

LEGISLATIVE DAY A HUGE SUCCESS

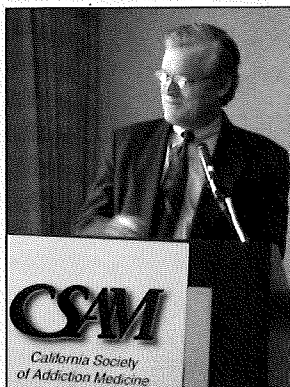
New Parity Bill (SB 101) Introduced in California Legislature

ON JANUARY 29th, speaking to a packed room at CSAM's first Annual Legislative Day, Senator Wesley Chesbro announced that earlier that morning he had introduced SB101, a new Substance Abuse Health Insurance Parity Bill and that he would lead the fight for this legislation in 2003.

Senator Chesbro's bill is an exact copy of SB599 introduced in the last year and drafted by Senator Chesbro with input from CSAM. SB599 passed the State Senate and Assembly Health Committee, but failed to make it out of the Assembly after governor Davis indicated that he would not sign the legislation. (See article *CSAM Public Policy Efforts Break New Ground* inside this issue.)

CSAM's Legislative Day was a huge success. Over 80 people participated in a half day educational workshop that featured presentations by lobbyist Jim Gonzalez (of Jim Gonzalez and Associates) and Bryce Docherty

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SENATOR
WESLEY CHESBRO
AT CSAM LEGISLATIVE
DAY ON JANUARY 29.

FDA Approves Buprenorphine

by Donald R. Wesson, M.D.

On October 8, 2002, the Food and Drug Administration (FDA) approved buprenorphine sublingual tablets Suboxone® and Subutex® for use in treatment of addiction.¹ The previous day, the Drug Enforcement Administration (DEA) issued its final ruling on the buprenorphine scheduling.² All formulations of buprenorphine approved for distribution in the U.S. – Buprenex®, Suboxone, and Subutex – will be schedule III *narcotics*. (As explained below, the class designation of *narcotic* has important regulatory and clinical ramifications independent of the schedule classification.) Reckitt Benckiser, the U.S. distributor for Subutex and Suboxone, has a toll-free help line (1-877-782-6966) to provide assistance with distribution to pharmacies and physician's offices. Additional information is available on their website, www.suboxone.com.

Suboxone will be hexagonal orange sublingual tablets available in two dosages: 2 mg of buprenorphine and 0.5 mg of naloxone, and 8 mg of buprenorphine and 2 mg of naloxone. Subutex will be oval white tablets containing either 2 or 8 mg of buprenorphine.³ All dosage forms will be distributed in bottles of 30 tablets.

Until recently, Schering-Plough seemed slated to be the distributor of Suboxone and Subutex in the U.S. Schering-Plough has marketed Subutex in France under a license from Reckitt Benckiser since its launch there in 1996. Since then, Subutex has been introduced into 24 countries.⁴ On October 31, 2002, however, Schering Plough issued a press release announcing an agreement under which Reckitt Benckiser plc will buy back U.S. marketing rights for Suboxone

and Subutex. The stated reason was for Schering-Plough to remain focused on its core U.S. therapeutic areas.⁵ The same day, Reckitt Benckiser announced that they were purchasing the rights in the U.S. but that Schering-Plough would retain the rights to distribute the two products internationally except for Japan, Taiwan, Korea, Australia and New Zealand. Reckitt Benckiser will market Subutex and Suboxone in the U.S.

Reckitt Benckiser plc is the world's largest household cleaning products company (excluding laundry detergent), and produces such products as Lysol, Spray 'n Wash, Woolite and Air Wick. With headquarters in England, Reckitt Benckiser's Healthcare division mainly produces over-the-counter medications such as Gaviscon and Senokot. Prescription medications are a legacy of Reckitt and Colman's research in the 1960's and 70's.⁶ Reckitt & Colman plc and Benckiser N.V. merged in 1999 to become Reckitt Benckiser plc.⁷ Reckitt Benckiser has manufactured and distributed Buprenex, an injectable formulation of buprenorphine for treatment of pain, in the U.S. since its introduction in the U.S. in the mid 80's.

DEA Scheduling

The "class" scheduling of all formulations of Suboxone and Subutex into a single schedule was contrary to the

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wishes of ASAM and CSAM. During the comment period on the DEA's proposed ruling, ASAM president, Larry Brown, submitted a letter to DEA pointing out the lower intravenous abuse potential of Suboxone and the desirability of a less restrictive scheduling for Suboxone to encourage physicians to prescribe Suboxone instead of Subutex. NIDA and Reckitt Benckiser had developed Suboxone specifically to reduce its intravenous abuse potential in opioid dependent patients. The DEA acknowledged the point, but concluded that "the combination product does not warrant lesser control than other buprenorphine products."

Buprenorphine, A Schedule III Narcotic

The Controlled Substances Act (CSA) defines five classes of drugs: narcotics, depressants, stimulants, hallucinogens, and anabolic steroids. Each class has distinguishing properties and drugs within a class often produce similar effects.⁸ Buprenorphine's "narcotic" classification brings it under prohibitions against prescribing narcotics for treatment of opioid dependence. The class and scheduling are independent dimensions. Diazepam, for example, is a schedule III medication, but is not classified as a narcotic.

Buprenorphine and the Three-Day Rule

There is a widely misunderstood provision in the Code of Federal Regulations that allows physicians to administer narcotic medications to an opioid addict to alleviate opiate withdrawal symptoms while arrangements are being made for the patient to enter drug abuse treatment. The wording of the applicable portion of the regulation (21 U.S.C. 1307.07) is:

(b) Nothing in this section shall prohibit a physician who is not specifically registered to conduct a narcotic treatment program from administering (but not prescribing) narcotic drugs to a person for the purpose of relieving acute withdrawal symptoms when necessary while arrangements are being made for referral for treatment. Not more than one day's medication may be administered to the person or for the person's use at one time. Such emergency treatment may be carried out for not more than three days and may not be renewed or extended.

