

1. **\_\_\_ Buprenorphine: An alternative to methadone. The Medical Letter on Drugs and Therapeutics, Feb. 17, 2003; Vol. 45 (W1150A). 3 pages.**

**Abstract:** Buprenorphine taken alone as Subutex or with naloxone as Suboxone appears to be an effective alternative to methadone for both opioid detoxification and maintenance treatment of opioid dependence. It appears to be safe than methadone, with a lower risk of illicit use, but may not be effective for patients maintained on high doses of methadone. Buprenorphine's availability for office-based treatment should make it more accessible than methadone, but its high cost may be a deterrent.

**Notes:** Available free online.

**URL:** <http://www.medletter.com/freedocs/buprenorphine.pdf>

**Pub. Type:** Web document; PDF.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; Pharmacology ; Pharmacotherapy for opiate dependence

2. **\_\_\_ Buprenorphine replacement therapy: a confirmed benefit. Prescribe International 1999 Aug;8(42):124-7.**

**Abstract:** (1) Three years after high-dose buprenorphine preparations were first marketed in France, we examine their use as replacement therapy for heroin addiction. (2) Various surveys of community pharmacists have shown that the prescribing and dispensing conditions are feasible in the routine ambulatory setting. However, teamwork between physicians and pharmacists is rarely optimal, and fractionated dispensing is under-used. This could lead to abuse by a minority of patients. (3) During ambulatory management, at a mean dose of 8 mg/day sublingually, long-term buprenorphine therapy seems to yield a reduction in drug consumption by most patients, and can help with social reintegration. (4) The risks of buprenorphine treatment are mainly linked to abuse (massive doses, intravenous injection). Fatalities have occurred after high doses of buprenorphine combined with benzodiazepines, especially when taken intravenously. (5) The limited data on buprenorphine intake during pregnancy are reassuring.

**ISSN:** 1167-7422.

**Pub Type:** Journal Article.

**Descriptors:** Ambulatory Care ; Benzodiazepines/adverse effects ; \*Buprenorphine/adverse effects/therapeutic use ; Female ; Heroin Dependence/\*drug therapy ; Human ; Infant, Newborn ; \*Narcotics/adverse effects/therapeutic use ; Physician's Practice Patterns ; Pregnancy ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Dosing/administration ; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence

3. **\_\_\_ Clinical concepts - How safe are methadone, LAAM, buprenorphine? Addiction Treatment Forum 2001 Spring;10(2). 6 p.**

**Abstract:** New medications have been proposed as welcome, superior, less

addictive alternatives to methadone in the treatment of opioid dependency. Are buprenorphine and LAAM improvements over methadone, the "gold standard" opioid agonist for the treatment of opioid dependency since the mid 1960's? Perhaps even more important, and the primary focus of this report, are the newer agents safe alternatives? AT Forum obtained from the US Food and Drug Administration Office of Postmarketing Drug Risk Assessment all adverse event reports from Nov. 1, 1997 to Nov. 1, 2000 regarding buprenorphine, LAAM and methadone with the focus solely on their use in the treatment of opioid addiction. This article is a brief overview of the report by Stewart B. Leavitt.

**Notes:** Available free online; See Leavitt for original report.

**Pub. Type:** Web document.

**URL:** [http://www.atforum.com/SiteRoot/pages/current\\_pastissues/spring2001.shtml#anchor1221360](http://www.atforum.com/SiteRoot/pages/current_pastissues/spring2001.shtml#anchor1221360)

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Pharmacology ; Pharmacotherapy for opiate dependence ; Special populations

4. **\_\_\_ Drugs approved for opiate dependence. [complete as cited]. FDA Consumer 2003 Jan-Feb;37(1):6.**

**Abstract:** In October 2002, the FDA approved Subutex and Suboxone tablets, which work by preventing symptoms of withdrawal from heroin and other opiates. The new products represent two new formulations of buprenorphine. Subutex (buprenorphine hydrochloride) is intended for use at the beginning of drug abuse treatment. Suboxone (buprenorphine hydrochloride and naloxone hydrochloride) is intended to be the formulation used in maintenance treatment for opiate addiction. Naloxone was added to Suboxone to guard against intravenous abuse of buprenorphine. Both drugs are supplied in 2 milligram and 8 milligram tablets, which are placed under the tongue and must be allowed to dissolve.

**ISSN:** 0362-1332.

**Pub. Type:** News ; Web document.

**Descriptors:** Buprenorphine/adverse effects/\*therapeutic use ; Drug Approval ; Drug Combinations ; Drug and Narcotic Control ; Naloxone/adverse effects/\*therapeutic use ; Narcotic Antagonists/adverse effects/\*therapeutic use; Opioid-Related Disorders/\*rehabilitation ; United States.

**URL:** [http://www.fda.gov/fdac/departs/2003/103\\_upd.html](http://www.fda.gov/fdac/departs/2003/103_upd.html)

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Dosing/administration ; Pharmacotherapy for opiate dependence

5. **\_\_\_ FDA approves buprenorphine for opiate addiction treatment. Alcoholism & Drug Abuse Weekly, Oct 14, 2002 v14 i39 p1 (3 pages)**

**Abstract:** Brief article announcing the FDA approval of buprenorphine for treating opiate dependence in the US, almost two years later than when most observers had expected it. In addition to making the treatment process more accessible and convenient for those who will be deemed appropriate for being

treated in an office-based setting, FDA's approval of buprenorphine should also significantly expand the overall capacity of the nation's opiate addiction treatment system.

**Pub. Type:** newsletter article; overview.

**ATTC Buprenorphine Topics:** Legal/regulatory issues; Pharmacotherapy for opiate dependence

6. **\_\_\_ High dose buprenorphine may be an effective interim treatment for long term heroin users waiting for drug-assisted rehabilitation. Analytic review of article by Krook A.L. et al (2003). Evidence-Based Mental Health, Feb 2003 v6 i1 p30(1 page).**

**Abstract:** EBMH reviews the study reported by Krook et al (2002), to provide analysis of the study's methods and conclusions, and to evaluate the strength of study's findings in support of the question: Can buprenorphine, without psychosocial treatment, help people waiting for drug-assisted rehabilitation from opiate dependency? [Krook article is included in this bibliography]

**Pub. Type:** analytic review.

**ATTC Buprenorphine Topics:** Psychosocial treatment aspects ; Treatment outcomes/effectiveness

7. **\_\_\_ Introducing Office-based Treatment for Opioid Addiction. Rockville, MD: Center for Substance Abuse Treatment, 2003.**

**Abstract:** This pamphlet describes buprenorphine, a new medicine developed to treat addiction to opioids such as heroin and prescription painkillers.

Discussed are how buprenorphine works, how it differs from methadone, and how someone in need of the medicine can obtain it.

**Pub. Type:** Pamphlet.

**Notes:** Available free from CSAT. NCADI Inventory # PHD992.

**URL:** <http://store.health.org/catalog/productDetails.aspx?ProductID=16524>

**ADAI Buprenorphine Topics:** Pharmacotherapy for opioid dependence

8. **\_\_\_ M.D.s optimistic about buprenorphine, but challenges remain: physician survey reveals information gaps in system. Alcoholism & Drug Abuse Weekly, Oct 20, 2003 v15 i40 p1(3 pages).**

**Abstract:** Physicians are generally optimistic about the potential of the drug buprenorphine for treating opiate addiction, but have reported encountering several obstacles to more widespread use of the medication. The organization Join Together this month stated these findings in a report generated from a telephone survey of physicians conducted in June and July. The survey, which used participants from the national online database of physicians qualified to prescribe buprenorphine, identified several barriers that physicians have faced, such as the drug's absence on certain formularies and some pharmacists' lack of familiarity with the medication. But given that the survey was conducted just a few months after the drug started to become widely available, even its

administrators admit that the situation has probably improved since early summer.

**Pub. Type:** newsletter article.

**Notes:** See entry for Join Together for survey

**Descriptors:** physicians; opinion survey.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence; Legal/regulatory issues

9. **\_\_\_ Opioid drugs in maintenance and detoxification treatment of opiate addiction; addition of buprenorphine and buprenorphine combination to list of approved opioid treatment medications. Interim final rule. Federal Register 2003 May 22;68(99):27937-9.**

**Abstract:** This interim final rule amends the Federal opioid treatment program regulations by adding buprenorphine and buprenorphine combination products to the list of approved opioid treatment medications that may be used in federally certified and registered opioid treatment programs. The Food and Drug Administration (FDA) recently approved Subutex[reg] (buprenorphine) and Suboxone[reg] (buprenorphine in fixed combination with naloxone) for the treatment of opiate dependence. These two products will join methadone and ORLAAM[reg] as medications that may be used in opioid treatment programs for the maintenance and detoxification treatment of opioid dependence. Opioid treatment programs that choose to use these new products in the treatment of opioid dependence will adhere to the same Federal treatment standards established for methadone and ORLAAM[reg]. The Secretary invites public comments on this action.

**ISSN:** 0097-6326.

**Pub Type:** Journal Article.

**Descriptors:** Buprenorphine/\*therapeutic use ; Drug Approval/\*legislation & jurisprudence ; Drug Therapy, Combination ; Human ; Naloxone/therapeutic use ; Opioid-Related Disorders/\*drug therapy ; Substance Withdrawal Syndrome/\*drug therapy ; United States.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Legal/regulatory issues ; Pharmacotherapy for opiate dependence

10. **\_\_\_ Pharmacists may dispense new opioid addiction treatment. Am J Health System Pharmacy 2002;59(22):2150-2152.**

**Abstract:** Perhaps little noticed by pharmacists when signed into law, the Drug Addiction Treatment Act of 2000 permits prescribers who meet certain requirements to obtain a waiver allowing them to prescribe or dispense Schedule III, IV or V controlled substances that have received FDA-approved labeling for the treatment of narcotic addiction. The agency's October approval for two such products - Subutex, containing buprenorphine hydrochloride alone, and Suboxone, containing buprenorphine hydrochloride and naloxone hydrochloride (both manufactured by Reckitt Benckiser) - means that

pharmacists may become involved in the outpatient treatment of opioid dependence.

**ISSN:** 1079-2082.

**Pub Type:** Journal article ; News.

**Descriptors:** Pharmacists.

**ATTC Buprenorphine Topics:** Dosing/administration ; Legal/regulatory issues

11. **\_\_\_ SAMHSA, ASAM discuss buprenorphine mentoring program. Alcoholism & Drug Abuse Weekly, Sept 1, 2003 v15 i33 p1(3 pages).**

**Abstract:** One of the challenges officials have encountered in trying to make buprenorphine, the new pharmacological treatment for opioid addictions, available to patients has been getting primary care physicians trained and certified to prescribe the drug. While federal officials have rolled out a national education initiative touting buprenorphine and federal and association professionals have conducted ongoing physician training sessions, some officials think more could be done to help primary care physicians become eligible to prescribe buprenorphine for opioid-addicted patients. Along these lines, officials with the Substance Abuse and Mental Health Services Administration (SAMHSA) and the American Society of Addiction Medicine (ASAM) are exploring the possibility of developing a mentoring program for physicians who are planning or beginning to treat opioid-dependent patients with buprenorphine. SAMHSA embarked on a community education initiative, "New Paths to Recovery," which included a 14-city tour to inform physicians and the public about buprenorphine.

**Pub. Type:** newsletter article.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

12. **Agar M ; Bourgois P ; French J ; Murdoch O. (2001) Buprenorphine: "field trials" of a new drug. Qual Health Res 2001 Jan;11(1):69-84.**

**Author Address:** Department of Anthropology, History and Social Medicine, University of San Francisco's School of Medicine, USA. magari@anth.umd.edu

**Abstract:** Buprenorphine is being introduced as a new treatment drug for narcotics addiction in the United States. The authors were asked by the National Institute on Drug Abuse to conduct a field trial to determine if buprenorphine might play a role in street markets. Because no street use of the drug existed in the United States, the authors used three sources of information: (a) "street readings" of clinical studies, (b) Internet discussion lists, and (c) research in other countries. By using an emergent style of analysis that relies on replication of patterns across disparate data sources, it was determined that buprenorphine has desirable characteristics from a street addict point of view. An evaluation of the field trial 5 years later evaluates its accuracy.

**ISSN:** 1049-7323.

**Notes:** This paper is on the NASADAD web site.

**Pub Type:** Evaluation Studies ; Journal Article.

**URL:** <http://www.nasadad.org/Departments/Buprenorphine/bupappens.htm#APPENDIX%20F>

**Descriptors:** Bibliometrics ; Buprenorphine/\*therapeutic use ; Forecasting ; Human ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/\*drug therapy ; Probability ; \*Street Drugs ; Support, U.S. Gov't, P.H.S. ; United States.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Pharmacotherapy for opiate dependence ; History, use and effectiveness in other countries

13. **Ahmadi J. (2002) Buprenorphine maintenance treatment of heroin dependence: the first experience from Iran. J Subst Abuse Treat 2002 Apr;22(3):157-9.**

**Author Address:** Shiraz University of Medical Sciences, Shiraz, Fars Province, Iran. jamshid\_ahmadi@yahoo.com

**Abstract:** The aim of this study was to assess the efficacy of 1-, 2-, and 4-mg-per-day sublingual doses of buprenorphine in the maintenance treatment of heroin-dependent patients over a 17-week treatment period. Subjects were randomized to three dosage groups. Participants consisted of 105 heroin addicts (102 men and 3 women) who met the DSM-IV criteria for opioid dependence and were seeking treatment. Subjects received buprenorphine at a dose of 1, 2, or 4 mg per day and were treated in an urban outpatient clinic, including a weekly 1-hour individual counseling session. Days retained in treatment were measured. Overall, 49 patients (46.7%) completed the 17-week study. Completion rates by dosage group were 34.3% for the 1 mg dose group, 42.9% for the 2 mg dose group, and 62.9% for the 4 mg dose group. Retention in the 4 mg dose group was significantly better than in the 1 mg dose group ( $P = .017$ ). None of the other comparisons was significant. The results support the efficacy and safety of buprenorphine for outpatient treatment of heroin dependence and seem to indicate that the highest dose (4 mg) of buprenorphine was the best of the three doses for Iranian heroin addicts to increase their retention in treatment.

**ISSN:** 0740-5472.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adolescent ; Adult ; Ambulatory Care Facilities ; Buprenorphine/administration & dosage/\*therapeutic use ; Comparative Study ; Female ; Heroin Dependence/\*drug therapy/epidemiology ; Human ; Iran/epidemiology ; Male ; Middle Age ; Narcotic Antagonists/administration & dosage/\*therapeutic use ; Patient Dropouts ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Dosing/administration ; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence

14. **Ahmadi J. (2002) A controlled trial of buprenorphine treatment for opium dependence: the first experience from Iran. Drug Alcohol Depend 2002 Apr 1;66(2):111-4.**

**Author Address:** Department of Psychiatry, Shiraz University of Medical

Sciences, PO Box 71345-1416, Shiraz, Iran. jamshid\_ahmadi@yahoo.com

**Abstract:** AIMS: To evaluate the effect of a 4 mg/day sublingual dose of buprenorphine in the maintenance treatment of opium dependence in comparison with a 1 mg/day dose over an 18-week treatment period. As a secondary objective, the results were determined concurrently for subjects treated with a 2 mg/day dose. DESIGN: Subjects were assigned randomly to three dosage groups. PARTICIPANTS: 330 consecutive (320 men and 10 women) opium addicts who met the DSM-IV criteria for opioid dependence and were seeking treatment. INTERVENTION: Subjects received a 1, 2 or 4 mg/day dose of buprenorphine and were treated in an outpatient clinic where they also received a weekly 1-hour clinical counseling session. MEASUREMENTS: Addiction Severity Index, retention in treatment, and illegal opioid use as determined by random urine testing. FINDINGS: The mean age was 37.5 years (SD=11.4, range 19-72). Overall, 194 (58.8%) of the patients completed the 18 week study. Completion rates by dosage groups were 47.3% for the 1 mg group, 58.2% for the 2 mg group and 70.9% for the 4 mg group ( $\chi^2=12.7$ ,  $df=2$ ,  $P=0.0017$ ). CONCLUSIONS: The results support the efficacy and safety of buprenorphine for opium addiction and suggest that an adequate dose of buprenorphine would help to increase the success rate.

ISSN: 0376-8716.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Aged ; Buprenorphine/\*therapeutic use ; Chi-Square Distribution ; Comparative Study ; Female ; Human ; Iran/epidemiology ; Male ; Middle Age ; Narcotic Antagonists/\*therapeutic use ; \*Narcotics ; Opioid-Related Disorders/\*drug therapy/epidemiology ; \*Opium.

**ATTC Buprenorphine Topics:** Dosing/administration ; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence

15. **Ahmadi J. (2002) A randomized, clinical trial of buprenorphine maintenance treatment for Iranian patients with opioid dependency. Addictive Disorders & Their Treatment. Vol 1(1) 2002, 25-27.**

**Author Address:** Ahmadi, Jamshid. Dept of Psychiatry, Hafez Hosp, PO Box 71345-1416, Shiraz Iran.

**Abstract:** This study assessed the effect of a 4-mg/d sublingual dosage of buprenorphine in the maintenance treatment of Iranian patients with opioid dependency by comparison with a 1-mg/d dosage over a 24-wk treatment period. As a secondary objective, results were determined concurrently for patients treated with a 2-mg/d dosage. Patients were randomized to three dosage groups. The participants included 420 consecutive patients (407 men and 13 women) with opioid dependency who met the criteria for opioid dependence of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, and were seeking treatment. Measurements included Addiction Severity Index, retention in treatment, and illegal opioid use as determined by random urine toxicology. The mean age was 36.3 years (range, 16-72). Overall, 237 (56.4%) of the patients completed the 24-wk study. Completion rates by dosage group were 45.7% for the 1-mg group, 55.7% for the 2-mg group, and 62.9% for the 4-mg group. No sex difference was observed. The results support the

efficacy and safety of buprenorphine for opioid dependence and suggest that an adequate dosage of buprenorphine is strongly recommended for Iranian patients with opioid dependence to increase their success rate.

ISSN: 1531-5754 (Print).

**Pub Type:** Journal article

**Descriptors:** opioid dependence; buprenorphine maintenance treatment; dosage; Iranian patients ; \*Drug Dependency ; \*Drug Dosages ; \*Drug Therapy; \*Maintenance Therapy ; \*Opiates ; Human. Male. Female. Outpatient. Adolescence (13-17 yrs). Adulthood (18 yrs & older). Young Adulthood (18-29 yrs). Thirties (30-39 yrs). Middle Age (40-64 yrs). Aged (65 yrs & older) ; Empirical Study.

**ATTC Buprenorphine Topics:** Dosing/administration ; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence

16. **Ahmadi J. (2003) Methadone versus buprenorphine maintenance for the treatment of heroin-dependent outpatients. J Subst Abuse Treat 2003 Apr;24(3):217-20.**

**Author Address:** Shiraz University of Medical Sciences, Abiverdi Street, Shiraz, Fars province, Iran. jamshid\_ahmadi@yahoo.com

**Abstract:** The aim of this study was to assess the efficacy of methadone compared with buprenorphine maintenance therapy in heroin-dependent patients over a treatment period of 18 weeks. Subjects were randomized to receive either methadone or buprenorphine in a comparative double-blind study and consisted of 164 heroin-dependent male patients who met the DSM-IV criteria for heroin dependence and were seeking treatment. The 164 subjects included 41 patients in 1-mg, 41 patients in 3-mg, and 41 patients in 8-mg dosage group of buprenorphine, and also 41 patients in the 30-mg dosage group of methadone. The mean age was 31.4 years for total buprenorphine group and 33.7 years for methadone group (the mean age differences in 4 groups were not statistically significant). Subjects received buprenorphine at a dose of 1, 3, or 8 mg per day or methadone at a dose of 30 mg per day and were treated in an urban outpatient clinic, offering a 1-hour weekly individual counseling session. Days retained in treatment were measured. Completion rates by buprenorphine dosage group were 29.3% for the 1-mg dose group, 46.3% for the 3-mg dose group, 68.3% for the 8-mg dose group, and 61% for the 30-mg methadone dose group. Retention in the 8-mg dose group was significantly better than in the 1-mg dose group ( $p=.00041$ ) and in the 3-mg dose group ( $p=.045$ ); other comparison (1 mg dose with 3 mg dose) was not significant. Methadone group was significantly better than 1 mg buprenorphine dose group ( $p=.004$ ), but was not significantly different from 3 mg buprenorphine dose group ( $p=.18$ ) or 8 mg buprenorphine dose group ( $p=.49$ ). The results support the efficacy of buprenorphine for outpatient treatment of heroin dependence and seem to indicate that the highest dose (8 mg) of buprenorphine was the best of the three doses of buprenorphine, and also support the superiority of 30 mg of methadone compared to 1 mg dose of buprenorphine for Iranian heroin-dependent patients to increase their retention in treatment.

ISSN: 0740-5472.

**Pub Type:** Journal Article.

**Descriptors:** Buprenorphine/\*administration & dosage/therapeutic use ; Methadone/\*therapeutic use.

**ATTC Buprenorphine Topics:** Dosing/administration ; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

17. **Ahmadi J ; Ahmadi K ; Ohaeri J. (2003) Controlled, randomized trial in maintenance treatment of intravenous buprenorphine dependence with naltrexone, methadone or buprenorphine: a novel study. Eur J Clin Invest 2003 Sep;33(9):824-9.**

**Author Address:** Shiraz University of Medical Sciences, Kuwait University, Iran. jamshid\_ahmadi@yahoo.com

**Abstract:** AIMS: To test the effect of a 50-mg day-1 dose of naltrexone in the maintenance treatment of intravenous-buprenorphine dependence in comparison with a 50-mg day-1 dose of methadone and also a 5-mg day-1 dose of buprenorphine over a 24-week treatment period. PARTICIPANTS: Two hundred and four intravenous-buprenorphine-dependent patients who met the DSM-IV criteria for opioid dependence were randomized to three equal groups and were treated in a clinic in Iran where they were also offered a weekly 0.5-h counselling session, in 2002. FINDINGS: The mean age was 31.2 years (range 17-53). The majority [63.2%] was between 20 and 34 years of age. The educational level of most of them [55.4%] was between 6 and 12 years of study. Completion rates by groups were 83.8% for the 50-mg dose methadone group, 58.8% for the 5-mg dose buprenorphine group and 20.6% for the 50-mg dose naltrexone group (P = 0.000). Retention in the 50-mg methadone group was significantly better than in the 5-mg dose buprenorphine group (P = 0.001) and the 50-mg dose naltrexone group (P = 0.000). Retention in the 5-mg buprenorphine group was significantly better than in the 50-mg naltrexone dose group (P = 0.000). CONCLUSIONS: Evaluation of the Iranian experience on this subject may be useful for other countries.

ISSN: 0014-2972.

**Pub Type:** Journal Article.

**Descriptors:** Methadone/\*therapeutic use ; Naltrexone/\*therapeutic use.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; History, use and effectiveness in other countries

18. **Ahmadi J ; Ahmadi M. (2003) Twelve-month maintenance treatment of heroin-dependent outpatients with buprenorphine. J Subst Use 2003;8(1):39-41.**

**Author Address:** Shiraz University of Medical Sciences, PO Box 71345-1416, Dept. of Psychiatry, Hafez Hospital, Shiraz, Iran

**Abstract:** The aim of this study was to assess the efficacy of 1-mg., 3-mg., and 8-mg/day doses of buprenorphine in the maintenance treatment of heroin-dependent patients over a 12-month treatment period. Subjects were allocated

randomly to three dosage groups. Participants consisted of 123 male heroin dependents who met the DSM-IV criteria for opioid dependence and were seeking treatment. Their mean age was 31.4 years ranging from 16 to 64 (SD = 9.4). Subjects received buprenorphine at a dose of 1 mg, 3 mg, or 8 mg/day and were treated in an urban outpatient clinic, offering a 1-h weekly individual counseling session. Days retained in treatment were measured. Overall, 49 patients (39.8%) completed the 12-month study. Completion rates by dosage group were 7 (17.1)% for the 1-mg dose group, 16 (39%) for the 3-mg dose group, and 26 (63.4%) for the 8-mg dose group. Retention in the 8-mg dose group was significantly better than in the 1-mg dose group (p = 0.0002) and in the 3-mg dose group (P = 0.027); other comparison (1-mg dose with 3-mg dose) was also significant (P = 0.027). The results support the efficacy and safety of buprenorphine for outpatient treatment of heroin dependence and seem to indicate that the highest dose (8 mg) of buprenorphine was the best of the three doses for Iranian heroin dependents to increase their retention in treatment.

**Pub. Type:** Journal article.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

19. **Ahmadi J ; Bahrami N. (2002) Buprenorphine treatment of opium-dependent outpatients seeking treatment in Iran. J Subst Abuse Treat 2002 Dec;23(4):415-7.**

**Author Address:** Shiraz University of Medical Sciences, Shiraz, Fars Province, Iran. jamshid\_ahmadi@yahoo.com

**Abstract:** The goal of this study was to evaluate the efficacy of 1-, 3-, and 8-mg per day doses of buprenorphine in the maintenance treatment of opium-dependent patients over a 6-month treatment period. Participants were 513 opium-dependent individuals who were seeking treatment in an urban outpatient clinic, offering a 1-hr weekly individual counseling session. Overall, 305 patients (59.5%) completed the 6-month study. Completion rates by dosage group were 33.9% for the 1-mg dose group, 64.3% for the 3-mg dose group, and 80.1% for the 8-mg dose group—each significantly different from the other two groups. The results support the efficacy and safety of buprenorphine for outpatient treatment of opium dependence and seem to indicate that the highest dose (8 mg) of buprenorphine was the best of the three doses for Iranian opium-dependent patients to increase their retention in treatment. ISSN: 0740-5472.

**Pub Type:** Clinical Trial ; Journal Article.

**Descriptors:** Adult ; Aged ; Aged, 80 and over ; Buprenorphine/\*therapeutic use ; Dose-Response Relationship, Drug ; Double-Blind Method ; Female ; Human ; Iran ; Male ; Middle Age ; Narcotics/\*therapeutic use ; Opioid-Related Disorders/\*drug therapy ; Outpatients ; \*Patient Acceptance of Health Care.

**ATTC Buprenorphine Topics:** Dosing/administration ; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence

20. **Ahmadi J ; Maany I ; Ahmadi M. (2003) Treatment of intravenous buprenorphine dependence: A randomized open clinical trial. German Journal of Psychiatry. Vol 6(1) 2003, 23-29.**

**Author Address:** Ahmadi, Jamshid. Hafez Hosp, P.O. Box 71345-1416, Shiraz Iran, jamshidahmadi@yahoo.com.

**Abstract:** Investigated the effectiveness of methadone in the maintenance treatment of iv buprenorphine dependence in comparison with sublingual buprenorphine and oral clonidine over a 12-wk treatment period. Another goal of the research was to characterize iv buprenorphine-dependent individuals with respect to socio-demographic and other background features. 108 male 19-46 yr old patients who met DSM--IV criteria for opioid dependence were randomized to 3 groups. The majority (86.1%) of the patients had a history of opium or heroin dependency before they were introduced to iv buprenorphine. The mean duration of buprenorphine dependence was 1.8 yrs and the mean ampoule per day was 4.6 ampoules (1 ampoule contains 0.3 mg of buprenorphine in 1 ml). Completion rates by groups were 83.3% for the methadone group, 58.3% for the buprenorphine group and 11.1% for the clonidine group. Retention in treatment was significantly better in the methadone group than in the buprenorphine and clonidine groups. Retention in the buprenorphine group was significantly better than in the clonidine group. It is concluded that the results support the efficacy and safety of oral methadone and sublingual buprenorphine tablets for iv buprenorphine-dependent patients.

**ISSN:** 1455-1033 (Electronic).

**URL:** <http://www.gjpsy.uni-goettingen.de/>

**Pub. Type:** journal article.

**Descriptors:** intravenous buprenorphine dependence; methadone maintenance; sublingual buprenorphine; oral clonidine; patient characteristics ; \*Drug Dependency ; \*Drug Rehabilitation ; \*Intravenous Drug Usage ; \*Methadone Maintenance ; \*Opiates ; Client Characteristics ; Clonidine ; Drug Administration Methods ; Narcotic Agonists ; Human. Male. Adulthood (18 yrs & older). Young Adulthood (18-29 yrs). Thirties (30-39 yrs). Middle Age (40-64 yrs) ; Empirical Study. Treatment Outcome Study.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; History, use and effectiveness in other countries ; Treatment outcomes/effectiveness

21. **Ahmed S ; Ara N. (2001) An exploratory study of buprenorphine use in Bangladesh: A note. Subst Use Misuse 2001 Jun;36(8):1071-83.**

**Author Address:** Central Drug Treatment Center, Tejgaon, Dhaka, Bangladesh.

**Abstract:** A pilot study was carried out in Bangladesh during August and September, 1995, using a "snowball" technique with 30 male multiple drug users in order to investigate buprenorphine use, characteristics of the users, their reasons for its use and the drug's effects.

**ISSN:** 1082-6084.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Bangladesh ; Buprenorphine/\*therapeutic use ; Female ; Heroin Dependence/drug therapy/psychology ; Human ; Male ; Narcotic Antagonists/\*therapeutic use ; Street Drugs/\*adverse effects ; Substance Withdrawal Syndrome/\*drug therapy ; Substance-Related Disorders/\*psychology.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; History, use and effectiveness in other countries ; Pharmacology

22. **Amanzio M ; Pollo A ; Maggi F ; Benedetti F. (2001) Response variability to analgesics: a role for non-specific activation of endogenous opioids. Pain 2001 Feb 15;90(3):205-15.**

**Author Address:** Department of Neuroscience, University of Torino Medical School, Corso Raffaello 30, 10125 Torino, Italy.

**Abstract:** Individual differences in pharmacokinetics and pharmacodynamics, the type of pain and the method of drug administration can account for the response variability to analgesics. By integrating a clinical and an experimental approach, we report here that another important source of variability is represented by individual differences in non-specific (placebo) activation of endogenous opioid systems. In the first part of this study, we analyzed the effectiveness of buprenorphine, tramadol, ketorolac and metamizol in the clinical setting, where the placebo effect was completely eliminated by means of hidden infusions. We found that the hidden injections were significantly less effective and less variable compared with open injections (in full view of the subject), suggesting that part of the response variability was due to non-specific factors (placebo). Since we could not administer the opioid antagonist, naloxone, to these patients, in the second part of this study, we induced experimental ischemic arm pain in healthy volunteers and found that, as occurred in clinical pain, the analgesic response to a hidden injection of the non-opioid ketorolac was less effective and less variable than an open injection. Most importantly, we obtained the same effects by adding naloxone to an open injection of ketorolac, thus blocking the opioid-mediated placebo component of analgesia. These findings indicate that both the psychological (hidden injection) and pharmacological (naloxone) blockade of the placebo response reduce the effectiveness of, and the response variability to, analgesic drugs. Therefore, an important source of response variability to analgesics appears to be due to differences in non-specific activation of endogenous opioid systems.

**ISSN:** 0304-3959.

**Pub Type:** Clinical Trial ; Journal Article.

**Descriptors:** Adult ; Aged ; Buprenorphine/administration & dosage/therapeutic use ; Dipyrrone/administration & dosage/therapeutic use ; Female ; Human ; Ketorolac/administration & dosage/therapeutic use ; Male ; Middle Age ; Opioid Peptides/\*administration & dosage/\*therapeutic use ; Pain Measurement ; Pain, Postoperative/\*drug therapy/physiopathology ; Support, Non-U.S. Gov't ; Tramadol/administration & dosage/therapeutic use.

**ATTC Buprenorphine Topics:** Pain management ; Pharmacology

23. **Amass L ; Kamien J ; Mikulich S. (2001) Thrice-weekly supervised dosing with the combination buprenorphine-naloxone tablet is preferred to daily supervised dosing by opioid-dependent humans. Drug Alcohol Depend 2001 Jan 1;61(2):173-81.**

**Author Address:** Department of Psychiatry, University of Colorado School of Medicine, Vine Street Center, 1741 Vine Street, Denver, CO 80206, USA. lamass@friendsresearch.org

**Abstract:** A sublingual tablet formulation of buprenorphine combining 8 mg of buprenorphine with 2 mg of naloxone is being targeted for use in settings where less than daily dosing strategies and/or prescription-based dispensing will likely be employed. This study determined patient preferences for, and clinical outcomes during, daily and 3-day per week supervised dosing schedules using the combination tablet. Twenty-four opioid-dependent subjects completing a 16-day baseline entered an outpatient triple crossover trial. Twenty-one days of daily dosing were compared to two different 21-day periods of 3-day per week supervised dosing: a 3-day per week clinic schedule and a 3-day per week take-home schedule in which tablets were provided to subjects to take at home on days between clinic visits. Thirteen patients completed the study.

Significantly more doses were ingested under the 3-day per week schedules. Illicit drug use did not differ across conditions and 45% of urine samples tested positive for illicit opioids. Subjects 'liked' both 3-day per week schedules more than the daily schedule, and ratings of feeling 'good' were higher for the 3-day take-home as opposed to 3-day clinic condition. Almost all subjects (91%) rated 3-day take-home as the most preferred schedule. Overall, reducing clinic attendance improved medication compliance and increased client satisfaction without impacting illicit drug use.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Analysis of Variance ; Buprenorphine/\*administration & dosage ; Chi-Square Distribution ; Drug Combinations ; Female ; Human ; Male ; Middle Age ; Naloxone/\*administration & dosage ; Narcotic Antagonists/\*administration & dosage ; Opioid-Related Disorders/\*drug therapy/psychology/urine ; Patient Compliance ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Dosing/administration ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

24. **Amass L ; Wing W. (2002) Symposium III : Ready, set, go : bringing buprenorphine to the U.S. treatment market. In: Harris LS (ed.). Problems of Drug Dependence, 2001: Proceedings of the 63rd Annual Scientific Meeting, College on Problems of Drug Dependence, Inc. / Bethesda, MD : National Institute on Drug Abuse, 2002, pp.27-37.**

**Abstract:** The face of opioid addiction treatment in the U.S. will change soon with the Food and Drug Administration approval and introduction of the sublingual buprenorphine-naloxone (BNX) tablet to the U.S. treatment market. The development of buprenorphine and BNX has brought with it

groundbreaking U.S. legislation permitting physicians to dispense and prescribe schedule III, IV or V narcotic drugs, or combinations thereof, to patients for opioid maintenance or detoxification treatment. For the first time in U.S. history, patients can be treated with an effective opioid medication in the privacy of the physician's office, i.e., outside the traditional narcotic treatment setting. In this symposium, national and international experts spoke on the developmental history, legislative processes, research experience, training of physicians and community providers, and potential therapeutic impact associated with bringing BNX to the U.S. treatment market.

**Notes:** ADAI Library: HV 5825 C617 2001.

**Pub Type:** book chapter.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Legal/regulatory issues ; Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

25. **American Academy of Addiction Psychiatry (AAAP). (ongoing) AAAP buprenorphine training sessions: Use of buprenorphine in the pharmacologic management of opioid dependence. American Academy of Addiction Psychiatry, 2003 +.**

**Abstract:** The "Drug Addiction Treatment Act of 2000" specifies several ways in which physicians can be considered "qualified" to prescribe and dispense buprenorphine in their offices for the treatment of opioid dependence. Some will need to complete training prior to notifying the U.S. Department of Health and Human Services (DHHS) of their intention to begin prescribing buprenorphine for the treatment of opioid dependence. Others, such as those certified in Addiction Medicine or Addiction Psychiatry or those who participated in clinical trials, are not required to complete any further training. However, it is likely that many physicians who are defined as qualified, by virtue of their subspecialty certification or specific experience, will elect to take part in an educational program to review the many elements involved in implementing this new treatment modality in a setting where pharmacological management of opioid dependence has not been provided before. AAAP is one of five organizations designated by DHHS to provide such training for physicians to dispense buprenorphine in office practice for treatment of opioid dependence. AAAP Buprenorphine Training Sessions meet the eight hour requirement. Places and dates for training are updated continually on this web site.

**URL:** <http://www.aaap.org/buprenorphine/buprenorphine.html>

**Pub. Type:** Web resource.

**Descriptors:** Physician training.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

26. **American Society of Addiction Medicine (ASAM). (2003) Buprenorphine Information [collection of web documents]. American Society of Addiction Medicine web site, 2003.**

**Abstract:** This is the main information page about buprenorphine on ASAM's website. The contains several forms and documents for clinicians to use with their patients. Forms include: Family Guide to Buprenorphine Maintenance Treatment, Information to give to patients in preparation for getting an informed consent for treatment with buprenorphine, DSM IV criteria with worksheet, History and Physical form, Patient Responsibilities and Agreement Form, Patient Treatment-Planning Questions, Protocol for Follow-up Visits, Commonly Abused Drugs, and Consent for Release of Information. Also has Links to materials on other sites such as CSAM, AAAP, and SAMHSA's Buprenorphine websites.

**URL:** [http://www.asam.org/info/buprenorphine\\_info.htm](http://www.asam.org/info/buprenorphine_info.htm)

**Pub. Type:** Web site ; numerous publications and resources

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Dosing/administration ; Legal/regulatory issues ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment protocols/physician guidelines

27. **Annitto W. (2000) Detoxification with buprenorphine of a pregnant heroin addict. Am J Addict 2000 Winter;9(1):92-3.**

**Abstract:** This is a case report and literature review concerning the use of buprenorphine for detoxification in a pregnant addict. It presents the clinical management of the complexities of opiate addiction and pregnancy. The author suggest a more vigorous study of buprenorphine for opiate withdrawal in motivated pregnant addicts.

**ISSN:** 1055-0496.

**Pub Type:** Letter; Case report.

**Descriptors:** Adult ; Buprenorphine/\*therapeutic use ; Case Report ; Female ; Heroin/pharmacokinetics ; Heroin Dependence/\*rehabilitation ; Human ; Metabolic Detoxication, Drug ; Narcotic Antagonists/\*therapeutic use ; Narcotics/pharmacokinetics ; Pregnancy ; \*Pregnancy Complications.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Special populations

28. **Atluri S ; Boswell M ; Hansen H ; Trescot A ; Singh V ; AE J. (2003) Guidelines for the use of controlled substances in the management of chronic pain. Pain Physician 6(3):233-257, 2003.**

**Abstract:** Controlled substance abuse has increased at an alarming rate. However, available evidence suggests a wide variance in the use of controlled substances, as documented by different medical specialties, medical boards, advocacy groups, and the Drug Enforcement Administration. The primary objective of controlled substance guidelines by American Society of Interventional Pain Physicians (ASIPP) is to provide guidance for the use of controlled substances for the treatment of chronic pain. It is anticipated that these practical guidelines will improve quality of care, patient access, and quality of life. Additional benefits include improved treatment efficiency and efficacy, and cost containment by improving the risk-benefit ratio of treating

patients with chronic pain. Further goals of this manuscript are to bring consistency in opioid philosophy among the many diverse groups involved, to improve the treatment of chronic pain patients with medically appropriate controlled substances, and to reduce the incidence of drug diversion. These guidelines also reinforce the need for systematic evaluation and ongoing care of patients with chronic or persistent pain. ASIPP controlled substance guidelines also provide a discussion of the epidemiology of chronic pain, the role of controlled substances in treating chronic pain, various aspects of drug abuse, pharmacological considerations, clinical effectiveness of controlled substances, options for treatment monitoring and drug testing and a review of terminology used in addiction medicine. These guidelines do not constitute inflexible treatment recommendations. It is expected that a provider will establish a plan of care on a case-by-case basis, taking into account an individual patient's medical condition, personal needs, and preferences, and the physician's experience. Based on an individual patient's needs, controlled substance prescribing and treatment different from that outlined here may be warranted.

**ISSN:** 1533-3159.

**Pub Type:** Journal article.

**ATTC Buprenorphine Topics:** Pain management ; Treatment protocols/physician guidelines

29. **Auriacombe M ; Franques P ; Tignol J. (2001) Deaths attributable to methadone vs buprenorphine in France. JAMA 2001 Jan 3;285(1):45.**

**Abstract:** Because buprenorphine has only partial opioid agonist activity and thus has a lower risk of overdose, 1 it may be an alternative to methadone in the treatment of heroin dependence. Buprenorphine has been used for this purpose in France, where general practitioners have been permitted to prescribe it since 1996 with less monitoring than methadone, which is available only in specialized treatment centers. 2 Buprenorphine thus has theoretically more risk of adverse effects and increased diversion than methadone. We computed the death rate from overdose of buprenorphine and methadone in France from 1994 to 1998.

**ISSN:** 0098-7484.

**Pub Type:** Letter.

**Descriptors:** Buprenorphine/\*adverse effects/therapeutic use ; France ; Heroin Dependence/\*rehabilitation ; Human ; Methadone/\*adverse effects/therapeutic use ; Narcotics/\*adverse effects/therapeutic use ; Overdose/\*mortality.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; History, use and effectiveness in other countries ; Pharmacology

30. **Banta-Green C. (2003) Note on the Epidemiology of Buprenorphine Abuse [personal communication]. Data from the Drug Abuse Warning Network, 2002, Office of Applied Studies, SAMHSA. (according to 03/2003 update).**

**Author Address:** Alcohol & Drug Abuse Institute, Box 354805, University of Washington, Seattle, WA 98105

**Abstract:** Emergency department visits involving buprenorphine totaled 6 in 2002 according to national estimates. These data represent a tiny proportion of the 119,185 visits for narcotic analgesics and 681,957 visits for major substances of abuse nationally. A total of 30 buprenorphine related visits were estimated for 1995-2002 (SAMHSA, 2003).

Other commonly available indicator data are unlikely to provide information on buprenorphine. Buprenorphine is only detectable via select toxicological methods, not routinely utilized in the U.S., so any estimates of deaths involving buprenorphine would be substantial underestimates. Treatment data are unlikely to reveal admissions for buprenorphine because most classification systems would categorize it as an 'other opiate' or a 'narcotic analgesic'. Other data sources have not historically tracked buprenorphine because of its limited use prior to approval for us in opioid addiction treatment.

**Notes:** Banta-Green is the Seattle representative to the Community Epidemiology Work Group (CEWG). CEWG members nationally were contacted for any unpublished data on the prevalence of abuse of buprenorphine.

**Pub Type:** Personal communication.

**Descriptors:** ER visits; overdose; epidemiology.

**ATTC Buprenorphine Topics:** Prevalence of use for opiate dependence

31. **Barclay L ; Lie D. (2003) Buprenorphine/Naloxone Safe, Effective as Office-Based Treatment for Opiate Addiction / CME. Medscape Medical News September 4, 2003 [online news**

**Abstract:** Office-based treatment with buprenorphine and naloxone is safe and effective for opiate addiction, according to the results of a study published in the Sept. 4 issue of the New England Journal of Medicine. This double-blind, placebo-controlled trial was terminated early because buprenorphine alone or in combination with naloxone had greater efficacy than did placebo.

**Notes:** Brief physician training article based on article in N Engl J Med. 2003;349:949-958. CME credit available for reading article and taking test; Valid for credit through September 4, 2004.

**URL:** <http://www.medscape.com/viewarticle/460951>

**Pub. Type:** online training.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

32. **Barnett P ; Rodgers J ; Bloch D. (2001) A meta-analysis comparing buprenorphine to methadone for treatment of opiate dependence. Addiction 2001 May;96(5):683-90.**

**Author Address:** Cooperative Studies Program and Health Economics Resource Center, VA Palo Alto Health Care System, US Department of Veterans Affairs, Menlo Park, CA 94025, USA. paul.barnett@med.va.gov

**Abstract:** BACKGROUND: The unique pharmacological properties of buprenorphine may make it a useful maintenance therapy for opiate addiction.

This meta-analysis considers the effectiveness of buprenorphine relative to methadone. METHODS: A systematic literature search identified five randomized clinical trials comparing buprenorphine to methadone. Data from these trials were obtained. Retention in treatment was analyzed with a Cox proportional hazards regression. Urinalyses for opiates were studied with analysis of variance and a common method of handling missing values. A meta-analysis was used to combine these results. RESULTS: Subjects who received 8-12 mg/day buprenorphine had 1.26 times the relative risk of discontinuing treatment (95% confidence interval 1.01-1.57) and 8.3% more positive urinalyses (95% confidence interval 2.7-14%) than subjects receiving 50-80 mg/day methadone. Buprenorphine was more effective than 20-35 mg/day methadone. There was substantial variation in outcomes in the different trials. CONCLUSIONS: The variation between trials may be due to differences in dose levels, patient exclusion criteria and provision of psychosocial treatment. The difference in the effectiveness of buprenorphine and methadone may be statistically significant, but the differences are small compared to the wide variance in outcomes achieved in different methadone treatment programs. Further research is needed to determine if buprenorphine treatment is more effective than methadone in particular settings or in particular subgroups of patients.

**ISSN:** 0965-2140.

**Pub Type:** Journal Article ; Meta-Analysis.

**Descriptors:** Analysis of Variance ; Buprenorphine/\*therapeutic use ; Human ; Methadone/\*therapeutic use ; Narcotics/\*therapeutic use/urine ; Opioid-Related Disorders/\*rehabilitation/urine ; Patient Compliance ; Patient Dropouts/statistics & numerical data ; Proportional Hazards Models ; Support, U.S. Gov't, Non-P.H.S. ; Support, U.S. Gov't, P.H.S. ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment outcomes/effectiveness

33. **Barnett P ; Zaric G ; Brandeau M. (2001) The cost-effectiveness of buprenorphine maintenance therapy for opiate addiction in the United States. Addiction 2001 Sep;96(9):1267-78.**

**Author Address:** Health Economics Resource Center, Veterans Affairs Palo Alto Health Care System, Menlo Park, CA, USA and the Department of Health Research and Policy, Stanford University, Stanford, CA, USA. paul.barnett@med.va.gov

**Abstract:** AIMS: To determine the cost-effectiveness of buprenorphine maintenance therapy for opiate addiction in the United States, particularly its effect on the HIV epidemic. DESIGN: We developed a dynamic model to capture the effects of adding buprenorphine maintenance to the current opiate dependence treatment system. We evaluated incremental costs, including all health-care costs, and incremental effectiveness, measured as quality-adjusted life years (QALYs) of survival. We considered communities with HIV prevalence among injection drug users of 5% and 40%. Because no price has been set in the United States for a dose of buprenorphine, we considered three prices per

dose: \$5, \$15, and \$30. **FINDINGS:** If buprenorphine increases the number of individuals in maintenance treatment by 10%, but does not affect the number of individuals receiving methadone maintenance, the cost-effectiveness ratios for buprenorphine maintenance therapy are less than \$45 000 per QALY gained for all prices, in both the low-prevalence and high-prevalence communities. If the same number of individuals enter buprenorphine maintenance (10% of the number currently in methadone), but half are injection drug users newly entering maintenance and half are individuals who switched from methadone to buprenorphine, the cost-effectiveness ratios in both communities are less than \$45 000 per QALY gained for the \$5 and \$15 prices, and greater than \$65 000 per QALY gained for the \$30 price. **CONCLUSIONS:** At a price of \$5 or less per dose, buprenorphine maintenance is cost-effective under all scenarios we considered. At \$15 per dose, it is cost-effective if its adoption does not lead to a net decline in methadone use, or if a medium to high value is assigned to the years of life lived by injection drug users and those in maintenance therapy. At \$30 per dose, buprenorphine will be cost-effective only under the most optimistic modeling assumptions.

**ISSN:** 0965-2140.

**Pub Type:** Journal Article ; Review ; Review, Tutorial.

**Descriptors:** Buprenorphine/economics/\*therapeutic use ; Cost-Benefit Analysis ; Human ; Narcotic Antagonists/economics/\*therapeutic use ; Opioid-Related Disorders/\*economics/rehabilitation ; Quality-Adjusted Life Years ; Support, U.S. Gov't, P.H.S. ; United States.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

consumed more heroin (12% vs. 8%) and engaged in more misuse, such as intravenous use, illicit acquisitions or irregular consumption. These practices were more frequent for patients consuming the drug "outwith protocol" or for patients obtaining the drug from a general practitioner. **CONCLUSION:** Our results suggest that patterns of consumption of methadone and buprenorphine are different in several respects: concomitant use of licit or illicit psychoactive substances, route of administration, and illegal acquisition. They also suggest that the behaviours of maintenance treatment users depend less on the nature of the maintenance drug (methadone or high dosage buprenorphine), than the nature of the delivery and monitoring practices.

**ISSN:** 0965-2140.

**Pub Type:** Journal Article ; Multicenter Study.

**Descriptors:** Adult ; Analgesics, Opioid/\*therapeutic use ; Buprenorphine/\*therapeutic use ; Comparative Study ; Female ; France ; Human ; Logistic Models ; Male ; Methadone/\*therapeutic use ; Odds Ratio ; Socioeconomic Factors ; Substance Abuse Treatment Centers/\*organization & administration ; Substance-Related Disorders/\*rehabilitation ; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Prevalence of use for opiate dependence

34. **Barrau K ; Thirion X ; Micallef J ; Chuniaud-Louche C ; Bellemin B ; San Marco J. (2001) Comparison of methadone and high dosage buprenorphine users in French care centres. Addiction 2001 Oct;96(10):1433-41.**

**Author Address:** Centre collaborateur du CEIP de Marseille, Laboratoire de Sante Publique, Faculte de Medecine, Marseille, France.

**Abstract:** AIMS: In France, maintenance programmes for opiate users were adopted later than in other countries. Two maintenance treatments are available: methadone is only delivered in specialized centres while high dosage (HD) buprenorphine can be prescribed by all general practitioners and in specialized centres. The aim of this study was to compare the socio-demographic profiles, the practices and drug consumption patterns of the two groups attending specialized centres. **METHODOLOGY:** The Oppidum Programme (observation of illegal drugs and misuse of psychotropic medications), a multi-centric survey, surveys drug-dependent subjects attending specialized care centres throughout France annually. Data were collected by questionnaire on socio-demographic variables and drug use during the preceding week. **RESULTS:** During October 1998, 46 centres took part in the survey. The methadone group (n = 424) was older, with a better economic situation; 16% used cocaine regularly. The HD buprenorphine group (n = 616)

35. **Barrett G. (2003) Model policy guidelines for opioid addiction treatment in the medical office. Pain Physician 6(2):217-221, 2003.**

**Abstract:** On October 17,2000, 'The Children's Health Act of 2000' (HR 4365) was signed into federal law. Section 3502 of that Act sets forth the 'Drug Addiction Treatment Act of 2000' (DATA). This legislation is of particular interest to state medical boards because it provides for significant changes in the oversight of the medical treatment of opioid addiction. For the first time in almost a century, physicians may treat opioid addiction with opioid medications in office-based settings. These opioid medications, Schedules III, IV, and V opioid drugs with Food and Drug Administration (FDA) approved indication for the treatment of opioid dependence, may be provided to patients under certain restrictions. This new treatment modality makes it possible for physicians to treat patients for opioid addiction with these Schedules III - IV narcotic controlled substances specifically approved by the FDA for addiction treatment in their offices without requirement that they be referred to specialised opioid treatment programs (OTP's) as previously required under federal law.

**ISSN:** 1533-3159.

**Pub Type:** journal article; overview.

**Descriptors:** Opioid Addiction; Dependence; Treatment.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

36. **Bartoletti M ; Gubellini C ; Gaiardi M. (2000) Sensitization to the morphine-like discriminative stimulus effects of buprenorphine in rats. Pharmacol**

**Res 2000 Sep;42(3):269-73.**

**Author Address:** Department of Pharmacology, University of Bologna, Via Irnerio 48, I-40126 Bologna, Italy.

**Abstract:** An experiment was performed to determine whether chronic non-contingent administration of morphine would produce cross-sensitization to the cueing properties of buprenorphine or D-amphetamine. To this end the sensitivity to the discriminative stimulus effects of morphine, buprenorphine and D-amphetamine was determined in rats trained to discriminate 10 mg kg<sup>-1</sup> morphine from saline in a food-reinforced operant task. Seven rats were given repeated non-contingent treatments with morphine (20 mg kg<sup>-1</sup>) on saline or no-test days and 10 mg kg<sup>-1</sup> on drug days) starting 20 days before the beginning of discrimination training; another six animals received injections of saline. Chronic administration of morphine resulted in sensitization to the discriminative stimulus effect of this drug and in cross-sensitization to the discriminative stimulus effect of buprenorphine. D-Amphetamine produced only saline lever selection in all rats. In conclusion, the present results confirm that the stimulus properties of opioid drugs may be enhanced, rather than decreased, in animals with a history of repeated non-contingent treatment with morphine. Sensitization to central-acting drugs is thought to play a role in the psychopathology of drug abuse. Hence, the present results point out the necessity of considering the effects of drugs which show tolerance, and those which show sensitization, under any particular drug regimen.

**ISSN:** 1043-6618.

**Pub Type:** Journal Article.

**Descriptors:** Animal ; Buprenorphine/\*pharmacology ; Dextroamphetamine/pharmacology ; Discrimination Learning/\*drug effects ; Dose-Response Relationship, Drug ; Male ; Morphine/\*pharmacology ; Narcotics/\*pharmacology ; Rats ; Rats, Sprague-Dawley.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Pharmacology

37. **Basu D ; Mattoo S ; Malhotra A ; Gupta N ; Malhotra R. (2000) A longitudinal study of male buprenorphine addicts attending an addiction clinic in India. Addiction 2000 Sep;95(9):1363-72.**

**Author Address:** Department of Psychiatry, Postgraduate Institute of Medical Education and Research, Chandigarh, India. medinst@pgi.chd.nic.in

**Abstract:** AIM: There is a lack of longitudinal studies of buprenorphine dependence, an important opioid dependence in several countries. We investigated the course and outcome of buprenorphine dependence in an Indian clinic-attending cohort. DESIGN: Retrospective longitudinal study. SETTING: An addiction clinic in northern India. PARTICIPANTS: Ninety-four male patients with buprenorphine dependence, registered for treatment between 1987 and 1993. Follow-up analyses were conducted for the 52 patients (55% of the index cohort) who completed more than a year of follow-up. In 48% of these 52 patients data were obtained from their clinical records of follow-up, while 52% were contacted specifically to obtain the required data on follow up. MEASUREMENT: Baseline demographic and clinical variables; time

spent in various phases of use or abstinence; outcome at the latest follow up; transition to other drugs during follow-up period. FINDINGS: Over an average follow-up duration of 3 years, 56% of the time was spent in dependent use, 12% in non-dependent use and 32% in abstinence. By the end of follow-up, 6% of patients were dead (annual death rate 1.9%), 33% were unchanged and 61% were classified as "improved". The proportion of patients with "improved" outcome increased over the years. Patients with poor outcome had shorter follow-up and hospital stay, and had used pentazocine and/or antihistaminic injections in the buprenorphine "cocktail" more often than those with better outcome. Thirty-two patients shifted to other drugs over the years, notably heroin or polydrug use. These "transition" patients had a family history of drug use more often, started their drug career earlier, had marital and legal complications more often, spent more time in dependent phase of drug use, underwent multiple hospital admissions but stayed for a shorter period and faced more deaths, when compared to those who did not shift. CONCLUSION: In clinic-attending male patients with buprenorphine dependence who were followed-up although dependent pattern of use of the drug continued for a long time in their career, there was a slow but progressive improvement. Transition to other drugs was associated with a worse course and outcome as compared to being stable on buprenorphine.

**ISSN:** 0965-2140.

**Pub Type:** Journal Article.

**Descriptors:** Adolescent ; Adult ; \*Buprenorphine ; Follow-Up Studies ; Human; India ; Male ; Middle Age ; \*Narcotics ; Opioid-Related Disorders/\*therapy ; Prognosis ; Retrospective Studies ; Risk Factors ; \*Substance Abuse Treatment Centers ; Support, Non-U.S. Gov't ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; History, use and effectiveness in other countries ; Treatment outcomes/effectiveness

38. **Becker A ; Strain E ; Bigelow G ; Stitzer M ; Johnson R. (2001) Gradual dose taper following chronic buprenorphine. Am J Addict 2001 Spring;10(2):111-21.**

**Author Address:** Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Md., USA.

**Abstract:** This paper describes the time course of withdrawal and relapse in opioid-dependent volunteers (n = 8) who completed a gradual outpatient buprenorphine dose taper (28 days). Compliance with treatment was very high, as evidenced by clinic attendance (96-100%). Urinalysis showed that 6 of the 8 volunteers had relapsed to opiates by the end of the dose taper, even though reports of withdrawal were generally low. Relapse may have been triggered by a desire to re-experience the drug's positive subjective effects, craving, or low motivation to remain drug-free. A longer taper combined with an expanded range of treatments may improve prognosis.

**ISSN:** 1055-0496.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Buprenorphine/administration & dosage/\*therapeutic use ;

Dose-Response Relationship, Drug ; Drug Administration Schedule ; Female ; Human ; Male ; Motivation ; Narcotic Antagonists/administration & dosage/\*therapeutic use ; Narcotics/\*adverse effects ; Opioid-Related Disorders/prevention & control/urine ; Questionnaires ; Recurrence ; Substance Withdrawal Syndrome/\*drug therapy/etiology ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

**39. Bell J ; Dru A ; Fischer B ; Levit S ; Sarfraz M. (2002) Substitution therapy for heroin addiction. *Subst Use Misuse* 2002 Jun-Aug;37(8-10):1149-78.**

**Author Address:** The Langton Centre, Sydney, NSW, Australia.

jamesb@sesahs.nsw.gov.au

**Abstract:** Substitution treatment for heroin addiction, defined here as maintenance prescribing of opioid agonist drugs to opioid dependent subjects, has increased in the last decade. The recent history of substitution treatment in five countries--Canada, the U.K., Australia, Israel, and France--is reviewed. In all five countries, the critical issues around substitution treatment are similar. The first key issue concerns the balance between making treatment accessible and attractive, and minimizing diversion to the black market. The second issue concerns the role of primary health care in delivering MMT. In general, there has been increasing involvement of primary health care, with training and support for practitioners. However, there remains uncertainty and official ambivalence over whether treatment should be restricted to specialist clinics and practitioners, or available through primary care. Most importantly, underlying these issues is the problem of stigma being associated with both addiction, and with substitution treatment. The underlying problem that treatment is often at odds with community values places enormous strains on substitution treatment, and makes the treatment system vulnerable to shifting community support and abrupt, politically-driven changes in policy.

**ISSN:** 1082-6084.

**Pub Type:** Journal Article.

**Descriptors:** Buprenorphine/therapeutic use ; Comparative Study ; Cross-Cultural Comparison ; Dose-Response Relationship, Drug ; Health Policy ; Heroin Dependence/psychology/\*rehabilitation ; Human ; Methadone/therapeutic use ; Narcotics/\*agonists/therapeutic use ; Patient Acceptance of Health Care/psychology ; Prescriptions, Drug ; Primary Health Care ; Substance Abuse, Intravenous/psychology/\*rehabilitation.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Legal/regulatory issues

**40. Beltrutti D ; Niv D ; Ben-Abraham R ; Di Santo S ; Weinbroum A. (2002) Late antinociception and lower untoward effects of concomitant intrathecal morphine and intravenous buprenorphine in humans. *J Clin Anesth* 2002 Sep;14(6):441-6.**

**Author Address:** Dept. of Anesthesia, S. Spirito Hospital, Alba-Bra, Italy.

**Abstract:** STUDY OBJECTIVE: To evaluate the perioperative antinociceptive effect of intrathecal morphine (a pure mu agonist), intravenous (IV) buprenorphine (a partial mu agonist) or their combination. DESIGN: Randomized, double-blind, placebo-controlled study. SETTINGS: Anesthesiology department of a university-affiliated public hospital. PATIENTS: 45 ASA physical status I, II, and III patients undergoing hysterectomy with general anesthesia. INTERVENTIONS: Preoperative and postoperative regimens consisted of intrathecal morphine 4.3 microg.kg(-1) plus IV 0.9% saline (Group 1), IV buprenorphine 1.3 microg.kg(-1) plus intrathecal saline (Group 2), and intrathecal morphine 4.3 microg.kg(-1) plus IV buprenorphine 1.3 microg.kg(-1) (Group 3; postoperative supplements consisting of IV buprenorphine 1.3 microg.kg(-1) plus intrathecal saline). MEASUREMENTS AND MAIN RESULTS: Group 2 and 3 patients were given three analgesic dosings compared with two dosings in Group 1 ( $p < 0.001$ ). The duration of action in Group 2 was significantly shorter ( $p = 0.001$ ) than in the other two groups. The 12-hour postoperative pain intensity and sedation in Group 3 was significantly lower ( $p < 0.05$ ) than in the other groups. Side effects (mainly pruritus and nausea and vomiting) were significantly fewer ( $p < 0.05$ ) in Groups 2 and 3 (26% and 28%, respectively) than in Group 1 (46%). CONCLUSIONS: The concomitant administration of intrathecal morphine and IV buprenorphine alleviates pain sensation and minimizes sedation more effectively than when given after the administration of either drug separately. In addition, IV buprenorphine affords a reduction in side effects.

**ISSN:** 0952-8180.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Analgesics, Opioid/\*administration & dosage/adverse effects ; Anesthesia, General ; Buprenorphine/\*administration & dosage/adverse effects ; Double-Blind Method ; Female ; Human ; Hysterectomy ; Injections, Intravenous ; Injections, Spinal ; Middle Age ; Morphine/\*administration & dosage/adverse effects ; Pain Measurement ; Pain, Postoperative/ diagnosis/\*prevention & control.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pain management ; Pharmacology

**41. Benson E. (2003) A new treatment for addiction. *APA Monitor* 2003; 24(6). 4p. (online and print version).**

**Abstract:** Short overview about Buprenorphine for psychologists, with web links to relevant sites. Approximately one million Americans are dependent on heroin, prescription painkillers and other opioids, but the vast majority of them--as many as 800,000--aren't receiving any treatment. Opiate substitutes that prevent withdrawal are among the most effective treatments for such addictions, when combined with psychological counseling, researchers say. But until recently, only two such drugs--methadone and levo-alpha-acetyl methadol (LAAM)--were available, and only licensed treatment clinics were authorized to dispense them. Many addicts avoid opiate treatment programs (OTPs) because of their inconvenience or perceived stigma, and even those who would like to enroll sometimes can't because of limited treatment slots. The approval of a

new medication by the Food and Drug Administration (FDA) last fall, however, could reshape the landscape of opiate addiction treatment in the United States, making pharmacotherapy available and attractive to patients who previously shunned it, say researchers. For its part, the APA has been trying to help build the buprenorphine network by encouraging appropriately trained psychologists to make themselves available as referral resources.

**Pub. Type:** Newsletter; Web document.

**Descriptors:** Overview; American Psychological Association.

**URL:** <http://www.apa.org/monitor/jun03/newtreat.html?CFID=2599890&CFTOKEN=84509744>

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence

42. **Berson A ; Gervais A ; Cazals D ; Boyer N ; Durand F ; Bernuau J ; Marcellin P ; Degott C ; Valla D ; Pessayre D. (2001) Hepatitis after intravenous buprenorphine misuse in heroin addicts. J Hepatol 2001 Feb;34(2):346-50.**

**Author Address:** INSERM U1481 and Service d'Hepatologie, H pital Beaujon, Clichy, France.

**Abstract:** BACKGROUND: Sublingual buprenorphine is used as a substitution drug in heroin addicts. Although buprenorphine inhibits mitochondrial function at high concentrations in experimental animals, these effects should not occur after therapeutic sublingual doses, which give very low plasma concentrations. CASE REPORTS: We report four cases of former heroin addicts infected with hepatitis C virus and placed on substitution therapy with buprenorphine. These patients exhibited a marked increase in serum alanine amino transferase (30-, 37-, 13- and 50-times the upper limit of normal, respectively) after injecting buprenorphine intravenously and three of them also became jaundiced. Interruption of buprenorphine injections was associated with prompt recovery, even though two of these patients continued buprenorphine by the sublingual route. A fifth patient carrying the hepatitis C and human immunodeficiency viruses, developed jaundice and asterixis with panlobular liver necrosis and microvesicular steatosis after using sublingual buprenorphine and small doses of paracetamol and aspirin. CONCLUSIONS: Although buprenorphine hepatitis is most uncommon even after intravenous misuse, addicts placed on buprenorphine substitution should be repeatedly warned not to use it intravenously. Higher drug concentrations could trigger hepatitis in a few intravenous users, possibly those whose mitochondrial function is already impaired by viral infections and other factors.

**ISSN:** 0168-8278.

**Pub Type:** Journal Article.

**Descriptors:** Administration, Sublingual ; Adult ; Animal ; Buprenorphine/administration & dosage/\*toxicity ; Case Report ; HIV Infections/complications ; Hepatitis C/complications ; Hepatitis, Toxic/\*etiology/pathology ; Heroin Dependence/\*complications/drug therapy ; Human ; Injections, Intravenous ; Male ; Narcotics/administration & dosage/\*toxicity.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; Pharmacology

43. **Bickel W ; Amass L ; Crean J ; Badger G. (1999) Buprenorphine dosing every 1, 2, or 3 days in opioid-dependent patients. Psychopharmacology (Berl) 1999 Sep;146(2):111-8.**

**Author Address:** Department of Psychiatry, University of Vermont, 38 Fletcher Place, Burlington, VT 05401, USA.

**Abstract:** RATIONALE: Administration of double the maintenance dose of buprenorphine has been shown to permit every-other-day dosing. Whether longer periods between dosing can be achieved is unknown. OBJECTIVES: To examine whether triple the maintenance dose can be administered every 72 h without opioid withdrawal or intoxication. METHODS: Sixteen opioid-dependent outpatients each received three conditions (1) the maintenance dose of buprenorphine every 24 h, (2) double the maintenance dose every 48 h, and (3) triple the maintenance dose every 72 h under double-blind placebo-controlled conditions. Each conditions was imposed in a random sequence for 21-22 days. Self report and observer measures were taken at 24-h intervals.

RESULTS: No significant differences were observed on measures of opioid agonist and withdrawal effects between the dosing conditions. However, averaging effects across conditions may obscure important within-condition effects. When conditions were analyzed by individual days within a condition, several significant effects were observed. For example, 24 h after administration of triple the maintenance dose, significant effects were observed in eight opioid agonist measures. Also, 72 h after administration of triple the maintenance dose, significant effects were observed on four measures of withdrawal. Neither adverse medical reactions nor excessive opioid intoxication were observed. CONCLUSIONS: These results suggest that buprenorphine may be administered safely every 72 h by tripling the maintenance dose, with only minimal withdrawal complaints. Importantly, this 72-h dosing may permit patients to attend clinic thrice weekly without the use of take-home doses.

**ISSN:** 0033-3158.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Buprenorphine/\*administration & dosage/\*therapeutic use ; Cross-Over Studies ; Double-Blind Method ; Female ; Human ; Male ; Narcotics/\*administration & dosage/\*therapeutic use ; Opioid-Related Disorders/psychology/\*rehabilitation ; Patient Compliance ; Psychiatric Status Rating Scales ; Pupil/drug effects ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

44. **Blanchon T ; Boissonnas A ; Vareseon I ; Vidal-Trecan G. (2003) Homelessness and high-dosage buprenorphine misuse. Subst Use Misuse 2003 Feb-May;38(3-6):429-42.**

**Author Address:** Department de Sante Publique, CHU Cochin-Port Royal, Assistance Publique Hopitaux de Paris, Universite Rene Descartes, Paris,

France.

**Abstract:** AIM: To determine whether intravenous drug users (IDUs) are more likely to misuse high dosage buprenorphine (HDB) if they are homeless.

**DESIGN:** We carried out a cross-sectional study using data collected from HDB users between 1998 and 1999. Data were collected by use of a structured questionnaire with questions about demographic characteristics, and use of HDB and other substances. IDUs were considered to be homeless if they did not live on their own or with their parents or friends. **SETTING:** IDUs were recruited from three centers for the treatment of drug users, three health care networks, one prison, one sleep-in, and two centers that provide psychosocial support for IDUs. **PARTICIPANTS:** Of the 788 eligible patients, 779 answered the questionnaire (response rate: 98.9%). **RESULTS:** Homeless IDUs were more likely to have injected HDB than those who were not homeless (67% vs. 47%;  $p < 0.001$ ), and their injection behaviors were more likely to be unsafe. The first HDB injection was more likely to result in medical complications in the homeless group than in the nonhomeless group (58% vs. 38%;  $p = 0.001$ ). Homeless IDUs were less likely to receive medical follow-up and were less well informed about the correct way of using HDB than nonhomeless IDUs. **CONCLUSION:** Homeless IDUs are more likely to misuse HDB. Thus, HDB maintenance therapy may not be the most appropriate maintenance therapy for this group.

**ISSN:** 1082-6084.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Buprenorphine/\*administration & dosage ; Cross-Sectional Studies ; Demography ; Drug Administration Schedule ; Female ; France/epidemiology ; Health Status ; Homeless Persons/\*psychology/\*statistics & numerical data ; Human ; Male ; Narcotics/\*administration & dosage ; Questionnaires ; Substance Abuse, Intravenous/\*epidemiology ; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** Dosing/administration ; Addiction potential/misuse of buprenorphine; Special populations

45. **Boatwright D. (2002) Buprenorphine and addiction: challenges for the pharmacist. J Am Pharm Assoc (Wash) 2002 May-Jun;42(3):432-8.**

**Author Address:** San Francisco Veterans Affairs Medical Center, Calif, USA. deborah.boatwright@mail.va.gov

**Abstract:** OBJECTIVE: To present an analysis of the Drug Addiction Treatment Act of 2000 (DATA) and its impact on the practice of pharmacy. DATA SOURCES: Statutes, codes, regulations, newspaper articles, journal articles; search of articles posted on MEDLINE identified using the search terms methadone, buprenorphine, treatment, opioid abuse, and opioid addiction. STUDY SELECTION: Not applicable. DATA EXTRACTION: Not applicable. DATA SYNTHESIS: DATA and Food and Drug Administration approval of sublingual tablets of buprenorphine and buprenorphine with naloxone (Reckitt and Benckiser) will dramatically expand opioid addicts' access to treatment and increase the number of opioid addicts receiving prescriptions for buprenorphine and buprenorphine with naloxone. The availability of buprenorphine will pose

unique challenges to pharmacists and suggests the need for education on addiction and greater awareness of the unique needs of patients recovering from addiction. **CONCLUSION:** The stage is being set to expand access to treatment and reach more untreated opioid addicts in the United States. Professional organizations such as the American Pharmaceutical Association should work with the U.S. Department of Health and Human Services and its Substance Abuse and Mental Health Services Administration to develop training materials, curricula, and guidelines for pharmacists on substance abuse with a special focus on outpatient opioid treatment. Such materials could be used in continuing education programs and materials and in pharmacy schools. **ISSN:** 1086-5802.

**Pub Type:** Journal Article ; Overview.

**Descriptors:** Analgesics, Opioid/\*therapeutic use ; Buprenorphine/\*therapeutic use ; Counseling ; Human ; \*Legislation, Drug ; Naloxone/therapeutic use ; Narcotic Antagonists/therapeutic use ; Opioid-Related Disorders/\*rehabilitation ; \*Pharmacists ; United States.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Legal/regulatory issues ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

46. **Bochud Torney C ; Favrat B ; Monnat M ; Daepfen J ; Schnyder C ; Bertschy G ; Besson J. (2003) Ultra-rapid opiate detoxification using deep sedation and prior oral buprenorphine preparation: long-term results. Drug Alcohol Depend 2003 Apr 1;69(3):283-8.**

**Author Address:** Department of Adult Psychiatry, Substance Abuse Unit, Cery Hospital, 1008, Prilly-Lausanne, Switzerland

**Abstract:** BACKGROUND: New methods of ultra-rapid opiate detoxification (URD) under intravenous sedation have been criticized because of limited data on safety and long-term follow-up. Premedication with buprenorphine has been advocated to improve safety by decreasing vomiting. Prior research has not explored URD in socially impaired patients. **METHOD:** Sixteen patients were detoxified with URD and prospectively evaluated over at least 30 months. Data of this procedure were compared with those of our previous study without buprenorphine preparation (Drug Alcohol Depend. 52(3) (1998) 243). The 16 patients were followed up by a general practitioner (GP) before and after URD. The GPs also supervised the 7-day course of buprenorphine treatment prescribed for the 16 patients prior to URD. **RESULTS:** During the procedure, only one episode of vomiting occurred instead of 13 out of 20 in our previous study. Post-procedure, only two patients experienced moderate withdrawal symptoms, such as persistent nausea, abdominal cramps and vomiting lasting from 24 to 48 h, in comparison with most patients in the previous study without buprenorphine. After a period of at least 30 months (36.0+/-6.38), the 16 patients were still alive and were regularly monitored by their GP. Only two of the 16 never relapsed after URD and reported total opiate abstinence. Fourteen patients relapsed; 12 of these were prescribed a licensed methadone substitution program and two were still using heroin. **CONCLUSION:** In this small sample, the data indicated that URD with buprenorphine preparation was

safe and that it markedly decreased post-procedure morbidity. No patient died over a minimum 30-month follow-up period. Furthermore, the procedure was employed with socially impaired patients. In the long term, a few patients were still free of opiates, while the majority opted for a methadone maintenance program, showing that URD can serve as one possible step in a long-term treatment program.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article.

**Descriptors:** ultra rapid opiate detoxification; buprenorphine; opiates; side effects ; \*Detoxification ; \*Opiates ; \*Side Effects (Treatment) ; Narcotic Agonists ; Human; Male ; Female; Adulthood (18 yrs & older) ; Empirical Study ; Longitudinal Study ; Prospective Study ; Treatment Outcome Study.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

47. **Bohme K. (2002) Buprenorphine in a transdermal therapeutic system--a new option. Clin Rheumatol 2002 Feb;21 Suppl 1:S13-6.**

**Author Address:** Group Practice for Anaesthesia, Burgfeld Hospital, Kassel, Germany. dr.boehme@t-online.de

**Abstract:** Advanced patch technology has yielded a novel transdermal therapeutic system (TDS) for the rate-controlled systemic delivery of buprenorphine. Buprenorphine TDS is available in three strengths with release rates of 35, 52.5 and 70 microg/h over 72 h, corresponding to daily doses of 0.8, 1.2 and 1.6 mg, respectively. In total, 445 patients with chronic pain of malignant or non-malignant origin requiring long-term treatment with potent opioid analgesics were enrolled in the clinical trial programme. The patients were treated with buprenorphine TDS in one of three dosage strengths or with placebo TDS in a randomised double-blind setting. Greater pain relief was documented in patients treated with buprenorphine TDS than in those treated with placebo. The benefit of buprenorphine TDS was further reflected in the larger number of patients who slept for longer than 6 h per night. Patients switching from Step 2 or Step 3 opioids to buprenorphine TDS encountered no problems with the conversion. Typical opioid-related adverse events were reported with a low incidence and mild intensity. In an open follow-up study 239 patients elected to continue treatment with buprenorphine TDS. The confirmation of clinical benefit, coupled with a high level of patient compliance and improved quality of life, substantiate the usefulness of buprenorphine TDS in a practical setting.

**ISSN:** 0770-3198.

**Pub Type:** Journal Article.

**Descriptors:** Administration, Cutaneous ; Administration, Sublingual ; Analgesics, Opioid/\*administration & dosage ; Buprenorphine/\*administration & dosage ; Dose-Response Relationship, Drug ; Double-Blind Method ; Drug Administration Schedule ; Female ; Human ; Male ; Pain/diagnosis/\*drug therapy ; Pain Measurement ; Randomized Controlled Trials ; Severity of Illness Index ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pain management ; Pharmacology

48. **Bohme K ; Likar R. (2003) Efficacy and tolerability of a new opioid analgesic formulation, buprenorphine transdermal therapeutic system (TDS), in the treatment of patients with chronic pain. A randomised, double-blind, placebo-controlled study. Pain Clinic. Vol 15(2):193-202, 2003.**

**Author Address:** Burgfeld Hospital, Pain Unit, Kassel; Germany.

**Abstract:** This randomised, double-blind, placebo-controlled study evaluated the efficacy and tolerability of buprenorphine TDS, a new transdermal formulation of the opioid analgesic buprenorphine. Patients (151) with severe to very severe chronic pain of malignant or non-malignant origin who maintained at least satisfactory pain relief with sublingual buprenorphine 0.8-1.2 mg/day during an open-label 5-day run-in phase, were randomly allocated to buprenorphine TDS in one of three dose strengths: 35 [mu]g/h, 52.5 [mu]g/h or 70 [mu]g/h, or placebo, receiving two patches consecutively, each applied for 72 hours. Rescue analgesic medication comprised sublingual buprenorphine tablets (0.2 mg). Responders were patients reporting at least satisfactory pain relief and taking no more than 0.2 mg/day rescue analgesic. The proportion of responders in each treatment group increased dose-dependently (34%, 37% and 50% for the 35 [mu]g/h, 52.5 [mu]g/h and 70 [mu]g/h groups, respectively). However, because of a high response rate in the placebo group (31%), these response rates failed to reach statistical significance ( $p = 0.374$ ). Twenty percent less patients in the placebo group reported good to complete pain relief while the proportion reporting moderate to very severe pain increased by 14%. In contrast, relative numbers of patients in the active treatment groups reporting good to complete pain relief increased by 5-13%, while the proportion reporting moderate to very severe pain fell by 3-14%. The duration of sleep uninterrupted by pain was shorter in the placebo than in the active treatment groups. The incidence of adverse events was 23%. Most local adverse events were mild to moderate erythema or pruritus.

**ISSN:** 0169-1112.

**Pub Type:** journal article.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pain management

49. **Borg L ; Kreek M. (2003) The pharmacology of opioids. In: Graham, Allen W ; Schultz, Terry K ; Mayo-Smith, Michael F ; Ries, Richard K ; Wilford, Bonnie B. Principles of Addiction Medicine / 3rd edition. Chevy Chase, MD : American Society of Addiction Medicine, Inc., 2003, pp. 141-153.**

**Abstract:** This chapter reviews the pharmacology and neurobiology of five exogenous opioids that are particularly significant in the area of opioid addiction and its pharmacotherapy: heroin, morphine, methadone, levo-alpha-acetylmethadol (LAAM), and buprenorphine.

**ISSN:** 1880425084.

**Pub Type:** book chapter.

**Notes:** ADAI Library: RC 644 M455 2003 [REF HAND]

**ATTC Buprenorphine Topics:** Pharmacology

50. **Borron S ; Monier C ; Risede P ; Baud F. (2002) Flunitrazepam variably alters morphine, buprenorphine, and methadone lethality in the rat. Hum Exp Toxicol 2002 Nov;21(11):599-605.**

**Author Address:** INSERM U26, Universite Paris 7, Hopital Fernand Widal, 200 rue du Fg St Denis, Paris 75475, France. sborron@intoxicon.com

**Abstract:** Opiates and substitution products are frequently abused, alone and in association with benzodiazepines. While this combination may result in severe respiratory depression and death, the quantitative relationship remains uncertain. We performed randomized, blinded intravenous median lethal dose (MLD) studies in Sprague-Dawley rats of morphine, buprenorphine, and methadone, alone and in combination with intraperitoneal flunitrazepam pretreatment. We employed the up-and-down method, performed in quadruplicate, comparing time to death following opioid injection. Results are expressed as median of four series (extremes). The MLDs of morphine, buprenorphine, and methadone alone were 64.0 (33.6:79.5), 234.6 (168.6:284.4), and 22.5 (19.3:24.1) mg/kg, respectively, and 60.6 (35.2:88.2), 38.4 (30.6:54.0), and 13.0 (9.7:13.8) mg/kg, respectively, after pretreatment with 40 mg/kg flunitrazepam. Times to death for morphine, buprenorphine, and methadone alone were 2.5 (0.8:24), 0.02 (0.0:24), and 2.0 (0.0:24) hours, respectively, and 13.5 (0.0:144), 24.0 (0.0:120), and 0.0 (0.0:24) hours, respectively, after pretreatment with flunitrazepam 40 mg/kg, ip. Flunitrazepam significantly altered methadone (P=0.02) and buprenorphine (P=0.02) but not morphine lethality (P=0.77). Flunitrazepam significantly prolonged time to death only for buprenorphine (P<0.01). Flunitrazepam-opioid drug-drug interactions are more complex than is generally believed. Mechanistic studies of flunitrazepam-opioid lethal interactions are needed.

