Both the subject of intense controversy and the most widely used illicit drug in the world, marijuana and its effects merit continued consideration. This issue examines current medical research into cannabis as well as the state of Oregon's recent Supreme Court decision about the use of marijuana in the workplace. Experts also document the convergent problems of drug trafficking and animal cruelty.

In our commentary, a consultant to the United Nations Office on Drugs and Crime describes the drug trafficking situation in Afghanistan and provides recommendations for future efforts to deal with the debilitating effects of the drug trade on the country and on the world.

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Edited by Eric A. Voth, MD, FACP and David A. Gross, MD, DFAPA, our intended readership includes clinicians, clinical researchers, policymakers, prevention specialists and the interested public.

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Early Findings in Controlled Studies of Herbal Cannabis: A Review
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Abstract
Despite the widespread public interest in the therapeutic potential of herbal cannabis, little rigorous data exist on its use for specific, chronic medical conditions. The Center for Medicinal Cannabis Research has funded research protocols which provide interesting results that may be useful in guiding future research programs. The data alone, however, fail to make the case that crude, smoked cannabis should be available to patients.

Introduction
Despite the widespread public interest in the therapeutic potential of the cannabis plant, little rigorous data exist reflecting on its safety and efficacy for the treatment of specific chronic medical conditions. Recently, the Center for Medicinal Cannabis Research (CMCR), based at the University of California San Diego, released a Report describing the results of research that it has funded since its inception ten years ago. That report, as well as the published studies it describes, has garnered considerable media coverage.

CMCR was created in 2000 as the result of legislation (California State Senate Bill 847) enacted in 1999 for the purpose of conducting research into cannabinoids, including smoked cannabis. CMCR reports it focused on medical conditions identified by the Institute of Medicine (in its 1999 publication Marijuana as Medicine: Assessing the Science Base) as those for which cannabis might have therapeutic effects. In total, CMCR approved fifteen clinical studies, including seven clinical trials. As of February, 2010, five of those trials had been completed, and two were in progress. CMCR also approved four preclinical studies, which have all been completed. Three of the clinical studies examined the use of smoked cannabis as an adjunctive treatment in pain conditions associated with injury or disease. Another examined the analgesic effect of smoked cannabis in experimental pain. Finally, an additional pilot study explored the use of vaporization as a cannabis delivery system. CMCR supported these studies with nine million dollars in funds appropriated by the California legislature. That funding source has not been renewed.

From the results of this research, CMCR concluded that there was “reasonable evidence” that cannabis is a “promising treatment” in certain pain syndromes and that the findings “provide a strong science-based context in which policy makers and the public can discuss the place of these compounds in medical care.”

This article will explore a number of issues raised by this research and clarify the limits and significance of the clinical trial results.

The following discussion suggests that the CMCR funded studies provide interesting data that may be useful in guiding future research programs. Those data, however, are quite inadequate to provide evidence that smoked cannabis should be made available directly to patients. In light of the short duration of treatment, small patient size, potential failure of blinding, and other considerations elucidated below, these studies cannot support such a conclusion. Similarly, they do not resolve other important public policy questions, such as whether it is appropriate to commit additional scarce governmental funding resources to smoked/inhaled cannabis research or to reconsider the status of cannabis under Schedule I of the Controlled Substances Act. Indeed, these studies demonstrate that patients using inhaled THC-predominant cannabis experience a range of significant CNS side effects, including cognitive impairment and intoxication. This further underlines the need for all cannabis-based products to develop a robust body of risk-benefit data in specific medical conditions and for patients using such products to be under the supervision of their personal physicians.

The Stages of Modern Medication Development
Modern medication development takes place in discrete stages. Research begins with very small trials, often in healthy subjects, and proceeds into larger trials in patients with specific medical conditions, through which a product’s efficacy, side effects, optimal dosing, pharmacological activity, and toxicity are increasingly better defined. Late stage clinical trials are often followed by open label extension studies, where the persistence of treatment effects, as well as additional safety information, can be assessed:

PHASE I TRIALS: Initial studies to determine the metabolism and pharmacologic actions of drugs in humans, the side effects associated with increasing doses, and to gain early evidence of effectiveness; may include healthy participants and/or patients.

PHASE II TRIALS: Controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks.
Smoked Cannabis as a Treatment for Neuropathic Pain Syndromes

In its report, CMCR indicated that its intention was to study cannabis as a treatment option for individuals with intractable symptoms, i.e., who do not respond or respond inadequately to currently available therapies. Accordingly, the report averred, cannabis was studied as an add-on to the patient’s existing treatments. Each study was conducted in a small number of patients and was of very short duration—limited even by Phase II standards. The patients/subjects were almost exclusively cannabis-experienced. All clinical studies were approved by the FDA and registered (licensed) by the DEA. Cannabis was obtained in varying potencies from the National Institute on Drug Abuse (NIDA). The clinical studies used a standard, timed method of smoke inhalation. Patients were generally excluded for schizophrenia or bipolar depression, uncontrolled hypertension, cardiovascular disease, chronic pulmonary disease (including asthma), active substance abuse, and history of cannabis dependence. All protocols were approved by experts on CMCR’s Scientific Review Board and the relevant institutional review board.

All the studies examined in this article were randomized, double blind, placebo-controlled trials (RCTs) investigating the use of smoked cannabis in the treatment of neuropathic pain syndromes. Abrams et al. conducted a parallel-group study in 55 patients with painful HIV-associated sensory neuropathy (28 randomized to placebo and 27 to smoked cannabis) with an in-patient treatment phase of five days. The THC content of the cannabis was 3.5%.

A trial conducted by Ellis et al. in the same pain syndrome involved 34 randomized patients, of whom 28 completed the study. After one 5-day treatment period and a 14-day washout period, the patients were crossed over to the other intervention for another 5-day treatment period. The THC content of the cannabis ranged from 1-8%. Patients were started at 4% THC and then titrated upwards or downwards in four smoking sessions depending on their symptom relief and tolerance of the dose.

Finally, a crossover study conducted by Wilsey et al. examined the use of smoked cannabis as a treatment for neuropathic pain of various origins. Thirty-eight patients were randomized, of whom 32 completed all the study sessions. Pain syndromes were diverse, rather than homogeneous: complex regional pain syndrome (22 patients), central neuropathic pain related to spinal cord injury or multiple sclerosis (10 patients), peripheral neuropathy related to diabetic neuropathy or nerve injury (6 patients).

These studies demonstrated a modest degree of efficacy; however, the extent of such efficacy was not fully consistent between the studies. In the Abrams study, the smoked cannabis group had a 34% reduction in daily pain vs. a 17% reduction in the placebo group (net 17% reduction); in addition, 52% of the patients in the cannabis group reported a 30% reduction in pain scores over the 5 days versus a 24% reduction in the placebo group (net 28%). In the Ellis study, 46% of patients in the cannabis group achieved 30% pain relief compared with 18% of those in the placebo group (net 28%).