Many physicians have assumed that this provides a three-day window in which they could administer narcotics, such as buprenorphine, methadone or other opioids, for detoxification. This is not the intent of the provision. In this context, detoxification is considered treatment. The provision enables a physician to administer an opiate for up to three days while arranging, for example, to get a patient into an inpatient program. On a frequently asked questions section of the DEA website, the prohibition against the use of Buprenex is explicit.

... It should be noted that although Buprenex, a Schedule V after [10/7/2002, a schedule III] controlled substance, is currently approved for the treatment of pain, it may not be prescribed or dispensed for use in narcotic addiction treatment, including the treatment of withdrawal symptoms as provided above under the three-day rule.⁹

Legal Requirements for Prescribing Subutex and Suboxone in Treatment of Opioid Dependence

CSAM physicians should be helpful to their colleagues by reminding them that they cannot prescribe buprenorphine for treatment of addiction unless they qualify under the conditions established by the Drug Addiction Treatment Act of 2000 and have sent notification of intent to prescribe to the Center for Substance Abuse Treatment (CSAT). After they have notified CSAT of their intention to prescribe it in treatment of addiction, qualified physicians¹⁰ may begin prescribing Suboxone or Subutex after they receive a response from CSAT and a "unique identifying number" from DEA. If no response is received after 45 days, physicians may begin to prescribe.

The "unique identifying number from DEA" will be your current DEA number with an X replacing the first letter. DEA has said that the unique identifying number should appear on each prescription for buprenorphine written for the treatment of opioid dependence.

The Subutex/Suboxone package insert does not alert physicians to this requirement, and it is likely that physicians outside the addiction treatment community will not know of the special requirements for prescribing Suboxone and Subutex. Only formulations of buprenorphine (i.e., Subutex and Suboxone) that are FDA approved for treatment of opiate dependence can be prescribed for treatment of addiction. Buprenex should not be used in treatment of addiction, and with the availability of Subutex and Suboxone, the only clinical indication for Buprenex in treatment of opioid dependence would be in a patient who was unable to hold a tablet under the tongue.

Additional information about buprenorphine and CSAT's notification process (including the opportunity to submit the notification form online) is available at: <http://buprenorphine.samhsa.gov/bwns/moreinfo.html>.

Patients on buprenorphine maintenance who are hospitalized for treatment of a medical or psychiatric illness (other than opioid dependence) could be maintained on buprenorphine during the hospitalization by the attending physician.

Use for Pain Management

Can Suboxone and Subutex be used for treatment of pain? The answer seems to be a qualified "yes." The FDA-approved label indication for Suboxone and Subutex is for treatment of opiate dependence. The use of the tablets for treatment of pain would be off label. Although the Controlled Substances Act prohibits physicians from using medications that are FDA approved for treatment of

pain (but not opioid dependence) for treatment of opioid addiction, the converse is not true. Physicians should be able to prescribe Suboxone or Subutex for pain control because there is a great deal of published medical literature about using buprenorphine for pain management.

There are reasons, however, why physicians would be leery of using Subutex or Suboxone for treatment of pain. First, the dosage formulations of Suboxone and Subutex are probably too high for initial treatment of pain in patients unless they have significant tolerance to opioids. Two milligrams of buprenorphine will make some patients nauseous.¹⁴ The usual sublingual buprenorphine dose for initial treatment of pain is 0.3 or 0.4 milligrams. Second, if a patient is opioid dependent by DSM-IV-TR¹² criteria, the physician could run afoul of the DEA. To be safe, drug abusing patients should be treated under the DATA provisions even if they have an uncontroversial pain syndrome.

Acute Pain Management in Patients with Buprenorphine

Buprenex, an injectable formulation of buprenorphine, is marketed for treatment of moderate to severe pain. In many parts of the world, sublingual buprenorphine tablets are marketed for treatment of pain. Patients who are already receiving opioid agonists for treatment of pain should not be switched to Subutex or Suboxone while they have opioids in their body. Buprenorphine is a partial opiate agonist at the mu opiate receptor. When a full opiate agonist (e.g., morphine, fentanyl, oxycodone, hydromorphone) is displaced from the mu receptor by a less potent one, opioid withdrawal may be precipitated. The analgesic effects of full opiates will be attenuated in patients who are being maintained on buprenorphine. Buprenorphine attaches to the mu opiate receptor with high affinity and in effect blocks access of the full opiate to the receptor (which is, of course, why it attenuates the effects of heroin). In addition, the patient may also have opiate tolerance. Trauma, surgery or an acute illness requiring treatment with full opioid agonists may require larger doses of opioid analgesics, but the patient must be carefully monitored while being treated with short-acting opioids. As the buprenorphine leaves the receptor and is metabolized, the patient's opioid requirements may decrease. Unfortunately there are not well-controlled clinical studies to guide clinicians concerning this.

Retail Cost of Suboxone or Subutex

According to the manufacturer, the cost at the pharmacy of Suboxone or Subutex will be something less than ten dollars a day for the usual maintenance dose.

Conclusion

Buprenorphine for treatment of opioid dependence has been a long time coming. The first publication suggesting that buprenorphine may have clinical utility in treatment of opioid dependence occurred in 1978.¹³

It is easy to miss in the hoopla over the long anticipated launch of Subutex and Suboxone that much more is happening than the availability of a new medication.