**ISSN:** 0960-3271.

**Pub Type:** Journal Article.

**Descriptors:** Animal ; Anti-Anxiety Agents, Benzodiazepine/\*toxicity ; Buprenorphine/toxicity ; Drug Interactions ; Flunitrazepam/\*toxicity ; Injections, Intraperitoneal ; Injections, Intravenous ; Lethal Dose 50 ; Male ; Methadone/toxicity ; Morphine/toxicity ; Narcotics/\*toxicity ; Rats ; Rats, Sprague-Dawley ; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** Basic laboratory research; Dosing/administration; Pharmacology

51. **Bose S ; Ravis W ; Lin Y ; Zhang L ; Hofmann G ; Banga A. (2001) Electrically-assisted transdermal delivery of buprenorphine. J Control Release 2001 Jun 15;73(2-3):197-203.**

**Author Address:** Department of Pharmacal Sciences, School of Pharmacy, Auburn University, Auburn, AL 36849-5503, USA.

**Abstract:** The objective of this study was to explore the electrically assisted transdermal delivery of buprenorphine. Oral delivery of buprenorphine, a

synthetic opiate analgesic, is less efficient due to low absorption and large first-pass metabolism. While transdermal delivery of buprenorphine is expected to avoid the first-pass effect and thereby be more bioavailable, use of electrical enhancement techniques (iontophoresis and/or electroporation) could provide better programmability. Another use of buprenorphine is for opiate addiction therapy. However, a patch type device is subject to potential abuse as it could be removed by the addict. This abuse can be prevented if drug particles are embedded in the skin. The feasibility of doing so was investigated by electro-incorporation. Buprenorphine HCl (1 mg/ml) in citrate buffer (pH 4.0) was delivered in vitro across human epidermis via iontophoresis using a current density of 0.5 mA/cm<sup>2</sup> and silver-silver chloride electrodes. Electroporation pulses were also applied in some experiments. For electro-incorporation, drug microspheres or particles were driven into full thickness human skin by electroporation. It was observed that the passive transdermal flux of buprenorphine HCl was significantly enhanced by iontophoresis under anodic polarity. The effectiveness of electro-incorporation seemed inconclusive, with pressure also playing a potential role. Delivery was observed with electro-incorporation, but the results were statistically not different from the corresponding controls.

**ISSN:** 0168-3659.

**Pub Type:** Journal Article.

**Descriptors:** Administration, Cutaneous ; Analgesics, Opioid/\*administration & dosage ; Animal ; Biological Transport ; Buprenorphine/\*administration & dosage/pharmacokinetics ; \*Electroporation ; Human ; \*Iontophoresis ; Skin/\*metabolism ; Swine.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pain management ; Pharmacotherapy for opiate dependence ; Pharmacology

52. **Bouchez J ; Beauverie P ; Touzeau D. (1998) Substitution with buprenorphine in methadone- and morphine sulfate-dependent patients. Eur Addict Res 1998;4(Suppl.1):8-12.**

**Author Address:** Clinique Liberte, Paris, France

**Abstract:** In France, during the 1990s, there have been some rapid developments in the treatment of opioid addiction with the introduction of legal substitution agents. Originally, some patients were treated with morphine sulfate, but this was superseded by high dose buprenorphine (Subutex(R)) and methadone. This resulted in those patients originally treated with morphine being transferred to either of these two licensed products. A study investigating the effects of the transition from morphine to either buprenorphine or methadone was undertaken. Supplementary to this, a trial investigating transition between these new compounds was also conducted. The primary outcome measures for these trials were retention rate, which was assessed at 5, 9 and 12 months, and the precipitation of withdrawal symptoms. The studies showed that transferring patients between substitution agents can be accomplished without severe withdrawal symptoms, although specific management may be required for transfer from high doses of methadone to buprenorphine. High long-term retention rates were observed in the studies,

with most drop-outs occurring directly after transfer. Results suggest that patients on long-term buprenorphine maintenance therapy may have good compliance in comparison with other agents.

**Pub. Type:** journal article.

**Descriptors:** Clinical Trial ; Adult ; Buprenorphine/therapeutic use\* ; Comparative Study ; Dose-Response Relationship, Drug ; Female ; Human; Male ; Methadone\* ; Morphine\*; Narcotics/therapeutic use\* ; Opioid-Related Disorders/rehabilitation\* ; Narcotics ; Buprenorphine ; Morphine ; Methadone.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence

53. **Boyarsky B ; McCance-Katz E. (2000) Improving the quality of substance dependency treatment with pharmacotherapy. Substance Use & Misuse. Vol 35(12-14) Oct-Dec 2000, 2095-2125.**

**Abstract:** Discusses current pharmacological treatments for alcohol, opioid, cocaine, and nicotine use disorders. For alcohol treatment, benzodiazepines, beta-blockers, alpha-sub-2 adrenergic agonists, and anticonvulsants such as carbamazepine and valproate are effective in attending to withdrawal symptoms; for maintenance, disulfiram and the opioid antagonist naltrexone are clinically effective in preventing relapse. Opioid withdrawal may be successfully treated with methadone replacement therapy, the opioid antagonist clonidine, and the alpha-sub-2 adrenergic agonist lofexidine. Maintenance may be enhanced with naltrexone, methadone, or levo-alpha-acetylmethadol, and possibly the partial opioid agonist buprenorphine. Cocaine dependence may be treated with dopamine agents, antidepressants, and other agents. Nicotine dependence may be treated with nicotine polacrilex gum, nicotine patches, or nicotine nasal spray. Psychotropic pharmacologic treatment of dually diagnosed patients with substance misuse and psychotic disorders is similar to that of patients with substance abuse disorders.

**ISSN:** 1082-6084 (Print).

**Pub Type:** Journal Article ; Overview.

**Descriptors:** pharmacological treatments for alcohol & opioid & cocaine & nicotine use disorders, clinicians & clients ; \*Alcohol Rehabilitation ; \*Cocaine ; \*Drug Rehabilitation ; \*Drug Therapy ; \*Opiates ; Clients ; Clinicians ; Nicotine ; Human.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence

54. **Boyd J ; Randell T ; Luurila H ; Kuisma M. (2003) Serious overdoses involving buprenorphine in Helsinki. Acta Anaesthesiol Scand 2003 Sep;47(8):1031-3.**

**Author Address:** Helsinki Emergency Medical Service, Helsinki University Central Hospital, Helsinki, Finland. james.boyd@hel.fi

**Abstract:** BACKGROUND: Buprenorphine is used as maintenance therapy for opioid-dependent patients. In comparison with other opioids it is thought to be safer because it is less likely to cause serious respiratory depression. However, concomitant use of psychotropics, especially benzodiazepines, and intravenous

injection of dissolved buprenorphine tablets increase the risk of a serious overdose. METHODS: As part of a larger retrospective study of opioid overdoses in Helsinki, the emergency medical services (EMS) records from January 1995 to April 2002 were reviewed for overdoses involving buprenorphine. Hospital records were reviewed when available. RESULTS: We report 11 overdoses in which buprenorphine was involved. The classic symptoms and signs of an opioid overdose (respiratory depression, miosis and central nervous system depression) were present in most of the cases. At least eight of the patients had an overdose that was potentially fatal. One of the patients had a heroin overdose and was reportedly 'treated' by his friends with intravenously administered buprenorphine. CONCLUSION: The high-dosage formulation of buprenorphine used for opioid-dependent patients might have caused several dangerous and potentially fatal overdoses in Helsinki. However, it does cause considerably less serious overdoses than heroin. Drug abusers might be intravenously administering buprenorphine themselves to treat heroin overdoses.

**ISSN:** 0001-5172.

**Pub Type:** Journal Article.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; History, use and effectiveness in other countries

55. **Breen C ; Harris S ; Lintzeris N ; Mattick R ; Hawken L ; Bell J ; Ritter A ; Lenne M ; Mendoza E. (2003) Cessation of methadone maintenance treatment using buprenorphine: transfer from methadone to buprenorphine and subsequent buprenorphine reductions. Drug Alcohol Depend 2003 Jul 20;71(1):49-55.**

**Author Address:** National Drug and Alcohol Research Centre, University of New South Wales, NSW 2052, Sydney, Australia.  
courtney.breen@unsw.edu.au

**Abstract:** BACKGROUND: Buprenorphine is used in the treatment of opioid dependence. Due to its pharmacology, the transfer from methadone to buprenorphine may precipitate withdrawal symptoms. METHODS: Methadone maintained patients with clinical indicators of stability who were seeking withdrawal from methadone were recruited from three Australian states. Patients on methadone doses between 30 and 40 mg were randomised to transfer to buprenorphine by a fixed dose (transfer at 30 mg methadone) or by a variable dose induction (transfer when 'uncomfortable'). A third group of patients with methadone doses less than 30 mg were transferred to buprenorphine at their entry methadone dose. Fifty-one patients were inducted onto buprenorphine using the same dosing protocol with the first dose of 4 mg buprenorphine. Following stabilisation on buprenorphine, patients gradually reduced the buprenorphine dose to 0 mg. Withdrawal severity and drug use was monitored. RESULTS: There were no significant difference between the transfer at 30 mg and transfer when 'uncomfortable' dosing protocols in severity of withdrawal on transfer from methadone to buprenorphine. Those on doses less than 30 mg reported significantly less withdrawal discomfort at transfer. All but one patient stabilised on buprenorphine. Thirty-eight of the 51 patients

inducted onto buprenorphine reached 0 mg. **CONCLUSIONS:** Transfer from methadone to buprenorphine can safely occur from doses of around 30 mg of methadone. Buprenorphine dose reductions were well tolerated. Thirty-one percent of patients were not using heroin or methadone at 1-month follow-up. **ISSN:** 0376-8716.

**Pub Type:** Journal Article.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

56. **Bridge T ; Fudala P ; Herbert S ; Leiderman D. (2003) Safety and health policy considerations related to the use of buprenorphine/naloxone as an office-based treatment for opiate dependence. Drug Alcohol Depend 2003 May 21;70(2 Suppl):S79-85.**

**Author Address:** Division of Treatment Research and Development, National Institute on Drug Abuse, 20892, Bethesda, MD, USA

**Abstract:** Opiate dependence remains a fundamental challenge confronting health delivery systems and is often characterized as a social and moral issue. The impact of this disorder on healthcare policy is changing with the increased incidence of HIV, hepatitis C, and tuberculosis infections in opiate-dependent patients. These medical illnesses have substantial effect on escalating healthcare costs, and, therefore, also affect healthcare policy priorities, which are responsive to these costs. Pharmacological treatments for opiate dependence have had limited success; often the consequence of limited access to care. Hence, there is a need to develop new pharmacotherapies for opiate dependence that extend the range of clinical options, including new first-line treatment approaches. This paper will focus on the safety and health policy considerations related to the use of buprenorphine and buprenorphine/naloxone based on data derived from clinical trials and post-marketing surveillance that provide evidence for the use of the medications as first-line treatments in an office-based environment. The evaluation of this evidence formed the basis by the National Institute on Drug Abuse to support and pursue the evaluation and registration of buprenorphine/naloxone and buprenorphine in a public/private sector cooperative effort to become an office-based, first-line treatment for opiate dependence.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Legal/regulatory issues ; Pharmacotherapy for opiate dependence

57. **Budd K. (2003) Buprenorphine and the transdermal system: the ideal match in pain management. Int J Clin Pract Suppl 2003 Feb;(133):9-14; discussion 23-4.**

**Author Address:** Mornington Clinic, Bradford, United Kingdom.

**Abstract:** A system for the transdermal administration of the opioid drug buprenorphine has recently been introduced. Buprenorphine has physico-

chemical properties, including a low molecular weight and high analgesic potency, that make it an excellent compound for transdermal drug delivery. The new technology (buprenorphine TDS, Transtec) is an advanced system that contains the active drug incorporated into a polymer matrix, which is at the same time the adhesive layer. The patch precisely controls the rate of drug delivery and produces stable plasma concentrations. It is available in three doses (release rates of 35, 52.5 and 70 microg/h), and the suggested duration of use per patch is three days. Buprenorphine TDS was developed for the treatment of moderate to severe cancer pain and severe pain which does not respond to non-opioid analgesics. Not only does this transdermal system provide excellent analgesia and a low incidence of adverse events, but its ease of use results in greater compliance. The patch provides excellent adhesion and has a low susceptibility to damage that might lead to toxicity or opioid abuse.

**ISSN:** 1368-504X.

**Pub Type:** Journal Article ; Review ; Review, Tutorial.

**Descriptors:** Administration, Cutaneous ; Administration, Sublingual ; Analgesics, Opioid/\*administration & dosage/pharmacokinetics ; Buprenorphine/\*administration & dosage/pharmacokinetics ; Dose-Response Relationship, Drug ; Human ; Pain/\*prevention & control.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pain management

58. **California Society of Addiction Medicine. (ongoing) Buprenorphine Information web page. CSAM web site; Various documents and resources.**

**Abstract:** The CSAM website includes much material listed elsewhere (such as on ASAM and CSAT websites), but has some unique resources and is a helpful place to look for information. Unique resources on the CSAM site are: (1) Buprenorphine Algorithm Slide set, which are an aid for making clinical decisions about the use of buprenorphine by medical practitioners; (2) Buprenorphine Discussion Forum, a web-based discussion of buprenorphine issues; it includes questions from physicians and answers from the experts. The CSAM Buprenorphine Discussion Forum is open to the public for viewing, but only registered user may post to the board.

**URL:** [http://csam-asam.org/buprenorphine\\_information.htm](http://csam-asam.org/buprenorphine_information.htm)

**Pub. Type:** Web site.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

59. **Cameron D ; Allen D ; Galway K. (2001) A pilot study of the effectiveness of buprenorphine and methadone as detoxication agents when choice is given to the consumer. Journal of Substance Use 2001; 6(2):101-109.**

**Author Address:** Department of Psychiatry, University of Leicester, Leicester Royal Infirmary, Leicester LE2 7LX; United Kingdom.

**Abstract:** A study was undertaken which provided for patients attending a community drug team (CDT) in the English Midlands the opportunity to decide

for themselves whether they received methadone or buprenorphine on a comparable five-week fixed dose regime for detoxification from opiates. All but one of the 26 participants chose which drug they would use with 13 choosing buprenorphine. Those who chose buprenorphine were more likely to be married or cohabiting. There was no difference in prior drug use. Those on buprenorphine reported less severe withdrawal symptoms from Week Three onwards. There was no difference in attrition rates between the two groups, but those on buprenorphine reported external reasons for defaulting from the study whereas those on methadone cited severity of withdrawal symptoms. Most participants used 'street drugs' on top of the prescribed regime, notably cannabis and heroin. Alcohol consumption in both groups increased during detoxification.

**ISSN:** 1465-9891.

**Pub Type:** journal article.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

60. **Candido K ; Winnie A ; Ghaleb A ; Fattouh M ; Franco C. (2002) Buprenorphine added to the local anesthetic for axillary brachial plexus block prolongs postoperative analgesia. Reg Anesth Pain Med 2002 Mar-Apr;27(2):162-7.**

**Author Address:** Department of Anesthesiology and Pain Management, Cook County Hospital, Chicago, IL 60611, USA. kcandido@msn.com

**Abstract:** BACKGROUND AND OBJECTIVES: Buprenorphine added to local anesthetic solutions for supraclavicular block was found to triple postoperative analgesia duration in a previous study when compared with local anesthetic block alone. That study, however, did not control for potentially confounding factors, such as the possibility that buprenorphine was affecting analgesia through intramuscular absorption or via a spinal mechanism. To specifically delineate the role of buprenorphine in peripherally mediated opioid analgesia, the present study controlled for these 2 factors. METHODS: Sixty American Society of Anesthesiologists (ASA) P.S. I and II, consenting adults for upper extremity surgery, were prospectively assigned randomly in double-blind fashion to 1 of 3 groups. Group I received local anesthetic (1% mepivacaine, 0.2% tetracaine, epinephrine 1:200,000), 40 mL, plus buprenorphine, 0.3 mg, for axillary block, and intramuscular (IM) saline. Group II received local anesthetic-only axillary block, and IM buprenorphine 0.3 mg. Group III received local anesthetic-only axillary block and IM saline. Postoperative pain onset and intensity were compared, as was analgesic medication use. RESULTS: The mean duration of postoperative analgesia was 22.3 hours in Group I; 12.5 hours in group II, and 6.6 hours in group III. Differences between groups I and II were statistically significant ( $P = .0012$ ). Differences both between groups I and III and II and III were also statistically significant ( $P < .001$ ). CONCLUSIONS: Buprenorphine-local anesthetic axillary perivascular brachial plexus block provided postoperative analgesia lasting 3 times longer than local anesthetic block alone and twice as long as buprenorphine given by IM injection plus local anesthetic-only block. This supports the concept of peripherally mediated opioid

analgesia by buprenorphine.

**ISSN:** 1098-7339.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Aged ; Analgesics, Opioid/\*administration & dosage ; Anesthetics, Local/\*administration & dosage/adverse effects ; \*Brachial Plexus ; Buprenorphine/\*administration & dosage/adverse effects ; Female ; Human ; Male ; Middle Age ; \*Nerve Block ; Pain, Postoperative/\*drug therapy.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pain management

61. **Caplehorn, J. (2003) Comments on Mattick et al.: The need for independent data re-analyses. Addiction 2003 Nov; 98(11):1633-4.**

**Author Address:** School of Public Health, A27, University of Sydney, Sydney, NSW 2006, Australia Email: johnc@health.usyd.edu.au

**Abstract:** Mattick et.al. (2003) presents the results of the world's largest comparative trial of buprenorphine and methadone maintenance. However, the report is disappointing because there are problems with the analysis and their presentation, and the discussion appears to undermine the finding that retention was significantly better in methadone maintenance.

**ISSN:** 0965-2140

**Pub. Type:** Commentary ; Letter

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

62. **Carrieri M ; Rey D ; Loundou A ; Lepeu G ; Sobel A ; Obadia Y. (2003) Evaluation of buprenorphine maintenance treatment in a French cohort of HIV-infected injecting drug users. Drug Alcohol Depend 2003 Oct 24;72(1):13-21.**

**Author Address:** ORS PACA-INSERM research Unit 379 'Epidemiology and Social Sciences Applied to Medical Innovation, Institut Paoli Calmettes, 23 Rue S. Torrents, 13006, Marseille, France

**Abstract:** BACKGROUND: Buprenorphine was approved in France for treating opiate dependence in July 1995 and can be prescribed by general practitioners (GPs). Most studies assessing buprenorphine maintenance treatment (BMT) outcomes have taken place in GP settings. An evaluation of BMT outcomes in patients already followed for their HIV-infection could supply additional information about the changes in addictive practices in a non-GP setting. METHODS: We assessed BMT discontinuations and the course of self-reported addictive behaviours and characteristics associated with buprenorphine-injection misuse in 114 HIV-infected patients on BMT who were followed in a hospital-based outpatient department. RESULTS: The continuous series of follow-up visits at which these 114 patients reported regular buprenorphine prescriptions accounted for 237.5 person-years of observation, i.e. 475 follow-up visits. Of the 114 patients on BMT, 43% continued BMT throughout the follow-up, 40% stopped it, and results for 17% were not available either because they did not answer the self-administered questionnaire (5%) or

because they were lost to follow-up (12%). Addictive behaviours declined but buprenorphine injection misuse remained stable. Depression measured by the CESD score (RR=1.04 95%CI [1.01-1.06]), cocaine use (RR=2.48 95%CI [1.31-4.68]) and alcohol consumption exceeding 4 alcohol units (AU) per day (RR=2.29, 95%CI [1.17-4.46]) were independently associated with buprenorphine injection misuse among stabilised BMT patients.

**CONCLUSIONS:** Despite the reduction in drug injection after starting BMT, buprenorphine injection misuse mainly involves patients with characteristics of severe addiction. Better monitoring of the illicit drug use patterns of patients on BMT may suggest new medical strategies for GPs to improve BMT outcomes.

**ISSN:** 0376-8716.

**Pub Type:** journal article.

**Descriptors:** Buprenorphine; Injecting drug users; HIV; Drug maintenance treatment.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Treatment outcomes/effectiveness

63. **Carrieri M ; Vlahov D ; Dellamonica P ; Gallais H ; Lepeu G ; Spire B ; Obadia Y. (2000) Use of buprenorphine in HIV-infected injection drug users: negligible impact on virologic response to HAART. The Manif-2000 Study Group. Drug Alcohol Depend 2000 Jul 1;60(1):51-4.**

**Author Address:** INSERM research Unit 379 'Epidemiology and Social Sciences Applied to Medical Innovation', Institut Paoli Calmettes, 23 rue Stanislas Torrents, Marseille, France.

**Abstract:** Some HIV-infected injecting drug users (IDUs) on drug abuse maintenance treatment have access to highly active antiretroviral therapy (HAART); this raises questions about the effects of individual treatments on the efficacy of HAART. The French Cohort Study of HIV-infected IDUs - MANIF-2000 - allowed one to assess whether buprenorphine differentially impacts efficacy of HAART. Of the 103 HAART-treated patients, (excluding active IDUs and patients on methadone), 20 were on buprenorphine substitution treatment and 83 were ex-IDUs. A linear regression model used the differences in viral load titre before and after treatment initiation, as a dependent variable, and showed that buprenorphine treatment was not significantly associated with viral load trend. This was also the case when adjusting for other potential confounders, and suggests that there is no major short-term influence of buprenorphine on HIV viral load in HAART-treated patients.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article ; Multicenter Study.

**Descriptors:** Adult ; Buprenorphine/\*therapeutic use ; Cohort Studies ; Female; France ; HIV Infections/\*drug therapy/etiology ; Human ; Linear Models ; Male ; Narcotics/\*therapeutic use ; Statistics, Nonparametric ; Substance Abuse, Intravenous/complications/\*drug therapy ; Support, Non-U.S. Gov't ; Support, U.S. Gov't, P.H.S. ; \*Viral Load.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence

64. **Cassadonte P. (2002) Dosing strategies: finding the right dose. Presentation at a meeting of the California Society of Addiction Medicine, Newport Beach, CA 10/9/02.**

**Abstract:** PowerPoint slide presentation about treatment for opiate addiction using buprenorphine. A clinical case is presented, and information on pre-induction to treatment, recommended inclusion criteria, possible exclusion factors, and concise dosing information and strategies are provided. (35 slides)

**URL:**<http://www.csam->

[asam.org/Bup%20Clinical%20Info/powerpoint%20presentations/Dosing.ppt](http://www.csam-asam.org/Bup%20Clinical%20Info/powerpoint%20presentations/Dosing.ppt)

**Pub. Type:** PowerPoint slides.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness ; Treatment protocols/physician guidelines

65. **Cassoux N ; Bodaghi B ; Lehoang P ; Edel Y. (2002) Presumed ocular candidiasis in drug misusers after intravenous use of oral high dose buprenorphine (Subutex). Br J Ophthalmol 2002 Aug;86(8):940-1.**

**Abstract:** Heroin drug misusers are a high risk group for disseminated candidiasis. Recently, an oral substitute for heroin with oral methadone or high dose sublingual buprenorphine tablets (Subutex) (HDSB) has proved to be effective in management of opioid addiction. We report the first four cases of presumed candida endophthalmitis following intravenous injection of HDSB.

**ISSN:** 0007-1161.

**Pub Type:** Letter; case report.

**Descriptors:** Adult ; Buprenorphine/administration & dosage/\*adverse effects ; Candidiasis/\*etiology ; Case Report ; Drug Contamination ; Endophthalmitis/\*microbiology ; Food Contamination ; \*Heroin Dependence ; Human ; Injections, Intravenous ; Male ; Narcotics/administration & dosage/\*adverse effects.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; Pharmacology

66. **Cavacuiti C ; Selby P. (2003) Managing opioid dependence. Comparing buprenorphine with methadone. Can Fam Physician 2003 Jul;49:876-7.**

**Author Address:** Department of Family and Community Medicine, University of Toronto.

**Abstract:** Community-based family physicians are uniquely suited to care for opioid-dependent patients. Buprenorphine, like methadone, is a substitution treatment for opioid dependence. Buprenorphine is available in Canada only through a special access program, which is not currently enrolling new patients. Now that the United States Food and Drug Administration has approved primary care physicians' prescribing of buprenorphine, we expect it will soon be available in Canada.

Current findings suggest that buprenorphine and methadone are relatively equal treatments for opioid dependence. At present, there is very little solid

evidence to guide doctor-patient decisions on treatment. Buprenorphine might be more beneficial for patients who find daily visits to a pharmacy very difficult. Buprenorphine might also be a better choice for patients likely to be successful with outpatient opioid detoxification.

**ISSN:** 0008-350X.

**URL:** <http://www.cfpc.ca/cfp/2003/Jul/vol49-jul-critical-1.asp>

**Pub. Type:** Journal article.

**Descriptors:** Buprenorphine/\*pharmacology/therapeutic use; Clinical Trials; Comorbidity; Comparative Study; Human Mental Disorders; Meta-Analysis ; Methadone/\*pharmacology/therapeutic use ; Narcotics/\*pharmacology/therapeutic use ; Opioid-Related Disorders/\*drug therapy ; Physicians, Family ; Research Design ; Treatment Outcome.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence

67. **Caviness S. (2002) Overview of the Drug Addiction Treatment Act (DATA 2000). SAMHSA Multimedia web page; Slide presentation on April 10, 2002.**

**Author Address:** Capt. Susanne Caviness (301) 443-7614 (email: [scavines@samhsa.gov](mailto:scavines@samhsa.gov)), CSAT Office of Pharmacologic & Alternative Therapies, SAMHSA / CSAT /OPAT [Rockwall II, Rm 7-222], 5600 Fishers Lane, Rockville, MD 20857

**Abstract:** This 27-slide presentation is a helpful, concise overview of information about the Drug Addiction Treatment Act: federal regulations; requirements for qualifying physicians; federal agencies and professional organizations involved in training and certification.

**URL:**[http://www.samhsa.gov/centers/csat/content/dpt/ppt\\_slices/data\\_bup/frame.htm](http://www.samhsa.gov/centers/csat/content/dpt/ppt_slices/data_bup/frame.htm)

**Pub. Type:** Powerpoint slides.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

68. **Center for Drug Evaluation and Research, U.S. Food and Drug Administration. (2002) Subutex (buprenorphine hydrochloride) and Suboxone tablets (buprenorphine hydrochloride and naloxone hydrochloride). U.S. Food and Drug Administration web site, updated Oct. 2002.**

**Abstract:** This is the main web site on Buprenorphine at the Center for Drug Evaluation and Research, under the U.S. Food and Drug Administration. The site includes basic information (leaflet for patients, documentation that comes with the medication when it is purchased, etc.); physician information (FDA Drug Label, training, applying for the waiver, basics about prescribing and preventing addiction, theft, etc.); pharmacist information (difference between two formulations, what the tablets look like, dependence/addiction potential, side effects, etc.); and a Q&A about the two formulations.

**Notes:** Site last updated in 2002.

**URL:** [http://www.fda.gov/cder/drug/infopage/subutex\\_suboxone/default.htm](http://www.fda.gov/cder/drug/infopage/subutex_suboxone/default.htm)

**Pub. Type:** Web site; government information.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; Legal/regulatory issues ; Pharmacology ; Pharmacotherapy for opiate dependence

69. **Chadderton A. (2000) Clinical issues in using buprenorphine in the treatment of opiate dependence. Drug Alcohol Rev 2000 Sep; 19(3):329-335.**

**Abstract:** Looks at the current role of buprenorphine in the treatment of opiate dependence. Buprenorphine is a partial agonist and a partial antagonist with a ceiling of opiate activity probably approximately equal to 30 mg methadone. Induction of buprenorphine may take slightly longer than for methadone and there is a higher dropout rate compared to methadone in the first two weeks. This is probably due to the antagonist action of buprenorphine causing more withdrawal symptoms in comparison to methadone. Also, the ceiling effect for buprenorphine means that some clients do not experience sufficient opiate activity to satisfy them. Buprenorphine has a long half-life and dissociates slowly from opiate receptors. Transferring from buprenorphine to methadone is straightforward and well tolerated by clients. Transferring from methadone to buprenorphine, however, is more difficult because of the partial antagonist action of buprenorphine. Clients experience withdrawal symptoms that can take up to two weeks to settle. Withdrawal from buprenorphine appears to be relatively easier than from methadone. It is concluded that buprenorphine will likely be useful in assisting detoxification methods from both methadone and heroin.

**ISSN:** 0959-5236 (Print), 1465-3362 (Electronic).

**Pub Type:** Journal Article ; Overview.

**Descriptors:** use of buprenorphine in the treatment of opiate dependence ; \*Drug Dependency ; \*Drug Rehabilitation ; \*Narcotic Agonists ; \*Opiates ; Human.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacology ; Pharmacotherapy for opiate dependence

70. **Champion R ; Gray J. (2003) May 1999 NSW Drug Summit. [Availability of buprenorphine treatment]. New South Wales Public Health Bull 2003 Mar;14(3):59-61.**

**Author Address:** Drug Programs Bureau, New South Wales Department of Health.

**Abstract:** Since 1999, there has been a reduction in heroin-related overdose events (defined as deaths and non-fatal incidents) from 400 in 1999 to 249 in 2000. There is an inverse relationship between the availability of methadone and buprenorphine treatment and the number of suspected opiate overdose deaths from early 1999 to March 2002. Access to pharmacotherapy treatment (methadone and buprenorphine) has improved significantly and there are now few parts of the state where there is a significant delay for patients wishing to

enter treatment. The successful introduction of buprenorphine as an alternative pharmacotherapy for the treatment of heroin addiction has attracted many new patients to treatment and provides more flexibility in the delivery of care.

**ISSN:** 1034-7674.

**URL:** <http://www.health.nsw.gov.au/public-health/phb/HTML2003/march03html/article9p59.html>

**Pub. Type:** Congresses; web document.

**Descriptors:** Buprenorphine/supply & distribution/therapeutic use ; Delivery of Health Care, Integrated ; Drug and Narcotic Control ; Health Services Accessibility ; Health Services Needs and Demand ; Human ; Methadone/supply & distribution/therapeutic use ; New South Wales ; Outcome Assessment (Health Care) ; Quality of Health Care ; Substance Abuse Treatment Centers/\*organization & administration ; Substance-Related Disorders/\*drug therapy.

**ATTC Buprenorphine Topics:** Dosing/administration ; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence

71. **Chawarski M ; Schottenfeld R ; O'Connor P ; Pakes J. (1999) Plasma concentrations of buprenorphine 24 to 72 hours after dosing. Drug Alcohol Depend 1999 Jun 1;55(1-2):157-63.**

**Author Address:** Department of Psychiatry, CMHC/SAC, Yale University School of Medicine, New Haven, CT 06519, USA.

**Abstract:** BACKGROUND: This study evaluated plasma buprenorphine concentrations 24-72 h following sublingual administration of a dose of buprenorphine solution, ranging from 16 mg/70 kg to 44 mg/70 kg, administered on a daily or thrice-weekly schedule. Additionally, this study evaluated the effects of different thrice-weekly buprenorphine dose schedules on opiate use and withdrawal symptoms. METHODS: Opiate dependent subjects (n = 10) were maintained in an outpatient clinic for two 3-week periods at each of three thrice-weekly buprenorphine dose schedules (providing a weekly total buprenorphine dose of 64, 84 and 112 mg) and for 1 week of a daily buprenorphine dose of 16 mg/70 kg. Plasma samples were obtained 24, 48 and 72 h following administration of buprenorphine. Urine samples were also collected and opiate withdrawal symptoms, agonist effects and the use of heroin, cocaine, alcohol and other drugs, were assessed. RESULTS: Plasma levels showed a wide range of intra- and inter-subject variability. Nonetheless, higher doses of buprenorphine resulted in higher plasma concentrations at each time point and plasma concentration decreased with time. There were no significant differences in heroin use across dosing. Rates of withdrawal symptoms were low and did not differ across dosing schedules.

CONCLUSIONS: In the two highest dose schedules, plasma levels 72 h following the administration of the highest dose and at 48 h after the lower dose, were comparable to plasma concentrations at 24 h following daily administration of 16 mg/70 kg of buprenorphine.

**ISSN:** 0376-8716.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Administration, Sublingual ; Buprenorphine/\*blood/therapeutic

use ; Cocaine/blood ; Comparative Study ; Dose-Response Relationship, Drug ; Double-Blind Method ; Ethanol/blood ; Female ; Heroin/blood ; Human ; Male ; Narcotics/\*blood/therapeutic use ; Opioid-Related Disorders/blood/rehabilitation/urine ; Substance Withdrawal Syndrome/blood/diagnosis/urine ; Support, U.S. Gov't, P.H.S. ; Time Factors.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

72. **Chiang C ; Hawks R. (2003) Pharmacokinetics of the combination tablet of buprenorphine and naloxone. Drug Alcohol Depend 2003 May 21;70(2 Suppl):S39-47.**

**Author Address:** Division of Treatment Research and Development, National Institute on Drug Abuse, 6001 Executive Blvd, Room 4123 20892, Bethesda, MD, USA

**Abstract:** The sublingual combination tablet formulation of buprenorphine and naloxone at a fixed dose ratio of 4:1 has been shown to be as effective as the tablet formulation containing only buprenorphine in treating opiate addiction. The addition of naloxone does not affect the efficacy of buprenorphine for two reasons: (1) naloxone is poorly absorbed sublingually relative to buprenorphine and (2) the half-life for buprenorphine is much longer than for naloxone (32 vs. 1 h for naloxone). The sublingual absorption of buprenorphine is rapid and the peak plasma concentration occurs 1 h after dosing. The plasma levels for naloxone are much lower and decline much more rapidly than those for buprenorphine. Increasing dose results in increasing plasma levels of buprenorphine, although this increase is not directly dose-proportional. There is a large inter-subject variability in plasma buprenorphine levels. Due to the large individual variability in opiate dependence level and the large variability in the pharmacokinetics (PK) of buprenorphine, the effective dose or effective plasma concentration is also quite variable. Doses must be titrated to a clinically effective level for individual patients.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Dosing/administration ; Pharmacology ; Pharmacotherapy for opiate dependence

73. **Cirimele V ; Kintz P ; Lohner S ; Ludes B. (2000) Buprenorphine to norbuprenorphine ratio in human hair. J Anal Toxicol 2000 Sep;24(6):448-9.**

**Author Address:** Institut de Medecine Legale, Strasbourg, France.

**Abstract:** Recently, publications concerning buprenorphine and norbuprenorphine dosage in human hair appeared in the international literature. The authors reported that the parent-to-metabolite ratio was generally lower than 1 in the hair specimens tested. For Vincent and colleagues, this ratio ranged from 0.34 to 0.66 in four hair samples and was 2.03 in only one case. For Wilkins et al, buprenorphine concentrations ranged from 4.5 to 156.8 pg/mg

and from 4.8 to 1438.5 pg/mg for norbuprenorphine in the hair of four subjects.

Some years previously, Kintz et al. and Tracqui co-workers published data concerning buprenorphine and norbuprenorphine dosage in human hair revealing higher concentrations for the parent drug than for the metabolite. Kintz et al. determined buprenorphine concentrations in the range 0.020 to 0.590 ng/mg in the hair of 14 young drug addicts admitted to a withdrawal program and norbuprenorphine concentrations ranged from not detected to 0.150 ng/mg in the same subjects. For Tracqui and co-workers, concentrations measured in the hair of six addicts undergoing substitutive therapy ranged from 0.004 to 0.140 ng/mg and from not detected to 0.067 ng/mg for buprenorphine and norbuprenorphine, respectively. It is generally admitted that the parent drug is present in hair in much higher concentrations than its corresponding metabolite(s).

The hypothesis of a better incorporation of the metabolite in hair in contrast to the parent buprenorphine has been proposed. The aim of this paper was to investigate complementary experimentations in order to explain these contradictory observations.

**ISSN:** 0146-4760.

**Pub Type:** Journal Article.

**Descriptors:** Buprenorphine/\*analogs & derivatives/\*analysis/metabolism ; Hair/\*chemistry ; Human ; Narcotics/\*analysis/metabolism ; Substance Abuse Detection/\*methods.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Pharmacology

74. **Cirimele V ; Kintz P ; Lohner S ; Ludes B. (2003) Enzyme immunoassay validation for the detection of buprenorphine in urine. J Anal Toxicol 2003 Mar;27(2):103-5.**

**Author Address:** Institut de Medecine Legale, Laboratoire de Toxicologie, 11, rue Humann, 67085 Strasbourg, France. [vincent.cirimele@medecine.u-strasbg.fr](mailto:vincent.cirimele@medecine.u-strasbg.fr)

**Abstract:** A solid-phase enzyme immunoassay involving microtiter plates was proposed by Microgenics to screen buprenorphine in urine. The intra-assay precision at 10 ng/mL was 7.7% (coefficient of variation). The immunoassay was determined to have no cross-reactivity with codeine, dihydrocodeine, morphine, ethylmorphine, 6-monoacetylmorphine, methadone, pholcodine, propoxyphene, dextromoramide, and dextromethorphan at 1 and 10 mg/L. A low cross-reactivity (3% at 1 ng/mL) was observed at low concentrations of norbuprenorphine. After comparing this new immunological test (Singlestep ELISA) for 76 urine specimens with our validated high-performance liquid chromatography-electrospray mass spectrometry (HPLC-ES-MS) procedure, an optimum cutoff concentration of 2 ng/mL was determined for the kit. At this cutoff, the screening assay was able to determine more than 90% of true results with 43.4% true positives and 48.7% true negatives. Four positive urines (5.3%) were not confirmed by HPLC-ES-MS. In only one case, the negative urine test was confirmed as positive by HPLC-ES-MS (buprenorphine: 62.5

ng/mL). Buprenorphine concentrations determined by HPLC-ES-MS ranged from 1.2 to 1052 ng/mL. Of the four potential adulterants (hypochloride 50 mL/L, sodium nitrite 50 g/L, liquid soap 50 mL/L, and sodium chloride 50 g/L) that might be added to a positive urine specimen, none were able to cause a false-negative response by the immunoassay. The results of this study support the concept that the Singlestep ELISA for buprenorphine determination in urine should be considered as a new, validated screening procedure.

**ISSN:** 0146-4760.

**Pub Type:** Journal Article.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Pharmacology

75. **Clark HW. (2001) A new era in opioid dependency treatment. Recent law allows qualified physicians to provide care in office setting. Postgrad Med 2001 Jun;109(6):15-6, 25.**

**Abstract:** Two drugs--buprenorphine hydrochloride (Subutex) and buprenorphine combined with naloxone (Suboxone)--are under consideration by the FDA, and approval is anticipated within several months. Buprenorphine is currently used in the United States as an analgesic, but it has long been used in Europe as a narcotic. A partial agonist that exerts significant effects on opioid receptors, buprenorphine at low doses is many times more potent than morphine. However, unlike morphine, it does not produce increasing effects with increasing doses. The agonist effects of buprenorphine are perceived by opioid-dependent patients as a mild subjective effect, which aids in patient compliance.

Primary care physicians, as well as addiction medicine specialists, are uniquely positioned to apply the new buprenorphine treatment options--and other new options that emerge in the years ahead--to intervene with opioid-addicted patients before they acquire HIV, hepatitis B or C, or sexually transmitted diseases. The epidemic of infectious diseases among opioid addicts underscores the critical need for primary care physicians to collaborate with the public health system to address treatment needs.

**ISSN:** 0032-5481.

**URL:** [http://www.postgradmed.com/issues/2001/06\\_01/editorial\\_jun.htm](http://www.postgradmed.com/issues/2001/06_01/editorial_jun.htm)

**Pub. Type:** Editorial, overview; web document.

**Descriptors:** Buprenorphine/\*therapeutic use ; Certification ; Communicable Diseases/etiology ; Family Practice/education/\*legislation & jurisprudence/\*methods ; Human ; Information Services ; \*Legislation, Medical ; Methadone/\*therapeutic use ; \*Office Visits ; Opioid-Related Disorders/complications/\*drug therapy/epidemiology ; Substance Abuse Treatment Centers/legislation & jurisprudence/statistics & numerical data ; United States ; United States Food and Drug Administration.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

76. **Clark HW. (2003) Office-based practice and opioid-use disorders. N Engl J Med 2003 Sep 4;349(10):928-30.**

**Author Address:** Center for Substance Abuse Treatment, Substance Abuse and Mental Health Services Administration, Department of Health and Human Services, Rockville, Md., USA.

**Abstract:** In the case of *Webb v. United States*, the U.S. Supreme Court ruled that the 1914 Harrison Narcotic Drug Act made it illegal for physicians to prescribe narcotics for the purpose of keeping a patient "comfortable by maintaining his customary use." For more than 80 years, it remained illegal in the United States for physicians to prescribe opioid medications for the treatment of opioid dependence. The exception was the dispensing of methadone or levomethadyl acetate through regulated programs. Physicians prescribing opioids such as morphine, fentanyl, codeine, hydrocodone, and oxycodone on a long-term basis needed to worry about whether their patients were truly in pain or whether they had become dependent on these pain medications. For patients found to be dependent on an illicit opioid, such as heroin, physicians were forced to treat withdrawal symptoms with nonnarcotic agents, which provided only symptomatic relief, or to refer patients to a regulated program.

The Harrison Narcotic Drug Act and decisions such as *Webb v. United States* essentially gave the following message to physicians: "Treat an addict; go to jail." Physicians consequently were reluctant to address the medical needs of those with opioid-use problems. But there is a wide gap between those who need treatment and the programs that are available to treat them. There are only about 1200 regulated opioid-treatment programs nationwide, and six states have no such programs.

On October 17, 2000, the Drug Addiction Treatment Act of 2000 was signed into law in the United States. This act allows Schedule III, IV, or V narcotic medications that have been approved by the Food and Drug Administration (FDA) for the treatment of narcotic-use disorders to be administered for either medically supervised tapering (detoxification) or long-term maintenance. On October 8, 2002, the FDA approved the use of buprenorphine (see Figure) and of buprenorphine in combination with naloxone — both Schedule III drugs — for either detoxification or maintenance. The purpose of the combination is to reduce the chance of drug diversion, since naloxone precipitates withdrawal symptoms if the combination tablet is misused and injected intravenously. The Drug Addiction Treatment Act and these FDA approvals create an opportunity for practicing physicians to provide critical assistance to patients.

Buprenorphine is already used in France and in Australia in physicians' offices. A benefit of office-based treatment is that it allows patients to obtain help without having to travel great distances or be put on a waiting list.

**ISSN:** 1533-4406.

**Pub Type:** Comment ; Journal Article.

**Descriptors:** \*Ambulatory Care ; Buprenorphine/chemistry/\*therapeutic use ; Drug Therapy, Combination ; Drug and Narcotic Control ; Human ; Naloxone/chemistry/\*therapeutic use ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/\*drug therapy ; United States.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Legal/regulatory issues ; Pharmacotherapy for opiate dependence

77. **Clark N. (2003) High dose buprenorphine may be an effective interim treatment for long term heroin users waiting for drug-assisted rehabilitation. Evidence-Based Mental Health 2003 Feb;6(1):30.**

**Author Address:** Turning Point Alcohol and Drug Centre and Department of Medicine, The University of Melbourne, St Vincent's Hospital, Australia.

**Abstract:** This article is an analytical review of Krook AL, Brors O, Dahlberg J, et al. "A placebo-controlled study of high dose buprenorphine in opiate dependents waiting for medication-assisted rehabilitation in Oslo, Norway." *Addiction* 2002;97(5):533-542.

**ISSN:** 1362-0347.

**Pub Type:** Journal article; analytical review.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

78. **Clark N ; Lintzeris N ; Muhleisen P. (2002) Severe opiate withdrawal in a heroin user precipitated by a massive buprenorphine dose. Med J Aust 2002 Feb 18;176(4):166-7.**

**Author Address:** Turning Point Alcohol & Drug Centre, Fitzroy, VIC. nicoc@turningpoint.org.au

**Abstract:** By diverting his dispensed medication, our patient collected 11 buprenorphine tablets (8 mg each), which he took in one day. The result was not respiratory depression, but instead severe opiate withdrawal lasting four days--this scenario has not previously been reported. This case highlights features of the unique pharmacology of buprenorphine and some key issues for its use in the management of heroin dependence.

**ISSN:** 0025-729X.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Buprenorphine/administration & dosage/\*adverse effects/pharmacology ; Case Report ; Heroin Dependence/\*rehabilitation ; Human ; Male ; Narcotic Antagonists/administration & dosage/\*adverse effects/pharmacology ; Overdose/complications ; Patient Compliance ; Receptors, Opioid/drug effects ; Self Medication/\*adverse effects ; Substance Withdrawal Syndrome/\*etiology ; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; Pharmacology

79. **Clarot F ; Proust B ; Vaz E ; Gouille J. (2003) Re: Tramadol-benzodiazepines and buprenorphine-benzodiazepines: Two potentially fatal cocktails? Journal of Clinical Forensic Medicine 2003; 10(2):125-126.**

**Author Address:** Department of Forensic Medicine, Rouen University Hospital, Rouen 76031; France.

**Abstract:** [abstract not available]

**ISSN:** 1353-1131.

**Pub Type:** Journal; Letter.

**Descriptors:** Adverse Reactions; Pharmacokinetics.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Combined treatment with other therapeutic medications

80. **Clay R. (2003) SAMHSA launches buprenorphine education initiative. SAMHSA News 2003; 11(1):3.**

**Abstract:** SAMHSA launched an initiative this winter to educate physicians and patients about buprenorphine—a new medication to treat addiction to heroin and other opioid drugs, including prescription painkillers. The Food and Drug Administration approved buprenorphine for treatment use in October 2002. SAMHSA launched the "New Paths to Recovery" educational initiative in December with a forum in Washington, DC. Similar events are planned to follow in 14 other cities. At the heart of the initiative is SAMHSA's new Buprenorphine Information Center.

**URL:** [http://www.samhsa.gov/news/click\\_samhsanews.html](http://www.samhsa.gov/news/click_samhsanews.html)

**Pub. Type:** Newsletter (print or online).

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

81. **Colker A. (2002) Behavioral health issue brief: Pharmacotherapy treatment of alcoholism and drug addiction: overview and bibliography: year end report-2002. Issue brief (Health Policy Tracking Service) 2002 Dec 31, p.1-6.**

**Abstract:** abstract not available

**Pub Type:** Journal Article ; Literature review.

**Descriptors:** Alcohol Deterrents/therapeutic use ; Alcoholism/\*drug therapy ; Analgesics, Opioid/administration & dosage/therapeutic use ; Buprenorphine/therapeutic use ; Drug Therapy/trends ; Human ; Methadone/administration & dosage/therapeutic use ; Methadyl Acetate/therapeutic use ; Naltrexone/therapeutic use ; Narcotic Antagonists/therapeutic use ; Substance-Related Disorders/\*drug therapy ; United States.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence

82. **College on Problems of Drug Dependence. (2003) Abstracts from the 65th Annual Meeting of the College on Problems of Drug Dependence, June 14-19, 2003, Miami Beach, Florida.**

**Abstract:** Abstracts on website: (1) Auriacombe M et al, Prevalence of abuse and dependence to benzodiazepines among buprenorphine patients in France: An ongoing study. (2) Chang Y, et al, Effect of benzodiazepines on the in vitro N-dealkylation of buprenorphine in human liver microsomes. (3) Conner SD, Reinforcing effects of intravenous buprenorphine compared to methadone in

non-dependent humans. (4) Correia,, et al, Acute and protracted blockade efficacy of buprenorphine/naloxone. (5) Courty P, et al. High-dose buprenorphine and injection practices: A study of 303 patients. (6) Cunningham-Rathner J, et al, Rapid induction with buprenorphine/naloxone (Suboxone) combination tablet. (7) Dubnernet J, et al, A comparison study of self-reported side effects in buprenorphine and methadone patients. (8) Eisenstein TK, et al, Comparison of morphine, methadone and buprenorphine for immunosuppressive capacity. (9) Fiellin DA, et al, Sustained abstinence and early urine toxicology analyses in office-based buprenorphine treatment. (10) Greenwald MK, et al, Buprenorphine tablet duration of action: Mu-receptor binding, plasma concentrations and opioid symptoms in heroin-dependent volunteers. (11) Harrer JM, et al, Effects of ketoconazole on the pharmacokinetics of buprenorphine (Subutex). (12) Knudsen HK, et al, Counselor attitudes toward buprenorphine: The importance of training and access to information. (13) Marsch, LA, et al, Pharmacological and behavioral interventions for opioid-dependent adolescents: A randomized, controlled trial. (14) Montoya ID, et al, The influence of counseling on buprenorphine treatment outcome. (15) Obert J., Matrix model for methamphetamine treatment: The Thai experience. (16) Pierre JD, et al, Prescription drug abuse among heroin-dependent volunteers receiving buprenorphine. (17) Schottenfeld RS, et al, Stability of abstinence during the first 6 months of opioid agonist maintenance treatment for patients with concurrent cocaine and opioid dependence. (18) Sigmon SC, et al, Evaluation of an injection depot formulation of buprenorphine: Placebo comparison. (19) Strain EC, et al, Abuse potential of parenteral buprenorphine/ naloxone in non-dependent opioid abusers. (20) Sullivan LE, et al, Office-based buprenorphine: Attracting new patients into treatment? **Notes:** Conference abstracts on the web. Search "buprenorphine" in the Keyword field to find all twenty abstracts listed here.

**URL:** [http://biopsych.com:81/cpdd03\\_web/](http://biopsych.com:81/cpdd03_web/)

**Pub. Type:** Conference abstracts; Web documents.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

83. **College on Problems of Drug Dependence. (2002) CPDD 64th Annual Scientific Meeting, June 8-13, 2002, Quebec City, Canada: Abstracts (Buprenorphine papers). Drug Alcohol Depend 2002 May 1; 66(Suppl 1):S1-S220.**

**Abstract:** Abstracts include: (1) Auriacombe MN, et.al., Office-based buprenorphine- and methadone-treated heroin-dependent individuals; a cross-sectional study of medical insurance data; (2) Batel, P et.al., Prospective evolution of alcohol consumption among opiate-dependent patients 6 months after inclusion in a buprenorphine maintenance program; (3) Comer ED, et.al., Reinforcing effects of intravenous buprenorphine compared to the buprenorphine/naloxone combination in non-dependent humans; (4) Fiellin DA, et.al., Office versus narcotic treatment program-based buprenorphine for opioid dependence; (5) Fischer G, et.al., Office-based prescription study with

buprenorphine; (6) Han Y, et.al., Liver enzyme abnormalities during buprenorphine versus methadone maintenance; (7) Harris A, et.al., Cost-effectiveness of buprenorphine maintenance treatment; (8) Lacroix L, et.al., High buprenorphine dosage in pregnancy: first data of a prospective study; (9) Lapeyre-Mestre M, et.al., A 24-week follow-up study of methadone and buprenorphine new users using data of a French prescription database; (10) Law FD, et.al., BD RCT of Suboxone vs methadone/lofexidine for stabilization and withdrawal of low dose outpatient opiate addicts; (11) Mendelson J, et.al., Simultaneous sublingual administration of multiple suboxone tablets does not alter buprenorphine pharmacokinetics to the delivered dose; (12) Moody DE, et.al., The terminal elimination half-life of buprenorphine; (13) Petitjean S, et.al., Buprenorphine versus methadone in opiate detoxification; (14) Ritter A, et.al., A randomized trial of buprenorphine maintenance compared to methadone maintenance: psycho-social outcomes; (15) Sobel BFX, et.al., Open-label trial of an injection depot formulation of buprenorphine in opioid detoxification; (16) Strain EC, et.al., Bioavailability of buprenorphine solution versus tablets during chronic dosing in opioid-dependent subjects; (17) Sullivan MA, et.al., Effects of detoxification modifications to retention in behavioral naltrexone therapy; (18) Zubieta JK, et.al., Buprenorphine sublingual tablet dose-dependently decreases mu-opioid receptor availability in heroin-dependent volunteers.

ISSN: 0376-8716.

URL: [http://biopsych.com:81/cpdd02\\_web/](http://biopsych.com:81/cpdd02_web/)

Pub. Type: Conference abstracts.

ATTC Buprenorphine Topics: Dosing/administration ; Pharmacotherapy for opiate dependence

antagonist currently under development as a maintenance medication for heroin dependence. Because of concerns about illicit diversion of buprenorphine, a combination tablet containing buprenorphine and naloxone has been developed. The present study evaluated the reinforcing effects of intravenously administered placebo, buprenorphine alone (BUP; 2 and 8 mg), and the buprenorphine/naloxone combination (BUP/NX; 2 mg of buprenorphine plus 0.5 mg of naloxone, and 8 mg of buprenorphine plus 2 mg of naloxone) in recently detoxified heroin abusers during a 6-week inpatient study. Participants (n = 6) were detoxified from heroin over approximately 1 week immediately after admission. During the next 5 weeks, the reinforcing effects of placebo, BUP, and BUP/NX were evaluated. Participants first received a dose of drug and \$20 and then were given the opportunity to self-administer either the dose or \$20 during choice sessions. Progressive ratio break point values were significantly higher after active drug, compared with placebo, but they did not significantly differ as a function of dose or drug. In contrast, positive subjective ratings were higher after administration of BUP compared with BUP/NX, and these ratings increased in a dose-dependent manner. BUP and the combination had few effects on performance. Relative to placebo, both BUP and BUP/NX decreased pupil diameter, but there were no significant differences in pupil diameter as a function of drug or dose. These results demonstrate that both BUP and BUP/NX served as reinforcers under these conditions and that they may have similar abuse liability in recently detoxified individuals who abuse heroin.

ISSN: 0022-3565.

Pub Type: Clinical Trial ; Journal Article.

Descriptors: Administration, Oral ; Adult ; Blood Pressure/drug effects ; Buprenorphine/\*pharmacology ; Dose-Response Relationship, Drug ; Drug Combinations ; Female ; Heroin Dependence/\*psychology ; Human ; Male ; Naloxone/\*pharmacology ; Narcotic Antagonists/\*pharmacology ; Narcotics/\*pharmacology ; Psychomotor Performance/drug effects ; Pupil/drug effects ; Questionnaires ; Reinforcement (Psychology) ; Self Administration ; Support, U.S. Gov't, P.H.S.

ATTC Buprenorphine Topics: Addiction potential/misuse of buprenorphine; Combined treatment with other therapeutic medications ; Dosing/administration; Pharmacology

84. **College on Problems of Drug Dependence. (ongoing) CPDD Consultants database; [including 35 with expertise on "Medications for Opioid Dependence."].**

Abstract: Searchable database of experts (consultants) in many areas of addiction research, including 35 researchers in the category of "Meds for Opioid Dependence." A form is provided to request contact with the consultant.

URL: <http://www.biopsych.com:81/consultants/>

Pub. Type: Web site ; directory

ATTC Buprenorphine Topics: Legal/regulatory issues ; Pharmacotherapy for opiate dependence ; Special populations

85. **Comer S ; Collins E. (2002) Self-administration of intravenous buprenorphine and the buprenorphine/naloxone combination by recently detoxified heroin abusers. J Pharmacol Exp Ther 2002 Nov;303(2):695-703.**

Author Address: Division on Substance Abuse, New York State Psychiatric Institute and Department of Psychiatry, College of Physicians and Surgeons of Columbia University, 1051 Riverside Drive, Unit 120, New York, NY 10032, USA. [sd10@columbia.edu](mailto:sd10@columbia.edu)

Abstract: Buprenorphine is a partial mu-opioid agonist and kappa-opioid

86. **Comer S ; Collins E ; Fischman M. (2001) Buprenorphine sublingual tablets: effects on IV heroin self-administration by humans. Psychopharmacology (Berl) 2001 Feb;154(1):28-37.**

Author Address: New York State Psychiatric Institute and Department of Psychiatry, College of Physicians and Surgeons of Columbia University, NY 10032, USA. [sd10@columbia.edu](mailto:sd10@columbia.edu)

Abstract: RATIONALE: Studies have shown that buprenorphine, a partial mu opioid agonist, effectively reduces heroin taking. While previous research with buprenorphine utilized a liquid formulation, a tablet formulation is proposed for clinical use. However, because recent research suggests that the liquid and tablet differ in bio-availability, it is unclear what dose of the buprenorphine tablet effectively antagonizes the reinforcing effects of heroin. OBJECTIVE: The

present study was designed to compare the effects of two sublingual doses of buprenorphine maintenance on heroin self-administration. **METHODS:** Eight heroin-dependent men participated in a 6-week, double-blind, placebo-controlled inpatient study to evaluate the reinforcing effects of intravenous heroin (0, 6.25, 12.5, 25 mg) during maintenance on 8 or 16 mg sublingual buprenorphine. Participants first sampled the available dose of heroin, and then were allowed to respond under a progressive ratio schedule for either heroin or \$20. For each heroin dose, one sample session and three choice sessions occurred. Two sessions per day were conducted. A sample session was followed by the first choice session on one day, and the second and third choice sessions occurred on the following day. These sessions were conducted while participants were maintained on daily doses of 8 or 16 mg buprenorphine (3 weeks each). **RESULTS:** Relative to placebo, 12.5 and 25 mg heroin produced significant increases in break point values under both maintenance dose conditions. The mean break point value for 12.5 mg heroin was significantly lower under 16 mg buprenorphine, compared to 8 mg. **CONCLUSIONS:** These results demonstrate that the reinforcing effects of heroin were not fully antagonized by these doses of the tablet formulation of buprenorphine, and that 16 mg buprenorphine reduced heroin self-administration relative to 8 mg.

**ISSN:** 0033-3158.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Administration, Sublingual ; Adult ; Buprenorphine/\*administration & dosage/pharmacokinetics/\*therapeutic use; Female ; Heroin/pharmacology ; Heroin Dependence/\*drug therapy/psychology ; Human ; Male ; Narcotic Antagonists/\*administration & dosage/pharmacokinetics/\*therapeutic use ; Narcotics/pharmacology ; Psychomotor Performance/drug effects ; Pupil/drug effects ; Self Administration; Support, U.S. Gov't, P.H.S. ; Tablets.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

87. **Comer S ; Collins E ; Fischman M. (2002) Intravenous buprenorphine self-administration by detoxified heroin abusers. J Pharmacol Exp Ther 2002 Apr;301(1):266-76.**

**Author Address:** Division on Substance Abuse, New York State Psychiatric Institute and Department of Psychiatry, College of Physicians and Surgeons of Columbia University, New York, New York 10032, USA. sdc10@columbia.edu

**Abstract:** Several sources indicate that intravenously administered buprenorphine may have significant abuse liability in humans. The present study evaluated the reinforcing effects of intravenously administered buprenorphine (0, 2, and 8 mg) in detoxified heroin-dependent participants during a 7.5-week inpatient study. Participants (n = 6) were detoxified from heroin over a 1.5-week period immediately after admission. Testing subsequently occurred in three 2-week blocks. During the first week of each 2-week block, the reinforcing effects of buprenorphine were evaluated. Participants first received a dose of buprenorphine and \$20 and then were

given either the opportunity to self-administer the dose or \$20 during choice sessions. During the second week of each 2-week block, the direct effects of heroin were measured to evaluate potential long-lasting antagonist effects of buprenorphine. Progressive ratio break-point values were significantly higher after 2 and 8 mg of buprenorphine compared with placebo. Correspondingly, several positive subjective ratings increased after administration of active buprenorphine relative to placebo. Although there were few differences in peak effects produced by 2 versus 8 mg of buprenorphine, the higher buprenorphine dose generally produced longer-lasting effects. Heroin also produced dose-related increases in several subjective effects. Peak ratings produced by heroin were generally higher than peak ratings produced by buprenorphine. There was little evidence of residual antagonism produced by buprenorphine. These results demonstrate that buprenorphine served as a reinforcer under these conditions, and that it may have abuse liability in nonopioid-dependent individuals who abuse heroin.

**ISSN:** 0022-3565.

**Pub Type:** Clinical Trial ; Journal Article.

**Descriptors:** Attention/drug effects ; Blood Pressure/drug effects ; Buprenorphine/administration & dosage/\*pharmacology ; Dose-Response Relationship, Drug ; Heroin/pharmacology ; Heroin Dependence/\*psychology/rehabilitation ; Human ; Male ; Narcotics/administration & dosage/\*pharmacology ; Psychomotor Performance/drug effects ; Pupil/drug effects ; Reinforcement (Psychology) ; Substance Abuse, Intravenous/physiopathology/\*psychology/rehabilitation ; Support, U.S. Gov't, P.H.S. ; Time Factors.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacology ; Psychosocial treatment aspects

88. **Comer S ; Evans S ; Pudiak C ; Foltin R. (2002) Effects of buprenorphine on candy and sweetened fluid self-administration by rhesus monkeys. Psychopharmacology (Berl) 2002 Nov;164(2):200-6.**

**Author Address:** Division on Substance Abuse, New York State Psychiatric Institute and Department of Psychiatry, College of Physicians and Surgeons of Columbia University, 1051 Riverside Drive, Unit 120, New York, NY 10032, USA. sdc10@columbia.edu

**Abstract:** RATIONALE: Previous studies have shown that buprenorphine differentially suppresses the reinforcing effects of different drugs (cocaine, alfentanil), drug versus nondrug reinforcers (food, drug), and the same reinforcer (food) maintained under different schedules of reinforcement. OBJECTIVES: The purpose of the present study was to determine whether buprenorphine (0.03, 0.1, 0.3 mg/kg) differentially affects candy versus sweetened fluid self-administration. The hypotheses were that (1) candy would maintain higher rates of responding and would be chosen on more occasions than sweetened fluid, and (2) buprenorphine would produce smaller disruptions in responding for the more-preferred reinforcer. METHODS: During separate sessions, rhesus monkeys self-administered candy alone, sweetened fluid alone, or had the opportunity to choose between candy and sweetened fluid.

Monkeys responded under a second order, two-chain schedule of reinforcement. RESULTS: Candy was a more-preferred reinforcer than sweetened fluid. Buprenorphine significantly decreased rates of responding for fluid, but increased rates of responding for candy. Although buprenorphine significantly decreased both candy and fluid intake, it produced a more robust, and longer-lasting suppression of sweetened-fluid intake than candy. Choice to self-administer candy or fluid was not affected by buprenorphine. CONCLUSIONS: These results demonstrate that behavior maintained by a less-preferred reinforcer is more easily disrupted by buprenorphine than is behavior maintained by a more-preferred reinforcer.

ISSN: 0033-3158.

**Pub Type:** Journal Article.

**Descriptors:** Analysis of Variance ; Animal ; Buprenorphine/\*pharmacology ; Candy ; Comparative Study ; Dose-Response Relationship, Drug ; Food Preferences/\*drug effects ; Macaca mulatta ; Male ; Narcotics/\*pharmacology ; Reinforcement Schedule ; \*Self Administration ; Support, Non-U.S. Gov't ; Support, U.S. Gov't, P.H.S. ; Sweetening Agents.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Dosing/administration ; Pharmacology

89. **Compton P ; Charuvastra V ; Ling W. (2001) Pain intolerance in opioid-maintained former opiate addicts: effect of long-acting maintenance agent. Drug Alcohol Depend 2001 Jul 1;63(2):139-46.**

**Author Address:** School of Nursing, University of California at Los Angeles (UCLA), Factor Building 4-246, Box 956918, Los Angeles, CA 90095-6918, USA. pcompton@sonnet.ucla.edu

**Abstract:** Patients on methadone maintenance therapy are relatively intolerant of pain, a finding hypothesized to reflect a hyperalgesic state induced by chronic opioid administration. To explore if the intrinsic activity of the opioid maintenance agent might affect expression of hyperalgesia in this population, withdrawal latency for cold-pressor (CP) pain was compared between small groups of methadone-maintained (n = 18), buprenorphine-maintained (n = 18), and matched control (n = 18) subjects. The opioid-maintained groups had equal and significantly shorter withdrawal latencies than controls, however it is possible that high rates of continued illicit opioid use precluded finding differences between methadone and buprenorphine groups. Differential effects of maintenance agent were found for the few subjects without illicit opioid use, such that withdrawal latencies for methadone-maintained (n = 5) were less than for buprenorphine-maintained (n = 7) which were less than controls (n = 18). Diminished pain tolerance in patients receiving opioid maintenance treatment has significant clinical implications. More research is needed to determine if buprenorphine offers advantages over methadone in this regard.

ISSN: 0376-8716.

**Pub Type:** Clinical Trial ; Journal Article.

**Descriptors:** Adult ; Buprenorphine/adverse effects/\*therapeutic use ; Cold/diagnostic use ; Comparative Study ; Female ; Human ; Male ; Methadone/adverse effects/\*therapeutic use ; Middle Age ; Opioid-Related

Disorders/psychology/\*rehabilitation ; Pain Threshold/\*drug effects ; Reaction Time/drug effects ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Pain management ; Pharmacology ; Pharmacotherapy for opiate dependence

90. **Cone E ; Preston K. (2002) Toxicologic aspects of heroin substitution treatment. Ther Drug Monit 2002 Apr;24(2):193-8.**

**Author Address:** ConeChem Research, Baltimore, Maryland, USA.

**Abstract:** Heroin abuse is an international problem with which all countries must continually cope. Many countries have implemented heroin substitution therapy as an effective means of decreasing illicit heroin use, crime, HIV risk, and death, and in improving employment and social adjustment. Although methadone is the most commonly used medication for heroin substitution, other agonists in current use include levomethadyl acetate (LAAM), buprenorphine, and pharmaceutical-grade heroin. This report reviews toxicologic issues that arise in these programs. A broad array of testing methodologies are available that allow selection of on-site testing or laboratory-based methodology. Urine specimens may be monitored for nonprescribed drugs on a qualitative or semiquantitative basis. Methods for differentiating opiate sources by urinalysis have been proposed to distinguish poppy seed consumption from heroin abuse and for distinguishing pharmaceutical-grade heroin from illicit heroin. Therapeutic drug monitoring for methadone in plasma continues to be evaluated for use in establishing adequate dosing and detecting diversion, and new methods have been devised for measurement of the optical isomers of methadone in plasma. Biologic specimens, in addition to plasma and urine, have been evaluated for use in drug monitoring, including sweat, hair, and oral fluid, with promising results. Overall, the many recent developments in testing methodology provide more effective means to assess patients in heroin substitution programs and should contribute to improvements in public health.

ISSN: 0163-4356.

**Pub Type:** Journal Article ; Review ; Review, Tutorial.

**Descriptors:** Buprenorphine/analysis/blood/toxicity/urine; Hair/chemistry; Heroin Dependence/\*rehabilitation; ethadone/analysis/blood/toxicity/urine; Methadyl Acetate/analysis/blood/toxicity/urine; narcotics/\*analysis/ ; narcotics/blood/\*toxicity/urine; Saliva/chemistry ; Sweat/chemistry.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

91. **CoreText.org. (ongoing) Buprenorphine Bibliography. Database produced by Reckitt Benckiser Pharmaceuticals, Inc.**

**Abstract:** Web-searchable database, from pharmaceutical company Reckitt/Benckiser; An-up-to-date, comprehensive, database of references to international papers, journal articles, and reports, most with an abstract, covering substance abuse treatment, analgesia, veterinary medicine, preclinical safety and efficacy. The database can be viewed as sorted by author, publication source, or reference (accession number). Search criteria include

author, year, title, or keyword. Non-English language literature is indexed, with English abstracts for most references. As of October 2003, there were over 6200 references, with frequent updates.

**URL:** <http://www.coretext.org/>

**Pub. Type:** Bibliography; Web Database.

**Note:** Moira Smith is credited as database author. The database sponsor, Reckitt Benckiser Pharmaceuticals, manufactures Buprenorphine.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Basic laboratory research ; Combined treatment with other therapeutic medications ; Dosing/administration ; History, use and effectiveness in other countries ; Legal/regulatory issues ; Pain management ; Pharmacology ; Pharmacotherapy for opiate dependence ; Prevalence of use for opiate dependence ; Psychosocial treatment aspects ; Special populations ; Treatment outcomes/effectiveness ; Treatment protocols/physician guidelines.

92. **Cozza K. (2003) Pharmacokinetic drug interactions of morphine, codeine, and their derivatives: theory and clinical reality, Part II. Psychosomatics 2003 Nov-Dec;44(6):515-20.**

**Author Address:** Center for Geriatric Psychiatry, Tuality Forest Grove Hospital, Forest Grove, OR 97116, USA. [scott.armstrong@tuality.org](mailto:scott.armstrong@tuality.org)

**Abstract:** Pharmacokinetic drug-drug interactions with codeine, dihydrocodeine, hydrocodone, oxycodone, and buprenorphine are reviewed in this column. These compounds have a very similar chemical structure to morphine. Unlike morphine, which is metabolized chiefly through conjugation reactions with uridine diphosphate glucuronosyl transferase (UGT) enzymes, these five drugs are metabolized both through oxidative reactions by the cytochrome P450 (CYP450) enzyme and conjugation by UGT enzymes. There is controversy as to whether codeine, dihydrocodeine, and hydrocodone are actually prodrugs requiring activation by the CYP450 2D6 enzyme or UGT enzymes. Oxycodone and buprenorphine, however, are clearly not prodrugs and are metabolized by the CYP450 2D6 and 3A4 enzymes, respectively. Knowledge of this metabolism assists in the understanding for the potential of drug-drug interactions with these drugs. This understanding is important so that clinicians can choose the proper dosages for analgesia and anticipate potential drug-drug interactions.

**ISSN:** 0033-3182

**Pub.Type:** Journal article

**Descriptors:** Drug interactions.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Combined treatment with other therapeutic medications

93. **Cracowski J ; Mallaret M ; Vanzetto G. (1999) Myocardial infarction associated with buprenorphine (letter). Annals of Internal Medicine 1999;130(6):537.**

**Abstract:** Buprenorphine, a mixed opioid agonist-antagonist, has been available in France since 1996 as a treatment for opioid dependence.

Buprenorphine has been abused by persons intravenously injecting crushed tablets. Administration is usually associated with hypotension (1) and has potential cardioprotective effects (2).

**ISSN:** 0003-4819.

**Pub Type:** Letter.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Pharmacology

94. **Danya Learning Institute ; Central East Addiction Technology Transfer Center. (2003) Danya Learning Institute Online Training Courses on Buprenorphine. 2003.**

**Abstract:** Offers two online courses on buprenorphine: 1) Buprenorphine in the Treatment of Opioid Dependence: Physicians' Course; 2) Buprenorphine Treatment of Opioid Addiction: A Counselors' Guide. These courses are recommended and partially funded by SAMHSA.

**URL:** <http://www.danyalearningcenter.org/>

**Pub. Type:** Web site; training calendar

**ATTC Buprenorphine Topics:** Treatment protocols/physician guidelines

95. **De Ducla M ; Gagnon A ; Mucchielli A ; Robinet S ; Vellay A. (2000) Comparison of high dose buprenorphine treatments of opiate dependent outpatients in four healthcare networks. Annales Medecine Interne (Paris) 2000 Oct;151 Suppl B:B9-15.**

**Author Address:** Reseau Renapsud, 2 place Louis-Barthou, 33000 Bordeaux.

**Abstract:** AIMS: The aim of this study was to compare the various clinical practices in four health care networks and to access how the variations in treatment effected the outcome in opiate-dependent patients. METHODS: A retrospective study was carried out with 71 participating general practitioners. These were chosen from a group of 354 practitioners from four health care networks. Each practitioner could enroll up to 5 patients who were currently undergoing treatment with high-dose buprenorphine (HDB). The patients' treatment had to have been initiated between the 1(st) of February 1996 and the 31(st) of October 1996, and excluded any patients who had lapsed on their treatment during the first month. Patients were selected until a total of 75 cases were enrolled from each network. Data were then collected retrospectively between June and December 1997. Information collected concerned the initial stage of treatment, the stabilizing stage or level of treatment and followed up data on the most recent prescriptions. RESULTS: The final patient maintenance totals were high for all four care networks (82.7 to 96% of patients were still being followed by their doctor at the final evaluation). A positive outcome as indicated by reduction of risk and decreased social vulnerability was also observed in all networks. Additionally, in each network there was a clear correlation between prescription practices and patient behavior. For example, the prescription of HDB at a daily dose of less than 6.2mg was associated with a higher rate of benzodiazepine use; and prescription of several daily doses of HDB was associated with a higher percentage of injecting patients.

CONCLUSION: This retrospective study provides evidence that general practitioner care of drug-dependent patients as outpatients, within a health care network helps to stabilize patient visits, allows treatment of associated comorbidities and favors social rehabilitation. The prescription of HDB as a single daily dose, individually adapted for each patient, optimizes the outcome and reduces misuse.

ISSN: 0003-410X.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Buprenorphine/\*administration & dosage ; Codeine ; Comparative Study ; Data Interpretation, Statistical ; Female ; Follow-Up Studies ; France ; Health Services ; Heroin Dependence/drug therapy ; Human; Male ; Narcotic Antagonists/\*administration & dosage ; Opioid-Related Disorders/\*drug therapy ; Retrospective Studies ; Risk-Taking ; Support, Non-U.S. Gov't ; Time Factors ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Dosing/administration ; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness ; Treatment protocols/physician guidelines

96. **de los Cobos J ; Martin S ; Etcheberrigaray A ; Trujols J ; Batlle F ; Tejero A ; Queraltó J ; Casas M. (2000) A controlled trial of daily versus thrice-weekly buprenorphine administration for the treatment of opioid dependence. Drug Alcohol Depend 2003 Jun; 59(3):223-233.**

**Abstract:** This study was aimed at determining whether thrice-weekly administration of buprenorphine is as effective as daily administration for treating opioid dependence. A total of 60 treatment-seeking opioid addicts were randomly assigned to take buprenorphine tablets sublingually either every day (8 mg) or thrice-weekly (16 mg on Mondays and Wednesdays and 24 mg on Fridays) over the course of a 12-week, double-blind, parallel trial. The buprenorphine dosing schedule had no significant effect on treatment retention. The rates of opioid-positive urine tests were significantly higher among those Ss who were given buprenorphine thrice weekly (58.5%) than among those who took it daily (46.6%). An analysis of the completers did not detect a significant effect of buprenorphine dosing schedule. The results obtained in our clinical trials indicate the advisability of daily doses of buprenorphine, at least at the beginning of a maintenance programme.

ISSN: 0376-8716 (Print).

**Pub Type:** Journal Article.

**Descriptors:** daily vs thrice-weekly administration of buprenorphine, treatment of opioid dependence, 21-45 yr old heroin addicts requesting methadone maintenance treatment ; \*Drug Dosages ; \*Drug Rehabilitation ; \*Methadone Maintenance ; \*Narcotic Agonists ; \*Opiates ; Cocaine ; Drug Dependency ; Heroin ; Human; Male;Female; Adulthood ; Empirical Study.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

97. **Des Jarlais D. (2001) Comment on Valenciano et al's "Unsafe injecting practices among attendees of syringe exchange programmes in France."**

**Addiction 2001 May;96(5):777-8.**

**Abstract:** Over the last 30 years, both injecting drug use and HIV infection among injecting drug users (IDUs) have spread to most countries throughout the world. The paper by Valenciano, Emmanuelli and Lert raises important issues about how to cope with the health and social problems associated with widespread injecting drug use. Valenciano and colleagues conducted a survey of drug use and HIV risk behavior among syringe exchange participants in France. The major findings from the study suggest that the syringe exchange programs are likely to be successful in controlling HIV transmission among their participants. Valenciano et al. also found a high proportion of syringe exchange participants injecting buprenorphine. In France, both methadone and buprenorphine are used as agonist chemotherapies for narcotic addiction. As a treatment for addiction, buprenorphine is supposed to be taken sublingually, and not injected. The French syringe exchange participants who are injecting buprenorphine are thus misusing the medication. Large-scale misuse of buprenorphine cannot be considered acceptable.

ISSN: 0965-2140.

**Pub Type:** Comment ; Letter.

**Descriptors:** \*Buprenorphine/therapeutic use ; Drug Therapy, Combination ; HIV Infections/complications/\*prevention & control ; Naloxone/therapeutic use ; \*Narcotic Antagonists/therapeutic use ; \*Needle-Exchange Programs ; Substance Abuse, Intravenous/complications/\*drug therapy.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine ; Special populations

98. **Deshmukh S ; Nanovskaya T ; Ahmed M. (2003) Aromatase is the major enzyme metabolizing buprenorphine in human placenta. J Pharmacol Exp Ther 2003 Sep;306(3):1099-105.**

**Author Address:** Department of Obstetrics and Gynecology, University of Texas Medical Branch, Galveston, TX 77555-0587, USA.

**Abstract:** Buprenorphine (BUP) is a partial opiate agonist used for treatment of the adult and the pregnant addicted to this class of narcotics. The kinetic parameters for transplacental transfer and the metabolism of BUP during its perfusion in a placental lobule were the subject of an earlier report from our laboratory. The aim of this investigation is to identify and characterize the enzyme catalyzing the metabolism of BUP in term human placenta. Norbuprenorphine (norBUP) is the only metabolite formed as determined by high performance liquid chromatography and mass spectrometry. The activity of the enzyme responsible for BUP metabolism is highest in the microsomal fraction and lowest in the cytosolic, with the mitochondrial in between. Compounds with selective affinity to the enzyme aromatase (CYP 19), namely 4-hydroxyandrostenedione and aminoglutethimide, caused >70% inhibition of norBUP formation. Monoclonal antibodies raised against CYP 19 were the most potent inhibitors of BUP dealkylation. A comparison between the data obtained from the saturation isotherm for BUP dealkylation by placental microsomes and a commercially available system of cDNA-expressed CYP 19 indicated similar

kinetic parameters, with apparent Km values of 12 +/- 4.0 and 14 +/- 8.0 microM, respectively. Therefore, aromatase is the major enzyme catalyzing the biotransformation of BUP to norBUP in term human placentas obtained from healthy pregnancies. The minor involvement of other cytochrome P450 isoforms or enzyme(s) in the metabolism of BUP in placental tissue cannot be ruled out.

**ISSN:** 0022-3565.

**Pub Type:** Journal Article.

**Descriptors:** Alkylation ; Antibodies/pharmacology ; Aromatase/antagonists & inhibitors/\*metabolism ; Buprenorphine/\*metabolism ; Cytochrome P-450 Enzyme System/antagonists & inhibitors/immunology/metabolism ; DNA, Complementary/drug effects/metabolism ; Enzyme Inhibitors/pharmacology ; Female ; Human ; Kinetics ; Mixed Function Oxygenases/metabolism ; Narcotics/metabolism ; Placenta/\*enzymology ; Pregnancy ; Subcellular Fractions ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Pharmacology ; Special populations

99. **Diamant K ; Fischer G ; Schneider C ; Lenzinger E ; Pezawas L ; Schindler S ; Eder H. (1998) Outpatient opiate detoxification treatment with buprenorphine. European Addiction Res 1998;4(4):198-202.**

**Author Address:** Drug Addiction Outpatient Clinic, Department of General Psychiatry, University Hospital of Vienna, Austria.