In the Wilsey study, by contrast, there was only a small—but statistically significant—difference in pain reduction from placebo (net less than 10 points on a 100-mm visual analogue scale of pain intensity). Furthermore, this separation from placebo did not occur until a cumulative 9 puffs at 240 minutes (4 hours) had taken place. This extended time to onset of analgesia, even longer than that in the Wallace study on experimental pain, infra, challenges the contentions of cannabis advocates that inhaling cannabis is necessary in order for patients to obtain rapid pain relief. No significant differences in analgesia were observed in the two different cannabis potency groups (3.5% and 7%).

The short duration of these studies, coupled with the small patient size and the variability of neuropathic pain syndromes (Wilsey), would afford them extremely limited significance in the FDA regulatory context. International regulatory standards call for randomized controlled clinical trials of 12 weeks duration in
order to demonstrate the safety and efficacy of an investigational product in chronic pain conditions. (11) Such a duration is necessitated because short term efficacy may not be maintained in chronic use, and/or side effects may become cumulative or more apparent over time, thereby affecting the risk/benefit profile.

Furthermore, the significance of the Abrams results must be considered against the fact that almost 50% of the patients were not taking a concurrent analgesic. In the Ellis study, only 68% of the patients were taking concomitant opioids; the remaining patients used acetaminophen and NSAIDs; it is unclear whether the NSAIDs comprised only aspirin, ibuprofen, and naproxen, or also included COX-2 inhibitors. In the Wilsey study, patients were instructed to “take all other concurrent medications,” but the prevalence and nature of such medications was not described. These discrepancies and omissions call into question the statement in the CMCR report that the trials were conducted in “treatment-refractory” patients, i.e., those who are not receiving adequate benefit from an optimized analgesic regimen.

**Extent of Side Effects**

All medications have side effects, and, in order to achieve marketing approval, an investigational product must have a favorable risk/benefit profile in a particular medical condition. In the studies described above, almost all patients were cannabis-experienced. (12) The side effect profile—particularly the incidence of adverse CNS events—exhibited by patients in these studies cannot be extrapolated to a more representative patient population, which would include cannabis-naïve patients. Indeed, in the Wilsey study, the authors noted that only cannabis experienced patients were entered into the study in order “to reduce the risk of adverse psychoactive effects in naïve individuals.” For example, in the Ellis study, one cannabis-naïve patient was withdrawn due to an “acute cannabis-induced psychosis.”

Despite the fact that most patients were cannabis-experienced, the extent and range of side effects were notable in these studies. Although the Abrams study investigators opined that “An acceptable safety margin has been shown in the present study,” the adverse event data seem to reveal considerable CNS impact and, while intoxication scores were not collected, the complex of symptoms identified suggests that intoxication was prominent.

**Table 1** (13)

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<th>Extent of Side Effects</th>
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| In the Wilsey study, the authors concluded that “psychoactive effects were minimal and well-tolerated,” but conceded that “neuropsychological impairment was problematic, particularly with the higher concentration of study medication.” Patients using the 7% cannabis demonstrated neurocognitive impairment in attention, learning and memory, and psychomotor speed, whereas the 3.5% cannabis resulted in a decline in learning and memory only. This, the authors opined, suggested a possible therapeutic window. They further cautioned, however, that severe pain coupled with psychological distress is associated with lower scores on cognitive performance tests, which was true of the patients in this study. Therefore, “[h] combination with the deficits in baseline neurocognitive performance...cannabis compounds this problem. This finding necessitates caution in the prescribing of medical marijuana for neuropathic pain, especially in instances in which learning and memory are integral to a patient’s work and lifestyle.” The authors speculated that, since the low and high doses were equally analgesic, it might be preferable to utilize a lower cannabis potency/dose, which would also reduce the diversion potential. This suggests that the high-potency cannabis available in dispensaries may seriously impact a patient’s neurocognitive functioning.

**Table 2** (14)

In the Ellis publication, little was described regarding safety issues. The authors stated only that “the frequency of some non-treatment-limiting side effects was greater for cannabis than placebo. These included concentration difficulties, fatigue, sleepiness or sedation, increased duration of sleep, reduced salivation and thirst.” However, they do warn that “Cannabis has potent psychotropic effects including ‘paradoxical’ effects (e.g., depersonalization, hallucination, suspiciousness) in an important minority of individuals.”

The CNS side effects reported in these controlled studies also suggest that many patients purchasing cannabis from dispensaries may be experiencing even more extreme reactions. Some of these patients are cannabis-naïve, and few receive proper evaluation and supervision from physicians. (13) Unlike the NIDA cannabis utilized in these studies, products from dispensaries vary widely in THC content. Many types of sinsemilla—buds from unfertilized female cannabis plants, generally cultivated indoors—exhibit THC concentrations of well over 15%. (14) Cannabis-infused honeys, cannabis resin, and hash/cannabis oil can reach THC concentrations of 60%. Patients who are 1) debilitated by serious medical conditions and 2) lack adequate physician guidance concerning product composition and dosing, may experience more undesirable or even frightening effects. For example, in a media report, one patient with advanced cancer ingested 1/8 teaspoon of cannabis-infused honey that she had purchased at a dispensary: “After a few hours, she was hallucinating, too dizzy and confused to dress herself for a doctor’s appointment. Then came vomiting far worse than her stomach upset before she took the drug.” (15) Such side effects may be quite unpredictable, since the cannabis products lack standardization. Patients also cannot be assured that they will experience the same effect from one cannabis purchase to the next.

**The Concern with Blinding**

Blinding is considered essential to the reliability and integrity of clinical trial results, particularly when the symptom being treated (such as pain) must be assessed by the patient, rather than by means of some objective measurement tool. As one expert stressed:
If participants are not blinded, knowledge of group assignment can affect responses to the intervention received. Participants who know that they have been assigned to a group who will receive a new treatment might harbor favourable expectations or increased apprehension. Those assigned to standard treatment, however, might feel deprived or relieved.....knowledge of the intervention received, and a perception of that treatment, can affect the psychological or physical responses of the participants. (16)

The fact that almost all of the patients in these studies were cannabis-experienced, coupled with the notable CNS side effects, calls into question the effectiveness of the blinding in these studies. In none of these studies did the researchers attempt to correlate the occurrences of side effects—particularly CNS side effects—with efficacy data. Therefore, it is impossible to know whether those patients on active medication who experienced notable CNS effects became unblinded and were influenced in their assessments of efficacy, i.e., whether those patients who believed they were on active medication were thereby influenced to think that they were obtaining greater pain relief. Furthermore, since almost all patients were cannabis-experienced, there was no way to attempt to correlate prior use of cannabis and efficacy, i.e., whether prior cannabis use was a predictive factor in determining clinical response. Since most of the patients were cannabis-experienced, it is very probable that the blinding was not successful. Indeed, in the Ellis study, the authors specifically noted that, when asked, the majority of patients who had been exposed to cannabis (either initially or during the cross over) correctly guessed the treatment. This calls into question the validity of the efficacy results.