The conjunction of the Drug Abuse Treatment Act of 2000 and the launch of Suboxone and Subutex reverses over 40 years of prohibition against physician agonist therapy of opioid dependence outside of specially licensed clinics. If office-based opiate agonist treatment using methadone or other opioids is to ever become accepted clinical practice, we have to show the FDA and DEA that we can responsibly prescribe opioid agonist to opioid dependent subjects without creating scandals or public health problems. This is an opportunity we want to cherish and protect.

Acknowledgements

Gail Jara, Walter Ling and Monika Koch reviewed drafts of the manuscript and provided many useful suggestions.

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THE POLITICAL EMPOWERMENT
OF ADDICTION PHYSICIANS

CSAM Public Policy Efforts Break New Ground

By Donald J. Kurth, M.D., FASAM
Chair, CSAM Committee on Public Policy

"We have lost our political virginity in Sacramento."
—CSAM Past President Peter Banys, M.D.

The CSAM Committee on Public Policy has come a long way since our inception as a standing CSAM committee barely three years ago. Hatched out of the reality of living in a world where "politically correct" often means discriminatory policies toward our patients who suffer from the disease of addiction, Past President Peter Banys, M.D., and current President Gary Jaeger, M.D., three years ago took the bold step to announce the formation of a new CSAM standing committee.

High on idealism but short on experience, they gathered together a handful of committed addiction doctors who believed that through political action we could achieve benefits for our patients that we could never hope to accomplish in the isolation of our daily practices. Let me be the first to tell you that we have done just that.

On the heels of a very successful Proposition 36 campaign (the very first treatment in place of incarceration law in the United States), we launched full bore into the addiction treatment parity campaign. We quickly learned, however, that not everybody shares our enthusiasm for providing treatment for addicts and alcoholics! The ferocity of the opposition from certain special interests groups has been enough to rattle my teeth at times. But, we have made progress, and we continue to make progress.

During the past year the CSAM Committee on Public Policy has reviewed dozens of bills. We have actively followed no less than thirty bills and have voted to recommend to the CSAM Executive Council positions on thirteen. Once approved by the Executive Council we sent letters of support, opposition, or support with amendments or changes for each of these thirteen bills to the authors and any other interested parties. CSAM members delivered testimony on a number of bills.

We have had our share of successes but things have not always gone the way we had hoped. Among our successes has been the passage of SB 1807 in 2001 which provided a framework for office-based treatment of opiate dependence and the passage of bills last year that eliminated the dose cap and take home limits for methadone. CSAM members testified in support of

pharmacy sale of syringes without prescription which passed both the Senate and the Assembly but was vetoed by the Governor. Success in politics has little to do with being scientifically correct and much more to do with being politically correct on any given bill.

Sometimes, we have had to be satisfied with just an opportunity to educate one or two of our lawmakers on the disease of addiction or as to just what are the realistic goals of addiction treatment. Sometimes, the best we can do is to set the footings for the foundation of a relationship that may help us sometime in the future. In order to have a political impact, we must form alliances and coalitions with others who have common interests and similar goals. The synergy of these relationships is often stronger than the sum of the individual parts and through these alliances we have learned that we can magnify our strength.

Update on Addiction Treatment Parity

Over the past two years we have made great strides in our quest for parity. Addiction treatment parity passed the Senate vote and passed the Assembly Health Committee vote. But, despite our valiant efforts on the Addiction Parity front, we took a setback in August of this year when we found we did not have the political strength to get the SB 599 out of its Assembly holding pattern and back to the Assembly floor for a vote. All in all, however, we have come a long way with addiction parity in California in the past three years.

Three years ago, we could not even get the Addiction Parity bill through the Senate Insurance Committee. Two years ago, after a vigorous grassroots lobbying effort and many phone calls and letters, we passed the Senate Insurance Committee and got the bill to the Senate floor for a vote. After an impassioned speech by Senator Liz Figueroa (her two brothers died of heroin overdoses, one just the week before the vote) we passed the Senate and moved on to the Assembly. We had learned how to count votes by that time and we knew we had Assembly support so we thought we were home free.

At that point, however, Governor Gray Davis let it be known that he would veto this bill if it came to his desk! Now, what do we do? At the end of the 2001 legislative year, we stood poised to bring our bill to a successful Assembly vote within just a matter of hours. Our allies met with the Governor's staff and we caucused by phone almost hourly during those last hectic days of the legislative session. Discussions with the Governor's staff seemed promising. He agreed to support the bill if we would agree to back off on the treatment requirements to a level that evidence has proven is ineffective. With just a few simple modifications, we could have addiction treatment parity here in California and bask in the glory of our success! But, would the parity law produced be in the best interests of our patients? Would it actually help those who suffer from this disease? After soul searching and head scratching, those of us on the front lines decided we just could not do that to the patients we were committed to serve. A watered down parity bill was not

going to receive the support of this group of addiction doctors!

We made SB 599 a two-year bill and restructured our strategy to bring it back last year for an Assembly vote. Despite scientific research supporting the cost effectiveness of addiction treatment, any addiction parity bill with any sort of effective treatment requirements was rejected by Governor Davis as too costly. We reformulated our strategy to try to reset the timing of our Assembly vote in an effort to leverage the upcoming gubernatorial campaign to our best advantage. However, as the close of the California legislative year approached, the financial crisis and budget issues began to overshadow all other legislative actions and nobody in Sacramento seemed to care much about the plight of drug addicts. Our bill got caught in the legislative meat grinder and we could not rally the political strength to get it out before the legislative session drew to a close.

Looking Ahead

Our success with Proposition 36 has shown us that we can be politically effective if we put our minds to the task. But, to do that we have to do our homework, develop alliances, meet face-to-face with the decision makers, and communicate our ideas in an effective manner. Others have been successful at this. We can be successful, too.