**Abstract:** In an open study design, 50 opioid-dependent subjects (DSM-IV: 304. 0) were investigated in a gradual detoxification treatment with buprenorphine. The study was performed at the drug addiction outpatient clinic of the Department of General Psychiatry at the University of Vienna. Subjects had to contact the outpatient clinic on a daily basis and buprenorphine was administered according to their clinical status. Withdrawal symptoms were evaluated by applying the WANG scale. Urine samples were screened for drug toxicology to exclude additional consumption. In this investigation buprenorphine was applied sublingually in a free dosage scheme aimed at completing detoxification treatment within 10 days by reducing buprenorphine on a daily basis. A mean daily dosage of 2.3 mg buprenorphine was required by patients on day 1 of the treatment period. The highest mean daily buprenorphine dosage was given on day 2, followed by a daily reduction over the study period. The result of this open study design revealed that a gradual daily reduction of buprenorphine might be a successful alternative outpatient detoxification treatment in opioid-dependent subjects. Compliance was 70%, the reported and evaluated withdrawal symptoms during the study period were moderate.

**Pub. Type:** Journal article.

**Descriptors:** Adult; Ambulatory Care; Buprenorphine/therapeutic use\*; Dose-Response Relationship, Drug; Female; Human; Male; Middle Age; Narcotic Antagonists/therapeutic use\*; Narcotics\*; Substance Abuse Treatment Centers; Substance-Related Disorders/rehabilitation\*; Narcotic Antagonists; Narcotics; Buprenorphine.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Dosing/administration ; Treatment protocols/physician guidelines

100. **DiPaula B ; Schwartz R ; Montoya I ; Barrett D ; Tang C. (2002) Heroin detoxification with buprenorphine on an inpatient psychiatric unit. J Subst Abuse Treat 2002 Oct;23(3):163-9.**

**Author Address:** University of Maryland, School of Pharmacy, 100 Penn St, Rm 505, Baltimore, MD 21201, USA. bdipaula@rx.umaryland.edu

**Abstract:** The purpose of this open-label, uncontrolled study was to evaluate the feasibility of administering off-label buprenorphine in combination with ancillary medications for inpatient short-term detoxification of heroin-dependent patients at a psychiatric facility. A sample of 20 heroin-dependent patients admitted to an urban psychiatric hospital was administered buprenorphine 6, 4, and 2 mg/day during the first, second, and third day of detoxification, respectively, and then observed during the fourth and fifth day. Eighty-five percent of the subjects abused other substances, 75% reported cocaine abuse/dependence, 75% had comorbid mood disorders. All subjects completed the medication phase of the study. No clinically significant adverse events were reported. There was a significant decrease in the Clinical Investigation Narcotic Assessment (CINA) total score between baseline and days 2 through 5. The results suggest that buprenorphine is well tolerated and may be beneficial for medically supervised short-term withdrawal from heroin for hospitalized psychiatric patients.

**ISSN:** 0740-5472.

**Pub Type:** Clinical Trial ; Journal Article.

**Descriptors:** Adult; Analgesics, Opioid/\*therapeutic use; Baltimore/epidemiology; Buprenorphine/\*therapeutic use ; Cocaine-Related Disorders/epidemiology ; Comorbidity ; Emergency Services, Psychiatric ; Female ; Heroin Dependence/\*drug therapy/epidemiology ; Human ; Male ; Middle Age ; Mood Disorders/epidemiology ; Narcotic Antagonists/\*therapeutic use ; Patient Satisfaction ; Pilot Projects ; Substance Withdrawal Syndrome/\*drug therapy.

**ATTC Buprenorphine Topics:** Psychosocial treatment aspects ; Pharmacotherapy for opiate dependence

101. **Division of Pharmacologic Therapies, Center for Substance Abuse Treatment. DPT Web site (ongoing)**

**Abstract:** CSAT's Division of Pharmacologic Therapies (DPT) manages the day-to-day regulatory oversight activities necessary to implement new SAMHSA regulations (42 CFR Part 8) on the use of Opioid agonist medications (methadone and LAAM) approved by the Food and Drug Administration (FDA) for addiction treatment. These activities include supporting the certification and accreditation of over 1,000 Opioid treatment programs that collectively treat over 200,000 patients annually. DPT also supports the training of medical and substance abuse professionals on a variety of treatment issues, including the use of new medications, such as Buprenorphine, that are anticipated to be

approved by FDA for use by physicians. The content of this web site is similar, or duplicates, other SAMHSA resources, but includes some unique resources.

**URL:** <http://dpt.samhsa.gov/>

**Pub. Type:** web site; resources in multiple formats.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

102. **Doran C ; Mattick R ; White J ; Shanahan M ; Bell J ; Ali R. (2001) Buprenorphine versus methadone maintenance: a cost analysis of preliminary findings. Research and Clinical Forums 2001;23(1):43-48.**

**Abstract:** This paper presents the preliminary results from a randomised controlled trial whose aim is to compare the safety, efficacy and cost-effectiveness of buprenorphine and methadone in the treatment of opioid dependence. Four hundred and five patients across three sites were randomised to receive buprenorphine or methadone, and the cost of treatment were recorded and analysed over a 6 month period. The combination of patient-level and facility-level data showed the two medications to be comparable in cost, with buprenorphine being marginally more expensive than methadone. However, these data do not take into account the impact of thrice weekly dosing with buprenorphine, which is likely to further reduce the cost associated with buprenorphine maintenance. Furthermore, full cost-effectiveness analyses and sensitivity analyses are yet to be carried out and will provide a more complete picture.

**ISSN:** 0143-3083.

**Notes:** Journal not readily available.

**Pub Type:** journal article.

**ATTC Buprenorphine Topics:** Treatment outcomes/effectiveness

103. **Doran C ; Shanahan M ; Mattick R ; Ali R ; White J ; Bell J. (2003) Buprenorphine versus methadone maintenance: a cost-effectiveness analysis. Drug Alcohol Depend 2003 Sep 10;71(3):295-302.**

**Author Address:** National Drug and Alcohol Research Centre, University of New South Wales, NSW 2052, Sydney, Australia. [c.doran@unsw.edu.au](mailto:c.doran@unsw.edu.au)

**Abstract:** This article presents the cost-effectiveness results of a randomised controlled trial conducted in two Australian cities. The trial was designed to assess the safety, efficacy and cost-effectiveness of buprenorphine versus methadone in the management of opioid dependence. The trial utilised a flexible dosing regime that was tailored to the clinical need of the patients, with high maximum doses, using the marketed formulation, under double-blind conditions. A total of 405 subjects were randomised to a treatment at one of three specialist outpatient drug treatment centres in Adelaide and Sydney, Australia. The perspective of the cost-effectiveness analysis was that of the service provider and included costs relevant to the provision of treatment. The primary outcome measure used in the economic analysis was change in heroin-free days from baseline to the sixth month of treatment. Treatment with methadone was found to be both less expensive and more effective than

treatment with buprenorphine, which suggests methadone dominates buprenorphine. However, statistical testing found that the observed difference between the cost-effectiveness of methadone and buprenorphine treatments was not statistically significant. The results of this study provide useful policy information on the costs and outcomes associated with the use of methadone and buprenorphine and indicate that buprenorphine provides a viable alternative to methadone in the treatment of opioid dependence.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

104. **Downey K ; Helmus T ; Schuster C. (2000) Treatment of heroin-dependent poly-drug abusers with contingency management and buprenorphine maintenance. Exp Clin Psychopharmacol 2000 May;8(2):176-84.**

**Author Address:** Department of Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine, Detroit, Michigan 48207, USA. [kdowney@med.wayne.edu](mailto:kdowney@med.wayne.edu)

**Abstract:** This study targeted poly-drug (cocaine plus heroin) abstinence among buprenorphine-maintained participants with a 12-week voucher-based reinforcement therapy (VBRT) phase versus a yoked control condition. Baseline levels of cocaine and heroin use were significant predictors of treatment outcome, regardless of treatment assignment. Overall, there were no significant group differences on treatment outcome. However, among the subsample that produced one or more poly-drug-free urine results, VBRT participants had significantly increased cocaine-but not heroin and poly-drug-abstinence, although all results were in the predicted direction. Results suggest that for those who achieve poly-drug abstinence, VBRT may enhance treatment outcome. However, improved interventions, perhaps targeting single-drug abstinence, increasing reinforcement magnitude, or both, may be necessary to promote initial poly-drug abstinence in this population.

**ISSN:** 1064-1297.

**Pub Type:** Clinical Trial ; Controlled Clinical Trial ; Journal Article. **Descriptors:** Adolescent ; Adult ; Breath Tests ; Buprenorphine/\*therapeutic use ; Cocaine-Related Disorders/complications/psychology/rehabilitation ; \*Cognitive Therapy; Combined Modality Therapy ; Female ; Heroin Dependence/complications/psychology/\*rehabilitation ; Human ; Male ; Middle Age ; Narcotic Antagonists/\*therapeutic use ; Psychiatric Status Rating Scales ; Substance Abuse Detection ; Substance-Related Disorders/ complications/psychology/\*rehabilitation ; Support, Non-U.S. Gov't ; Support, U.S. Gov't, P.H.S. ; Time Factors ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment outcomes/effectiveness

105. **Drug Enforcement Administration. (2002) Schedule of controlled substances: Proposed rule: Rescheduling of buprenorphine from Schedule V to Schedule III. Federal Register Volume 67, Number 55,**

**March 21, 2002.**

**Abstract:** This proposed rule is issued by the Administrator of the Drug Enforcement Administration (DEA) to increase the regulatory controls placed on buprenorphine by rescheduling buprenorphine from a Schedule V narcotic to a Schedule III narcotic. This proposed action is based on a formal rescheduling recommendation by the Department of Health and Human Services (DHHS) and a DEA review indicating that buprenorphine meets the definition of a Schedule III narcotic. If finalized, this action will impose the regulatory controls and criminal sanctions of a Schedule III narcotic on those person who handle buprenorphine or products containing buprenorphine.

**URL:** [http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=2002\\_register&docid=02-6767-filed](http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=2002_register&docid=02-6767-filed)

**Pub. Type:** Web document.

**ATTC Buprenorphine Topics:** Legal/regulatory issues

**106. Drug Enforcement Administration. (2002) Schedules of controlled substances: rescheduling of buprenorphine from schedule V to schedule III. Final rule. Federal Register 2002 Oct 7;67(194):62354-70.**

**Abstract:** This final rule is issued by the Deputy Administrator of the Drug Enforcement Administration (DEA) to reschedule buprenorphine from a Schedule V narcotic to a Schedule III narcotic under the Controlled Substances Act (CSA). This action is based on a rescheduling recommendation by the Department of Health and Human Services (DHHS) and a DEA review indicating that buprenorphine meets the criteria of a Schedule III narcotic. The DEA published a proposed rule to reschedule buprenorphine on March 21, 2002 (67 FR 13114). The comment period was extended for an additional 30 days until May 22, 2002 (67 FR 20072). The DEA received ten comments but no requests for hearings. This final action will impose the regulatory controls and criminal sanctions of a Schedule III narcotic on those persons who handle buprenorphine or products containing buprenorphine

**ISSN:** 0097-6326.

**Pub Type:** Journal Article.

**Descriptors:** Buprenorphine/\*classification/therapeutic use ; Drug Evaluation ; Drug Therapy, Combination ; Drug and Narcotic Control/\*legislation & jurisprudence ; Human ; Naloxone/therapeutic use; Narcotics/\*classification/therapeutic use ; Substance-Related Disorders/drug therapy ; United States ; United States Food and Drug Administration.

**ATTC Buprenorphine Topics:** Legal/regulatory issues

**107. Eder H ; Fischer G ; Gombas W ; Jagsch R ; Stuhlinger G ; Kasper S. (1998) Comparison of buprenorphine and methadone maintenance in opiate addicts. Eur Addict Res 1998;4(Suppl 1):3-7.**

**Author Address:** Department of General Psychiatry, University Hospital of Psychiatry, Wahringer Gurtel, Vienna, Austria. drogenambulanz@akh-wien.ac.at

**Abstract:** As a maintenance agent for opioid dependency, buprenorphine offers advantages such as a lower level of dependence and minimal withdrawal symptoms, due to its partial agonist properties at the micro-opioid receptor. Previous studies have shown 8 mg sublingual buprenorphine to be equivalent to 60 mg oral methadone in terms of retention rate and opioid-negative urine levels. In a 24-week, ongoing European study, 34 opioid-dependent subjects were assessed; 16 receiving buprenorphine and 18 methadone. A free dosing schedule was used with no upper limit for methadone dosing but with a maximum buprenorphine dose of 8 mg. Screening prior to the study excluded subjects with polysubstance dependence, somatic disease and/or HIV infection. Primary outcome measures were abstinence from other drugs, for which subjects provided weekly urine samples for analysis of opioids, cocaine and benzodiazepines, and retention in treatment. Patients in the buprenorphine group provided a greater proportion of negative urine samples, in particular cocaine-negative samples, compared with the methadone group, although this was not statistically significant. Retention in the buprenorphine group was significantly lower than in the methadone group, suggesting that the 8 mg buprenorphine limit may have biased the results in favour of methadone, and that this dose may have been too low for those subjects with high levels of dependence. However, buprenorphine is clearly effective in the more motivated subjects and further investigation in this subgroup is recommended.

**Pub. Type:** journal article.

**Descriptors:** Clinical Trial ; Controlled Clinical Trial; Adolescent; Adult; Buprenorphine/therapeutic use\*; Comparative Study; Dose-Response Relationship, Drug; Female; Human;Male; Methadone/therapeutic use\*; Narcotics/therapeutic use\*; Opioid-Related Disorders/rehabilitation\*; Narcotics; Buprenorphine; Methadone.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Dosing/administration

**108. Evans H ; Easthope S. (2003) Transdermal buprenorphine. Drugs 2003;63(19):1999-2010.**

**Author Address:** Adis International Limited, Auckland, New Zealand.

**Abstract:** Buprenorphine is a low molecular weight, lipophilic, opioid analgesic. Recently, a transdermal matrix patch formulation of buprenorphine has become available in three dosage strengths designed to release buprenorphine at 35, 52.5 and 70 micro g/h over a 72-hour period. At least satisfactory analgesia with minimal requirement for rescue medication ( $\leq 0.2$  mg/day sublingual buprenorphine) was achieved by 34-50% of patients with chronic pain treated with transdermal buprenorphine 35, 52.5 or 70 micro g/h and 31% of placebo recipients, in one double-blind, placebo-controlled, randomised trial. In one trial involving patients unsuccessfully treated with weak opioids or morphine, 36.6% and 47.5% of buprenorphine 35 micro g/h and 52.5 micro g/h recipients, respectively, experienced at least satisfactory analgesia and received  $\leq 0.2$  mg/day of sublingual buprenorphine compared with 16.2% of placebo recipients (both  $p \leq 0.032$ ). The requirement for rescue medication was reduced from baseline in  $>50\%$  of patients treated with transdermal buprenorphine, in two

trials. Furthermore, despite the availability of rescue medication to all patients, those receiving transdermal buprenorphine tended to experience greater pain relief, reduced pain intensity and longer pain-free sleep. Transdermal buprenorphine was generally well tolerated. Systemic adverse events were typical of opioid treatment or were attributable to the underlying disease.

ISSN: 0012-6667.

Pub Type: Journal Article.

ATTC Buprenorphine Topics: Dosing/administration ; Pain management

109. **Farre M ; Mas A ; Torrens M ; Moreno V ; Cami J. (2002) Retention rate and illicit opioid use during methadone maintenance interventions: a meta-analysis. Drug Alcohol Depend 2002 Feb 1;65(3):283-90.**

**Author Address:** Pharmacology Unit (Institut Municipal d'Investigacio Medica-IMIM), Carrer Doctor Aiguador 80, E-08003, Barcelona, Spain. mfarre@imim.es

**Abstract:** The efficacy of methadone maintenance in opioid addiction was assessed in terms of programme retention rate and reduction of illicit opioid use by means of a meta-analysis of randomised, controlled and double blind clinical trials. The results were compared with interventions using buprenorphine and levo-acetylmethadol (LAAM). Trials were identified from the PubMed database from 1966 to December 1999 using the major medical subject headings 'methadone' and 'randomised controlled trial'. Data for a total of 1944 opioid-dependent patients from 13 studies were analysed. Sixty-four percent of patients received methadone, administered either as fixed or adjusted doses. Thus, 890 patients received  $\geq$  50 mg/day (high dose group) and 392 were given  $<$  50 mg/day (low dose group). Of 662 controls, 131 received placebo, 350 buprenorphine (265 at doses  $\geq$  8 mg/day and 85 at doses  $<$  8 mg/day) and 181 LAAM. High doses of methadone were more effective than low doses in the reduction of illicit opioid use (odds ratio [OR] 1.72, 95% confidence interval [CI] 1.26--2.36). High doses of methadone were significantly more effective than low doses of buprenorphine ( $<$  8 mg/day) for retention rates and illicit opioid use, but similar to high doses of buprenorphine ( $\geq$  8 mg/day) for both parameters. Patients treated with LAAM had more risk of failure of retention than those receiving high doses of methadone (OR 1.92, 95% CI 1.32--2.78). It is proposed that in agonist-maintenance programmes, oral methadone at doses of 50 mg/day or higher is the drug of choice for opioid dependence.

ISSN: 0376-8716.

Pub Type: Journal Article ; Meta-Analysis.

**Descriptors:** Buprenorphine/therapeutic use ; Human methadone/\*therapeutic use ; Methadyl Acetate/therapeutic use ; Narcotics/\*therapeutic use ; Opioid-Related Disorders/\*rehabilitation ; Patient Dropouts/\*statistics & numerical data; Randomized Controlled Trials; Substance Abuse Detection ; Support, Non-U.S. Gov't ; Treatment Outcome.

ATTC Buprenorphine Topics: Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

110. **Farre M ; Torrens M. (2003) Maintenance buprenorphine for opioid users. Lancet 2003 May 31;361(9372):1906-7; author reply 1907-8.**

**Abstract:** The internal and external validity of Johan Kakko and colleagues' study results (Feb 22, p 662) are limited by important flaws in design. Furthermore, the selection of placebo as a control is ethically questionable. The study is not a true two-group, parallel controlled, 1-year retention trial; although patients were randomly assigned to one of the groups, the interventions were not comparable. The control group was in fact a 6-day detoxification trial, which resulted in a high drop-out rate during the first 2 weeks of follow-up. Time to relapse corresponds well with the delayed onset of withdrawal noted after buprenorphine. With respect to the buprenorphine group, the trial should be considered an independent before-after study, since the placebo group did not act as a control. The high number of individuals in the buprenorphine group who completed the study can only be explained by the recruitment of a very select group of patients, the use of high-dose buprenorphine (16 mg), and the intensive psychosocial therapy offered. As indicated in the accompanying Commentary by Fergus Law and David Nutt (Feb 22, p 634) and noted by Kakko and colleagues, the generalisability of the results is limited.

ISSN: 0140-6736.

Pub Type: Comment ; Letter.

**Descriptors:** Buprenorphine/\*therapeutic use ; Ethics, Clinical ; Heroin Dependence/\*drug therapy ; Human ; Narcotic Antagonists/\*therapeutic use; Reproducibility of Results ; Research Design/standards.

ATTC Buprenorphine Topics: Pharmacotherapy for opiate dependence

111. **Federation of State Medical Boards of the United States. (2002) Model Policy Guidelines for Opioid Addiction Treatment in the Medical Office; Report of the Center for Substance Abuse Work Group. Signed by officials of government agencies and professional societies, April 2002.**

**Abstract:** On October 17, 2000, "The Children's Health Act of 2000" (HR 4365) was signed into federal law. Section 3502 of that Act sets forth the "Drug Addiction Treatment Act of 2000" (DATA). This legislation is of particular interest to state medical boards because it provides for significant changes in the oversight of the medical treatment of opioid addiction. For the first time in almost a century, physicians may treat opioid addiction with opioid medications in office-based settings. These opioid medications, Schedules III, IV, and V opioid drugs with Food and Drug Administration (FDA) approved indication for the treatment of opioid dependence, may be provided to patients under certain restrictions. This new treatment modality makes it possible for physicians to treat patients for opioid addiction with these Schedules III-V narcotic controlled substances specifically approved by the FDA for addiction treatment in their offices without the requirement that they be referred to specialized opioid treatment programs (OTP's) as previously required under federal law.

The DATA requires changes in the oversight systems within the Department of Health and Human Services (HHS) and the Drug Enforcement Administration

(DEA). The Secretary of HHS has delegated authority in this area to the Center for Substance Abuse Treatment (CSAT), within the Substance Abuse and Mental Health Services Administration (SAMHSA). Bringing the treatment of opioid addicted patients into the scope of individual physician practice significantly increases the role of the state medical board in overseeing opioid addiction treatment. For this reason, the Federation of State Medical Boards entered into an agreement with CSAT to develop model guidelines for use by state medical boards in regulating the office-based treatment of opioid addiction.

The following model guidelines are designed to encourage state medical boards to adopt consistent standards, promote public health by availing opioid addicted patients of appropriate treatment, and educating the regulatory and physician communities on new treatment modalities offering an alternative in the treatment of opioid addiction. The recommendations contained herein were adopted as policy by the House of Delegates of the Federation of State Medical Boards of the United States, Inc. April 2002

**Notes:** "The recommendations contained herein were adopted as policy by the House of Delegates of the Federation of State Medical Boards of the United States, Inc. April 2002."

**URL:** <http://buprenorphine.samhsa.gov/model.html>

**Pub. Type:** Policy statement; Web document.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

112. **Feeney G ; Fairweather P. (2003) Groin necrosis requiring skin graft following parental abuse of buprenorphine tablets. Drug and Alcohol Review 22(3): 359-361, 2003.**

**Abstract:** In May 2002, Buprenorphine (Subutex) was listed on the Australian Pharmaceutical Benefits Schedule for treatment in opioid dependence. In addition to broadening treatment options, buprenorphine has the advantage of an improved safety profile. The risk of overdose is lessened but other risks remain due to diversion. French experience reports widespread [diversion] of buprenorphine sublingual tablets to intravenous injection. We report a case of attempted parental administration of buprenorphine tablets, which resulted in abscess. Stringent protocols for dispensing are advised.

**ISSN:** 1465-3362.

**Pub Type:** journal article; case report.

**Descriptors:** abscess; buprenorphine tablets; parental abuse.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine

113. **Feingold A ; Oliveto A ; Schottenfeld R ; Kosten T. (2002) Utility of crossover designs in clinical trials: efficacy of desipramine vs. placebo in opioid-dependent cocaine abusers. Am J Addict 2002 Spring;11(2):111-23.**

**Author Address:** Department of Psychiatry, Yale University School of Medicine, VA Connecticut Healthcare System, West Haven 06516, USA.

**Abstract:** The utility of the crossover design in substance abuse research was examined in a 26-week, double-blind clinical trial that evaluated the efficacy of desipramine (0 or 150 mg/day) in 109 male and female cocaine- and opiate-dependent patients maintained on buprenorphine (12 mg/day) or methadone (65 mg/day). After being stabilized on buprenorphine or methadone (weeks 1-2), half of the patients were randomly assigned to receive desipramine for the first half of the trial and placebo for the second, with the order reversed for the second half. Analyses using hierarchical linear models (HLM) indicated that desipramine reduced the use of opiates only when administered at the start (rather than the middle) of the trial, whereas cocaine use was reduced when desipramine was introduced at either time.

**ISSN:** 1055-0496.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Analgesics, Opioid/therapeutic use ; Antidepressive Agents, Tricyclic/\*therapeutic use ; Buprenorphine/therapeutic use ; Clinical Trials/\*methods; Cocaine-related disorders/complications/psychology; Cocaine-related disorders/\*rehabilitation ; Cross-Over Studies ; Desipramine/\*therapeutic use ; Double-Blind Method ; Female ; Human ; Male ; Methadone/therapeutic use ; Middle Age ; Narcotics/therapeutic use ; Opioid-Related Disorders/complications/psychology/\*rehabilitation ; Placebos ; Support, U.S. Gov't, P.H.S. ; Time Factors ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacotherapy for opiate dependence

114. **Fiellin D. (2001) Training physicians in the use of buprenorphine. NIDA Research Monograph 182. "Problems of Drug Dependence, 2001. Proceedings of 63rd Annual Scientific Meeting, CPDD," 2001, pp. 33-34.**

**Abstract:** The limited capacity of the current treatment system has resulted in roughly 600,000 - 800,000 untreated opioid-dependent patients in the United States (ONDCP, 1999). The need to expand access to treatment identified by the Institute of Medicines and Federal agencies, has resulted in broad support for the use of physician's offices, including primary care settings, for the treatment of opioid-dependent patients using pharmacotherapies including buprenorphine (ONDCP, 1999; National Consensus Development Panel, 1988; Rettig and Yarmolinsky 1995; O'Connor and Fiellin 2000). As of July 2001, approximately 1200 US physicians have received training in the care of opioid-dependent patients using buprenorphine by three of the organizations designated in the Drug Addiction Treatment Act of 2000 (American Society of Addiction Medicine [ASAM], American Academy of addiction Psychiatry [AAAP], and the American Osteopathic Academy of Addiction Medicine [AOAAM]).

**Pub. Type:** conference abstract.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

115. **Fiellin D ; O'Connor P. (2002) Office-based treatment of opioid dependent patients. New England Journal of Medicine 347(22):817-823, 2002.**

**Author Address:** Department of Internal Medicine, Yale University School of Medicine, 333 Cedar St., P.O. Box 208025, New Haven, CT 06520-8025, or at david.fiellin@yale.edu.

**Abstract:** This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations. The authors conclude that buprenorphine would be a first-line agent for treatment of the patient described in the case vignette, adding that treatment should be continued indefinitely in most patients. Psychosocial services should also be provided routinely. Characteristics of the patient, the training and experience of the physician, and regulatory issues must be factored into decisions about whether office-based treatment is right for a given patient. For appropriate patients, this approach has the potential to improve the coordination of care and access to treatment.

**Pub. Type:** article.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

116. **Fiellin D ; Pantaloni M ; Pakes J ; O'Connor P ; Chawarski M ; Schottenfeld R. (2002) Treatment of heroin dependence with buprenorphine in primary care. Am J Drug Alcohol Abuse 2002;28(2):231-41.**

**Author Address:** Department of Internal Medicine, Yale University School of Medicine, New Haven, CT 06520-8025, USA. david.fiellin@yale.edu

**Abstract:** Buprenorphine is an effective treatment for heroin dependence. The feasibility and potential efficacy of buprenorphine with brief counseling in primary care is unknown. We enrolled 14 heroin dependent patients in a 13-week clinical trial using thrice weekly buprenorphine along with brief counseling in the primary care center of an urban medical center. Primary outcomes included urine toxicology and treatment retention. Opioid-positive urine toxicology tests reduced over the 13-week period from 95 to 25% ( $p < 0.05$ ). Eleven patients (79%) had greater than or equal to one week of opioid-free urine toxicologies. Nine patients (64%) had greater than or equal to three weeks of opioid-free urine toxicologies. Eleven patients (79%) were retained through the maintenance phase. We conclude that buprenorphine maintenance is feasible in a primary care setting.

**ISSN:** 0095-2990.

**Pub Type:** Journal Article.

**Descriptors:** Administration, Sublingual ; Adult ; \*Ambulatory Care ; Buprenorphine/\*administration & dosage/adverse effects ; Combined Modality Therapy ; Connecticut ; Counseling ; Dose-Response Relationship, Drug ; Drug Administration Schedule ; Feasibility Studies ; Female ; Heroin Dependence/\*rehabilitation ; Human ; Male ; Middle Age ; Primary Health Care ; Social Support ; Support, U.S. Gov't, P.H.S. ; Treatment Outcome ; \*Urban Population.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment outcomes/effectiveness

117. **Fiellin D ; Rosenheck R ; Kosten T. (2001) Office-based treatment for opioid dependence: reaching new patient populations. Am J Psychiatry 2001 Aug;158(8):1200-4.**

**Author Address:** VISN 1 Mental Illness Research, Education, and Clinical Center, New Haven, CT USA. david.fiellin@yale.edu

**Abstract:** Heroin addiction is a costly and personally destructive public health problem that is often portrayed in the nonprofessional media as a problem primarily facing the lower socioeconomic segment of the U.S. population. Epidemiologic studies, however, show that opioid addiction affects 810,000 people each year, representing all segments of American society, as well as their families and communities, with annual costs estimated at \$21 billion. The most effective treatment for this disorder is opioid maintenance with medications such as methadone or levo-alpha-acetyl methadol. In this treatment, legal, long-acting, medically managed medications replace illegal drugs and block both the painful withdrawal syndrome and craving as well as the subjective drug high that motivate continued use. This treatment, however, has been significantly restricted by limited public funding, local opposition to the establishment of new clinics, state licensing restrictions, and stringent federal regulations designed to prevent the medication from being diverted from its medical use and resold as a substance of abuse on the street. These regulations restrict the delivery of these medications to specialized methadone clinics that are often located in undesirable neighborhoods, are inconvenient to reach, and require almost daily attendance. For these reasons, only about 15% of the total heroin-dependent population participates in methadone or levo-alpha-acetyl methadol treatment, although studies clearly demonstrate that this therapy is more effective than drug-free outpatient care in promoting sustained abstinence. Although progress has been made in developing more cost-effective methods for outpatient detoxification, this approach has limited long-term usefulness because of frequent relapses after detoxification, even in well-motivated patients with good social supports.

**ISSN:** 0002-953X.

**Pub Type:** Clinical Conference ; Journal Article.

**Descriptors:** Adult ; Buprenorphine/\*therapeutic use ; Case Report ; Cocaine-Related Disorders/drug therapy/prevention & control/rehabilitation ; Heroin Dependence/drug therapy/prevention & control/\*rehabilitation ; Human ; Male ; Office Visits/\*utilization ; Private Practice ; Psychiatry/\*methods/organization & administration.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

118. **Fiellin D ; Rosenheck R ; Kosten T. (2003) Coordination of medical care and opioid dependence treatment in primary care: a case report. Subst Abuse 2003 Mar;24(1):43-6.**

**Author Address:** Department of Internal Medicine, Yale University School of Medicine, New Haven, Connecticut. david.fiellin@yale.edu

**Abstract:** JV is a 45-year-old woman with a past medical history significant for Hepatitis C, hypothyroidism, adult onset diabetes mellitus, and opioid dependence who presents with a chief complaint of "I want my life back." Her substance use history is significant for intravenous heroin since 18. She currently uses four bags per day of heroin. Her prior treatments include outpatient detoxification, naltrexone maintenance, and methadone maintenance. She is reluctant to try methadone again because she noted harassment and too many temptations to use heroin at the narcotic treatment program. She has also resisted treatment because of the stigma associated with narcotic treatment programs and the impact that this would have on her family and job. On the basis of JV's diagnosis of opioid dependence, her long-term history of heroin use, prior success with opioid agonist maintenance, and her need for coordinated medical and substance use care, she was offered treatment with buprenorphine -- a partial opioid agonist with efficacy in the treatment of opioid dependence -- in a primary care setting. This article discusses the outcome of her treatment with buprenorphine.

**ISSN:** 0889-7077.

**Pub Type:** Journal Article; case report.

**Descriptors:** Buprenorphine/\*therapeutic use ; Case Report ; \*Continuity of Patient Care ; Delivery of Health Care ; Female ; Human ; Middle Age ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/drug therapy/\*therapy ; \*Primary Health Care ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment outcomes/effectiveness

\*Outpatient Treatment ; Clonidine ; Detoxification ; Drug Rehabilitation ; Human. Male. Female. Outpatient. Adulthood (18 yrs & older) ; Empirical Study.  
**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

120. **Fischer G ; Eder H ; Peterzell A ; Topitz A ; Kraigher D. (2000) Experience with Buprenorphine. Paper presented at the 13th Congress of the European College of Neuropsychopharmacology, Munich, Germany, September 9 - 13, 2000. European Neuropsychopharmacology 2000;10(S3):S137-S138.**

**Abstract:** Psychopharmacological treatment interfering with opioid receptors is supporting the treatment in opioid dependence, especially maintenance therapy with substances acting as opioid receptor agonists have proved to be effective. Methadone and LAAM (Leva-alpha-methyl-methadone) have been standard agents in the US and Europe, oral-slow release morphine has been successfully administered in this indication in some European countries. In France, buprenorphine, a partial my-agonist and kappa-antagonist has been registered for the treatment of opioid dependence since 1995 being followed by other European countries in 1999.

**Pub. Type:** journal article, conference abstract.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries

119. **Fingerhood M ; Thompson M ; Jasinski D. (2001) A comparison of clonidine and buprenorphine in the outpatient treatment of opiate withdrawal. Substance Abuse. Vol 22(3) Sep 2001, 193-199.**

**Author Address:** Fingerhood, Michael I. Johns Hopkins Bayview Medical Center, 4940 Eastern Avenue, Baltimore, MD US 21224.

**Abstract:** The opiate withdrawal syndrome, although not life threatening, is a major obstacle in the treatment of opiate dependence. Over a 12 wk period, 124 patients (63% female and 37% male, mean age 32.6 yrs) underwent 5 day treatment for opiate withdrawal. Patients treated in the first 6 wks received clonidine based treatment while patients treated in the latter 6 wks received buprenorphine. Both groups received supportive medications for diarrhea, cramps, aches, and nausea, had clonidine patches placed on day 4, and were offered naltrexone upon completion. Based on age, gender, and race the 2 treatment groups were similar. The completion rate was 75.4% for the buprenorphine group and 47.5 for the clonidine group. In conclusion, buprenorphine was superior to clonidine in enabling opiate dependent patients to successfully complete an outpatient detoxification program.

**ISSN:** 0889-7077.

**URL:** <http://www.wkap.nl>

**Pub. Type:** Journal Article.

**Descriptors:** opiate withdrawal; buprenorphine; clonidine; outpatient treatment; detox ; \*Drug Therapy ; \*Drug Withdrawal ; \*Narcotic Agonists ; \*Opiates ;

121. **Fischer G ; Etzersdorfer P ; Eder H ; Jagsch R ; Langer M ; Weninger M. (1998) Buprenorphine maintenance in pregnant opiate addicts. European Addiction Research 1998;4(Suppl.1):32-36.**

**Author Address:** Department of General Psychiatry, University Hospital of Psychiatry, Vienna, Austria. gabriele.fischer@akh-wien.ac.at

**Abstract:** Opioid maintenance agents such as methadone and slow-release morphine have provided beneficial effects in pregnant opioid-dependent women in both themselves and their child. However, one of the major drawbacks involved with these agents is that they cause an increase in the severity of neonatal abstinence syndrome (NAS) when compared to mothers using heroin. Consequently, a trial was performed to investigate the effects of buprenorphine use during pregnancy. A total of nine pregnant opioid-dependent women were transferred from either a mean daily dose of 39.7 mg methadone or 400 mg slow-release morphine to a mean daily dose of 8.1 mg buprenorphine. The buprenorphine-maintained patients were integrated into an already established outpatient maintenance treatment programme covering all aspects of prenatal and perinatal care. Results demonstrated that buprenorphine administration in opioid-dependent pregnant patients is efficacious and well tolerated. Babies born to buprenorphine-maintained patients had birthweight and Apgar scores within the normal range (2,500-4,500 g and 9-10, respectively) and no evidence of opioid-related NAS was observed. The results from this preliminary study indicate the potential for buprenorphine maintenance therapy in pregnant

addicts, although further research is required to confirm this hypothesis.

**Pub. Type:** journal article.

**Descriptors:** Adult ; Buprenorphine/therapeutic use\*; Dose-Response Relationship, Drug; Female; Human; Infant, Newborn; Narcotics/therapeutic use\*; Neonatal Abstinence Syndrome/diagnosis; Opioid-Related Disorders/rehabilitation\*; PregnancyComplications/rehabilitation\*.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Dosing/administration ; Special populations

122. **Fischer G ; Gombas W ; Eder H ; Jagsch R ; Peternell A ; Stuhlinger G ; Pezawas L ; Aschauer H ; Kasper S. (1999) Buprenorphine versus methadone maintenance for the treatment of opioid dependence. Addiction 1999 Sep;94(9):1337-47.**

**Author Address:** Department of General Psychiatry, University Hospital of Vienna, Austria.

**Abstract:** AIMS: To evaluate the effectiveness of buprenorphine compared with methadone maintenance therapy in opiate addicts over a treatment period of 24 weeks. DESIGN: Subjects were randomized to receive either buprenorphine or methadone in an open, comparative study. SETTING: Subjects were recruited and treated at the drug addiction outpatient clinic at the University of Vienna. PARTICIPANTS: Sixty subjects (19 females and 41 males) who met DSM-IV criteria for opioid dependence and were seeking treatment. INTERVENTION: Subjects received either sublingual buprenorphine (2-mg or 8-mg tablets; maximum daily dose 8 mg) or oral methadone (racemic D +/- L-methadone; maximum daily dose 80 mg). A stable dose was maintained following the 6-day induction phase. MEASUREMENT: Assessment of treatment retention and illicit substance use (opiates, cocaine and benzodiazepines) was made by urinalysis. FINDINGS: The retention rate was significantly better in the methadone maintained group ( $p < 0.05$ ) but subjects completing the study in the buprenorphine group had significantly lower rates of illicit opiate consumption ( $p = 0.04$ ). CONCLUSION: The results support the superiority of methadone with respect to retention rate. However, they also confirm previous reports of buprenorphine use as an alternative in maintenance therapy for opiate addiction, suggesting that a specific subgroup may be benefiting from buprenorphine. This is the first comparative trial to use sublingual buprenorphine tablets: previously published comparison studies refer to 30% solutions of buprenorphine in alcohol.

**ISSN:** 0965-2140.

**Pub Type:** Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adolescent ; Adult ; Ambulatory Care ; Ambulatory Care Facilities; Buprenorphine/\*therapeutic use ; Female ; Human ; Male ; Methadone/\*therapeutic use ; Narcotics/\*therapeutic use ; Opioid-Related Disorders/\*rehabilitation ; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

123. **Fischer G ; Johnson R ; Eder H ; Jagsch R ; Peternell A ; Weninger M ; Langer M ; Aschauer H. (2000) Treatment of opioid-dependent pregnant women with buprenorphine. Addiction 2000 Feb;95(2):239-44.**

**Author Address:** Department of General Psychiatry, University Hospital of Vienna, Austria. gabriele.fischer@akh-wien.ac.at

**Abstract:** AIMS: To assess the maternal and fetal acceptability of buprenorphine and neonatal abstinence syndrome (NAS) in children born to buprenorphine-maintained mothers. DESIGN AND SETTING: Open-label, flexible dosing, inpatient induction with outpatient maintenance, conducted at the University of Vienna within the existing pregnancy and drug addiction program. PARTICIPANTS: Fifteen opioid-dependent pregnant women. INTERVENTION: Sublingual buprenorphine tablets (1-10 mg/day). MEASUREMENTS: Mothers: withdrawal symptoms (Wang Scale), nicotine dependence (Fagerstrom Scale: FTQ) and urinalysis. Neonates: birth outcome and NAS (Finnegan Scale). FINDINGS: All subjects were opioid-, nicotine- and cannabis-dependent. Buprenorphine was well tolerated during induction (Wang Score  $< \text{or} = 4$ ) and illicit opioid use was negligible (91% opioid-negative). All maternal, fetal and neonatal safety laboratory measures were within normal limits or not of clinical significance. Mean birth outcome measures including gestational age at delivery (39.6 +/- 1.5 weeks), Apgar scores (1 min = 8.9; 5 min = 9.9; and 10 min = 10), birth weight (3049 +/- 346 g), length (49.8 +/- 1.9 cm) and head circumference (34.1 +/- 1.8 cm) were within normal limits. The NAS was absent, mild (without treatment) and moderate (with treatment) in eight, four and three neonates, respectively. The mean duration of NAS was 1.1 days. CONCLUSIONS: Buprenorphine appears to be well accepted by mother and fetus, and associated with a low incidence of NAS. Further investigation of buprenorphine as a maintenance agent for opioid-dependent pregnant women is needed.

**ISSN:** 0965-2140.

**Pub Type:** Journal Article.

**Descriptors:** Buprenorphine/\*therapeutic use ; Delivery, Obstetric ; Female ; Human ; Infant, Newborn ; Narcotics/\*therapeutic use ; Opioid-Related Disorders/\*rehabilitation ; Pregnancy Complications/\*rehabilitation ; Support, Non-U.S. Gov't ; Treatment Outcome.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Special populations ; Treatment outcomes/effectiveness

124. **Fischer G ; Peternell A. (1999) The use of buprenorphine in pregnancy. Research & Clinical Forums. Vol 21(3) (pp 17-27), 1999.**

**Author Address:** University Hospital of Vienna, Vienna; Austria

**Abstract:** Various maintenance treatments, including methadone, LAAM (levo-alpha-acetyl-methadol) and buprenorphine, are available for the treatment of opiate dependence across Europe and in the US. Few studies have investigated the use of opioid maintenance treatment in high-risk subsets of the population, such as pregnant women. Studies at the University Hospital for

Psychiatry in Vienna have addressed this deficit, comparing the use of slow-release morphine and buprenorphine with the current standard maintenance therapy, methadone. A multidisciplinary approach to the treatment of addiction was deployed, which incorporated psychosocial counselling and behavioural psychotherapy. Methadone and slow-release morphine proved to be safe and efficacious but were found to cause neonatal abstinence syndrome (NAS) in infants of treated mothers. Buprenorphine, however, was associated with no or mild NAS and could provide a useful alternative to methadone in the maintenance treatment of opiate-dependent pregnant women  
**ISSN:** 0143-3083.

**Pub Type:** journal article.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Special populations

**125. Food and Drug Administration. (2002) FDA Talk Paper: Subutex and suboxone approved to treat opiate dependence. U.S. Food and Drug Administration. FDA Talk Paper, T02-38, October 8, 2002.**

**Abstract:** The Food and Drug Administration (FDA) announced the approval of Subutex (buprenorphine hydrochloride) and Suboxone tablets (buprenorphine hydrochloride and naloxone hydrochloride) for the treatment of opiate dependence. Subutex and Suboxone treat opiate addiction by preventing symptoms of withdrawal from heroin and other opiates. These products represent two new formulations of buprenorphine. The first of these formulations, Subutex, contains only buprenorphine and is intended for use at the beginning of treatment for drug abuse. The other, Suboxone, contains both buprenorphine and the opiate antagonist naloxone, and is intended to be the formulation used in maintenance treatment of opiate addiction. Naloxone has been added to Suboxone to guard against intravenous abuse of buprenorphine by individuals physically dependent on opiates. Both drugs are supplied in 2 mg and 8 mg tablets which are placed under the tongue and must be allowed to dissolve.

**URL:** <http://www.fda.gov/bbs/topics/ANSWERS/2002/ANS01165.html>

**Pub. Type:** Web document.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacology ; Pharmacotherapy for opiate dependence

**126. Food and Drug Administration. (2002) Suboxone and Subutex : Drug label. U.S. Food and Drug Administration; Reckitt Benckiser Pharmaceuticals, Inc.**

**Abstract:** This is the information contained in the FDA drug label for both Suboxone and Subutex. It includes information on the pharmacology of both formulations, as well as information about clinical studies, side effects, contraindications, and drug interactions and adverse effects, and storage and dispensing information. The last page of the label is a "patient information leaflet" with an abbreviated version of the information from the rest of the label.

**URL:** <http://www.fda.gov/cder/foi/label/2002/20732lbl.pdf> ;

<http://www.suboxone.com/Suboxone/pdfs/SuboxonePI.pdf>

**Pub. Type:** Web document ; patient leaflet; PDF.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; Pharmacology ; Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

**127. Food and Drug Administration. (2002) Suboxone and subutex : Physician information.**

**Abstract:** Information for physicians on how to become qualified to prescribe buprenorphine, including information on prescription regulations, record-keeping, safety, and how to find training sessions.

**URL:** <http://www.fda.gov/cder/foi/label/2002/20732mdinfo.pdf>

**Pub. Type:** Web document; PDF.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Treatment protocols/physician guidelines

**128. Food and Drug Administration. (2002) Suboxone and Subutex : Information for pharmacists.**

**Abstract:** Information for pharmacists, including a description of the two formulations, how they are supplied, the risks of dependence or opioid withdrawal, possible side effects, and information pharmacists should relay to patients.

**URL:** <http://www.fda.gov/cder/foi/label/2002/20732pharmacist.pdf>

**Pub. Type:** Web document; PDF.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; Legal/regulatory issues ; Pharmacology

**129. Ford C. (2003) Use of buprenorphine in primary care. [London] RCGP Drug and Alcohol Misuse Training Programme; RCGP Sex, Drugs and HIV Task Group; SMMGP, April 2003.**

**Abstract:** This presentation of 33 slides compares buprenorphine and methadone for use by physicians, and gives practical advice for the use of either medication. It uses a case study of "Annie" to elicit issues and examples about care of a heroin-using patient.

**Notes:** Royal College of General Practitioners (RCGP); Substance Misuse Management in General Practice (SMMGP).

**URL:** <http://www.smmgp2.demon.co.uk/download/articles/art021.zip>

**Pub. Type:** Powerpoint slides, web document (zipped).

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

**130. Ford C ; Morton S ; Lintzeris N ; Bury J ; Gerada C. (2003) Guidance for the Use of Buprenorphine for the Treatment of Opioid Dependence in Primary Care. Royal College of General Practitioners, (RCGP) Drug & Alcohol Misuse Training Programme; RCGP Sex, Drugs and HIV Task Group, February 2003, 16 p.**

**Abstract:** This guidance has been produced to aid medical practitioners in the use of buprenorphine as a substitute medication for opioid dependence for detoxification and maintenance. It should be read in conjunction with 'Drug Misuse and Dependence: Guidelines on Clinical Management' issued by the UK Department of Health in 1999.' Full text online.

**Notes:** Revision due Feb. 2004.

**URL:** <http://www.smmgp.demon.co.uk/html/articles.htm#016>

**Pub. Type:** Web document, PDF, and Word formats; includes patient information sheet.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines ; History, use and effectiveness in other countries

131. **Fraser D. (1998) Addiction medicine: Substitute prescribing - Buprenorphine maintenance prescribing. In: Karch SB (ed.) Drug Abuse Handbook. Boca Raton, FL : CRC Press, 1998, pp. 510-511, (complete text).**

**Abstract:** Generally, the more efficacious the drug is at producing its pharmacological effect, the greater the addiction potential and value as an illicit drug. Drugs with lower efficacy are called partial agonists. Buprenorphine is a partial agonist for opioid receptors. The pharmacological profile of partial agonists is such that they are useful in substitution therapy because they provide some reinforcement of the opiate effect but should also reduce illicit heroin use. In analgesic terms it is approximately 25 to 40 times more potent than morphine. There is mounting evidence that buprenorphine is a safe and effective therapeutic agent for use in the treatment of opiate dependence. Buprenorphine has a high affinity but a low intrinsic activity at the mu opiate receptors. This means that although buprenorphine has agonist activity at the mu receptors, this activity is not as potent as that achieved by a pure opiate agonist such as morphine. The high affinity results in a long duration of action in the order of 24 to 48 hours. A study was conducted which compared daily buprenorphine administration with alternate day administration. Objectively there was no significant difference between the two groups on measures of opiate withdrawal symptoms. The group receiving alternate day treatment reported subtle withdrawal symptoms subjectively whereas the daily treatment group reported no such problems. A 24-hour dosage interval is most commonly recommended. Opiate dependent subjects find buprenorphine an acceptable treatment for their dependence and report a "morphine-like" effect. It is possible to convert people from heroin or methadone to buprenorphine with minimal withdrawal problems. Due to its wide therapeutic index buprenorphine is relatively safe in overdose. It has been shown that there is a ceiling effect at higher doses of buprenorphine. This is due to its intrinsic opiate antagonist activity and means that it is possible for a non-dependent person to tolerate a single dose of buprenorphine up to 70 times the recommended analgesic dose without life threatening consequences. Buprenorphine can be administered by subcutaneous or sublingual routes for opiate dependence. Due to concerns

about the likelihood of injectable opiate preparations finding their way onto the black market, the sublingual route is considered the safest route. Sublingual preparations have been shown to be as effective as subcutaneous preparations and to have a similar profile of effects in opiate dependent subjects.

**ISSN:** 0849326370.

**Notes:** ADAI Library Call no: RM 316 D76 1998 [REF HAND].

**Pub Type:** book entry (encyclopedia).

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Dosing/administration

132. **French M. (2001) Cost-effectiveness of buprenorphine maintenance versus methadone maintenance. Addiction 2001 Oct;96(10):1515-7.**

**Abstract:** Buprenorphine maintenance therapy is a potentially important treatment for opiate addiction due to its recognized clinical efficacy, its potential for office-based dispensing and its capacity to reach more opiate users in need of treatment (Johnson et al., 2000). Despite the high expectations for buprenorphine maintenance therapy, little is known about its economic viability. Barnett, Zaric and Brandeau (2001) recently published one of the first prospective economic evaluations of buprenorphine maintenance therapy. The authors determined whether buprenorphine therapy would be cost-effective under three possible dosage prices: \$5, \$15, and \$30. Under various assumptions, and using quality-adjusted life-years (QALYs) gained as the measure of treatment effectiveness, they found that buprenorphine maintenance would be cost effective at a price of \$5 per dose or less under all scenarios. Buprenorphine maintenance would be cost-effective under some scenarios at \$15 per dose, but only under very extreme scenarios at \$30 per dose.

**ISSN:** 0965-2140.

**Pub Type:** Comment ; Letter.

**Descriptors:** Buprenorphine/\*economics/therapeutic use ; Cost-Benefit Analysis/methods ; Heroin Dependence/rehabilitation ; Human ; Methadone/\*economics/therapeutic use ; Narcotics/\*economics/therapeutic use ; Quality-Adjusted Life Years.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

133. **Fudala P. (2002) Quintuple the daily maintenance dose of buprenorphine given every 5 days was associated with opioid withdrawal symptoms. Evidence-Based Mental Health 2002 Feb;5(1):21.**

**Author Address:** University of Pennsylvania/VA Medical Center, Philadelphia, Pennsylvania, USA.

**Abstract:** A comment on the study by Petry et al which provides information for clinicians regarding the maximal interdose interval of buprenorphine for the treatment of opioid addiction. The study showed the maximum interval to be <5 days when 5 times the daily maintenance dose was given. A number of factors will influence the degree to which less than daily dosing of buprenorphine will

be used in clinical practice. These include the patient's response and acceptance, and the clinicians' willingness and ability to prescribe take home medication doses (which in many cases could obviate the need for or advantages of less than daily dosing).

**ISSN:** 1362-0347.

**Pub Type:** Comment ; Journal Article.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

134. **Fudala P ; Bridge T. (2003) Foreword to: Buprenorphine and buprenorphine/naloxone: a guide for clinicians. Drug Alcohol Depend 2003 May 21;70(2 Suppl):S1-2.**

**Author Address:** Behavioral Health Service, Ward 7 East (116-7E), VA Medical Center, School of Medicine, University and Woodland Avenues, 19104, Philadelphia, PA, USA

**Abstract:** Introduction of a special supplement to the journal Drug and Alcohol Dependence, entitled Buprenorphine and Buprenorphine/Naloxone, A Guide for Clinicians. Buprenorphine is a mu-opioid partial agonist that has been used as an analgesic for approximately the last 25 years. For many readers of this journal, however, their primary interest in buprenorphine derives from its demonstrated utility as a treatment for opioid addiction. As a mu-opioid partial-agonist, buprenorphine fills the treatment gap between the full agonists, methadone and levomethadyl acetate, and the antagonist naltrexone. More recently, a combination product containing both buprenorphine and naloxone for sublingual administration has been developed to reduce the potential for abuse of buprenorphine itself. Both buprenorphine and the buprenorphine/naloxone combination have recently been approved for the treatment of opioid addiction by the U.S. Food and Drug Administration.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article; Overview.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Pharmacology

135. **Fudala P ; Bridge T ; Herbert S ; Williford W ; Chiang C ; Jones K ; Collins J ; Raisch D ; Casadonte P ; Goldsmith R ; Ling W ; Malkernek U ; McNicholas L ; Renner J ; Stine S ; Tusel D. Group Buprenorphine/Naloxone Collaborative Study. (2003) Office-based treatment of opiate addiction with a sublingual-tablet formulation of buprenorphine and naloxone. New England Journal of Medicine 2003 Sep 4;349(10):949-58.**

**Author Address:** Veterans Affairs (VA) Medical Center, University of Pennsylvania School of Medicine, Philadelphia, USA.

**Abstract:** BACKGROUND: Office-based treatment of opiate addiction with a sublingual-tablet formulation of buprenorphine and naloxone has been proposed, but its efficacy and safety have not been well studied. METHODS: We conducted a multicenter, randomized, placebo-controlled trial involving 326

opiate-addicted persons who were assigned to office-based treatment with sublingual tablets consisting of buprenorphine (16 mg) in combination with naloxone (4 mg), buprenorphine alone (16 mg), or placebo given daily for four weeks. The primary outcome measures were the percentage of urine samples negative for opiates and the subjects' self-reported craving for opiates. Safety data were obtained on 461 opiate-addicted persons who participated in an open-label study of buprenorphine and naloxone (at daily doses of up to 24 mg and 6 mg, respectively) and another 11 persons who received this combination only during the trial. RESULTS: The double-blind trial was terminated early because buprenorphine and naloxone in combination and buprenorphine alone were found to have greater efficacy than placebo. The proportion of urine samples that were negative for opiates was greater in the combined-treatment and buprenorphine groups (17.8 percent and 20.7 percent, respectively) than in the placebo group (5.8 percent,  $P < 0.001$  for both comparisons); the active-treatment groups also reported less opiate craving ( $P < 0.001$  for both comparisons with placebo). Rates of adverse events were similar in the active-treatment and placebo groups. During the open-label phase, the percentage of urine samples negative for opiates ranged from 35.2 percent to 67.4 percent. Results from the open-label follow-up study indicated that the combined treatment was safe and well tolerated. CONCLUSIONS: Buprenorphine and naloxone in combination and buprenorphine alone are safe and reduce the use of opiates and the craving for opiates among opiate-addicted persons who receive these medications in an office-based setting.

**ISSN:** 1533-4406.

**Pub Type:** Journal Article ; Multicenter Study ; Randomized Controlled Trial.

**Descriptors:** Administration, Sublingual ; Adult ; \*Ambulatory Care ; Buprenorphine/\*therapeutic use ; Double-Blind Method ; Drug Therapy, Combination ; Female ; Human ; Male ; Middle Age ; Naloxone/\*therapeutic use ; Narcotic Antagonists/\*therapeutic use ; Narcotics/urine ; Office Visits ; Opioid-Related Disorders/\*drug therapy ; Support, U.S. Gov't, Non-P.H.S. ; Support, U.S. Gov't, P.H.S. ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

136. **Fudala P ; Bridge Te. (2003) Buprenorphine and Buprenorphine/Naloxone: A Guide for Clinicians. Drug and Alcohol Dependence 70(2 Suppl): S1-S104, May 2003.**

**Abstract:** This is a supplemental issue to the journal Drug and Alcohol Dependence, vol. 70 (May 2003). It contains nine articles (plus a foreword from the editors) on clinical aspects of using buprenorphine in opioid dependence treatment. Authors of the articles were chosen by the editors for their expertise in the particular area of study on the topic of buprenorphine, and all articles were peer-reviewed. The individual articles are included in this bibliography under the name of the authors.

**ISSN:** 0376-8716.

**Notes:** Publication of journal supplement supported by Reckitt Benckiser

Pharmaceuticals, Inc.; This journal issue can be purchased from Elsevier Science, PO Box 945, New York NY 10159-0945; tel: (212) 633-3770, or 1-888-4ES-INFO.

**URL:** <http://www.elsevier.com/locate/drugalcdep>

**Pub. Type:** theme issue; journal supplement.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Dosing/administration ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment outcomes/effectiveness

137. **Gandhi D ; Jaffe J ; McNary S ; Kavanagh G ; Hayes M ; Currens M. (2003) Short-term outcomes after brief ambulatory opioid detoxification with buprenorphine in young heroin users. *Addiction* 2003 Apr;98(4):453-62.**

**Author Address:** Department of Psychiatry, University of Maryland School of Medicine, Baltimore, MD 21201, USA. [dgandhi@psych.umaryland.edu](mailto:dgandhi@psych.umaryland.edu)

**Abstract:** AIMS: This study examines the outcomes at 1, 3 and 6 months after a very brief outpatient detoxification with buprenorphine in 18-25-year-old heroin users. DESIGN: Prospective follow-up study. SETTING: Outpatient drug treatment clinic, providing brief detoxification in downtown Baltimore, Maryland, USA. PARTICIPANTS: One hundred and twenty-three subjects between 18 and 25 years old; 56% male; 95% Caucasian; seeking detoxification; living in Baltimore City and five surrounding counties. INTERVENTION: Detoxification with buprenorphine over 3 days. Follow-up at 1, 3 and 6 months.

MEASUREMENTS: Drug use history, the Addiction Severity Index at baseline and follow-up, urine drug screens, evaluation of the detoxification experience. FINDINGS: By self-report, 37% of the total sample were not currently using heroin at 1 month, 32% at 3 months and 29% at 6 months, and 6.7%, 10.1% and 11.8% had an opioid negative urine test at 1, 3 and 6 months, respectively. There was a significant reduction from the baseline in mean Addiction Severity Index drug use composite score, as well as the mean number of days of heroin and cocaine use during past 30 days, that was sustained over the three follow-up points. Engagement in aftercare was generally poor. CONCLUSIONS: The findings show a reduced frequency and intensity of drug use, suggesting a possible role for brief outpatient detoxification in reducing the severity of dependence for some younger heroin users who may not yet be ready to engage in long-term abstinence-oriented or opioid substitution treatments. **ISSN:** 0965-2140.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adolescent ; Adult ; Ambulatory Care/\*methods ; Buprenorphine/\*therapeutic use ; Drug Administration Schedule ; Female ; Follow-Up Studies ; Heroin Dependence/\*rehabilitation ; Human ; Male ; Narcotic Antagonists/\*therapeutic use ; Patient Satisfaction ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Special populations ; Treatment outcomes/effectiveness

138. **Garcia-Fernandez M ; Fernandez-Abedul M ; Costa-Garci A. (2001) Determination of buprenorphine in biological samples by high**

**performance liquid chromatography with electrochemical detection. *Chromatographia* 2001 ; 53(11-12):704-708.**

**Abstract:** A simple, selective and rapid reversed phase high-performance liquid chromatography method with electrochemical detection is described for the analysis of buprenorphine in human serum and urine. Biological samples are easily prepared and separated on a C18 column employing acetonitrile, tetrahydrofuran and sodium acetate as mobile phase. The composition and pH of this phase is discussed. Electrochemical detection is carried out on a glassy carbon electrode held at +0.70 V (vs. Ag/AgCl). The limit of detection is  $4 \times 10^{-8}$  M; the linearity extends between  $5 \times 10^{-8}$  and  $3 \times 10^{-6}$  M. High precision and recoveries were obtained. Separation from norbuprenorphine, its metabolite, is achieved in serum and urine. No interferences from the 13 substances checked were found.

**ISSN:** 0009-5893.

**Pub Type:** Journal article.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Pharmacology

139. **Gasquet I ; Lancon C ; Parquet P. (1999) Predictive factors for patient maintenance on buprenorphine high dosage treatment: A naturalistic study in primary care. *Encephale* vol 25(6) Nov-Dec 1999, 645-651. [abstract only]**

**Abstract:** Conducted a naturalistic study in a primary care setting to determine the prognostic factors concerning patient response to high-dose buprenorphine treatment in daily practice. Sociodemographic, medical, and addiction histories were collected for 956 patients of 200 general practitioners in France. A quantitative sociobehavioral and medical indicator was used. Simple and multivariate analyses were performed. The results indicate that patients with good social adjustment and past withdrawal respond well to high-dose buprenorphine. Outcome was improved if patients were treated for more than 1 yr in a clear-cut therapeutic program.

**ISSN:** 0013-7006 (Print).

**Pub Type:** Journal Article in French; English abstract

**Descriptors:** prognostic & predictive factors for response & maintenance on high dosage buprenorphine, primary care patients ; \*Drug Addiction ; \*Drug Dosages ; \*Drug Therapy ; \*Drugs ; \*Primary Health Care ; Medical Patients; Prediction ; Risk Taking ; Human ; Empirical Study.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment outcomes/effectiveness

140. **Gaulier J ; Marquet P ; Lacassie E ; Dupuy J ; Lachatre G. (2000) Fatal intoxication following self-administration of a massive dose of buprenorphine. *J Forensic Sci* 2000 Jan;45(1):226-8.**

**Author Address:** Department of Pharmacology and Toxicology, University Hospital, Limoges, France.

**Abstract:** Several drug packages, including Subutex (high-dose buprenorphine, as sublingual tablets) boxes, were found near the corpse of a 25-year-old male drug addict, who apparently had committed suicide. The autopsy revealed a fatal respiratory depression. The toxicological investigations concluded that death resulted from massive buprenorphine intoxication. The determination of buprenorphine (BU) and norbuprenorphine (NBU) in all biological specimens was performed by liquid chromatography-electrospray mass spectrometry (LC-ES-MS) after hydrolysis (for solid tissues), deproteinization of the matrices, and solid-phase extraction of the compounds. Exceptionally high concentrations of BU and NBU were found in blood (3.3 and 0.4 mg/L, respectively), urine (3.4 and 0.6 mg/L), bile (2035 and 536 mg/L) and brain (6.4 and 3.9 microg/g). The high concentration of BU (899 mg/L) and the absence of NBU in gastric liquid suggested oral intake. High concentrations of amino-7-flunitra/epam, the main metabolite of flunitra/epam, were also found in blood, urine and gastric liquid. This benzodiazepine may have been a co-factor in the toxic effects of BU.

**ISSN:** 0022-1198.

**Pub Type:** Journal Article.

**Descriptors:** Analgesics, Opioid/\*poisoning ;Buprenorphine/\*poisoning ; Case Report ; Human ; Male ; \*Suicide.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; Pharmacology

141. **George T ; Chawarski M ; Pakes J ; Carroll K ; Kosten T ; Schottenfeld R. (2000) Disulfiram versus placebo for cocaine dependence in buprenorphine-maintained subjects: a preliminary trial. Biol Psychiatry 2000 Jun 15;47(12):1080-6.**

**Author Address:** Department of Psychiatry, Yale University, School of Medicine, New Haven, CT 06508, USA.

**Abstract:** BACKGROUND: We examined the effects of disulfiram versus placebo on cocaine dependence in buprenorphine-maintained subjects.

**METHODS:** Opioid and cocaine dependent subjects (n = 20) were induced onto buprenorphine maintenance, then randomized to disulfiram (250 mg q.d. ; n = 11) or placebo (n = 9) treatment for 12 weeks. **RESULTS:** Groups were comparable at baseline on demographic measures and on baseline measures of drug-use severity. Fifteen subjects completed the study, including 8 subjects randomized to disulfiram (72.7%) and 7 subjects randomized to placebo (77.8%). The total number of weeks abstinent from cocaine was significantly greater on disulfiram versus placebo (mean +/- SD: 7.8 +/- 2.6 vs. 3.3 +/- 0.5, p <.05) and the number of days to achieving 3 weeks (24.6 +/- 15.1 vs. 57.8 +/- 7.7, p <.01) of continuous cocaine abstinence was significantly lower in disulfiram compared with placebo. The number of cocaine-negative urine tests during the trial were also higher on disulfiram (14.7) than on placebo (8.6); furthermore, subjects in the disulfiram group achieved consistently higher rates of cocaine-negative urine tests in each 3-week interval and the increase over time was faster in the disulfiram compared with placebo. **CONCLUSIONS:** This preliminary study suggests the potential efficacy of disulfiram versus placebo

for treatment of cocaine dependence in buprenorphine-maintained patients. **ISSN:** 0006-3223.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Alcohol Deterrents/adverse effects/\*therapeutic use ; Buprenorphine/\*therapeutic use ; Chi-Square Distribution ; Cocaine-Related Disorders/psychology/\*rehabilitation ; Disulfiram/adverse effects/\*therapeutic use ; Female ; Heroin Dependence/psychology/rehabilitation ; Human ; Male ; Narcotic Antagonists/\*therapeutic use ; Substance Abuse Detection ; Support, Non-U.S. Gov't ; Support, U.S. Gov't, P.H.S. ; Time Factors.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacotherapy for opiate dependence

142. **Gerlach R. (2002) Drug-substitution treatment in Germany: A critical overview of its history, legislation and current practice. Journal of Drug Issues. Vol 32(2) Spr 2002, 503-521.**

**Author Address:** Gerlach, Ralf. INDRO e.V., Bremer Platz 18-20, Munster Germany, 48155, INDROeV@t-online.de.

**Abstract:** Maintains that, within a global context, Germany was relatively late in its acceptance of substitution treatment, having first introduced methadone maintenance treatment (MMT) in the late 1980s. Since the early 1990s, Germany has taken a number of legal steps which favor harm reduction, assistance and treatment, rather than the law enforcement approach that was dominant before. As a result of this new commitment, Germany now also allows the use of non-methadone substitutes such as buprenorphine, LAAM, dihydrocodeine, and codeine. A heroin maintenance trial has been scheduled to begin in early 2002. Despite the fact that the overall number of participants in drug-substitution treatment has risen over the past decade from about 1,000 in the early 1990s to more than 55,000 in 2001 and that MMT has been comprehensively evaluated in Germany with favorable outcomes, there remains a lack of availability of and accessibility to substitution treatment, due to rigid entry and treatment criteria imposed by the social health insurers.

**ISSN:** 0022-0426 (Print).

**Pub Type:** Journal Article.

**Descriptors:** drug substitution treatment; methadone maintenance treatment; history; legislation ; \*Drug Laws ; \*Drug Rehabilitation ; \*History ; \*Methadone Maintenance.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence

143. **Giacomuzzi S ; Riemer Y ; Ertl M ; Kemmler G ; Rossler H ; Hinterhuber H ; Kurz M. (2003) Buprenorphine versus methadone maintenance treatment in an ambulant setting: a health-related quality of life assessment. Addiction 2003 May;98(5):693-702.**

**Author Address:** University Department of Psychiatry, Innsbruck, Austria. salvatore.giacomuzzi@uibk.ac.at

**Abstract:** BACKGROUND: To compare the effects on quality of life (QOL) of

oral methadone with sublingual buprenorphine. **METHODS:** We performed an open-label, non-randomized, two-site (methadone-buprenorphine) study. During 6 months we assessed the quality of life status of 53 opioid-dependent patients admitted to a methadone or buprenorphine maintenance programme using the German version (Berlin Quality of Life Profile) of the Lancashire Quality of Life Profile. Physical symptoms were measured using the Opioid Withdrawal Scale. Five hundred and thirty urine screening tests were carried out randomly to detect additional consumption. **RESULTS:** Sixty-seven opioid-dependent subjects (38 on methadone and 29 on buprenorphine) were enrolled in the study, and 53 completed it (30 subjects treated with buprenorphine and 23 subjects with racemic methadone). The subjects were comparable on all baseline measures. At the first follow-up (week 8), the buprenorphine-maintained group showed significantly less additional consumption of opioids ( $P = 0.013$ ) compared with the methadone group. Patients retained in the buprenorphine or methadone programme (week 24) showed no significant differences in all quality of life scores. At the end of the study period, the buprenorphine-maintained group showed significantly less additional consumption of opioids ( $P = 0.001$ ) and cocaine ( $P = 0.018$ ) compared with the methadone group. The outcome measures for withdrawal symptoms after 24 weeks of treatment with buprenorphine showed slight advantages in stomach cramps, fatigue or tiredness, feelings of coldness and heart pounding. **CONCLUSIONS:** These results suggest that buprenorphine treatment is as effective as methadone regarding effects on quality of life and withdrawal symptoms. Buprenorphine has the potential to reduce the harm caused by drug abuse. Further research is needed to determine if buprenorphine is more effective than methadone in particular subgroups of patients.

**ISSN:** 0965-2140.

**Pub Type:** Journal Article ; Multicenter Study.

**Descriptors:** Adult ; Buprenorphine/\*therapeutic use ; Comparative Study ; Female ; Human ; Male ; Methadone/\*therapeutic use ; Narcotics/\*therapeutic use ; Opioid-Related Disorders/\*rehabilitation ; Quality of Life ; Treatment Outcome.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

144. **Gibson A ; Doran C ; Bell J ; Ryan A ; Lintzeris N. (2003) A comparison of buprenorphine treatment in clinic and primary care settings: a randomised trial. Med J Aust 2003 Jul 7;179(1):38-42.**

**Author Address:** National Drug and Alcohol Research Centre, University of New South Wales, UNSW Randwick Campus, King Street, Randwick, NSW 2052, Australia. amy.gibson@unsw.edu.au

**Abstract:** **OBJECTIVE:** To compare outcomes, costs and incremental cost-effectiveness of heroin detoxification performed in a specialist clinic and in general practice. **DESIGN AND SETTING:** Randomised controlled trial set in a specialist outpatient drug treatment centre and six office-based general practices in inner city Sydney, Australia. **PARTICIPANTS:** 115 people seeking

treatment for heroin dependence, of whom 97 (84%) were reinterviewed at Day 8, and 78 (68%) at Day 91. **INTERVENTIONS:** Participants were randomly allocated to primary care or a specialist clinic, and received buprenorphine for 5 days for detoxification, then were offered either maintenance therapy with methadone or buprenorphine, relapse prevention with naltrexone, or counselling alone. **MAIN OUTCOME MEASURES:** Completion of detoxification, engagement in post-detoxification treatment, and heroin use assessed at Days 8 and 91. Costs relevant to providing treatment, including staff time, medication use and diagnostic procedures, with abstinence from heroin use on Day 8 as the primary outcome measure. **RESULTS:** There were no significant differences in the proportions completing detoxification (40/56 [71%] primary care v 46/59 [78%] clinic), participating in postwithdrawal treatment (28/56 [50%] primary care v 36/59 [61%] clinic), reporting no opiate use during the withdrawal period (13/56 [23%] primary care v 13/59 [22%] clinic), and in duration of postwithdrawal treatment by survival analysis. Most participants in both groups entered postwithdrawal buprenorphine maintenance. On an intention-to-treat basis, self-reported heroin use in the month before the Day 91 interview was significantly lower than at baseline (27 days/month at baseline, 14 days/month at Day 91;  $P < 0.001$ ) and did not differ between groups. Buprenorphine detoxification in primary care was estimated to be \$24 more expensive per patient than treatment at the clinic. The incremental cost-effectiveness ratio reveals that, in this context, it costs \$20 to achieve a 1% improvement in outcome in primary care. **CONCLUSIONS:** Buprenorphine-assisted detoxification from heroin in specialist clinic and primary care settings had similar efficacy and cost-effectiveness. Buprenorphine treatment can be initiated safely in primary care settings by trained GPs.

**ISSN:** 0025-729X.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**URL:** [http://www.mja.com.au/public/issues/179\\_01\\_070703/gib10877\\_fm.html](http://www.mja.com.au/public/issues/179_01_070703/gib10877_fm.html)

**Descriptors:** Adolescent ; Adult ; Ambulatory Care Facilities/\*economics/statistics & numerical data ; Buprenorphine/economics/\*therapeutic use ; Comparative Study ; Cost-Benefit Analysis ; Family Practice/economics/statistics & numerical data ; Female ; Health Care Costs/statistics & numerical data ; Heroin Dependence/\*drug therapy ; Human ; Male ; Middle Age ; New South Wales; Outcome and Process Assessment (Health Care) ; Primary Health Care/\*economics/statistics & numerical data ; Support, Non-U.S. Gov't ; Treatment Outcome.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Legal/regulatory issues ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

145. **Giordano L ; Bickel W ; Loewenstein G ; Jacobs E ; Marsch L ; Badger G. (2002) Mild opioid deprivation increases the degree that opioid-dependent outpatients discount delayed heroin and money. Psychopharmacology. Vol 163(2) Sep 2002, 174-182.**

**Author Address:** Giordano, Louis A. U Vermont, Dept of Psychiatry,

Burlington, VT US 05401, giord003@mc.duke.edu.

**Abstract:** Examined the extent to which opioid deprivation affects how opioid-dependent individuals discount small, medium and large quantities of delayed heroin and money. 13 29.9-45.1 yr old opioid-dependent individuals maintained on buprenorphine completed a hypothetical choice task in which they choose between a constant delayed reward amount and an immediate reward amount that was adjusted until they expressed indifference between both outcomes. The task was completed for 3 values of heroin and money rewards during 8 sessions under conditions of opioid deprivation and satiation. Results show that across conditions, hyperbolic functions provided a good fit for the discounting data. Degree of discounting was significantly higher when Ss were opioid deprived. Degree of discounting was higher for heroin than money and inversely related to the magnitude of the reward. It is concluded that opioid deprivation increased the degree to which dependent individuals discounted delayed heroin and money. Understanding the conditions that affect how drug-dependent individuals discount delayed rewards might help us understand the myopic choices made by such individuals and help improve treatment outcomes.

**ISSN:** 0033-3158 (Print), 1430-2072 (Electronic).

**Pub Type:** Journal Article.

**Descriptors:** opioid-dependency; opioid deprivation; reward amount; reward delay ; \*Drug Dependency ; \*Drug Withdrawal ; \*Heroin Addiction ; \*Opiates ; \*Rewards ; Human. Male. Female. Adulthood (18 yrs & older). Young Adulthood (18-29 yrs). Thirties (30-39 yrs). Middle Age (40-64 yrs) ; Empirical Study.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

146. **Gonzalez G ; Feingold A ; Oliveto A ; Gonsai K ; Kosten T. (2003) Comorbid major depressive disorder as a prognostic factor in cocaine-abusing buprenorphine-maintained patients treated with desipramine and contingency management. Am J Drug Alcohol Abuse 2003 Aug;29(3):497-514.**

**Author Address:** Department of Psychiatry, Yale University School of Medicine, and VA Connecticut Healthcare System, West Haven, Connecticut 06516, USA. gerardo.gonzalez-haddad@yale.edu

**Abstract:** Depression is common among patients who abuse both opiates and cocaine, and its treatment has had mixed success. This study compares buprenorphine-maintained patients with lifetime major depressive disorder (MDD, N = 53) with those never depressed (ND, N = 96) on cocaine and opiate-free urines during a 12-week outpatient double-blind, placebo-controlled, randomized clinical trial. The 149 subjects were assigned to four groups: 1) desipramine (DMI) + contingency management (CM); 2) DMI + noncontingency management (NCM); 3) placebo + CM; and 4) placebo + NCM. Depression assessments included Hamilton Depression Rating Scale, Center for Epidemiological Studies Depression Inventory, and Structured Clinical Interview for DSM-IV interview for diagnosis of lifetime MDD. Urine toxicologies were

performed thrice weekly and the CES-D was performed monthly. The MDD group had a larger proportion of females (45% vs 21%, P = 0.02) and were more likely to be married (13.2% vs 7.3%, P = 0.02) than the ND group. Treatment retention did not vary by depression status. Hierarchical Linear Modeling found that depressive symptoms decreased comparably across the four treatment groups. Although participation in CM improved drug-free urines more for patients with MDD than for the ND group (Z = 2.44, P = 0.01), treatment with DMI was significantly more efficacious for the ND group than for the MDD group (Z = -2.89, P = 0.003). These results suggest that patients with MDD may respond better to behavioral treatments such as CM than to desipramine plus buprenorphine. The ND cocaine-abusing, opiate-dependent patients may be more responsive to the anticraving effects of DMI.

**ISSN:** 0095-2990.

**Pub Type:** Journal Article ; Clinical trial.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

147. **Gonzalez G ; Oliveto A ; Kosten T. (2002) Treatment of heroin (diamorphine) addiction: current approaches and future prospects. Drugs 2002;62(9):1331-43.**

**Author Address:** Department of Psychiatry, Division of Substance Abuse, Yale University School of Medicine, VA Connecticut Healthcare System, West Haven, Connecticut 06516, USA. Geraldo.Gonzales-Haddad@yale.edu

**Abstract:** New pharmacological treatments for heroin (diamorphine) addiction include drugs that reduce opiate withdrawal symptoms and agents that are given during the maintenance phase of treatment. A variety of different types of pharmacological agents (opioid agonists, partial opioid agonists, opioid antagonists and alpha(2)-adrenoreceptor agonists) are reviewed and the evidence of their use during managed withdrawal and maintenance are presented. Experimental approaches attempting to reduce the time of opiate withdrawal and to accelerate the transition to abstinence are being developed. The combination tablet of buprenorphine and naloxone that is to be introduced for office-based maintenance is currently undergoing intense evaluation in the US. This new approach may facilitate the expansion of treatment while reducing the potential for medication diversion and intravenous use.

**ISSN:** 0012-6667.

**Pub Type:** Journal Article ; Review ; Review, Tutorial.

**Descriptors:** Heroin Dependence/\*drug therapy/rehabilitation ; Human ; Narcotic Antagonists/therapeutic use ; Receptors, Adrenergic, alpha-2/agonists; Receptors, Opioid/agonists/antagonists & inhibitors ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacology ; Pharmacotherapy for opiate dependence

148. **Gopal S ; Tzeng T ; Cowan A. (2001) Development and validation of a sensitive analytical method for the simultaneous determination of**

**buprenorphine and norbuprenorphine in human plasma. Eur J Pharm Biopharm 2001 Mar;51(2):147-51.**

**Author Address:** Department of Pharmaceutical Sciences, School of Pharmacy, Temple University, 3307 N. Broad Street, Philadelphia, PA 10140, USA. sumithrag@hotmail.com

**Abstract:** A sensitive, specific, and robust capillary gas chromatography-mass spectrometry method has been developed and validated for simultaneous determination of buprenorphine and its active metabolite, norbuprenorphine, in human plasma. Sample preparation involved a clean-up procedure using a Bond Elut Certify cartridge followed by derivatization with pentafluoropropionic anhydride. Separation was carried out on a HP-1 fused silica capillary column using helium as the carrier gas. Selected ion monitoring was used in the electron impact mode. Excellent linearity was found between 0.10 and 20.0 ng/ml with a limit of quantitation of 0.05 and 0.10 ng/ml for buprenorphine and norbuprenorphine, respectively. Interday and intraday assay precisions (%CV) and accuracies were within 15.0% for buprenorphine and norbuprenorphine, respectively. Recoveries were quantitative and concentration-independent. This method will be applied to pharmacokinetic/pharmacodynamic/bioequivalence studies of buprenorphine in humans.