**Effect of Smoked Cannabis on the Immune System**

Although not funded by CMCR, another trial published by Abrams et al. in 2003 is of relevance to the current discussion. This study investigated the short-term effects of smoked cannabis on the viral load in HIV-infected patients receiving a stable antiretroviral treatment regimen of either indinavir or nelfinavir. Because the same systems metabolize cannabinoids and protease inhibitors, it was hypothesized that cannabinoids might alter viral loads in HIV-infected patients taking protease inhibitors. Patients were required to have a stable viral load for the previous 16 weeks and must have had previous smoked marijuana experience (6 or more times) in order “to ensure that they knew what neuropsychiatric effects to expect.”

The 62 study participants were randomized to cannabis cigarettes, a synthetic THC (dronabinol) capsule or placebo capsules three times daily for 21 days of in-patient treatment. NIDA provided the cannabis (3.95% THC). Patients randomized to smoked cannabis utilized a standardized puff procedure. Interestingly, the investigators noted that they had chosen not to include a smoked placebo group because they thought it “would be impossible to blind marijuana in study participants with previous marijuana experience.” (17)

The investigators concluded that short-term use of cannabinoids, either smoked or oral, does not substantially elevate viral load in HIV-infected persons receiving specified antiretroviral regimens. The results also showed increased weight in both cannabinoid groups compared to placebo, although the weight gained was not in lean body mass but in fat. The investigators acknowledged that their conclusions were “limited by the short duration of the study” and that it would be desirable to produce additional safety information over longer exposure periods. They also noted that the effect of government-supplied cannabis of known potency and content cannot be extrapolated to the potential effects of cannabis available from other sources. Finally, the lack of a blinded control group for the smoked marijuana could bias the interpretation of some of the results, such as weight changes.

As with later CMCR studies (and as acknowledged by the authors), this study provided at best short-term data about the effect of either oral or smoked cannabinoids on viral load in HIV infected persons. It took place in a controlled environment (in-hospital!) with government-standardized cannabis. The results fail to establish that the chronic use of smoked cannabis will not impair immune function. Nor does it suggest that the many types of cannabis dispensary products—which may be contaminated with pesticides or dangerous microbes—will not cause injury to the immune system. A patient whose immune system has been compromised, either by disease process or by treatment (e.g., cancer chemotherapy), is likely to be particularly susceptible to harm from such contaminants. (18)

**Smoked Cannabis and Experimental Pain**

Using a human experimental pain model, Wallace et al. hypothesized that smoked cannabis would reduce the pain and hyperalgesia induced by intradermal capsaicin. (19) In an RCT with a crossover design, capsaicin was injected into opposite forearms of 15 active cannabis-using (20) healthy volunteers, 5 and 45 minutes after exposure to smoked cannabis. Subjects were exposed to placebo, low (2%), medium (4%), and high (3%) potency NIDA cannabis. They adhered to an observed, standardized smoking procedure, taking three inhalations at each dose, with 40 seconds between inhalations, followed by a one-week washout period. Pain, hyperalgesia, THC plasma levels, and side effects (including a “high”) were assessed. (21)

The results demonstrated that 5 minutes after cannabis exposure, there was no effect on induced pain at any dose. Not until 45 minutes after cannabis exposure was there a significant decrease in capsaicin-induced pain with the medium dose. As with the Wilsey study, this undermines the claims of cannabis advocates that smoking or otherwise inhaling cannabis is necessary in order for patients to obtain rapid pain relief. Moreover, a significant increase in pain was seen with the high dose. There was no effect with
the low dose, and there was no effect on hyperalgesia at any dose. There was also no effect on the pain quality.

Side effects were dose-dependent, with many more reported at the high potency, despite the fact that patients took only 3 inhalations. Tests of neuropsychological functioning showed no significant difference at any dose, although this may be inconsistent with the impairment in cognitive functioning displayed in the Wilsey study. (22) Subjective reports of a "high" were also dose-dependent. Five minutes after cannabis exposure, subjects rated a significant (7/10) "high" at the highest dose; although a prominent (5.4/10) "high" was still reported at the lowest dose. Intoxication scores were lower, but still notable, 40 minutes after exposure: 3/10 for the lowest dose, 4/10 for the medium, and 4/10 for the highest dose.

The biphasic effects (analgiesia at a lower dose, hyperalgesia at a higher dose) reported in this study have been identified previously, (23) although they were apparently not consistent with the Wilsey study, where there was an equal analgiesic response with both low and high dose cannabis. As the authors noted with concern, such an effect may suggest that there is a narrow therapeutic window of efficacy for inhaled cannabis and perhaps cannabinoids as a class. This indicates (particularly in light of the discrepant Wilsey results) that more research is needed to determine the therapeutic window for different cannabinoid formulations and modes of delivery. For example, a product containing both THC and CBD (cannabidiol) may have a different therapeutic window from a formulation that is almost exclusively THC. (24, 25) High-THC cannabis may be more likely to produce psychotic symptoms. (26, 27) Cannabis generally available in cannabis dispensaries is essentially devoid of CBD. (28) This is also true of the NIDA cannabis used in this and other CMCR studies.

The authors candidly acknowledge that the results of this study cannot be generalized to clinical research because of the small sample size and use of only healthy volunteers who were cannabis-experienced and able to tolerate the highest study dose of cannabis. They do conclude that more information is needed regarding abuse potential, tolerance, efficacy in neuropathic pain, and safety issues. Consequently, they "[could] not advocate a place for using cannabis in the treatment armamentarium at this time." Pointing to the health-related harms resulting from the long-term use of smoked cannabis, including respiratory symptoms "suggestive of obstructive lung disease," and the "paradoxical" psychotropic effects (e.g., dysphoria, dejection, depressed mood) often associated with cannabis use, they cautioned that: "[S]uch effects must be carefully considered in work addressing the future clinical application of cannabinoids."