Changing public policy through the legislative process requires a three-tiered treatment plan: political contributions (monetary donations), professional lobbying, and grassroots lobbying. Political contributions will need to be organized, professional lobbying we can acquire and develop, but grassroots lobbying we can start right now. (Actually, of the three, grassroots lobbying can actually have the strongest impact if applied correctly.) And, we can begin to educate ourselves as to how to change public policy in the process.

There exists a political void at the very highest levels in our state with regard to addiction policy. We are the experts. Nobody in our society knows more than we do about the treatment of addictions. If we do not step up to fill that void, somebody else will.

In fact, people with less knowledge and less experience than you or I are filling that void right now. Insurance company lobbyists, law enforcement lobbyists, and others with a vested financial interest in the process are filling the void that we, as physicians, have neglected to fill. And, none of us like the results that follow when these others fill the public policy void that we, as physicians, should rightfully fill. But, what can we do about it?

The time has come for us to begin to work smarter, not just harder. The time has come for us, as physicians, to begin to learn to become an effective force in advocating for sensible addiction medicine public policy. The time has come for us to fill that void for our patients, our specialty, and our future in addiction medicine.

If you would like to become active in CSAM's Public Policy efforts contact Dr. Kurth at 909-980-2273 or via e-mail at donkurth@aol.com.

Experience of Large Employers Supports Parity for Substance Abuse Treatment



CSAM MEMBER KEN SAFFIER, MD
AND DELEGATION MEETING WITH
SENATOR TORLAKSON OF ANTIOCH

ACCORDING TO A REPORT prepared by the Washington Business Group on Health in June 2001 the experience of some of the nation's largest employers "provide strong support for economic analyses that predict that parity can be implemented without significant increases in

cost." The companies studied in the report which all offer forms of substance abuse and mental health parity were American Airlines, AT&T, Delta Air Lines, Eastman Kodak, General Motors, IBM, the Massachusetts Group Insurance Commission, and PepsiCo. The Washington Business Group on Health is a non-profit membership organization consisting primarily of large Fortune 500 employers that purchase health care for more than 39 million people. **The full report is available on the CSAM website: www.csam-asam.org.**

CSAM Legislative Day a Huge Success

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of the California Medical Association. Five CSAM members gave presentations on public policy issues: Gary Jaeger, MD (parity), Peter Banyas, MD (Proposition 36 issues), Diana Sylvestre, MD (syringe exchange legislation), Jack McCarthy, MD (methadone) and Ihor Galarnyk, MD (prevention and treatment of adolescent substance abuse).

In addition to Senator Chesbro, two other legislators, Assembly Members Keith Richman and Gloria Negrete McLeod, addressed the group. Richard Figueroa representing Governor Davis also spoke.

Besides for CSAM physicians, CSAM's legislative day involved drug abuse counselors from CAADAC, methadone treatment providers, patient and treatment advocates, and other addiction professionals. The broad turnout is the result of alliances that CSAM has built over recent years.

After the educational workshop CSAM members participated in a silent vigil and memorial for those who died of preventable illnesses and a rally on the capitol steps as part of Public Health Advocacy Day organized by Diana Sylvestre, MD.

In the afternoon, teams of CSAM physicians engaged in face-to-face meetings with 30 legislators and their aides. CSAM President Gary Jaeger said that legislators were much more open to hearing CSAM's message than they had been just a few years ago.

Driving with Benzodiazepines: Is it Safe?

New study from the Netherlands examines the effects of alprazolam on driving, psychomotor performance

Reprinted with permission from *The Brown University Psychopharmacology Update*, September 2002

Researchers who examined the effects of alprazolam (Xanax) on driving skills on primary highways in normal traffic conclude that driving under the influence of alprazolam and other benzodiazepines should be prohibited.

"The thing that surprised us most was the huge impact of alprazolam on the weaving index," says Joris C. Verster, M.S., the lead investigator of the team from the University of Utrecht, the Netherlands, who performed the research. "Approximately 30 percent of the drivers did not complete the driving test because they fell asleep while driving. In those cases, the driving instructor drove them back to the Institute."

Verster and his colleagues, Edmund R. Volkerts, Ph.D., and Marinus N. Verbaten, Ph.D., have performed many studies of the effects of benzodiazepines on psychomotor performance over the last 20 years. Their ability to test drug effects in drivers on primary highways during normal traffic conditions is unique. Their latest research was published in the August issue of *Neuropsychopharmacology*.

"Never have other investigators performed such a study because they are simply not allowed in the rest of the world, not even in the United States," says Volkerts.

During the 100-km driving test, 20 healthy participants were instructed to drive with a constant speed and steady lateral position within the right (slower) traffic lane. The amount of weaving – Standard Deviation of Lateral Position (SDLP) – and the standard deviation of speed (SDS) give an impression of the amount of vehicle control. A licensed driving instructor who has access over dual controls is present to guard the subject's safety.

"In contrast, driving studies performed on closed roads or in a driving simulator lack the presence of other traffic, risk-taking is not involved, etc.," says Verster. "In other words they do not resemble normal driving optimally."

The real-life driving conditions revealed that drivers taking alprazolam showed a 9 cm increment change in SDLP, which is comparable to someone driving with a blood alcohol content of 0.15 percent.

Volkerts explains that after conducting more than 60 studies, they have discovered that skilled driving results in a placebo SDLP between 18 cm (7 1/8") and 22 cm (8 5/8").

"The effect that we found for alprazolam, the 9 cm, is after extraction of the corresponding placebo. That is very serious," says Volkerts.