**ISSN:** 0939-6411.

**Pub Type:** Journal Article ; Validation Studies.

**Descriptors:** Analgesics, Opioid/\*blood ; Animal ; Buprenorphine/analogs & derivatives/\*blood ; Calibration ; Human ; Mass Fragmentography/\*methods; Molecular Structure ; Reproducibility of Results ; Sensitivity and Specificity.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Pharmacology

149. **Govindarajan R ; Bakalova T ; Michael R ; Abadir A. (2002) Epidural buprenorphine in management of pain in multiple rib fractures. Acta Anaesthesiol Scand 2002 Jul;46(6):660-5.**

**Author Address:** Brookdale University Hospital and Medical Center, Brooklyn, NY 11212, USA. rmsm7007@aol.com

**Abstract:** BACKGROUND: Pain from multiple rib fractures may affect pulmonary function, morbidity, and length of stay in the intensive care units. This study describes some clinical characteristics of epidural buprenorphine, a lipophilic and partial opiate agonist with a higher micro receptor affinity than morphine, in combating the pain in multiple rib fractures. METHODS: The study was conducted prospectively over a 15-month period. A total of 27 patients admitted to the hospital with multiple rib fractures were studied. Buprenorphine at a concentration of 0.3 mg in 5-10 ml normal saline was administered epidurally, twice daily the first 24 h, thereafter once daily. Ventilatory function tests (including vital capacity, tidal volume, respiratory rate, and minute volume) and assessment of pain intensity using a simple, categorical, verbal rating scale were obtained before and after institution of analgesia. Any nausea, vomiting, hypotension, urinary retention, respiratory depression or pruritis were recorded. RESULTS: We found a significant improvement in ventilatory function tests during the 1st, 2nd, and 3rd day after epidural analgesia when compared with

the preanalgesia levels ( $P < 0.001$ ). Changes in the verbal rating scale demonstrated that epidural buprenorphine was associated with marked improvement in pain at rest and pain during coughing and deep breathing. None of our patients developed hypotension ( $<10\%$  of the baseline), urinary retention or respiratory depression. Nausea, vomiting, and mild pruritis were the only reported complications. CONCLUSIONS: Epidurally introduced narcotic, like buprenorphine in saline, has been found to be effective in our study to achieve adequate analgesia in treatment of patients with multiple rib fractures. In addition, this methodology of pain relief eliminates the costly delivery system and early discharge, and allows walking epidurals and follow-up on outpatient basis.

**ISSN:** 0001-5172.

**Pub Type:** Clinical Trial ; Journal Article.

**Descriptors:** \*Analgesia, Epidural ; Analgesics, Opioid/\*therapeutic use ; Buprenorphine/\*therapeutic use ; Female ; Human ; Male ; Middle Age ; Pain/\*drug therapy/physiopathology ; Pain Measurement ; Prospective Studies ; Pulmonary Ventilation/drug effects ; Respiratory Function Tests ; Rib Fractures/\*drug therapy ; Tidal Volume/drug effects ; Time Factors ; Vital Capacity/drug effects.

**ATTC Buprenorphine Topics:** Pain management

150. **Gowing L ; Ali R ; White J. (2000) Buprenorphine for the management of opioid withdrawal. Cochrane Database of Systematic Reviews 2000;(3):CD002025. (see Gowing, et al, 2002 for update).**

**Author Address:** Evidence-Based Practice Unit, Drug and Alcohol Services Council, 161 Greenhill Road, Parkside, SA, Australia, 5067.

gowing.linda@saugov.sa.gov.au

**Abstract:** BACKGROUND: Managed withdrawal, or detoxification, is not in itself a treatment for opioid dependence, but it is a required first step for many forms of longer-term treatment. It may also represent the end point of an extensive period of treatment such as methadone maintenance. As such, managed withdrawal is an essential component of an effective treatment system. This review is one of a series that aims to assess the evidence as to the effectiveness of the variety of approaches to managing opioid withdrawal. OBJECTIVES: To assess the effectiveness of interventions involving the short-term use of buprenorphine to manage the acute phase of opioid withdrawal. SEARCH STRATEGY: Multiple electronic databases, including Medline, Embase, Psyclit, Australian Medical Index and Current Contents, were searched using a strategy designed to retrieve references broadly addressing the management of opioid withdrawal. Reference lists of retrieved studies, reviews and conference abstracts were handsearched. SELECTION CRITERIA: We included randomised or quasi-randomised controlled clinical trials or prospective controlled cohort studies comparing buprenorphine (treatment 10 days or less) with another form of treatment. Studies were required to provide detailed information on the type and dose of drugs used and the characteristics of patients treated. Studies were also required to provide information on the nature of withdrawal signs and symptoms experienced, the

occurrence of adverse effects OR rates of completion of the withdrawal episode. DATA COLLECTION AND ANALYSIS: Potentially relevant studies were assessed for inclusion by one reviewer (LG). Inclusion decisions were confirmed by consultation between reviewers. Included studies were assessed by all reviewers. One reviewer (LG) undertook data extraction with the process confirmed by consultation between all three reviewers. MAIN RESULTS: Five studies met the criteria for inclusion in the review. No data tables are included in this review and no meta-analysis has been undertaken because of differences in treatment regimes and the assessment of outcomes in these studies. Four studies compared buprenorphine with clonidine. All found withdrawal to be less severe in the buprenorphine treatment group. In three of these studies all participants were withdrawing from heroin. Participants in one study were withdrawing from methadone, with doses reduced to 10mg/day prior to treatment with buprenorphine. Three of the studies commented on residual symptoms experienced by participants treated with buprenorphine to manage heroin withdrawal. Aches, restlessness, yawning, mydriasis, tremor, insomnia, nausea and mild anxiety were reported as being experienced by some participants. Rates of completion of withdrawal were able to be calculated for all studies included in the review but the definition of completion varied between studies. Rates ranged from 65% to 100%. None of the studies included in the review reported adverse effects. However, approximately approximately Lintzeris 1999a approximately approximately (a single-group study which therefore did not meet the inclusion criteria) reported 50% of participants withdrawing from heroin experienced headaches, 28% sedation, 21% nausea, 21% constipation, 21% anxiety, 17% dizziness and 17% itchiness during withdrawal. These adverse effects were most common in the first 2-3 days of treatment and then subsided. In four of the five studies treatment was undertaken on an inpatient basis. Only approximately approximately O'Connor 1997 approximately approximately provided outpatient treatment. However, two studies that did not meet the inclusion criteria ( approximately approximately Diamant 1998 approximately approximately and approximately approximately Lintzeris 1999a approximately approximately ) also provided outpatient treatment. The findings of these studies support the feasibility of heroin withdrawal being managed with buprenorphine on an outpatient basis  
**ISSN:** 1469-493X.

**Pub Type:** Meta-analysis ; Review.

**Descriptors:** Acute Disease ; Buprenorphine/\*therapeutic use ; Human ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/ complications/\*drug therapy ; Randomized Controlled Trials ; Substance Withdrawal Syndrome/\*drug therapy.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

151. **Gowing L ; Ali R ; White J. (2000) The management of opioid withdrawal. Drug & Alcohol Review. Vol 19(3) Sep 2000, 309-318.**

**Abstract:** Reviews 213 published reports of interventions to manage opioid withdrawal. Rates of completion and severity of withdrawal are similar when

managed with either alpha-sub-2-adrenergic agonists or reducing doses of methadone, but alpha-sub-2-adrenergic agonists, particularly clonidine, are associated with a higher incidence of hypotensive side effects. The use of opioid antagonists may increase completion rates, but with the risk of more severe withdrawal. Buprenorphine has considerable promise for the management of opioid withdrawal, being associated with lower withdrawal severity, fewer side effects, and similar completion rates to withdrawal managed with alpha-sub-2-adrenergic agonists. Withdrawal in an in-patient setting is found to be associated with higher completion rates than withdrawal in an out-patient setting. Psychological state prior to and during withdrawal may be important in determining withdrawal outcomes. It is concluded that future studies should include long-term outcomes in any consideration of effectiveness of the management of opioid withdrawal.

**ISSN:** 0959-5236 (Print), 1465-3362 (Electronic).

**Pub Type:** Journal Article.

**Descriptors:** interventions for the management of opioid withdrawal ; \*Drug Rehabilitation ; \*Drug Withdrawal ; \*Opiates ; Drug Addiction ; Drug Dependency ; Human. Inpatient. Outpatient. ; Literature Review/Research Review.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

152. **Gowing L ; Ali R ; White J. (2002) Buprenorphine for the management of opioid withdrawal. Cochrane Database of Systematic Reviews, 2002(2): CD002025. (update of Gowing 2000).**

**Author Address:** Evidence-Based Practice Unit, Drug and Alcohol Services Council, 161 Greenhill Road, Parkside, SA, Australia, 5063.  
gowing.linda@saugov.sa.gov.au

**Abstract:** BACKGROUND: Managed withdrawal (detoxification) is a necessary step prior to drug-free treatment. It may also represent the end point of long-term opioid replacement treatment such as methadone maintenance. The availability of managed withdrawal is essential to an effective treatment system. OBJECTIVES: To assess the effectiveness of interventions involving the short-term use of buprenorphine to manage the acute phase of opioid withdrawal. SEARCH STRATEGY: Multiple electronic databases were searched using a strategy designed to retrieve references broadly addressing the management of opioid withdrawal. Reference lists of retrieved studies, reviews and conference abstracts were handsearched. SELECTION CRITERIA: Randomised or quasi-randomised controlled clinical trials or prospective controlled cohort studies that compared different buprenorphine regimes, or that compared buprenorphine with another form of treatment (or placebo) to modify the signs and symptoms of withdrawal in participants who were primarily opioid dependent. DATA COLLECTION AND ANALYSIS: Potentially relevant studies were assessed for inclusion by one reviewer. Inclusion decisions were confirmed by consultation between reviewers. One reviewer undertook data extraction with the process confirmed by consultation between all three reviewers. MAIN RESULTS: Six studies (5 RCTs and 1 controlled prospective study), involving 357 participants,

met the criteria for inclusion in the review. Four studies compared buprenorphine with clonidine. All found withdrawal to be less severe in the buprenorphine treatment group. In three of these studies all participants were withdrawing from heroin. Participants in one study were withdrawing from methadone (10mg/day). Aches, restlessness, yawning, mydriasis, tremor, insomnia, nausea and mild anxiety were reported as being experienced by some participants. Rates of completion of withdrawal ranged from 65% to 100%. None of the studies included in the review reported adverse effects. However a single-group study which therefore did not meet the inclusion criteria, reported the occurrence in some participants of headaches, sedation, nausea, constipation, anxiety, dizziness and itchiness, particularly in the first 2-3 days of treatment. In one of the six studies, and in two studies that did not meet the inclusion criteria, treatment was provided on an outpatient basis. REVIEWER'S CONCLUSIONS: Buprenorphine has potential as a medication to ameliorate the signs and symptoms of withdrawal from heroin, and possibly methadone, but many aspects of treatment protocol and relative effectiveness need to be investigated further.

**ISSN:** 1469-493X.

**Pub Type:** Meta-analysis ; Review.

**Descriptors:** Acute Disease ; Buprenorphine/\*therapeutic use ; Human ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/ complications/\*drug therapy ; Randomized Controlled Trials ; Substance Withdrawal Syndrome/\*drug therapy.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

153. **Great Britain. Dept. of Health. Medical Working Group. (1999) Drug Misuse and Dependence ; Guidelines on Clinical Management. London: Department of Health; Scottish Office Department of Health ; Welsh Office ; Department of Health and Social Services, Northern Ireland: The Stationery Office, 1999, 138 p.**

**Author Address:** Copyright Unit, Her Majesty's Stationery Office, St Clements House, 2-16 Colegate, Norwich NR3 1BQ

**Abstract:** These Guidelines are written for all doctors in Great Britain. They are intended for doctors who are 'generalists' (e.g. general practitioners, physicians, surgeons and obstetricians); and for those practitioners who have varying degrees of training and expertise treating drug misusers, including specialists in drug misuse and some general practitioners. The Guidelines make a number of recommendations (e.g. those on supervised consumption), which for practical reasons, may need to be phased in over a time period in some cases. For the purpose of these Guidelines, treatment is divided into assessment, management of withdrawal and dependence, and preventing relapse. Information about Buprenorphine is included in the sections on management of withdrawal and dependence.

**ISBN:** 0 11 322277 7.

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PO Box 276, London SW8 5DT. / Telephone orders: 020 7873 9090 / Fax orders: 020 7873 8200.

**URL:** <http://www.smmgp.demon.co.uk/html/clinical.htm>

**Pub. Type:** Monograph ; web document ; clinical guidelines.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

154. **Greenwald M ; Johanson C ; Moody D ; Woods J ; Kilbourn M ; Koeppe R ; et.al. (2003) Effects of buprenorphine maintenance dose on mu-opioid receptor availability, plasma concentrations, and antagonist blockade in heroin-dependent volunteers. Neuropsychopharmacology 2003 Nov;28(11):2000-9.**

**Author Address:** Department of Psychiatry and Behavioral Neurosciences, Wayne State University, Detroit, MI 48207, USA. [mgreen@med.wayne.edu](mailto:mgreen@med.wayne.edu)

**Abstract:** The clinical effectiveness of opioid maintenance for heroin dependence is believed to result from a medication's ability to decrease mu-opioid receptor (microOR) availability thereby replacing agonist effects, alleviating withdrawal symptoms and attenuating heroin effects. We empirically tested this hypothesis in five heroin-dependent volunteers who were successively maintained on 32, 16, 2, and 0 mg daily buprenorphine (BUP) tablet doses. We predicted and confirmed that higher BUP doses would decrease in vivo microOR availability (measured with PET and [(11)C]carfentanil), increase plasma levels of BUP and its metabolite nor-BUP, and decrease withdrawal symptoms and hydromorphone (HYD) responses. Relative to placebo, BUP significantly decreased mean (+/-SEM) whole-brain microOR availability 41 +/-8, 80 +/-2, and 84 +/-2% at 2, 16, and 32 mg, respectively. Regions of interest (ROIs) (prefrontal cortex, anterior cingulate, thalamus, amygdala, nucleus accumbens, caudate) showed similar dose-dependent effects. Changes in microOR availability varied across ROIs (prefrontal cortex, 47% vs amygdala, 27%) at BUP 2 mg, but were more homogeneous across ROIs at BUP 32 mg (94-98%; except thalamus, 88%). Relative to placebo (0 ng/ml), peak plasma levels of BUP and nor-BUP were comparable and dose-dependent (0.5-1, 5-6, and 13-14 ng/ml at 2, 16, and 32 mg, respectively). microOR availability decreases were negatively correlated with BUP plasma level and positively correlated with questionnaire-based opioid withdrawal symptoms and attenuation of HYD symptoms. These findings suggest that high-dose BUP maintenance produces near-maximal microOR occupation, microOR availability correlates well with plasma levels, and BUP-related opioid symptoms and antagonist blockade exhibit concentration-effect relationships.

**ISSN:** 0893-133X.

**Pub Type:** Journal article.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacology ; Pharmacotherapy for opiate dependence

**155. Greenwald M ; Johanson C ; Schuster C. (1999) Opioid reinforcement in heroin-dependent volunteers during outpatient buprenorphine maintenance. Drug Alcohol Depend 1999 Oct 1;56(3):191-203.**

**Author Address:** Department of Psychiatry and Behavioral Neurosciences, Wayne State University, Detroit, MI 48207, USA. mgreen@med.wayne.edu

**Abstract:** This study examined the reinforcing effects of hydromorphone (HYD) (0, 4, 8, and 16 mg/70 kg i.m.) in heroin-dependent outpatient volunteers maintained on buprenorphine (BUP) at doses of 2, 4, and 8 mg, each for 2 weeks. Following a week of maintenance at each dose, volunteers received injections of one of the four HYD doses under double-blind conditions. Eight volunteers (abstainers) were heroin-free during HYD test weeks, whereas six volunteers remained heroin-positive (nonabstainers). Among abstainers, HYD had minimal reinforcing value, whereas in nonabstainers there were marked dose-related increases in HYD reinforcing value, which were not attenuated by increasing doses of BUP. A similar pattern was found for HYD subjective agonist effects. Heroin craving among nonabstainers was significantly higher compared with abstainers, and was reduced in a dose-related manner by HYD. Although BUP and HYD produced dose-related miosis, abstinence status had no differential effect. In summary, BUP effects on opioid reinforcement were consistent from outpatient setting (heroin abstinence) to laboratory setting (decreased HYD reinforcement), supporting the validity of this laboratory model. **ISSN:** 0376-8716.

**Pub Type:** Clinical Trial ; Controlled Clinical Trial ; Journal Article. **Descriptors:** Adult ; Analysis of Variance ; Behavior, Addictive/\*drug therapy/psychology ; Buprenorphine/\*therapeutic use ; Double-Blind Method ; Drug Synergism ; Female ; Heroin Dependence/psychology/ \*rehabilitation/urine ; Human ; Hydromorphone/\*administration & dosage ; Male ; Middle Age ; Narcotic Antagonists/\*therapeutic use ; Narcotics/ \*administration & dosage ; Outpatients/psychology ; Pupil/drug effects ; Questionnaires ; Reinforcement (Psychology) ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

**156. Greenwald M ; Schuh K ; Hopper J ; Schuster C ; Johanson C. (2002) Effects of buprenorphine sublingual tablet maintenance on opioid drug-seeking behavior by humans. Psychopharmacology (Berl) 2002 Apr;160(4):344-52.**

**Author Address:** Addiction Research Institute, Wayne State University School of Medicine, 2761 E. Jefferson, Detroit, MI 48207, USA. mgreen@med.wayne.edu

**Abstract:** RATIONALE: Buprenorphine can decrease opioid self-administration by humans and animals, but its ability to decrease drug-seeking behavior and craving (i.e. motivational measures) among outpatient volunteers using clinically relevant dosing schedules has not been extensively studied. OBJECTIVES: We investigated whether daily versus alternating-day administration of high versus low buprenorphine doses influenced choice of,

and operant responding for, hydromorphone versus money. METHODS: Fourteen heroin-dependent outpatients were maintained under four buprenorphine sublingual tablet (double blind) dose conditions using a within-subject, randomized crossover design. All participants received, for 2 weeks each, buprenorphine doses of 2 mg daily, 4 mg/placebo on alternating days, 16 mg daily, and 32 mg/placebo on alternating days. In each laboratory test session, participants chose between money (\$2/choice) and drug (1/8 of total hydromorphone, 4 or 24 mg IM in different sessions) alternatives using an eight-trial non-independent progressive ratio schedule (FR 100, 200, 12,800). The drug dose and money amount earned was delivered after the end of the 2.5-h work period. RESULTS: Hydromorphone 24 mg was more reinforcing than 4 mg. Higher versus lower average buprenorphine doses (regardless of daily versus alternate-day schedule) significantly decreased hydromorphone 24 mg choice and increased money choice. Baseline heroin craving questionnaire scores predicted drug choice, and craving scores were significantly decreased by high-dose buprenorphine. CONCLUSIONS: High-dose buprenorphine attenuated opioid drug-seeking behavior, heroin craving self-reports and increased sensitivity to alternative reinforcement. These beneficial effects were retained when high-dose buprenorphine was administered on alternate days. **ISSN:** 0033-3158.

**Pub Type:** Journal Article.

**Descriptors:** Administration, Sublingual ; Adolescent ; Adult ; Analysis of Variance ; Behavior, Addictive/\*drug therapy/psychology ; Buprenorphine/\*administration & dosage ; Comparative Study ; Cross-Over Studies ; Female ; Heroin Dependence/\*drug therapy/psychology ; Human ; Male ; Middle Age ; Narcotic Antagonists/\*administration & dosage ; Support, U.S. Gov't, P.H.S. ; Tablets.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

**157. Greenwald M ; Schuh K ; Stine S. (2003) Transferring methadone-maintained outpatients to the buprenorphine sublingual tablet: a preliminary study. Am J Addict 2003 Jul-Aug;12(4):365-74.**

**Author Address:** Substance Abuse Research Division, Department of Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine, Detroit, Mich.

**Abstract:** There is no accepted algorithm to transfer opioid-dependent patients from methadone (METH) to its new alternative, buprenorphine (BUP). Five outpatients transferred (double blind, double dummy) from METH 60 mg/day (with one day at 45 mg) to BUP 8 mg s.l. tablet. Relative to METH maintenance, BUP decreased opioid agonist symptoms (transfer day 1) and increased withdrawal symptoms (days 1 and 2) and blood pressure (day 2). Self-reported heroin use did not increase from METH maintenance levels. It may be feasible to transfer outpatients on METH 60 mg/day to BUP 8 mg/day s.l. tablet, although this pilot protocol needs refinements to improve tolerability and clinical efficacy. (Am J Addict 2003;12:365-374)

**ISSN:** 1055-0496.

**Pub Type:** Journal Article.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacology ; Pharmacotherapy for opiate dependence

158. **Gringauz M ; Rabinowitz R ; Stav A ; Korczyn A. (2001) Tolerance to the analgesic effect of buprenorphine, butorphanol, nalbuphine, and cyclorphan, and cross-tolerance to morphine. Journal of Anesthesia 2001; 15(4):204-209).**

**Author Address:** Dept. of Physiology/Pharmacology, Tel-Aviv University, Sackler School of Medicine, Ramat-Aviv 69978; Israel.

**Abstract:** Purpose. The increased use of opioids in the chronic treatment of pain, especially with oncologic patients, encourages the search for drugs with potent analgesic activity, but with minimal induced tolerance and cross-tolerance to morphine. Methods. Four agonist-antagonist opioid derivatives (buprenorphine, butorphanol, nalbuphine, and cyclorphan) were examined. Tolerance to the analgesic effect of the four drugs and their cross-tolerance effects with morphine were evaluated in ICR albino mice by the 'hot plate method'. Measurements of the analgesic effect were taken before and after chronic treatment (of 14 days duration) with these drugs, as well as morphine. Results. All tested drugs produced tolerance after 14 days of treatment. Chronic treatment with morphine reduced the effects of nalbuphine and cyclorphan, but not those of buprenorphine and butorphanol. After 14 days treatment with buprenorphine and cyclorphan, the analgesic action of morphine was reduced, but this reduction did not occur after butorphanol and nalbuphine treatments. Conclusion. Of the four agonist-antagonists tested, butorphanol seems to be least likely to produce cross-tolerance with morphine

**Pub. Type:** Journal article.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pain management

159. **Gross A ; Jacobs E ; Petry N ; Badger G ; Bickel W. (2001) Limits to buprenorphine dosing: a comparison between quintuple and sextuple the maintenance dose every 5 days. Drug Alcohol Depend 2001 Sep 1;64(1):111-6.**

**Author Address:** Substance Abuse Treatment Center, University of Vermont, 1 South Prospect Street, Burlington, VT 05401, USA. agross@zoo.uvm.edu

**Abstract:** The relative efficacy of quintuple and sextuple buprenorphine dosing in abating withdrawal symptoms for 120 h was compared in opioid-dependent outpatients. Fourteen subjects received buprenorphine in a double-blind, placebo-controlled, cross-over design. Daily sublingual maintenance doses were 4 mg/70 kg (n=4) and 8 mg/70 kg (n=10). After a stabilization period of daily maintenance administration, subjects received quintuple (5x daily maintenance dose) and sextuple (6x daily maintenance dose) doses every 120 h. Measures of opioid agonist and withdrawal effects were assessed daily. Subjective ratings of withdrawal were significantly greater than baseline ratings beyond 96-h post dosing under both regimens. There was no evidence,

however, that those subjective ratings of withdrawal differed between the two regimens. Thus, these data suggest that sextuple buprenorphine dosing, administered every 5 days, does not abate opioid-withdrawal beyond 96 hours. **ISSN:** 0376-8716.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Analysis of Variance ; Buprenorphine/\*administration & dosage ; Comparative Study ; Female ; Human ; Male ; Middle Age ; Outcome Assessment (Health Care) ; Substance Withdrawal Syndrome/\*drug therapy ; Support, Non-U.S. Gov't ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

160. **Gueye P ; Megarbane B ; Borron S ; Adnet F ; Galliot-Guilley M ; Ricordel I ; Tournau J ; Goldgran-Toledano D ; Baud F. (2002) Trends in opiate and opioid poisonings in addicts in north-east Paris and suburbs, 1995-99. Addiction 2002 Oct;97(10):1295-304.**

**Author Address:** Reanimation Medicale et Toxicologique, Groupe hospitalier Lariboisiere - Fernand Widal Assistance Publique-Hopitaux de Paris and INSERM U-26, Paris, France. p.gueye@wanadoo.fr

**Abstract:** AIMS: (1). To assess the trends in the number, mortality and the nature of severe opiate/opioid poisonings from 1995 to 1999 in north-east Paris and adjacent suburbs and (2). to examine the effects of the introduction of high-dose buprenorphine on these parameters. DESIGN: Retrospective, 5-year study with review of pre-hospital, hospital and post-mortem data. SETTING AND PARTICIPANTS: Eighty patients from the toxicological intensive care unit (TICU) in north-east Paris, 421 patients from the pre-hospital emergency medical service in a north-east suburb of Paris (SAMU 93) and 40 deaths from the coroner's office in Paris. MEASUREMENTS AND RESULTS: We found that the number of pre-hospital opiate/opioid poisonings and deaths decreased over 5 years. During the same time frame, opiate/opioid poisoning admissions to our TICU remained steady, but the number of deaths declined. From 1995 to 1999, the detection of buprenorphine among opiate/opioid-poisoned TICU patients increased from two to eight occurrences per year while detection of opiates diminished from 17 to 10 occurrences per year. Increased buprenorphine detection correlated directly with increasing sales over this time period. In spite of the increased use of buprenorphine, the mortality associated with opiate/opioid poisonings has diminished in the pre-hospital environment from 9% in 1995 to 0% in 1999, and in the TICU from 12% in 1995 to 0% in 1997 and thereafter. We found a high frequency of multiple opiate/opioid use in severe poisonings, as well as the frequent association of other psychoactive drugs including ethanol. CONCLUSIONS: The number and the mortality of opiate/opioid poisonings appear to be stable or decreasing in our region. The association of multiple opiates/ opioids appears nearly as common as the association with other psychoactive drugs. The introduction of high-dose buprenorphine coincides with a decrease in opiate/opioid poisoning mortality. Further study will be necessary to clarify this observation. **ISSN:** 0965-2140.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Buprenorphine/therapeutic use ; Female ; Hospitalization/trends ; Human ; Male ; Narcotic Antagonists/therapeutic use ; Opioid-Related Disorders/\*epidemiology/rehabilitation ; Overdose/epidemiology ; Paris/epidemiology ; Retrospective Studies ; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; History, use and effectiveness in other countries ; Prevalence of use for opiate dependence.

161. **Guichard, A ; Lert, F ; Calderon, C ; Gaigi, H ; Maguet, O ; Soletti, J ; Brodeur, J; Richard, L ; Benigeri, M ; Zunzunegui M. (2003) Illicit drug use and injection practices among drug users on methadone and buprenorphine maintenance treatment in France. *Addiction* 2003 Nov; 98(11):1585-1597.**

**Author Address:** INSERM U88, Hopital National de Saint-Maurice, 14 rue du Val d'Osne, 94415 Saint-Maurice Cedex, France, email: anne.guichard@st-maurice.inserm.fr

**Abstract:** A cross-sectional study to evaluate the associations between methadone and high-dose buprenorphine maintenance treatment and illicit drug use and injection among drug users in France.

**ISSN:** 0965-2140

**Pub. Type:** Journal article

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; History, use and effectiveness in other countries ; Psychosocial treatment aspects

162. **Haanstra C. (1999) Alternatives to methadone offer heroin addicts options -- but in Canada? *CAMH The Journal*, vol. 2 no. 6, 1999; Nov/Dec.**

**Abstract:** Several U.S. studies have indicated that buprenorphine and LAAM are as effective as methadone. They also suppress patients' withdrawal symptoms without inducing the high someone would normally get from heroin. And they have the advantage of reducing cravings and blocking opioid-induced euphoria. However experts are divided on the need for methadone alternatives to be introduced into Canada. (For now, they are available in Canada only by making an onerous application to the Special Access Program of the Bureau of Drug Surveillance.)

**URL:**[http://www.camh.net/journal/journalv2no6/alternatives\\_methadone.html](http://www.camh.net/journal/journalv2no6/alternatives_methadone.html)

**Pub. Type:** Journal article; web document.

**Descriptors:** Canada.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence

163. **Hao W ; Zhao M. (2000) A comparative clinical study of the effect of WeiniCom, a Chinese herbal compound, on alleviation of withdrawal symptoms and craving for heroin in detoxification treatment. *J Psychoactive Drugs* 2000 Jul-Sep;32(3):277-84.**

**Author Address:** Mental Health Institute, Hunan Medical University, Changsha, Hunan, China. haowei@bigfoot.com

**Abstract:** WeiniCom is a Chinese herbal compound. The purposes of this double blind study were to evaluate (1) the efficacy of WeiniCom in reducing acute opioid withdrawal symptoms and craving, and (2) the side effects of WeiniCom, in each instance by comparing WeiniCom with Buprenorphine, an established opioid detoxification treatment agent. Forty-two heroin addicts meeting the criteria of dependence in DSM-IV were randomly assigned to two treatment groups: a WeiniCom group (21 cases), and a buprenorphine group (21 cases). The Withdrawal Symptom Rating Scale and the Craving Rating Scale were employed to assess acute withdrawal symptoms and craving for heroin, and the Side Effects Rating Scale was used to measure side effects in the 14-treatment period. Both the WeiniCom and buprenorphine treatments are well-tolerated and very safe. Overall, the relief from opioid withdrawal symptoms and craving was better in the WeiniCom group than in the buprenorphine group. The rate of reduction in the severity of the withdrawal symptoms was faster in the WeiniCom group than in the buprenorphine group. By day nine to 10, the WeiniCom group showed very few withdrawal symptoms. In contrast, from day five on, the buprenorphine group continued to report relatively high scores for withdrawal symptoms and craving. WeiniCom demonstrated positive effects quickly, and required a shorter treatment period to achieve a desired degree of elimination of acute withdrawal symptoms and craving.

**ISSN:** 0279-1072.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Animal ; Buprenorphine/adverse effects/\*therapeutic use ; Comparative Study ; Demography ; Drugs, Chinese Herbal/adverse effects/\*therapeutic use ; Female ; Heroin/\*adverse effects ; Human ; \*Motivation ; Narcotic Antagonists/adverse effects/\*therapeutic use ; Substance Withdrawal Syndrome/\*drug therapy ; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacology ; Pharmacotherapy for opiate dependence

164. **Harris D ; Jones R ; Welm S ; Upton R ; Lin E ; Mendelson J. (2000) Buprenorphine and naloxone co-administration in opiate-dependent patients stabilized on sublingual buprenorphine. *Drug Alcohol Depend* 2000 Dec 22;61(1):85-94.**

**Author Address:** Drug Dependence Research Center, Langley Porter Psychiatric Institute, and Department of Biopharmaceutical Sciences, University of California, San Francisco, 401 Parnassus Avenue, 94143-0984, San Francisco, CA 94143-0984, USA.

**Abstract:** Buprenorphine and naloxone sublingual (s.l.) dose formulations may

decrease parenteral buprenorphine abuse. We evaluated pharmacologic interactions between 8 mg s.l. buprenorphine combined with 0, 4, or 8 mg of naloxone in nine opiate-dependent volunteers stabilized on 8 mg s.l. buprenorphine for 7 days. Combined naloxone and buprenorphine did not diminish buprenorphine's effects on opiate withdrawal nor alter buprenorphine bioavailability. Opiate addicts stabilized on buprenorphine showed no evidence of precipitated opiate withdrawal after s.l. buprenorphine-naloxone combinations. Buprenorphine and naloxone bioavailability was approximately 40 and 10%, respectively. Intravenous buprenorphine and naloxone produced subjective effects similar to those of s.l. buprenorphine and did not precipitate opiate withdrawal.

**ISSN:** 0376-8716.

**Pub Type:** Clinical Trial ; Controlled Clinical Trial ; Journal Article. **Descriptors:** Administration, Sublingual ; Adult ; Blood Pressure/drug effects ; Buprenorphine/administration & dosage/pharmacology/\*therapeutic use ; Female ; Heart Rate/drug effects ; Human ; Injections, Intravenous ; Male ; Naloxone/administration & dosage/pharmacology/\*therapeutic use ; Narcotic Antagonists/administration & dosage/pharmacology/\*therapeutic use ; Opioid-Related Disorders/\*rehabilitation ; Support, U.S. Gov't, P.H.S. ; Time Factors. **ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Dosing/administration ; Pharmacology ; Pharmacotherapy for opiate dependence

165. **Hayase T ; Yamamoto Y ; Yamamoto K. (2002) Antidotal effects of buprenorphine on the behavioral alterations accompanying cocaine and combined cocaine-ethanol toxicity. Pharmacol Biochem Behav 2002 Jan-Feb;71(1-2):19-27.**

**Author Address:** Department of Legal Medicine, Faculty of Medicine, Kyoto University Graduate School of Medicine, Yoshidakonoe-cho, Sakyo-ku, Kyoto 606-8501, Japan. hayaselab@jweb.co.jp

**Abstract:** The present study examined the effects of buprenorphine (BUP), a mixed opioid agonist-antagonist, on the behaviors accompanying cocaine (COCA) and combined cocaine-ethanol (EtOH) toxicity in the surviving mice. Using the activity-counting instrument Supermex, the relationship between the toxic signs and the corresponding behavioral alterations could be assessed. In the COCA-only group, a prolonged increase in the activity counts was caused by a high dose of COCA (75 mg/kg ip). Furthermore, this COCA-induced hyperactivity included ataxic behaviors that were accompanied by visible toxic signs, which were not observed in the mice with no drug treatment. A depressive dose of EtOH (3 g/kg ip) did not significantly modify the mortality rate in the COCA-only group in spite of its anticonvulsant effects. However, the peak activity counts in the survivors were attenuated in the COCA-EtOH group as compared to the COCA-only group. BUP attenuated the mortality rate in both COCA and COCA-EtOH groups, even without any anticonvulsant effects, but the most effective dose differed between the COCA (BUP: 0.25 mg/kg ip) and COCA-EtOH (BUP: 0.5 mg/kg ip) groups. At these BUP doses, the prolonged suppression of the morbid hyperactivity in the COCA-BUP group and

the restoration of normal behavior in the COCA-EtOH-BUP group both seemed to be correlated with a good prognosis in the survivors; there was an early recovery from an increased blood pressure (BP), increased heart rate (HR) and decreased respiratory rate (RR) in the COCA-BUP group, and an early recovery from a decreased BP, decreased HR and decreased RR in the COCA-EtOH-BUP group.

**ISSN:** 0091-3057.

**Pub Type:** Journal Article.

**Descriptors:** Animal ; Antidotes/\*pharmacology ; Behavior, Animal/drug effects/physiology ; Buprenorphine/\*pharmacology ; Central Nervous System Depressants/toxicity ; Cocaine/\*toxicity ; Comparative Study ; Dopamine Uptake Inhibitors/toxicity ; Drug Combinations ; Ethanol/\*toxicity ; Male ; Mice ; Mice, Inbred ICR ; Motor Activity/\*drug effects/physiology ; Narcotic Antagonists/pharmacology ; Respiratory Insufficiency/chemically induced ; Seizures/chemically induced/mortality.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Dosing/administration ; Pharmacology

166. **Heading C. (2003) Recent advances against substance abuse. IDrugs (Investigational Drugs) 6(7):681-687, 2003.**

**Abstract:** Pharmacotherapy for substance abuse is rarely offered to willing recipients without some form of psychosocial support. Pharmacotherapy must match the needs of the patient at the time it is offered, as patients often progress through one or more cycles of use and abstinence. Increasingly, long-acting formulations of agonists and antagonists are being developed as substitution or relapse-prevention products, respectively, in order to aid compliance. Products which target use-reinforcement pathways are starting to progress through clinical trials, as are vaccines that potentially prevent the abused substance reaching the brain. For cocaine abuse, the main focus is on products targeting the dopamine reuptake system.

**ISSN:** 1369-7056.

**Pub Type:** Review article.

**Descriptors:** Pharmacology; Abuse.

**ATTC Buprenorphine Topics:** Pharmacology ; Pharmacotherapy for opiate dependence

167. **Helmus T ; Downey K ; Arfken C ; Henderson M ; Schuster C. (2001) Novelty seeking as a predictor of treatment retention for heroin dependent cocaine users. Drug Alcohol Depend 2001 Feb 1;61(3):287-95.**

**Author Address:** Research Division on Substance Abuse, Department of Psychiatry and Behavioral Neurosciences, School of Medicine, Wayne State University, 2761 E. Jefferson, Detroit, MI 48207, USA. thelmus@gopher.chem.wayne.edu

**Abstract:** This study examined the relationship between novelty seeking between treatment retention and among heroin dependent cocaine users. Participants were treated with buprenorphine maintenance and contingency

management. The Tridimensional Personality Questionnaire's (TPQ) Novelty Seeking scale was administered to 68 participants prior to buprenorphine induction. Demographics, mood and anxiety disorders, antisocial personality disorder, and substance use were also assessed. Variables with significant relationships with overall retention were entered into a logistic regression analysis. In addition, using a survival analysis, all variables with significant relationships with time to drop-out were entered into a multivariate proportional hazards regression with time dependent covariates. Results demonstrated that although high novelty seekers, in comparison to low novelty seekers, were more likely to drop-out by the end of treatment, they had higher retention rates during the early phases of treatment. It is suggested that buprenorphine and contingency management were viewed by participants as novel treatment components and thus facilitated high novelty seekers' success early in treatment. If replicated, results suggest that inclusion of novel treatment components might facilitate retention among this at-risk group.

ISSN: 0376-8716.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Age Factors ; \*Buprenorphine/therapeutic use ; Chi-Square Distribution ; Cocaine-Related Disorders/\*psychology/therapy ; Confidence Intervals ; \*Exploratory Behavior ; Female ; Heroin Dependence/\*psychology/rehabilitation ; Human ; Logistic Models ; Male ; Middle Age ; \*Narcotics/therapeutic use ; Patient Dropouts/\*psychology ; Support, Non-U.S. Gov't ; Support, U.S. Gov't, P.H.S. ; Survival Analysis ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment outcomes/effectiveness

168. **Henderson S ; Huey M ; Roman P. (2003) Substance Abuse Treatment Philosophy and the Adoption of Pharmaceutical innovations: An organizational approach. Paper presented at the annual meeting of the Southern Sociological Society, 2003.**

**Author Address:** University of Georgia, Department of Sociology, Athens GA, 30602.[e-mail: hender@arches.uga.edu]

**Abstract:** With an increase in pharmacotherapies in substance abuse treatment, it is imperative to understand the adoption of these pharmaceutical innovations, as well as clinical outcomes. The purpose of this analysis is twofold, to assess the influence of treatment philosophy on the adoption of pharmaceutical innovations, & to evaluate the extent to which the predictive models of adoption, including organizational structure, caseload & staff characteristics, & philosophy vary depending on the type of pharmacotherapy. At the organizational level, this study has implications for understanding similarities & differences in the adoption of different innovations. For the substance abuse treatment field, it provides an assessment of center characteristics that are enhancing or impeding the diffusion & adoption of these pharmaceutical innovations, & the role of treatment philosophy in this process.

The data used for this analysis is taken from nationally representative sample of

400 private substance abuse treatment centers. Onsite interviews were used to collect data on center characteristics including but not limited to organizational structure, caseload & staff characteristics, & new treatment techniques. Current use of the three general types of pharmacotherapies, antagonists, partial agonists, & agonists, by centers that reported some knowledge of them was found in varying degrees in this sample. Antagonists such as antabuse & naltrexone were used in 66% & 52% of centers respectively. The partial agonist buprenorphine was used in 28% & the agonists methadone & LAAM in 25% & 6% respectively. With such variance in adoption, it is essential to understand any organizational & philosophical differences that are influencing the adoption of these pharmaceutical innovations.

**Notes:** Request copy from author; CORK database is source of reference.

**Pub Type:** Conference presentation.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

169. **Hinton A. (2003) Pharmacy aspects of Buprenorphine (Subutex) treatment. [London] Substance Misuse Service, Central & North West London Mental Health NHS Trust, April 2003.**

**Abstract:** This is a 13-slide presentation by a pharmacist who has been prescribing Buprenorphine for approximately 2 years. The speaker discusses the procedures and criteria for supervised consumption of buprenorphine at the clinic, and then discusses take-home medication and when it should and should not be prescribed. Advantages and disadvantages of both approaches are included.

**URL:** <http://www.smmgp2.demon.co.uk/download/articles/art020.zip> (zipped)

**Pub. Type:** Powerpoint slides; web document.

**Descriptors:** training; pharmacists.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

170. **Hossain M. (2000) Injecting drug users, HIV risk behaviour and shooting galleries in Rajshahi, Bangladesh. Drug & Alcohol Review. Vol 19(4) Dec 2000, 413-417.**

**Abstract:** The purpose of this study was to investigate HIV risk behaviors of injecting drug users (IDUs) and the drug scene in Bangladesh. 64 male clients (mean age 32 yrs) of a drug treatment agency were surveyed about their drug use, drug injecting, sexual behavior, and knowledge about HIV and AIDS. All participants had injected drugs, primarily buprenorphine. The majority of participants were long-term drug users who had begun injecting drugs recently-70% had commenced injecting in the last 3 years. Sexual contact with sex workers and with casual partners was common among participants. Although most participants had heard of AIDS, few knew how HIV is transmitted. Most participants injected in groups at shooting galleries where they paid another to inject them. The shooting galleries operated without concern for hygiene or user safety. It is concluded that the potential for HIV to spread among IDUs and onto

their non-injecting sexual partners in Bangladesh is cause for concern. A rapid assessment of HIV prevalence among IDUs in Bangladesh is urged.

ISSN: 0959-5236 (Print), 1465-3362 (Electronic).

**Pub Type:** Journal Article.

**Descriptors:** HIV risk knowledge & behavior among injecting drug users, Bangladesh ; \*At Risk Populations ; \*Human Immunodeficiency Virus ; \*Intravenous Drug Usage ; \*Risk Perception ; \*Risk Taking ; Health Behavior; Human; Male; Adulthood (18 yrs & older) ; Empirical Study.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; History, use and effectiveness in other countries ; Psychosocial treatment aspects

171. **Huang P ; Kehner G ; Cowan A ; Liu-Chen L. (2001) Comparison of pharmacological activities of buprenorphine and norbuprenorphine: norbuprenorphine is a potent opioid agonist. J Pharmacol Exp Ther 2001 May;297(2):688-95.**

**Author Address:** Department of Pharmacology, Temple University Medical School, Philadelphia, Pennsylvania 19140, USA.

**Abstract:** Buprenorphine (BUP) is an oripavine analgesic that is beneficial in the maintenance treatment of opiate-dependent individuals. Although BUP has been studied extensively, relatively little is known about norbuprenorphine (norBUP), a major dealkylated metabolite of BUP. We now describe the binding of norBUP to opioid and nociceptin/orphanin FQ (ORL1) receptors, and its effects on [(35)S]guanosine-5'-O-(gamma-thio)triphosphate [(35)S]GTP gamma S binding mediated by opioid or ORL1 receptors and in the mouse acetic acid writhing test. Chinese hamster ovary cells stably transfected with each receptor were used for receptor binding and [(35)S]GTP gamma S binding. NorBUP exhibited high affinities for mu-, delta-, and kappa-opioid receptors with K(i) values in the nanomolar or subnanomolar range, comparable to those of BUP. NorBUP and BUP had low affinities for the ORL1 receptor with K(i) values in the micromolar range. In the [(35)S]GTP gamma S binding assay, norBUP displayed characteristics distinct from BUP. At the delta-receptor, norBUP was a potent full agonist, yet BUP had no agonist activity and antagonized actions of norBUP and DPDPE. At mu- and kappa-receptors, both norBUP and BUP were potent partial agonists, with norBUP having moderate efficacy and BUP having low efficacy. At the ORL1 receptor, norBUP was a full agonist with low potency, while BUP was a potent partial agonist. In the writhing test, BUP and norBUP both suppressed writhing in an efficacious and dose-dependent manner, giving A(50) values of 0.067 and 0.21 mg/kg, s.c., respectively. These results highlight the similarities and differences between BUP and norBUP, each of which may influence the unique pharmacological profile of BUP.

ISSN: 0022-3565.

**Pub Type:** Journal Article.

**Descriptors:** Acetic Acid/diagnostic use ; Adenylate Cyclase/antagonists & inhibitors ; Analgesics, Opioid/\*pharmacology ; Animal ; Buprenorphine/analogs & derivatives/\*pharmacology ; CHO Cells ; Cell Membrane/drug

effects/metabolism ; Comparative Study ; Forskolin/pharmacology ; Guanosine 5'-O-(3-Thiotriphosphate)/metabolism ; Hamsters ; Mice ; Pain Measurement/drug effects ; Receptors, Opioid/\*agonists/antagonists & inhibitors/biosynthesis ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Pharmacology

172. **Husbands S ; Lewis J. (2003) Opioid ligands having delayed long-term antagonist activity: potential pharmacotherapies for opioid abuse. Mini Rev Med Chem 2003 Mar;3(2):137-44.**

**Author Address:** Department of Pharmacy and Pharmacology, University of Bath, UK. S.M.Husbands@bath.ac.uk

**Abstract:** Buprenorphine is a partial agonist at the micro-opioid receptor with long duration of action and also exhibits delayed antagonist activity. Buprenorphine is finding increasing use as a treatment agent for opioid abuse, though its low efficacy is not well tolerated by all addicts. There is interest in developing a higher efficacy version of buprenorphine and in this mini-review some of the ligands recently discovered, that share with buprenorphine a profile of agonism followed by delayed antagonism, are discussed.

ISSN: 1389-5575.

**Pub Type:** Journal Article; Literature Review.

**Descriptors:** Analgesics, Opioid/chemistry/\*pharmacology/therapeutic use ; Animal ; Buprenorphine/adverse effects/chemistry/\*pharmacology/ therapeutic use ; Drug Evaluation, Preclinical ; Etorphine/\*analogs & derivatives/chemistry/pharmacology ; Human ; Hydromorphone/analogs & derivatives/pharmacology ; Ligands ; Morphinans/chemistry/pharmacology ; Narcotic Antagonists/chemistry/\*pharmacology/therapeutic use ; Receptors, Opioid, mu/agonists/\*antagonists & inhibitor ; Structure-Activity Relationship; Substance-Related Disorders/\*drug therapy.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Pharmacology ; Pharmacotherapy for opiate dependence

173. **Hylar S ; Tahil F. (2002) APA Online CME: Buprenorphine for office-based treatment of opiate dependent patients. Journal of Psychiatric Practice 2002 Nov; 8(6):393-397.**

**Abstract:** Reviews the American Psychiatric Association online CME training program Buprenorphine for Office-Based Treatment of Opiate Dependent Patients. It is concluded that the site is easy to access and user friendly. It is suggested that for any psychiatrist interested in obtaining certification for office-based treatment of opiate addicted patients, this program serves as a reasonable alternative to taking an in-person course.

ISSN: 1527-4160 (Print).

**Pub Type:** Journal Article.

**Descriptors:** American Psychiatric Association; online CME training program; buprenorphine; office-based treatment; opiate dependence ; \*Computer Assisted Instruction ; \*Continuing Education ; \*Drug Dependency; \*Outpatient Treatment ; \*Psychiatric Training ; Analgesic Drugs ; Professional

Organizations ; Psychiatry.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

174. **Infant Development Center, Women & Infants Hospital (Rhode Island)]. (2003) Methadone and Buprenorphine: Ante- and Post-partum. Report of research study conducted at Infant Development Center, Rhode Island, 2003. (complete as cited here).**

**Author Address:** Women & Infants Hospital, 101 Dudley Street, Providence, RI, 02905 (tel) 401-274-1100, email:wihinfo@wihri.org

**Abstract:** Approximately 1/3 of opioid addicts are women of child-bearing age. Compared to non-drug exposed infants, opioid exposed infants have longer and more costly neonatal hospitalizations and display neurophysiological and behavioral disruption. It is estimated that 55%-94% of infants exposed to opioids in utero will show signs of opioid withdrawal. Methadone is the only medication currently recommended for the treatment of pregnant opioid-dependent women. Buprenorphine offers the potential of providing benefits comparable to methadone with fewer medical problems. Buprenorphine is reported to produce only a mild abstinence syndrome following abrupt withdrawal. This pilot feasibility study will enroll 45 subjects (15 maintained on buprenorphine, 15 maintained on methadone, and 15 non-drug using) over 3 years and will provide additional efficacy and safety for buprenorphine in this special population of opioid dependent women. The study sites will be located in the New Bedford, Massachusetts area where heroin use in pregnant women is a significant and an increasing problem. Currently, the methadone doses in this area are high and there is concern by the pregnant women and their clinicians over the effects of methadone on the baby. The specific objectives of this pilot, open-label study are to determine the: 1) number and characteristics of pregnant women who can be enrolled; 2) ability of an additional site to adopt elements from the ongoing double-blind, randomized clinical trial; 3) elements necessary to develop the infrastructure for a future randomized clinical trial; 4) neurobehavioral outcome of the fetus and infant whose mother is maintained on buprenorphine, methadone or no drug during her pregnancy; and to provide additional data relative to the: 1) safety and efficacy of buprenorphine in pregnant opioid dependent women and their fetus; and 2) magnitude and duration of any neonatal abstinence syndrome observed in the infant exposed to buprenorphine and methadone in utero.

**URL:** <http://www.womenandinfants.org/body.cfm?id=452#section5>

**Pub. Type:** Web page ; report of research study in progress.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Special populations ; Pharmacology ; Dosing/administration

175. **International Center for Advancement of Addiction Treatment. Opiate Addiction Rx: Information for Physicians Worldwide Web site.**

**Abstract:** The mission of The International Center for Advancement of Addiction Treatment is to promote among medical professionals the humane

treatment of people who are living with opioid addiction by making available to healthcare providers relevant medical, legal and policy information and by advocating for change in attitudes that constrain optimal treatment delivery. A search of the ICAAT web site found 105 hits, with summaries and commentary on articles and news stories about opioid treatment.

**Pub. Type:** Web site, almost a Web Log (blog) about buprenorphine.

**URL:** <http://www.opiateaddictionrx.info>

**ATTC Buprenorphine Topics:** Legal/regulatory issues; Pharmacotherapy for opiate dependence

176. **Jacobs E ; Bickel W. (1999) Precipitated withdrawal in an opioid-dependent outpatient receiving alternate-day buprenorphine dosing. Addiction 1999 Jan;94(1):140-1.**

**Abstract:** Due to its pharmacological profile, buprenorphine, a high-affinity partial mu-agonist, can precipitate withdrawal syndrome in physically dependent individuals under some circumstances (Strain et al, 1995; Walsh et al, 1995). Buprenorphine-precipitated withdrawal may result from its low intrinsic agonist activity, coupled with its relatively high affinity for mu-receptors. When receptor occupancy by full-agonist opiates is high, buprenorphine may displace the full-agonist, resulting in an overall decrease in agonist activity and precipitated withdrawal. Although precipitated withdrawal may reduce the abuse liability of buprenorphine, such an effect may also prove to be a barrier to the initiation of continuation of treatment. We have recently observed an instance of buprenorphine-precipitated withdrawal that provides significant implications for the applicability of alternate-day buprenorphine dosing.

**ISSN:** 0965-2140.

**Pub Type:** Letter.

**Descriptors:** Adult ; Buprenorphine/\*adverse effects ; Case Report ; Female ; Human ; Narcotic Antagonists/\*adverse effects ; Opioid-Related Disorders/\*rehabilitation ; Substance Withdrawal Syndrome/\*etiology.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacology ; Pharmacotherapy for opiate dependence

177. **Jaffe J ; O'Keeffe C. (2003) From morphine clinics to buprenorphine: regulating opioid agonist treatment of addiction in the United States. Drug Alcohol Depend 2003 May 21;70(2 Suppl):S3-S11.**

**Author Address:** Department of Psychiatry, Division of Alcohol and Drug Abuse, University of Maryland School of Medicine, 701 West Pratt Street, 21201, Baltimore, MA, USA

**Abstract:** The practice of prescribing opioid drugs for opioid dependent patients in the U.S. has been subjected to special government scrutiny for almost 100 years. From 1920 until 1964, doctors who used opioids to treat addicts risked federal and/or state criminal prosecution. Although that period ended when oral methadone maintenance was established as legitimate medical practice, public concern about methadone diversion and accidental

overdose fatalities, combined with political pressure from both hostile bureaucracies and groups committed to drug-free treatments, led to the development of unprecedented and detailed Food and Drug Administration (FDA) regulations that specified the manner in which methadone (and later, levo-alpha-acetyl methadol, or levomethadyl acetate, (LAAM)) could be provided. In 1974, Congress gave the Drug Enforcement Administration (DEA) additional oversight of methadone treatment programs. Efforts to liberalize the FDA regulations over the past 30 years have been resisted by both the DEA and existing treatment providers. Additional flexibility for clinicians may evolve from the most recent effort to create an accreditation system to replace some of the FDA regulations. The development of buprenorphine, a partial opioid agonist, as an effective treatment for opioid addiction reopened the possibility for having a less burdensome oversight process, especially because of its reduced toxicity if ingested by non-tolerant individuals. New legislation, the Drug Addiction Treatment Act (DATA) of 2000, created an opportunity for clinicians with special training to be exempted from both federal methadone regulations and the requirement to obtain a special DEA license when using buprenorphine to treat addicts. Some details of how the DATA was developed, moved through Congress, and signed into law are described.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article ; Overview.

**Descriptors:** buprenorphine; methadone maintenance; office-based pharmacotherapy; opioid agonists; regulations; treatment; history; policy.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

178. **Jia Y. (2001) Effect of methadone plus buprenorphine on the alleviation of heroin withdrawal symptoms. Chinese Journal of Clinical Psychology. Vol 9(1) 2001, 60-62. [abstract only]**

**Author Address:** Clinical Psychological Research Ctr.

**Abstract:** Studied the effect of methadone plus buprenorphine on the treatment of heroin withdrawal symptoms. Ss were 120 patients with heroin withdrawal symptoms (according to the criteria of the Mental Disorders-IV (DSM-IV)) in detoxification treatment in Guangzhou, China, between December, 1998 and August, 1999. Ss were divided into a methadone plus buprenorphine group (60 Ss), using methadone in the first 4 days (20-60 mg/day reducing to 5-10 mg/day) and buprenorphine in 5-8 days and a buprenorphine alone group for a 8-9 day treatment (using doses of 0.90, 1.20, 0.90, 0.75, 0.60, 0.45, 0.30, and 0.15 mg/day for the Ss with mild or moderate symptom and 0.90, 1.20, 1.20, 0.90, 0.75, 0.60, 0.45, 0.30, and 0.15 mg/day for Ss with severe symptoms). The effects were assessed with 23 indexes of symptoms and a urine test measured by an enzyme analysis instrument. The results show that Ss in the methadone plus buprenorphine group had fewer withdrawal symptoms in the 1st 4 days and considered the combined treatment more acceptable. The results prove methadone plus buprenorphine to be a favorable treatment that improves the short-term detoxification success rate especially for Ss with severe symptoms.

**ISSN:** 1005-3611 (Print).

**Pub Type:** Journal Article (Chinese) with English abstract

**Descriptors:** methadone & buprenorphine treatment; heroin withdrawal symptoms; detoxification treatment ; \*Drug Interactions ; \*Drug Withdrawal ; \*Heroin Addiction ; \*Methadone ; \*Narcotic Agonists ; Detoxification ; Drug Therapy ; Symptoms ; Human ; Empirical Study.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence

179. **Johnson R. (2001) Buprenorphine: clinical use from maintenance to special populations. Research and Clinical Forums 2001;23(1):25-41.**

**Abstract:** Buprenorphine has only recently been licensed for the treatment of opioid-dependent patients in Australia; however, there is a wealth of data available worldwide supporting its safety and efficacy in this indication. Four recent American studies have provided further support for the use of buprenorphine in the maintenance of opioid-dependent individuals using less than daily dosing protocols, in dose taper and transfer to naltrexone, and in the maintenance of opioid-dependent pregnant women. While the majority of American studies have compared buprenorphine with methadone for efficacy in maintenance therapy. LAAM and buprenorphine have not previously been directly compared. The data presented here compare all three treatments and show thrice-weekly buprenorphine and LAAM provide effective maintenance therapy comparable to daily high-dose methadone and superior efficacy to daily low-dose methadone. In reviewing two pilot studies, buprenorphine dose taper is also shown to be associated with mild withdrawal symptomatology and to allow a shortening of the window between the cessation of agonist treatment and the initiation of low-dose naltrexone therapy. In a further pilot study, buprenorphine treatment of three pregnant women is shown to be associated with a limited form of neonatal abstinence syndrome (NAS) with tremor, hyperactive Moro and sleeping less than 3 hours after feeding being the three major symptoms. The expression of NAS in these infants was sufficiently mild that it did not require treatment. Acoustic cry analysis of 30 cry samples, assessed by a non-blind investigator, did not indicate that the infants were experiencing withdrawal.

**ISSN:** 0143-3083.

**Notes:** Journal not readily available.

**Pub Type:** journal article.

**ATTC Buprenorphine Topics:** Dosing/administration ; Special populations ; Treatment outcomes/effectiveness

180. **Johnson R ; Chutuape M ; Strain E ; Walsh S ; Stitzer M ; Bigelow G. (2000) A comparison of levomethadyl acetate, buprenorphine, and methadone for opioid dependence. N Engl J Med 2000 Nov 2;343(18):1290-7.**

**Author Address:** Department of Psychiatry and Behavioral Sciences, Johns

Hopkins University School of Medicine, Baltimore, MD 21224, USA.

**Abstract:** BACKGROUND: Opioid dependence is a chronic, relapsing disorder with important public health implications. METHODS: In a 17-week randomized study of 220 patients, we compared levomethadyl acetate (75 to 115 mg), buprenorphine (16 to 32 mg), and high-dose (60 to 100 mg) and low-dose (20 mg) methadone as treatments for opioid dependence. Levomethadyl acetate and buprenorphine were administered three times a week. Methadone was administered daily. Doses were individualized except in the group assigned to low-dose methadone. Patients with poor responses to treatment were switched to methadone. RESULTS: There were 55 patients in each group; 51 percent completed the trial. The mean (+/-SE) number of days that a patient remained in the study was significantly higher for those receiving levomethadyl acetate (89+/-6), buprenorphine (96+/-4), and high-dose methadone (105+/-4) than for those receiving low-dose methadone (70+/-4, P<0.001). Continued participation was also significantly more frequent among patients receiving high-dose methadone than among those receiving levomethadyl acetate (P=0.02). The percentage of patients with 12 or more consecutive opioid-negative urine specimens was 36 percent in the levomethadyl acetate group, 26 percent in the buprenorphine group, 28 percent in the high-dose methadone group, and 8 percent in the low-dose methadone group (P=0.005). At the time of their last report, patients reported on a scale of 0 to 100 that their drug problem had a mean severity of 35 with levomethadyl acetate, 34 with buprenorphine, 38 with high-dose methadone, and 53 with low-dose methadone (P=0.002). CONCLUSIONS: As compared with low-dose methadone, levomethadyl acetate, buprenorphine, and high-dose methadone substantially reduce the use of illicit opioids.

ISSN: 0028-4793.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Analgesics, Opioid/adverse effects/\*therapeutic use ; Buprenorphine/adverse effects/\*therapeutic use ; Cocaine-Related Disorders/complications ; Comparative Study ; Double-Blind Method ; Drug Administration Schedule ; Female; Human ; Male ; Methadone/administration & dosage/adverse effects/\*therapeutic use ; Methadyl Acetate/adverse effects/\*therapeutic use ; Middle Age ; Narcotics/urine ; Opioid-Related Disorders/complications/\*drug therapy ; Support, Non-U.S. Gov't ; Support, U.S. Gov't, P.H.S. ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

181. **Johnson R ; Jones H ; Fischer G. (2003) Use of buprenorphine in pregnancy: Patient management and effects on the neonate. Drug Alcohol Depend 2003;70(2 Suppl):S87-S101.**

**Author Address:** Behav. Pharmacology Research Unit, Dept. of Psychiat./Behav. Sciences, Johns Hopkins Univ. Sch. of Medicine, Baltimore, MD 21224

**Abstract:** It is estimated that 55-94% of infants born to opioid-dependent mothers in US will show signs of opioid withdrawal. Buprenorphine has been

reported to produce little or no autonomic signs or symptoms of opioid withdrawal following abrupt termination in adults. To date, there have been 21 published reports representing approximately 15 evaluable cohorts of infants exposed to buprenorphine in utero. Of approximately 309 infants exposed, a neonatal abstinence syndrome (NAS) has been reported in 62% infants with 48% requiring treatment; apparently greater than 40% of these cases are confounded by illicit drug use. The NAS associated with buprenorphine generally appears within 12-48 h, peaks at approximately 72-96 h, and lasts for 120-168 h. These results appear similar to or less than that observed following in utero exposure to methadone. From a review of the literature, buprenorphine appears to be safe and effective in both mother and infant with an NAS that may differ from methadone both qualitatively and quantitatively

ISSN: 0376-8716.

**Pub Type:** Review article.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Special populations

182. **Johnson R ; Jones H ; Jasinski D ; Svikis D ; Haug N ; Jansson L ; Kissin W ; Alpan G ; Lantz M ; Cone E ; Wilkins D ; Golden A ; Huggins G ; Lester B. (2001) Buprenorphine treatment of pregnant opioid--dependent women: maternal and neonatal outcomes. Drug Alcohol Depend 2001 Jun 1;63(1):97-103.**

**Author Address:** Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Johns Hopkins Bayview Medical Center, Baltimore, MD 21224-6823, USA.

**Abstract:** This open-label prospective study examined maternal and neonatal safety and efficacy outcome measures during and following prenatal buprenorphine exposure. Three opioid-dependent pregnant women received 8 or 12 mg sublingual buprenorphine tablets daily for 15-16 weeks prior to delivery. Results showed that buprenorphine in combination with comprehensive prenatal care was safe and effective in these women. Prenatal exposure to buprenorphine resulted in normal birth outcomes, a mean of 4.33 days (minimum possible=4) hospitalization, and a 'relatively mild' neonatal abstinence syndrome comprised primarily of tremors (disturbed), hyperactive Moro and shortened sleep after feeding. The infants required no pharmacological treatment. Onset of neonatal abstinence signs occurred within the first 12 h after birth, peaked by 72 h and returned to below pre-12 h levels by 120 h. It is concluded that buprenorphine has potential utility for the treatment of pregnant opioid-dependent women.

ISSN: 0376-8716.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Buprenorphine/administration & dosage/\*therapeutic use ; Female ; Health Status ; Human ; Infant ; Narcotic Antagonists/administration & dosage/\*therapeutic use ; Opioid-Related Disorders/\*drug therapy ; Pregnancy ; \*Pregnancy Complications ; \*Pregnancy Outcome ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for

opiate dependence ; Prevalence of use for opiate dependence ; Special populations

**183. Johnson R ; McCagh J. (2000) Buprenorphine and naloxone for heroin dependence. Curr Psychiatry Rep 2000 Dec;2(6):519-26.**

**Author Address:** Johns Hopkins University School of Medicine, Department of Psychiatry and Behavioral Sciences, 5510 Nathan Shock Drive, Baltimore, Maryland 21224, USA. rejohnso@jhmi.edu

**Abstract:** The pharmacology of buprenorphine is unique because of its partial agonist profile at the mu-opioid receptor (ie, high affinity, low intrinsic activity and slow dissociation). This unique profile results in greater safety, less physical dependence, and greater flexibility in dose scheduling. Buprenorphine has been investigated in combination with the opioid antagonist, naloxone, with the goal of decreasing abuse, misuse, and diversion. When combined with naloxone in a sublingual tablet, buprenorphine has been shown to be effective 1) in retaining patients in treatment, 2) in reducing opioid use and craving, and 3) when dosed less-than-daily. The pharmacologic effects of buprenorphine are not altered by the addition of naloxone when administered to the population in an appropriate combination ratio. However, if taken intravenously by individuals dependent on short- or long-acting opioids a precipitated withdrawal syndrome is observed, which should reduce its abuse potential. This review discusses the rationale for development and evidence supporting the use of a buprenorphine/naloxone combination product. The buprenorphine/naloxone combination product should be considered for use in primary care office-based settings as a safe and effective treatment that is likely to increase the availability of agonist treatment for opioid dependence.

**ISSN:** 1523-3812.

**Pub Type:** Journal Article ; Review ; Review, Tutorial.

**Descriptors:** Buprenorphine/adverse effects/\*therapeutic use ; Clinical Trials ; Heroin Dependence/\*rehabilitation ; Human ; Naloxone/adverse effects/\*therapeutic use ; Narcotic Antagonists/adverse effects/\*therapeutic use.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Combined treatment with other therapeutic medications ; Pharmacology ; Pharmacotherapy for opiate dependence

**184. Johnson R ; Strain E ; Amass L. (2003) Buprenorphine: how to use it right. Drug Alcohol Depend 2003 May 21;70(2 Suppl):S59-77.**

**Author Address:** Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, 5510 Nathan Shock Drive, 21224, Baltimore, MD, USA

**Abstract:** The unique pharmacology of buprenorphine at the mu-opioid receptor (i.e. high affinity, low intrinsic activity and slow dissociation) results in buprenorphine having: (1) a good safety profile, (2) low physical dependence, and (3) flexibility in dose scheduling. Early studies assessed the effectiveness of buprenorphine for the treatment of opioid dependence using a sublingual solution formulation. More recently, a combination tablet

(buprenorphine/naloxone in a 4:1 ratio) has been assessed with the goal of decreasing diversion and abuse. Controlled studies with buprenorphine solution, buprenorphine mono-tablet, and buprenorphine/naloxone combination tablet have uniformly demonstrated the effectiveness of buprenorphine for opioid dependence treatment and the combination tablet appears to decrease (but not eliminate) abuse potential. There is general agreement across studies regarding buprenorphine induction and maintenance dose schedules. The clinical effects of buprenorphine and buprenorphine/naloxone are similar and most patients can be treated initially with and maintained on a daily buprenorphine/naloxone dose of 4:1-24:6 mg. Dosing is possible on a less-than-daily schedule; however, multiples of the daily-dose should be administered to cover the increased interval between doses. If buprenorphine withdrawal is indicated, gradual dose reduction is recommended over a rapid dose reduction or abrupt cessation. Both tablet formulations are approved by the US FDA for opioid dependence treatment as Schedule III narcotics and are, therefore, available for use in office-based practice. The buprenorphine plus naloxone combination product should provide additional safeguards for use in office-based practice by decreasing risk of diversion, and office-based treatment should expand the availability of services to opioid dependent patients.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

**185. Join Together. (2003) National Poll of Physicians on Barriers to Widespread Buprenorphine Use. Join Together, October 2003.**

**Abstract:** In the summer of 2003, Join Together, a project of the Boston University School of Public Health, conducted a brief poll of physicians who are qualified to prescribe buprenorphine for opioid addiction. The intent was to learn about the availability and use of the medication following the FDA's approval of office-based treatment. Join Together was interested in finding out directly from authorized physicians what barriers, if any, are preventing further use and their overall impressions and experiences. Results of the survey indicated that most physicians seem optimistic about buprenorphine, and many of the physicians who are not yet prescribing indicated that they planned to start treating patients with the medication soon.

**URL:** <http://www.jointogether.org/sa/files/pdf/bupereport.pdf>

**Pub. Type:** web document ; PDF.

**ATTC Buprenorphine Topics:** Psychosocial treatment aspects ; Pharmacotherapy for opiate dependence ; Legal/regulatory issues

**186. Join Together. Hot Issue: Buprenorphine. Join Together web site (ongoing).**

**Abstract:** This section of the Join Together web site focuses on the "hot issue"

of Buprenorphine; it conveniently pulls together news items, resources such as the Physician Locator, and selected web sites with information on buprenorphine.

**URL:** [http://www.jointogether.org/sa/issues/hot\\_issues/bupe/](http://www.jointogether.org/sa/issues/hot_issues/bupe/)

**Pub. Type:** web site.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Psychosocial treatment aspects ; Treatment outcomes/effectiveness

187. **Jones H ; Johnson R (Symposium Chairs) (2003) How Far have We Come Baby? The Current Knowledge about Exposure to Buprenorphine during Pregnancy and Lactation [symposium]. CPDD Annual Meeting 2003, Symposium VI, June 16, 2003.**

**Abstract:** This site notes a symposium (poster session?) on buprenorphine and pregnancy & lactation at the 2003 CPDD annual meeting; the speakers/titles are listed on the conference website, but abstracts are not included. Listed are (1) Ahmed, "Placental Transfer and Metabolism of Buprenorphine and LAAM;" (2) Fischer, "Neonatal outcome After Buprenorphine Treatment at Conception — Clinical and Pharmacokinetic Features;" and (3) Finnegan, "Are We There Yet?"

**URL:** [http://biopsych.com:81/CPDD03\\_Web/FMPPro](http://biopsych.com:81/CPDD03_Web/FMPPro)

**Pub. Type:** web document; conference poster.

**ATTC Buprenorphine Topics:** Pharmacology ; Special populations

188. **Karger S ; Backmund M ; Walcher S ; Soyka M. (2002) Buprenorphine maintenance treatment and driving performance – Results of an experimental study. Suchtmedizin in Forschung und Praxis 4(1):17-24. [abstract only]**

**Abstract:** Buprenorphine has become an attractive alternative to methadone in the treatment of opioid dependence because of its unique psychopharmacology. Only a few studies so far have tested the influence of buprenorphine on subjects' psychomotor functioning, especially with regard to driving performance. In the laboratory, driving performance is tested with computer aided tests, which measure the subject's visual perception, attention span and reaction response behavior. We examined driving performance in 27 opioid-dependent out-patients under buprenorphine in our laboratory. Data of these subjects were compared with a similar study of our work-group (n = 28) (Dittert, Naber, Soyka, *Der Nervenarzt* 1999, Vol. 5, 457-462). In three of five psychomotor tests subjects under buprenorphine achieved significant higher scores than subjects under methadone treatment. Additional tests revealed no differences. Overall, our data suggest a better psychomotor functioning under buprenorphine compared to methadone. Thus, maintenance treatment with buprenorphine does not seem to impair driving fitness in general.

**ISSN:** 1437-5567.

**Pub Type:** journal article (GERMAN) with English abstract.

**Descriptors:** Clinical Study; Dependence; Treatment; Human; Driving.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Pharmacology ;

Pharmacotherapy for opiate dependence

189. **Kakko J ; Svanborg K ; Kreek M ; Heilig M. (2003) 1-year retention and social function after buprenorphine-assisted relapse prevention treatment for heroin dependence in Sweden: a randomised, placebo-controlled trial. Lancet 2003 Feb 22;361(9358):662-8.**

**Author Address:** Division of Psychiatry, Neurotec, Karolinska Institute, Huddinge University Hospital, S-141 86, Stockholm, Sweden.

**Abstract:** BACKGROUND: The partial opiate-receptor agonist buprenorphine has been suggested for treatment of heroin dependence, but there are few long-term and placebo-controlled studies of its effectiveness. We aimed to assess the 1-year efficacy of buprenorphine in combination with intensive psychosocial therapy for treatment of heroin dependence. METHODS: 40 individuals aged older than 20 years, who met DSM-IV criteria for opiate dependence for at least 1 year, but did not fulfil Swedish legal criteria for methadone maintenance treatment were randomly allocated either to daily buprenorphine (fixed dose 16 mg sublingually for 12 months; supervised daily administration for at least 6 months, possible take-home doses thereafter) or a tapered 6 day regimen of buprenorphine, thereafter followed by placebo. All patients participated in cognitive-behavioural group therapy to prevent relapse, received weekly individual counselling sessions, and submitted thrice weekly supervised urine samples for analysis to detect illicit drug use. Our primary endpoint was 1-year retention in treatment and analysis was by intention to treat. FINDINGS: 1-year retention in treatment was 75% and 0% in the buprenorphine and placebo groups, respectively (p=0.0001; risk ratio 58.7 [95% CI 7.4-467.4]). Urine screens were about 75% negative for illicit opiates, central stimulants, cannabinoids, and benzodiazepines in the patients remaining in treatment. INTERPRETATION: The combination of buprenorphine and intensive psychosocial treatment is safe and highly efficacious, and should be added to the treatment options available for individuals who are dependent on heroin.

**ISSN:** 0140-6736.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Buprenorphine/\*therapeutic use ; Counseling ; Female ; Heroin Dependence/classification/\*drug therapy/prevention & control ; Human; Male ; Narcotic Antagonists/\*therapeutic use ; \*Psychotherapy, Group ; Severity of Illness Index ; Support, Non-U.S. Gov't ; Support, U.S. Gov't, P.H.S. ; Sweden ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment outcomes/effectiveness

190. **Kastelic A ; Scott R ; (editors). (1998) Buprenorphine: Current Perspectives; Proceedings from a symposium at the European Opiate Addiction Treatment Association meeting, "Heroin Addiction in Europe." European Addiction Research 1998 Oct;4(Suppl 1): S1-S36 [special issue].**

**Abstract:** Proceedings from a conference held in Ljubljana, Slovenia,

September 17-20, 1997. Individual papers are included in this bibliography. The Symposium editors conclude that in light of the evidence from buprenorphine trials in the US, France, and Switzerland, the expansion of buprenorphine treatment for opioid addiction into more countries seems inevitable and should be welcomed.

**Pub Type:** Journal supplement [whole issue].

**Descriptors:** Substitution Therapy; \*Opiate Addiction ; Drug Dependence ; Heroin Dependence ; Doctor Patient Relation ; Pregnancy ; Drug Withdrawal \*Buprenorphine.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence

191. **Kayemba-Kay's, S ; Laclede, JP. (2003) Buprenorphine withdrawal syndrome in newborns: a report of 13 cases. Addiction 2003 Nov; 98(11):1599-1604.**

**Author Address:** Unite de Neonatologie et Soins Intensifs Neonatals, Service de Pediatrie, Centre Hospitalier Universitaire de Poitiers, Rue de la Miletrie, BP 577-F 86021, Poitiers cedex, France, Email: k.kayemba-kays@chu-poitiers.fr

**Abstract:** To assess neonatal abstinence syndrome (NAS) and neurodevelopmental outcome in infants born to addicted mothers under buprenorphine substitution therapy. Buprenorphine substitution seems to be safe during pregnancy, and has had no teratogenic effects reported to date.

**ISSN:** 0965-2140

**Pub. Type:** Journal article

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacology ; Special populations

192. **Khan F ; Memon G ; Kamal R. (2002) Effect of route of buprenorphine on recovery and postoperative analgesic requirement in paediatric patients. Paediatric Anaesthesia 2002; 12(9): 786-790.**

**Author Address:** Department of Anaesthesia, Aga Khan University Hospital (AKUH), Karachi; Pakistan.

**Abstract:** Background: We compared the effects of extradural with intravenous (i.v.) buprenorphine on postoperative pain and recovery characteristics.

Methods: Thirty patients, aged 11-13 years, who were undergoing inguinal hernia repair with or without orchidopexy, were randomly allocated to receive either caudal 0.5% bupivacaine alone (group A) or were additionally given i.v. buprenorphine 2.5 [mu]g[middle dot]kg<sup>-1</sup> (group B) or caudal buprenorphine in the same dose (group C). Patients were followed for 8 h after the end of surgery. Results: All patients remained haemodynamically stable during the study period and no clinical respiratory depression was seen. Nausea, vomiting, urinary retention and pruritus were more common in the extradural buprenorphine group. Three patients in group A, five in group B and eight in group C did not require any additional analgesia during the study period. The incidence of vomiting was 20%, 50% and 80% in groups A, B and C, respectively. Four patients in group C had urinary retention compared with one

each in the other two groups. Conclusions: Administration of buprenorphine resulted in a higher incidence of side-effects.

**ISSN:** 1155-5645.

**Pub Type:** journal article.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pain management ; Special populations

193. **Kilicarslan T ; Sellers E. (2000) Lack of interaction of buprenorphine with flunitrazepam metabolism. Am J Psychiatry 2000 v.157(7):1164-6.**

**Author Address:** Department of Pharmacology, University of Toronto, Ontario, Canada.

**Abstract:** OBJECTIVE: The authors' goal was to determine if the reported clinical adverse interaction of flunitrazepam and buprenorphine was caused by inhibition of drug metabolism. METHOD: Inhibition of flunitrazepam metabolism by buprenorphine and norbuprenorphine were determined in three human liver microsome preparations carrying the CYP2C19\*1/\*1 allele. Omeprazole metabolism mediated by CYP2C19 and CYP3A4 was used as a control reaction. Apparent K(i) values were determined. RESULTS: Norbuprenorphine did not inhibit the metabolism of flunitrazepam or omeprazole. Buprenorphine inhibited the formation of CYP3A4-mediated pathways of 3-hydroxyflunitrazepam and omeprazole sulfone formation (K(i) 118 and 16 microM) in human liver microsomes. Corresponding values were 38 and 90 microM in cDNA-expressed CYP3A4 microsomes. Projected in vivo inhibition of CYP3A4-mediated metabolism of flunitrazepam by buprenorphine is 0.1%-2.5%. Estimated inhibition of buprenorphine N-dealkylation by flunitrazepam in vivo is 0.08%. CONCLUSIONS: The clinical interaction of flunitrazepam and buprenorphine is likely based on a pharmacodynamic mechanism.

**ISSN:** 0002-953X.

**Pub Type:** Journal Article.

**Descriptors:** Buprenorphine/analogs & derivatives/\*pharmacokinetics/pharmacology ; Cytochrome P-450 Enzyme System/metabolism ; DNA, Complementary/metabolism ; Dealkylation/drug effects; Drug Interactions; Flunitrazepam/\*metabolism /pharmacokinetics Flunitazepam/pharmacology ; Human ; Microsomes, Liver/drug effects/metabolism ; Mixed Function Oxygenases/metabolism ; Omeprazole/metabolism/pharmacokinetics/pharmacology.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Combined treatment with other therapeutic medications ; Pharmacology

194. **Kintz P. (2001) Deaths involving buprenorphine: a compendium of French cases. Forensic Sci Int 2001 Sep 15;121(1-2):65-9.**

**Author Address:** Institut de Medecine Legale, Universite Louis Pasteur (ULP), 11 rue Humann, 67000 Strasbourg, France. pascal.kintz@wanadoo.fr

**Abstract:** Buprenorphine at high dosage became available in France in 1996, as a substitution treatment for heroin addicts. Since this date, numerous deaths were attributed to this drug. This paper reports two original series of 39 and 78

fatalities involving buprenorphine observed at the Institute of Legal Medicine of Strasbourg and at 13 other French forensic centers, respectively. The files were recorded from January 1996-May 2000. The first 20 fatalities that were previously published were excluded from this epidemiological study. From these 117 subjects, 96 were male (82%). Buprenorphine and its primary metabolite norbuprenorphine were assayed in post-mortem blood by HPLC/MS (n=11 labs) or by GC/MS (n=3 labs). Blood levels for buprenorphine ranged from 0.5 to 51.0ng/ml (mean 10.2ng/ml) and 0.1 to 76ng/ml (mean 12.6ng/ml) in Strasbourg and the other centers, respectively. Blood levels for norbuprenorphine ranged from 0.2 to 47.1ng/ml (mean 8.2ng/ml) and <0.1 to 65ng/ml (mean 10.6ng/ml) in Strasbourg and the other centers, respectively. The mean values appear to be within the therapeutic range. Buprenorphine was identified in 24 of the 26 hair samples assayed in Strasbourg, at concentrations ranging from 10 to 1080pg/mg. Intravenous injection of crushed tablets, a concomitant intake of psychotropics (especially benzodiazepines and neuroleptics) and the high dosage of the buprenorphine formulation available in France appear as the major risk factors for such fatalities. In addition, two suicide-related deaths were also observed, with blood buprenorphine concentrations at 144 and 3276ng/ml.