Vaporization as an Alternate Delivery System

Cannabis is generally smoked. (29) Cannabis smoke contains many of the components of tobacco smoke. Smoking a cannabis cigarette can deposit as much as four times the amount of tar in the lungs, compared to smoking a tobacco cigarette. (30) This effect results from the fact that cannabis cigarettes lack filters, and cannabis smokers inhale more deeply and hold their breath longer than tobacco smokers hold theirs. (31) There is no doubt that chronic cannabis smoking is harmful to the lungs. (32, 33, 34)

Recognizing this concern, CMCR funded a study to examine vaporization as a potential cannabis delivery system. As the study investigators stated: "The Institute of Medicine sends a clear message suggesting that smoking is not a desirable delivery system for the potential therapeutic effects of cannabis." (35)

Abrams et al. conducted a 6-day in-patient pilot study involving 18 healthy subjects (not individuals with medical conditions), all of whom were active (rather than merely past) cannabis users. They were exposed to three separate cannabinoid concentrations (1.7%, 3.4%, and 6.8%), either by smoking or by vaporizing. Subjects were exposed to one type of intervention each day and were blinded to the THC concentration. The primary endpoint was the measurement of plasma concentrations of THC at specific time points for each strength of THC. The secondary outcome measure was the level of exhaled carbon monoxide (CO). Vaporization was accomplished by means of a device called the Volcano®. (36)

The study results demonstrated that the vaporizer actually resulted in higher concentrations of THC compared to smoked cannabis at 30 and 60 minutes, at both potencies. (37, 38) Subjects also reported their "high" on a 100-mm VAS scale; this "high" did not differ during vaporization compared to smoking, although it did increase in both instances with increasing strength of THC. Since these were active cannabis users, it is evident that vaporization, even at low levels of THC, produces intoxication. This would be even more pronounced in cannabis-naive individuals, potentially more so in those afflicted with serious medical conditions. Surprisingly, the investigators stated that "no adverse events were reported," indicating that the subjects (and perhaps the investigators) did not consider such intoxication to be an adverse event. Seriously ill patients, however, generally consider intoxication to be an undesirable side effect of a medication.

Levels of exhaled CO, the secondary outcome, increased very little after vaporization, whereas there was a substantial increase after smoking. From this finding, Abrams et al. concluded that vaporization produced "little or no exposure to gaseous combustion toxins" and that the Volcano® device is an "effective and apparently safe vehicle for THC delivery." The lowered levels of exhaled CO, however, do not support that "did not measure, since the study "did not measure other combustion products such as polycyclic aromatic hydrocarbons and oxidant gases."

Another recent non-CMCR study belies this conclusion. Noting that several previous vaporizer studies had examined only the presence of high molecular weight pyrolysis products, Bloor and colleagues analyzed the extent of low molecular weight toxic products, such as ammonia, resulting from vaporization versus smoking of both street cannabis and NIDA cannabis (3% THC). (39)
Two vaporizers, the Blue Meanie and the Volcano®, were examined. The Blue Meanie consists of an electrically heated metal cup which is enclosed in a glass container. The cup is temperature-controlled but not adjustable and reaches a temperature of about 250°C, which (according to the investigators) is below the temperature at which cannabis leaf combusts. The Volcano® consists of a ceramic heater with a heat vent; a removable chamber is positioned above the heat vent into which the cannabis sample is placed. Hot air is blown through the chamber to release vapors from the sample without combustion. The vapor inflates a disposable plastic balloon, which can be detached when filled; the vapor can then be inhaled. The device was set to its highest setting of 9, which equates to 218°C at the heater screen and 155°C at the sample surface.

Smoked cannabis from NIDA produced (in mainstream smoke) acetaldehyde at 45 ppm and ammonia at 10 ppm. Ammonia was the most abundant species in sidestream smoke, reaching the level of 250 ppm. The Blue Meanie produced ammonia (NH3) at a mean of 205 ppm from street cannabis, compared with 4 ppm from NIDA cannabis; methanol at 212 ppm for street cannabis, compared to 73.8 ppm for NIDA cannabis; acetaldehyde at 24.5 ppm for street cannabis, compared with 36.8 from NIDA cannabis. The Volcano® produced ammonia at 60 ppm for street cannabis and 4.3 ppm for NIDA cannabis; methanol at 4.6 ppm for street cannabis and 13.8 ppm for NIDA cannabis.

The results demonstrated that, with street cannabis, the Volcano® produced levels of exposure to ammonia that are 1) greater than the maximum short-term occupational exposure limits of 35 ppm and 2) higher than levels reported from tobacco smoke (10-12 ppm). This is extremely concerning, since an industrial accident resulting in relatively low levels of ammonia resulted in significant neurocognitive impairment even after 22 months. Furthermore, a recent study demonstrated that eye irritation, headache, dizziness and short-term intoxication result from short-term exposure to only 5 ppm of NH3. The Volcano® lowered the ammonia content of the vapor only by 40-50% as compared to smoking NIDA cannabis; it did not even approach total elimination.

It certainly cannot be said that vaporizers as a class, fully or even adequately eliminate toxic products. In fact, Bloor et al. noted that closed system vaporizers may actually expose the user to higher levels of ammonia than would be created by smoking tobacco, since with smoking, most toxic combustion products are dispersed into the atmosphere through sidestream smoke: "The use of closed systems to produce cannabis vapour results in the inhalation of most of the products of pyrolysis and thus exposure to higher levels of toxic products, such as ammonia, which may otherwise have been mainly lost in sidestream smoke." This would not be acceptable to regulatory agencies such as the FDA.

An earlier study with the Volcano® also demonstrated that at its highest setting of nine, it reduced, but did not fully eliminate poly aromatic hydrocarbons, as compared with smoking cannabis. Furthermore, the efficiency of THC delivery was poor. Using 200 mg samples of 4.15% THC NIDA cannabis, an average of 1.95% of the sample weight was recovered as THC after vaporization (3.9 mg—47% of the maximum), compared to 3.24% with smoked cannabis (78% of the maximum, but without sidestream smoke loss or any residual butt). In previous smoking machine tests, THC efficiencies of 30-60% had been demonstrated, with approximately 30% loss by heat destruction of THC and additional loss in sidestream smoke. Earlier vaporizer studies also demonstrated that vaporization can be a very inefficient way of delivering THC, which is a significant concern in its own right, considering the high cost of much cannabis herbal material available in dispensaries. Moreover, vaporizers such as the Volcano® are not portable and cannot easily be used outside the patient's residence. Many non-smoking facilities, such as hospitals, will not permit the use of cannabis vaporizers, further limiting their usability by patients.

In addition, vaporizers cannot ensure a reliable and reproducible medication dose if the underlying cannabis material lacks standardization. Cannabis available in dispensaries varies significantly in THC and other cannabinoid content. Cannabis material may also be contaminated with pesticides and/or dangerous microbes. These contaminants are not necessarily eliminated by vaporization, particularly at lower temperatures.