According to the RxList 2000, alprazolam is one of the most frequently prescribed drugs in the U.S. It begins working to relieve anxiety in less than one week, as compared to two to four weeks for such medications as buspirone (BuSpar) or the selective serotonin reuptake inhibitors (SSRIs). It has anticonvulsant and antidepressant properties, and a relatively short half-life, all of which make it attractive to consumers and easy to prescribe. The recommended starting dose is 0.5 mg, but "physicians upgrade the prescribed dose even to 2 mg or 3 mg," says Volkerts.

But unlike the SSRIs or buspirone, alprazolam, like all benzodiazepines, is nonselective, and its action enhances the inhibitory effects of the neurotransmitter GABA, which causes a general slowing of brain activity. A low dose of a benzodiazepine such as diazepam (Valium) results in sedation (5 mg 3 times/day for anxiety), a higher dose results in sleep (10 mg at bedtime), and an even higher dose results in anesthesia (20 mg intravenous for a minor surgical procedure).

"Indeed, [driving] should be prohibited while using alprazolam," says Verster. "However, this is equally true for several other psychoactive drugs. Legislative changes would be welcome, but seem difficult to implement."

Verster points out that in most countries the law is very clear about driving and alcohol, but less clear in the case of medicinal drugs.

"In the Netherlands, for example, the law states that it is forbidden to operate a vehicle while using a medicinal drug if you feel or can reasonably suspect that the drug will impair your driving behavior," says Verster. "Clear drug labeling and advice from physicians and the pharmacist should prevent patients from driving after using alprazolam."

The Experiment

In a double-blind, crossover design, 1 mg of alprazolam or placebo was administered to the eight male and 12 female participants 30 minutes before a standardized breakfast and one hour before the driving test and 2.5 hours before the laboratory test battery. *The three skills evaluated in the research were:*

- **Motor control:** Driving 100 km on a primary highway with a constant speed (90km/h) (55.9 MPH) while maintaining a steady lateral position within the right traffic lane. A licensed driving instructor provided with a brake and clutch system accompanied the participant, and could correct driving maneuvers if warranted. Motor control was tested under controlled laboratory conditions with two versions of a tracking test, one easy and one difficult.
- **Working memory:** This skill was tested with the Sternberg memory scanning test.
- **Divided attention:** The participants were asked to perform the easy version of the tracking test and a Sternberg memory scanning test simultaneously. Reaction time and percentage of errors were measured.

Results

All 20 participants performed the laboratory test battery. Six participants were unable to complete their driving test after taking alprazolam because of seriously unsafe driving. Although these six subjects put considerable effort into driving carefully and remaining alert, all of them fell asleep while driving within the first half of their driving test. Four of these subjects were women.

"It is common knowledge that females are more sensitive to drug-induced sedation than males," says Volkerts. "Women have a different balance between fat and muscle, and when the drug is metabolized the drug molecules bind to fat. Women are also lower in weight than men, so they are more affected in terms of impairment."

An analysis of variance revealed, relative to placebo, a significantly elevated SDLP after alprazolam. Second, relative to placebo, speed variability significantly increased after alprazolam, although the mean speed did not differ between the treatments. Third, excursions out of lane were commonly observed in the alprazolam condition, but generally absent in the placebo condition.

The findings also indicate detrimental effects on laboratory tracking, memory functioning and divided attention after acute treatment with alprazolam.

The clinical relevance of these results is limited by the fact that the researchers administered a single dose of alprazolam to healthy young volunteers, while in practice, alprazolam is used chronically by patients suffering from anxiety or panic attacks. Verster says that in chronic users it can be assumed that some tolerance will develop for the adverse effects accompanying alprazolam use. However, tolerance will develop only slowly. Several studies showed tolerance to the performance-impairing effects of alprazolam, he says, but their tests were relatively simple to perform and of relatively short duration, whereas driving is an example of complex behavior.

"Our driving test takes about 75 minutes, which prevents motivational factors compensating the impairment," Verster says.

"However, if alprazolam is chronically used on an as-needed basis, it can be expected that tolerance to its effects will not develop easily," says Verster. "Each time treatment is initiated, it can be expected that driving will be impaired again, especially if doses are higher than 1 mg."

Research in the future should focus on the effects of chronic alprazolam use on driving ability and its dose-response relationship in the intended patient population. "We are very interested in studying this drug further to see when tolerance begins to appear after chronic use," says Volkerts.

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For more information, visit: www.pharm.uu.nl/drugdriving

Comments from the Editor of *The Brown University Psychopharmacology Update*

THE LEAD ARTICLE in this month's issue of *The Brown University Psychopharmacology Update* is sure to provoke reaction from our readers. The study serving as its basis is notable enough – a clinically relevant dosage of alprazolam given to healthy volunteers caused meaningful impairment in driving skills in a real-world test on primary highways in normal traffic. The interview comment of the lead investigator, Joris C. Verster, M.S., is even more eye-opening: "[Driving] should be prohibited while using alprazolam."

Obviously, there is nothing unique about alprazolam in this regard; if one accepts Verster's thesis, then driving should be prohibited while using any benzodiazepine. Since most psychiatrists, myself included, treat large numbers of patients with these agents, the clinical implications are staggering.

Some perspective is in order. Recall that the benzodiazepines were introduced in the 1950s as a safer alternative to the sedative/hypnotics of the day, the barbiturates (truly dangerous drugs that now have little place in general psychiatric practice). The benzodiazepines have been alternately lionized and demonized throughout their tenure in the pharmacopoeia. It would be reasonable to say that the current consensus holds them to be effective in the acute relief of anxiety symptoms, relatively well-tolerated, and generally safe, with the main concerns pertaining to their abuse liability and their effects on cognitive and psychomotor function.