**ISSN:** 0379-0738.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Buprenorphine/analysis/blood/\*poisoning ; Female ; \*Forensic Medicine ; France ; Hair/chemistry ; Human ; Injections, Intravenous ; Male ; Mass Fragmentography ; Narcotics/analysis/blood/\*poisoning ; Retrospective Studies ; Risk Factors ; Substance-Related Disorders/\*mortality ; Suicide.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Prevalence of use for opiate dependence ; History, use and effectiveness in other countries

**195. Kintz P. (2002) A new series of 13 buprenorphine-related deaths. Clinical Biochemistry 2002 Oct;35(7):513-6.**

**Author Address:** Institut de Medecine Legale, 11 rue Humann, 67000 Strasbourg, France. pascal.kintz@wanadoo.fr

**Abstract:** OBJECTIVES: Buprenorphine at high dosage became available in France in 1996, as a substitution treatment for heroin addicts. Since this date, numerous deaths were attributed to this drug. This paper reports a new series of 13 fatalities involving buprenorphine observed at the Institute of Legal Medicine of Strasbourg, between August 2000 to October 2001. DESIGN AND METHODS: During the mentioned period, about 800 forensic cases were screened at the laboratory. Buprenorphine and its primary metabolite norbuprenorphine were assayed in postmortem specimens by HPLC/MS. From these 13 subjects, 11 were male. Blood levels ranged from 0.3 to 7.7 ng/mL (mean 3.5 ng/mL) and 0.3 to 16.2 ng/mL (mean 2.9 ng/mL) for buprenorphine and norbuprenorphine, respectively. The mean values appear to be within the therapeutic range. CONCLUSIONS: IV injection of crushed tablets, a concomitant intake of psychotropics (especially benzodiazepines and

neuroleptics) and the high dosage of the buprenorphine formulation available in France appear as the major risk factors for such fatalities

**ISSN:** 0009-9120.

**Pub Type:** Journal Article.

**Descriptors:** Analgesics, Opioid/blood/\*poisoning ; Autopsy ; Buprenorphine/\*analogs & derivatives/blood/\*poisoning ; Death ; Drug Interactions ; Female ; Forensic Medicine/methods ; Human ; Injections, Intravenous ; Male ; Mass Fragmentography ; Poisoning/mortality ; Psychotropic Drugs/adverse effects/poisoning ; Risk Factors.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; History, use and effectiveness in other countries ; Prevalence of use for opiate dependence

**196. Kintz P ; Marquet P ; (editors). (2002) Buprenorphine Therapy of Opiate Addiction (Book). Totowa, NJ: Humana Press, 2002, 168 p.**

**Abstract:** In Buprenorphine Therapy of Opiate Addiction, participating physicians and toxicologists summarize and evaluate their experiences with five years of intensive buprenorphine therapy. They cover all aspects of its use, including the pharmacology, conditions of delivery, risks from use with other psychoactive drugs, toxicology and related deaths, as well as its testing in blood, urine, tissue, and hair. Special attention is given to comparing the long-term care of opiate-dependent patients using high-dose buprenorphine vs methadone, and to explaining the differences in treatment, administration, and delivery. The authors also describe how buprenorphine is currently prescribed and monitored in France and Australia, and review all the latest advances in analytical techniques for the determination of buprenorphine and its metabolites in biological fluids and tissues.

**ISSN:** 1-59259-282-1.

**Notes:** Also sold as E-Book (\$89.00) Read chapter abstracts online for free: <http://www.humanapress.com/BookTOC.pasp?isbn=1-59259-282-1&returntoisbn=1-59259-282-1>; In NIDA Library collection [Call no: RC 568 .O45B87 2002 ].

**Pub Type:** Book.

**Descriptors:** Pharmacokinetic;Abuse; Dependence Treatment; Pregnancy.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Dosing/administration ; History, use and effectiveness in other countries ; Pharmacology ; Pharmacotherapy for opiate dependence ; Special populations ; Treatment outcomes/effectiveness

**197. Kleber H. (2003) Pharmacologic treatments for heroin and cocaine dependence. Am J Addict 2003;12 Suppl 2:S5-S18.**

**Author Address:** Division on Substance Abuse, Columbia University, New York, NY 10032, USA. HDK3@columbia.edu

**Abstract:** Given the difficulty of achieving sustained recovery, pharmacotherapy of opioid and cocaine addiction is more effective when combined with behavioral and psychosocial approaches. Effective

pharmacotherapies for opioid dependence and withdrawal include methadone, L-alpha acetylmethadol (LAAM), naltrexone, buprenorphine, and clonidine. Treatment of cocaine addiction includes anti-craving agents, dopamine agonists or blocking agents, antidepressants, and treatment of co-morbid psychiatric disorders, but all with mixed results. In this paper, we discuss the use of medication in the context of general principles of opioid and cocaine addiction treatment. Both established medications and promising directions in pharmacotherapy will be addressed.

ISSN: 1055-0496.

**Pub Type:** Journal Article ; Overview.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

**198. Kosten T ; O'Connor P. (2003) Management of Drug and Alcohol Withdrawal. N Engl J Med 2003;348:1786-95.**

**Abstract:** Good review article of managing withdrawal, including use of opiate substitution medication. Pharmacologic treatment of drug withdrawal often involves substituting a long-acting agent for the abused drug and then gradually tapering its dosage. The desirable qualities for outpatient medications include administration by mouth, low potential for abuse and overdose, and low incidence of side effects. Adequate dosages of appropriate substitute medications are important. Patients often safely attain abstinence without pharmacologic interventions, however, and the threshold for pharmacotherapy differs among abused drugs. The need for medication is signaled by both symptoms and signs in patients withdrawing from alcohol, by severe objective signs in those withdrawing from stimulants, and by specific signs during withdrawal in those withdrawing from opioids. For patients addicted to heroin, sustained opioid stabilization is often a better treatment option than detoxification and abstinence.

ISSN: 0028-4793.

**Pub Type:** Review article.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

**199. Kosten T ; Oliveto A ; Feingold A ; Poling J ; Sevarino K ; McCance-Katz E ; Stine S ; Gonzalez G ; Gonsai K. (2003) Desipramine and contingency management for cocaine and opiate dependence in buprenorphine maintained patients. Drug Alcohol Depend 2003 Jun 5;70(3):315-25.**

**Author Address:** Department of Psychiatry, Yale University School of Medicine, VA New England MIRECC, VA Connecticut Healthcare System, 950 Campbell Avenue, Bldg. 35, West Haven, CT 06516, USA. thomas.kosten@yale.edu

**Abstract:** Co-dependence on opiates and cocaine occurs in about 60% of patients entering methadone treatment and has a poor prognosis. However, we recently found that desipramine (DMI) could be combined with buprenorphine to significantly reduce combined opiate and cocaine use among these dually

dependent patients. Furthermore, contingency management (CM) has been quite potent in reducing cocaine abuse during methadone maintenance. To test the efficacy of combining CM with these medications we designed a 12-week, randomized, double blind, four cell trial evaluating DMI (150 mg/day) or placebo plus CM or a non-contingent voucher control in 160 cocaine abusers maintained on buprenorphine (median 16 mg daily). Cocaine-free and combined opiate and cocaine-free urines increased more rapidly over time in those treated with either DMI or CM, and those receiving both interventions had more drug-free urines (50%) than the other three treatment groups (25-29%). Self reported opiate and cocaine use and depressive and opioid withdrawal symptoms showed no differences among the groups and symptom levels did not correlate with urine toxicology results. Lower DMI plasma levels (average 125 ng/ml) were associated with greater cocaine-free urines. DMI and CM had independent and additive effects in facilitating cocaine-free urines in buprenorphine maintained patients. The antidepressant appeared to enhance responsiveness to CM reinforcement.

ISSN: 0376-8716.

**Pub Type:** Journal Article.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

**200. Kosten T ; Poling J ; Oliveto A. (2003) Effects of reducing contingency management values on heroin and cocaine use for buprenorphine- and desipramine-treated patients. Addiction 2003 May;98(5):665-71.**

**Author Address:** Department of Psychiatry, Yale University School of Medicine, VA New England MIRECC, West Haven, CT 06516, USA. thomas.kosten@yale.edu

**Abstract:** AIMS: During 3 months where contingency management (CM) had an escalating value for each consecutive drug-free urine (escalating CM), cocaine- and heroin-abusing patients significantly increased drug-free urines. The 'escalating CM' was eliminated during months 4-6 to assess any reduction in drug-free urines. DESIGN: Patients who completed a 3-month, randomized, double-blind, trial evaluating CM versus non-CM and desipramine (DMI) versus placebo, had an 'escalating CM' eliminated during months 4-6. The CM and non-CM groups were compared using thrice-weekly urine samples. SETTING: Out-patient buprenorphine maintenance for 6 months. PARTICIPANTS: All 75 of the 160 original study patients who completed month 3 of the clinical trial. INTERVENTION: The 'escalating CM' was eliminated for all 3 months and during months 5 and 6 the response requirement was also increased to two and then three consecutive drug-free urines in order to obtain a voucher. MEASUREMENTS: Urine toxicology for opiates and cocaine. FINDINGS: After eliminating the 'escalating CM', the CM group showed a decline in combined opioid- and cocaine-free urines. This decline within the CM group was greater in those treated with DMI than placebo. CONCLUSIONS: Buprenorphine with DMI maintained drug abstinence after eliminating the 'escalating CM', but not after increasing the response requirement, suggesting the need for more

intensive psychosocial interventions during CM.

**ISSN:** 0965-2140.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Antidepressive Agents, Tricyclic/therapeutic use ; Behavior Control/\*methods ; Buprenorphine/therapeutic use ; Cocaine-Related Disorders/\*drug therapy/urine ; Desipramine/therapeutic use ; Double-Blind Method ; Drug Therapy, Combination ; Female ; Human ; Male ; Narcotics/therapeutic use ; Opioid-Related Disorders/\*drug therapy/urine ; Support, U.S. Gov't, Non-P.H.S. ; Support, U.S. Gov't, P.H.S. ; Token Economy; Treatment Outcome.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

201. **Kotler S. (2003) Under my tongue : the new face of the anti-addiction drug buprenorphine -- safer, easier and FDA-approved. LA Weekly, August 22-28, 2003.**

**Abstract:** For almost as long as people have been chasing the dragon, people have been trying to slay it as well. The list of heroin-addiction cures comes in all forms. Urban legend says light-bulb inventor Thomas Alva Edison came up with a multispiced detox wonder called either "Poly-Form" or "Golden Liquid Beef Tonic," the historical records being a little unclear. Just past the turn of the 19th century, two New York doctors, Alexander Lambert and Charles Towns, doled out a wondrous concoction containing the poisonous plant belladonna, among other things. There was a pre-World War II eugenic program designed to weed out the junkie bad seeds, which sounds mildly similar to the warehousing of addicts via government-approved methadone clinics or the recent suggestion that the ingestion of Tetrodotoxin, the toxin found in puffer fish, could work as well. And last year, on October 9, the FDA approved a new potion, the drug buprenorphine, for the treatment of heroin addiction.

Buprenorphine didn't start out as a heroin cure-all. It was discovered 30 years ago at a time when drug companies were rushing to fill the pharmacological gap that existed between mild analgesics like codeine and hardcore painkillers like Percocet. Buprenorphine is a wonderful dampener with an analgesic potency 20 to 30 times stronger than morphine. For this purpose, it was first sold in the United States as an injectable, under the brand name Buprenex. But before Buprenex was allowed onto the market, the FDA ordered a series of abuse liability tests, required by the DEA to ensure that any drugs capable of becoming recreationally abused are not. The results were startling. First published in a 1978 issue of *The Archives of General Psychology*, they showed that buprenorphine — a derivative of thebaine, a major constituent of opium — is a narcotic agonist-antagonist, a partial agonist or an "opioid partial agonist." Buprenorphine is more powerful than heroin — not in terms of high, but in terms of chemistry — and it binds to the same receptors in an addict's brain that opium uses. So if you're taking buprenorphine, heroin won't work. Unlike methadone, which can be (and often is) teamed up with heroin and taken as a

speedball, buprenorphine doesn't cocktail.

**URL:** <http://www.laweekly.com/ink/03/40/features-kotler.php>

**Pub. Type:** newspaper feature article; web document.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

202. **Kreek M. (2000) Methadone-related opioid agonist pharmacotherapy for heroin addiction. History, recent molecular and neurochemical research and future in mainstream medicine. Ann N Y Acad Sci 2000;909:186-216.**

**Author Address:** Laboratory of the Biology of Addictive Diseases, Rockefeller University, New York, New York 10021, USA. [kreek@mail.rockefeller.edu](mailto:kreek@mail.rockefeller.edu)

**Abstract:** In 1963, Professor Vincent P. Dole at the Rockefeller University formed a small team to develop a pharmacotherapy for the management of heroin addiction. They hypothesized that heroin addiction is a disease of the brain with behavioral manifestations, and not merely a personality disorder or criminal behavior and began to address the specific question of whether a long-acting opioid agonist could be used in the long-term maintenance treatment of heroin addiction. Over the next 35 years, many studies documented the safety, efficacy and effectiveness of methadone pharmacotherapy for heroin addiction, but Federal regulations and stigmatization of heroin addiction prevented implementation of treatment. Finally, in 1999, NIH published a report unequivocally supporting methadone maintenance pharmacotherapy for heroin addiction. Two other effective opioid agonist treatments have been developed: the even longer acting opioid agonist l-alpha-acetylmethadol (LAAM) has been approved for pharmacotherapy for heroin addiction, and still under study is the opioid partial agonist-antagonist buprenorphine-naloxone combination. A variety of studies, both laboratory based and clinical, have revealed the mechanisms of action of long-acting opioid agonists in treatment, including prevention of disruption of molecular, cellular and physiologic events and, in fact, allowing normalization of those functions disrupted by chronic heroin use. Recent molecular biological studies have revealed single nucleotide polymorphisms of the human mu opioid receptor gene; the mu opioid receptor is the site of action of heroin, the major opiate drug of abuse, analgesic agents such as morphine, and the major treatment agents for heroin addiction. These findings support the early hypotheses of our laboratory that addiction may be due to a combination of genetic, drug-induced and environmental (including behavioral) factors and also, that atypical stress responsivity may contribute to the acquisition and persistence of, as well as relapse to, use of addictive drugs. **ISSN:** 0077-8923.

**Pub Type:** Journal Article ; Review ; Review, Tutorial.

**Descriptors:** Corticotropin/secretion ; Corticotropin-Releasing Hormone/secretion ; Heroin Dependence/\*drug therapy/metabolism ; Human; Hypothalamo-Hypophyseal System/drug effects ; Methadone/pharmacology/\*therapeutic use ; Methadyl Acetate/therapeutic use ; Pituitary-Adrenal System/drug effects ; Pro-Opiomelanocortin/metabolism ; Support, Non-U.S. Gov't ; Support, U.S. Gov't, P.H.S. ; beta-

Endorphin/physiology.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacology ; Pharmacotherapy for opiate dependence

**203. Kreek M ; LaForge K ; Butelman E. (2002) Pharmacotherapy of addictions. Nat Rev Drug Discov 2002 Sep;1(9):710-26.**

**Author Address:** Laboratory of the Biology of Addictive Diseases, Rockefeller University, 1230 York Avenue, New York, New York 10021, USA.  
kreek@mail.rockefeller.edu

**Abstract:** Addiction to drugs, such as heroin, cocaine and alcohol, exacts great human and financial costs on society, but the development of pharmacotherapies for addiction has been largely neglected by the pharmaceutical industry. With advances in our understanding of the underlying biology of addictions now opening the door for the development of novel pharmacotherapies, it could be time for a reassessment of involvement in this increasingly important therapeutic area. Here, we summarize the current approved and implemented pharmacotherapeutic approaches to the treatment of addiction, and then highlight the most promising areas for future drug development from the perspective of our laboratory and our National Institutes of Health (NIH) National Institute on Drug Abuse (NIDA) Research Center.  
**ISSN:** 1474-1776.

**Pub Type:** Journal Article ; Review.

**Descriptors:** Alcoholism/\*drug therapy ; Buprenorphine/\*therapeutic use ; Human ; Methadone/\*therapeutic use ; Naltrexone/\*therapeutic use ; Narcotic Antagonists/\*therapeutic use ; Receptors, Opioid, mu/\*agonists ; Substance-Related Disorders/\*drug therapy/psychology ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence

**204. Kreek M ; Vocci F. (2002) History and current status of opioid maintenance treatments: blending conference session. J Subst Abuse Treat 2002 Sep;23(2):93-105.**

**Author Address:** The Laboratory of the Biology of Addictive Diseases, The Rockefeller University and The Rockefeller University Hospital, New York, NY 10021, USA.

**Abstract:** Opiate addiction is a chronic, relapsing disorder. Left untreated, high morbidity and mortality rates are seen. Pharmacotherapies for this disorder using mu opiate agonists (methadone and levomethadyl acetate) and partial agonists have been developed in the last 40 years. Agonist pharmacotherapy with oral methadone for the treatment of opiate dependence was developed in clinical pharmacology studies at Rockefeller University by Dole, Nyswander, and Kreek. Further studies by this laboratory and others established that moderate to high dose treatment with methadone (80-120 mg) reduced or eliminated opiate use in outpatient settings with consequent reductions in morbidity and up to 4-fold reductions in mortality. Levomethadyl acetate (LAAM), a congener of methadone, is biotransformed to active metabolites responsible for its longer duration of action. The Federal Regulations regarding

the dispensation of methadone and LAAM have recently been revised to facilitate the treatment of patients under a "medical maintenance" model. Future regulatory reform will likely involve the establishment of rules for "office based opioid treatment."

**ISSN:** 0740-5472.

**Pub Type:** Historical Article ; Journal Article ; Review. **Descriptors:** Buprenorphine/therapeutic use ; Clinical Trials ; History of Medicine, 20th Cent ; Human ; Methadone/history/\*therapeutic use ; Methadyl Acetate/history/\*therapeutic use ; Naloxone/therapeutic use ; Narcotic Antagonists/therapeutic use ; Narcotics/history/\*therapeutic use ; Opioid-Related Disorders/history/physiopathology/\*rehabilitation ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

**205. Krook A ; Brors O ; Dahlberg J ; Grouff K ; Magnus P ; Roysamb E ; Waal H. (2002) A placebo-controlled study of high dose buprenorphine in opiate dependents waiting for medication-assisted rehabilitation in Oslo, Norway. Addiction 2002 May;97(5):533-42.**

**Author Address:** Centre of Medication Assisted Rehabilitation in Oslo, Rusmiddelstaten, Oslo County, Norway.

**Abstract:** **AIMS:** To evaluate whether buprenorphine, even without additional control and psychosocial treatment and support, alleviates the problems faced by patients waiting for medication assisted rehabilitation (MAR). **DESIGN:** A randomized, double-blind, 12-week study of Subutex versus placebo without additional support as an interim therapy. **PARTICIPANTS:** One hundred and six patients, 70 males and 36 females, waiting for MAR in Oslo. The average age was 38 years with an average history of heroin use of 20 years. Fifty-five patients were assigned to buprenorphine and 51 to a placebo. **INTERVENTION:** Subutex or placebo sublingual tablets were given under supervision in a daily dose of 16 mg with the exception of a double dose on Saturday and no dose on Sunday. **MEASUREMENT:** Retention, compliance, self-reported drug-abuse, wellbeing and mental health. **FINDINGS:** The average number of days of participation was significantly higher in the buprenorphine group, 42 (median: 29) compared to 14 (median: 11) for the placebo group ( $P < 0.001$ ). The retention of patients after 12 weeks was 16 patients in the buprenorphine group and one patient in the placebo group. The buprenorphine group had a larger decrease in reported opioid use ( $p < 0.001$ ) and in reported use of other drugs, tablets and alcohol abuse ( $p < 0.01$ ). The group also showed a stronger increase in wellbeing ( $p < 0.01$ ) and life satisfaction ( $p < 0.05$ ). None of the participants died. **CONCLUSION:** The patients waiting for MAR benefited significantly from the buprenorphine as an interim therapy according to retention, self-reported use of drugs and wellbeing. However, the patients had difficulties in remaining in treatment over time without psychosocial support.

**ISSN:** 0965-2140.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Buprenorphine/\*therapeutic use ; Double-Blind Method ; Female ; Human ; Male ; Middle Age ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/\*rehabilitation ; Patient Compliance ; Support, Non-U.S. Gov't ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

206. **Kumar M ; Mudaliar S ; Thyagarajan S ; Kumar S ; Selvanayagam A ; Daniels D. (2000) Rapid assessment and response to injecting drug use in Madras, south India. Int J Drug Policy 2000 Mar 1;11(1-2):83-98.**

**Author Address:** SAHAI Trust, 12 Vaidyaram Street, T. Nagar, Madras, India

**Abstract:** HIV infection among injecting drug users (IDUs) is preventable, and in order to develop appropriate interventions, an assessment was carried out at Madras, South India using the Rapid Assessment and Response Guide on Injecting Drug Use developed by WHO. Data were collected with multiple methods from multiple sources using the principles of triangulation and induction. A total of 100 IDUs were interviewed. These interviews were complemented by focus groups and observations. A community advisory board ensured community ownership and participation. Findings showed that heroin, buprenorphine, diazepam and avil were the drugs most commonly injected. The use of pharmaceutical preparations as a 'cocktail' was also prevalent. Drug injectors interviewed were males, and most (81%) were from low-income groups living in slums. Direct (69%) as well as indirect sharing (94%) was common. Such unhygienic injecting practices, and the lack of access to sterile water, contribute to the high incidence of adverse health consequences. Compared with the buprenorphine injectors, heroin injectors were more likely to share injecting equipment ( $P=0.0022$ ), inject more frequently ( $P=0.0013$ ), have more drug using network members ( $P=0.0104$ ), frequent 'shooting' locations ( $P=0.002$ ), use the dealer's place to inject ( $P=0.0317$ ), and face threats of arrest ( $P=0.0023$ ). Many buprenorphine injectors managed their life without serious crises, and seemed to adopt a 'natural' harm reduction response. Sexual risk behaviour was prevalent among opioid users, and a history of commercial sex was associated with daily alcohol use ( $P=0.0221$ ). The assessment led to an action plan which was presented and endorsed in an advocacy meeting by key stakeholders and decision-makers. The critical importance of implementing quality, accessible, community-oriented, and effective HIV interventions with the capacity to reach the majority of IDUs is discussed. Public health responses to injecting drug use must target changes among individuals at-risk, as well as in the community and risk environment.

**ISSN:** 0955-3959.

**Pub Type:** Journal article.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; History, use and effectiveness in other countries ; Prevalence of use for opiate dependence

207. **Kuo I ; Fischer B ; Vlahov D. (2000) Consideration of a North American heroin-assisted clinical trial for the treatment of opiate-dependent individuals. Int J Drug Policy 2000 Sep 1;11(5):357-370.**

**Author Address:** Department of Epidemiology, Johns Hopkins School of Public Health, 615 North Wolfe Street, Room E6005, 21205, Baltimore, MD, USA

**Abstract:** Untreated opiate addiction remains a major public health problem in North America (US and Canada). Increased morbidity and mortality as well as criminal behavior related to untreated opiate dependence constitute significant social and economic burdens. While the principal treatment modality to opiate addiction in North America has been methadone treatment since the 1960s, its reach and effectiveness has been limited; at any given time, only about 25% (US) and 15-20% (Canada) of all opiate addicts are in methadone treatment. Reasons for low levels of treatment participation among this subset of users include perceptions among users that treatment programs are punitive and that the medication is fraught with side effects. In the meantime, alternatives to methadone have been recently approved or are in development, including levo-alpha acetylmethadol and buprenorphine. However, the extent to which they will solve the current problem is still unknown, and therefore development of additional treatment strategies needs to continue. Recent studies of heroin-assisted treatment in Europe (Switzerland, the Netherlands and Great Britain) produced preliminary yet encouraging results in attracting and retaining long-term, treatment-resistant addicts in treatment, as well as improving treatment outcomes. However encouraging, the North American context differs from Europe. A study performed in North America would provide critical information on whether utilizing injectable opiates enhances the overall therapeutic attractiveness and effectiveness of substance abuse treatment to a subset of recalcitrant users. Implications of positive results would expand the continuum of effective interventions in the US and Canada, and increase the number of long-term, treatment-resistant opiate addicts in treatment.

**ISSN:** 0955-3959.

**Pub Type:** Journal article ; overview.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; History, use and effectiveness in other countries

208. **Kutz I ; Reznik V. (2001) Rapid heroin detoxification using a single high dose of buprenorphine. J Psychoactive Drugs 2001 vol. 33(2):191-3.**

**Author Address:** Psychiatric Services, Meir General Hospital, Kfar-Saba, Israel. ikutz@netvision.net.il

**Abstract:** To test the effect of 32 mg of buprenorphine on the withdrawal process from heroin, 10 street-heroin using subjects were given 32 mg of sublingual buprenorphine, following heroin abstinence of 24 hours. Withdrawal symptoms were monitored during the first few hours, and followed for six days after buprenorphine administration, after which naltrexone (50 mg) was introduced to prevent future heroin use. Nine subjects completed detoxification with negligible withdrawal symptoms and a smooth transition to naltrexone. One

subject was excluded from the study due to methadone ingestion prior to experiment. These results strongly suggest that painless detoxification from heroin can be obtained by a single high dose of buprenorphine.

ISSN: 0279-1072.

**Pub Type:** Journal Article.

**Descriptors:** Administration, Sublingual ; Buprenorphine/\*administration & dosage ; Drug Administration Schedule ; Follow-Up Studies ; Heroin Dependence/\*drug therapy/psychology ; Human; Male ; Narcotic Antagonists/\*administration & dosage ; Substance Withdrawal Syndrome/\*drug therapy/psychology.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

209. **Kutz I ; Reznik V. (2002) Heroin detoxification with a single high dose of buprenorphine. Isr J Psychiatry Relat Sci 2002;39(2):113-9.**

**Author Address:** Meir General Hospital, Kfar Saba, Israel.

ikutz@netvision.net.il

**Abstract:** Twenty street-heroin dependent subjects were given 32 mg of sublingual buprenorphine, following heroin abstinence of 24 hours. Withdrawal symptoms were monitored during the first few hours, and followed for six days after buprenorphine administration, after which naltrexone 50 mg was introduced to prevent future heroin use. All 20 subjects completed the seven-day trial with negligible withdrawal symptoms, and smooth transition to naltrexone. These results strongly demonstrate that symptom-free detoxification from heroin can be obtained by a single high dose of buprenorphine.

ISSN: 0333-7308.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Buprenorphine/administration & dosage/\*therapeutic use ; Drug Administration Schedule ; Heroin Dependence/\*rehabilitation ; Human ; Male ; Metabolic Detoxification, Drug ; Narcotic Antagonists/ administration & dosage/\*therapeutic use.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Basic laboratory research

210. **Lavignasse P ; Lowenstein W ; Batel P ; Constant M ; Jourdain J ; Kopp P ; Reynaud-Maurupt C ; Riff B ; Videau B ; Mucchielli A. (2002) Economic and social effects of high-dose buprenorphine substitution therapy. Six-month results. Annales Medecine Interne (Paris) 2002 May;153(3 Suppl):1S20-6.**

**Author Address:** CSST Bizia-Medecins du Monde/Bayonne, Centre Hospitalier de la Cote Basque, 64109 Bayonne Cedex, France.

MDM.bayonne@wanadoo.fr

**Abstract:** The purpose of this study was to analyze the impact of high-dose buprenorphine substitution therapy in opiate-dependent patients in terms of use of psychoactive substances, associated risks, social integration, and the social cost generated by the use of these substances. This was a longitudinal

quantitative survey carried out in 1083 patients who were evaluated at three times: at the beginning of substitution therapy (D0), at 6 months and then at 12 months follow up (M6, M12). Data were collected with an anonymous self-administered questionnaire, completed in the presence of an investigating physician. Results demonstrated that patients treated with high-dose buprenorphine for 6 months, consumed fewer psychoactive drugs (heroin, cocaine, benzodiazepines) and had fewer associated risks. Additionally, several criteria involved in social integration showed improvement; morbidity and mortality decreased after the first 6 months of substitution therapy. These improvements were followed by a reduction in the social cost of drug use generated by the group of patients considered. These initial results require confirmation in the final analysis of the study taking into account the 12-month follow up.

ISSN: 0003-410X.

**Pub Type:** Journal Article.

**Descriptors:** Adolescent ; Adult ; Buprenorphine/administration & dosage/\*economics/\*therapeutic use ; \*Cost of Illness ; Dose-Response Relationship, Drug ; Female ; Human ; Longitudinal Studies ; Male ; Middle Age ; Morbidity ; Mortality ; Narcotic Antagonists/administration & dosage/\*economics/\*therapeutic use ; Opioid-Related Disorders/\*economics/\*rehabilitation ; Psychotropic Drugs/administration & dosage ; Risk Factors ; \*Social Behavior ; Support, Non-U.S. Gov't ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

211. **Law F ; Nutt D. (2003) Maintenance buprenorphine for opioid users [Comment on Kakko et al 2003]. Lancet 2003 Feb 22;361(9358):634-5.**

**Author Address:** Psychopharmacology Unit, University of Bristol, School of Medical Sciences, BS8 1TD, Bristol, UK. Fergus.Law@bristol.ac.uk

**Abstract:** Comments on the article by Kakko et al (2003) in Lancet. Kakko and colleagues report a small but well designed double-blind randomised controlled trial from Sweden in which buprenorphine was compared with placebo as long-term maintenance therapy in opioid users. This trial is likely to become a classic. The results have far-reaching implications for the treatment of opioid dependence in general, and the role of psychological treatments and buprenorphine in particular. The proven efficacy of opioid-substitution treatment means that long-term placebo studies in this field are rare, and are typically only done in a context in which opioid-maintenance treatment is strictly rationed (which makes such a study ethically acceptable). There are no other long-term placebo-controlled trials with buprenorphine, and only three with methadone.

ISSN: 0140-6736.

**Pub Type:** Comment;Journal Article.

**Descriptors:** Buprenorphine/\*therapeutic use ; Human ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/\*drug therapy/mortality/therapy ; Patient Dropouts ; Psychotherapy, Group/\*statistics & numerical data ; Randomized Controlled Trials ; Sweden.

**ATTC Buprenorphine Topics:** Treatment outcomes/effectiveness ; History, use and effectiveness in other countries

212. **Leavitt S. (2001) The safety of methadone, LAAM, buprenorphine in the treatment of opioid dependency. Addict Treat Forum Mar 20, 2001.**  
**Abstract:** New medications have been proposed as welcome, superior, less addictive alternatives to methadone in the treatment of opioid dependency. Are buprenorphine and LAAM improvements over methadone, the "gold standard" opioid agonist for the treatment of opioid dependency since the mid 1960's? Perhaps even more important, and the primary focus of this report, are the newer agents safe alternatives? AT Forum obtained from the US Food and Drug Administration Office of Postmarketing Drug Risk Assessment all adverse event reports from Nov. 1, 1997 to Nov. 1, 2000 regarding buprenorphine, LAAM and methadone with the focus solely on their use in the treatment of opioid addiction.  
**Notes:** This research is supported by Mallinckrodt Inc., a manufacturer of methadone and naltrexone. Available free online.  
**URL:** [http://www.atforum.com/SiteRoot/pages/current\\_pastissues/safety\\_methadone.shtml](http://www.atforum.com/SiteRoot/pages/current_pastissues/safety_methadone.shtml)  
**Pub. Type:** Web document.  
**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Pharmacology ; Pharmacotherapy for opiate dependence ; Special populations
213. **Lenne M ; Dietze P ; Rumbold G ; Redman J ; Triggs T. (2001) Preliminary results on the effects of prescribed opioid pharmacotherapies on driving skills. Research and Clinical Forums 2001;23(1):19-23.**  
**Abstract:** Until recently, methadone has represented the mainstay of treatment for opioid dependence in Australia. The introduction of buprenorphine and the possible future introduction of levo-alpha-acetylmethadol (LAAM) will enhance the quality of treatment provision by expanding treatment options and offering alternatives to methadone treatment, which may not be suitable for all individuals. While the safety of these compounds in terms of their direct effects on physical well-being has been evaluated in extensive clinical trials, it is also important to determine whether clients receiving buprenorphine and LAAM are subject to any increase in accident risk when compared either with clients receiving methadone or with ex-user controls. In the present study, the effects of buprenorphine, methadone and LAAM on driving skills, with or without the influence of alcohol, were compared with one another and with the effects of alcohol on the driving skills of ex-user and non-drug user controls. Driving skills were assessed in a 75 minute test in a driving simulator. Preliminary results show that, when compared with control results, the driving performance of clients maintained on buprenorphine, methadone or LAAM did not appear to be impaired by their treatment.  
**ISSN:** 0143-3083.  
**Notes:** Journal not readily available.  
**Pub Type:** Journal article.

**Descriptors:** Driving ; effect on psychomotor ability.

**ATTC Buprenorphine Topics:** Psychosocial treatment aspects

214. **Leshner A. (2003) Accessing opiate dependence treatment medications: buprenorphine products in an office-based setting. Drug Alcohol Depend 2003 May 21;70(2 Suppl):S103-4.**  
**Author Address:** Leshner, Alan I. American Assn for the Advancement of Science, 1200 New York Avenue, NW, Washington, DC US 20005, [aleshner@aaas.org](mailto:aleshner@aaas.org).  
**Abstract:** Alan Leshner (former NIDA director) argues that there is a significant need to expand access to opioid addiction treatment in this country. We have come a long distance in our approaches to understanding and treating drug addiction, but we still have quite a distance ahead of us. Bringing new drugs like buprenorphine from clinical trials into the clinical toolboxes of certified and trained physicians in their own office-based settings is a significant step in closing the treatment access gap. It is concluded that we can improve the quality and availability of treatment in the United States if we use the power of science to put treating addiction on equal footing with treatments for other chronic diseases.  
**ISSN:** 0376-8716.  
**Pub Type:** Journal Article; Overview.  
**Descriptors:** opioid addiction treatment; opiate addiction; buprenorphine; office-based setting.  
**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence
215. **Likar R. (2003) Transdermal buprenorphine: a viewpoint by Rudolf Likar. Drugs 2003;63(19):2011-2.**  
**Author Address:** Pain Clinic, General Hospital Klagenfurt, Klagenfurt, Austria.  
**Abstract:** Persistent pain requires continuous analgesia and sustained-release formulations of strong opioids are the mainstay in current treatment modalities. One of the most potent opioids is buprenorphine, a partial agonist at mu-opioid receptors. Its broad application in pain management was in the past restricted by the fact that buprenorphine is subject to a high first-pass metabolism, reducing its bioavailability after oral administration. Until now, buprenorphine was only available in a sublingual and various parenteral (intravenous, intramuscular, and subcutaneous) preparations. Recently, a transdermal therapeutic system containing buprenorphine was introduced into pain management. Transdermal buprenorphine works like a sustained-related formulation, but the active substance enters circulation by permeation through the skin, thus avoiding gastrointestinal passage and first-pass metabolism.  
**ISSN:** 0012-6667.  
**Pub Type:** Journal Article.  
**ATTC Buprenorphine Topics:** Dosing/administration ; Pain management
216. **Ling W. (2001) Changing the face of addiction medicine: The role of buprenorphine in opiate pharmacotherapy. NIDA Research Monograph**

182:34-36, 2001.

**Abstract:** When we talk about the face of addiction medicines, we are not only talking about how we, the medical profession, specifically treat our addicted patients but also about how we, as a society, deal with our addicted population. In the US, this face changes every couple of decades depending on our national mood. In the present context it seems appropriate to limit remarks to the treatment of opiate dependence as exemplifying how Americans view addicts in general and heroin addicts in particular, and how we treat them. By way of introduction, let us refresh our memory with a glimpse of a face from the past. The Report of the Committee on Narcotic Drug Situation in the US published in JAMA in 1920 typecast addicts as either correctional cases, degenerates, social misfits or otherwise normal and made treatment recommendations based on this typology. This did not come from radical extremist group; it was the official recommendation of the AMA some 80 years ago.

**Notes:** Presented at Problems of Drug Dependence, 2001. Proceedings of 63rd Annual Scientific Meeting, CPDD.

**Pub Type:** conference presentation (print).

**Descriptors:** Addiction; Dependence Treatment.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

217. **Ling W. (2001) Buprenorphine: what's known, what's new and what's next? Research and Clinical Forums 2001;23(1):11-17.**

**Abstract:** The introduction of buprenorphine into the Australian opioid dependence treatment system is underpinned by decades of clinical experience and research. Buprenorphine is a partial agonist whose unique pharmacological properties make it safer and less addictive than full agonists like methadone and levo-acetylmethadol (LAAM) while providing comparable levels of efficacy in treatment. As the opportunities for take-home dosing of opioid maintenance therapies are restricted in most countries by concerns over possible diversion and misuse, a formulation that combines buprenorphine and naloxone has been developed to decrease the likelihood of abuse or resale. When taken sublingually, the formulation (Suboxone) provides the same benefits as the buprenorphine mono-tablets (Subutex), but if injected the naloxone content of the tablet becomes manifest and will precipitate an acute withdrawal in opiate-dependent individuals. Interim results from a multicentre study of this combination product show that it is well accepted and well tolerated by patients. The place of buprenorphine in the treatment of opioid dependence is discussed in a treatment model using buprenorphine as a first-line treatment agent.

**ISSN:** 0143-3083.

**Notes:** Journal not readily available.

**Pub Type:** journal article.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

218. **Ling W ; Huber A ; Rawson R. (2001) New trends in opiate pharmacotherapy. Drug & Alcohol Review. Vol 20(1) 2001, 79-94.**

**Abstract:** Focuses on medication development and on the evolution of alternative treatment strategies. Specifically, the authors highlight key developments in pharmacotherapeutic approaches to the treatment of opiate dependence. Buprenorphine is discussed in considerable detail given the recently completed research indicating its efficacy and clinical utility as well as the imminent approval of its use in the US. Levo-alpha-acetylmethadol, methadone, lofexidine, and naltrexone and ultra-rapid opiate detoxification are also discussed.

**ISSN:** 0959-5236 (Print), 1465-3362 (Electronic).

**Pub Type:** Journal Article.

**Descriptors:** medication development & evolution of alternative treatment strategies in opiate pharmacotherapy ; \*Drug Addiction ; \*Drug Therapy ; \*Opiates ; \*Prescription Drugs ; \*Strategies ; Treatment ; Human.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence Treatment outcomes/effectiveness

219. **Ling W ; Rawson R ; Compton M. (2003) Clinical treatment of opioid addiction and dependence. Methods in Molecular Medicine 2003; 84:285-95.**

**Author Address:** Integrated Substance Abuse Programs, University of California Los Angeles, Los Angeles, CA, USA.

**Abstract:** This chapter discusses the use of opioids for maintenance and detoxification of opiate dependence, including the use of buprenorphine, methadone, LAAM, and naltrexone. The authors conclude that buprenorphine is a highly desirable medication in that it satisfies both medical and social criteria; they state clearly that opioid medications should be used in the context of a comprehensive treatment environment.

**ISSN:** 1543-1894.

**Pub Type:** Book chapter.

**Descriptors:** Administration, Oral ; Administration, Sublingual; Buprenorphine/administration&dosage/\*pharmacokinetics/pharmacology/\*therapeutic use ; Human ; Metabolic Detoxication, Drug ; Methadone/administration & dosage/\*pharmacokinetics/ pharmacology/\*therapeutic use ; Methadyl Acetate/administration & dosage/pharmacology/\*therapeutic use ; Naltrexone/administration & dosage/pharmacology/\*therapeutic use ; Narcotic Antagonists/administration & dosage/\*therapeutic use ; Opioid-Related Disorders/\*drug therapy/psychology/rehabilitation ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

220. **Ling W ; Smith D. (2002) Buprenorphine: blending practice and research. J Subst Abuse Treat 2002 Sep;23(2):87-92.**

**Author Address:** Integrated Substance Abuse Programs, University of California, Los Angeles, 11075 Santa Monica Boulevard, Suite 200, Los Angeles, CA 90025, USA. lwalter@ucla.edu

**Abstract:** Although pharmacotherapy has been a mainstay in opiate addiction, not much research in the development of new opiate medications has been translated into clinical practice. In part, this is because opiate pharmacotherapy has not been an integral element of mainstream medical practice and because new medications developed by research are not available to clinicians. All that will change with the availability of buprenorphine for addiction treatment. For the first time in nearly a century, clinicians will be able to treat opiate addicts in the general medical setting, in the same manner they treat other patients. The unique pharmacological properties of buprenorphine, with its high patient acceptance, favorable safety profile, and ease of clinical administration, should facilitate its clinical integration. However, successful implementation will require changes in the understanding and attitude of clinicians, policymakers, and society.

**ISSN:** 0740-5472.

**Pub Type:** Journal Article ; Review ; Review, Tutorial.

**Descriptors:** Australia;Buprenorphine; Opiate dependence; Pharmacotherapy; Policy; Research; Practice ; Buprenorphine/ pharmacology/\*therapeutic use ; Clinical Trials ; France ; Human ; Narcotic Antagonists/pharmacology/\*therapeutic use ; Opioid-Related Disorders/ \*drug therapy/rehabilitation ; Substance Abuse Treatment Centers ; Support, U.S. Gov't, P.H.S. ; United States.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; History, use and effectiveness in other countries

221. **Ling W ; Wesson D. (2003) Clinical efficacy of buprenorphine: comparisons to methadone and placebo. Drug Alcohol Depend 2003 May 21;70(2 Suppl):S49-57.**

**Author Address:** Integrated Substance Abuse Programs, Department of Psychiatry and Biobehavioral Sciences, School of Medicine, University of California Los Angeles, 11075 Santa Monica Boulevard, Suite 200, 90025, Los Angeles, CA, USA

**Abstract:** Buprenorphine has been studied extensively since 1978 when it was initially proposed as an alternative to methadone for treatment of opioid dependence. Early work by and their colleagues demonstrated buprenorphine's low physical abuse potential and its ability to substitute for heroin and reduce heroin self-administration in opiate-dependent humans. The subsequent early clinical studies suggested that, in clinical settings, buprenorphine was a safe and efficacious opiate dependence pharmacotherapy. Formal approval for general clinical use, however, required that systematic data be gathered on buprenorphine's safety and efficacy in larger groups and a series of controlled clinical trials was designed to evaluate its utility from a medication development perspective. In general, these trials adhered to one of three basic protocol designs: comparison of buprenorphine to methadone; dose comparisons using dose response as an indicator of efficacy; and comparison of buprenorphine to

placebo. Retention in treatment, reduction in illicit drug use and craving, and patient and staff ratings of improvements were the most frequently used outcome indicators in these trials. Additional data collected included optimum dosing and dosage schedules, adverse reactions and common side-effects, and other information intended to clarify buprenorphine's benefit-risk relationship and to help prepare guidelines for its safe marketing and utilization by physicians in general clinical practice. This paper presents a review of the buprenorphine/methadone comparison trials conducted in the United States and two such trials conducted in Europe. Also reviewed are three placebo-controlled trials and a buprenorphine/methadone detoxification study. Overall, this series of studies did firmly establish the efficacy of buprenorphine alone and in comparison to methadone.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article ; Literature Review.

**Descriptors:** Treatment; Pharmacotherapy; Buprenorphine.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Dosing/administration ; Pharmacotherapy for opiate dependence

222. **Lintzeris N. (2002) Buprenorphine dosing regime in the management of out-patient heroin withdrawal. Drug Alcohol Rev 2002 Mar;21(1):39-45.**

**Author Address:** Turning Point Alcohol and Drug Centre and Australian National University, Victoria, Australia.

**Abstract:** This study aimed to establish a buprenorphine regime suitable for the short-term management of out-patient heroin withdrawal using an open-label, single-group case series. Eighteen dependent injecting heroin users underwent an 8-day withdrawal episode with supervised dosing of sublingual Subutex tablets. Buprenorphine doses were titrated daily over a 5-day period. Fifteen subjects (83%) completed the 5-day regime, and 14 (78%) completed the 8-day withdrawal episode. The mean doses ((SD) were 6.1 (1.2) mg on day 1; 9.6 (1.7) mg on day 2; 10.1 (1.9) mg on day 3; 8.9 (2.0) mg on day 4; 4.1 (1.5) mg on day 5; and a total regime dose of 38.9 (5.8) mg. Withdrawal severity was mild, with minimal rebound upon the cessation of dosing. Five subjects reported no heroin use, and five subjects reported using on only one occasion during the 8 days. An out-patient buprenorphine regime is recommended.

**ISSN:** 0959-5236.

**Pub Type:** Journal Article.

**Descriptors:** Ambulatory Care/\*methods/statistics & numerical data ; Buprenorphine/\*administration & dosage/adverse effects ; Drug Administration Schedule ; Female ; Heroin Dependence/\*drug therapy/psychology ; Human ; Male ; Patient Satisfaction/statistics & numerical data ; Severity of Illness Index; Substance Withdrawal Syndrome/\*drug therapy/psychology ; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

223. **Lintzeris N. (2003) Buprenorphine: What Is It & Why Use It? [London] National Addiction Centre, Institute of Psychiatry, July 2003.**

**Abstract:** A presentation with 50 slides, providing an overview of the clinical pharmacology of buprenorphine and its effects on the body; overview of evidence of its effectiveness; comparison of buprenorphine vs methadone and clonidine for maintenance and detox; and practical aspects of using buprenorphine in treatment for opiate dependence.

**URL:** <http://www.smmgp2.demon.co.uk/download/articles/art019.zip>

**Pub. Type:** Powerpoint slides.

**ATTC Buprenorphine Topics:** Pharmacology ; Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

224. **Lintzeris N ; Bammer G ; Rushworth L ; Jolley D ; Whelan G. (2003) Buprenorphine dosing regime for inpatient heroin withdrawal: a symptom-triggered dose titration study. Drug Alcohol Depend 2003 Jun 5;70(3):287-94.**

**Author Address:** Turning Point Alcohol and Drug Centre, Victoria, Australia. [n.lintzeris@iop.kcl.ac.uk](mailto:n.lintzeris@iop.kcl.ac.uk)

**Abstract:** The study aimed to identify the range of buprenorphine doses required to comfortably alleviate symptoms in patients undergoing inpatient heroin withdrawal using a symptom-triggered titration dosing regime, and to identify the patient characteristics that impact upon the buprenorphine dose requirements. The study was conducted in two Australian inpatient withdrawal units, recruiting 63 dependent, injecting heroin users with no recent methadone treatment, dependence on other drugs, or other active medical or psychiatric conditions. In a single (patient) blinded case series, placebo or 2 mg sublingual buprenorphine tablets was administered four times a day according to severity of withdrawal (assessed with Subjective Opiate Withdrawal Scale). Up to 16 mg buprenorphine was available over the first 4 days of the admission, up to 8 mg on day 5, and placebo continued until day 6. Thirty-two subjects completed the dosing regime, with mean (+/-S.D.) daily doses of 3.8+/-2.8 on day 1, 5.8+/-3.2 on day 2, 4.8+/-3.3 on day 3, 2.3+/-2.6 on day 4, 0.8+/-1.3 on day 5, and a total dose of 17.4+/-9.7. Higher buprenorphine doses were required by those patients with more severe psychosocial dysfunction, women, those with more frequent heroin use, and those with more severe dependence on heroin at intake. A dosing regime using sublingual buprenorphine tablets for short inpatient heroin withdrawal is proposed.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article.

**Descriptors:** Buprenorphine; Heroin withdrawal; Detoxification; Inpatient titration regime.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Special populations

225. **Lintzeris N ; Bell J ; Bammer G ; Jolley D ; Rushworth L. (2002) A randomized controlled trial of buprenorphine in the management of short-term ambulatory heroin withdrawal. Addiction 2002 Nov;97(11):1395-404.**

**Author Address:** Turning Point Alcohol and Drug Centre, Fitzroy, Victoria, Australia. [N.Lintzeris@iop.kcl.ac.uk](mailto:N.Lintzeris@iop.kcl.ac.uk)

**Abstract:** AIM: To determine whether buprenorphine is more effective than clonidine and other symptomatic medications in managing ambulatory heroin withdrawal. DESIGN: Open label, prospective randomized controlled trial examining withdrawal and 4-week postwithdrawal outcomes on intention-to-treat. SETTING: Two specialist, out-patient drug treatment centres in inner city Melbourne and Sydney, Australia. PARTICIPANTS: One hundred and fourteen dependent heroin users were recruited. Participants were 18 years or over, and with no significant other drug dependence, medical or psychiatric conditions or recent methadone treatment. One hundred and one (89%) participants completed a day 8 research interview examining withdrawal outcomes, and 92 (81%) completed day 35 research interview examining postwithdrawal outcomes. INTERVENTIONS: Participants randomized to control (n = 56) (up to 8 days of clonidine and other symptomatic medications) or experimental (n = 58) (up to 5 days of buprenorphine) withdrawal groups. Following the 8-day withdrawal episode, participants could self-select from range of postwithdrawal options (naltrexone, substitution maintenance, or counselling). MEASUREMENTS: Retention in withdrawal; heroin use during withdrawal; and retention in drug treatment 4 weeks after withdrawal. SECONDARY OUTCOMES: Withdrawal severity; adverse events, and heroin use in the postwithdrawal period. FINDINGS: The experimental group had better treatment retention at day 8 (86% versus 57%, P = 0.001, 95% CI for numbers needed to treat (NNT) = 3-8) and day 35 (62% versus 39%, P = 0.02, 95% CI for NNT = 4-18); used heroin on fewer days during the withdrawal programme (2.6 +/- 2.5 versus 4.5 +/- 2.3, P < 0.001, 95% CI = 1-2.5 days) and in the postwithdrawal period (9.0 +/- 8.2 versus 14.6 +/- 10, P < 0.01, 95% CI = 1.8-9.4); and reported less withdrawal severity. No severe adverse events reported. CONCLUSIONS: Buprenorphine is effective for short-term ambulatory heroin withdrawal, with greater retention, less heroin use and less withdrawal discomfort during withdrawal; and increased postwithdrawal treatment retention than symptomatic medications.

**ISSN:** 0965-2140.

**Pub Type:** Clinical Trial ; Journal Article ; Multicenter Study ; Randomized Controlled Trial.

**Descriptors:** Adult ; Ambulatory Care/methods ; Buprenorphine/\*therapeutic use ; Clonidine/\*therapeutic use ; Comparative Study ; Female ; Heroin Dependence/\*rehabilitation ; Human ; Male ; Narcotics/\*therapeutic use ; Patient Compliance ; Substance Abuse Treatment Centers ; Substance Withdrawal Syndrome/\*prevention & control ; Support, Non-U.S. Gov't ; Sympatholytics/therapeutic use.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness ; Treatment protocols/physician guidelines

226. **Lintzeris N ; Clark N ; Muhleisen P ; Ritter A ; Ali R ; Bell J ; Gowing L ; Hawkin L ; Henry E ; Mattick R ; Monheit B ; Newton I ; Quigley A ; Whicker S ; White J. (2001) Clinical Guidelines : Buprenorphine Treatment**

**of Heroin Dependence. [Australia] Commonwealth Department of Health and Aged Care, under the auspices of the National Expert Advisory Committee on Illicit Drugs (NEACID), March 2001, 74 p.**

**Abstract:** This set of guidelines has been developed through a consensus process by a working party of senior Australian clinicians and researchers who have experience in the use of buprenorphine in a variety of jurisdictions. The original draft of the guidelines was developed as part of the Buprenorphine Implementation Trial by the Turning Point Alcohol and Drug Centre. The Clinical Guidelines for the Buprenorphine Implementation Trial were piloted by over 20 medical practitioners (both specialists and general practitioners) and 30 pharmacies involved in delivering buprenorphine maintenance treatment. In addition to the participants (patients, doctors, pharmacists, and researchers) of the Trial, a number of other individuals contributed to the development of the guidelines, including researchers and doctors from the U.S., France, and the UK.

The guidelines have been endorsed by the Royal Australian College of General Practitioners, the Royal Australian College of Physicians and the Australian Professional Society on Alcohol and other Drugs. The guidelines contain information on clinical pharmacology (withdrawal syndrome, safe and side effects, drug interactions); entry into treatment (suitability for buprenorphine treatment, assessment procedures, informed consent, registration of patients); guidelines for treatment (commencing buprenorphine from heroin, transferring from methadone to buprenorphine, stabilization, dosing, missed doses, ancillary interventions); guidelines for the management of heroin withdrawal (what to expect, supportive care, role of bup in withdrawal, preventing withdrawal by using bup, transition to post-withdrawal treatment); complications or adverse events with bup treatment (side effects, intoxicated presentations, incorrect dosages, analgesia requirements for patients on bup, pregnancy/lactation); writing prescriptions and dispensing bup (protocols).

**URL:** <http://www.dhs.vic.gov.au/phd/buprenorphine/bupguidelines.pdf>

**Pub. Type:** monograph ; PDF.

**Descriptors:** Clinical guidelines and procedures for the use of buprenorphine in the treatment of heroin dependence.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Combined treatment with other therapeutic medications ; Dosing/administration; History, use and effectiveness in other countries ; Legal/regulatory issues ; Pharmacology ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment outcomes/effectiveness ; Treatment protocols/physician guidelines

dependence has required a clear implementation strategy to maximise the uptake of these treatment options. Within Victoria, under the auspices of the New Pharmacotherapies Project, implementation trials have been ongoing for both buprenorphine and levo-alpha-acetylmethadol (LAAM). These compounds have demonstrable and observable advantages over existing treatments, such as the possibility of thrice-weekly dosing and the utility of buprenorphine in the treatment of heroin withdrawal. Furthermore, these compounds are both relatively straightforward to prescribe and administer. However, much of the treatment experience that exists for either medication has been confined to the specialist clinic setting, which is of little relevance to the community-based setting that provides the majority of treatment for opioid dependence in Victoria, and increasingly around Australia. Therefore, the implementation trials have focused on examining the use of these treatments within community-based treatment settings. The trials have involved the development and refinement of a set of training programs, learning objectives and clinical guidelines for doctors and pharmacists.

**ISSN:** 0143-3083.

**Notes:** Journal not readily available.

**Pub Type:** journal article; overview.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

- 228. Lintzeris N ; Ritter A ; Dunlop A ; Muhleisen P. (2002) Training primary health care professionals to provide buprenorphine and LAAM treatment. Subst Abuse 2002 Dec;23(4):245-54.**

**Author Address:** Turning Point Alcohol and Drug Centre, Melbourne, Australia.

**Abstract:** This paper describes the development and implementation of training programs for primary care medical practitioners and pharmacists in the delivery of buprenorphine and LAAM treatment in the management of opiate dependence. Separate training programs were developed for each medication. Each training package included learning objectives, training materials, and assessment instruments. Findings of the evaluation of these initiatives and the subsequent Australian postregistration training program for buprenorphine are described.

**ISSN:** 0889-7077.

**Pub Type:** Journal Article.

**Descriptors:** Buprenorphine/\*therapeutic use ; Education, Medical, Continuing/\*methods/standards ; Education, Pharmacy, Continuing/\*methods/standards ; Human ; Methadyl Acetate/\*therapeutic use ; Opioid-Related Disorders/\*rehabilitation ; Pharmacists ; Physicians, Family/education ; Professional Competence ; Quality of Health Care ; Receptors, Opioid/\*agonists ; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines ; History, use and effectiveness in other countries

- 227. Lintzeris N ; Dunlop A ; Muhleisen P ; Connolly K ; Ritter A. (2001) Buprenorphine and LAAM implementation trials: training practitioners and pharmacists to deliver buprenorphine and LAAM treatment. Research and Clinical Forums 2001;23(1):61-65.**

**Abstract:** The expansion of the available treatment options for heroin

229. **Lintzeris N ; Rushworth L ; Bammer G ; Main N ; Bell J ; Weeks C ; Jolley D ; Mazengarb J ; Mac Queen R ; Whelan G. (2001) Randomised controlled trials of buprenorphine in the management of inpatient and outpatient heroin withdrawal. Research and Clinical Forums 2001;23(1):49-60.**

**Abstract:** Buprenorphine's pharmacological profile makes it an ideal treatment for heroin withdrawal, since it reduces cravings by exerting opioid effects, blocks the effects of additional heroin use, has a ceiling effect that increases its safety, is associated with minimal rebound withdrawal after short courses and facilitates a wide-range of continuing treatment options. This paper reports the preliminary outcomes of two multi-site withdrawal studies, one of which was placebo-controlled and was conducted in the inpatient setting, the other being comparative and conducted in the outpatient setting. Ninety percent of participants in the inpatient study reported mild withdrawal symptoms and 61% did not experience side effects. In the outpatient study, buprenorphine treatment was associated with significant reductions in heroin use and resulted in significantly superior buprenorphine over symptomatic medications such as clonidine and benzodiazepines

**ISSN:** 0143-3083.

**Notes:** Journal not readily available.

**Pub Type:** journal article.

**ATTC Buprenorphine Topics:** Treatment outcomes/effectiveness

230. **Liu Z ; Lu X ; Lian Z ; Mu Y ; Guo P ; An X. (2003) Evaluation on drug dependence of buprenorphine. Acta Pharmacol Sin 2003 May;24(5):448-52.**

**Author Address:** National Institute on Drug Dependence, Peking University, Beijing 100083, China. zhiminliu@bjmu.edu.cn

**Abstract:** AIM: To survey and assess the drug dependence and abuse potential liability of buprenorphine among opiate abusers. METHODS: Subjects of opiate dependence with history of buprenorphine use for 3 d at least were surveyed by interview. Physical dependence of buprenorphine was assessed using 30 items opiate withdrawal scale (OWS), which composed of 30 symptoms/signs. A 4-point scale was used to rate each symptoms/signs: zero (0), mild (1), moderate (2), and severe (3). Subjects were asked to rate their symptoms according to severity of previous experienced buprenorphine withdrawal. The estimate of the degree of subjective euphoria for buprenorphine was assessed using visual analogue scale (VAS). RESULTS: Subjects 1235 who met the research criteria cases completed this survey in multi-detoxification treatment centers. The main initial purposes of buprenorphine use were detoxification (77.4 %) and protracted abstinence treated (26.6 %) respectively. The scores of OWS of buprenorphine were between 0.2 to 1.3; The mean scores of OWS in 3 different categories of frequency of buprenorphine use on "continuous use", "un-continuous use", and "sometimes continuous, sometimes un-continuous" were 0.9+/-0.9, 0.4+/-0.5, and 0.7+/-0.4, respectively (F=70.846, P<0.05). The degree of subjective

euphoria for buprenorphine was slight to sub-moderate (mean score of VAS was 27 mm+/-24 mm). The mean scores of VAS in different routes of buprenorphine administration of sublingual and injection were (24+/-23) mm and (27+/-24) mm, respectively. No significant difference was found between sublingual and injection use of buprenorphine ( $u=1.516$ ,  $P>0.05$ ). CONCLUSION: Both physical and psychic dependence of buprenorphine were low.

**ISSN:** 1671-4083.

**Notes:** Free access to full text online.

**URL:** <http://www.chinaphar.com/1671-4083/24/448.pdf>

**Pub. Type:** Journal Article.

**Descriptors:** Adolescent ; Adult ; Buprenorphine/\*adverse effects/therapeutic use ; Drug Evaluation ; Female ; Human ; Male ; Narcotic Antagonists/\*adverse effects/therapeutic use ; Opioid-Related Disorders/drug therapy ; Substance Withdrawal Syndrome/\*etiology.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Psychosocial treatment aspects

231. **Lohmann A ; Smith F. (2001) Buprenorphine substitution ameliorates spontaneous withdrawal in fentanyl-dependent rat pups. Pediatr Res 2001 Jan;49(1):50-5.**

**Author Address:** Department of Pharmacology and Toxicology, Virginia Commonwealth University School of Medicine, Richmond, Virginia 23298-0613, USA.

**Abstract:** Iatrogenic physical dependence has been documented in human infants infused i.v. with fentanyl or morphine to maintain continuous analgesia and sedation during extracorporeal membrane oxygenation and mechanical ventilation. Many infants are slowly weaned from the opioid. However, this approach requires extended hospital stays. Little is known about the potential benefits of substitution therapy to prevent abstinence. Therefore, the hypothesis was tested that s.c. and p.o. buprenorphine substitution would ameliorate spontaneous withdrawal in fentanyl-dependent rat pups. Analgesia in the tail-flick test was used to indicate behaviorally active doses of buprenorphine in opioid-naive postnatal day 17 rats. Other postnatal day 14 rat pups were surgically implanted with osmotic minipumps that infused saline (1 microL/h) or fentanyl (60 microg/kg/h) for 72 h. Vehicle or buprenorphine was administered s.c. or p.o. before the initiation of spontaneous withdrawal brought about the removal of the osmotic minipumps. The major withdrawal signs of wet-dog shakes, jumping, wall climbing, forepaw tremor, and mastication were counted during a 3-h period of withdrawal. The major scored sign, scream on touch, was assessed every 15 min for 3 h. Injection of naloxone after the 3-h observation did not reveal any residual dependence. Subcutaneous buprenorphine administration significantly ameliorated all signs of withdrawal. Surprisingly, p.o. buprenorphine was nearly as efficacious as the s.c. route of administration. These results indicate that buprenorphine substitution therapy may be effective in fentanyl-dependent human infants.

**ISSN:** 0031-3998.

**Pub Type:** Journal Article.

**Descriptors:** Administration, Oral ; Animal ; Buprenorphine/\*therapeutic use; Female ; Fentanyl/\*adverse effects ; Injections, Subcutaneous Narcotic Antagonists/\*therapeutic use ; Rats ; Rats, Sprague-Dawley ; Substance Withdrawal Syndrome/\*drug therapy ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Pharmacology

232. **Lopatko O ; White J ; Huber A ; Ling W. (2003) Opioid effects and opioid withdrawal during a 24 h dosing interval in patients maintained on buprenorphine. Drug Alcohol Depend 2003 Apr 1;69(3):317-22.**

**Author Address:** Department of Clinical and Experimental Pharmacology, University of Adelaide, 5005, SA, Adelaide, Australia

**Abstract:** In maintenance patients methadone has been shown to produce considerable changes in opioid effects and withdrawal over the dosing interval. As a partial agonist buprenorphine may be expected to produce smaller changes, but the nature and magnitude of these changes have only been described for single doses. In the present study opioid effects and withdrawal were described in patients maintained on buprenorphine. Twenty four opioid dependent subjects were administered 16 mg buprenorphine tablets sublingually for 10 days. On day 10 plasma samples were collected and physiological, subjective and observer-rated measures collected pre-dose and at 14 time points during the dosing interval. No significant respiratory depression was observed. Consistent with the partial agonist properties of buprenorphine, other physiological and subjective changes were also of small magnitude. However, even at a once daily dose of 16 mg some patients experienced significant opioid withdrawal that was maximal at the end of the dosing interval. Buprenorphine maintenance should be associated with a high level of safety and a low level of disruption caused by changing opioid effects over the dosing interval, but some patients may require high doses or other strategies to completely suppress withdrawal.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacology ; Pharmacotherapy for opiate dependence

233. **MacDonald D ; Obert J. (2003) A new combination treatment for opiate dependence : office-based buprenorphine and Matrix relapse prevention. Counselor 2003;4(2):66-71.**

**Abstract:** More than one million Americans are chronically opiate dependant. Most go without meaningful treatment or recovery counseling. While existing treatment systems reduce harm, they still leave the majority of opiate users outside the mainstream of professional treatment, and without the benefits enjoyed by those in recovery from other addictive substances. Clients are often reluctant to use current Narcotic Treatment Programs. Methadone clinics can only treat a fraction of the addicted and are not often structured to provide extensive counseling. In a revolutionary development, opiate substitution

therapy combined with professional counseling is becoming available through private physician's offices, narcotic treatment centers, and outpatient recovery centers. On October 8, 2002, the Food and Drug Administration (FDA) announced approval of Subutex and Suboxone, Buprenorphine-based medications, to be prescribed by physicians in their offices and clinics for the treatment of opiate dependence. This is to be combined with the physicians' newly certified capacity to refer to immediate and long-term relapse prevention counseling as part of a whole recovery plan. We had the opportunity at the Matrix Institute on Addictions to be a test site for the counseling groups and a medication clinic prior to the FDA approval. We observed opiate-addicted clients over a six-month to one-year period as they worked to halt relapse using buprenorphine replacement therapy.

**Pub. Type:** Journal article.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment outcomes/effectiveness

234. **Mandal T. (1999) Development of biodegradable drug delivery system to treat addiction. Drug Dev Ind Pharm 1999 Jun;25(6):773-9.**

**Author Address:** Division of Pharmaceutics, College of Pharmacy, Xavier University of Louisiana, New Orleans 70125, USA. tmandal@xula.edu

**Abstract:** Opiate addiction is a serious problem that has now spread worldwide to all levels of society. Buprenorphine has been used for several years for the treatment of opiate addiction. The objective of this project was to develop sustained-release biodegradable microcapsules for the parenteral delivery of buprenorphine. Biodegradable microcapsules of buprenorphine/poly(lactide-co-glycolide) were prepared using two main procedures based on an in-water drying process in a complex emulsion system. These procedures differ in the way the organic solvent was eliminated: evaporation or extraction. The effect of drug loading and the effect of partial saturation of the aqueous phase with the core material during the in-water solvent evaporation were also studied. The efficiency of encapsulation increased from 11% to 34% when the drug loading was decreased from 20% to 5%. There was no significant change in the efficiency of encapsulation when the aqueous phase was partially saturated with buprenorphine. In changing the solvent removal process from evaporation to extraction, no significant change in the efficiency of encapsulation was observed. The microcapsules prepared by the solvent evaporation were smooth and spherical. However, the microcapsules prepared by the extraction of the organic solvent lost their surface smoothness and became slightly irregular and porous compared with the other batches. The average particle size of the microcapsules was between 14 and 49 microns. The cumulative drug release was between 2% and 4% within the first 24 hr. A sustained drug release continued over 45 days.

**ISSN:** 0363-9045.

**Pub Type:** Journal Article.

**Descriptors:** Absorbable Implants ; Biocompatible Materials/chemistry ; Buprenorphine/\*administration & dosage ; Delayed-Action

Preparations/\*therapeutic use ; \*Drug Compounding ; Drug Delivery Systems/\*methods ; Emulsions ; Human ; Lactic Acid/\*chemistry ; Microscopy, Electron, Scanning ; Microspheres ; Opioid-Related Disorders/\*drug therapy ; Particle Size ; Polyglycolic Acid/\*chemistry ; Polymers/\*chemistry ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacology

235. **Manisses Communication Group Inc. (ongoing) Alcoholism and Drug Abuse Weekly [newsletter, numerous articles]. Published by Manisses Communication Group, Inc., 48 issues / year.**

**Abstract:** This newsletter is a good source for current news about the policy and regulation of buprenorphine, with updates from the FDA, SAMHSA, and other government offices. In addition, the publication presents brief summaries of recent research and clinical publications (e.g. Lancet, JAMA), and stories from newspapers such as the NY Times. It is included here as a source here because it is a publication available to many practitioners and others in the AOD field. In this bibliography, we have included only a few of the individual articles on buprenorphine that have been published in ADAW.

**ISSN:** 1042-1394.

**URL:** <http://www.manisses.com/2newsletters/newsletters/adaw/adaw.htm>

**Pub. Type:** newsletter.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

236. **Margolin A ; Avants S. (1999) Should cocaine-abusing, buprenorphine-maintained patients receive auricular acupuncture? Findings from an acute effects study. J Altern Complement Med 1999 Dec;5(6):567-74.**

**Author Address:** Department of Psychiatry, Yale University School of Medicine, New Haven, Connecticut 06519, USA. [arthur.margolin@yale.edu](mailto:arthur.margolin@yale.edu)

**Abstract:** OBJECTIVE: Buprenorphine is a synthetic opioid with micro-agonist properties currently pending Food and Drug Administration (FDA) approval as a maintenance agent for treating heroin-addicted individuals. Unlike methadone, a widely used opioid maintenance agent, buprenorphine is a kappa-receptor antagonist. Research linking the effects of acupuncture to the release of dynorphin, the endogenous ligand for the kappa-receptor, raised the possibility that buprenorphine may block acupuncture's effects. In this study, we sought to gather preliminary data on this issue in order to guide the clinical care of cocaine-abusing, buprenorphine-maintained patients. DESIGN: Between-group analysis comparing buprenorphine- and methadone-maintained patients on ratings of acute effects after a single session of auricular acupuncture. SUBJECTS: Thirty-four (34) cocaine-abusing, opioid-dependent patients, eighteen (18) maintained on buprenorphine, and sixteen (16) maintained on methadone. Intervention: A single, 40-minute session of auricular acupuncture; four needles were inserted in each auricle. OUTCOME MEASURES: Acute effect ratings in four domains: pain, de qi sensations, relaxation effects, subjective experiences. RESULTS: There were no significant differences in

acute-effects ratings between the two groups. Patients in both groups reported positive effects. CONCLUSIONS: These preliminary findings are consistent with the interpretation that buprenorphine does not block auricular acupuncture, supporting the provisional recommendation that cocaine-abusing patients maintained on buprenorphine should not be excluded from receiving auricular acupuncture or from participating in clinical studies of this treatment modality. Further, controlled research on this issue, with clinical outcomes, is needed.

**ISSN:** 1075-5535.

**Pub Type:** Journal Article.

**Descriptors:** \*Acupuncture, Ear ; Adult ; Analgesics, Opioid/\*therapeutic use ; Buprenorphine/\*therapeutic use ; Cocaine-Related Disorders/\*rehabilitation ; Comparative Study ; Female ; Human ; Male ; Methadone/\*therapeutic use ; Substance Abuse Treatment Centers/methods; Support, U.S. Gov't, P.H.S. ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pain management ; Pharmacology ; Treatment outcomes/effectiveness

237. **Martin J. (2002) Drug Addiction Treatment Act of 2000. Presentation at a meeting of the California Society of Addiction Medicine, Newport Beach, CA 10/9/02.**

**Abstract:** PowerPoint slide presentation about the Drug Addiction Treatment Act of 2000, including information about physician waivers.

**URL:** [http://www.csam-](http://www.csam-asam.org/Bup%20Clinical%20Info/powerpoint%20presentations/Data2000.ppt)

[asam.org/Bup%20Clinical%20Info/powerpoint%20presentations/Data2000.ppt](http://www.csam-asam.org/Bup%20Clinical%20Info/powerpoint%20presentations/Data2000.ppt)

**Pub. Type:** PowerPoint slides ; web document.

**ATTC Buprenorphine Topics:** Legal/regulatory issues

238. **Martin J. (2002) Monitoring treatment progress and managing threats to stability. Presentation at a meeting of the California Society of Addiction Medicine, Newport Beach, CA 10/9/02.**

**Abstract:** PowerPoint slide presentation discussing the maintenance phase of buprenorphine treatment, including retention, patient agreements, ways to integrate pharmacological and psychological care, the stages of adjustment to chronic disease, and how best to monitor patients in maintenance phase.

**URL:** [http://www.csam-](http://www.csam-asam.org/Bup%20Clinical%20Info/powerpoint%20presentations/Maintenance.ppt)

[asam.org/Bup%20Clinical%20Info/powerpoint%20presentations/Maintenance.ppt](http://www.csam-asam.org/Bup%20Clinical%20Info/powerpoint%20presentations/Maintenance.ppt)

**Pub. Type:** PowerPoint slides; web document.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

239. **Martin K. (2002) Combining medications may be effective treatment for "speedball" abuse. NIDA Notes 2002;17(3).**

**Abstract:** NIDA-supported researchers from Harvard Medical School-McLean Hospital, in Belmont, Massachusetts, discovered that a combination of the

drugs buprenorphine and indatraline reduced the self-administration of "speedball" by monkeys. Speedball is a cocaine-heroin mixture that is taken by some injecting drug users and may increase the adverse consequences of drug abuse, such as greater severity of psychiatric disorders, higher incidence of failure in drug abuse treatment, and increased risk of contracting HIV infection.

**URL:** [http://www.drugabuse.gov/NIDA\\_notes/NNVol17N3/Combining.html](http://www.drugabuse.gov/NIDA_notes/NNVol17N3/Combining.html)

**Pub. Type:** Newsletter article.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications; Basic laboratory research

240. **Mattick R ; Ali R ; White J ; O'Brien S ; Wolk S ; Danz C. (2003) Buprenorphine versus methadone maintenance therapy: a randomized double-blind trial with 405 opioid-dependent patients. *Addiction* 2003 Apr;98(4):441-52.**

**Author Address:** National Drug and Alcohol Research Centre, University of New South Wales, Sydney, Australia. [r.mattick@unsw.edu.au](mailto:r.mattick@unsw.edu.au)

**Abstract:** AIMS: To assess the efficacy of buprenorphine compared with methadone maintenance therapy for opioid dependence in a large sample using a flexible dosing regime and the marketed buprenorphine tablet.

**DESIGN:** Patients were randomized to receive buprenorphine or methadone over a 13-week treatment period in a double-blind, double-dummy trial.

**SETTING:** Three methadone clinics in Australia. **PARTICIPANTS:** Four hundred and five opioid-dependent patients seeking treatment.

**INTERVENTION:** Patients received buprenorphine or methadone as indicated clinically using a flexible dosage regime. During weeks 1-6, patients were dosed daily. From weeks 7-13, buprenorphine patients received double their week 6 dose on alternate days. **MEASUREMENTS:** Retention in treatment, and illicit opioid use as determined by urinalysis. Self-reported drug use, psychological functioning, HIV-risk behaviour, general health and subjective ratings were secondary outcomes. **FINDINGS:** Intention-to-treat analyses revealed no significant difference in completion rates at 13 weeks. Methadone was superior to buprenorphine in time to termination over the 13-week period (Wald chi 2 = 4.371, df = 1, P = 0.037), but not separately for the single-day or alternate-day dosing phases. There were no significant between-group differences in morphine-positive urines, or in self-reported heroin or other illicit drug use. The majority (85%) of the buprenorphine patients transferred to alternate-day dosing were maintained in alternate-day dosing. **CONCLUSIONS:** Buprenorphine did not differ from methadone in its ability to suppress heroin use, but retained approximately 10% fewer patients. This poorer retention was due possibly to too-slow induction onto buprenorphine. For the majority of patients, buprenorphine can be administered on alternate days.

**ISSN:** 0965-2140.

**Pub Type:** Clinical Trial ; Journal Article ; Multicenter Study ; Randomized Controlled Trial.

**Descriptors:** Buprenorphine/\*therapeutic use ; Double-Blind Method; Drug Administration Schedule ; Female ; Human ; Male ; Methadone/\*therapeutic use ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related

Disorders/\*rehabilitation ; Support, Non-U.S. Gov't ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

241. **Mattick R ; Kimber J ; Breen C ; Davoli M. (2002) Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database of Systematic Reviews* 2002;(4):CD002207. (See Mattick et al 2003 for update).**

**Author Address:** National Drug and Alcohol Research Centre, University of New South Wales, National Drug and Alcohol Research Centre, University of New South Wales, Sydney, New South Wales, Australia, 2052.

[R.MATTICK@UNSW.EDU.AU](mailto:R.MATTICK@UNSW.EDU.AU)

**Abstract:** BACKGROUND: Buprenorphine has recently been reported to be an alternative to methadone and LAAM for maintenance treatment of opioid dependent individuals, differing results are reported concerning its relative effectiveness indicating the need for an integrative review. OBJECTIVES: To evaluate the effects of buprenorphine maintenance against placebo and methadone maintenance in retaining patients in treatment and in suppressing illicit drug use. SEARCH STRATEGY: We searched the following databases up to 2001, inclusive: Cochrane Drugs and Alcohol Review Group Register, the Cochrane Controlled Trials Register, MEDLINE, EMBASE, Current Contents, Psychlit, CORK [[www.state.vt.su/adap/cork](http://www.state.vt.su/adap/cork)], Alcohol and Drug Council of Australia (ADCA) [[www.adca.org.au](http://www.adca.org.au)], Australian Drug Foundation (ADF -VIC) [[www.adf.org.au](http://www.adf.org.au)], Centre for Education and Information on Drugs and Alcohol (CEIDA) [[www.ceida.net.au](http://www.ceida.net.au)], Australian Bibliographic Network (ABN), and Library of Congress databases, available NIDA monographs and the College on Problems of Drug Dependence Inc. proceedings, the reference lists of all identified studies and published reviews and authors of identified RCT's were asked about any other published or unpublished relevant RCT. SELECTION CRITERIA: Randomised clinical trials of buprenorphine maintenance compared with either placebo or methadone maintenance for opioid dependence. DATA COLLECTION AND ANALYSIS: Reviewers evaluated the papers separately and independently, rating methodological quality of concealment of allocation; data were extracted independently for meta-analysis and double-entered. MAIN RESULTS: Thirteen studies met the inclusion criteria, all were randomised clinical trials, all but one were double-blind. The method of concealment of allocation was not clearly described in 11 of the studies, otherwise methodological quality was good. Buprenorphine given in flexible doses appeared statistically significantly less effective than methadone in retaining patient in treatment (RR= 0.82; 95% CI: 0.69-0.96). Low dose buprenorphine is not superior to low dose methadone. High dose buprenorphine does not retain more patients than low dose methadone, but may suppress heroin use better. There was no advantage for high dose buprenorphine over high dose methadone in retention (RR=0.79; 95% CI:0.62-1.01), and high dose buprenorphine was inferior in suppression of heroin use. Buprenorphine was statistically significantly superior to placebo medication in retention of patients in treatment at low doses (RR=1.24; 95% CI: 1.06-1.45), high doses (RR=1.21;

95% CI: 1.02-1.44), and very high doses (RR=1.52; 95% CI: 1.23-1.88). However, only high and very high dose buprenorphine suppressed heroin use significantly above placebo. REVIEWER'S CONCLUSIONS: Buprenorphine is an effective intervention for use in the maintenance treatment of heroin dependence, but it is not more effective than methadone at adequate dosages. ISSN: 1469-493X.

**Pub Type:** Journal Article ; Meta-analysis ; Review article.

**Descriptors:** Buprenorphine/\*therapeutic use ; Human ; Methadone/\*therapeutic use ; Narcotic Antagonists/\*therapeutic use ; Narcotics/\*therapeutic use ; Opioid-Related Disorders/\*rehabilitation ; Randomized Controlled Trials.