Current vaporization systems, therefore, do not mitigate many of the concerns and problems associated with cannabis smoking. Importantly, inhalation (whether vaporization or smoking) results in rapid delivery of a bolus of active substance to the lungs and consequently to the body and brain. As demonstrated by the Abrams pilot study, vaporized cannabis (even of low THC potency), produces significant intoxication and abuse liability.

Patients with chronic conditions—the large majority of those using cannabis for medical purposes—do not require an immediate onset method of medication delivery. For example, patients with chronic pain are often prescribed an extended release opioid, such as OxyContin®. Oral transmucosal fentanyl (e.g.. Actiq®), by contrast, is reserved for patients with breakthrough (rather than persistent background) pain, which necessitates a medication with very rapid onset. Perhaps not surprisingly, the FDA has never approved a vaporizer for the home administration of a psychoactive substance for treatment of a chronic condition. Indeed, because of the technological and regulatory obstacles, development by the pharmaceutical industry of vaporization systems is in its infancy. One company describes the challenges:

Traditional dry powder and aerosolized inhalation delivery systems have been designed and used primarily for local delivery of the drugs to the respiratory airways, not to the delivery for rapid systemic drug delivery. Certain recent variants of these systems, however, can provide systemic delivery of drugs, either for the purpose of rapid onset of action or to enable noninvasive delivery of drugs that are not orally bioavailable.
Nevertheless, many of these systems have difficulty generating appropriate drug particle sizes and consistent emitted doses for deep lung delivery. To achieve appropriate drug particle sizes and consistent emitted doses, most traditional inhalation systems require the use of excipients and additives such as detergents, stabilizers and solvents, which may potentially cause toxicity or allergic reactions. Many traditional inhalation devices require patient coordination to deliver the correct drug dose, leading to potentially wide variations in the amount of drug delivered to a patient. (50)

These studies by Abrams and others demonstrate that vaporization technology is extremely challenging, particularly when it is used to deliver a potent psychoactive substance such as cannabis. Vaporizers differ significantly in the extent to which they reduce toxic substances and deliver THC and other cannabinoid components. This fact highlights the need for manufacturers of such products to seek FDA approval as medical devices through established regulatory channels. (51)

The Federal Government and Cannabis Research

Cannabis advocates often claim that the federal government is suppressing research into the therapeutic potential of the cannabis plant. The CMCR studies demonstrate that this contention is false. The CMCR report states that all protocols (15 clinical studies and 4 pre-clinical studies) were submitted to, and approved by, the Office of Public Health and Science of the federal Department of Health and Human Services (DHHS), the Food and Drug Administration (FDA), the National Institute on Drug Abuse (NIDA), and the Drug Enforcement Administration (DEA). In all instances, these studies involved collaboration with NIH as NIDA provided the research cannabis. Indeed, in the 2003 Abrams study, which was conducted outside of the CMCR umbrella, NIDA provided the grant funding.

It is far from clear whether further funding of public or private -of smoked cannabis research is a wise use of resources. In 2001, Lyle E. Craker, a Professor in the Department of Plant, Soil and Insect Sciences at the University of Massachusetts Amherst, submitted an application to DEA to become registered as a bulk manufacturer/cultivator of cannabis for research purposes. The cannabis cultivation would be funded not by the federal government, but through a grant from the Multidisciplinary Association for Psychedelic Studies (MAPS). (52) Dr. Craker, sponsored by MAPS, argued (53) that a second, privately-funded source of research cannabis was necessary in order for any cannabis-derived medications to achieve marketing approval from the FDA:

No privately funded sponsor (such as MAPS, or alternatively, a for-profit pharmaceutical company) will invest significant sums in a realistic drug development research program aimed at obtaining FDA approval for the prescription use of marijuana without first obtaining its own independent source of supply of a drug whose quality, price and availability it determines. (54)

A number of factors undermine the credibility of this claim. First, it would be unprecedented for the FDA to approve herbal material for direct prescription, due to the difficulties in standardizing the dose. The FDA has provided a pathway for the marketing approval of prescription medication derived from botanical materials. (55) This Guidance permits some leniency at the very early stages of research and development. However, by the stage of advanced clinical trials and New Drug Application, the product must meet all the stringent requirements (e.g., specifications for product composition, clear dosing parameters, testing for carcinogenicity, reproductive toxicity, etc.) applicable to any new medication.

The FDA guidance document identifies three stages of development for a botanically derived medication: Botanical Raw Material (BRM), Botanical Drug Substance (BDS) and Botanical Drug Product (BDP). (56) Because of the difficulties in identifying a method of administration that provides a reproducible dose without producing carcinogens, it is unlikely that the FDA would approve cannabis herbal material itself. Rather, the agency would probably require that the plant components be extracted and formulated into an appropriate delivery system. As the American Medical Association recently recognized: "The future of cannabinoid-based medicine lies in the rapidly evolving field of botanical drug substance development, as well as the design of molecules that target various aspects of the endocannabinoid system." (57) Currently, Sativex®, an investigational product derived from cannabis extracts, is proceeding through the FDA process pursuant to the Guidance.

Second, herbal cannabis need not be cultivated in the United States in order for a specific cannabis-derived product to enter into the FDA approval process. For over 85 years, it has been the policy of the U.S. not to cultivate or produce narcotic raw material (NRM), such as opium or poppy straw. (58) By longstanding international practices, the U.S. is a country that imports and manufactures, rather than one that cultivates and supplies, NRM for the development of pharmaceutical products. (59) The U.S. relies on a specific list of countries authorized to import NRM into the U.S. in order to meet legitimate medical needs. This list is deliberately kept very short, in order to prevent a proliferation of NRM-producing countries. (60) The same approach could be taken to the cultivation of cannabis for the production of pharmaceutical products. Private foreign companies may, under circumstances permitted by their domestic laws, cultivate cannabis to provide the starting materials of a pharmaceutical development program. The resulting extracts or formulated finished products can then be imported into the U.S. for research (61) and, upon FDA approval, for marketing.

Impact of the CMCR Studies on Public Policy Questions

In its report, CMCR states that the results of its studies provide physicians and policy makers with "solid scientific data" to inform not only future medical research, but also "policy decisions." With regard to the
direction of future medical research. CMCR acknowledges that the current Phase II published studies have generated only the early stages of data elucidating the therapeutic potential of cannabis. If funding were available, CMCR would advance its program into the next stages, which would involve larger (Phase III) RCTs to develop “definitive data” on therapeutic merit; head-to-head comparisons of cannabis with other therapies; studies evaluating whether cannabis, when added to other analgesics, can allow for a reduced dose of those analgesics without sacrificing pain relief (e.g., opioid-sparing effects); research exploring the safety and effectiveness of alternative (non-smoked) delivery forms of cannabis and cannabis preparations; models of take-home treatment; long-term studies to assess emerging toxicities, stability of treatment effects and possible development of tolerance to treatment over time; and research into synthetic agents that would affect/modulate the endocannabinoid receptor system. CMCR did not elaborate on its statement that its current studies could inform “policy decisions.”