Many clinicians and clinics refuse to prescribe benzodiazepines as a matter of policy because of concerns about potential abuse. Although benzodiazepine abuse is clearly a cause for caution, dispassionate examination of the evidence has generally failed to support the no-use position (Posternak and Mueller 2001). Similarly, that benzodiazepines can impair psychomotor performance has long been recognized. In a 1996 study of impaired drivers, however, 10 percent had positive urine toxicology for benzodiazepines, while 67 percent were positive for marijuana and 33 percent for cocaine and other stimulants (Tomaszewski et al. 1996). Benzodiazepines are the least of our problems on the road.

I don't mean to be glib. These are serious drugs and they should be prescribed with care. The work of the Verster group must be extended to look at patients receiving ongoing benzodiazepine treatment. At the same time, recent findings concerning the utility of benzodiazepines as adjunctive agents in the treatment of depression (Smith et al. 2002) and panic disorder (Goddard et al. 2001) should be kept in mind. Each of our patients deserves an individualized consideration of the risks and benefits of these drugs rather than a blanket policy (Moller 1999). — *Lawrence H. Price, M.D.*

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ADDICTION MEDICINE IN GERMANY:

A Personal Perspective from a Year in Mannheim/Germany

by Monika Koch, MD

EDITOR'S NOTE: *To a great extent, the idea of addiction medicine/psychiatry began in the U.S. as did many other innovations in addiction treatment. Alcoholics Anonymous and other twelve-step oriented treatments began here, methadone maintenance was a U.S. invention, and the National Institute on Drug Abuse funds about 80 percent of the world's research on drug abuse treatment. The opportunity and need for drug abuse innovation would appear to be greatest here because the U.S. is the world's largest consumer country of illicit drugs. But our days of innovation are largely in the past and addiction medicine in the U.S. is falling behind practice in countries of Europe and Australia. Addiction medicine in the U.S. is hampered by a fractionated and uncoordinated health care delivery, archaic regulation enforced by bureaucrats with little clinical knowledge or incentives for innovation, managed care organizations whose main function is to reduce costs by being a barrier to treatment services, and many special interest groups that are more interested in protecting their turf and profits than in providing better health care. It can be informative to see how addiction medicine/psychiatry has evolved in other countries. Monika Koch has had an unusual opportunity to observe the practices of addiction medicine in a variety of settings in the U.S.: as a substance abuse fellow at the San Francisco Veterans Administration Medical Center and San Francisco General Hospital, as an addiction psychiatrist at Kaiser, and as an investigator in a multicenter research study of office-based buprenorphine at Friends Research Associates in Berkeley. In June 2001, she returned to Germany and worked for a year at the Central Institute for Mental Health CIMH (Zentralinstitut für Seelische Gesundheit) in Mannheim, which is affiliated with Ruprechts-Karls-Universität in Heidelberg. Here she shares some of her observations about the similarities and differences in the way addiction medicine is practiced in the U.S. and Germany. Dr. Koch currently works part-time in addiction psychiatry at Kaiser Vallejo.*

Returning to my home country after 11 years in the U.S. was quite an experience. Even though my psychiatric training was quite comprehensive (4 years residency, 2 years fellowship), it did not satisfy the requirements for the German Medical Boards. Therefore, I worked as a resident in the only Department of Addiction Medicine of a German University in Mannheim.

The chairman, Professor Dr. Karl Mann, is an internationally-renowned researcher in the field of substance abuse and the first chairman of the department, which was founded in March of 1999¹. It is the only department for addiction medicine in Germany. Advocating for this specialty and evidence-based approaches to chemical dependency treatment is definitely not an easy undertaking in a country with many traditions, not the least of which is making beer.

Professor Mann was a very supportive mentor and made it possible for me to work relatively independently, which I appreciated even more after remembering how intricate etiquette and hierarchy in a German University hospital can be. I was welcomed warmly into a young and dynamic department and would not want to have missed this opportunity to get to know the German perspective on substance abuse disorders.

Most of the medical component of substance abuse work is done on an inpatient basis. So my first job was being "Stationsärztin" on one of the two 12-bed inpatient detoxification units of our department. In our department, patients were usually admitted for a 21-day program, called "qualified detoxification" (qualifizierter Entzug), which focused mostly on alcohol and prescription sedatives and had many similarities to the American 28-day programs. An integral part was connecting patients to outpatient treatment, which is mostly done through community organizations, such as Caritas and others. AA is available, however it lacks the wide range of different meetings, that I know from the Bay Area, and was considered just one and not necessarily the most attractive of several options. Our program did not focus on the 12 steps at all.

Our program was accepted by the national insurance carriers and could be extended as needed, e.g. for treatment of psychiatric co-morbid disorders. I was pleasantly surprised to learn (and remember) that those insurance companies do not have access to patient records routinely. They can request a review by a separate organization (Medizinischer Dienst der Krankenkassen). The clinicians, usually physicians or nursing staff, will report to the insurance on their overall opinion, e.g. about the appropriateness of length of stay. They will not, however, share individual information about a patient. In some cases when extension of the hospital stay was required, we had to fill in a brief form describing the reasons for extension. Usually it was accepted without problems.

Sometimes the Medizinischer Dienst der Krankenkassen (a central service agency for handling individual medical cases for public health insurance companies) requested copies of the discharge summaries, which are routinely sent to the primary care and referring physician. Most of the time, we did not comply with this request, as it was felt, that this information would be too confidential and we would rather respond to specific questionnaires. This resulted in delay of payment to the hospital in some occasions, but was generally accepted by most public insurance companies. Private insurance

¹ He is also organizing the 12th World Conference on Biomedical Alcohol Research in 2004 (www.isbra2004.de)

agencies (see explanation below), on the other hand, usually did not cover primary addiction treatment and would accept it only in context of treating a primary psychiatric disorder.

National Health Care System

The German national health system is a two-tiered system, public insurance companies participating in the national public health system (öffentliche Krankenkassen) and private insurance companies.