**ATTC Buprenorphine Topics:** Dosing/administration ; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

**242. Mattick R ; Kimber J ; Breen C ; Davoli M. (2003) Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database of Systematic Reviews 2003;(2):CD002207. (update of Mattick et al 2002).**

**Author Address:** National Drug and Alcohol Research Centre, University of New South Wales, National Drug and Alcohol Research Centre, University of New South Wales, Sydney, New South Wales, Australia.  
R.MATTICK@UNSW.EDU.AU

**Abstract:** BACKGROUND: Buprenorphine has recently been reported to be an alternative to methadone and LAAM for maintenance treatment of opioid dependent individuals, differing results are reported concerning its relative effectiveness indicating the need for an integrative review. OBJECTIVES: To evaluate the effects of buprenorphine maintenance against placebo and methadone maintenance in retaining patients in treatment and in suppressing illicit drug use. SEARCH STRATEGY: We searched the following databases up to 2001, inclusive: Cochrane Drugs and Alcohol Review Group Register, the Cochrane Controlled Trials Register, MEDLINE, EMBASE, Current Contents, Psychlit, CORK [www.state.vt.su/adap/cork], Alcohol and Drug Council of Australia (ADCA) [www.adca.org.au], Australian Drug Foundation (ADF -VIC) [www.adf.org.au], Centre for Education and Information on Drugs and Alcohol (CEIDA) [www.ceida.net.au], Australian Bibliographic Network (ABN), and Library of Congress databases, available NIDA monographs and the College on Problems of Drug Dependence Inc. proceedings, the reference lists of all identified studies and published reviews and authors of identified RCT's were asked about any other published or unpublished relevant RCT. SELECTION CRITERIA: Randomised clinical trials of buprenorphine maintenance compared with either placebo or methadone maintenance for opioid dependence. DATA COLLECTION AND ANALYSIS: Reviewers evaluated the papers separately and independently, rating methodological quality of concealment of allocation; data were extracted independently for meta-analysis and double-entered. MAIN RESULTS: Thirteen studies met the inclusion criteria, all were randomised clinical trials, all but one were double-blind. The method of concealment of

allocation was not clearly described in 11 of the studies, otherwise methodological quality was good. Buprenorphine given in flexible doses appeared statistically significantly less effective than methadone in retaining patient in treatment (RR= 0.82; 95% CI: 0.69-0.96). Low dose buprenorphine is not superior to low dose methadone. High dose buprenorphine does not retain more patients than low dose methadone, but may suppress heroin use better. There was no advantage for high dose buprenorphine over high dose methadone in retention (RR=0.79; 95% CI:0.62-1.01), and high dose buprenorphine was inferior in suppression of heroin use. Buprenorphine was statistically significantly superior to placebo medication in retention of patients in treatment at low doses (RR=1.24; 95% CI: 1.06-1.45), high doses (RR=1.21; 95% CI: 1.02-1.44), and very high doses (RR=1.52; 95% CI: 1.23-1.88). However, only high and very high dose buprenorphine suppressed heroin use significantly above placebo. REVIEWER'S CONCLUSIONS: Buprenorphine is an effective intervention for use in the maintenance treatment of heroin dependence, but it is not more effective than methadone at adequate dosages. ISSN: 1469-493X.

**Pub Type:** Journal Article ; Meta-analysis ; Review.

**Descriptors:** Buprenorphine/\*therapeutic use ; Human ; Methadone/\*therapeutic use ; Narcotic Antagonists/\*therapeutic use ; Narcotics/\*therapeutic use ; Opioid-Related Disorders/\*rehabilitation ; Randomized Controlled Trials.

**ATTC Buprenorphine Topics:** Dosing/administration ; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

**243. Mattick R ; Oliphant D ; Ward J ; Hall W. (1998) The effectiveness of other opiate replacement therapies: LAAM, heroin, buprenorphine, naltrexone and injectable maintenance. In: Ward JM, Mattick RP, Hall W (eds.) Methadone Maintenance Treatment and Other Opioid Replacement Therapies. Harwood Academic Publishers, 1998, pp. 123-157.**

**Abstract:** The need to consider and develop alternative methods of management of opioid-dependent patients is based on the belief that there is an important element of patient choice that affects the decision to enter and stay in treatment, and hence the benefits achieved. With that in mind, the authors of this chapter review research evidence on the safety and effectiveness of alternative opioid maintenance agents, such as buprenorphine, LAAM, naltrexone, and injectable heroin and maintenance.

ISSN: 90-5702-239-7.

**Pub Type:** Book chapter.

**ATTC Buprenorphine Topics:** Pharmacology ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment outcomes/effectiveness

**244. McAleer SD ; Mills R ; Polack T ; Hussain T ; Rolan P ; Gibbs A ; Mullins F ; Hussein Z. (2003) Pharmacokinetics of high-dose buprenorphine following single administration of sublingual tablet formulations in opioid**

**naive healthy male volunteers under a naltrexone block. Drug and Alcohol Dependence 72(1):75-83, 2003.**

**Author Address:** Medeval Limited, Skelton House, Manchester Science Park, Lloyd Street North, M15 6SH, Manchester, UK

**Abstract:** Sublingual buprenorphine formulations have been developed as treatments for opioid dependence. In three studies, opioid naïve healthy male subjects received Subutex® tablets (buprenorphine 2 and 8 mg [N=27] or 12 and 16 mg [N=27]) or Suboxone® (two formulations) tablets (buprenorphine 8 mg/naloxone 2 mg [N=36]) sublingually, under a naltrexone block for assessment of buprenorphine pharmacokinetics and tablet disintegration times. Plasma buprenorphine was quantified up to 72 h post-dose using a sensitive LC-MS/MS assay. Mean C<sub>max</sub> values ranged from 1.6 to 6.4 ng/ml and t<sub>max</sub> from 0.5 to 3 h. Concentrations declined bi-exponentially and fluctuations after a meal suggested enterohepatic recirculation of buprenorphine. The terminal half-life was approximately 26 h (range 9-69). C<sub>max</sub> and AUC appeared to increase in proportion to Subutex® dose over 8-16 mg. The Suboxone® formulations were bioequivalent. The least squares mean (90% CI) treatment ratio for C<sub>max</sub> was 1.00 (0.92-1.10) and AUC was 1.00 (0.95-1.06). Median times of disintegration were similar for all doses and formulations (range 6-12 min). Sublingual buprenorphine, up to 40 times the 400 g analgesic dose, was well tolerated in these opioid naïve subjects, as administration of naltrexone 50-150 mg was sufficient to attenuate anticipated adverse effects in this population of subjects.

**Pub. Type:** journal article.

**Descriptors:** Naltrexone; Opioid; Sublingual; Subutex.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacology ; Dosing/administration

245. **McCance-Katz E ; Rainey P ; Friedland G ; Kosten T ; Jatlow P. (2001) Effect of opioid dependence pharmacotherapies on zidovudine disposition. Am J Addict 2001 Fall;10(4):296-307.**

**Author Address:** Department of Psychiatry and Behavioral Sciences, Albert Einstein College of Medicine, Bronx, NY 10461, USA. emccance@montefiore.org

**Abstract:** Injection drug users are frequently infected with human immunodeficiency virus (HIV) and receive opioid dependence pharmacotherapies and zidovudine (ZDV), the latter as a component of highly active antiretroviral therapy. We previously reported that methadone substantially increases ZDV concentrations. We now report on oral ZDV pharmacokinetics in 52 subjects receiving the opioid dependence pharmacotherapies l-alpha-acetylmethadol LAAM, buprenorphine, or naltrexone, and 17 non-opioid-treated controls. Relative to the area under the time-concentration curve (AUC) of ZDV in control subjects, no statistically significant differences in ZDV AUC were observed in participants treated with LAAM (p = .75), buprenorphine (p = .37), or naltrexone (p = .34). While methadone maintenance may result in ZDV toxicity and possibly require dose

adjustments, other opioid pharmacotherapies should not produce ZDV toxicity. ISSN: 1055-0496.

**Pub Type:** Journal Article.

**Descriptors:** Anti-HIV Agents/blood/\*pharmacokinetics/therapeutic use ; Buprenorphine/therapeutic use ; Drug Interactions ; Female ; HIV Infections/blood/\*drug therapy ; Human ; Male ; Methadyl Acetate/therapeutic use ; Naltrexone/therapeutic use ; Narcotic Antagonists/therapeutic use ; Narcotics/therapeutic use ; Opioid-Related Disorders/\*drug therapy ; Radioimmunoassay ; Substance Abuse Detection ; Support, Non-U.S. Gov't ; Support, U.S. Gov't, Non-P.H.S. ; Support, U.S. Gov't, P.H.S. ; Time Factors ; Zidovudine/blood/\*pharmacokinetics/therapeutic use.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacotherapy for opiate dependence ; Special populations

246. **McClellan M. (2002) From the Food and Drug Administration: Two drugs for opiate dependence. JAMA 2002 Dec 4;288(21):2678.**

**Abstract:** The FDA has approved buprenorphine hydrochloride and buprenorphine hydrochloride combined with naloxone hydrochloride (Subutex and Suboxone; Reckitt Benckiser Pharmaceuticals, Slough, England) for the treatment of opioid dependence. Buprenorphine is a partial agonist at the  $\mu$ -opioid receptor and an antagonist at the [kappa]-opioid receptor. Naloxone is an antagonist at the  $\mu$ -opioid receptor.

The FDA approval was based on the results of three studies involving 1219 heroin-addicted subjects: two 4-month double-blind, randomized studies of an ethanolic solution of buprenorphine (one active-controlled and one dose-controlled), and a 1-month, double-blind, randomized, placebo-controlled study of Subutex and Suboxone tablets. Based on retention in treatment and the percentage of negative urine test results for nonstudy opiates collected 3 times per week, Subutex and Suboxone at doses of approximately 12 to 16 mg/d were shown to be effective in the treatment of opiate dependence. ISSN: 0098-7484.

**Pub Type:** Journal Article.

**Descriptors:** Antiviral Agents/\*therapeutic use ; Buprenorphine/\*therapeutic use ; Hepatitis C, Chronic/\*drug therapy ; Human ; Interferon Alfa-2a/\*therapeutic use ; Naloxone/\*therapeutic use ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/\*drug therapy ; \*Patents ; Polyethylene Glycols/\*therapeutic use ; United States ; United States Food and Drug Administration.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Dosing/administration ; Pharmacotherapy for opiate dependence

247. **McNicholas L (Consensus Panel Chair) CSAT Buprenorphine Practice Guidelines, (in press).**

**Abstract:** CSAT Practice Guidelines: A panel of experts from outside of DHHS were assembled to prepare practice guidelines using CSAT consensus process. The pharmacist information document was developed from these

guidelines. Practice Guidelines include: Overview of addictions treatment systems; Buprenorphine and applied pharmacology; Patient assessment and treatment protocols

**Notes:** Physicians are referred to the Buprenorphine Clinical Practice Guidelines, available at the CSAT/SAMHSA, Office of Pharmacologic and Alternative Therapies, Rockwall II, Room 7-222, 5515 Security Lane, Rockville, MD 20857; (301) 443-7614 or <http://dpt.samhsa.gov>.

**Pub Type:** Monograph ; Practice Guidelines.

**ATTC Buprenorphine Topics:** Pharmacology ; Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

**248. Meadows M. (2002) Prescription drug abuse: FDA and SAMHSA join forces. FDA Consumer 37(2):36, 2002.**

**Abstract:** The recent approval by the FDA of buprenorphine to treat prescription drug abuse, and the office-based use of other addiction medications likely to be approved in the years ahead, makes the role of primary care physicians more vital than ever. In October 2002, the FDA approved Subutex (buprenorphine) and Suboxone (buprenorphine and naloxone) - the first narcotic drugs available to treat opiate dependence that can be prescribed in an office setting.

**Pub. Type:** brief overview.

**Descriptors:** Opiate; Dependence; Addiction; Abuse.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

**249. Media Awareness Project (MAP) Inc. (1997-2000) MAP, Inc. -- Drug News Archive. DrugSense, Irvine, California.**

**Abstract:** The MAP web site contains over 100,000 drug-related full-text news articles (from 1997-April 2000), including editorials, op-ed pieces, and letters to the editor. In November, there were 171 items that referred to Buprenorphine, mostly newspaper stories from the US and elsewhere. This is an activist site that is oriented toward drug policy reform and changing public policy away from the current War on Drugs. Despite political bias, posted articles are from any point of view; they need only to be about licit and illicit drugs and/or drug policy to qualify to be added to the database. Built and maintained by activists and volunteers. Updated daily, and thus contains up-to-the-minute articles. Hits come in one list, rather than in small groups. Searches can be done by subject, country, state, news source, and type of article, and limited by date.

**URL:** <http://www.mapinc.org/drugnews/index.htm>

**Pub. Type:** web site; News.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

**250. Mello N ; Negus S. (2001) Effects of indatraline and buprenorphine on self-administration of speedball combinations of cocaine and heroin by**

**rhesus monkeys. Neuropsychopharmacology 2001 Jul;25(1):104-17.**

**Author Address:** Alcohol and Drug Abuse Research Center, McLean Hospital-Harvard Medical School, Belmont, MA 02478, USA.

**Abstract:** The simultaneous intravenous (i.v.) administration of heroin and cocaine, called a "speedball," is often reported clinically, and identification of effective pharmacotherapies is a continuing challenge. We hypothesized that treatment with combinations of a dopamine reuptake inhibitor, indatraline, and a mu partial agonist, buprenorphine, might reduce speedball self-administration by rhesus monkeys more effectively than either drug alone. Speedballs (0.01 mg/kg/inj cocaine + 0.0032 mg/kg/inj heroin) and food (1 g banana pellets) were available in four daily sessions on a second-order schedule of reinforcement [fixed ratio (FR)4; variable ratio (VR)16:S]. Monkeys were treated for 10 days with saline or ascending dose combinations of indatraline (0.001-0.032 mg/kg/day) and buprenorphine (0.00032-0.01 mg/kg/day). Two combinations of indatraline (0.32 and 0.56 mg/kg/day) + buprenorphine (0.10 and 0.18 mg/kg/day) significantly reduced speedball self-administration in comparison to the saline treatment baseline ( $p < .01-.001$ ), whereas the same doses of each compound alone had no significant effect on speedball-maintained responding. Daily treatment with 0.56 mg/kg/day indatraline + 0.18 mg/kg/day buprenorphine produced a significant downward shift in the speedball dose-effect curve ( $p < .01$ ) and transient changes in food-maintained responding. These findings suggest that medication mixtures designed to target both the stimulant and opioid component of the speedball combination may be an effective approach to polydrug abuse treatment.

**ISSN:** 0893-133X.

**Pub Type:** Journal Article.

**Descriptors:** Animal ; Buprenorphine/\*pharmacology ; Cocaine/pharmacology ; Cocaine-Related Disorders/\*drug therapy/physiopathology ; Dopamine Uptake Inhibitors/pharmacology ; Dose-Response Relationship, Drug ; Drug Administration Schedule ; Drug Combinations ; Drug Interactions/\*physiology ; Female ; Heroin/pharmacology ; Heroin Dependence/\*drug therapy/physiopathology;Indans/ \*pharmacology ; Macaca mulatta ; Methylamines/\*pharmacology ; Narcotics/\*pharmacology ; Neurotransmitter Uptake Inhibitors/\*pharmacology ; Self Administration ; Support, U.S. Govt, P.H.S.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Pharmacology

**251. Mendelson J. (2002) Buprenorphine and naloxone: clinical pharmacology abuse liability. Presentation at a meeting of the California Society of Addiction Medicine, Newport Beach, CA 10/9/02.**

**Abstract:** PowerPoint slide presentation about the pharmacology of buprenorphine and naloxone, including information on abuse and dependence, tolerable dose ranges, and absorption and distribution rates of the drug through the body.

**URL:** <http://www.csam->

[asam.org/Bup%20Clinical%20Info/powerpoint%20presentations/BupPharm.ppt](http://www.csam-asam.org/Bup%20Clinical%20Info/powerpoint%20presentations/BupPharm.ppt)

**Pub. Type:** PowerPoint slides.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacology ; Addiction potential/misuse of buprenorphine

252. **Mendelson J ; Jones R. (2003) Clinical and pharmacological evaluation of buprenorphine and naloxone combinations: Why the 4:1 ratio for treatment? Drug & Alcohol Dependence. Vol 70(Suppl2) May 2003, S29-S37.**

**Author Address:** Mendelson, John. Drug Dependence Research Ctr, Langley Porter Psychiatric Inst, U California, 401 Parnassus Avenue, San Francisco, CA US 94143-0984, jemnd@itsa.ucsf.edu.

**Abstract:** Although only a partial mu-opiate agonist, buprenorphine can be abused and diverted from medical therapy to the illicit drug market. A combination of buprenorphine and naloxone for sublingual administration may discourage diversion and abuse by precipitating opiate withdrawal when taken parenterally. Because opiate-abusing populations are not homogeneous and have varying levels of opiate dependence, the efficacy of buprenorphine and naloxone in precipitating opiate withdrawal or in attenuating the pleasurable effects of buprenorphine may vary. This chapter describes the effects of sublingual and parenteral buprenorphine and naloxone combinations in several populations of opiate-dependent people. We conclude that buprenorphine and naloxone combinations should not diminish the efficacy of sublingual buprenorphine, but should have lower abuse liability than buprenorphine alone. **ISSN:** 0376-8716 (Print).

**Pub Type:** Literature Review.

**Descriptors:** buprenorphine; naloxone; combination therapy; pharmacology; opiate addiction ; \*Drug Therapy ; \*Naloxone ; \*Narcotic Agonists ; \*Opiates ; \*Pharmacology ; Drug Abuse Liability ; Drug Addiction ;

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Dosing/administration ; Pharmacotherapy for opiate dependence

253. **Mendelson J ; Jones R ; Welm S ; Baggott M ; Fernandez I ; Melby A ; Nath R. (1999) Buprenorphine and naloxone combinations: the effects of three dose ratios in morphine-stabilized, opiate-dependent volunteers. Psychopharmacology (Berl) 1999 Jan;141(1):37-46.**

**Author Address:** Drug Dependence Research Center, Langley Porter Psychiatric Institute, University of California, San Francisco 94143-0984, USA. jemnd@itsa.ucsf.edu

**Abstract:** Sublingual buprenorphine is a promising new treatment for opiate dependence, but its opioid agonist effects pose a risk for parenteral abuse. A formulation combining buprenorphine with the opiate antagonist naloxone could discourage such abuse. The effects of three intravenous (IV) buprenorphine and naloxone combinations on agonist effects and withdrawal signs and symptoms were examined in 12 opiate-dependent subjects. Following stabilization on a daily dose of 60 mg morphine intramuscularly, subjects were challenged with IV doses of buprenorphine alone (2 mg) or in combination with naloxone in ratios of 2:1, 4:1, and 8:1 (1, 0.5, or 0.25 mg naloxone), morphine

alone (15 mg) or placebo. Buprenorphine alone did not precipitate withdrawal and had agonist effects similar to morphine. A naloxone dose-dependent increase in opiate withdrawal signs and symptoms and a decrease in opioid agonist effects occurred after all drug combinations. Buprenorphine with naloxone in ratios of 2:1 and 4:1 produced moderate to high increases in global opiate withdrawal, bad drug effect, and sickness. These dose ratios also decreased the pleasurable effects and estimated street value of buprenorphine, thereby suggesting a low abuse liability. The dose ratio of 8:1 produced only mild withdrawal symptoms. Dose combinations at 2:1 and 4:1 ratios may be useful in treating opiate dependence.

**ISSN:** 0033-3158.

**Pub Type:** Clinical Trial; Journal Article.

**Descriptors:** Affect/drug effects ; Buprenorphine/\*administration & dosage/economics/therapeutic use ; Dose-Response Relationship, Drug ; Drug Therapy, Combination ; Female ; Human ; Male ; Middle Age ; Morphine/administration & dosage ; Naloxone/\*administration & dosage/economics/therapeutic use ; Narcotic Antagonists/\*administration & dosage/economics/metabolism/therapeutic use ; Narcotics/metabolism ; Opioid-Related Disorders/\*drug therapy/physiopathology ; Substance Withdrawal Syndrome/drug therapy/physiopathology; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Dosing/administration ; Pharmacotherapy for opiate dependence

254. **Merrill J. (2002) Policy progress for physician treatment of opiate addiction. J Gen Intern Med 2002 May;17(5):361-8.**

**Author Address:** Division of General Internal Medicine, Harborview Medical Center, Department of Medicine, and the Alcohol and Drug Abuse Institute, University of Washington, Seattle 98104, USA. joem@u.washington.edu

**Abstract:** Medical treatment of heroin addiction with methadone and other pharmacotherapies has important benefits for individuals and society. However, regulatory policies have separated this treatment from the medical care system, limiting access to care and contributing to the social stigma of even effective addiction pharmacotherapy. Increasing problems caused by heroin addiction have added urgency to the search for policies and programs that improve the access to and quality of opiate addiction treatment. Recent initiatives aiming to reintegrate methadone maintenance and other addiction pharmacotherapies into medical practice may promote both expanded treatment capacity and increased physician expertise in addiction medicine. These initiatives include changes in federal oversight of the opiate addiction treatment system, the approval of physician office-based methadone maintenance programs for stabilized patients, and federal legislation that could enable physicians to treat opiate addiction with new medications in regular medical practice.

**ISSN:** 0884-8734.

**Pub Type:** Journal Article.

**Descriptors:** Buprenorphine/therapeutic use ; Human ; Methadone/therapeutic use ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/\*drug

therapy ; \*Physicians, Family ; \*Public Policy ; Substance Abuse Treatment Centers ; Support, Non-U.S. Gov't ; United States.

**ATTC Buprenorphine Topics:** Legal/regulatory issues

255. **Miotto K. (2002) Pain management in patients maintained on buprenorphine. Presentation at a meeting of the California Society of Addiction Medicine, Newport Beach, CA 10/9/02.**

**Abstract:** This PowerPoint slide presentation addresses the issue of pain treatment for patients maintained on buprenorphine. Buprenorphine is an effective analgesic, but must be administered several times a day for successful treatment of pain. Acute pain is not addressed by maintenance dosages of buprenorphine, but some sort of opioid maintenance medication should be continued while the patient is under treatment for pain. If the patient needs treatment for chronic pain, physicians should consider using LAAM or methadone for maintenance instead of buprenorphine.

**URL:** [http://www.csam-](http://www.csam-asam.org/Bup%20Clinical%20Info/powerpoint%20presentations/Pain.ppt)

[asam.org/Bup%20Clinical%20Info/powerpoint%20presentations/Pain.ppt](http://www.csam-asam.org/Bup%20Clinical%20Info/powerpoint%20presentations/Pain.ppt)

**Pub. Type:** PowerPoint slides.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pain management ; Pharmacotherapy for opiate dependence

256. **Mitka M. (2003) Office-based primary care physicians called on to treat the "new" addict. JAMA 2003 Aug 13;290(6):735-6.**

**Abstract:** Office-based physicians in general practice are being called to treat the "new" heroin addict-young professionals who dwell in tree-lined suburbs rather than disadvantaged youth scrabbling in the asphalt jungle. While heroin traditionally has been associated with inner-city drug addicts, today's user is more and more likely to be an employed young professional living in the suburbs, said John F. Schneider, MD, PhD, immediate past president of the Illinois State Medical Society.

**ISSN:** 1538-3598.

**Pub Type:** News.

**Descriptors:** Buprenorphine/therapeutic use ; \*Family Practice ; Human ; Narcotic Antagonists/therapeutic use ; Opioid-Related Disorders/epidemiology/\*therapy ; United States/epidemiology.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

257. **Mitka M. (2003) Agency offers guidance on office-based drug treatment for opioid addiction. JAMA 2003 Feb 12;289(6):690.**

**Abstract:** For the first time, a medication to treat addiction to opioids, such as prescription painkillers and heroin, can be prescribed by physicians in their own offices. Buprenorphine, an opioid partial agonist that blocks the craving for opioids, received US Food and Drug Administration approval on October 8,

2002. It is the first narcotic drug for the treatment of opioid dependence that may be provided in a physician's office-as allowed under the Drug Addiction Treatment Act (DATA) of 2000-rather than through special treatment facilities, as is the case with methadone.

**ISSN:** 0098-7484.

**Pub Type:** News.

**Descriptors:** Buprenorphine/\*therapeutic use ; Human ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/\*drug therapy ; United States ; United States Substance Abuse and Mental Health Services Administration.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

258. **Moatti J ; Carrieri M ; Spire B ; Gastaut J ; Cassuto J ; Moreau J. (2000) Adherence to HAART in French HIV-infected injecting drug users: the contribution of buprenorphine drug maintenance treatment. The Manif 2000 study group. AIDS 2000 Jan 28;14(2):151-5.**

**Author Address:** INSERM Research Unit 379, Marseille, France.

**Abstract:** OBJECTIVES: To assess adherence to highly active antiretroviral therapies (HAART) in a cohort of French patients infected by HIV through injection drug use (IDU), and the impact on adherence of buprenorphine ambulatory drug maintenance treatment (DMT) which has been widely introduced since 1996. DESIGN: Adherence assessment at first visit after initiation of HAART in the MANIF2000 cohort study. METHODS: Patient's face-to-face and self-administered questionnaires. Univariate and logistic regression adjusted odds ratios (OR) to compare characteristics of non-adherent versus adherent patients. RESULTS: Of the 164 patients, 34.8% took less than 80% of the prescribed HAART doses during the previous week. Decrease in viral load titres after initiation of HAART was significantly lower among non-adherent patients. After adjustment by logistic regression, non-adherence was associated with younger age, alcohol consumption, frequency of negative life-events during the prior 6 months and active drug use. However, IDU in buprenorphine DMT reached higher levels of adherence (78.1%) than ex-IDU (65.5%), although this difference did not reach statistical significance. CONCLUSION: Prescription of buprenorphine DMT may increase adherence to HAART among HIV-infected opiate-dependent patients. Reducing the negative impact of stressful life-events through psychosocial interventions should be considered, even for those who have stopped using drugs.

**ISSN:** 0269-9370.

**Pub Type:** Clinical Trial ; Journal Article.

**Descriptors:** Adolescent ; Adult ; Anti-HIV Agents/\*therapeutic use ; Buprenorphine/\*therapeutic use ; Cohort Studies ; Drug Therapy, Combination ; Female ; HIV Infections/\*drug therapy ; Human ; Longitudinal Studies ; Male ; Narcotics/\*therapeutic use ; Patient Compliance ; Questionnaires ; Substance Abuse, Intravenous/\*drug therapy/psychology ; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other

countries ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

259. **Moatti J ; Souville M ; Escaffre N ; Y O. (1998) French general practitioners' attitudes toward maintenance drug abuse treatment with buprenorphine. *Addiction*. 1998; 93(10): pp. 1567-1575.**

**Author Address:** INSERM Research Unit 379, Institut Paoli-Calmettes, Marseille, France. u379@marseille.inserm.fr

**Abstract:** Aims. To assess attitudes of general practitioners (GPs) toward buprenorphine maintenance drug abuse treatment just after its introduction in French ambulatory care (February, 1996). Design. Cross-sectional survey by telephone interviews in a national random sample of French GPs (n= 1,186; response rate= 70.3 %) carried out in April 1996. Measurements. GPs' experience with care for IDU patients and HIV infection during the last 12 months. Logistic regression model to identify GPs' characteristics associated with readiness to prescribe buprenorphine for maintenance treatment. Findings. A minority (24.0 %) of GPs took care of IDU patients and 30.8 % of these were prepared to prescribe buprenorphine (vs. only 7.5 % in the rest of the sample). A positive attitude toward buprenorphine was related to GPs' experience with care for IDUs and with prescription of opiates for pain management and palliative care, tolerance toward drug use and personal characteristics such as tobacco use and interest in psychoanalysis. Conclusions. Giving general freedom of prescription of buprenorphine (rather than methadone) to all GPs did not lead to widespread acceptance of the drug's use in treating IDUs. The development of organized networks between specialist services for drug abuse treatment and motivated GPs may be necessary to maximize appropriate prescribing practices.

**URL:** <http://www.drugpolicy.org/library/moatti2.cfm>

**Pub. Type:** Journal article ; Web document.

**Descriptors:** Adult ; Aged; Attitude of Health Personnel\*; Attitude to Health\*; Buprenorphine/therapeutic use\*; Family Practice; Female; France; Human; Male; Middle Age; Narcotics/therapeutic use\*; Physicians, Family/ psychology\*; Professional Practice; Substance Abuse, Intravenous/ psychology; Substance Abuse, Intravenous/rehabilitation\*; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines ;

260. **Moatti J ; Vlahov D ; Feroni I ; Perrin V ; Obadia Y. (2001) Multiple access to sterile syringes for injection drug users: vending machines, needle exchange programs and legal pharmacy sales in Marseille, France. *Eur Addict Res* 2001 Mar;7(1):40-5.**

**Author Address:** INSERM Research Unit 379, 'Social Sciences Applied to Medical Innovation', Institut Paoli Calmettes, Marseille, France.

**Abstract:** OBJECTIVE: In Marseille, southeastern France, HIV prevention

programs for injection drug users (IDUs) simultaneously include access to sterile syringes through needle exchange programs (NEPs), legal pharmacy sales and, since 1996, vending machines that mechanically exchange new syringes for used ones. The purpose of this study was to compare the characteristics of IDUs according to the site where they last obtained new syringes. METHODS: During 3 days in September 1997, all IDUs who obtained syringes from 32 pharmacies, four NEPs and three vending machines were offered the opportunity to complete a self-administered questionnaire on demographics, drug use characteristics and program utilization. RESULTS: Of 485 individuals approached, the number who completed the questionnaire was 141 in pharmacies, 114 in NEPs and 88 at vending machines (response rate = 70.7%). Compared to NEP users, vending machine users were younger and less likely to be enrolled in a methadone program or to report being HIV infected, but more likely to misuse buprenorphine. They also had lower financial resources and were less likely to be heroin injectors than both pharmacy and NEP users. CONCLUSIONS: Our results suggest that vending machines attract a very different group of IDUs than NEPs, and that both programs are useful adjuncts to legal pharmacy sales for covering the needs of IDUs for sterile syringes in a single city. Assessment of the effectiveness and cost-effectiveness of combining such programs for the prevention of HIV and other infectious diseases among IDUs requires further comparative research.

**ISSN:** 1022-6877.

**Pub Type:** Journal Article.

**Descriptors:** Adolescent ; Adult ; Confidence Intervals ; Female ; France/epidemiology ; HIV Infections/prevention & control ; Human ; Male ; Needle-Exchange Programs/\*methods/statistics & numerical data ; Odds Ratio; \*Pharmacies/statistics & numerical data ; \*Questionnaires ; Substance Abuse, Intravenous/epidemiology/\*psychology ; Support, Non-U.S. Gov't ; Support, U.S. Gov't, P.H.S. ; Syringes/supply & distribution.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; History, use and effectiveness in other countries

261. **Moody D ; Slawson M ; Strain E ; Laycock J ; Spanbauer A ; Foltz R. (2002) A liquid chromatographic-electrospray ionization-tandem mass spectrometric method for determination of buprenorphine, its metabolite, norbuprenorphine, and a coformulant, naloxone, that is suitable for in vivo and in vitro metabolism studies. *Anal Biochem* 2002 Jul 1;306(1):31-9.**

**Author Address:** Center for Human Toxicology, University of Utah, Salt Lake City, Utah 84112, USA. dmoody@alanine.pharm.utah.edu

**Abstract:** A liquid chromatographic-electrospray ionization-tandem mass spectrometric method has been developed and validated for determination of the antiabuse medication, buprenorphine, its primary metabolite, norbuprenorphine, and a proposed coformulant, naloxone. The method uses deuterated internal standards and a simple liquid-liquid extraction. Mass spectrometry employed selected reaction monitoring of the transitions of m/z 468 to 396 for buprenorphine, 472 to 400 for [2H4]buprenorphine, 414 to 101

for norbuprenorphine, 423 to 110 for [2H9]norbuprenorphine, 328 to 310 for naloxone, and 345 to 327 for its internal standard, [2H3]naltrexone. The method was accurate and precise across the dynamic range of 0.1 to 10 ng/ml. All analytes were stable in human plasma stored at room temperature for up to 24 h and after three freeze-thaw cycles. Reconstituted extracts were stable at -20 degrees C for up to 3 days. In human subjects receiving a sublingual tablet of 8 mg buprenorphine and 2 mg naloxone, buprenorphine and norbuprenorphine were detected for up to 24 h with respective maximum concentrations at 1 and 1.5 h. Maximal concentrations ranged from 2.2 to 2.8 and 1.5 to 2.4 ng/ml for buprenorphine and norbuprenorphine, respectively (i.e., approximately 6 nM). The method detected norbuprenorphine formation in human liver microsomes incubated with 5-82 nM buprenorphine, which encompasses the therapeutic plasma concentration range. When cDNA-expressed P450s were incubated with 21 nM buprenorphine, norbuprenorphine formation was detected for P450s 3A4, as previously described, but also for 3A5, 3A7, and 2C8. Buprenorphine utilization generally exceeded norbuprenorphine formation, suggesting that P450s 2C18, 2C19, 2D6, and 2E1 may also be involved in buprenorphine metabolism to other products. These results suggest this method is suitable for both in vivo and in vitro studies of buprenorphine metabolism to norbuprenorphine.

ISSN: 0003-2697.

**Pub Type:** Journal Article.

**Descriptors:** Buprenorphine/\*analogs & derivatives/\*blood/chemistry/\*metabolism/pharmacology ; Chromatography, Liquid/\*methods ; Human ; Liver/drug effects/metabolism ; Models, Chemical; Molecular Structure ; Naloxone/\*blood/chemistry/\*metabolism ; Spectrometry, Mass, Electrospray Ionization/\*methods ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacology

examined in 23 adult men with DSM III-R diagnosis of concurrent opiate and cocaine dependence. After admission to a clinical research ward, subjects were detoxified with methadone (10-50 mg/day), then were drug-free for 6 days before random assignment to either 4 or 8 mg/day of buprenorphine. Gradually increasing daily sublingual doses of buprenorphine were administered for 5 days, then subjects were maintained on 4 or 8 mg/day of buprenorphine for 12 days. Each subject's preferred brand of cigarettes was available ad libitum throughout the study. Five responses (FR 5) on a key were required to earn each cigarette. The time and number of cigarettes were recorded by an automated cigarette dispenser. Subjects acquired significantly more cigarettes during the buprenorphine induction and maintenance phases (25.5+/-2.0) than during the drug-free phase (18.5+/-1.8; p<0.0002). During buprenorphine induction, the number of cigarettes acquired was positively correlated with increasing doses of buprenorphine (p<0.001) and the inter-cigarette interval was significantly shorter during buprenorphine maintenance than during drug-free conditions (p<0.001). These data showed that daily administration of the partial mu opioid agonist buprenorphine was associated with increased smoking in men concurrently dependent on opiates and cocaine. These findings are consistent with previous reports of opioid-cigarette interactions.

ISSN: 1462-2203.

**Pub Type:** Clinical Trial ; Journal Article.

**Descriptors:** Administration, Sublingual ; Adult ; Buprenorphine/ administration & dosage/\*pharmacology ; Cocaine-Related Disorders/\*drug therapy ; Human ; Inpatients ; Male ; Narcotic Antagonists/administration & dosage/\* pharmacology ; Opioid-Related Disorders/\*drug therapy ; \*Smoking; Support, U.S. Gov't, P.H.S. ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacology ; Pharmacotherapy for opiate dependence

262. Muhleisen P ; al el. (2003) Buprenorphine dispensing in a cohort of community pharmacies in Victoria. *Australian Pharmacist*. Vol 22 (3) March 2003. pp 229-234.

**Abstract:** Abstract not available.

**Notes:** Source: DrugInfo JA AUS 223229.

**Pub Type:** Journal article.

**Descriptors:** Buprenorphine - Therapeutic use; pharmacists; Australia.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries

263. Mutschler N ; Stephen B ; Teoh S ; Mendelson J ; Mello N. (2002) An inpatient study of the effects of buprenorphine on cigarette smoking in men concurrently dependent on cocaine and opioids. *Nicotine Tob Res* 2002 May;4(2):223-8.

**Author Address:** Alcohol and Drug Abuse Research Center, Harvard Medical School, McLean Hospital, 115 Mill Street, Belmont, MA 02478, USA.

**Abstract:** The effect of sublingual buprenorphine on cigarette smoking was

264. Nanovskaya T ; Deshmukh S ; Brooks M ; Ahmed M. (2002) Transplacental transfer and metabolism of buprenorphine. *J Pharmacol Exp Ther* 2002 Jan;300(1):26-33.

**Author Address:** Division of Pharmacology, School of Medicine, University of Missouri, Kansas City, Missouri 64108-2792, USA.

**Abstract:** Information on the direct and indirect effects of buprenorphine (BUP) on the fetus is essential for determining its potential for treatment of the pregnant opiate addict. The goal of this investigation is to determine the transplacental transfer of BUP to the fetal circulation, its metabolism, and effects on the tissue. The technique of dual perfusion of placental lobule is used. The range of BUP concentrations investigated included its peak plasma levels (10 ng/ml) in patients under treatment. A biphasic decline in concentration of the drug in the maternal circulation was observed, initially rapid then slow. During the initial (60 min), the tissue sequestered most of BUP resulting in a low (<10%) transplacental transfer of the drug to the fetal circulation. The concentration ratios of the drug in tissue/maternal and tissue/fetal were 13 +/- 6.5 and 27.4 +/- 0.4. The drug sequestered did not have any adverse effects on placental tissue viability and functional parameters. Less

than 5% of the perfused BUP was metabolized to norbuprenorphine during the 4 h of perfusion and the metabolite was distributed between the tissue, maternal, and fetal circulations. Taken together, these data suggest that the therapeutic levels of BUP in the maternal circulation may have no indirect effects (via the placenta) on the fetus. The observed low transplacental transfer of BUP to the fetal circuit may explain the moderate/absence of neonatal withdrawal in the limited number of reports on mothers treated with the drug during pregnancy.

**ISSN:** 0022-3565.

**URL:** <http://jpet.aspetjournals.org/cgi/content/full/300/1/26>

**Pub. Type:** Clinical Trial ; Journal Article.

**Descriptors:** Adult ; Anti-Inflammatory Agents, Non-Steroidal/ pharmacokinetics; Antipyrene/pharmacokinetics ; Biotransformation ; Buprenorphine/\*pharmacokinetics ; Female ; Human ; \*Maternal-Fetal Exchange ; Narcotic Antagonists/\*pharmacokinetics ; Placenta/ \*metabolism/physiology ; Pregnancy ; Receptors, Opioid/metabolism ; Receptors, Opioid, kappa/metabolism ; Support, U.S. Gov't, P.H.S. ; Tissue Distribution.

**ATTC Buprenorphine Topics:** Pharmacology ; Special populations

265. **Nath R ; Upton R ; Everhart E ; Cheung P ; Shwonek P ; Jones R ; Mendelson J. (1999) Buprenorphine pharmacokinetics: relative bioavailability of sublingual tablet and liquid formulations. J Clin Pharmacol 1999 Jun;39(6):619-23.**

**Author Address:** Drug Dependence Research Center, Langley Porter Psychiatric Institute, University of California, San Francisco 94143-0984, USA.

**Abstract:** Buprenorphine is an effective new treatment for opiate dependence. This study compared the bioavailability of buprenorphine from a tablet to that from a reference solution. Six men experienced with, but not dependent on, opiates (DSM-III-R) were each administered 7.7 mg of buprenorphine in liquid form and 8 mg in tablet form 1 week apart in a balanced crossover design. Plasma levels were measured by electron capture capillary gas chromatography (GC), and concentration-time curves were constructed. Pharmacokinetic data were analyzed by analysis of variance. The bioavailability from the tablet was approximately 50% that from the liquid and was not affected by saliva pH. Lower bioavailability from the tablet may be due to slow dissolution.

**ISSN:** 0091-2700.

**Pub Type:** Clinical Trial ; Journal Article.

**Descriptors:** Administration, Sublingual ; Adult ; Analgesics, Opioid/administration & dosage/\*pharmacokinetics ; Area Under Curve ; Biological Availability ; Buprenorphine/administration & dosage/\*pharmacokinetics ; Comparative Study ; Cross-Over Studies ; Heart Rate/drug effects ; Human ; Male ; Narcotics/adverse effects ; Pharmaceutical Solutions ; Substance Withdrawal Syndrome/physiopathology ; Support, U.S. Gov't, P.H.S. ; Tablets.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacology

266. **National Advisory Committee on Drugs Working Party, National Medicines Information Centre (Ireland). (2002) Report to the National Advisory Committee on Drugs on Use of Buprenorphine as an intervention in the treatment of Opiate Dependence Syndrome. (Ireland). National Advisory Committee on Drugs, 2003, 96 p.**

**Abstract:** A systematic review was undertaken in order to evaluate the potential usefulness of buprenorphine as an intervention in the treatment of opiate dependence. All available data were retrieved by means of a comprehensive search of the published literature and clinical trials databases. Authors of pivotal studies were contacted for further information, for inclusion in a meta analysis. Contact was made with experts in the UK and France, to evaluate the practical issues associated with buprenorphine in a clinical setting. Pharmacoeconomic data were retrieved from the GMS, ERHA and the manufacturer for the purposes of analysis. The review suggests that buprenorphine may be viewed as an effective treatment option in the management of opiate dependence syndrome, with an acceptable safety profile. **ISBN:** 0 7557 1308 7.

**Notes:** To be purchased directly from the Government Publications Sales Office, Sun Alliance House, Molesworth Street, Dublin 2, or by mail order from Government Publications, Postal Trade Section, 4 -5 Harcourt Road, Dublin 2, (Tel:01 476834/35/36/37; Fax:01-4752760).

**URL:** <http://www.nacd.ie/buprenorphine.pdf>

**Pub. Type:** monograph; review; PDF

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

267. **National Association of State Alcohol and Drug Abuse Directors. (2002) States' Perspectives on Buprenorphine and Office-Based Treatment. Paper prepared for the Center on Substance Abuse Treatment, July 2002. 4 p., plus appendices**

**Abstract:** At the request of CSAT, NASADAD convened a State Buprenorphine Focus Group to gather input on the issues surrounding approval of buprenorphine, and its rollout in the US. The intent was to inform CSAT and other stakeholders as to the perspective of state AOD agencies, and to provide guidance to CSAT about the nature of information and technical assistance that may be required by the States when buprenorphine is introduced. Issues raised included cost, consumer or public opinion, impact on existing opioid treatment programs, and access to counseling and other traditional services for buprenorphine patients due to waiting lists.

**Pub. Type:** Opinion paper; Web document

**Notes:** See also Witter M (2002) for conference presentation (slides) on same report.

**URL:** <http://www.nasadad.org/Departments/Buprenorphine/bupreport.htm>

**ATTC Buprenorphine Topics:** Legal/regulatory issues

**268. National Institute on Drug Abuse. (2001) Buprenorphine Update: Questions and Answers. NIDA web site, January 2001.**

**Abstract:** Two-page document containing Q&A on safety and efficacy as well as regulations for administration and delivery of buprenorphine to patients. **CONTENTS:** Question No. 1. Is buprenorphine (alone and in combination) a safe and effective treatment for drug addiction? Question No. 2. Do current regulations properly set forth the rules for administration, delivery, and use of these drugs? Question No. 3. Should more physicians be permitted to dispense these drugs under controlled circumstances? Brief answers are given to common questions.

**URL:** <http://165.112.78.61/Bupupdate.html>

**Pub. Type:** Q&A format; web document.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; Pharmacotherapy for opiate dependence

**269. National Institute on Drug Abuse. (2003) Buprenorphine/naloxone and clonidine: A medication comparison study. Should I join? NIDA Clinical Trials Network, participant brochure, 2003.**

**Abstract:** This is a patient brochure for people interested in joining the NIDA Clinical Trials Network research study comparing the effectiveness of buprenorphine/naloxone with clonidine in the treatment of opioid withdrawal. It describes the medications, their side effects, and what to expect from being a participant in the study. (Available in both HTML and PDF formats.)

**URL:** [http://www.nida.nih.gov/CTN/brochures/BupNx\\_should.pdf](http://www.nida.nih.gov/CTN/brochures/BupNx_should.pdf)  
[http://www.nida.nih.gov/CTN/brochures/BupNx\\_P\\_shouldijoin.html](http://www.nida.nih.gov/CTN/brochures/BupNx_P_shouldijoin.html)

**Pub. Type:** web document; brochure.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

**270. National Institute on Drug Abuse. (2003) Buprenorphine/naloxone and clonidine: A medication comparison study. Now that I've joined. . . NIDA. Clinical Trials Network, participant brochure, March 2003.**

**Abstract:** This is a patient brochure for people who have joined the National Drug Abuse Treatment Clinical Trials Network research study comparing the effectiveness of buprenorphine/naloxone with clonidine in the treatment of opioid withdrawal. It describes the study's procedures, the symptoms of withdrawal, and several effective methods of birth control (as the effects of buprenorphine on a fetus are not yet known). Available in both HTML and PDF formats.

**URL:** [http://www.nida.nih.gov/CTN/brochures/BupNx\\_P\\_joined.html](http://www.nida.nih.gov/CTN/brochures/BupNx_P_joined.html)  
[http://www.nida.nih.gov/CTN/brochures/BupNx\\_joined.pdf](http://www.nida.nih.gov/CTN/brochures/BupNx_joined.pdf)

**Pub. Type:** web document; pdf; patient brochure.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic

medications ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

**271. National Institute on Drug Abuse. (ongoing) [Various articles]. NIDA Notes, quarterly newsletter. (available in print and online).**

**Abstract:** NIDA Notes is a free publication published in print and on the NIDA web site. It covers drug abuse research in the areas of treatment and prevention, epidemiology, neuroscience, behavioral science, health services, and AIDS, and medication development, including NIDA's activities related to Buprenorphine development and use. The publication reports on research; identifies resources; and promotes communication among clinicians, researchers, administrators, policymakers, and the public. The web site is searchable, and searching for "buprenorphine" results in 32 documents, including, "Buprenorphine Treatment Option," "Buprenorphine Taken Three Times per Week is as Effective as Daily Doses in Treating Heroin Addiction," and "Buprenorphine Proves Effective, Expands Options for Treatment." Some of the articles on buprenorphine are summaries of research published in medical or addiction journals (and are in this bibliography under the original author citation). All materials appearing in NIDA Notes are in the public domain and may be reproduced without permission; citation of the source is appreciated.

**URL:** [http://www.drugabuse.gov/NIDA\\_Notes/NNIndex.html](http://www.drugabuse.gov/NIDA_Notes/NNIndex.html)

**Pub. Type:** Overviews; Newsletter articles; Web newsletter.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment outcomes/effectiveness

**272. National Institutes of Health. National Institutes of Health. (1997) Effective Medical Treatment of Opiate Addiction. NIH Consensus Statement Online no. 108, November 17-19, 1997; [cited 11/14/03]: 15(6):1-38.**

**Abstract:** This older document is included here because it is an excellent summary of the state of medical knowledge on the medical treatment of opiate addiction, including use of buprenorphine up to November 1997. The NIH panel that prepared this document was an independent panel of experts from the fields of psychology, psychiatry, behavioral and family medicine, drug abuse, epidemiology, and the public. NIH Consensus Statements provide a "snapshot in time" of objective, science-based evidence for health care providers, patients, and the general public.

**Pub. Type:** Review article; Web document

**URL:** [http://consensus.nih.gov/cons/108/108\\_intro.htm](http://consensus.nih.gov/cons/108/108_intro.htm)

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness; Treatment protocols/physician guidelines

**273. National Library of Medicine. (ongoing) MEDLINEplus. Web site.**

**Abstract:** This is a consumer health information web site created and

maintained by the National Library of Medicine and the National Institutes of Health. MedlinePlus is intended to be a gateway for the public to all sorts of health topics, with contents screened for appropriate, and authoritative information. For example, entering the term "buprenorphine" in the Search box on the main page turns up a variety of articles from news sources and governmental web sites (SAMHSA, NIDA, etc.) as well as consumer information, medical dictionary entries, and drug information. Spanish-language versions of the web pages are also available.

**URL:** <http://medlineplus.gov/>

**Pub. Type:** web site.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Combined treatment with other therapeutic medications ; Legal/regulatory issues ; Pain management ; Pharmacology ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment outcomes/effectiveness

**274. New South Wales Health Department. (2001) New South Wales Policy for the Use of Buprenorphine in the Treatment of Opioid Dependence. New South Wales Health Department, Australia, 2001. (63 pages).**

**Abstract:** This Booklet is primarily about the policies for use and prescription in Australia, but also contains sections on selecting buprenorphine (instead of methadone or another medication), contraindications, side effects, dosing and administration, ongoing and maintenance treatment, and drug interactions.

**URL:** [http://www.health.nsw.gov.au/public-health/dpb/publications/pdf/use\\_of\\_buprenorphine\\_treatmentofopioid\\_dependence.pdf](http://www.health.nsw.gov.au/public-health/dpb/publications/pdf/use_of_buprenorphine_treatmentofopioid_dependence.pdf)

**Pub. Type:** Booklet; PDF.

**ATTC Buprenorphine Topics:** Dosing/administration ; History, use and effectiveness in other countries ; Legal/regulatory issues ; Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

**275. Newman R. (2003) Maintenance buprenorphine for opioid users. Lancet 2003 May 31;361(9372):1907; author reply 1907-8.**

**Abstract:** Ethical concerns about the comparison of buprenorphine with placebo in association with intensive psychosocial therapy for heroin addiction cannot be as readily dismissed as Johan Kakko and colleagues and Fergus Law and David Nutt suggest. Kakko and co-workers note that without concomitant agonist treatment "... psychosocial interventions have consistently failed to show effectiveness" in the management of heroin dependence. Their own findings confirm this statement: within 2 weeks a quarter of controls had been lost to follow-up, and by the end of the second month all had dropped out. At that point, the randomised, placebo-controlled trial was over. And yet, the investigation continued, and none of the controls was offered active treatment. Within 1 year 20% of controls had died of an overdose, compared with none in the buprenorphine group. The findings of the study suggest that buprenorphine could have prevented this outcome in at least some of the individuals.

Furthermore, the omission of an offer of agonist medication after drop-out was particularly serious in this instance because of the protocol of the study--i.e., individuals in the control group were detoxified, then exposed to what was "generally reported [as] a massive heroin craving that was triggered during sessions of relapse-prevention". Craving among addicts whose tolerance has been reduced substantially as a result of detoxification can be life threatening, and while cause cannot be proven, the fact is four of 20 controls died.

**ISSN:** 0140-6736.

**Pub Type:** Comment ; Letter.

**Descriptors:** Buprenorphine/\*therapeutic use ; Ethics, Clinical ; Heroin Dependence/\*drug therapy ; Human ; Narcotic Antagonists/\*therapeutic use; Reproducibility of Results ; Research Design/standards.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

**276. Nutt D ; Lingford-Hughes A ; Daglish M. (2003) Future directions in substance dependence research. J Neural Transm 64:95 - 103, 2003.**

**Abstract:** The current and future developments in the diagnosis and management of substance dependence are reviewed. The brain circuits of substance dependence are described. The role of various neurotransmitter (dopamine, opioid, GABA, glutamate and substance P) systems in the occurrence and treatment of substance dependence is discussed. The use of GBR-12909, BP-897, bupropion, buprenorphine, heroin, methadone, L-822179, acamprosate and substance P antagonists is explained. The new pharmacological approaches to treatment based on receptor targets and improved kinetic profiles are likely to lead to improved diagnosis and outcome for future generations of substance abusers. (Conference paper: 5th Neuropsychiatry Symposium of the European Institute of Healthcare, 2003)

**Pub. Type:** Journal article; conference paper.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Pharmacology ; Pharmacotherapy for opiate dependence

**277. Obadia Y ; Perrin V ; Feroni I ; Vlahov D ; Moatti J. (2001) Injecting misuse of buprenorphine among French drug users. Addiction 2001 Feb;96(2):267-72.**

**Author Address:** Regional Center for Disease Control of South-Eastern France (ORS PACA), ORS PACA-INSERM U379, 23 rue Stanislas Torrents, 13006 Marseille, France. [orspaca@wanadoo.fr](mailto:orspaca@wanadoo.fr)

**Abstract:** **AIMS:** To evaluate the extent to which the introduction (February 1996) of ambulatory prescriptions of buprenorphine for drug maintenance treatment (DMT) has been associated with its intravenous illicit use by French injecting drug users (IDUs). **DESIGN:** Cross-sectional survey (September 1997), using self-administered questionnaires, in a sample of IDUs recruited at 32 pharmacies, four needle exchange programmes and three syringe vending machines. **SETTING:** Thirty-nine sites where IDUs have access to sterile syringes in the city of Marseille (South-Eastern France). **PARTICIPANTS:**

Sample of IDUs attending community pharmacies, vending machines and needle exchange programs to obtain equipment. MEASUREMENT: To compare characteristics of IDUs who declared that they only injected buprenorphine in the prior 6 months versus the rest of the sample. FINDINGS: Among the 343 respondents (response rate = 70.7%), 33.8% were polydrug users who occasionally injected buprenorphine in parallel to heroin and/or cocaine, while 23.9% only injected buprenorphine in the previous 6 months. IDUs in this latter group were younger, injected more frequently, and were more frequently on buprenorphine DMT, but they were less likely to be HIV-infected and to declare HIV-related injecting risky behaviours. CONCLUSIONS: Substantial risk of injecting misuse is associated with large-scale diffusion of buprenorphine DMT. A more stringent regulation for medical dispensation of buprenorphine than the current French general freedom of prescription for all physicians, including general practitioners in ambulatory care, may be necessary in other countries which are considering the diffusion of buprenorphine DMT.

ISSN: 0965-2140.

**Pub Type:** Journal Article.

**Descriptors:** Adolescent ; Adult ; Buprenorphine/\*administration & dosage ; Cross-Sectional Studies ; Female ; France/epidemiology ; \*Health Services Accessibility ; Human ; Male ; Opioid-Related Disorders/\*epidemiology ; \*Preventive Health Services ; Substance Abuse, Intravenous/etiology /\*rehabilitation ; Support, Non-U.S. Gov't ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Dosing/administration ; History, use and effectiveness in other countries ; Prevalence of use for opiate dependence

**278. O'Connor P. (2000) Treating opioid dependence--new data and new opportunities. N Engl J Med 2000 Nov 2;343(18):1332-4.**

**Abstract:** Heroin use in the United States has grown considerably over the past decade. Approximately 3 million Americans have used heroin, a fact that has led to increasing concern about heroin-related problems such as overdose, human immunodeficiency virus (HIV) infection, unemployment, and crime. Finding effective treatments for heroin dependence is critical. The report by Johnson et al. in this issue of the Journal represents an important step toward expanding the options for treatment.

ISSN: 0028-4793.

**Pub Type:** Comment ; Editorial.

**Descriptors:** Analgesics, Opioid/\*therapeutic use ; Buprenorphine/\*therapeutic use ; Drug Administration Schedule ; Human ; Methadone/administration & dosage/\*therapeutic use ; Methadyl Acetate/\*therapeutic use ; Opioid-Related Disorders/\*drug therapy.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

**279. O'Connor P. (2001) "A comparison of levomethadyl acetate, buprenorphine, and methadone for opioid dependence": Reply. New England Journal of Medicine. Vol 344(7) Feb 2001, 531.**

**Abstract:** Replies to comments by B. Stimmel and T. V. Reese, Sr. on the article by R. E. Johnson et al (2000) that compared levomethadyl acetate, buprenorphine, and high (60-100 mg/day) and low (20 mg/day) dose methadone for the treatment of opioid dependence, and on the accompanying editorial by P. G. O'Connor (see record 2000-12281-003). O'Connor suggests that, as Stimmel and Reese point out, the dose of methadone is clearly related to its effectiveness in the treatment of opioid dependence. He also suggests that while buprenorphine has a potential for abuse, as a partial opioid agonist, it may have less potential for abuse than pure opioid agonists such as methadone. O'Connor also discusses the use of office-based maintenance therapy for opioid dependence, suggesting that while the approach may be useful in areas that do not have maintenance programs (as suggested by Reese), it will also be useful in areas where programs exist but access to them is limited due to an insufficient number of treatment slots or other barriers. Studies of office-based methadone maintenance suggest that selected patient can do well in the office setting.

ISSN: 0028-4793 (Print).

**Pub Type:** Journal Article.

**Descriptors:** levomethadyl acetate vs buprenorphine vs high vs low-dose methadone, study retention & abstinence & severity of drug problem, adults with opioid dependence, 17 week study, commentary reply ; \*Drug Dependency ; \*Drug Therapy ; \*Methadone Maintenance ; \*Narcotic Agonists ; \*Opiates ; Drug Abstinence ; Drug Dosages ; Drug Rehabilitation ; Experimental Attrition ; Maintenance Therapy ; Severity (Disorders) ; Human. Male. Female. Adulthood (18 yrs & older) ; Comment. Letter.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Pharmacotherapy for opiate dependence

**280. O'Connor P ; Fiellin D. (2000) Pharmacologic treatment of heroin-dependent patients. Ann Intern Med 2000 Jul 4;133(1):40-54.**

**Author Address:** Yale University School of Medicine and Yale-New Haven Hospital Primary Care Center, New Haven, Connecticut 06520, USA.

**Abstract:** Patients with heroin dependence frequently present to internists and other physicians for heroin-related medical, psychiatric, and behavioral health problems and often seek help with reducing their heroin use. Thus, physicians should be familiar with the identification and diagnosis of heroin dependence in their patients and be able to initiate treatment of heroin dependence both directly and by referral. Recent research has provided much information concerning effective pharmacologically based treatment approaches for managing opioid withdrawal and helping patients to remain abstinent. Methadone maintenance and newer approaches using L-alpha acetylmethadol and buprenorphine seem to be particularly effective in promoting relapse prevention. Although these treatments are currently provided in special drug treatment settings, recent and ongoing research indicates that the physician's office may be an effective alternative site for these treatments.

ISSN: 0003-4819.

**Pub Type:** Journal Article ; Review.

**Descriptors:** Analgesics, Opioid/therapeutic use ; Buprenorphine/therapeutic use ; Counseling ; Heroin Dependence/\*drug therapy/psychology/\*rehabilitation; Human ; Mental Disorders/complications ; Methadone/therapeutic use ; Methadyl Acetate/analogs & derivatives/therapeutic use ; Naltrexone/therapeutic use ; Narcotic Antagonists/therapeutic use ; Physician's Role ; Substance Withdrawal Syndrome/diagnosis/therapy ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

281. O'Connor P ; Kosten T ; Stine S. (2003) Management of opioid intoxication and withdrawal. In: Graham, Allen W ; Schultz, Terry K ; Mayo-Smith, Michael F ; Ries, Richard K ; Wilford, Bonnie B. Principles of Addiction Medicine / 3<sup>rd</sup> edition. Chevy Chase, MD : American Society of Addiction Medicine, Inc., 2003, pp. 651-669.

**Abstract:** This chapter reviews the clinical features of opioid intoxication and withdrawal. Several pharmacologic therapies for withdrawal are discussed, including detoxification using methadone, clonidine, naltrexone, and buprenorphine.

**ISSN:** 1880425084.

**Pub Type:** Book chapter; Review.

**Notes:** ADAI Library: RC 644 M455 2003 [REF HAND]

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence

282. Oliveto A ; Feingold A ; Schottenfeld R ; Jatlow P ; Kosten T. (1999) Desipramine in opioid-dependent cocaine abusers maintained on buprenorphine vs methadone. Arch Gen Psychiatry 1999 Sep;56(9):812-20.

**Author Address:** Department of Psychiatry, Yale University School of Medicine, West Haven, Conn, USA. oliveto.alison\_h@west-haven.va.gov

**Abstract:** BACKGROUND: Cocaine abuse occurs in 40% to 60% of patients entering opioid maintenance treatment, and effective pharmacotherapies are needed for this combined dependence. METHODS: This 13-week, randomized, double-blind, placebo-controlled trial evaluated the efficacy of desipramine hydrochloride (0 or 150 mg/d) plus buprenorphine hydrochloride (12 mg/d) or methadone hydrochloride (65 mg/d) in 180 opioid-dependent cocaine abusers (124 men, 56 women). Supervised urine samples were obtained thrice weekly, and self-reported cocaine and heroin use was reported once weekly.

Desipramine plasma levels were determined at weeks 4 and 10. RESULTS: In men, opioid abstinence was increased more rapidly over time when treated with methadone than with buprenorphine, whereas cocaine abstinence was increased more with buprenorphine than with methadone. In women, opioid abstinence was increased the least rapidly when treated with buprenorphine plus placebo, while cocaine abstinence was increased more rapidly over time when treated with methadone than with buprenorphine. Regardless of sex or

opioid medication, desipramine increased opioid and cocaine abstinence more rapidly over time than placebo. Self-reported opioid use confirmed these findings. Desipramine plasma levels were higher in women than in men, particularly those on buprenorphine maintenance. Higher desipramine plasma levels were associated with greater opioid, but not cocaine, abstinence.

CONCLUSIONS: Desipramine may be a useful adjunctive medication in facilitating opioid and cocaine abstinence in opioid-maintained patients. The efficacy of opioid medications to treat opioid or cocaine dependence may differ by sex. These findings highlight the importance of including sex as a factor when examining treatment outcome in these types of trials.

**ISSN:** 0003-990X.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Analgesics, Opioid/\*therapeutic use ; Antidepressive Agents, Tricyclic/\*therapeutic use ; Buprenorphine/\*therapeutic use ; Cocaine-Related Disorders/\*drug therapy/epidemiology ; Comorbidity ; Comparative Study ; Desipramine/\*therapeutic use ; Drug Administration Schedule ; Drug Therapy, Combination ; Female ; Heroin Dependence/epidemiology/rehabilitation ; Human ; Male ; Methadone/\*therapeutic use ; Middle Age ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/epidemiology/\*rehabilitation ; Sex Factors ; Support, U.S. Gov't, P.H.S. ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacotherapy for opiate dependence ; Special populations

283. Oliveto A ; Kosten T. (1997) Buprenorphine. In: Stine SM ; Kosten TR (eds.) New Treatments for Opiate Dependence. New York : Guilford Press, 1997, pp. 254-267.

**Abstract:** Buprenorphine was developed as part of an intense interest in the synthesis and study of opioid compounds with mixed action agonist-antagonist effects (Hart & McCawley, 1944; Lewis, 1982). Marketed as an injectable analgesic, buprenorphine was shown to be 25-40 times more potent than morphine (Houde, 1979; Jasinski et al., 1978; Lewis et al., 1982). Jasinski and colleagues (1978) then demonstrated that buprenorphine could relieve acute opioid withdrawal and craving and thus began more than a decade of clinical and behavioral pharmacological research on buprenorphine. This research has substantiated buprenorphine's potential as a treatment for opiate dependence, and buprenorphine is presently undergoing the U.S. Food and Drug Administration approval process.

**Pub. Type:** Book chapter.

**Notes:** Older reference included as good summary up to 1997. ADAI Library: RC 568 O58 N49 1997

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration

284. Pacini M ; Maremmani I. (2002) Buprenorphine: Evidence for Effectiveness. Heroin Addiction & Related Clinical Problems 4(1):13 - 24, 2002.

**Abstract:** In all cases, opiate addiction is best treated by the use of opiate agonist agents. A maintenance regimen based on an opiate agonist leads to a gradual dwindling of the subjective effects due to street opiates, thanks to the blockade achieved by these agents on the receptors that are reached by heroin. Buprenorphine looms as the most useful of the latest generation of agonist agents for the treatment of opioid use disorders. It is equivalent to other opiates as regards retention rates and control of street opiate use. Apart from maintenance programmes for opiate addiction, buprenorphine has proved effective in short-term programmes for opiate detoxification. Buprenorphine treatment should be regarded as first-line in subjects with low level of craving and low severity of addictive behaviours, as long as: 1) it is documented that low methadone doses produce complete and stable remission; or 2) after a period of ongoing abstinence in drug-free conditions, the patient has recently relapsed into use of street opiates, so that their tolerance threshold is presumably still low. For subjects, whose tolerance is unknown, or when anamnestic or objective elements suggest there may be a high tolerance threshold, or else in cases comparing a recent history of unresponsiveness to low dose methadone treatments (below 60 mg), methadone should be the first choice for the therapy of opiate addiction. Subjects who have proved to be refractory to buprenorphine, even at higher dosages, can reasonably be directed to a methadone treatment programme.

**ISSN:** 1592-1638.

**Notes:** EUROPAD official journal.

**URL:** <http://www.europad.org>

**Pub. Type:** Journal Article.

**Descriptors:** Addiction; Dependence Treatment; Human.

**ATTC Buprenorphine Topics:** Dosing/administration ; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence

285. **Pani P ; Maremmani I ; Pirastu R ; Tagliamonte A ; Gessa G. (2000) Buprenorphine: a controlled clinical trial in the treatment of opioid dependence. Drug Alcohol Depend 2000 Jul 1;60(1):39-50.**

**Author Address:** Servizio Tossicodipendenze Azienda USL 8, Cagliari, Italy. pallolo@tin.it

**Abstract:** Clinical trials carried out to compare methadone and buprenorphine in the treatment of opioid dependence have generally employed an alcoholic solution of buprenorphine, which has a bioavailability superior to that of the tablets. Since the product available for large scale use is in tablet form, one intended to verify the efficacy of this formulation. In a multicentre randomised controlled double blind study, 72 opioid dependent patients were assigned to treatment with buprenorphine (8 mg/day) or methadone (60 mg/day) for a period of 6 months. The two compounds did not show any significant difference with regard to urinalyses: the average percentage of analyses proving negative was 60.4% for patients assigned to buprenorphine, and 65.5% for those assigned to methadone. With regard to retention, a non-significant trend in favour of methadone was observed. Patients completing the trial improved

significantly in terms of psychosocial adjustment and global functioning, as ascertained by the DSM-IV-GAF and symptom checklist-90 (SCL-90) scales, and this was independent of the treatment group. Finally, in the case of buprenorphine, patients who dropped out differed significantly from those who stayed, in terms of a higher level of psychopathological symptoms, and a lower level of psychosocial functioning. The results of the study further support the utility of buprenorphine for the treatment of opioid dependence.

**ISSN:** 0376-8716.

**Pub Type:** Clinical Trial ; Journal Article ; Multicenter Study ; Randomized Controlled Trial.

**Descriptors:** Adolescent ; Adult ; Behavior, Addictive/\*drug therapy/psychology; Buprenorphine/\*therapeutic use/urine ; Double-Blind Method ; Female ; Human ; Male ; Methadone/\*therapeutic use/urine ; Multivariate Analysis ; Narcotics/\*therapeutic use/urine ; Opioid-Related Disorders/\*drug therapy/rehabilitation ; Support, Non-U.S. Gov't ; Tablets.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Special populations

286. **Perez de los Cobos J ; Martin S ; Etcheberrigaray A ; Trujols J ; Batlle F ; Tejero A ; Queraltó J ; Casas M. (2000) A controlled trial of daily versus thrice-weekly buprenorphine administration for the treatment of opioid dependence. Drug Alcohol Depend 2000 Jun 1;59(3):223-33.**

**Author Address:** Addictive Behaviours Unit, Department of Psychiatry, Hospital de la Santa Creu i Sant Pau, Barcelona Autonomous University School of Medicine, Sant Antoni Ma Claret, 167, 08025, Barcelona, Spain.

**Abstract:** This study was aimed at determining whether thrice-weekly administration of buprenorphine is as effective as daily administration for treating opioid dependence. A total of 60 treatment-seeking opioid addicts were randomly assigned to take buprenorphine tablets sublingually either every day (8 mg) or thrice-weekly (16 mg on Mondays and Wednesdays and 24 mg on Fridays) over the course of a 12-week, double-blind, parallel trial. The buprenorphine dosing schedule had no significant effect on treatment retention. The rates of opioid-positive urine tests were significantly higher among those subjects who were given buprenorphine thrice weekly (58.5%) than among those who took it daily (46.6%). An analysis of the completers did not detect a significant effect of buprenorphine dosing schedule. The results obtained in our clinical trials indicate the advisability of daily doses of buprenorphine, at least at the beginning of a maintenance programme.

**ISSN:** 0376-8716.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Analysis of Variance ; Behavior, Addictive/drug therapy/urine ; Buprenorphine/\*administration & dosage/blood ; Double-Blind Method ; Female ; Human ; Male ; Middle Age ; Narcotic Antagonists/\*administration & dosage/blood ; Opioid-Related Disorders/\*drug therapy/urine ; Support, Non-U.S. Gov't ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

287. **Petitjean S. (2003) Buprenorphine may be more effective than clonidine and other symptomatic medications for short term ambulatory heroin withdrawal. Evid Based Ment Health 2003 Aug;6(3):92.**

**Author Address:** University of Basel, Basel, Switzerland.

**Abstract:** Comment on article by Lintzeris N, Bell J, Bammer G, Jolley DJ, Rushworth L., "A randomized controlled trial of buprenorphine in the management of short-term ambulatory heroin withdrawal." *Addiction*. 2002 Nov;97(11):1395-404.

**ISSN:** 1362-0347.

**Pub Type:** Comment ; Journal Article.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

288. **Petitjean S ; Stohler R ; Deglon J ; Livoti S ; Waldvogel D ; Uehlinger C ; Ladewig D. (2001) Double-blind randomized trial of buprenorphine and methadone in opiate dependence. Drug Alcohol Depend 2001 Mar 1;62(1):97-104.**

**Author Address:** Department of Psychiatry, University of Basel Wilhelm Klein-Strasse 27, CH-4025 Basel, Switzerland. sylvie.petitjean@pukbasel.ch

**Abstract:** This study compared the safety and efficacy of sublingual buprenorphine tablets with oral methadone in a population of opioid-dependent individuals in a double-blind, randomized, 6-week trial using a flexible dosing procedure. Fifty-eight patients seeking treatment for opioid dependence were recruited in three outpatient facilities and randomly assigned to substitution with buprenorphine or methadone. The retention rate was significantly better in the methadone maintained group (90 vs. 56%;  $P < 0.001$ ). Subjects completing the study in both the treatment groups had similar proportions of opioid positive urine samples (buprenorphine 62%; methadone 59%) and positive urine specimens, as well as mean heroin craving scores decreased significantly over time ( $P = 0.035$  and  $P < 0.001$ ). The proportion of cocaine-positive toxicology results did not differ between groups. At week six mean stabilization doses were 10.5 mg per day for the sublingual buprenorphine tablet, and 69.8 mg per day for methadone, respectively. Patient performance during maintenance was similar in both the groups. The high attrition rate in the buprenorphine group during the induction phase might reflect inadequate induction doses. Thus, buprenorphine is a viable alternative for methadone in short-term maintenance treatment for heroin dependence if treatment induction is done with adequate dosages.

**ISSN:** 0376-8716.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Analysis of Variance ; Behavior, Addictive/\*psychology ; Buprenorphine/\*therapeutic use ; Chi-Square Distribution ; Double-Blind Method ; Female ; Heroin Dependence/psychology/\*rehabilitation/urine ; Human ; Male ; Methadone/\*therapeutic use ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/psychology/rehabilitation/urine ;

Patient Compliance ; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

289. **Petry N ; Bickel W. (1999) Buprenorphine dose self-selection: effects of an alternative reinforcer, behavioral economic analysis of demand, and examination of subjective drug effects. Exp Clin Psychopharmacol 1999 Feb;7(1):38-48.**

**Author Address:** Department of Psychiatry, University of Vermont, USA. petry@psychiatry.uvm.edu

**Abstract:** Buprenorphine (BUP)-maintained patients were first exposed to various BUP doses and then chose between BUP doses and money. In the choice phase, they had 10 units exchangeable for units of BUP (constant at 3 mg/unit) or money (varied from \$0.30 to \$20/unit). They chose BUP exclusively (30 mg) when the money alternative was low. As available money increased, they selected lower daily BUP doses (down to 3 mg). An economic analysis indicated demand for BUP was inelastic; changes in drug intake were proportionally lower than changes in price. Subjective reports of agonist and withdrawal effects increased  $> 200\%$  when high and low BUP doses, respectively, were given during the exposure phase. In the choice phase, subjective drug effects were constant regardless of the BUP dose selected. Thus, BUP dose selection varies with the magnitude of alternative reinforcers, and subjective drug effects depend on whether doses are self- or experimenter-selected.

**ISSN:** 1064-1297.

**Pub Type:** Clinical Trial ; Journal Article.

**Descriptors:** Adult ; Analgesics, Opioid/administration & dosage/\*economics/\*pharmacology ; Behavior/\*drug effects ; Buprenorphine/administration & dosage/\*economics/\*pharmacology ; Human ; Male ; Opioid-Related Disorders/\*psychology/urine ; Reinforcement (Psychology) ; Self Administration ; Substance Withdrawal Syndrome/psychology ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

290. **Petry N ; Bickel W. (2000) Gender differences in hostility of opioid-dependent outpatients: Role in early treatment termination. Drug & Alcohol Dependence. Vol 58(1-2) Feb 2000, 27-33.**

**Abstract:** Evaluated gender differences in hostility and the role of hostility in predicting early treatment termination of opioid-dependent outpatients. Demographic characteristics and Addiction Severity Index (ASI) ratings were collected from 104 patients (68 males and 36 females) at intake to a buprenorphine treatment program. Hostility was assessed using the Buss-Durkee Hostility Scale. Compared to male opioid-dependent patients, females scored significantly higher on this scale. 13% of males and 25% of females were classified as early terminators. Stepwise logistic regression identified

predictors of early treatment termination. Severity of legal and employment problems and the interaction between hostility and gender predicted early treatment termination status. Patients with less severe legal problems and patients with greater employment problems were more likely to terminate early. Higher levels of hostility predicted early treatment termination of female patients, but hostility levels were not associated with treatment termination in male patients. Results from this study show that female heroin addicts have high levels of hostility and suggest that hostility may be an important predictor of premature discharge from opioid substitution programs, especially among women.

**ISSN:** 0376-8716 (Print).

**Pub Type:** Journal Article; Empirical Study.

**Descriptors:** gender differences in & role of hostility, early treatment termination prediction, opioid dependent outpatients in buprenorphine treatment program ; \*Drug Rehabilitation ; \*Hostility ; \*Human Sex Differences ; \*Treatment Termination ; Drug Addiction ; Drug Therapy ; Narcotic Agonists ; Opiates ; Prediction ; Human. Male. Female. Outpatient. Adulthood (18 yrs & older).

**ATTC Buprenorphine Topics:** Psychosocial treatment aspects ; Special populations

291. **Petry N ; Bickel W ; Badger G. (1999) A comparison of four buprenorphine dosing regimens in the treatment of opioid dependence. Clin Pharmacol Ther 1999 Sep;66(3):306-14.**

**Author Address:** University of Vermont, Department of Psychiatry, Substance Abuse Treatment Center, Burlington, USA.

**Abstract:** OBJECTIVES: This study compared 24-, 48-, 72-, and 96-hour buprenorphine dosing regimens in opioid-dependent outpatients. METHODS: Fourteen subjects received buprenorphine in a double-blind, placebo-controlled crossover trial. Daily sublingual maintenance doses were 4 mg/70 kg (n = 5) and 8 mg/70 kg (n = 9). After a stabilization period of maintenance administration, subjects received, in a random order, four dosing regimens for five repetitions of each regimen: a maintenance dose every 24 hours, a doubled maintenance dose every 48 hours, a tripled maintenance dose every 72 hours, and a quadrupled maintenance dose every 96 hours. In the latter three dosing regimens, subjects received placebo on the interposed day(s). Study participation was contingent on opioid abstinence and daily clinic attendance. Measures of subjective opioid agonist and withdrawal effects were assessed daily. RESULTS: Relative to standard maintenance dosing, none of the higher doses induced agonist effects. Changes in indices of subjective withdrawal effects were noted as the time since the last active dose increased during intermittent dosing regimens, but the magnitude of these effects was relatively low and was comparable to those found in other alternate-day dosing studies. CONCLUSIONS: These results support the feasibility and safety of twice weekly buprenorphine dosing regimens.

**ISSN:** 0009-9236.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Buprenorphine/\*administration & dosage ; Comparative Study ; Cross-Over Studies ; Dose-Response Relationship, Drug ; Double-Blind Method ; Drug Administration Schedule ; Feasibility Studies ; Female ; Human ; Male ; Middle Age ; Narcotics/\*administration & dosage ; Opioid-Related Disorders/\*drug therapy ; Support, U.S. Gov't, P.H.S. ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

292. **Petry N ; Bickel W ; Badger G. (2000) A comparison of four buprenorphine dosing regimens using open-dosing procedures: is twice-weekly dosing possible? Addiction 2000 Jul;95(7):1069-77.**

**Author Address:** Department of Psychiatry, University of Vermont, Burlington, USA. petry@psychiatry.uhc.edu

**Abstract:** AIMS: To compare opioid withdrawal symptoms during 24-, 48-, 72- and 96-hour buprenorphine dosing regimens and to evaluate subjects' preferences for these different dosing schedules. SUBJECTS: Fourteen opioid-dependent subjects participated in this study. They received daily sublingual maintenance doses of 4 mg/70 kg (n = 4) or 8 mg/70 kg (n = 10) of buprenorphine. INTERVENTION: In the first study subjects received, in a random order, four dosing regimens for five repetitions of each: daily maintenance doses every 24 hours (4 or 8 mg/70 kg), double the daily maintenance dose every 48 hours (8 or 16 mg/70 kg), triple the daily maintenance dose every 72 hours (12 or 24 mg/70 kg), and quadruple the daily maintenance dose every 96 hours (16 or 32 mg/70 kg). Measures of subjective and observer opioid withdrawal symptoms were assessed prior to receipt of each dose. In a second study, subjects chose between the different dosing regimens. FINDINGS: Some withdrawal ratings increased during the less frequent dosing schedules in the first study. In the second study, 46% of subjects preferred the quadruple-every-fourth-day dosing regimen over every other option, and only 14% preferred to be dosed daily. CONCLUSIONS: These results suggest that some opioid-dependent outpatients are willing and able to endure the withdrawal symptoms associated with less than daily dosing, and a twice-weekly dosing regimen may be possible.

**ISSN:** 0965-2140.

**Pub Type:** Clinical Trial ; Controlled Clinical Trial;Journal Article.

**Descriptors:** Adult ; Analysis of Variance ; Buprenorphine/\*administration & dosage/adverse effects ; Comparative Study ; Drug Administration Schedule ; Female ; Human ; Male ; Middle Age ; Narcotics/\*administration & dosage/adverse effects ; Opioid-Related Disorders/\*rehabilitation ; Substance Withdrawal Syndrome/diagnosis/etiology ; Support, U.S. Gov't, P.H.S. ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

293. **Petry N ; Bickel W ; Badger G. (2001) Examining the limits of the buprenorphine interdosing interval: daily, every-third-day and every-fifth-day dosing regimens. Addiction 2001 Jun;96(6):823-34.**

**Author Address:** Departments of Psychiatry and Psychology, University of Vermont, USA. petry@psychiatry.uhc.edu

**Abstract:** AIMS: Opioid-dependent outpatients may be more likely to present for pharmacological treatment if less than daily dosing can be arranged. These studies compared opioid withdrawal symptoms during 24-, 72-, and 120-hour buprenorphine dosing regimens and evaluated participants' preferences for these different dosing regimens. PARTICIPANTS: Thirty-three opioid-dependent participants received daily sublingual maintenance doses of 4 mg/70 kg (n = 14) or 8 mg/70 kg (n = 19) of liquid buprenorphine. METHODS: In Study I participants received, in a random order, three dosing regimens for five repetitions of each: daily maintenance doses every 24 hours (4 or 8 mg/70 kg), triple the daily maintenance dose every 72 hours (12 or 24 mg/70 kg) and quintuple the daily maintenance dose every 120 hours (20 or 40 mg/70 kg). Doses were administered under double-blind procedures, and placebos were administered on the interposed days during the latter two regimens. Subjective and observer ratings of opioid withdrawal symptoms were assessed daily prior to receipt of each dose. In Study II, a new group of participants received each of the three dosing regimens under open-dosing procedures and then chose between the different dosing regimens. FINDINGS: Opioid withdrawal symptoms increased significantly during the every-fifth-day dosing regimen in both the blind- and open-dosing studies. In the choice phase of Study II, only one participant (7%) chose quintuple-every-fifth-day dosing over all other dosing options. CONCLUSIONS: These results suggest that the maximum duration of action of buprenorphine is less than 5 days when five times the daily maintenance dose is provided.