Certainly, the CMCR results could be used as promising data to encourage pharmaceutical companies and other sponsors of medication development to pursue the next stages of research outlined above. The results could also be used in a public policy discussion concerning the appropriateness of allocating scarce governmental funding resources to such research. What other “public policy” questions, however, could the CMCR data inform?

Contrary to the report’s statement, these studies, for the reasons stated above, do not constitute “reasonable evidence” that smoked cannabis is a “promising treatment” for certain painful conditions. In addition to the reasons outlined above, the studies obscure the fact that “cannabis” is not an identifiable, homogeneous material. Even in these studies, the cannabis potencies differed significantly. Outside the boundaries of government-approved studies utilizing NIDA cannabis in cannabis dispensaries, for example, the quality and composition of cannabis and cannabis-based products vary enormously. Cannabis may differ significantly in THC and other cannabinoid constituents, depending on the cannabis strain, as well as the cultivation, harvesting, and storage practices. As mentioned above, cannabis products may be contaminated with pesticides or dangerous microbes. Therefore, the CMCR studies do not provide evidence that cannabis—in any and all iterations—should be made available directly to patients without meeting the requirements of the FDA process.

The studies also do not meaningfully inform the debate over whether cannabis should be moved from Schedule I to Schedule II of the Controlled Substances Act. Substances in Schedule I have:

A high potential for abuse;
No currently accepted medical use in treatment in the U.S.; and
A lack of accepted safety for use under medical supervision. (62)

Substances in Schedule II have:
A high potential for abuse;
A currently accepted use in treatment in the US or a currently accepted medical use with severe restrictions; and
Abuse of the substance may lead to severe psychological or physiological dependence. (63)

In order for a substance to have a “currently accepted medical use” in the U.S., the following criteria must be met:

The drug’s chemistry must be known and reproducible;
There must be adequate safety studies;
There must be adequate and well-controlled studies proving efficacy;
The drug must be accepted by qualified experts; and
The scientific evidence must be widely available. (64)

The preliminary safety and efficacy data from the CMCR studies do not satisfy these demanding requirements; in light of the short duration and small sample size, coupled with the serious blinding issues, they cannot be said to be the type of pivotal studies contemplated by these criteria. Furthermore, even if cannabis were rescheduled, that would not make it available directly to patients by prescription. Physicians may prescribe, and pharmacists may dispense, only those medications that have received FDA marketing approval. The FDA does not approve active ingredients or bulk botanical material for prescription and marketing. As one cannabinoid expert has stated: “In order for a Schedule II substance to be made available by prescription, it must be contained in one or more specific dosage forms, as is the case for opium. Each and every one of such dosage forms must pass FDA muster.” (65) FDA approval of a specific cannabis Botanical Drug Product would constitute “currently accepted medical use in the US,” thereby allowing that product to be rescheduled into Schedule II or below. (66) Cannabis itself need not be rescheduled in order for that to occur.

Conclusion
CMCR is to be commended for having contributed to the scientific discussion concerning the therapeutic potential of the cannabis plant. It is important, too, to emphasize that these studies would not have been possible without the sponsorship and support of the State of California and numerous federal governmental agencies, including NIDA, DEA, and FDA. This fact demonstrates the falsity of the
argument of cannabis advocates that the federal government is actively suppressing cannabis-related research. Despite being the first RCTs in smoked cannabis in 20 years, the Phase II CAMCR studies do not offer data on quality, safety, and efficacy that are sufficiently robust either to have regulatory significance or to determine important public policy issues. With such short treatment duration, small patient numbers, and potential blinding failure, these studies should be characterized, at most, as preliminary guides for future research. The prevalence of CNS side effects, probable pulmonary damage with chronic use, and challenges of dose standardization, suggest that future research cannot focus productively on smoked cannabis. Vaporization of cannabis produces a sharp spike in THC blood levels and accompanying intoxication/abuse liability, as well as a still-unacceptable level of toxic byproducts. In sum, inhaled cannabis would seem to be a potential delivery system only for the small number of patients who suffer from intractable breakthrough pain and/or terminal disease, for whom a different risk/benefit calculus may be appropriate.

Further research into the direct use of inhaled cannabis herbal material, therefore, appears to be of limited usefulness. Government resources are scarce and precious. Accordingly, those resources should be devoted only to research likely to result in products that can achieve FDA approval and thereby become available to patients by prescription. Pharmaceutical companies, similarly, will sponsor only that research likely to produce definitive data on quality, safety, and efficacy and products with an acceptable risk/benefit profile in a broad patient population, which includes cannabis-naïve patients.

A look at modern history reveals that smoking cannabis for therapeutic purposes is largely an anachronism arising out of the general increase in the use of smoked cannabis in the 1960s. In 1839, William B. O'Shaughnessy introduced the Western world to the therapeutic properties of cannabis. In his studies, however, cannabis was formulated into tinctures and extracts; it was not smoked or inhaled. Unfortunately, the technology available throughout the 1800s and most of the 1900s was not adequate to permit these and other formulations to be developed in accordance with modern medical standards, and they gradually fell out of favor with the medical profession. That technology has now emerged, and many cannabis-derived and cannabinoid products are currently in various stages of development. These products will be comprised of various cannabinoids/ratios (rather than solely THC), may target CB2 rather than CB1 receptors (thereby minimizing psychoactivity), or modulate the endocannabinoid receptor system. Funding further studies into smoked cannabis would be retrogressive.

Author Information

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Andrea Grubb Barthwell, M.D., F.A.S.A.M., is the founder and Chief Executive Officer of the global health care and policy-consulting firm EMGlobal LLC and Director at Two Dreams Outer Banks Treatment Center. President George W. Bush nominated Dr. Barthwell in December 2001 to serve as Deputy Director for Demand Reduction in the Office of National Drug Control Policy (ONDCP). The United States Senate confirmed her nomination on January 28, 2002. As a member of the President's sub-cabinet, Dr. Barthwell was a principal advisor in the Executive Office of the President (EOP) on policies aimed at reducing the demand for illicit drugs.

During Dr. Barthwell's tenure, the Bush Administration widely publicized the science-based facts about the dangers of marijuana use and the harms of drug legalization. The Administration encouraged student drug testing as a deterrent to the initiation of drug use and as an early identification tool, and it promoted the expansion and improvement of drug courts. The ONDCP 25-Cities Initiative fostered local coordination of drug control efforts.