The public insurance company system covers health care of about 90% of all Germans and immigrants. There are several hundred insurance companies, however they vary little in their policies and coverage and are all "öffentliche Krankenkassen", "public health insurance companies". Their network functions as one entity in most respects. This system is paid for by premiums, which are about 14% of the gross income of any employee and is usually split by the employers and employees. Unemployment and welfare recipients, as well as immigrants with pending immigration proceedings, are covered by government agencies (Sozialamt und Arbeitsamt), which participate in the national insurance system. Representatives of the public insurance system, the hospitals, the private practitioner organization "Kassenärztliche Vereinigung" and other providers negotiate fees for provider services. The fees are binding for all public insurance companies (Krankenkassen). Prescriptions are routinely covered with co-payments usually under \$10.

If your income is higher than a certain limit (4000 Euro/month) or if you are self-employed, you may opt out of the public insurance system and join a private insurance company. Often their rates are lower and benefits better, since they can pick desirable customers and are not required by law to accept all clients. Their premiums have a wider range, as do their policies, e.g. they usually exclude addiction treatment. Physicians can charge significantly higher fees and most physician's private offices try to have as many private patients as possible; however, only few private offices can exist solely on private patients.

If you work in substance abuse, this system has some interesting consequences. For example, many long-term alcoholics exist on unemployment and welfare for years, are able to maintain their own apartments and keep full health coverage. Thus it is often difficult to use the incentives and structure provided by regular work as a component of treatment plans. Of course, on the other hand, I rarely encountered problems with homeless patients; the few treated in our facility could be discharged to transitional housing or halfway houses. I did not see any patients without insurance, nor did I ever have to check, what was and what was not covered.

Health insurance companies are not usually paying for outpatient programs, which are a separate track from the medical care system. They pay relatively low fees for programs associated with specialized clinics or private practices. Continuity of care is not easy. Often primary care physicians or psychiatrists treat patients enrolled in

outpatient programs, but only rarely is there a regular communication between counselors and physicians. In the CIMH in Mannheim, counselors from several outpatient programs came to the inpatient ward and introduced their programs to the patients. In addition going to several meetings (such as AA or other) while still an inpatient was mandatory for the patients; however transitioning to outpatient aftercare was often difficult and patients needed frequent reminders to actually go to the meetings.

Overall, university outpatient clinics are not well liked by the private practitioner community and are seen as competition rather than complementary resources. Thus university clinics are usually small and very specific. Hospitals usually just provide inpatient care and have their own staff rather than being staffed by private practitioners.

Treatment of Opioid Dependence

When I started, the CIMH was about to launch an opiate replacement clinic. A demand was noted by the city and, after a lot of work by the local addiction specialist, it was supported and financed by the city of Mannheim in cooperation with CIMH and the KV. It was designed to meet the need for treatment of about 600 estimated opiate dependent patients in the area, provide care as comprehensive as possible in cooperation with the local counseling center and be involved in research projects of the CIMH. When I went to the town meeting discussing this issue, two supportive comments were heard and then the measure was passed – miracles do happen.

So far the opiate dependent patients, who were in treatment, were seen for counseling in the Drogenberatung, a low threshold entry into the treatment system. [By U.S. standards, it might almost be considered harm reduction. It has a lot of pragmatic motivational enhancing approaches such as needle exchange (at times just providing needles for free). In Frankfurt and Hamburg they also provide shooting rooms with adjacent social work and medical care, which is controversial, but legal if not vetoed by the state government.] Private practitioners provide most of the opiate replacement treatment. They have to complete 50 hours of continuing education in substance abuse (there is no substance abuse specialty certification like ASAM) and limit the number of patients treated at any given time to 10 or fewer. Drugs used are methadone, sublingual Buprenorphine (Subutex®), and at times codeine. LAAM is phased out because of cardiac side effects. Since not enough practitioners were found in Mannheim, the KV decided to fund a practice focusing on opiate replacement, which cares for about 100 patients and employs one full and two part-time physicians, four medical assistants and social work care about 8 hours/week. This practice does not support itself (its cost of providing services are greater than what the insurance companies pay). However, it is continued because it covers a demand, that cannot be met otherwise. Usually patients are referred by their physicians, assessed and admitted

Continued on page ten

CSAM AWARDS



CSAM presents the Vernelle Fox Award to WALTER LING, MD

In recognition of his vision and leadership in advancing clinical trial research methodology, his role as principal investigator in pivotal clinical trials of naltrexone, LAAM, and buprenorphine in treatment of opiate dependence, and his role – worldwide – as a teacher, clinician and advocate for evidence-based treatment of addiction.



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- For publicly acknowledging his own recovery – a courageous act for a person holding political office.
- For his personal example of recovery, which serves to enlighten politicians and the citizenry of the State that addiction is a disease and treatment is effective in rehabilitating addicts and restoring them to productive lives.
- For his work in the legislature creating opportunities for citizens of all walks of life who are afflicted with addiction, mental illness, or social ills to be treated with dignity and respect.
- For his bold and innovative legislative efforts to create diversion programs to rehabilitate professionals as an alternative to discipline; he is a true leader in advancing a substance agenda to benefit the professions of law and medicine and the public they serve.
- For his mentorship in supporting the recovery of others.

Presented on October 11, 2002 in Newport Beach, California.

CSAM news

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ADDICTION MEDICINE IN GERMANY

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by the practice physicians. Then an application for approval of treatment is sent to the KV and usually accepted and paid for by the insurance carrier.

Of note is, that allowing office-based methadone maintenance did not result in a rush by practitioners to treat as many addicts as they could. They often remain difficult patients who require a lot of time and resources, therefore few physicians were willing to treat too many with methadone. However having access to treatment without at times having to change your doctor is an invaluable benefit.