**ISSN:** 0965-2140.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** ; Analysis of Variance ; Appointments and Schedules ; Buprenorphine/\*administration & dosage ; Comparative Study ; Double-Blind Method ; Drug Administration Schedule ; Female ; Human ; Male ; Middle Age ; Narcotics/\*administration & dosage ; Opioid-Related Disorders/\*drug therapy ; Patient Compliance ; Patient Satisfaction ; Substance Withdrawal Syndrome/drug therapy ; Support, U.S. Gov't, P.H.S. ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

294. **Petry N ; Bickel W ; Piasecki D ; Marsch L ; Badger G. (2000) Elevated liver enzyme levels in opioid-dependent patients with hepatitis treated with buprenorphine. Am J Addict 2000 Summer;9(3):265-9.**

**Author Address:** Department of Psychiatry, University of Connecticut School of Medicine, Farmington 06030-1517, USA. petry@psychiatry.uhc.edu

**Abstract:** The purpose of this study was to assess changes in liver enzyme levels among opioid-dependent patients treated with buprenorphine. Liver enzyme levels were evaluated among 120 individuals before treatment and following a minimum of 40 days of buprenorphine treatment (2, 4, or 8 mg/70 kg/day). Among patients with a history of hepatitis, AST and ALT levels

significantly increased ( $p < .05$ ) with buprenorphine treatment. The odds of observing an increase in AST were determined to be dependent upon buprenorphine dose ( $p < .05$ ; odds ratio = 1.23 per 1 mg increase in dose). These results suggest that liver enzyme levels should be monitored carefully when patients with hepatitis are treated with buprenorphine.

**ISSN:** 1055-0496.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Aged ; Buprenorphine/\*adverse effects/therapeutic use ; Female ; Hepatitis/\*complications ; Human ; Liver/drug effects/\*enzymology ; Male ; Middle Age ; Narcotic Antagonists/\*adverse effects/therapeutic use ; Opioid-Related Disorders ; Support, U.S. Gov't, P.H.S. ; Transaminases/drug effects/\*metabolism.

**ATTC Buprenorphine Topics:** Pharmacology ; Pharmacotherapy for opiate dependence

295. **Polettini A ; Huestis M. (2001) Simultaneous determination of buprenorphine, norbuprenorphine, and buprenorphine-glucuronide in plasma by liquid chromatography-tandem mass spectrometry. J Chromatograph -- B: Biomed Sci Appl. vol 754: 447-459, 2001.**

**Author Address:** Chemistry and Drug Metabolism Section, IRP, NIDA, NIH, Baltimore, MD 21224, USA

**Abstract:** For the first time, an LC-MS-MS method has been developed for the simultaneous analysis of buprenorphine (BUP), norbuprenorphine (NBUP), and buprenorphine-glucuronide (BUPG) in plasma. Analytes were isolated from plasma by C18 SPE and separated by gradient RP-LC. Electrospray ionization and MS-MS analyses were carried out using a PE-Sciex API-3000 tandem mass spectrometer. The m/z 644-->m/z 468 transition was monitored for BUPG, whereas for BUP, BUP-d4, NBUP, and NBUP-d3 it was necessary to monitor the surviving parent ions in order to achieve the required sensitivity. The method exhibited good linearity from 0.1 to 50 ng/ml ( $r^2 > 0.998$ ). Extraction recovery was higher than 77% for BUPG and higher than 88% for both BUP and NBUP. The LOQ was established at 0.1 ng/ml for the three analytes. The method was validated on plasma samples collected in a controlled intravenous and sublingual buprenorphine administration study. Norbuprenorphine-glucuronide was also tentatively detected in plasma by monitoring the m/z 590-->m/z 414 transition.

**ISSN:** 1387-2273.

**Notes:** NIDA Library reprint.

**Pub Type:** article.

**Descriptors:** Analgesics, Opioid/blood\* ; Buprenorphine/analogs & derivatives ; Buprenorphine/blood\* ; Chromatography, Liquid/methods\* ; Human ; Quality Control ; Spectrum Analysis, Mass/methods\*.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Pharmacology

296. **Preston K ; Bigelow G. (2000) Effects of agonist-antagonist opioids in humans trained in a hydromorphone/not hydromorphone discrimination. Journal of Pharmacology & Experimental Therapeutics. Vol 295(1) Oct**

2000, 114-124.

**Abstract:** Examines the discrimination of agonist-antagonist opioids in 8 male Ss (aged 31-40 yrs) trained in a two-choice hydromorphone/not hydromorphone discrimination. Ss were trained to discriminate the mu receptor agonist hydromorphone (3 mg/70 kg, i.m.) ("Drug A") from a "Not Drug A" saline placebo. Ss received financial reinforcement for correct responses. After training, generalization dose-effect curves for hydromorphone, butorphanol, pentazocine, nalbuphine, and buprenorphine were determined. Other subjective, behavioral, and physiological measures were concurrently collected in all sessions. In generalization testing hydromorphone and buprenorphine produced dose-related increases in hydromorphone-appropriate responses. Pentazocine produced an inverted U-shaped dose-response curve with complete substitution at 32 mg/70 kg but not at 64 mg/70 kg. Butorphanol and nalbuphine did not completely substitute for hydromorphone at any dose tested. After Drug/Not Drug instructions the behavioral discriminations of agonist-antagonist opioids were more consistent with their putative agonist activities at the mu opioid receptor and with their subjective effects profiles than was the case after Drug A versus Drug B instructions.

**ISSN:** 0022-3565 (Print).

**URL:** <http://www.aspet.org>

**Pub. Type:** Journal Article.

**Descriptors:** discrimination of agonist-antagonist opioids under different training conditions in two-choice hydromorphone/not hydromorphone discrimination, adult males with opioid abuse histories ; \*Drug Discrimination; \*Experimental Instructions ; \*Opiates; \*Psychopharmacology ; \*Side Effects (Drug) ; Human. Male. Adulthood (18 yrs & older). Thirties (30-39 yrs). Middle Age (40-64 yrs) ; Empirical Study.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Pharmacology

297. Price L. (2002) Buprenorphine (generic)~Subutex (brand) Buprenorphine/Naloxone (generic)~Suboxone (brand). *Psychopharmacology Update, Nov 2002 v13 i11 p4a, (2 pages).*

**Abstract:** Brief guidelines for pharmacists about the medications Subutex and Suboxone, their common usages, recommended dosage, side effects and interactions.

**Pub. Type:** brief article.

**Descriptors:** Pharmacists ; Guidelines.

**ATTC Buprenorphine Topics:** Dosing/administration

298. Radbruch L. (2003) Buprenorphine TDS: use in daily practice, benefits for patients. *Int J Clin Pract Suppl 2003;(133):19-22; discussion 23-4.*

**Author Address:** University of Cologne, Germany.

**Abstract:** In Germany and many other countries, buprenorphine has been used for a long time for the management of pain in both cancer and non-cancer patients. Although a transdermal delivery system for buprenorphine (Transtec)

has recently been introduced, the clinical experience in daily practice with this drug, delivered in a matrix patch, is only now being evaluated. In preliminary data from a survey of 3,255 patients with chronic pain, 26% had cancer pain, while the most common diagnoses of the other respondents included back pain (33%), osteoarthritis (22%), osteoporosis (17%), and neuropathic pain (10%, multiple entries). Before being switched to the buprenorphine patch, most patients had been pretreated with World Health Organization (WHO) Step II opioids (47%) or WHO Step III opioids (18%), including tramadol (in 35% of patients) and a tilidin/naloxone combination (15%); 9% had not been prescribed any opioids in advance of receiving transdermal buprenorphine. Most patients (77%) in the survey had been started on the lowest dose of the buprenorphine patch (35 microg/h), and nearly half (49%) were placed on adjuvant analgesics, including tramadol or tilidin/naloxone. Pain relief was rated as good or very good by 81% of the respondents. Adverse effects were similar to those seen on other opioids, although their intensity was mild in most cases. Local side effects, including erythema (4% of cases) and pruritus (1%), were transitory. Based on the survey results, transdermal buprenorphine is considered an effective opioid treatment for patients with stable cancer and non-cancer pain; it may prove particularly useful in patients who have experienced side effects taking oral analgesic preparations, as well as in those who are taking extensive co-medications.

**ISSN:** 1368-504X.

**Pub Type:** Journal Article.

**Descriptors:** Administration, Cutaneous ; Adult ; Analgesics, Opioid/\*administration & dosage ; Buprenorphine/\*administration & dosage ; Case Report ; Female ; Germany ; Human ; Middle Age ; Pain/\*drug therapy/etiology ; Tramadol/administration & dosage.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pain management

299. Radbruch L ; Vielvoye-Kerkmeier A. (2003) Buprenorphine TDS: the clinical development rationale and results. *Int J Clin Pract Suppl 2003 Feb;(133):15-8; discussion 23-4.*

**Author Address:** University of Cologne, Germany.

**Abstract:** Buprenorphine, a powerful opioid, is newly available for delivery in a transdermal formulation. The transdermal system's matrix patch provides rate-controlled administration of the drug. Three double-blind, placebo-controlled trials were conducted to evaluate efficacy and tolerability of the buprenorphine transdermal system (buprenorphine TDS, Transtec). A total of 445 patients were enrolled in the studies. All suffered from moderate to severe and very severe pain, both cancer- or non-cancer-related. The percentage of responders increased as the rate of buprenorphine delivered by the transdermal system rose, ranging from a 29% (cancer) and 36% (non-cancer) response rate associated with the lowest dose (35 microg/h), to 40% (cancer) and 46% (non-cancer) with the highest dose (70 microg/h). Patients receiving buprenorphine TDS slept longer, uninterrupted by pain, than patients from the placebo group. Systemic adverse effects reported in the drug cohorts included nausea, vomiting and dizziness, and were typical of those reported in other studies of

opioids; local adverse events, most commonly erythema and pruritus, were transient and mild to moderate. In an open-label, follow-up trial, in which 239 patients from the original clinical studies participated, 90% of patients reported that their analgesia was satisfactory or even better over a mean duration of 4.7 months; nearly 95% of patients found the patch to be user-friendly. The new buprenorphine TDS appears to be an important new modality for administering analgesia in patients with non-acute pain.

**ISSN:** 1368-504X.

**Pub Type:** Journal Article ; Review ; Review, Tutorial.

**Descriptors:** Analgesics, Opioid/\*administration & dosage/adverse effects ; Attitude to Health ; Buprenorphine/\*administration & dosage/adverse effects ; Human ; Multicenter Studies ; Pain/\*prevention & control/psychology ; Randomized Controlled Trials ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pain management ; Pharmacology

**300. Radomska M ; Bisaga A ; Popik P. (2000) Contemporary methods in pharmacotherapy in the opiate dependent treatment. Przegląd Lekarski 2000;57(10):509-18.**

**Author Address:** Klinika Toksykologii KMPiChS, Collegium Medicum, Uniwersytetu Jagiellońskiego w Krakowie.

**Abstract:** In this review, we present methods of pharmacotherapy in opiate dependence currently used in Poland and worldwide. As problems associated with drug abuse increase in severity, it is particularly important to bring these methods to the attention of medical professionals, governmental agencies and the general public. Here we describe pharmacotherapeutic approaches used in detoxification as well as relapse prevention. The presented methods of detoxification include classical treatments with clonidine and methadone as well as newer methods of rapid and ultrarapid detoxification. Agonists, partial agonists, and antagonists can be used in preventing relapse in detoxified patients. Experimental therapeutic approaches in the treatment of drug dependence are also presented. Psychotherapy and psychiatric care, central to the successful treatment of opiate dependence, are reviewed as well.

**ISSN:** 0033-2240.

**Notes:** (article in English, Polish).

**Pub Type:** Editorial ; Review ; Review, Tutorial.

**Descriptors:** Adrenergic alpha-Agonists/pharmacokinetics/\*therapeutic use; Buprenorphine/pharmacokinetics/therapeutic use; Clonidine/pharmacokinetics/\*therapeutic use ; Heroin Dependence/\*rehabilitation ; Human ; Metabolic Detoxication, Drug ; Methadone/pharmacokinetics/\*therapeutic use ; Naltrexone/pharmacokinetics/therapeutic use ; Narcotic Antagonists/pharmacokinetics/therapeutic use ; Narcotics/pharmacokinetics/\*therapeutic use.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacology ; Pharmacotherapy for opiate dependence

**301. Raffa R ; Cowan A ; Budd K ; Radbruch L. (2002) Transdermal Buprenorphine: A New Therapeutic Option in Chronic Pain Control. 10th World Congress on Pain, San Diego, August 17-22, 2002. [Symposia Highlighter issue 1, 2002, 6 p.].**

**Abstract:** Summary of 5 presentations at the 10th World Congress on Pain on August 19, 2002 in San Diego, California, in which a panel of experts summarized the evolving understanding of the basic pharmacology of buprenorphine, described the pharmacokinetic and clinical attributes and advantages of buprenorphine use in a patch formulation, reviewed the TRANSTEC® clinical studies, and described the clinical experience with TRANSTEC® in Germany.

**URL:** [http://www.symposiahighlighter.com/old\\_issues/10wcp.pdf](http://www.symposiahighlighter.com/old_issues/10wcp.pdf)

**Pub. Type:** Presentation summary ; Web document.

**ATTC Buprenorphine Topics:** Pain management ; Dosing/administration ; Pharmacology

**302. Raisch D ; Fye C ; Boardman K ; Sather M. (2002) Opioid dependence treatment, including buprenorphine/naloxone. Ann Pharmacother 2002 Feb;36(2):312-21.**

**Author Address:** Veterans Affairs Cooperative Studies Program, Clinical Research Pharmacy Coordinating Center, 2401 Centre, SE, Albuquerque, NM 87106-4180, USA. [dwr raisch@unm.edu](mailto:dwr raisch@unm.edu)

**Abstract:** OBJECTIVE: To review opioid dependence (OD) and its treatment. Pharmacologic treatments, including the use of buprenorphine/naloxone, are presented. Pharmaceutical care functions for outpatient OD treatment are discussed. DATA SOURCES: Primary and review articles were identified by MEDLINE and HEALTHSTAR searches (from 1966 to November 2000) and through secondary sources. Tertiary sources were also reviewed regarding general concepts of OD and its treatment. STUDY SELECTION/DATA EXTRACTION: Relevant articles were reviewed after identification from published abstracts. Articles were selected based on the objectives for this article. Studies of the treatment of OD with buprenorphine were selected based on the topic (pharmacology, pharmacokinetics, adverse reactions) and study design (randomized, controlled clinical trials in patients with OD with active/placebo comparisons and/or comparisons of active OD treatments). Articles regarding pharmacists' activities in the treatment and prevention of OD were reviewed for the pharmaceutical care section. DATA SYNTHESIS: OD is considered a medical disorder with costly adverse health outcomes. Although methadone maintenance treatment (MMT) is cost-effective for OD, only about 12% of individuals with OD receive this treatment. Psychological and pharmacologic modalities are used to treat OD, but patients often relapse. Drug therapy includes alpha 2-agonists for withdrawal symptoms, detoxification regimens with or without opioids, opioid antagonists, and opioid replacement including methadone, levomethadyl acetate, and buprenorphine. The Drug Addiction Treatment Act of 1999 allows for office-based opioid replacement therapies. Sublingual buprenorphine with naloxone can be used in this milieu.

Buprenorphine with naloxone is currently under new drug application review with the Food and Drug Administration. Clinical research shows buprenorphine to be equal in effectiveness to methadone, but safer in overdose due to its ceiling effect on respiratory depression. It has lower abuse potential and fewer withdrawal symptoms when discontinued. Naloxone is included to decrease diversion and injection of the tablets. Pharmacists in outpatient settings who are familiar with OD have opportunities to provide pharmaceutical care to patients receiving this treatment. Pharmaceutical care functions for OD include ensuring appropriate drug administration, monitoring adverse effects, alleviating withdrawal symptoms, treating intercurrent illnesses, minimizing diversion, and preventing relapse. CONCLUSIONS: OD is a critical unmet health problem in the US. Buprenorphine combined with naloxone represents an innovative treatment for OD in outpatient settings. This new treatment has advantages over MMT.

**ISSN:** 1060-0280.

**Pub Type:** Journal Article ; Review ; Review, Tutorial.

**Descriptors:** Administration, Sublingual ; Buprenorphine/\*therapeutic use ; Clinical Trials ; Databases, Bibliographic ; Human ; Naloxone/\*therapeutic use ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/\*drug therapy; Support, Non-U.S. Gov't ; Support, U.S. Gov't, Non-P.H.S. ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

**303. Rawson R ; McCann M ; Hasson A ; Ling W. (2000) Addiction pharmacotherapy 2000: new options, new challenges. J Psychoactive Drugs 2000 Oct-Dec;32(4):371-8.**

**Author Address:** UCLA Integrated Substance Abuse Programs, Los Angeles, California 90025, USA.

**Abstract:** There are many indicators that substance abuse research and treatment are going to become better integrated. Hopefully, this development will produce new treatment options and will improve access and effectiveness of care. Among the most significant factors in this period of change are the advances in addiction pharmacotherapy. For the treatment of alcoholism, disulfiram has been joined by naltrexone, and soon acamprosate will be added to the list of available pharmacotherapies. Individuals with opiate dependence who, for 25 years, were limited to a single medication (methadone) now have LAAM as an available treatment. Furthermore, there is eager anticipation that buprenorphine/naloxone will bring many more opiate users into treatment since it appears that this medication will be available to doctors outside the traditional narcotics treatment program settings. Other opiate addiction treatment options, including sustained-release naltrexone and lofexidine, are in active development. The greatest area of challenge for pharmacotherapy research is the search for stimulant addiction medications. NIDA has extensive efforts underway to discover/develop medicines that can help in the treatment of cocaine and methamphetamine users. During the next decade, those who

embrace these new treatments and integrate them into standard care will offer their patients the best chance for recovery.

**ISSN:** 0279-1072.

**Pub Type:** Journal Article ; Review ; Review Literature.

**Descriptors:** Alcohol Deterrents/\*therapeutic use ; Alcoholism/\*drug therapy ; Analgesics, Opioid/\*therapeutic use ; Clonidine/analogs & derivatives/therapeutic use ; Cocaine-Related Disorders/drug therapy ; Disulfiram/therapeutic use ; Human ; Methadone/therapeutic use ; Methadyl Acetate/therapeutic use ; Methamphetamine ; Naloxone/therapeutic use ; Naltrexone/therapeutic use ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/\*drug therapy ; Substance-Related Disorders/drug therapy ; Taurine/\*analogs & derivatives/therapeutic use.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacotherapy for opiate dependence

**304. Reckitt Benckiser Pharmaceuticals Inc. (2002) Subutex ; Buprenorphine Hydrochloride ; Opening new doors in opiate dependence / New Drugs to Treat Opiate Dependence in Doctor's Office. FDA New Products Bulletin Board; Show #11, January 2003.**

**Abstract:** Short video (from pharmaceutical manufacturer) aimed at health care professionals. The video plays on the FDA web site, and has 2 speakers. Complete transcript:

"The FDA recently approved two new formulations of the drug buprenorphine that can be used to treat opiate addiction in physicians' offices. The products are called Subutex and Suboxone, and they're manufactured by Reckitt Benckiser Pharmaceuticals. These drugs prevent withdrawal symptoms when the patient stops taking heroin or other opiates.

Subutex and Suboxone are the first narcotic drugs available for the treatment of opiate dependence that can be prescribed in an office setting under a new law passed in the year 2000. Physicians prescribing these drugs must be specially trained.

Until recently, the narcotic drugs used to treat opiate dependence, such as methadone, could only be dispensed in a very limited number of clinics that specialize in addiction treatment. Historically, there haven't been enough of these clinics for all the patients who want withdrawal therapy. Providing this treatment in physicians' offices should provide patients with greater access to needed treatment.

Subutex, which is used at the beginning of drug abuse treatment, contains only buprenorphine. Suboxone, which is used in the maintenance stage, also contains an opiate antagonist, naloxone. The naloxone is added to discourage drug abusers from crushing and injecting the Suboxone tablets.

To help deter misuse of these drugs, a comprehensive plan has been

developed that includes education, tailored drug distribution, and supervised dose induction. Active and passive surveillance are also being used to allow early detection of any problems. If it becomes clear in the future that buprenorphine is being widely diverted and misused, tighter regulations can be enacted. [end of video]

**URL:** <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/psn/transcript.cfm?show=11#1>

**Pub. Type:** video clip, about 4 minutes; play in Windows Media and Real Player formats.

**Descriptors:** Subutex; Healthcare professionals; Opiates.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence

305. **Reckitt Benckiser Pharmaceuticals Inc. (2003) Treating opioid dependence with Suboxone; In the Office (Physicians and health care professionals); In Confidence (Patients, family & friends). Reckitt Benckiser Pharmaceuticals, Inc. Web site for Suboxone.**

**Abstract:** Physicians who meet qualifying criteria can now prescribe medication for treatment of opioid dependence, thanks to recent US legislation. The physician's role is changing, and the results will change opioid dependence therapy for the better. The "In the Office" link provides introductory information for physicians who are considering the implications of this new treatment paradigm on their practices, as well as a link to the registry and information for pharmacists. Additional content on new developments, research, and treatment options will be added as the information becomes available. The "In Confidence" link allows patients and families to explore this site, and return here often to read about new treatment options and information about opioid dependence and recovery. Links to the MD locator and other resources are provided.

**URL:** <http://www.suboxone.com/Suboxone/home.htm>

**Pub. Type:** Web site.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

306. **Reese T. (2001) "A comparison of levomethadyl acetate, buprenorphine, and methadone for opioid dependence": Comment. New England Journal of Medicine. Vol 344(7) Feb 2001, 530.**

**Abstract:** Comments on the article by R. E. Johnson et al (see record 2000-12281-001) that compared levomethadyl acetate, buprenorphine, and high (60-100 mg/day) and low (20 mg/day) dose methadone for the treatment of opioid dependence. Reese suggests that a maintenance dose of 20 mg/day is homeopathic and that a dose of 60-100 mg/day is a standard rather than a high dose. Reese also suggests that while allowing private physicians to prescribe methadone to opioid addicts has its advances (e.g., it assists addicts who live in states without methadone treatment programs and allows for greater patient

privacy), the complex problems associated with opioid dependence are better addressed in large clinics.

**ISSN:** 0028-4793 (Print).

**Pub Type:** Letter.

**Descriptors:** levomethadyl acetate vs buprenorphine vs high vs low-dose methadone, study retention & abstinence & severity of drug problem, adults with opioid dependence, 17 week study, commentary ; \*Drug Dependency ; \*Drug Therapy ; \*Methadone Maintenance ; \*Narcotic Agonists ; \*Opiates ; Drug Abstinence ; Drug Dosages ; Drug Rehabilitation ; Experimental Attrition ; Maintenance Therapy ; Severity (Disorders) ; Human; Male; Female; Adulthood (18 yrs & older).

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence

307. **Resnick R. (2003) Food and Drug Administration approval of buprenorphine-naloxone for office treatment of addiction. Ann Intern Med 2003 Feb 18;138(4):360.**

**Abstract:** Many persons addicted to opium decline available treatment methods but accept buprenorphine, particularly when it is offered in a private office (1). On 8 October 2002, the U.S. Food and Drug Administration approved buprenorphine, a schedule III partial morphine agonist, for treatment of opioid dependence. This approval, together with provisions in the Drug Addiction Treatment Act of 2000, expands the venues for the treatment of opioid dependence from specially licensed methadone facilities to physicians' private offices, where schedule III to schedule V drugs can be prescribed. Expansion of treatment to private practice creates opportunities to provide holistic care for addicted patients with AIDS, hepatitis, or other conditions that are complicated by opioid dependence. In addition, this expansion could have substantial public health benefits by reducing heroin demand.

**ISSN:** 1539-3704.

**Pub Type:** Letter.

**Descriptors:** Buprenorphine/\*therapeutic use ; \*Drug Approval ; Drug Combinations; Human ; Naloxone/\*therapeutic use ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/\*drug therapy ; \*Private Practice ; United States ; United States Food and Drug Administration.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

308. **Resnick R ; Galanter M ; Resnick E ; Pycha C. (2001) Buprenorphine treatment of heroin dependence (detoxification and maintenance) in a private practice setting. J Addict Dis 2001;20(2):75-83.**

**Author Address:** New York University Medical Center, USA.

**Abstract:** At the conclusion of a 3-year demonstration project in a medical setting in which refusal to accept methadone was an inclusion criterion, 12 subjects were unable to detoxify from buprenorphine and remained adamant in their refusal to enroll in a MMTP. In order to study the feasibility of expanding opportunities for treatment previously unavailable to this under-served

population of heroin addicts, these 12 subjects plus an additional 11 subjects (N = 23) were recruited for a 12 months trial of buprenorphine treatment conducted in an office-based setting on a fee-for-service basis. An additional cohort of 40 heroin dependent subjects were entered in a protocol for detoxification only. The findings demonstrate both feasibility and patient acceptance of office based fee-for-service buprenorphine treatment, supporting the need for (1) additional studies of this population and (2) changes in government regulations to reintroduce addiction treatment under physician auspices in private practice settings.

**ISSN:** 1055-0887.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Buprenorphine/administration & dosage/\*therapeutic use ; \*Drug Monitoring ; Female ; Follow-Up Studies ; Heroin Dependence/\*rehabilitation ; Human ; Male ; \*Metabolic Detoxication, Drug ; Middle Age ; Narcotics/administration & dosage/\*therapeutic use ; \*Private Practice.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

**309. Reuter P. (2001) Cost-effectiveness estimates for buprenorphine should factor in crime. *Addiction* 2001 Oct;96(10):1515.**

**Abstract:** What Barnett, Zaric, and Brandeau (2001) offer is the very stuff of contemporary policy analysis, synthesizing a wide range of research to provide decision makers with an easily understood heuristic. Their results suggest that, at most plausible prices and ranges of effects, buprenorphine lowers cost per quality-adjusted life-years (QALY) more than most standard interventions. What is striking is that it does so well, given that the model excludes some of the most significant gains from increasing the number of heroin users in treatment. Two omissions include the low addiction potential of buprenorphine and the reduction in crime.

**ISSN:** 0965-2140.

**Pub Type:** Comment ; Letter.

**Descriptors:** Buprenorphine/\*economics ; Cost-Benefit Analysis/methods ; Crime/economics ; Heroin Dependence/rehabilitation ; Human ; Narcotics/\*economics.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Psychosocial treatment aspects

**310. Reynaud-Maurupt C ; Carrieri M ; Gastaud J ; Pradier C ; Obadia Y ; Moatti J. (2000) Impact of drug maintenance treatment on injection practices among French HIV-infected IDUs. The MANIF 2000 Study Group. *AIDS Care* 2000 Aug;12(4):461-70.**

**Author Address:** INSERM Research Unit 379 Marseilles, France.

**Abstract:** Drug maintenance treatment (DMT) has only been recently introduced in France (methadone programmes in March 1995, buprenorphine prescriptions in ambulatory medicine in February 1996) in relation to risk reduction policies for HIV infection among intravenous drug users (IDUs).

Impact of DMT was assessed in the period of inclusion (October 1995-December 1997) of a French cohort of patients HIV infected through intravenous drug use the MANIF 2000 study). Among the 429 patients, 48.2% were ex-IDUs, 20.3% were active users not in DMT and 31.5% were in DMT. A majority (73.3%) of patients in DMT had persisted in their injection behaviours and their social and psychological characteristics were similar to those of active users not in DMT. Among the 186 active IDUs, those in DMT were more likely to have injected cocaine (42.4%) and buprenorphine or methadone (21.3%) than those who were not (respectively 27.6% and 2.4%), and 23.6% declared direct needle-sharing behaviours during the prior six months. Among younger IDUs (< or = 33 years of age) (n = 100), needle-sharing was associated with polydrug use and cocaine injection but was not significantly reduced by participation in DMT. These results suggest the need for taking into account differences between type of HIV-infected drug users and developing appropriate multidrug maintenance treatment programmes, which may imply adaptations of current dosages of methadone and buprenorphine.

**ISSN:** 0954-0121.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Buprenorphine/therapeutic use ; Female ; France/epidemiology ; HIV Infections/\*complications/prevention & control ; Human ; Male ; Methadone/therapeutic use ; Narcotics/therapeutic use ; Needle Sharing ; Risk-Taking ; Substance Abuse, Intravenous/ complications/epidemiology/\*rehabilitation.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Prevalence of use for opiate dependence

**311. Ritter A. (2001) Buprenorphine for the treatment of heroin dependence. *Drug & Alcohol Review* 2001;20(1): 5-7.**

**Abstract:** Discusses the use of buprenorphine for the treatment of heroin dependence. With the approval of buprenorphine by the Therapeutic Goods Administration, it is the author's opinion that this is an important leap forward in heroin treatment in Australia. Benefits and pitfalls of the drug's use in withdrawal and maintenance treatment are discussed. Research supporting the efficacy of buprenorphine maintenance, as compared to other forms of maintenance, are presented.

**ISSN:** 0959-5236 (Print), 1465-3362 (Electronic).

**Pub Type:** Journal Article; editorial.

**Descriptors:** buprenorphine in treatment of heroin dependence, Australia ; \*Drug Therapy ; \*Heroin Addiction ; \*Narcotic Agonists ; Human.

**ATTC Buprenorphine Topics:** Dosing/administration ; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence

**312. Ritter A. (2002) Naltrexone in the treatment of heroin dependence: Relationship with depression and risk of overdose. *Australian & New Zealand Journal of Psychiatry* Apr 2002;36(2):224-228.**

**Author Address:** Ritter, Alison J. Turning Point Alcohol & Drug Ctr, 54 Gertrude Street, Fitzroy, VIC Australia 3065, Alisonr@turningpoint.org.au.  
**Abstract:** Examined the use of naltrexone (NAL) in the treatment of heroin dependence. The relationship between NAL and depression as well as risk of overdose was examined. Literature was reviewed along with recent interim data from clinical trials underway in Victoria, Australia. NAL is a recent addition to treatment for heroin dependence in Australia. The relationship between depression and NAL has been examined in previous literature. Underlying rates of depression in heroin users are high and treatment may resolve or exacerbate depression. Research demonstrates that the addition of NAL does not necessarily increase depression in patients. The risk of non-fatal heroin overdose is significantly elevated after NAL treatment as a result of reduced tolerance. Data from clinical trials underway demonstrate a significantly elevated rate of non-fatal overdose in NAL patients compared to those in substitution maintenance treatment. The mortality rate subsequent to NAL treatment appears to be equivalent to or greater than that for untreated heroin users. Clinicians need to carefully monitor depression in patients, and warn patients of the risks of reduced tolerance to opiates following NAL treatment. Agonist treatments such as methadone and buprenorphine carry much less risk of overdose.

**ISSN:** 0004-8674 (Print).

**Pub Type:** Journal Article; Literature Review/Research Review. **Descriptors:** naltrexone; heroin dependence; depression; overdose risk ; \*At Risk Populations ; \*Drug Overdoses ; \*Heroin Addiction ; \*Major Depression ; \*Naltrexone ; Drug Dependency ; Drug Therapy ; Side Effects (Drug) ; Human. **ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence

**313. Robinson S. (2002) Buprenorphine: an analgesic with an expanding role in the treatment of opioid addiction. CNS Drug Rev 2002 Winter;8(4):377-90.**

**Author Address:** Department of Pharmacology and Toxicology, P O Box 980613, Virginia Commonwealth University, Richmond, VA 23298-0613, USA. serobins@hsc.vcu.edu.

**Abstract:** Buprenorphine, a long-acting opioid with both agonist and antagonist properties, binds to mu-opioid (OP(3)), kappa-opioid (OP(2)), delta-opioid (OP(1)), and nociceptin (ORL-1) receptors. Its actions at these receptors have not been completely characterized, although buprenorphine is generally regarded as a mu-opioid receptor partial agonist and a kappa-opioid receptor antagonist. Its pharmacology is further complicated by an active metabolite, norbuprenorphine. Although buprenorphine can be used as an analgesic agent, it is of greater importance in the treatment of opioid abuse. Because of its partial agonist activity at mu-opioid receptors and its long half-life, buprenorphine has proven to be an excellent alternative to methadone for either maintenance therapy or detoxification of the opioid addict. Although buprenorphine may ultimately prove to be superior to methadone in the maintenance of the pregnant addict, its effects on the developing fetus must be carefully evaluated.

**ISSN:** 1080-563X.

**Pub Type:** Journal Article ; Review.

**Descriptors:** Analgesics, Opioid/adverse effects/pharmacology/\*therapeutic use ; Animal ; Buprenorphine/adverse effects/pharmacology/\*therapeutic use ; Female ; Human ; Infant, Newborn ; Narcotic Antagonists/adverse effects/pharmacology/\*therapeutic use ; Neonatal Abstinence Syndrome/etiology ; Opioid-Related Disorders/complications/\*drug therapy/rehabilitation ; Pregnancy ; Pregnancy Complications/drug therapy/rehabilitation ; Receptors, Opioid/\*drug effects/metabolism ; Receptors, Opioid, delta/drug effects/metabolism ; Receptors, Opioid, kappa/drug effects/metabolism ; Receptors, Opioid, mu/drug effects/metabolism.

**ATTC Buprenorphine Topics:** Pharmacology ; Pharmacotherapy for opiate dependence ; Special populations

**314. Robinson S ; Wallace M. (2001) Effect of perinatal buprenorphine exposure on development in the rat. J Pharmacol Exp Ther 2001 Aug;298(2):797-804.**

**Author Address:** Department of Pharmacology and Toxicology, Medical College of Virginia Campus, Virginia Commonwealth University, Richmond, Virginia, USA. serobins@hsc.vcu.edu

**Abstract:** The developmental effects of exposure to various doses of buprenorphine, methadone, or water during the perinatal period were studied in the rat. Rats were exposed to buprenorphine (0.3, 1.0, or 3.0 mg/kg/day), methadone (9 mg/kg/day), and/or water prenatally, postnatally, or both pre- and postnatally, via maternally implanted osmotic minipumps. Fetal and maternal mortality and morbidity were assessed, as well as the acquisition of several developmental milestones, pup weight gain, precipitated withdrawal, and the antinociceptive effect of morphine. Although perinatal exposure to buprenorphine failed to produce severe maternal and fetal or neonatal mortality, it was associated with a significant amount of perinatal mortality and perturbations of pup development. Pups developed physical dependence to both drugs, as evidenced by the ability of naloxone challenge to precipitate withdrawal. Both drugs induced tolerance to the antinociceptive effects of morphine in the tail-flick test. The effects of buprenorphine varied with the dose used, and the highest dose did not always produce the greatest effect. There were some similarities between the effects of perinatal buprenorphine and perinatal methadone; however, differences were also observed between the effects of the two drugs, which may be related to the different affinities and efficacies of the drugs at different opioid receptor subtypes.

**ISSN:** 0022-3565.

**Pub Type:** Journal Article.

**Descriptors:** Animal ; Animals, Newborn/\*physiology ; Buprenorphine/ adverse effects/\*toxicity ; Drinking/drug effects ; Eating/drug effects ; Female ; Growth/\*drug effects ; Litter Size/drug effects ; Methadone/adverse effects/pharmacology ; Narcotics/adverse effects/\*toxicity ; Pain Measurement/drug effects ; Rats ; Rats, Sprague-Dawley ; Substance Withdrawal Syndrome/psychology ; Support, U.S. Gov't, P.H.S. ; Weight

Gain/drug effects.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Dosing/administration ; Pharmacology

315. **Rosenberg H ; Melville J ; McLean P. (2002) Acceptability and availability of pharmacological interventions for substance misuse by British NHS treatment services. *Addiction* 2002 Jan;97(1):59-65.**

**Author Address:** Psychology Department, Bowling Green State University, Ohio 43403, USA.

**Abstract:** AIMS: Despite their potential advantages, many of the pharmacological interventions available to treat substance misuse are controversial and their acceptability within the United Kingdom (and other countries) has only recently begun to be investigated. DESIGN: A questionnaire mailed to British National Health Service (NHS) alcohol and drug treatment services asked respondents to rate the acceptability and availability of 11 pharmacological interventions for substance misuse employed to relieve withdrawal, reduce the likelihood of relapse and opiate overdose and substitute pharmaceuticals for illicit drugs. PARTICIPANTS: A sample of NHS substance misuse services (n = 265) listed in one or more directories of services in England, Wales and Scotland. FINDINGS: Substitute methadone for opiate addiction, substitute benzodiazepines for benzodiazepine-dependent patients, lofexidine for opiate detoxification, naltrexone for opiate relapse prevention andacamprostate for alcohol relapse prevention were widely acceptable and available interventions. Another subset of medications-buprenorphine for opiate detoxification, take-home naloxone for overdose prevention and substitute prescribing of levo-alpha-acetyl-methadol (LAAM), heroin and dexamphetamine-garnered less support, but the majority of participants rated even these therapies as acceptable. Ultra-rapid detoxification under sedation was the intervention rated as least acceptable to, and was one of the two least frequently available from, responding NHS services. CONCLUSIONS: Differences among specific medications notwithstanding, a wide range of harm-reduction and abstinence-orientated interventions were acceptable to and available from NHS services. Acceptance and availability are probably limited by a combination of practical, economic, safety, efficacy and theoretical considerations.

**ISSN:** 0965-2140.

**Pub Type:** Journal Article.

**Descriptors:** \*Attitude of Health Personnel ; Great Britain ; \*Health Services Accessibility ; Human ; Questionnaires ; State Medicine; \*Substance Abuse Treatment Centers ; Substance-Related Disorders/\*drug therapy.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence

316. **Rosenheck R ; Kosten T. (2001) Buprenorphine for opiate addiction: potential economic impact. *Drug Alcohol Depend* 2001;63(3):253-62.**

**Author Address:** Department of Psychiatry, Yale School of Medicine, New

Haven, CT 06519, USA. robert.rosenheck@yale.edu

**Abstract:** This study evaluated the potential economic impact of the buprenorphine/naloxone combination in the context of practice in the United States of America. In comparison to treatment provided through methadone clinics, buprenorphine/naloxone therapy in office practice may be associated with increased medication, physician, and nursing costs, but reduced costs for dispensing, toxicology screens, counseling and administration. It may also result in markedly reduced costs for patients, especially travel costs, resulting in net savings for society as a whole. A review of controlled studies suggest that buprenorphine/naloxone is not likely to be any more or less effective than methadone, but since it will be less expensive in the long run, it may be more cost-effective than methadone when provided to comparable groups of patients. Because of the convenience of office-based treatment, buprenorphine/naloxone may increase access to opiate substitution for some addicts. To the extent that treatment is provided to additional high-cost patients who are involved in extensive criminal activity or who undergo multiple detoxifications each year, net cost savings could be substantial. To the extent that treatment is extended to better adjusted addicts who are employed, married and experience fewer adverse effects from their addiction, costs could increase. The total cost impact will depend on which addict sub-populations make greatest use of the treatment opportunity presented by buprenorphine/naloxone.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article.

**Descriptors:** Buprenorphine/\*economics/\*therapeutic use ; Comparative Study; Cost-Benefit Analysis ; Counseling/economics ; Drug Evaluation, Preclinical/economics ; \*Health Care Costs ; Human ; Methadone/economics/therapeutic use ; Opioid-Related Disorders/\*drug therapy/\*economics ; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Legal/regulatory issues ; Pharmacotherapy for opiate dependence

317. **Rothman R ; Gorelick D ; Heishman S ; Eichmiller P ; Hill B ; Norbeck J; Liberto J. (2000) An open-label study of a functional opioid kappa antagonist in the treatment of opioid dependence. *J Subst Abuse Treat* 2000 Apr;18(3):277-81.**

**Author Address:** National Institute on Drug Abuse, National Institutes of Health, 5500 Nathan Shock Drive, Baltimore, MD 21224, USA. rrothman@intra.nida.nih.gov

**Abstract:** Several lines of evidence, including the well-established observation that kappa opiate agonists produce dysphoria and psychotomimetic effects in humans, suggest that dysfunction of the endogenous kappa opioid system may contribute to opioid and cocaine addiction. The objective of this open-label study was to determine the effectiveness of a functional kappa antagonist as a treatment for opioid dependence. This was accomplished by combining a partial mu agonist/kappa antagonist (buprenorphine, 4 mg, sublingual) with a mu antagonist (naltrexone, 50 mg by mouth), theoretically leaving kappa

antagonism as the major medication effect. Subjects were treatment-seeking heroin-dependent (as per Diagnostic and Statistical Manual of Mental Disorders, 4th ed.) men (41 +/- 7 years old; 19 +/- 8 years heroin use) eligible for methadone maintenance. After inpatient detoxification and a naloxone-challenge test to verify that they were not physically dependent on opioids, subjects received naltrexone. Starting on the fourth day, patients also received liquid buprenorphine. All patients received medication at the clinic 6 days per week and a full program of psychosocial treatment. The major endpoints of the study were: pupil diameter to determine if the mu agonist effects of buprenorphine were blocked by naltrexone, urine toxicology, and retention in treatment. Five patients (33%) completed the 3-month study. Four were abstinent from opioids and cocaine for the entire study, and one was abstinent from opioids and cocaine for the last 9 weeks. Six subjects dropped out due to either minor side effects or disliking the sensation of sublingual buprenorphine. There were no significant changes in pupillary diameter. The positive response to treatment exceeds that expected from naltrexone alone (90% dropout). These promising results suggest that controlled studies of this medication combination should be conducted.

**ISSN:** 0740-5472.

**Pub Type:** Clinical Trial ; Journal Article.

**Descriptors:** Administration, Sublingual ; Adult ; Affect ; Buprenorphine/pharmacology/\*therapeutic use ; Drug Therapy, Combination ; Heroin Dependence/\*drug therapy/physiopathology/psychology ; Human ; Male ; Middle Age ; Naltrexone/pharmacology/\*therapeutic use ; Narcotic Antagonists/pharmacology/\*therapeutic use ; Patient Dropouts/\*psychology ; Psychiatric Status Rating Scales ; Pupil/drug effects ; Receptors, Opioid, kappa/\*antagonists & inhibitors ; Recurrence ; Substance Abuse Detection ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

318. **Schindler S ; Eder H ; Ortner R ; Rohrmeister K ; Langer M ; Fischer G. (2003) Neonatal outcome following buprenorphine maintenance during conception and throughout pregnancy. *Addiction* 2003 Jan;98(1):103-10.**

**Author Address:** Department of General Psychiatry, University Hospital of Vienna, Vienna, Austria.

**Abstract:** AIMS: To assess the effects of maternal buprenorphine treatment at conception and during pregnancy on neonates in terms of birth outcomes and neonatal abstinence syndrome (NAS). DESIGN AND SETTING: Prospective, open-label, out-patient maintenance, case report study, conducted at the drug addiction out-patient clinic at the University Hospital Vienna. PARTICIPANTS: Two buprenorphine-maintained pregnant women who had conceived during buprenorphine treatment. Both patients had previously given birth to healthy neonates following induction on to buprenorphine maintenance therapy in the second trimester. MEASUREMENTS: Mothers: urinalysis. Neonates: gestational age at delivery, Apgar scores, birth weight, length and NAS

(Finnegan Scale). FINDINGS: Urinalyses were negative for both women for 25 and 38 months, respectively, during the pregnancy period. There were no complications during the course of the pregnancy. The newborns delivered by both women were healthy, birth outcomes were within normal ranges and there were no NAS symptoms requiring treatment. CONCLUSIONS: To our knowledge this is the first report detailing the pregnancies of women treated with buprenorphine at the time of conception and investigated in a prospective study. The NAS noted in neonates born to buprenorphine-maintained mothers appears to be less severe than the NAS observed in neonates born to methadone-maintained mothers. These preliminary data indicate that, in our patient cohort, buprenorphine maintenance at the time of conception and during pregnancy did not seem to affect birth outcome measurements such as pregnancy complications, week of delivery, birth weight, length, umbilical pH or neurodevelopmental progress. Future prospective studies with larger study populations are warranted.

**ISSN:** 0965-2140.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Buprenorphine/\*adverse effects ; Case Report ; Female ; Human ; Infant, Newborn ; Narcotics/\*adverse effects ; Neonatal Abstinence Syndrome/\*etiology ; Opioid-Related Disorders/\*rehabilitation ; Preconception Care/methods ; Pregnancy ; Pregnancy Complications/etiology/\*rehabilitation ; Pregnancy Outcome ; Prenatal Care/methods ; Prospective Studies ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Pharmacology ; Pharmacotherapy for opiate dependence ; Special populations

319. **Schneider U ; Paetzold W ; Eronat V ; Huber T ; Seifert J ; Wiese B ; Emrich H. (2000) Buprenorphine and carbamazepine as a treatment for detoxification of opiate addicts with multiple drug misuse: A pilot study. *Addiction Biology* 2000;5(1):65-69.**

**Author Address:** Dept. Clin. Psychiatry Psychotherapy, School of Medicine, 30625 Hannover; Germany.

**Abstract:** The growing tendency of opioid addicts to misuse multiple other drugs leads to the investigation of new pharmacostategies to prevent patients from suffering life-threatening complications and minimize the withdrawal symptoms. The short-term efficacy of a 10-day low-dose buprenorphine/19-day carbamazepine regime (n = 15) to a 14-day oxazepam/19-day carbamazepine regime (n = 12) in an open-labelled 21-day inpatient detoxification treatment was compared. Twenty-seven men and women dependent on opioids and misusing other drugs admitted to a detoxification unit were included in this protocol. Eighteen of 27 patients (67%) completed the study. Four non-completers (27%) received buprenorphine/carbamazepine (four of 15) and five non-completers (42%) were treated with oxazepam/carbamazepine (five of 12), but the difference in the dropout rate between the two treatment strategies was not significant. The buprenorphine/carbamazepine regime provided significantly more effective relief of withdrawal symptoms during the first week of treatment. No severe side effects occurred during treatment in both groups. The present

study supports the hypothesis that buprenorphine/carbamazepine in rapid opioid detoxification in patients with additional multiple drug misuse and both regimens were safe with no unexpected side effects.

**ISSN:** 1355-6215.

**Pub Type:** Journal article.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

**320. Schnoll S. (2001) Treatment of opioid addiction in physicians' offices: it's about time. J Addict Dis 2001;20(2):1-3.**

**Abstract:** The famous philosopher/physician of the middle ages, Moses Maimonides, stated ". . . the physician should not treat the disease, but the patient who is suffering from it." Despite this admonition, most physicians often fail to see the whole patient and address only the immediate problem. Addiction has at times been an exception to this with both behavioral and medication treatments being offered in the same setting with attempts to provide comprehensive services that address the array of patient needs. In 1965, Dole and Nyswander reported on the use of methadone to treat heroin addicts as part of a treatment program that offered numerous services in addition to the methadone. Since that time, methadone maintenance treatment programs have become a mainstay for the treatment of opioid addicted patients. However, unlike other diseases, which are treated in the privacy of the physician's office, the treatment of opioid addicted patients with methadone was relegated to specially licensed clinics, where numerous regulations were imposed on the treatment process. No other disease had its treatment so regulated. The rules and the locations of the clinics were often so onerous that many potential patients refused to come to treatment in the clinics. In addition to the strict rules governing the clinic, until recently, only on agonist medication was available for the treatment of opioid addiction. This is in contrast to other diseases where there are few regulations imposed on the physician, and numerous medications that can be used either singly or in combination to provide the optimal outcome. These rules and regulations have served to stigmatize the patients and the treatment process.

**ISSN:** 1055-0887.

**Pub Type:** Comment ; Editorial.

**Descriptors:** Buprenorphine/\*therapeutic use ; Human ; Methadone/\*therapeutic use ; Narcotics/\*therapeutic use ; Opioid-Related Disorders/\*rehabilitation ; \*Physicians' Offices.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

**321. Schottenfeld R ; Pakes J ; O'Connor P ; Chawarski M ; Oliveto A ; Kosten T. (2000) Thrice-weekly versus daily buprenorphine maintenance. Biol Psychiatry 2000 Jun 15;47(12):1072-9.**

**Author Address:** Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06519, USA.

**Abstract:** BACKGROUND: Buprenorphine is a promising alternative to methadone or levo-acetyl alpha methadol for opioid agonist maintenance treatment, and thrice-weekly dosing would facilitate its use for this purpose. METHODS: After a 3-day induction, opioid-dependent patients (n = 92) were randomly assigned to daily clinic attendance and 12-weeks maintenance treatment with sublingual buprenorphine administered double blind either daily (n = 45; 16 mg/70 kg) or thrice weekly (n = 47; 34 mg/70 kg on Fridays and Sundays and 44 mg/70 kg on Tuesdays). Outcome measures include retention, results of 3x/week urine toxicology tests, and weekly self-reported illicit drug use. RESULTS: There were no significant differences at baseline in important social, demographic, and drug-use features. Retention was 71% in the daily and 77% in the 3x/week conditions. The proportion of opioid-positive urine tests decreased significantly from baseline in both groups and averaged 57% (daily) and 58% in 3x/week. There were no significant differences between groups in self-reported number of bags of heroin used for any day of the week, including Thursdays (48-72 hours following the last buprenorphine dose for subjects in the 3x/week condition), or in medication compliance (92%, 91%) and counseling attendance (82%, 82%). CONCLUSIONS: At an equivalent weekly dose of 112 mg/70 kg, thrice-weekly and daily sublingual buprenorphine appear comparable in efficacy with regard to retention and reductions in illicit opioid and other drug use. These findings support the potential for utilizing thrice-weekly buprenorphine dosing in novel settings.

**ISSN:** 0006-3223.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Buprenorphine/administration & dosage/blood/\*therapeutic use ; Cocaine-Related Disorders/psychology/rehabilitation ; Double-Blind Method ; Female ; Heroin Dependence/psychology/rehabilitation ; Human ; Male ; Narcotic Antagonists/administration & dosage/blood/\*therapeutic use ; Opioid-Related Disorders/psychology/\*rehabilitation ; Psychiatric Status Rating Scales ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

**322. Schottenfeld R ; Pantalon M ; Chawarski M ; Pakes J. (2000) Community reinforcement approach for combined opioid and cocaine dependence. Patterns of engagement in alternate activities. J Subst Abuse Treat 2000 Apr;18(3):255-61.**

**Author Address:** CMHC/SAC, Room S-205, 34 Park Street, New Haven, CT 06519, USA. richard.schottenfeld@yale.edu

**Abstract:** We compared outcomes for agonist-maintained patients with combined opioid and cocaine dependence who were treated in an earlier clinical trial with group drug counseling (DC; n = 57) or in a current trial with the Community Reinforcement Approach (CRA; n = 60). The association between engagement in nondrug-related activities and abstinence was also evaluated. There were no significant differences between the treatments in retention or drug use. The total number of hours and average hours per week engaged in nondrug-related activities was significantly higher for CRA-treated patients who

achieved abstinence from opioids, cocaine, or both combined than for those who never achieved abstinence. Although CRA was not more effective overall than DC, the finding that engagement in reinforcing community activities unrelated to drug use (e.g., planned pleasurable events or parenting activities) was associated with abstinence suggests that the planning and reinforcement of specific nondrug-related social, vocational, and recreational activities is a crucial component of CRA.

**ISSN:** 0740-5472.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Buprenorphine/\*therapeutic use ; Clinical Trials ; Cocaine-Related Disorders/complications/\*rehabilitation ; Community Networks/\*utilization ; Comparative Study ; \*Counseling ; Female ; Human ; Male ; Methadone/\*therapeutic use ; Narcotics/\*therapeutic use ; Opioid-Related Disorders/complications/\*rehabilitation ; Recurrence ; Social Support ; Socioenvironmental Therapy/methods ; Support, U.S. Gov't, P.H.S. ; Temperance ; Treatment Outcome ; United States.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment outcomes/effectiveness

- 323. Schuh K ; Johanson C. (1999) Pharmacokinetic comparison of the buprenorphine sublingual liquid and tablet. Drug Alcohol Depend 1999 Aug 2;56(1):55-60.**

**Author Address:** Wayne State University School of Medicine, Department of Psychiatry and Behavioral Neurosciences, Detroit, MI 48207, USA. kschuh@med.wayne.edu

**Abstract:** Buprenorphine is a mu opioid partial agonist being developed as a treatment for opioid dependence. Buprenorphine, usually administered as a sublingual liquid, is now being developed as a sublingual tablet for clinical use. The present study compared participants' plasma concentrations after daily maintenance on three buprenorphine liquid doses (2, 4 and 8 mg) and one tablet dose (8 mg). Fourteen opioid-dependent individuals (11 males, three females) participated. Plasma samples were collected over a 24-h period after at least 7 days of maintenance on each dose. Results showed that the liquid doses produced dose-related increases in plasma concentrations. The 8-mg tablet produced mean plasma concentrations significantly lower than those of the 8-mg liquid, although there was substantial individual variability. Thus, the buprenorphine tablet dose might have to be adjusted to produce plasma concentrations equivalent to those of the liquid.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article.

**Descriptors:** Administration, Sublingual ; Adult ; Analgesics, Opioid/administration & dosage/blood/\*pharmacokinetics ; Analysis of Variance ; Buprenorphine/administration & dosage/blood/\*pharmacokinetics ; Female ; Human ; Male ; Middle Age ; Support, Non-U.S. Gov't ; Support, U.S. Gov't, P.H.S. ; Tablets.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacology

- 324. Schuh K ; Walsh S ; Stitzer M. (1999) Onset, magnitude and duration of opioid blockade produced by buprenorphine and naltrexone in humans. Psychopharmacology (Berl) 1999 Jul;145(2):162-74.**

**Author Address:** Department of Psychiatry and Behavioral Science, Johns Hopkins University School of Medicine, Baltimore, MD 21224, USA.

**Abstract:** RATIONALE: One therapeutic benefit of mu opioid agonist or antagonist maintenance is the resultant attenuation of the effects of illicit opioids. It is important to characterize the development and duration of opioid blockade produced by buprenorphine, a novel opioid dependence pharmacotherapy. OBJECTIVE: This study characterized the ability of buprenorphine to attenuate opioid effects during treatment initiation and discontinuation compared to naltrexone and placebo. METHODS: Opioid-experienced volunteers (n = 8) participated in this 10-week, inpatient, double-blind, within-subject, crossover study. Five randomized conditions [buprenorphine (2 and 8 mg, sublingually), naltrexone (25 and 100 mg, PO) and placebo] were each examined during a 2-week period; the test drug was given for 7 days followed by a 7-day placebo wash-out. Cumulative doses of hydromorphone (0, 2 and 4 mg, IM, 45 min apart) were administered thrice-weekly corresponding with treatment and wash-out days 1, 3, and 5; behavioral, physiological and pharmacokinetic measures were collected. RESULTS: Buprenorphine alone produced dose-related prototypic agonist effects during induction (i.e., positive mood, respiratory depression, miosis); tolerance developed only to the subjective effects. Buprenorphine 2 mg partially attenuated the effects of hydromorphone, while nearly complete attenuation was observed with 8 mg that lasted up to 72 h after discontinuation. Both naltrexone doses produced complete hydromorphone blockade after a single dose; blockade of the behavioral, but not physiological, effects persisted for 5 days after discontinuation of 100 mg. CONCLUSIONS: These data suggest that 2 mg buprenorphine is a sub-therapeutic maintenance dose, both buprenorphine 8 mg and naltrexone produce immediate and efficacious opioid blockade, and adequate protection against illicit opioids may be achieved with less-than-daily dosing.

**ISSN:** 0033-3158.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Buprenorphine/blood/\*pharmacology ; Cross-Over Studies ; Double-Blind Method ; Human ; Hydromorphone/pharmacology ; Male ; Middle Age ; Naltrexone/blood/\*pharmacology ; Narcotic Antagonists/\*pharmacology ; Support, U.S. Gov't, P.H.S. ; Time Factors.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacology

- 325. Seifert J ; Metzner C ; Paetzold W ; Borsutzky M ; Passie T ; Rollnik J ; Wiese B ; Emrich H ; Schneider U. (2002) Detoxification of opiate addicts with multiple drug abuse: a comparison of buprenorphine vs. methadone. Pharmacopsychiatry 2002 Sep;35(5):159-64.**

**Author Address:** Department of Clinical Psychiatry and Psychotherapy,

Medical School, Hannover, Germany. Seifert.Juergen@mh-hannover.de

**Abstract:** Over the last few years, there has been a growing tendency for opioid addicts to abuse multiple drugs, although many patients are in substitution therapy with methadone. Abuse of multiple drugs leads to a more complicated withdrawal syndrome; it is therefore necessary to investigate new drug strategies as a treatment for detoxification. Buprenorphine appears to be an effective and safe drug in opioid-addicted patient detoxification. In this study, we have compared the short-term efficacy of an 11-day low-dose buprenorphine/14-day carbamazepine regime [BPN/CBZ] (n = 14) to an 11-day methadone/14-day carbamazepine regime [MET/CBZ] (n = 12) in a double-dummy, randomized 14-day inpatient detoxification treatment study. Twenty-six inpatients met the DSM-IV criteria for opioid dependence and were included in this study. All patients abused various additional drugs. Fourteen of 26 patients (53.8 %) completed the study. Seven non-completers (seven of 12 = 58.3 %) were treated with methadone/carbamazepine and five non-completers (five of 14 = 35.7 %) received buprenorphine/carbamazepine, but the difference in the dropout rate was not significant. However, patients with buprenorphine/carbamazepine showed significantly fewer withdrawal symptoms after the first two weeks of treatment. The present study supports the hypothesis that buprenorphine/carbamazepine is more effective than methadone/carbamazepine in detoxification strategies for opioid addict with additional multiple drug abuse. No severe side effects occurred during treatment in either group.

**ISSN:** 0176-3679.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Anticonvulsants/therapeutic use ; Buprenorphine/administration & dosage/\*therapeutic use ; Carbamazepine/therapeutic use ; Double-Blind Method ; Drug Administration Schedule ; Female ; Human ; Male ; Methadone/administration & dosage/\*therapeutic use ; Narcotic Antagonists/administration & dosage/\*therapeutic use ; Narcotics/administration & dosage/\*therapeutic use ; Opioid-Related Disorders/\*drug therapy ; Substance-Related Disorders/drug therapy ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Dosing/administration ; Pharmacotherapy for opiate dependence

326. **Seivewright N ; Iqbal M. (2002) Prescribing to drug misusers in practice--often effective, but rarely straightforward. Addict Biol 2002 Jul;7(3):269-77.**

**Author Address:** Substance Misuse Service, Community Health Sheffield NHS Trust, Sheffield, UK. amyh@chsheff-tr.trent.nhs.uk

**Abstract:** Many reviews describe the effectiveness of methadone treatment in reducing illicit drug use and associated behaviours among opiate misusers. The strongest evidence includes social outcomes such as reduced debt and crime, and relates overwhelmingly to maintenance rather than detoxification treatment. Drug clinics are often dominated by individuals unable to withdraw fully from methadone, while the "harm reduction" model accepts some ongoing drug use,

with attendant risks. Security measures are necessary to avoid abuse of treatments, but these may be undermined by the agenda of "partnerships with patients" in decision-making. Buprenorphine appears both safer and less addictive than methadone, and lofexidine is effective as a non-substitute detoxification method. Naltrexone can clearly reduce relapse rates, provided consumption is assured, while for individuals unable to detoxify or avoid euphoriant opiates, morphine and diamorphine are sometimes used. In non-opiate misuse, clinical studies of a wide range of medications have produced relatively few positive findings.

**ISSN:** 1355-6215.

**Pub Type:** Evaluation Studies ; Journal Article ; Review.

**Descriptors:** Comparative Study ; Euphoria/drug effects ; Human ; Methadone/\*administration & dosage/adverse effects ; Narcotic Antagonists/\*administration & dosage/adverse effects ; Narcotics/\*administration & dosage/adverse effects ; Opioid-Related Disorders/prevention & control/psychology/\*rehabilitation ; Patient Compliance/psychology ; Prescriptions, Drug ; Risk Factors.

**ATTC Buprenorphine Topics:** Pharmacology ; Pharmacotherapy for opiate dependence

327. **Sevarino K ; Oliveto A ; Kosten T. (2000) Neurobiological adaptations to psychostimulants and opiates as a basis of treatment development. Ann N Y Acad Sci 2000;909:51-87.**

**Author Address:** Department of Psychiatry, Connecticut V.A. Healthcare System, West Haven 06516, USA. kevin.sevarino@yale.edu

**Abstract:** Abuse of illicit substances, in particular psychostimulants and opiates, is a worldwide public health issue. Chronic use of cocaine and amphetamine causes common neurobiological adaptations that may guide new treatment development. These include perturbations in dopamine and serotonin neurotransmission, leading to trials of antidepressants, and serotonin and dopamine augmentation strategies. The detection of cerebral perfusion abnormalities caused by psychostimulants has led to examination of antiplatelet and excitatory amino acid (EAA) antagonist therapies. Further, development of cocaine vaccines allows for testing of peripheral blockade approaches to cocaine addiction. New approaches to behavioral treatments for cocaine dependence are also reviewed. For opiate dependence, understanding of heroin's effects on mu and kappa opiate receptors has led to investigations of the partial mu agonist buprenorphine in opiate maintenance. Evidence for hyper-excitability of locus coeruleus (LC) noradrenergic neurons and EEA inputs to the LC guides trials of new alpha 2-adrenergic agonists and EEA antagonists to alleviate opiate withdrawal. Finally, clinical experience with withdrawal from methadone and LAAM has led to trials of antagonist-accelerated opiate withdrawal. Improved treatment of psychostimulant and opiate addiction is critically needed, and likely to have wide-reaching impact in health care and society.

**ISSN:** 0077-8923.

**Pub Type:** Journal Article ; Review ; Review, Tutorial.

**Descriptors:** Adaptation, Physiological ; Antidepressive Agents/therapeutic use; Brain Ischemia/drug therapy ; Cocaine-Related Disorders/\*drug therapy ; Dopamine Agonists/therapeutic use ; Dopamine Antagonists/therapeutic use ; Excitatory Amino Acid Antagonists/therapeutic use ; Human ; Opioid-Related Disorders/\*drug therapy ; Platelet Aggregation Inhibitors/therapeutic use ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Pharmacology ; Pharmacotherapy for opiate dependence

328. **Shreeram S ; Dennison S. (2001) The future of pharmacologic interventions for addictive disorders. *Psychiatric Annals.* 31(12) Dec 2001, 723-728.**

**Abstract:** Presents an overview of medications that are potentially useful for the treatment of addictive disorders, some of which may become available in the US in the near future. Drugs for treatment of alcohol dependence include acamprosate, tiapride, nalmefene, and gabapentin. For treatment of opiate addiction, drugs include buprenorphine and naloxone. When used in conjunction with nicotine replacement therapy, mecamylamine has further increased smoking abstinence. For cocaine addiction, drugs include gabapentin, buprenorphine, dopamine receptor partial agonists, and active and passive immunization.

**ISSN:** 0048-5713.

**Pub Type:** Journal Article ; Review.

**Descriptors:** medications; pharmacologic treatment; addictions; alcohol dependence; cocaine addiction; opiate addiction ; \*Addiction ; \*Drug Addiction ; \*Drug Rehabilitation ; \*Drug Therapy ; Alcohol Abuse ; Cocaine ; Drug Dependency ; Opiates ; Human ; Literature Review/Research Review.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence

329. **Sindelar J. (2001) Opioid maintenance: The politics matter. *Addiction* 2001 Oct;96(10):1517-8.**

**Abstract:** The paper by Barnett, Zaric and Brandeau (2001) highlights a perplexing and important policy dilemma. Buprenorphine, the relatively new pharmacological treatment for treating opiates, could help to expand access to treatment. It is likely that new regulations in the US will allow, under some circumstances, prescribing by physicians in office-based practices, thus increasing access to treatment. One might expect that buprenorphine could be relatively cost-effective because it can be prescribed by office-based physicians. This negates the need for a dedicated addiction clinic and eliminates the overhead of a dedicated clinic.

**ISSN:** 0965-2140.

**Pub Type:** Comment ; Letter.

**Descriptors:** Buprenorphine/\*economics ; Cost-Benefit Analysis/economics ; Human ; Methadone/\*economics ; Narcotics/\*economics.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

330. **Sindelar J ; Fiellin D. (2001) Innovations in treatment for drug abuse: solutions to a public health problem. *Annual Review in Public Health* 2001;22:249-72.**

**Author Address:** Yale University School of Public Health, New Haven, Connecticut 06520, USA. jody.sindelar@yale.edu

**Abstract:** Treatment reduces drug use and crime and increases individuals' functioning. However, programs that treat drug dependence have high dropout rates and low completion rates. In addition, some individuals continue to use drugs while in treatment, and relapse is common. Furthermore, only a fraction of those who need treatment receive it. Recently, there have been important innovations that reduce barriers and increase effectiveness of treatment. These innovations include new pharmacological agents, novel counseling strategies, promising ways to motivate, and treatment in new settings. This paper describes standard treatments and recent innovations designed to increase (a) effectiveness of treatment, (b) motivation to seek care, (c) access, (d) retention, and (e) cost-effectiveness. We provide criteria on how these innovations should be evaluated in order to determine which should be adopted, funded, and transferred to existing and future treatment programs. This is a good review of current drug abuse treatment approaches, including use of buprenorphine.

**Pub. Type:** Journal article; Review.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness ; Treatment protocols/physician guidelines

331. **Sittl R. (2003) Transdermal buprenorphine: a viewpoint by Reinhard Sittl. *Drugs* 2003;63(19):2011-2.**

**Author Address:** Pain Clinic, University of Erlangen, Erlangen, Germany.

**Abstract:** Buprenorphine is the second transdermal formulation of a strong opioid to be introduced into pain management, following the fentanyl transdermal therapeutic system. Although the two systems function in a similar manner, they differ from each other not only in the contained opioids' profiles, but also in the technology of their transdermal delivery systems. While transdermal fentanyl uses the reservoir patch technology, the buprenorphine transdermal system (TDS) is a matrix system. In a matrix system, the substance is an integral part of the polymer structure of the patch, rendering the buprenorphine patch more robust in handling. While damaging the reservoir patch might result in "dose-dumping" and potentially overdosing the patient, damaging a matrix patch does not interfere with the controlled release of the drug.

**ISSN:** 0012-6667.

**Pub Type:** Journal article.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pain management

332. **Sittl R ; Griessinger N ; Likar R. (2003) Analgesic efficacy and tolerability of transdermal buprenorphine in patients with inadequately controlled chronic pain related to cancer and other disorders: a multicenter,**

**randomized, double-blind, placebo-controlled trial. Clin Ther 2003 Jan;25(1):150-68.**

**Author Address:** University of Erlangen, Pain Clinic, Erlangen, Germany. Reinhard.Sittl@kfa.imed.uni-erlangen.de

**Abstract:** BACKGROUND: Buprenorphine is a potent opioid analgesic that is available in sublingual and parenteral formulations. A new formulation, buprenorphine transdermal delivery system (TDS), has been developed. OBJECTIVE: The aim of this study was to compare the analgesic efficacy and tolerability of the 3 available dosages of buprenorphine TDS (35.0, 52.5, and 70.0 microg/h) with placebo. METHODS: This was a randomized, double-blind, placebo-controlled, multicenter study. Patients with chronic, severe pain related to cancer or other diseases and inadequately controlled with weak opioids were randomized to receive buprenorphine TDS 35.0, 52.5, or 70.0 microg/h or placebo patch for up to 15 days. A new patch was applied every 72 hours, for a total of 5 patches. All patients were permitted rescue analgesia with sublingual buprenorphine tablets (0.2 mg) as required for breakthrough pain. RESULTS: A total of 157 patients (86 women, 71 men; mean [SD] age, 58.7 [11.8] years) were initially enrolled in the study. Buprenorphine TDS was associated with significantly higher response rates than was placebo at the 35.0- and 52.5-microg/h dosages (36.6% and 47.5%, respectively, vs 16.2%; P=0.032 and P=0.003, respectively) and a numerically higher response rate at 70.0 microg/h (33.3%), although this difference did not reach statistical significance. Patients treated with buprenorphine TDS experienced a 56.7% reduction in use of sublingual rescue analgesic during the study compared with an 8% reduction with the placebo patch. A total of 43.5% of patients treated with buprenorphine TDS reported good or complete pain relief compared with 32.4% in the placebo group. Pain intensity decreased in a dose-dependent manner with buprenorphine TDS, and the duration of sleep uninterrupted by pain was improved by the end of the study. More than three fourths (78.8%) of patients in the placebo and buprenorphine TDS groups reported at least 1 adverse event (AE) during the study. The most common AEs were central nervous system and gastrointestinal symptoms. The majority of treatment-related AEs were mild or moderate in intensity and were typical of those occurring at the beginning of therapy with a strong opioid. CONCLUSIONS: Buprenorphine TDS was shown to be an effective analgesic against chronic, severe pain in this study population. Patients treated with this new formulation of buprenorphine showed improved duration of sleep and reduced need for additional oral analgesics. **ISSN:** 0149-2918.

**Pub Type:** Clinical Trial ; Journal Article ; Multicenter Study ; Randomized Controlled Trial.

**Descriptors:** Administration, Cutaneous ; Administration, Sublingual ; Adult ; Aged ; Aged, 80 and over ; Analgesics, Opioid/\*administration & dosage/adverse effects/\*therapeutic use ; Buprenorphine/\*administration & dosage/adverse effects/\*therapeutic use ; Chronic Disease ; Comparative Study ; Dose Forms ; Dose-Response Relationship, Drug ; Double-Blind Method ; Female ; Human ; Male ; Middle Age ; Neoplasms/\*complications ; Pain/\*drug therapy/etiology ; Pain Measurement ; Sleep/drug effects ; Support,

Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pain management

333. **Solberg U ; Burkhart G ; Nilson M. (2002) An overview of opiate substitution treatment in the European Union and Norway. International Journal of Drug Policy. Vol 13(6) Dec 2002, 477-484.**

**Author Address:** Solberg, Ulrik., ulrik.solberg@emcdda.org.

**Abstract:** This paper aims to provide an overview on the delivery and coverage of opiate substitution treatment in the European Union (EU) and Norway by the year 2000. It sketches which substitution substances are being used and when they were introduced in which countries, to what extent they are used, and how the delivery of substitution substances is organized in the EU Member States and Norway. Substitution treatments were introduced at different stages in the EU countries and although such measures now exist in all Member States there are considerable differences in coverage. Methadone remains predominant although other substitution substances such as buprenorphine, dihydrocodeine, slow-release morphine and heroin have been launched or are on trial in some Member States. The organization of the delivery of substitution treatment varies considerably but may tentatively be categorized into four overall 'organization modes': firstly, countries offering this treatment through general practitioners; secondly, those offering it through specialized centers; thirdly, those who provide it through specialized centers but with a limited number of treatment slots; and lastly, 'mixed modes' in which both general practitioners and specialized centers deliver substitution treatment services.

**ISSN:** 0955-3959 (Print).

**Pub Type:** Journal Article; Overview.

**Descriptors:** opiate substitution treatment; delivery; coverage; European Union; Norway; substitution substances ; \*Drug Therapy ; \*Health Care Delivery ; \*Methadone Maintenance ; \*Opiates ; Human.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries

334. **Soyka M ; Horak M ; Dittert S ; Kagerer S. (2001) Less driving impairment on buprenorphine than methadone in drug-dependent patients? J Neuropsychiatry Clin Neurosci 2001 Fall;13(4):527-8.**

**Abstract:** Buprenorphine is a low-efficacy, partial mu-opioid agonist that has long been under investigation as an alternative to methadone for treatment of drug dependence, with encouraging clinical results. The drug has been introduced into clinical practice in many countries, including Germany, in recent years. Its unique profile includes a ceiling on agonist activity that decreases toxicity and risk for overdose. Its slow dissociation from the mu-opioid receptor results in a long duration of action, which offers the possibility of alternate-day dosing schedules. A possible benefit from buprenorphine treatment may also be less impairment of psychomotor performance and driving ability than has been described in drug-dependent patients under methadone maintenance. **ISSN:** 0895-0172.

**Pub Type:** Letter.

**Descriptors:** Adult ; Attention/drug effects ; Automobile Driving/\*legislation & jurisprudence ; Buprenorphine/administration & dosage/\*adverse effects ; Comparative Study ; Female ; Human ; Male ; Methadone/administration & dosage/\*adverse effects ; Opioid-Related Disorders/\*rehabilitation ; Psychomotor Performance/\*drug effects ; Reaction Time/drug effects ; Support, Non-U.S. Gov't ; Visual Fields/drug effects.

**ATTC Buprenorphine Topics:** Pharmacology ; Psychosocial treatment aspects

335. **Stimmel B. (2001) Treating opioid dependence. N Engl J Med 2001 Feb 15;344(7):530; author reply 530-1.**

**Abstract:** The article by Johnson et al. on the treatment of opioid dependence (Nov. 2 issue) and the accompanying editorial by O'Connor serve an important purpose in making physicians and, one hopes, the public more aware of the effectiveness of methadone maintenance for heroin dependence. It is discouraging, however, that the ineffectiveness of low-dose methadone therapy still has to be demonstrated. The effectiveness of methadone, at an average dose of 100 mg per day, was shown by Dole et al. more than 30 years ago and has been repeatedly confirmed since then, with some patients needing a dose higher than 100 mg per day. If the high-dose group in the study by Johnson et al. had actually received a high dose of methadone (i.e., higher than 100 mg per day), its effectiveness might have been even more impressive. The low-dose group received a daily dose of 20 mg of methadone, which would not even be an analgesic dose if used for chronic pain. Unfortunately, most programs are using inadequate doses of methadone with, not surprisingly, poor results.

Buprenorphine has been shown to be effective as maintenance therapy for heroin dependence; however, the authors do not mention its high potential for abuse. It is one of the most frequently abused drugs in Australia and Scotland. It would have been helpful if Johnson et al. and O'Connor had mentioned the risk of addiction with buprenorphine as well as its effectiveness as maintenance therapy.

**ISSN:** 0028-4793.

**Pub Type:** Comment ; Letter.

**Descriptors:** Analgesics, Opioid/\*administration & dosage ; Buprenorphine/\*therapeutic use ; Human ; Methadone/\*administration & dosage ; Narcotic Antagonists/therapeutic use ; Opioid-Related Disorders/\*drug therapy.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; Pharmacotherapy for opiate dependence

336. **Stimmel B. (2001) Maintenance therapy for opioid addiction with methadone, LAAM and buprenorphine: the Emperor's New Clothes phenomenon. J Addict Dis 2001;20(4):1-5.**

**Abstract:** Since its inception in the late 1960's, methadone maintenance has been consistently shown to be one of the most effective methods of managing heroin addiction, even in cases refractory to other forms of therapy. This has been confirmed by numerous, independent assessments as well as by the number of persons enrolled in methadone maintenance as compared to other treatment modalities for opioid addiction. Methadone has been perhaps one of the most closely scrutinized therapies for treatment of any medical condition, and studies assessing its efficacy have found its side effects to be few, its benefits many. Yet, despite this, it remains one of the most controversial forms of therapy and is consistently denigrated not only by the public but, unfortunately, by those in the health professions as well.

**ISSN:** 1055-0887.

**Pub Type:** Comment ; Editorial.

**Descriptors:** Buprenorphine/\*therapeutic use ; Comparative Study ; Electrocardiography/drug effects ; Heroin Dependence/\*rehabilitation ; Human ; Methadone/\*therapeutic use ; Methadyl Acetate/\*therapeutic use ; Naltrexone/therapeutic use ; Narcotic Antagonists/therapeutic use ; Narcotics/\*therapeutic use ; Opioid-Related Disorders/\*rehabilitation ; Time Factors.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Pharmacotherapy for opiate dependence

337. **Stimmel B. (2001) "A comparison of levomethadyl acetate, buprenorphine, and methadone for opioid dependence": Comment. New England Journal of Medicine. Vol 344(7) Feb 2001, 530.**

**Abstract:** Comments on the article by R. E. Johnson et al (2000) that compared levomethadyl acetate, buprenorphine, and high (60-100 mg/day) and low (20 mg/day) dose methadone for the treatment of opioid dependence. Stimmel suggests that the "high-dose" group was not actually receiving a high dose, and that the low dose of 20 mg/day would not even be an analgesic dose if used for chronic pain. Stimmel also comments that Johnson et al, as well as P. G. O'Connor in his accompanying editorial failed to mention the risk addiction associated with buprenorphine.

**ISSN:** 0028-4793 (Print).

**Pub Type:** Journal Article ; Letter.

**Descriptors:** levomethadyl acetate vs buprenorphine vs high vs low-dose methadone, study retention & abstinence & severity of drug problem, adults with opioid dependence, 17 week study, commentary ; \*Drug Dependency ; \*Drug Therapy ; \*Methadone Maintenance ; \*Narcotic Agonists ; \*Opiates ; Drug Abstinence ; Drug Dosages ; Drug Rehabilitation ; Experimental Attrition ; Maintenance Therapy ; Severity (Disorders) ; Human; Male; Female; Adulthood (18 yrs & older).

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; Pharmacotherapy for opiate dependence

338. **Stine S ; Greenwald M ; Kosten T. (2003) Pharmacologic interventions for opioid addiction. In: Graham, Allen W ; Schultz, Terry K ; Mayo-Smith,**

**Michael F ; Ries, Richard K ; Wilford, Bonnie B. Principles of Addiction Medicine / 3rd edition. Chevy Chase, MD : American Society of Addiction Medicine, Inc., 2003, pp. 735-748.**

**Abstract:** Studies on the nature of opioid addiction have described an abstinence syndrome characterized by two phases: a relatively brief initial phase in which opioid-dependent patients experience acute withdrawal, followed by a protracted abstinence syndrome. Current pharmacotherapeutic strategies are based on this distinction. Four pharmacologic agents and the ways that each addresses both the biological and psychosocial concomitants of opioid dependence are discussed in this chapter: naltrexone, methadone, LAAM, and buprenorphine.

**ISSN:** 1880425084.

**Pub Type:** Book Chapter

**Notes:** ADAI Library: RC 644 M455 2003 [REF HAND].

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

339. **Stoil M. (2003) Buprenorphine and the future of addiction medicine. (Washington Insights). Behavioral Health Management, March-April 2003 v23(2) p8, (2 pages).**

**Abstract:** This is an overview of issues about the approval of buprenorphine for treatment of opioid dependence, particularly by primary care physicians. The author notes implications for current addiction specialists, adding that "Behavioral health practitioners and addiction specialists perhaps should remind their primary care colleagues that psychological counseling and support could be important in helping patients cope with the beginning and end of buprenorphine treatment."