While serving in the EOP, Dr. Barthwell was an active member of the White House Task Force on Disadvantaged Youth and the White House Domestic Violence Working Group. The United States Senate confirmed her nomination on January 28, 2002. As a member of the President's sub-cabinet, Dr. Barthwell was a principal advisor in the Executive Office of the President (EOP) on policies aimed at reducing the demand for illicit drugs.

While serving in the EOP, Dr. Barthwell was an active member of the White House Task Force on Disadvantaged Youth and the White House Domestic Violence Working Group. She worked closely with the National Institute on Drug Abuse (NIDA) to define the scope of its Health Services Research portfolio.

Dr. Barthwell received a Bachelor of Arts degree in Psychology from Wesleyan University, where she serves on the Board of Trustees, and a Doctor of Medicine from the University of Michigan Medical School. Following post-graduate training at the University of Chicago and Northwestern University Medical Center, she began her practice in the Chicago area. Dr. Barthwell served as President of the Encounter Medical Group (EMG, an affiliate of EMGlobal), was a founding member of the Chicago Area AIDS Task Force, hosted a weekly local cable show on AIDS, and is a past president of the American Society of Addiction Medicine.

In 2003, Dr. Barthwell received the Betty Ford Award, given by the Association for Medical Education and Research in Substance Abuse. In 1997, Dr. Barthwell's peers named her one of the "Best Doctors in America" in addiction medicine.

Conflict of Interest Statement

I declare that I have no proprietary, financial, professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the position presented in, or the review of, the manuscript entitled Early Findings in Controlled Studies of Herbal Cannabis: A Review except for the following:

GW Pharma, consultant, stock
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1. Center for Medicinal Cannabis Research, Report to the Legislature and Governor of the State of California presenting findings pursuant to SB 847 which created the CMCR and provided state funding, www.cmcr.ucsd.edu (Feb. 11, 2010) (hereinafter CMCR Report).

2. Another clinical study has completed but the results have been published thus far only as an abstract. Corey-Bloom J et al. Short-Term Effects of Medicinal Cannabis on Spasticity in Multiple Sclerosis, www.cmcr.ucsd.edu. This randomized cross over study involved a small number of patients (30) and was of short duration (one cannabis or placebo cigarette smoked once daily for 3 days). The results showed statistically significant reduction in spasticity as measured on the Ashworth Scale and also pain reduction measured on a VAS scale. Since the full data have not been published, however, this study cannot be rigorously assessed in the present article.


   After demonstrating positive results in a Phase II study, dexamabinol (a synthetic cannabinoid) failed in Phase III, in which it was tested on 861 patients with head trauma in 86 trauma centers in 15 countries.

6. CMCR Report at p. 16.


10. The FDA generally will approve a product only for a specific type of neuropathic pain. This further reduces the regulatory significance of the study results.


12. Although patients were asked to refrain from cannabis use for a period of time before the study, the Abrams study did not take urine screens to confirm compliance. In that study, 78% of the patients were not merely cannabis-experienced, but were current cannabis users.


15. Many physicians blatantly fail to adhere to the standard of care in recommending cannabis to their patients. In California, despite the existence of strict guidelines promulgated by the state medical board, a substantial number of physicians advertise on the internet, accept cash only, and offer recommendations without following the basic professional requirements of good patient care: a physical examination, medical history, review of past medical treatments, development of a treatment plan, follow up and continuing oversight. Lopez S. A visit to the medical marijuana doctor. Los Angeles Times (Oct. 28, 2009).

16. The University of Mississippi has been analyzing the THC levels of seized cannabis for over 30 years. In that period, those levels (for domestic cannabis seizures) have increased from an average of 1.7% to 13%. See National Center for Natural Products Research, University of Mississippi, Quarterly Report: Potency Monitoring Project, Report 104 (Dec. 16, 2008-Mar. 15, 2009), www.whitehousedrugpolicy.gov/publications/pdf/mpmp_report_104.pdf.


19. In fact, 17 of 22 participants receiving THC identified their treatment correctly, as compared with 9 of 20 in the placebo group. It was unclear how many of the 17 were receiving THC capsules, which have a different onset of action and potentially a somewhat different side effect profile, which might have been more difficult for smoked cannabis-experienced patients to identify.


21. According to the authors, intradermal capsaicin results in a brief pain state that is replaced by an enlarged area of tactile allodynia and thermal hyperalgesia that persists for an extended interval.

22. The subjects must have used cannabis within the last six months. Furthermore, all subjects were exposed to a preliminary high-dose training session. Those who were unable to tolerate the highest dose of THC were excluded from the study.

23. As with the other CMCR analgesic studies, blinding was questionable. It is likely that cannabis experienced subjects could identify accurately when they were receiving placebo.

24. Patients in that study took 2 puffs (40 seconds between puffs) after baseline measurements, followed one hour later by 3 puffs, and after another hour, 4 puffs.


39. Interestingly, the plasma THC AUC was progressively lower at higher THC concentrations, and the investigators were uncertain whether this suggested higher bioavailability and/or more intensive puffing at lower THC potency. Despite the use of the standardized puff procedure, the investigators could not resolve this issue, since the number of puffs taken using vaporized cannabis tended to decrease with increasing THC potency, but this trend was not significant.
40. See also Miller J, Meuwsen I, ZumBrunnen T., de Vries M. A Phase I evaluation of pulmonary dronabinol administered via a pressurized metered dose inhaler in healthy volunteers. Paper presented at: American Academy of Neurology; April 14, 2005; Miami Beach, FL.


44. Author’s note: readers are reminded that no vaporizer has been tested or approved by the FDA as a medical device (see below).


Pawns of Pot: The Coexistence of Marijuana and Animal Crimes

Dr. Kris Otteman DVM, Director of Shelter Medicine, Oregon Humane Society and Emily Davidsohn, Oregon

Abstract

Animals are commonly exploited by the drug using community, and investigation of this exploitation often leads to discovery of drug crimes. Guard dogs are utilized in the production and trafficking business and may spend their lives on a chain. Companion animals can be exploited by dealers as a means to control their customers. Marijuana does not cause people to commit animal cruelty, but animal cruelty and marijuana crimes are undeniably connected.

A timeless human and canine duo is Shaggy and his partner in crime Scooby-Doo. This pair entertains children as well as adults around the country with their crazy behavior. However, their antics are construed differently by children and more mature audiences. An internet search of “Shaggy and Scooby” paired with any slang word for marijuana returns hundreds of links. Adults enjoy the marijuana innuendos that can be interpreted throughout any given episode, such as the constant craving for “Scooby Snacks,” the cloud of smoke billowing out of the Mystery Machine when the back doors open, and the constant paranoia both Shaggy and Scooby exhibit. Shaggy embodies the typical “stoner” portrayed most often through the media; a relaxed person who laughs easily and craves snack food often. This comedic duo, however, fails to demonstrate the reality of marijuana use and its link to animal abuse. The Massachusetts Society for the Prevention of Cruelty to Animals found that people who abuse animals are three times more likely to have a record for drug or disorderly conduct offenses. Marijuana does not cause people to commit animal cruelty, but animal cruelty and marijuana crimes are undeniably connected.