Methadone

Methadone maintenance is a relatively new treatment in Germany. In the 70's, a temporary experimental program in northern Germany was the only site for opiate replacement. Methadone treatment was effectively outlawed by federal law, which favored an abstinence-oriented approach and supported long-term residential treatment. In the mid 80's HIV became a public health concern for the estimated 100 – 150,000 opiate dependent patients. Individual states, especially cities like Hamburg and Berlin, started to stretch state laws and establish opiate replacement clinics. In 1992 the federal government established guidelines to prevent further spread of unregulated opiate replacement treatment. However interpretation of these guidelines and treatment practice varies widely from state to state. In 1996 there were about 15,000 patients in MMT and the enrollment numbers are rising with increasing acceptance of the treatment, as I could see in Mannheim. In fact, at present, a major research program has been started comparing methadone with heroin maintenance, a project, which has shown some benefit for selected patients in the Netherlands and Switzerland and would be hard to imagine in the U.S.

These are just some of the situations that made my stay very interesting. Of course, there is the difference in culture overall. There are hardly any non-alcohol establishments (legal drinking age is 16). I did not encounter any smoke-free restaurant, usually not even non-smoking zones. I also did not encounter any physician or treatment professional who was openly in recovery. The professionals amongst my patients did not volunteer this information at work. There is no "war on drugs" in Europe, the prisons are less dominated by drug-related offenders and politicians focus less on the supply side of drug use. My patients had a lot less legal problems, partially because drug laws are less rigid, e.g. possession of a small amount of marijuana is legal. The way you practice medicine is less affected by the threat of lawsuits and more affected by the authority of your Chefarzt. And then of course there is the fairy castle Neuschwanstein, centuries to millennia old traditions of all kinds of things, a lot of German sausage, bread and pastries and much more ... but that is another story.

BOOK REVIEW

Pain Management by Andrew Vachss

Vintage Crime/Black Lizard, a division of Random House (paperback) 2002. 308 pages. \$13.00

Review by Donald R. Wesson, MD

FROM JUST THE TITLE, one might think that this is a textbook for physicians, but it's not. It's a novel in the genre of crime/fiction. A subplot involves a heist of a fictional new opiate, Ultracet, which a group of friends and relatives of pain patients are planning to make available outside medical channels for treatment of patients with intractable pain. The members of the renegade group have one thing in common: they've all watched someone they cared deeply about suffer excruciating pain. A woman describes the treatment of her younger brother before she took matters into her own hands.

And the pain, it took everything from him. It ... degraded him. He had no dignity. They wouldn't give him what he needed. Kept telling me what the 'dose' was suppose to be – like he was a fucking gas tank and they were reading a gauge to know when he was full.

The renegades have their own pain management manual that sometimes challenges conventional medical wisdom. Ann, the principal character in the subplot, reads from it:

During the first two or three days of *effective* pain relief, the patient may sleep for many hours. This can be misinterpreted as the effect of excessive analgesic dosing rather than the first sign of relief in a pain-exhausted patient.

Part of the recitation could have come straight from a recent medical textbook on pain management.

In treating the terminally ill patient, the benefit of pain relief may outweigh the possibility of drug dependence. The chance of drug dependence is substantially reduced when the patient is placed on scheduled narcotic programs instead of 'a pain to relief of pain' cycle typical of a PRN regimen.

Physicians don't take all the heat. Ann brings the relationship between pain management and moral high ground of mainstream society into sharp focus.

... Somebody's dying, what possible difference could it make if they were a damn drug addict? That's the legacy of Nancy-Fucking-Reagan, a country where we're so psycho about 'drug addicts' that we sentence millions to be tortured to death. Doctors are so freaked about the DEA that they won't write the scrips. People are in absolute agony, and what they get is sanctimonious babbling about the 'war on drugs.'

The pain focused parts of the narrative, such as the snippets quoted above, if collected together, would occupy only a few of the book's 308 pages. The bulk of the novel revolves around the main story, set in Portland, Oregon. The father of a missing girl engages Burke – an ex-con, non-licensed private investigator who gives his name as B.B. Hazard – to locate his teen daughter. Burke's forays into Portland's underbelly to tap into the "whisper stream" for clues about the whereabouts of the missing girl and the characters he finds there comprise the primary grist for the mill.

The snippets about physicians' treatment of pain have verisimilitude and accurately capture some of the current debate between physicians involved in pain management, physicians in addiction medicine, and mainstream society.

For the past several years, aggressive treatment of pain with opioids and hospice care of the terminally ill is now mainstream medical practice. Physicians can be taken to task for under treatment of pain as well as for over treatment. Less well understood is the relationship between aggressive pain management and abuse of prescription opioids. Physicians who specialize in pain management in their zeal to allay concerns about opioid addiction, have cited studies to show how rare iatrogenic drug dependence is among pain patients.¹ Addiction medicine physicians see the fallouts of more liberal prescribing of opioids – not necessarily the opioid-addicted, terminally-ill patient with severe pain – more commonly opioid addiction among health care workers and opioid addicts who abuse prescription opioids that are diverted from pain patients.

¹Some members of the pain treatment community are beginning to acknowledge that iatrogenic addiction may be a more significant problem than previously acknowledged, see, for example, Passik, S.D. 2001. Responding rationally to recent report of abuse/diversion of Oxycontin. *J Pain Symptom Manage* 21(5):359.

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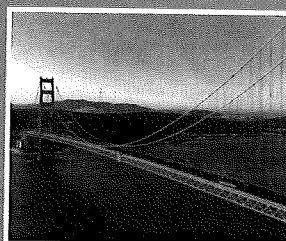
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