**Pub. Type:** magazine article.

**ATTC Buprenorphine Topics:** Legal/regulatory issues; Pharmacotherapy for opiate dependence

340. **Stoller K ; Bigelow G ; Walsh S ; Strain E. (2001) Effects of buprenorphine /naloxone in opioid-dependent humans. Psychopharmacology (Berl) 2001 Mar;154(3):230-42.**

**Author Address:** Behavioral Pharmacology Research Unit, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, 5510 Nathan Shock Drive, Baltimore, MD 21224, USA.

kstolle@jhmi.edu

**Abstract:** RATIONALE: Buprenorphine is a partial mu opioid agonist under development as a sublingual (SL) medication for opioid dependence treatment in the United States. Because buprenorphine may be abused, tablets combining buprenorphine with naloxone in a 4:1 ratio have been developed to reduce that risk. Low doses of injected buprenorphine/naloxone have been tested in opioid-dependent subjects, but higher doses (more than 2 mg of either

medication) and direct comparisons to SL buprenorphine/naloxone have not been examined. OBJECTIVES: To assess and compare the effects of intramuscular (i.m.) versus SL buprenorphine/naloxone in opioid-dependent volunteers. METHODS: Opioid-dependent volunteers were maintained on 40 mg per day of oral hydromorphone while on a residential research ward. After safety testing in two pilot subjects, participants (n = 8) were tested with both i.m. and SL buprenorphine/naloxone (1/0.25, 2/0.5, 4/1, 8/2, 16/4 mg); i.m. hydromorphone (10 mg) and naloxone (0.25 mg); both i.m. and SL buprenorphine alone (8 mg); and placebo. Test sessions were twice per week; dosing was double-blind. RESULTS: Intramuscular buprenorphine/naloxone produced dose-related increases on indices of opioid antagonist effects. Effects were consistent with naloxone-precipitated withdrawal, and were short-lived. As withdrawal effects dissipated, euphoric opioid agonist effects from buprenorphine did not appear. Sublingual buprenorphine/naloxone produced neither opioid agonist nor antagonist effects. CONCLUSIONS: Intramuscular injection of buprenorphine/naloxone precipitates withdrawal in opioid dependent persons; therefore, the combination has a low abuse potential by the injection route in this population. Sublingual buprenorphine/naloxone by tablet is well tolerated in opioid dependent subjects, and shows neither adverse effects (i.e., precipitated withdrawal) nor a high abuse potential (i.e., opioid agonist effects). **ISSN:** 0033-3158.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Administration, Sublingual ; Adolescent ; Adult ; Affect/drug effects/physiology ; Buprenorphine/\*administration & dosage ; Dose-Response Relationship, Drug ; Drug Therapy, Combination ; Female ; Human ; Hydromorphone/administration & dosage ; Injections, Intramuscular; Male ; Middle Age ; Naloxone/\*administration & dosage ; Narcotic Antagonists/\*administration & dosage ; Narcotics/administration & dosage ; Observer Variation ; Opioid-Related Disorders/\*drug therapy/psychology ; Psychomotor Performance/drug effects/physiology ; Substance Withdrawal Syndrome/drug therapy/psychology ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Dosing/administration ; Pharmacotherapy for opiate dependence

341. **Stone S. (2002) Brief Clinical Report: Case report of buprenorphine hydrochloride (Subutex) in a 4-year old asthmatic male. Journal of Substance Use 7(3):124, 2002.**

**Author Address:** Merthyr Home Detox Team, 34 Victoria Street, Merthyr Tydfil CF47 8BW Wales, UK,

**Abstract:** In this case report a child accidentally ingested buprenorphine hydrochloride (Subutex). The regional poisons unit was contacted and there was an eventual favorable outcome. In company literature, 8 mg of Subutex is the approximate equivalent to 60 ml of methadone mixture (1 mg/ml). Recommendations are made for preventing or treating accidental ingestion.

**ISSN:** 1465-9891

**Pub. Type:** Journal article; Case report.

**Descriptors:** Human; Adverse Reactions.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Special populations

342. **Strain, E. (2002) Pharmacology, Safety and Efficacy of Buprenorphine for the Treatment of Opioid Dependence. Presentation to the State Systems Development Program Conference, Nov. 20-22, 2002, Washington DC.**

**Abstract:** This is a 33-slide conference presentation on the topics: Overview to opioid pharmacology; Pharmacology of buprenorphine; and Efficacy and safety of buprenorphine. It was presented to the SSDP conference on "Closing the Treatment Gap / No Wrong Doors" as part of a panel titled "An Overview of Buprenorphine for the Treatment of Opioid Dependence."

**Pub. Type:** Conference presentation; Slides (in PDF document)

**URL:** [http://www.treatment.org/ssdpvi/handouts/friday/C3\\_Eric\\_Strain.pdf](http://www.treatment.org/ssdpvi/handouts/friday/C3_Eric_Strain.pdf)

**ATTC Buprenorphine Topics:** Pharmacology; Pharmacotherapy for opiate dependence

343. **Strain E ; Clarke HW ; Auriacombe M ; Lagier G ; Mallaret M ; Thirion X. (2002) French Experience with Buprenorphine [symposium]. NIDA Research Monograph 183:134 –141, 2002.**

**Abstract:** Summary of a symposium presentation at 64th Annual meeting of College on Problems of Drug Dependence (CPDD). Sections: (1) Clinical Data on Buprenorphine Use in France; (2) Epidemiological Studies of Diverted Use of Buprenorphine in France. (3) Buprenorphine: Toxic and Adverse Effects.

**Pub. Type:** Conference presentation.

**Descriptors:** Addiction; Clinical Study; Dependence Treatment; Adverse Effects.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Prevalence of use for opiate dependence

344. **Strain E ; Stoller K ; Walsh S ; Bigelow G. (2000) Effects of buprenorphine versus buprenorphine/naloxone tablets in non-dependent opioid abusers. Psychopharmacology (Berl) 2000 Mar;148(4):374-83.**

**Author Address:** Department of Psychiatry and Behavioral Sciences, The Johns Hopkins University School of Medicine, Baltimore, MD 21224, USA. [ecsgss@aol.com](mailto:ecsgss@aol.com)

**Abstract:** RATIONALE: Buprenorphine is an opioid agonist-antagonist under development in the United States as a sublingual medication for treatment of opioid dependence. Buprenorphine may be abused; therefore, tablets combining buprenorphine with naloxone have been developed with the intent of reducing the abuse risk in people physically dependent upon opioids. The characteristics and abuse potential of buprenorphine and buprenorphine/naloxone tablets in non-dependent opioid abusers have not been determined. Non-parenteral abuse of opioids such as buprenorphine may

be more likely in people who have less severe substance abuse disorders (e.g., are not physically dependent upon opioids). OBJECTIVES: To assess the abuse potential of sublingual buprenorphine and buprenorphine/naloxone tablets in non-dependent opioid abusers. METHODS: Subjects (n=7) were tested with sublingual buprenorphine (4, 8, 16 mg), sublingual buprenorphine/naloxone (1/0.25, 2/0.5, 4/1, 8/2, 16/4 mg), as well as intramuscular hydromorphone as an opioid agonist control (2, 4 mg) and placebo in laboratory sessions conducted twice per week. Dosing was double-blind and double-dummy. RESULTS: The higher doses of both buprenorphine and buprenorphine/naloxone produced similar opioid agonist-like effects. The onset of these effects was slowed, consistent with the sublingual route of administration, and the magnitude of effects was moderate. There was no evidence to suggest the addition of naloxone attenuated buprenorphine's opioid agonist effects in this population when buprenorphine was delivered by the sublingual route. CONCLUSIONS: These results suggest that sublingual buprenorphine and buprenorphine/naloxone may both be abused by opioid users who are not physically dependent upon opioids.

**ISSN:** 0033-3158.

**Pub Type:** Clinical Trial ; Controlled Clinical Trial ; Journal Article. **Descriptors:** Administration, Sublingual ; Adult ; Analgesics, Opioid/administration & dosage/therapeutic use ; Buprenorphine/administration & dosage/\*therapeutic use ; Comparative Study ; Drug Combinations ; Human ; Hydromorphone/administration & dosage/therapeutic use ; Injections, Intravenous ; Male ; Middle Age ; Motor Activity/drug effects ; Naloxone/administration & dosage/\*therapeutic use ; Narcotic Antagonists/administration & dosage/\*therapeutic use ; Opioid-Related Disorders/\*drug therapy/psychology ; Support, U.S. Gov't, P.H.S. ; Tablets ; Time Factors.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Dosing/administration ; Pharmacotherapy for opiate dependence

345. **Strain E ; Walsh S ; Bigelow G. (2002) Blockade of hydromorphone effects by buprenorphine/naloxone and buprenorphine. Psychopharmacology (Berl) 2002 Jan;159(2):161-6.**

**Author Address:** Behavioral Pharmacology Research Unit, Department of Psychiatry and Behavioral Sciences, The Johns Hopkins University School of Medicine, 5510 Nathan Shock Drive, Baltimore, MD 21224, USA. [ecsgss@aol.com](mailto:ecsgss@aol.com)

**Abstract:** RATIONALE: Buprenorphine is an opioid agonist-antagonist used in the treatment of opioid dependence. Naloxone has been combined with buprenorphine to decrease the parenteral abuse potential of buprenorphine. This addition of naloxone may also confer further opioid blockade efficacy. OBJECTIVES: To test the opioid blockade efficacy of sublingual buprenorphine/naloxone versus buprenorphine alone and determine whether: (1) the blockade efficacy of buprenorphine/naloxone varies between the time of expected maximal and minimal effects of naloxone, (2) the blockade efficacy of buprenorphine/naloxone and buprenorphine varies as a function of

maintenance dose level, and (3) there are adaptive changes over time associated with repeated daily dosing of buprenorphine/naloxone and buprenorphine. **METHODS:** Residential subjects ( n=6) were maintained on different double-blind dose levels of buprenorphine/naloxone (4/1, 8/2, 16/4, 32/8 mg) and buprenorphine (32 mg) for 6-day periods and challenged with parenteral doses of hydromorphone (12 mg) in laboratory sessions. **RESULTS:** There was no evidence of additional opioid blockade efficacy conferred by combining naloxone with buprenorphine. Higher doses of buprenorphine/naloxone provided greater blockade of hydromorphone effects. Changes over time associated with repeated daily dosing of buprenorphine/naloxone and buprenorphine were minimal. **CONCLUSIONS:** The addition of naloxone to buprenorphine may deter the parenteral abuse of buprenorphine/naloxone, but it does not enhance the therapeutic efficacy of buprenorphine. The blockade efficacy of buprenorphine/naloxone is dose related; however, doses up to 32/8 mg buprenorphine/naloxone provide only partial blockade when subjects receive a high dose of an opioid agonist. **ISSN:** 0033-3158.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Analgesics, Opioid/\*antagonists & inhibitors/ pharmacology; Buprenorphine/\*pharmacology/therapeutic use ; Comparative Study ; Dose-Response Relationship, Drug ; Double-Blind Method ; Drug Therapy, Combination ; Female ; Human ; Hydromorphone/\*antagonists & inhibitors/pharmacology ; Male ; Naloxone/\*pharmacology/therapeutic use ; Narcotic Antagonists/\*pharmacology/therapeutic use ; Opioid-Related Disorders/drug therapy/psychology ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacology ; Pharmacotherapy for opiate dependence

- 346. Substance Abuse and Mental Health Services Administration. (2002) Draft Buprenorphine Curriculum for Physicians. From SAMHSA web site; DRAFT form is currently being updated based on the recent FDA approval of Subutex® and Suboxone® for opioid therapy. (as of October 2003).**

**Abstract:** The purpose of the Curriculum is to assist in preparing lectures and other medical education activities related to prescribing of buprenorphine for the treatment of opioid dependence. It includes the core information unique to buprenorphine and its use in the pharmacological management of opioid dependence, as well as a comprehensive overview of treatment for opioid dependence. It does not describe a standard of care. Treatment decisions should be made based upon the individual patient and the level of available resources. The Curriculum is based on the CSAT document Buprenorphine Clinical Practice Guidelines (DRAFT) which is also in the process of being updated and finalized. The Curriculum was developed by a consensus panel with members from the American Academy of Addiction Psychiatry, the American Osteopathic Academy of Addiction Medicine, and the American Society of Addiction Medicine. Development of the Curriculum was supported by CSAT.

**URL:** <http://buprenorphine.samhsa.gov/curriculum.html>

**Pub. Type:** web document.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

- 347. Substance Abuse and Mental Health Services Administration. (2002) Buprenorphine approved for opioid addiction treatment. SAMHSA News 2002 Fall;10(4):3.**

**Abstract:** The medication buprenorphine was approved by the Food and Drug Administration on October 9, 2003 for the detoxification and maintenance treatment of heroin and other narcotic addiction. The new medication enables physicians, for the first time, to treat opioid addiction in an office-based setting provided they meet criteria mandated by Congress and they obtain a waiver through SAMHSA to dispense and prescribe it.

**URL:** <http://www.samhsa.gov/news/2002News/index.html>

**Pub. Type:** Newsletter (print or online).

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

- 348. Substance Abuse and Mental Health Services Administration. (2003) Opioid treatment programs can now offer buprenorphine. SAMHSA News 2003; 11(2):19.**

**Abstract:** SAMHSA has announced an interim final rule that will permit opioid treatment programs serving persons addicted to heroin or narcotic pain relievers to offer buprenorphine treatment along with methadone and ORLAAM.

**URL:** [http://www.samhsa.gov/news/click\\_samhsanews.html](http://www.samhsa.gov/news/click_samhsanews.html)

**Pub. Type:** Newsletter (print and online).

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

- 349. Substance Abuse and Mental Health Services Administration. Buprenorphine : Physician waiver qualifications. Substance Abuse and Mental Health Administration, on website in October 2003.**

**Abstract:** The Drug Addiction Treatment Act of 2000 (DATA 2000) enables qualifying physicians to receive a waiver from the special registration requirements in the Controlled Substances Act for the provision of medication-assisted opioid therapy. This waiver allows qualifying physicians to practice medication-assisted opioid addiction therapy with specially FDA-approved Schedule III, IV, or V narcotic medications. On October 8, 2002 Subutex® (buprenorphine hydrochloride) and Suboxone® tablets (buprenorphine hydrochloride and naloxone hydrochloride) received FDA approval for the treatment of opioid dependence.

To receive a waiver to practice opioid addiction therapy with approved Schedule III, IV, or V narcotics a physician must notify the Center for Substance Abuse Treatment (CSAT, a component of the Substance Abuse and Mental

Health Services Administration) of his or her intent to begin dispensing or prescribing this treatment. This Notification of Intent must be submitted to CSAT before the initial dispensing or prescribing of opioid therapy. The "waiver notification" section on this web site provides information on how to obtain and submit a Notification of Intent form. The Notification of Intent can be submitted on-line from this Web site, or via ground mail or fax.

**URL:** [http://buprenorphine.samhsa.gov/waiver\\_qualifications.html](http://buprenorphine.samhsa.gov/waiver_qualifications.html)

**Pub. Type:** web resource.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Treatment protocols/physician guidelines

**350. Substance Abuse and Mental Health Services Administration. (ongoing) SAMHSA Buprenorphine Home Page. Substance Abuse and Mental Health Administration [web site].**

**Abstract:** This is the main SAMHSA site on buprenorphine. Contains: 1) General information about buprenorphine; 2) Text of the Drug Addiction Treatment Act of 2000 (act that permits physicians to prescribe narcotics for opioid addiction); 3) Physician Waiver Qualifications and Waiver Notification (instructions on how to apply for permission to prescribe buprenorphine, including the actual application form); 4) FAQ (primarily for physicians with questions about legal and procedural issues); 5) Physician Buprenorphine Curriculum (a curriculum to assist in preparing lectures and other medical education activities related to prescribing buprenorphine); 6) Model State Medical Board Policy Guidelines (guidelines designed to encourage state medical boards to adopt consistent standards, promote public health by availing opioid addicted patients of appropriate treatment, and educating the regulatory and physician communities on new treatment modalities offering an alternative in the treatment of opioid addiction).

**URL:** <http://buprenorphine.samhsa.gov/>

**Pub. Type:** web site; documents in multiple formats.

**ATTC Buprenorphine Topics:** Dosing/administration ; Legal/regulatory issues; Pharmacology ; Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

**351. Substance Abuse and Mental Health Services Administration. (ongoing) Buprenorphine Physician Locator. Substance Abuse and Mental Health Services Administration [web site].**

**Abstract:** The Buprenorphine Physician Locator is a service of the Center for Substance Abuse Treatment (CSAT), Substance Abuse and Mental Health Services Administration (SAMHSA). The Locator is an on-line resource designed to assist the States, medical and addiction treatment communities, potential patients, and/or their families in finding information on locating physicians who can prescribe buprenorphine (Suboxone® and Subutex®) for treatment of opioid addiction. The Locator lists:

Physicians authorized to prescribe a class of medications for opioid (narcotic) addiction treatment, of which Suboxone® and Subutex® are the only ones

approved at this time. CSAT provides the on-line Physician Locator as a source of information for persons seeking physician treatment for themselves or another person. CSAT compiles the information in the Physician Locator from its information on qualified physicians who have waivers to prescribe or dispense specially approved classes of narcotic medications for the treatment of narcotic addiction. Of these drugs, Subutex® and Suboxone® are the only ones approved by the FDA thus far. The list includes only physicians who have met qualifications under the Drug Addiction Treatment Act of 2000 (DATA 2000), and who have authorized the use of their names in the Locator. Please note that CSAT is not a treatment referral agency and cannot make specific recommendations or endorsements regarding physicians on the Locator.

**URL:** [http://buprenorphine.samhsa.gov/bwns\\_locator/index.html](http://buprenorphine.samhsa.gov/bwns_locator/index.html)

**Pub. Type:** Web site ; Searchable Directory.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

**352. Summers Z ; Stone S. (2002) A description of opiate detoxification using buprenorphine in a community setting. J Subst Use 2002;7(2):96-99.**

**Abstract:** There is a need to test a range of suitable and appropriate methods of opiate detoxification in addition to the use of methadone. This paper describes the use of Subutex (Buprenorphine) in opiate detoxification regimes in two outpatient settings. The first setting is a home detoxification programme and the second a community detoxification programme. The paper demonstrates the safe and effective use of Subutex in the community. The medication was administered by a community psychiatric nurse in the home detoxification team in the first setting and by a community pharmacist, with a voluntary sector worker assisting in the supervision of the administration of the drug, in the second setting. The paper also demonstrates the high success rate of initiation onto Naltrexone and maintenance of Naltrexone to 3 months post-detoxification. It is thought that there were several factors that contributed to this success. These include the local culture and the manner in which the detoxification process and initiation of Naltrexone were presented to the client. Other important factors include the use of adjunctive medication, the close involvement of family members and co-reporters and the assiduous follow-up of compliance of supervised consumption by a family support worker.

**Pub. Type:** journal article.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects

**353. Swift R. (2001) Can medication successfully treat substance addiction? (Special report part II). Psychopharmacology Update, Dec 2001 v12(12) p1 (3 pages).**

**Abstract:** This is the second part of a special two-part report on using medications to treat addiction. Part II examines pharmacotherapy for opioid

and cocaine dependence and dual diagnosis, including buprenorphine. Patients with combined opiate and cocaine dependence, receiving buprenorphine maintenance treatment, show significant reductions in their use of cocaine, compared to patients receiving methadone maintenance.

**Pub. Type:** brief article.

**Descriptors:** pharmacists.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence

354. Swoboda J. (2003) Improving opioid dependency treatment. *J Am Board Fam Pract* 2003 Mar-Apr;16(2):185-6.

**Abstract:** Physicians have played an outsider role in the treatment of opioid dependency. We are called upon as the purveyors of authoritative signature when it comes to prescribing the controlled substances that are frequently used to replace illegal sources, and thus we contribute reluctantly to the drug diversion problem. We have been simultaneously prohibited from knowingly prescribing opiate agonist therapy for opioid addiction unless we are employed by one of 1,200 narcotic treatment programs that dispense methadone and levo-alpha acetylmethadol (LAAM). We are held responsible for treating the growing population of needle-use victims who have human immunodeficiency virus infection and hepatitis. We contribute through taxation to the burdensome and expensive systems designed to punish (but rarely rehabilitate) addicts and dealers, although hopeful is the idea of introducing methadone clinics into correctional settings. Two and one-half million persons have used heroin in this country, and nearly 1 million do so currently. Approximately 1 in 5 are engaged in treatment. In that addictive medicine might be one of the quintessential subspecialties of family practice, given the solid evidence of genetic involvement in dependency disorders and the profound impact that substance abuse has on family function, it follows that the family physician might be an indispensable part of diagnosing and treating addiction in this large population. **ISSN:** 0893-8652.

**Pub Type:** Letter.

**Descriptors:** Buprenorphine/\*therapeutic use ; Delivery of Health Care ; Human ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/\*drug therapy/epidemiology ; \*Primary Health Care ; United States.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Pharmacotherapy for opiate dependence

355. Sylvestre D. (2002) Common medical problems in opioid addicted patients. Presentation at a meeting of the California Society of Addiction Medicine, Newport Beach, CA October 9, 2002.

**Abstract:** This PowerPoint slide presentation uses a case study to address some of the common medical problems found in opioid addicted patients. As in the case study, the majority of long-term IDUs presenting for buprenorphine therapy will have a number of comorbid medical conditions that need to be addressed, including Hepatitis, HIV, and Tuberculosis, as well as a variety of STDs and other bacterial infections. Offers suggestions on screening methods,

and the impact these diseases may have on buprenorphine treatment.

**URL:**<http://www.csam-asam.org/Bup%20Clinical%20Info/powerpoint%20presentations/MedicalProblems.ppt>

**Pub. Type:** PowerPoint slides.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

356. Tacke U. (2002) Abuse of buprenorphine by intravenous injection--the French connection. *Addiction* 2002 Oct;97(10):1355.

**Abstract:** Recently, drug tourism was mentioned in this journal (Lemmons 2002) in relation to the Dutch cannabis policy. I would like to draw your attention to a problem of drug tourism, which has been brought about by differences in treatment policy within the European Union (EU). In Finland, opiate addiction has been a smaller problem than in many other European countries and, traditionally, the threshold for drug maintenance treatment (DMT) with methadone or buprenorphine has been high. However, more liberal treatment regulations have come into effect starting 1 May 2002, making it possible to use opioids for withdrawal or DMT in authorized community health-care centres all over the country.

In recent times the use of buprenorphine for DMT has increased in the United States and Europe, with France representing one of the leading countries in this respect. During recent years many Finnish opiate addicts have made 1-day trips to Paris, where they have obtained prescriptions of buprenorphine by French general practitioners (GPs). There is evidence that these trips have been used for drug-trafficking and to lead to buprenorphine addiction in individuals without previous abuse of opiates.

**ISSN:** 0965-2140.

**Pub Type:** Comment ; Letter.

**Descriptors:** \*Buprenorphine ; Drug and Narcotic Control ; France ; Human ; \*Narcotics ; Opioid-Related Disorders/\*etiology ; \*Travel.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; History, use and effectiveness in other countries

357. Telias D ; Nir-Hod J. (2000) Buprenorphine-Ketorolac vs. Clonidine-Naproxen in the Withdrawal from Opioids. *Int J Psychosocial Rehabilitation* 2000;4(4):441-446.

**Author Address:** Dr. Darwin Telias, POBox 4600, Beer-Sheva, Israel, Tel. 972-7-6401702, Fax 972-7-6401622, email: [teliaska@zahav.net.il](mailto:teliaska@zahav.net.il)

**Abstract:** The authors analyzed the comparative results of two groups of patients undergoing detoxification from opiates: one group received a Clonidine-Naproxen protocol, and the other received Buprenorphine-Ketorolac. Success rate of Clonidine-Naproxen (CN) was 81%. and success rate of Buprenorphine-Ketorolac (B-K) was 73%, success defined as patients who finished detoxification procedures and were drug-free at the end. Despite the

better results for the CN group, BK was much better accepted by patients. One of the advantages of the Buprenorphine protocol was that it did not require close supervision and monitoring, thus abating the costs significantly. Buprenorphine doses used were lower than average reported in literature, and the authors attribute this to the concomitant use of Ketorolac. The authors recommend the use of BK in order to increase the number of patients asking for treatment. The addictive potential of Buprenorphine is emphasized but also the misuse of Clonidine by patients attempting at self detoxification is brought to attention.

**URL:** <http://www.psychosocial.com/addiction/buprenorphine-ketorolac.html>

**Pub. Type:** journal article; web document.

**Descriptors:** ambulatory detoxification; using a combination of Buprenorphine and Ketorolac.

**ATTC Buprenorphine Topics:** Dosing/administration ; Combined treatment with other therapeutic medications; Treatment outcomes/effectiveness

358. **Thirion X ; Lapierre V ; Micallef J ; Ronfle E ; Masut A ; Pradel V ; Coudert C ; Mabriez J ; Sanmarco J. (2002) Buprenorphine prescription by general practitioners in a French region. Drug Alcohol Depend 2002 Jan 1;65(2):197-204.**

**Author Address:** Centre for Evaluation and Information on Pharmacodependence, Public Health Department, School of Medicine, 27 Boulevard Jean Moulin, 13005 Marseilles, France. [oppidum@medecine.univ-mrs.fr](mailto:oppidum@medecine.univ-mrs.fr)

**Abstract:** Since 1996 French general practitioners (GPs) may prescribe sublingual buprenorphine tablets as maintenance treatment for opiate dependence. The computerised data management of the main French health reimbursement system now allows surveillance of the use of this drug, and how it is prescribed. The purpose of this study is to determine the profile of maintained patients, prescribed doses, associated psychotropic treatments and how practitioners prescribe these treatments. This study analyses the 11186 buprenorphine prescriptions electronically transmitted for reimbursement between September and December 1999 in a specific French region. It was found that the 2078 treated patients consumed a mean of 11.5 mg of buprenorphine per day and 12% of them procured prescriptions from more than two prescribers. 43% of maintained patients had an associated benzodiazepine prescription, mainly flunitrazepam, often on the same prescription form. 61% of patients had regular follow-up, others had occasional consultations (21%) and another 18% had deviant maintenance treatment (more than two prescribers or more than 20 mg per day of daily buprenorphine dose). Benzodiazepine consumption was much higher in the 'deviant group' (71.4%). 85% of buprenorphine prescriptions were made by GPs. 21% of GPs prescribed buprenorphine and 61% of those had only one or two maintained patients. Buprenorphine prescription by French GPs is a procedure with no particular requirements, allowing many patients to easily access maintenance treatments. However, a high risk of abuse exists, which demands extensive investigation and evaluation of these practices.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article.

**Descriptors:** Administration, Sublingual ; Adult ; Analgesics, Opioid/ administration & dosage/\*therapeutic use ; Buprenorphine/administration & dosage/\*therapeutic use ; Drug Administration Schedule ; Female ; Flunitrazepam/therapeutic use ; France/epidemiology ; GABA Modulators/therapeutic use ; Human ; Male ; Middle Age ; Opioid-Related Disorders/epidemiology/\*rehabilitation ; Prescriptions, Drug/\*statistics & numerical data ; \*Primary Health Care.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Prevalence of use for opiate dependence

359. **Thirion X ; Micallef J ; Barrau K ; Djeddar S ; Lambert H ; Sanmarco J ; Lagier G. (2001) Recent evolution in opiate dependence in France during generalisation of maintenance treatments. Drug Alcohol Depend 2001 Feb 1;61(3):281-5.**

**Author Address:** Centre collaborateur du CEIP Marseille et Laboratoire de Sante Publique, Faculte de Medecine, 27 Bd. Jean Moulin 13005 Marseille, France. [oppidum@medecine.univ-mrs.fr](mailto:oppidum@medecine.univ-mrs.fr)

**Abstract:** Two maintenance drugs had been used in France since 1996, methadone and high-dosage buprenorphine. This study aimed to examine changes in drug use from observations gathered between 1995 and 1997, within the framework of the French program for the monitoring of drug dependence (OPPIDUM). This annual survey studies psychoactive substances consumed by drug addicts attending specialised drug care centres. During the last three surveys, 16 centres collected a total of 1597 patient-files. This study shows an increase in the number of patients undergoing maintenance treatment (from 14 to 69%), a reduction in the number of intravenous drug users (from 55 to 22%) and a reduction in consumption of psychoactive substances. However, poly-drug addiction behaviour continues and high-dose buprenorphine subjects frequently use the substance intravenously and in association with benzodiazepines.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article ; Multicenter Study.

**Descriptors:** Adult ; \*Buprenorphine/administration & dosage ; Chi-Square Distribution ; Female ; France/epidemiology ; Human ; Male ; \*Methadone/administration & dosage ; \*Narcotics/administration & dosage ; Opioid-Related Disorders/\*epidemiology/rehabilitation ; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; History, use and effectiveness in other countries ; Prevalence of use for opiate dependence

360. **Thirion X ; Micallef J ; Barrau K ; Djeddar S ; Sanmarco J ; Lagier G. (2001) Observation of psychoactive substance consumption: methods and**

**results of the French OPPIDUM programme. Eur Addict Res 2001 Mar;7(1):32-6.**

**Author Address:** CEIP de Marseille (centre associe) et Laboratoire de Sante Publique, Faculte de Medecine, Marseille, France. oppidum@medecine.univ-mrs.fr

**Abstract:** This study presents a French programme designed to observe and evaluate psychoactive substance dependence and abuse. Annual surveys lasting 4 weeks are performed with drug users in drug centres. Its usefulness is discussed using examples from the study: potential for antidepressant dependence (amineptine), monitoring benzodiazepine use and consumption associated with maintenance treatments. Flunitrazepam is the most consumed benzodiazepine and often got by deal (29%). There are important differences between buprenorphine consumption in a maintenance treatment context (9/10) and beyond this context (1/10). The main methodology problems encountered are representativeness and validity of data. The limits of the programme and its role in the French health care system are discussed.

**ISSN:** 1022-6877.

**Pub Type:** Journal Article.

**Descriptors:** Adolescent ; Adult ; Anti-Anxiety Agents, Benzodiazepine ; Buprenorphine ; Data Collection ; Female ; France/epidemiology ; Human ; Male ; Methadone ; \*Narcotics ; Program Evaluation ; \*Psychotropic Drugs ; Substance Abuse Treatment Centers/\*methods/statistics & numerical data ; Substance-Related Disorders/\*epidemiology/therapy ; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; History, use and effectiveness in other countries ; Prevalence of use for opiate dependence

**361. Traynor K. (2002) Pharmacists may dispense new opioid addiction treatment. Am J Health Syst Pharm 2002 Nov 15;59(22):2150, 2152.**

**Abstract:** abstract not available

**ISSN:** 1079-2082.

**Pub Type:** News.

**Descriptors:** Buprenorphine/\*administration & dosage ; \*Drug and Narcotic Control ; Human ; Naloxone/\*administration & dosage ; Narcotic Antagonists/\*administration & dosage ; Opioid-Related Disorders/\*rehabilitation; \*Pharmacists ; United States.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

**362. Tzschentke T. (2002) Behavioral pharmacology of buprenorphine, with a focus on preclinical models of reward and addiction. Psychopharmacology (Berl) 2002 Apr;161(1):1-16.**

**Author Address:** Grunenthal GmbH, Biomedical Research, Department of Pharmacology, Postfach 500444, 52088 Aachen, Germany. thomas.tzschentke@grunenthal.de

**Abstract:** RATIONALE: Buprenorphine is a potent mu-receptor partial agonist and is widely used as an analgesic drug. It is also increasingly considered to be an alternative to methadone in the maintenance and eventual detoxification of heroin addicts, and also in the treatment of cocaine addiction. So far, buprenorphine has been available as a sublingual tablet and as a solution for IV injection. Recently, a new transdermal formulation of buprenorphine in slow-release matrix patches has been introduced (Transtec) for the treatment of intermediate to severe pain. OBJECTIVES: The aim of this paper is to review, from a preclinical perspective, the current status of what is known about the behavioral pharmacology of buprenorphine, with a particular emphasis on the issues of reward, addiction, and dependence. It will also point to open questions that should be addressed in the future to improve our understanding of the effects and the mechanisms of action of this drug. RESULTS AND CONCLUSIONS: Since buprenorphine is a potent opioid drug, the issue of addiction and dependence in this context is an important one. Although there are still some gaps in the behavioral pharmacological characterization of buprenorphine, the general conclusion that can be drawn from the reviewed literature is that despite the high affinity of buprenorphine for the mu receptor it appears to be a remarkably safe drug, with a benign overall side effect profile and low addictive and dependence-inducing potential. This favorable side effect profile appears to be due, to a large extent, to the partial agonistic properties of the drug, in combination with its particular receptor kinetics (i.e. very slow dissociation from the mu receptor after binding).

**ISSN:** 0033-3158.

**Pub Type:** Journal Article ; Review ; Review, Tutorial.

**Descriptors:** Analgesics, Opioid/\*pharmacology ; Animal ; Buprenorphine/\*pharmacology ; Conditioning (Psychology)/drug effects ; Discrimination Learning/drug effects ; Human ; Motor Activity/drug effects ; Naloxone ; \*Reward ; Self Administration ; Substance-Related Disorders/\*etiology.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Pharmacology ; Pharmacotherapy for opiate dependence

**363. U.S. Congress, 106<sup>th</sup> Congress (2000) Drug Addiction Treatment Act of 2000 [Full title: Waiver Authority for Physicians who Dispense or Prescribe Certain Narcotic Drugs for Maintenance Treatment or Detoxification Treatment]. Public Law 106-310, 106th Congress, Page 114 Stat. 1101.**

**Abstract:** Full text of the Drug Addiction Treatment Act of 2000, (DATA) which provides a waiver authority for physicians who dispense or prescribe certain narcotic drugs for maintenance treatment or detoxification treatment.

**URL:** <http://buprenorphine.samhsa.gov/fulllaw.html>

**Pub. Type:** US federal law ; web document.

**ATTC Buprenorphine Topics:** Legal/regulatory issues ; Treatment protocols/physician guidelines

364. **Uchtenhagen A. (2003) Substitution management in opioid dependence. Journal of Neural Transmission Supplementum. 2003;(66):33-60.**

**Author Address:** Addiction Research Institute, Zurich, Switzerland.  
uchtenhagen@isf.unizh.ch

**Abstract:** Substitution treatment (replacement therapy) is the most widespread and the most frequently researched therapeutic approach to heroin dependence. At present, the "gold standard" is methadone maintenance, but the use of other agonists and of combined compounds with antagonists are increasingly used, especially Buprenorphine. This paper reviews the main findings from research and their consequences for best practice rules. The evolution and organisation of substitution treatment in Europe is described, indicating a major discrepancy in administrative regulations. Emerging trends are also mentioned, as well as the merits and limitations that mark the place of substitution treatment in a comprehensive therapeutic network for opioid dependence.

**ISSN:** 0303-6995.

**Pub Type:** Review article.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness ; Treatment protocols/physician guidelines

365. **Uehlinger C ; Deglon J ; Livoti S ; Petitjean S ; Waldvogel D ; Ladewig D. (1998) Comparison of buprenorphine and methadone in treatment of opioid dependence. Eur Addict Res 1998;4(Suppl.1):13-18.**

**Author Address:** Psychosocial Centre of Fribourg, Fribourg, Switzerland.

**Abstract:** A three-centre, randomised, double-blind study was designed to compare the efficacy and safety of buprenorphine and methadone. This was the first European study to compare these agents and was based on a previous trial performed in the US. Opioid-dependent subjects were randomised to receive either sublingual buprenorphine or oral methadone daily. Both objective and subjective measures of efficacy were monitored weekly, and safety parameters were regularly monitored over the entire six-week study. Urinalysis showed that the two treatments were similar with a slight increase in opioid-negative urines noted in both groups. The retention rate in the buprenorphine group was lower than in the methadone group, although it has been suggested that the buprenorphine dose may have been too low for some patients. None of the side effects noted were considered serious and all were attributable to chronic opioid dependence. Experience of two years substitution treatment in Fribourg suggests that initial induction onto buprenorphine allows for patients to be subgrouped before being given the most appropriate maintenance agent. Further investigation is required into the different dose-related effects of buprenorphine seen in particular subsets of addicts.

**Pub. Type:** journal article.

**Descriptors:** Clinical Trial ; Multicenter Study; Randomized Controlled Trial; Adult; Buprenorphine/therapeutic use\*; Comparative Study; Double-Blind Method; Female;Human; Male; Narcotics/therapeutic use\*; Opioid-Related

Disorders/rehabilitation\*; Switzerland.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

366. **Umbricht A ; Hoover D ; Tucker M ; Leslie J ; Chaisson R ; Preston K. (2003) Opioid detoxification with buprenorphine, clonidine, or methadone in hospitalized heroin-dependent patients with HIV infection. Drug Alcohol Depend 2003 Apr 1;69(3):263-72.**

**Author Address:** National Institute on Drug Abuse Intramural Research Program, 5500 Nathan Shock Drive, 21224, Baltimore, MD, USA

**Abstract:** With the growing role of intravenous drug use in the transmission of HIV infection, HIV-infected patients frequently present with comorbid opioid dependence. Yet, few empirical evaluations of the efficacy and consequences of opioid detoxification medications in medically ill HIV-infected patients have been reported. In a randomized, double-blind clinical trial, we evaluated the impact of three medications on the signs and symptoms of withdrawal and on the pain severity in heroin-dependent HIV-infected patients (N=55) hospitalized for medical reasons on an inpatient AIDS service. Patients received a 3-day pharmacologic taper with intramuscular buprenorphine (n=21), oral clonidine (n=16), or oral methadone (n=18), followed by a clonidine transdermal patch on the fourth day. Observed and self-reported measures of opioid withdrawal and pain were taken 1-3 times daily for up to 4 days. Opiate administration used as medically indicated for pain was also recorded. Observer- and subject-rated opiate withdrawal scores decreased significantly following the first dose of medication and overall during treatment. Among all 55 subjects, self-reported and observer-reported pain decreased after treatment (on average observer-rated opioid withdrawal scale (OOWS) scores declined 5.6 units and short opioid withdrawal scale (SOWS) declined 4.8 units,  $P < 0.001$ , for both) with no indication of increased pain during medication taper. There were no significant differences of pain decline and other measures of withdrawal between the three treatment groups. During the intervention period, supplemental opiates were administered as medically indicated for pain to 45% of the patients; only 34% of men versus 62% of women received morphine ( $P < 0.05$ ). These findings suggest buprenorphine, clonidine, and methadone regimens each decrease opioid withdrawal in medically ill HIV-infected patients.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pain management ; Pharmacotherapy for opiate dependence

367. **Umbricht A ; Montoya I ; Hoover D ; Demuth K ; Chiang C ; Preston K. (1999) Naltrexone shortened opioid detoxification with buprenorphine. Drug Alcohol Depend 1999 Oct 1;56(3):181-90.**

**Author Address:** NIDA Intramural Research Program, Addiction Research Center, Baltimore, MD, USA. aumbri@intra.nida.nih.gov

**Abstract:** This double-blind, randomized, placebo-controlled clinical trial evaluated the impact on withdrawal symptoms of (i) combining naltrexone with a 4-day buprenorphine taper for short opioid detoxification (NB Group), compared to (ii) using a 4-day buprenorphine taper alone, followed by naltrexone on day 8 (PB Group). Sublingual buprenorphine was administered on days 1-4 (26 mg total). For the NB Group (n = 32) escalating doses of oral naltrexone were given on days 2-8 (placebo day 1). For the PB Group (n = 28) placebo was given on days 1-7 and naltrexone on day 8. Main outcome measures were Observed Opioid Withdrawal scores (OOW, 0-30) and use of medications to treat opioid withdrawal. Of 32 patients in the NB group, 59% experienced clinically relevant withdrawal (defined as OOW > or = 5) on day 2, but, after day 5, none experienced withdrawal. In the PB group, the number of patients experiencing withdrawal increased over time. The first naltrexone dose induced comparable withdrawal in both groups: peak OOW scores were (mean +/- SD) 5.2 +/- 3.3 on day 2 for the NB group, and 4.0 +/- 3.9 on day 8 for the PB group (NS), though, on day 2, 7 patients dropped out in the NB group and none in the PB group, while only one patient dropped out in the PB group on day 8. Throughout the 8-day study, patients in both groups received similar amount of adjunct medication: 0.64 +/- 0.07 mg (NB group) of clonidine vs 0.73 +/- 0.15 mg (PB group; NS). Only 25% of patients required use of sedatives (up to 20 mg diazepam). Starting naltrexone on day 2 appeared to abolish withdrawal symptoms after day 5 and, thus, to shorten the duration of withdrawal symptoms. Peak withdrawal symptoms after naltrexone were of moderate intensity, suggesting that naltrexone combined with buprenorphine is an acceptable and safe treatment for shortened opioid detoxification and induction of naltrexone maintenance.

**ISSN:** 0376-8716.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Analgesics/therapeutic use ; Area Under Curve ; Buprenorphine/\*therapeutic use ; Clonidine/therapeutic use ; Double-Blind Method ; Drug Interactions ; Drug Therapy, Combination ; Female ; Heroin/\*adverse effects ; Heroin Dependence/\*rehabilitation ; Human ; Male ; Naltrexone/\*therapeutic use ; Narcotic Antagonists/\*therapeutic use ; Substance Withdrawal Syndrome/\*drug therapy/physiopathology ; Support, U.S. Gov't, P.H.S.

**ATTC Buprenorphine Topics:** Combined treatment with other therapeutic medications ; Dosing/administration ; Pharmacotherapy for opiate dependence

368. **Valenciano M ; Emmanuelli J ; Lert F. (2001) Unsafe injecting practices among attendees of syringe exchange programmes in France. *Addiction* 2001 Apr;96(4):597-606.**

**Author Address:** Institut de Veille Sanitaire, St-Maurice, France.

**Abstract:** AIMS: To describe syringe exchange programme attendees and their injection practices. DESIGN: Cross-sectional study (one week in 1998). Data were collected through a standardized questionnaire. SETTING: 60/74 syringe exchange programmes (SEPs) in France. PARTICIPANTS: Clients requesting syringes in 60 SEPs. MEASUREMENTS: Self-reports of drug use, injecting

behaviour, sexual behaviour, serological status (HIV, HBV, HCV). Prevalence of unsafe injecting practices in the previous month such as: syringe sharing; and sharing other injection paraphernalia. FINDINGS: 1004 questionnaires were collected (response rate: 50%). The mean age of respondents was 30 years, and 70% were males. Among individuals tested, HIV reported prevalence was 19.2%, HCV 58.4% and HBV 20.8%. The mean duration of drug use was 11 years. Eighty-five percent were polydrug users and buprenorphine high-dosage was the substance most used (73%). In the previous month, 45% of the participants had re-used a syringe, 93% injected at least daily (mean 3.6 injections per day), 18% shared a syringe and 71% shared injection paraphernalia. In multivariate analyses, unsafe injecting practices were associated with heroin and cocaine use and with living in a couple. The cluster analysis identified five categories of IDUs: users of buprenorphine-HD (45% of the responders), morphine-sulphate (17%), benzodiazepines and other legal drugs (13%), methadone associated with other legal drugs (13%) and crack-cocaine (13%). The buprenorphine-HD group had better social status and safer injection practices. CONCLUSIONS: In France, despite an increase in the accessibility to syringes and substitution treatments, unsafe injecting practices persist among SEP attenders. Interventions should stress the importance of using sterile material for each injection, even with a steady sex partner.

**ISSN:** 0965-2140.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Cross-Sectional Studies ; Female ; France/epidemiology ; HIV Infections/\*epidemiology ; Human ; Male ; Needle Sharing/\*adverse effects ; \*Needle-Exchange Programs ; Questionnaires ; Risk Factors ; \*Risk-Taking ; Substance Abuse, Intravenous/\*epidemiology.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; History, use and effectiveness in other countries ; Prevalence of use for opiate dependence

369. **Vastag B. (2003) In-office opiate treatment "not a panacea": physicians slow to embrace therapeutic option. *JAMA* 2003 Aug 13;290(6):731-5.**

**Abstract:** A drug trumpeted as a major advance in opiate addiction treatment is garnering a tepid response from physicians, despite its status as the first such treatment available outside licensed drug treatment clinics. Bureaucratic hurdles, lack of clinical guidelines, and unfamiliarity with addiction have all hampered physician adoption of the drug, buprenorphine. While less strictly regulated than methadone, buprenorphine can be prescribed only by physicians who complete an eight-hour course and register with the Department of Health and Human Services and the Drug Enforcement Agency (DEA). But even after receiving a special DEA number, individual physicians and physician group practices-no matter how large-are limited by law to 30 buprenorphine patients, a figure several people interviewed for this article called absurd. "That [limit] is going to have to change before there's widespread use," said Michael G. Hayes, MD, director of the Center for Addiction Medicine, part of the University of Maryland Medical System, Baltimore.

ISSN: 1538-3598.

**Pub Type:** News.

**Descriptors:** Buprenorphine/\*therapeutic use ; \*Drug and Narcotic Control ; France ; Human ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/\*drug therapy ; United States.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Legal/regulatory issues ; Treatment protocols/physician guidelines

- 370. Vidal-Trecan G ; Varescon I ; Nabet N ; Boissonnas A. (2003) Intravenous use of prescribed sublingual buprenorphine tablets by drug users receiving maintenance therapy in France. Drug Alcohol Depend 2003 Mar 1;69(2):175-81.**

**Author Address:** Departement de Sante Publique and service de Sante publique, AP-HP, CHU Cochin-Port Royal, Universite Rene Descartes, Paris, France. genaelle.vidal-trecan@cochin.univ-paris5.fr

**Abstract:** BACKGROUND: In 1996, sublingual buprenorphine was authorized for prescription in France for maintenance therapy (MT). MT should facilitate the rehabilitation of opioid-dependent drug users and reduce the risks associated with injection. However, misuse and side effects have been reported. OBJECTIVES: To assess the frequency of buprenorphine injection in 404 subjects on buprenorphine MT and to determine the factors associated with the injection of buprenorphine. METHODS: A cross-sectional survey was used to collect data from subjects on buprenorphine MT seeking treatment from health care networks, specialized structures, a prison and a hostel in three different regions of France (1998-1999). Information was collected by trained interviewers using a structured questionnaire. RESULTS: About half (46.5%) of the subjects on MT (188/404) had ever injected buprenorphine; 67.2% of this subgroup had since used both injected and sublingual buprenorphine. Variables associated with buprenorphine injection were having injected a substance other than buprenorphine (odds ratio (OR): 13.18; 95% CI: 5.36-32.42), cannabis use (OR: 2.34; 95% CI: 1.51-3.63) and having a source of income other than a salary (OR: 1.58; 95% CI: 1.02-2.45) and heroin use (OR: 0.23; 95% CI: 0.09-0.61). CONCLUSIONS: To decrease buprenorphine injection, prescribers of buprenorphine should participate in networks with specialized centers, and social and professional rehabilitation programs should be implemented for subjects on buprenorphine MT.

ISSN: 0376-8716.

**Pub Type:** Journal Article.

**Descriptors:** Administration, Sublingual ; Adolescent ; Adult ;

\*Buprenorphine/administration & dosage/therapeutic use ; Comparative Study ; Cross-Sectional Studies ; Data Collection ; Female ; France/epidemiology ; Human ; Male ; \*Narcotics/administration & dosage/therapeutic use ; Opioid-Related Disorders/epidemiology/\*rehabilitation ; Substance Abuse, Intravenous/epidemiology/\*rehabilitation ; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Dosing/administration ; History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence

- 371. Vignau J. (1998) Preliminary assessment of a 10-day rapid detoxification programme using high dosage buprenorphine. Eur Addict Res 1998;4(Suppl.1):29-31.**

**Author Address:** Centre Hospitalier et Universitaire, Lille, France.

jvignau@nordnet.fr

**Abstract:** The original French therapeutic strategy for the treatment of opioid addiction was a rapid detoxification occasionally accompanied by treatment for withdrawal symptoms. In 1995, substitution therapy using opioids was introduced with the aim of maintenance, utilising methadone and the partial agonist buprenorphine, introduced in 1996. As well as being a maintenance agent, buprenorphine has been prescribed for rapid detoxification due to its reduced tendency to cause any withdrawal effects and its ability to block the effects of other opioids. This trial was initiated to measure the efficacy of buprenorphine in rapid detoxification and to assess whether additional medication would be required. Participants in this open study had requested rapid detoxification and were referred to the addiction clinic as inpatients. Patients were assessed by the clinician and during counselling sessions, and an initial dose was agreed upon. This dose was then gradually decreased over ten days in a flexible dosing schedule, with concurrent toxicological urinalysis to ensure no illicit drug use. During the trial, 25% of patients transferred to a maintenance programme and 58% remained in the study. The large transfer of patients to maintenance programmes may indicate that many people requesting rapid detoxification are actually asking for a more generalised form of assistance. No opioid-positive urines were noted after the fourth day in any patients, and the study indicates that buprenorphine should prove to be a useful detoxification agent, particularly in less hardened addicts. Step-down buprenorphine detoxification minimises withdrawal symptoms and, therefore, reduces the need for concurrent medication

**Pub. Type:** journal article.

**Descriptors:** Clinical Trial ; Adolescent; Adult; Buprenorphine/therapeutic use\*; Dose-Response Relationship, Drug; Female; Human; Male; Metabolic Detoxication, Drug; Narcotics/pharmacokinetics\*; Narcotics/therapeutic use\*; Substance-Related Disorders/diagnosis\*; Substance-Related Disorders/rehabilitation\*; Time Factors; Treatment Outcome;.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment outcomes/effectiveness ; Treatment protocols/physician guidelines

- 372. Vignau J ; Duhamel A ; Catteau J ; Legal G ; Pho A ; Grailles I ; Beauvillain J ; Petit P ; Beauvillain P ; Parquet P. (2001) Practice-based buprenorphine maintenance treatment (BMT): how do French healthcare providers manage the opiate-addicted patients? J Subst Abuse Treat 2001 Oct;21(3):135-44.**

**Author Address:** University Hospital, Lille, France. jvignau@nordnet.fr

**Abstract:** France was the first country to promote the extensive use of buprenorphine for the treatment of drug-addicted subjects through the primary care system. To assess both professional commitment and patients' characteristics, all the physicians and pharmacists of a French area having prescribed/dispensed buprenorphine from 2/12/96 (the official release date) to 1/31/98 were identified from data files of the Health Insurance and then interviewed. During the first 61 weeks of buprenorphine maintenance treatment (BMT), 27.5% of physicians and 51.2% of pharmacists of that area were involved; 142 patient records were documented. Features of the clinical routines spontaneously implemented for practice-based BMT were: a high level of on-site supervised dispensation by the pharmacist (71% at treatment induction and 23% thereafter); the absence of objective measurement of illicit drug use; and a low buprenorphine dosage. These features are consistent with the lack of physicians' experience and training, and also the relatively good status of the population treated (no HIV-positives, heroin use duration averaging 4.2 +/- 3.1 years, and 81.7% with stable accommodations). Despite liberal regulations guiding BMT, a negligible proportion of cases had a "nomadic" attitude (multiple buprenorphine prescribers/deliverers). The treatment outcomes (no deaths, three drug overdoses, improvement in occupational status) are encouraging. **CONCLUSION:** Practice-based BMT appears to be a safe and acceptable response to moderate heroin addiction, but further training of the professionals involved and longitudinal investigations of individual outcomes are needed.

**ISSN:** 0740-5472.

**Pub Type:** Journal Article.

**Descriptors:** Buprenorphine/\*therapeutic use ; Drug Utilization Review ; Family Practice/legislation & jurisprudence/\*statistics & numerical data ; Female ; France ; Heroin Dependence/\*rehabilitation ; Human ; Narcotic Antagonists/\*therapeutic use ; National Health Programs/legislation & jurisprudence ; Outcome Assessment (Health Care) ; Pharmacies/legislation & jurisprudence/\*statistics & numerical data ; Questionnaires ; Retrospective Studies.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Legal/regulatory issues ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

**373. Vignau J ; E B. (1998) Differences between general practitioner- and addiction centre-prescribed buprenorphine substitution therapy in France. Eur Addict Res 1998;4(Suppl.1):24-28.**

**Author Address:** Centre Hospitalier et Universitaire, Lille, France.

[jvignau@nordnet.fr](mailto:jvignau@nordnet.fr)

**Abstract:** The treatment of heroin addiction in France relies on either general practitioners (GP) or specialist Addiction Centres (ACs). In general, the GPs offer a more flexible approach regarding frequency of consultations, urine tests and dosing regimen while the AC approach is more structured. A cohort study was undertaken to compare the treatment strategies of buprenorphine therapy between these medical environments. To determine the efficacy of each

treatment, a number of outcomes were measured including the Addiction Severity Index, retention rates at 90 and 180 days, the average dose prescribed, quality of life assessment, body weight and two self-reported measures: treatment perception and predictive total duration. A total of 69 patients were enrolled; 32 treated by GPs and 37 treated in ACs. Significant differences, including average age, addiction severity and employment status were apparent between each group. Nevertheless, significant improvements in the social and medical status were observed in all patients after 3 months, continuing after 6 months in both groups. Treatment retention was good in both groups with 65% of the total sample remaining after 180 days. The usually more flexible GP approach was more rigid in this study, resulting in an equally positive treatment outcome as seen in the ACs. The study highlights the effectiveness of buprenorphine in addicts with different social and medical backgrounds, regardless of the therapeutic approach.

**Pub. Type:** journal article.

**Descriptors:** Clinical Trial ; Adult; Buprenorphine/therapeutic use\*; Comparative Study; Family Practice\*; Follow-Up Studies; France; Human; Methadone/therapeutic use\*;Narcotics/therapeutic use\*; Prospective Studies; Substance Abuse Treatment Centers\*; Substance-Related Disorders/rehabilitation\*.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment outcomes/effectiveness

**374. Walsh S ; Eissenberg T. (2003) The clinical pharmacology of buprenorphine: Extrapolating from the laboratory to the clinic. Drug Alcohol Depend 2003 May 21;70(2 Suppl):S13-27.**

**Author Address:** Behavioral Pharmacology Research Unit, Department of Psychiatry and Behavioral Sciences, John Hopkins University, 5510 Nathan Shock Drive, 21224, Baltimore, MD, USA

**Abstract:** This paper will review clinical pharmacology studies on buprenorphine, a mixed opioid agonist-antagonist currently approved as a treatment for opioid dependence. The focus is on studies characterizing buprenorphine's pharmacodynamic actions, including its safety, abuse liability, withdrawal suppression and withdrawal precipitation capacity, physical dependence potential, cross-tolerance and duration of action as well as a review of the pharmacological profile of buprenorphine/naloxone combinations. The findings from these clinical pharmacology studies are synthesized and presented in a framework designed to (1) inform clinicians about the advantages and disadvantages of buprenorphine as an opioid maintenance agent, and (2) provide information about dosing procedures that may optimize the use of buprenorphine in the clinic.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article; Review article.

**ATTC Buprenorphine Topics:** Addiction potential/misuse of buprenorphine; Combined treatment with other therapeutic medications ; Dosing/administration;

Pharmacology ; Pharmacotherapy for opiate dependence ; Treatment protocols/physician guidelines

375. **Welsh C ; Cargiulo T. (2000) Response to "detoxification with buprenorphine of a pregnant heroin addict". Am J Addict 2000 Fall;9(4):340-1.**

**Abstract:** The Winter 2000 edition of The American Journal of Addictions contained a letter entitled "Detoxification with buprenorphine of a pregnant heroin addict" that described the use of buprenorphine and clonidine to detoxify a heroin-dependent woman who was 28-weeks pregnant and had been admitted to an obstetrical service for fetal monitoring. Although this certainly makes intuitive and clinical sense, in the highly litigious climate of American medicine, we feel that there are some issues that must be mentioned concerning this.

**ISSN:** 1055-0496.

**Pub Type:** Comment ; Letter.

**Descriptors:** Buprenorphine/adverse effects/\*therapeutic use ; Drug Approval ; Female ; Heroin Dependence/\*rehabilitation ; Human ; Infant, Newborn ; Neonatal Abstinence Syndrome/prevention & control ; Pregnancy; Pregnancy Complications/\*rehabilitation ; United States ; United States Food and Drug Administration.

**ATTC Buprenorphine Topics:** Pharmacology ; Pharmacotherapy for opiate dependence ; Legal/regulatory issues ; Special populations

376. **Welsh C ; Suman M ; Cohen A ; Broyles L ; Bennett M ; Weintraub E. (2002) The use of intravenous buprenorphine for the treatment of opioid withdrawal in medically ill hospitalized patients. Am J Addict 2002 Spring;11(2):135-40.**

**Author Address:** Department of Psychiatry, Division of Alcohol and Drug Abuse, University of Maryland School of Medicine, Baltimore 21201, USA. cwelsh@psych.umaryland.edu

**Abstract:** The aim of this study was to assess the safety of buprenorphine administered intravenously for the treatment of opioid withdrawal in medically ill hospitalized patients. Data regarding demographic information, number of doses of buprenorphine, and measures of buprenorphine's effects were collected via chart reviews for 30 heroin-dependent patients who received buprenorphine intravenously during their hospitalization for an acute medical problem. No respiratory depression was observed, and no patients reported feeling "high." All patients reported that buprenorphine decreased withdrawal symptoms. Thus, intravenous administration of buprenorphine appears to be safe for the treatment of opioid withdrawal.

**ISSN:** 1055-0496.

**Pub Type:** Clinical Trial ; Journal Article.

**Descriptors:** Acute Disease ; Adult ; Buprenorphine/\*therapeutic use ; Female; Heroin/adverse effects; Heroin Dependence/complications/\*drug therapy ; Human ; Injections, Intravenous ; Male ; Middle Age ; Narcotic

Antagonists/\*therapeutic use ; Substance Withdrawal Syndrome/drug therapy/psychology.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

377. **Wesson D. (2002) Opiate receptor pharmacology. Presentation at a meeting of the California Society of Addiction Medicine, Newport Beach, CA, October 9, 2002.**

**Abstract:** PowerPoint slide presentation about the pharmacology of opiate receptors; the difference between agonists, partial agonists, and antagonists; and the pharmacology of buprenorphine.

**URL:** <http://www.csam-asam.org/Bup%20Clinical%20Info/powerpoint%20presentations/OpiatePharm.ppt>

**Pub. Type:** PowerPoint slides.

**ATTC Buprenorphine Topics:** Pharmacology ; Addiction potential/misuse of buprenorphine

378. **Wesson D. (2002) Therapeutic discontinuation of buprenorphine. Presentation at a meeting of the California Society of Addiction Medicine, Newport Beach, CA, October 9, 2002.**

**Abstract:** This PowerPoint slide presentation is about the discontinuation of buprenorphine treatment for opiate dependence. It primarily offers suggestions to physicians on how best to end treatment for patients (both voluntary discontinuation and involuntary), including advice on how best to phrase the need for discontinuation to patients so as to avoid alarm or stress. It is not recommended that both pharmacological treatment and psychosocial treatment be stopped at the same time. Information on tapering the dosage of buprenorphine is also provided.

**URL:** <http://www.csam-asam.org/Bup%20Clinical%20Info/powerpoint%20presentations/Discontinuation.ppt>

**Pub. Type:** PowerPoint slides.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Psychosocial treatment aspects ; Treatment protocols/physician guidelines

379. **Wesson D. (2003) Prescribing buprenorphine for the treatment of opioid addiction. In: Graham, Allen W ; Schultz, Terry K ; Mayo-Smith, Michael F; Ries, Richard K ; Wilford, Bonnie B. Principles of Addiction Medicine / 3rd edition. Chevy Chase, MD : American Society of Addiction Medicine, Inc., 2003, pp. 749-750.**

**Abstract:** Brief overview of the prescribing qualifications and cautions for buprenorphine, as well as the use of buprenorphine in pain management.

**ISSN:** 1880425084.

**Pub Type:** book chapter.

**Notes:** ADAI Library: RC 644 M455 2003 [REF HAND]

**ATTC Buprenorphine Topics:** Dosing/administration ; Pain management

380. **Wesson D ; Ling W. (2003) The Clinical Opiate Withdrawal Scale (COWS). J Psychoactive Drugs 2003 Apr-Jun;35(2):253-9.**

**Author Address:** CNS Medications Development, Oakland, California, USA. dwesson@mindspring.com

**Abstract:** The clinical opiate withdrawal scale (COWS) is a clinician-administered, pen and paper instrument that rates eleven common opiate withdrawal signs or symptoms. It is meant to be helpful during the initial evaluation. It should help the practitioner decide when it is safe to give the induction dose of buprenorphine. The summed score of the eleven items can be used to assess a patient's level of opiate withdrawal and to make inferences about their level of physical dependence on opioids. With increasing use of opioids for treatment of pain and the availability of sublingual buprenorphine in the United States for treatment of opioid dependence, clinical assessment of opiate withdrawal intensity has received renewed interest. Buprenorphine, a partial opiate agonist at the mu receptor, can precipitate opiate withdrawal in patients with a high level of opioid dependence who are not experiencing opioid withdrawal. Since development of the first opiate withdrawal scale in the mid-1930s, many different opioid withdrawal scales have been used in clinical and research settings. This article reviews the history of opiate withdrawal scales and the context of their initial use. A template version of the COWS that can be copied and used clinically is appended. PDF formatted versions of the COWS are also available from the websites of the American Society of Addiction Medicine, the California Society of Addiction Medicine, the UCLA Integrated Substance Abuse Programs, and AlcoholMD.com.

**ISSN:** 0279-1072.

**Pub Type:** Journal Article ; Review ; Review, Tutorial.

**Descriptors:** Human ; Mental Status Schedule/statistics & numerical data ; Opioid-Related Disorders/\*diagnosis/psychology ; Substance Withdrawal Syndrome/\*diagnosis/psychology.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

381. **West S ; O'Neal K ; Graham C. (2000) A meta-analysis comparing the effectiveness of buprenorphine and methadone. J Subst Abuse 2000;12(4):405-14.**

**Author Address:** Texas Tech University, Lubbock, TX, USA.

**Abstract:** Increases in the use of illicit opiates have refocused attention on these drugs. One outgrowth of this attention has been the increased consideration of pharmacotherapies to provide alternatives to methadone maintenance. Buprenorphine is one new tool used in the attenuation of illicit opiate use. Like methadone, buprenorphine produces cross-tolerance to other opiates. However, it may have advantages over methadone including a longer duration, limited withdrawal syndrome, and increased safety. Buprenorphine's

ability to serve as a replacement drug for illicit opiate use is well documented, and efforts have recently been made to compare the drug with methadone. The purpose of this study was to provide a meta-analysis of all available research reporting a controlled comparison of buprenorphine and methadone. This analysis provided a rating of the comparative efficacy of each drug, thus giving clinicians an additional guide when selecting an appropriate course of treatment. Findings suggest a relative equality in the efficacy of buprenorphine and methadone, although patients receiving methadone were less likely to test positive for illicit opiate use. Past experience with methadone maintenance acted as a moderating variable, however, such that those receiving buprenorphine were more likely to stay drug-free in studies that included patients with prior methadone experience.

**ISSN:** 0899-3289.

**Pub Type:** Journal Article ; Meta-Analysis.

**Descriptors:** Buprenorphine/adverse effects/\*therapeutic use ; Comparative Study ; Female ; Human ; Male ; Methadone/adverse effects/\*therapeutic use ; Opioid-Related Disorders/\*rehabilitation ; Substance Withdrawal Syndrome/etiology/prevention & control ; Treatment Outcome.

**ATTC Buprenorphine Topics:** Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

382. **White R ; Alcorn R ; Feinmann C. (2001) Two methods of community detoxification from opiates: an open-label comparison of lofexidine and buprenorphine. Drug Alcohol Depend 2001 Dec 1;65(1):77-83.**

**Author Address:** St Lukes Woodside Hospital, Woodside Avenue, Muswell Hill, N10 3HU, London, UK. rupert.white@virgin.net

**Abstract:** There is currently no consensus on the best approach to the management of opiate detoxification. In the current open-label study, 69 opiate-dependent individuals requesting outpatient detoxification were allocated to two different medication regimes: lofexidine and buprenorphine. Allocation was dependent on the timing of their presentation. Lofexidine is a structural analogue of clonidine, and used widely in the UK. Buprenorphine is a partial opiate agonist with unusual pharmacological properties. Outcomes were better for the buprenorphine-receiving group (n=38). Clients receiving buprenorphine had a less severe withdrawal syndrome, and were more likely to complete their detoxification. In addition, for the buprenorphine-receiving group it was found that the withdrawal syndrome was least in those prescribed an initial dose of 4 mg. The findings and their implications are discussed. The design of the study precludes definitive conclusions regarding relative efficacy.

**ISSN:** 0376-8716.

**Pub Type:** Journal Article.

**Descriptors:** Adult ; Buprenorphine/\*therapeutic use ; Chi-Square Distribution ; Clonidine/\*analogs & derivatives/\*therapeutic use ; Community Health Services/\*methods ; Comparative Study ; Female ; Human ; Logistic Models ; Male ; Narcotic Antagonists/\*therapeutic use ; Opioid-Related Disorders/\*drug therapy ; Outcome Assessment (Health Care) ; Prospective Studies ; Statistics, Nonparametric ; Substance Withdrawal Syndrome/\*drug therapy ; Support,

Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence ; Treatment outcomes/effectiveness

383. **Wilkins D ; Rollins D ; Valdez A ; Mizuno A ; Krueger G ; Cone E. (1999) A retrospective study of buprenorphine and norbuprenorphine in human hair after multiple doses. J Anal Toxicol 1999 Oct;23(6):409-15.**

**Author Address:** Center for Human Toxicology, Department of Pharmacology and Toxicology, University of Utah, Salt Lake City 84112, USA.

**Abstract:** The analysis of hair has been proposed as a tool for monitoring drug-treatment compliance. This study was performed to determine if buprenorphine (BPR) and norbuprenorphine (NBPR) could be detected in human hair after controlled administration of drug and to determine if segmental analysis of hair was an accurate record of the dosing history. Subjects with dark hair (six males, six females) received 8 mg sublingual BPR for a maximum of 180 days. Single hair collections were made once after BPR treatment and stored at -20 degrees C until analysis. Hair was aligned scalp-end to tip and then segmented in 3-cm sections. For this study, it was assumed that the mean hair growth rate was 1.0 cm/month. Deuterated internal standard was added to hair segments (2-20 mg of hair) and digested overnight at room temperature with 1 N NaOH. Specimens were extracted with a liquid-liquid procedure and analyzed by liquid chromatography-tandem mass spectrometry. The limits of quantitation for BPR and NBPR were 3 pg/mg and 5 pg/mg, respectively, for 20 mg of hair. BPR and NBPR concentrations were highest for all subjects in hair segments estimated to correspond to the subject's period of drug treatment. With one exception, NBPR was present in higher concentrations in hair than was the parent compound. BPR concentrations in hair segments ranged from 3.1 pg/mg to 123.8 pg/mg. NBPR concentrations ranged from 4.8 pg/mg to 1517.8 pg/mg. In one subject, BPR and NBPR were not detected in any hair segment. In some subjects, BPR and NBPR were detected in hair segments that did not correspond to the period of drug treatment, suggesting that drug movement may have occurred by diffusion in sweat and other mechanisms. The data from this study also indicate that there is a high degree of intersubject variability in measured concentration of BPR and NBPR in hair segments, even when subjects receive the same dose for an equivalent number of treatment days. Future prospective studies involving controlled drug administration will be necessary to evaluate whether hair can serve as an accurate historical record of variations in the pattern of drug use.

**ISSN:** 0146-4760.

**Pub Type:** Journal Article.

**Descriptors:** Administration, Sublingual ; Adult ; Analgesics, Opioid/administration & dosage/\*analysis/metabolism ; Buprenorphine/administration & dosage/\*analogs & derivatives/\*analysis/metabolism ; Female ; Hair/\*chemistry ; Human ; Male; Mass Fragmentography ; Pharmacogenetics ; Retrospective Studies ; Support, U.S. Gov't, P.H.S. ; Time Factors.

**ATTC Buprenorphine Topics:** Basic laboratory research ; Dosing/administration ; Pharmacology

384. **Williams H ; Remedios A ; Oyefeso A ; Bennett J. (2002) Buprenorphine detoxification treatment for heroin dependence: A preliminary experience in an outpatient setting. Irish Journal of Psychological Medicine 2002 Sep;19(3):80-83.**

**Author Address:** Williams, Hugh. Substance Misuse Service, South Downs Health NHS Trust, Brighton England BN1 4SF.

**Abstract:** Evaluated buprenorphine as a detoxification agent for heroin dependence in an outpatient setting. The authors specifically sought to establish the rate of completion of detoxification and retention in treatment, the duration of successful detoxification and dose requirements. The study was an open prospective evaluation of routinely collected clinical data on the 1st 60 consecutive heroin dependent patients who underwent buprenorphine detoxification. A flexible dosing regime was adopted with the dose of buprenorphine being adjusted daily against the previous day's withdrawal symptoms. The majority of patients (67%) completed detoxification. The median duration of treatment for completers was 17 days (range 9-30 days) with 90% of detoxification episodes completed within 21 days. Patients were started on an initial median dose of 4 mg buprenorphine (range 2 mg-6 mg) and the median stabilization dose for the sample was 10 mg daily (range 6 mg-14 mg). The median final dosage of buprenorphine required by patients retained in treatment was 1.2 mg (range 0.4 mg-2 mg). Older patient age was a significant predictor of treatment completion. Based on the study findings the authors propose a standard 21-day fixed-dose detoxification schedule.

**ISSN:** 0790-9667 (Print).

**URL:** <http://www.ijpm.org>

**Pub. Type:** Journal article.

**Descriptors:** buprenorphine; heroin detoxification; outpatients ; \*Detoxification ; \*Heroin ; \*Heroin Addiction ; \*Narcotic Agonists ; \*Outpatients ; Drug Therapy ; Human. Male. Female. Outpatient. Adulthood (18 yrs & older) ; Empirical Study. Longitudinal Study. Prospective Study. Treatment Outcome Study.

**ATTC Buprenorphine Topics:** Dosing/administration ; Pharmacotherapy for opiate dependence

385. **Witter M. (2002) State Perspectives on Buprenorphine and Office-Based Treatment. Presentation to the State Systems Development Program Conference, Nov. 20-22, 2002, Washington DC.**

**Abstract:** This is a 14-slide conference presentation about the NASADAD Treatment Committee opinions and concerns about Buprenorphine. It was presented to the SSDP conference on "Closing the Treatment Gap / No Wrong Doors."

**Pub. Type:** PowerPoint Slides Notes: See also NASADAD Focus Group report on same matter.

**URL:**http://www.treatment.org/ssdpvi/handouts/friday/C3\_Melanie\_Whitter.ppt  
**ATTC Buprenorphine Topics:** Legal/regulatory issues

**386. World Health Organization. Expert Committee on Drug Dependence. (2001) Thirty-second report. World Health Organization Technical Report Series 903: i-v, 1-26.**

**Abstract:** This report presents the recommendations of a WHO Expert Committee responsible for reviewing information on dependence-producing drugs to assess the need for their international control. The first part of the report contains a general discussion of the new guidelines for the review of dependence-producing psychoactive substances and their implications for the scheduling of ephedrine and of the guidelines that were drafted to clarify the scope of control of stereoisomers. A summary follows of the Committee's evaluations of six substances (4-bromo-2,5-dimethoxyphenethylamine (2C-B), 4-methylthioamphetamine (4-MTA), gamma-hydroxybutyric acid (GHB), N-methyl-1-(3,4-methylenedioxyphenyl)-2-butanamine (MDBD), diazepam and zolpidem), four of which (2C-B, 4-MTA, GHB and zolpidem) were recommended for international control. The report also discusses the substances that were pre-reviewed by the Committee, five of which (amfepramone, amineptine, buprenorphine, dronabinol and tramadol) were recommended for critical review at a future meeting.  
**ISSN:** 0512-3054.

**Pub Type:** Technical Report; review; guideline.

**Descriptors:** Amphetamines/adverse effects/pharmacology ; Buprenorphine/adverse effects/pharmacology ; Carisoprodol/adverse effects/pharmacology ; Diazepam/adverse effects/pharmacology ; Dibenzocycloheptenes/adverse effects/pharmacology ; Diethylpropion/adverse effects/pharmacology ; \*Drug and Narcotic Control ; Guidelines ; Human ; Hydroxybutyrates/adverse effects/pharmacology ; Narcotics/\*adverse effects/classification/pharmacology ; Papaver/adverse effects ; Pentazocine/adverse effects/pharmacology ; Psychotropic Drugs/\*adverse effects/classification/pharmacology ; Pyridines/adverse effects/pharmacology ; Substance-Related Disorders/\*etiology/prevention & control ; Tetrahydrocannabinol/adverse effects/pharmacology ; Tramadol/adverse effects/pharmacology ; World Health Organization.

**ATTC Buprenorphine Topics:** Pharmacology

**387. World Health Organization. Expert Committee on Drug Dependence. (2003) World Health Organization Technical Report Series 915: i-v,1-26.**

**Abstract:** This report presents the recommendations of a WHO Expert Committee responsible for reviewing information on dependence-producing drugs to assess the need for their international control. The first part of the report contains a description of the procedure for the review of dependence-producing substances. This is followed by a critical review of five psychoactive substances (amfepramone, amineptine, buprenorphine, delta-9-tetrahydrocannabinol and tramadol). The report also discusses the substances

that were pre-reviewed by the Committee, four of which (ketamine, zopiclone, butorphanol and khat) were recommended for critical review at a future meeting. The final section discusses the problems of the terminology used in reporting abuse-related adverse drug reactions and describes how confusion affects the reporting of adverse effects using the example of the selective serotonin reuptake inhibitors.

**ISSN:** 0512-3054.

**Pub Type:** Review; guideline.

**Descriptors:** Advisory Committees ; Drug Evaluation ; \*Drug and Narcotic Control ; Human ; Practice Guidelines ; Product Surveillance, Postmarketing; Psychotropic Drugs/adverse effects/classification/ pharmacology/ \*therapeutic use ; Substance-Related Disorders/\*prevention & control ; \*World Health Organization.

**ATTC Buprenorphine Topics:** History, use and effectiveness in other countries ; Legal/regulatory issue; Treatment protocols/physician guidelines

**388. Wunsch M ; Stanard V ; Schnoll S. (2003) Treatment of pain in pregnancy. Clin J Pain 2003 May-Jun;19(3):148-55.**

**Author Address:** Department of Pediatrics, Edward Via Virginia College of Osteopathic Medicine, Blacksburg 24060, USA. mwunsch@evvcom.org

**Abstract:** BACKGROUND: The treatment of pain during pregnancy other than that of labor is a clinical issue that has not been addressed in a systematic manner. MATERIALS AND METHODS: To assess current knowledge, a review of the human and animal literatures was undertaken using MEDLINE. In addition, the dynamics of three pharmacological compartments, the mother, the placenta, and the fetus, and fate of drugs given in pregnancy, was reviewed. RESULTS: The literature review yielded little information except for a few case studies in which opiates, nonsteroidal anti-inflammatory drugs, antidepressants, mu agonists, and anticonvulsants were used in the treatment of pain in pregnancy. In contrast, there is extensive information in the addiction medicine literature concerning the use of opioids in recovering pregnant addicts. Methadone, buprenorphine, and morphine have been used to treat women seeking recovery from opioids, and neonatal outcomes have been closely monitored with no evidence of harm to the newborn. CONCLUSIONS: Experience in women seeking recovery from opioids and their newborns illustrates that opioids are an effective and safe pharmacological option for the treatment of pain during pregnancy. Controlled studies are needed to expand knowledge in this clinical area.

**ISSN:** 0749-8047.

**Pub Type:** Journal Article ; Review ; Review, Tutorial.

**Descriptors:** Analgesics, Opioid/\*therapeutic use ; Animal ; Female ; Human ; Narcotics/therapeutic use ; Opioid-Related Disorders/drug therapy/\*rehabilitation ; Pain/\*drug therapy/physiopathology ; Pregnancy ; Pregnancy Complications/\*drug therapy ; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** Pain management ; Pharmacotherapy for opiate dependence ; Special populations

389. Zubieta J ; Greenwald M ; Lombardi U ; Woods J ; Kilbourn M ; Jewett D ; Koeppe R ; Schuster C ; Johanson C. (2000) Buprenorphine-induced changes in mu-opioid receptor availability in male heroin-dependent volunteers: a preliminary study. *Neuropsychopharmacology* 2000 Sep;23(3):326-34.

**Author Address:** Neurosciences, University of Michigan, Ann Arbor 48104-1687, USA.

**Abstract:** A principle of opioid pharmacotherapy is that high medication doses should occupy fractionally more opioid receptors that mediate heroin effects. In this preliminary study we examined in vivo mu opioid receptor (muOR) binding in three healthy opioid-dependent volunteers during maintenance on 2 and 16 mg sublingual buprenorphine (BUP) liquid, and after detoxification (0 mg) under double-blind, placebo-controlled conditions, and once in matched controls. Binding measures were obtained with the muOR-selective radioligand [<sup>11</sup>C]carfentanil (CFN) and PET 4 hrs after BUP administration. BUP induced dose-dependent reductions in muOR availability, 36-50% at 2 mg and 79-95% at 16 mg relative to placebo. Heroin abusers also had greater muOR binding potential in the inferofrontal cortex and anterior cingulate regions during placebo, compared to matched controls. Further studies are warranted to examine the relationship of muOR availability with BUP therapeutic actions, and the clinical implications of increased muOR binding during withdrawal.

**ISSN:** 0893-133X.

**Pub Type:** Clinical Trial ; Journal Article ; Randomized Controlled Trial.

**Descriptors:** Adult ; Analgesics, Opioid/diagnostic use ; Brain/radionuclide imaging ; Brain Chemistry ; Buprenorphine/\*pharmacology ; Double-Blind Method ; Fentanyl/analogs & derivatives/diagnostic use ; Heroin Dependence/\*metabolism/radionuclide imaging ; Human ; Image Processing, Computer-Assisted ; Male ; Middle Age ; Narcotics/\*pharmacology ; Receptors, Opioid, mu/\*drug effects ; Support, U.S. Gov't, P.H.S. ; Tomography, Emission-Computed.

**ATTC Buprenorphine Topics:** Pharmacology ; Pharmacotherapy for opiate dependence

390. Zylberberg H ; Fontaine H ; Correas J ; Carnot F ; Brechot C ; Pol S. (2000) Dilated bile duct in patients receiving narcotic substitution: an early report. *J Clin Gastroenterol* 2000 Sep;31(2):159-61.

**Author Address:** Unite d'HepatoLOGIE, Hopital Necker, Paris, France.

**Abstract:** Narcotic substitution is now widely used. Morphine can induce a spasm of the sphincter of Oddi but dilation of bile duct has been reported only in an anecdotal case. In June 1995, we observed a first case of dilation of the common bile duct without organic obstacle in a hepatitis C virus (HCV)-infected patient who was under narcotic substitution, suggesting a causal relationship. We conducted a prospective study to evaluate the precise prevalence of bile duct abnormalities related to narcotic substitution in active intravenous drug or ex-intravenous drug users referred to our liver unit for histologic evaluation of HCV infection. We conducted a prospective study in a 30-month period of 334

HCV-infected patients, including 36 receiving narcotic substitution with methadone or buprenorphine. Biliary tract was analyzed by ultrasonography and by endoscopy ultrasound in cases of bile duct abnormalities. Of the 36 patients under narcotic substitution, 3 (8.3%) had asymptomatic dilated bile duct without organic obstacle--defined as a common bile duct > or =9 mm--compared to 1 of 298 (0.03%; p < 0.001) of those who did not receive substitution. Narcotic substitution may lead to bile duct dilation that does not require invasive diagnosis procedures.

**ISSN:** 0192-0790.

**Pub Type:** Journal Article; case report.

**Descriptors:** Adult ; Bile Duct Diseases/\*chemically induced/pathology/ultrasonography ; Bile Ducts/pathology ; Biopsy ; Buprenorphine/\*adverse effects ; Case Report ; Common Bile Duct/pathology ; Common Bile Duct Diseases/chemically induced/pathology/ultrasonography ; Dilatation, Pathologic ; Endoscopy ; Female ; HIV Seronegativity ; Hepatitis C/complications/diagnosis/pathology ; Human ; Liver/pathology ; Liver Function Tests ; Male ; Methadone/\*adverse effects ; Middle Age ; Narcotics/\*adverse effects ; Prospective Studies ; Substance Abuse, Intravenous/\*complications/\*rehabilitation ; Support, Non-U.S. Gov't.

**ATTC Buprenorphine Topics:** Pharmacology