A common exploitation of animals in the marijuana production and trafficking business is the use of guard dogs. These dogs spend their life on a chain on drug producing property and alert their owners when strangers approach. This exploitation easily crosses over into the realm of animal cruelty when those dogs are not provided “minimum care” as defined under Oregon law. Oregon requires that animals, at a minimum, be provided with sufficient food, water, and shelter. Failing to provide minimum care to an animal constitutes neglect, which is a misdemeanor in Oregon.

Companion animals can also be exploited by dealers as a means to control their “customers.” Similar to circumstances in domestic violence situations, the dealer can threaten or actually injure a pet in order to get the animal’s owner to give them what they want. In Oregon this type of animal cruelty, known as Aggravated Animal Abuse, is a felony. Although this crime is more severe and the injuries are more apparent, it is difficult for humane officers to investigate because drug users are not likely to come forward with their injured animals for fear of incriminating themselves and their dealers, as well as the daunting repercussions that would ensue.

Cases in Oregon substantiate the argument that investigating an animal cruelty complaint can lead to a crime involving marijuana. In March of this year, in Benton County, Oregon, a search warrant executed in a marijuana investigation led to the discovery of a dog fighting ring. In that case fourteen pounds of marijuana were seized as well as fifteen dogs. In the fall of 2009 an 18 year old from Corvallis, Oregon participated in the torture of a duck using a homemade blowgun and razor-tipped arrows, ultimately killing the duck by wringing its neck. Five days after the duck killing, the teen was charged with manufacture of marijuana, delivery of marijuana, and possession of marijuana.

The coexistence of marijuana and animal abuse is also evident on a national scale. The now infamous Atlanta dog fighter, Michael Vick, tested positive for marijuana while under house arrest. Vick was responsible for severe cruelty to over fifty dogs, and the costs of rehabilitating the dogs in that case totaled $928,073. In 2009, Acea Schomaker of Lincoln, Nebraska trapped his six month old kitten in a homemade bong while he smoked in order to “keep it calm” because it was “high-strung.” As recently as March of 2010, a teen from North Carolina was charged with misdemeanor animal cruelty for feeding marijuana to a pit bull.

The presence of marijuana in animal cruelty incidents can be documented through cases over the span of many years. Just recently a young man rushed his large dog to the hospital at the Oregon Humane Society. The dog could not retain its balance and its personality was listless. The doctors treated the dog...
with fluids and ran some tests but the next morning the dog was fine, showing none of the symptoms from the previous day. The doctors treating this dog suspected that it had ingested marijuana and impressed upon its owner that it would be important for the veterinarians to know if that were the case in order to treat the dog accordingly. True to the trend in investigations like this, the owner refused to admit to anything. In this case the dog was lucky and it survived; so many other animals that fall victim to this trade do not.

On the surface Shaggy appears to be a good dog owner; Scooby is neutered, socialized, and well fed. However, if Shaggy is in fact the “stoner” adult fans make him out to be then, in reality, there is a chance that Scooby is being exploited and abused behind the closed doors of the Mystery Machine.

Author Information
Dr. Kris Otteman, DVM
Dr. Kris Otteman, OSU graduate 1986, College of Veterinary Medicine, has enjoyed a diverse and challenging career in veterinary medicine. Post graduate Dr. Otteman returned to her home town in southern Oregon to build a three doctor mixed animal practice. During this 8 year stint she focused on client relationships, quality medicine and tracking medical AND service outcomes while building a high quality full service community hospital.

In 1993 Dr. Otteman and her husband Jeff moved to Portland, Oregon to join a veterinary school classmate and founded what was then called VetSmart and is now known as Banfield, the Pet Hospital. While with Banfield, Dr. Otteman worked as Vice President of Team Resources and Education. She worked actively in doctor recruiting and retention, development of support systems for training and hospital openings and completed many special projects including the 1999 merger of Banfield with PetSmart Veterinary Services.

Dr. Otteman’s next career stop was with CAT Adoption Team - the Pacific Northwest’s largest non-profit, no-kill cat shelter where she and her team have built an on-site full service medical facility to serve the needs of the cats and kittens in their care. During her five year tenure, she led CAT in the housing of about 600 cats continuously and the adoption of over 3000 cats in 2006. The shelter has grown at least 30% per year for the past 5 years in terms of rescue, adoptions, collaboration and medical services.

For the past 2.5 years Dr. Otteman has served as Director of Shelter Medicine for Oregon Humane Society. Her role at OHS includes oversight of the medical center and investigations department. The medical center provides services for the 10,000 animals that come to the shelter per year and provides a required course for OSU’s College of Veterinary Medicine designed to provide valuable hands-on surgical and medical experience for 4th year veterinary students. The team handles animal neglect and abuse cases for the Portland community and collaborates with local law enforcement to address animal cases as well.

Dr. Otteman and family - including husband Jeff and children Jessica, Jarrett, and Kameron - make their home in Camas, Washington with their dogs Rose and Sky, cats Doodle, Pepper and Dolly and two horses.

References
2. In 2005, the Ninth Circuit affirmed a decision that found police officers in violation of the Fourth Amendment when they shot and killed multiple guard dogs seconds before executing a search warrant in an investigation of the Hells Angels gang. San Jose Charter of the Hells Angels Motorcycle Club v. City of San Jose, 402 F.3d 962 (9th Cir. 2005). The officers had prior knowledge that the dogs were present and made no arrangements for them when planning the raid, other than to shoot them. This case has been positively referenced by several courts since it was published and simply emphasizes the need for law enforcement to work together with humane investigators when animal are involved in a case.
5. Studies have established a link between animal abuse and domestic violence. In a survey done by the Wisconsin Community Coalition Against Violence, of the women seeking domestic violence prevention services, 80% had experienced their partners committing cruelty to animals. Frank R. Ascione, Claudia V. Weber & David S. Wood, The Abuse of Animals and Domestic Violence: A National Survey of Shelters for Women who are Battered, 5 Society and Animals 205, 208 (1997). In a survey of animal owning families in which physical child abuse took place 88% reported that animal abuse also took place. Elizabeth DeViney, Jeffery Dickert & Randall Lockwood, The Care of Pets Within Child Abusing Families, 4 International Journal for the Study of Animal Problems 321, 327 (1983).


Medical Marijuana Laws: Obstructing Congress?
Paula A. Barran, A.B. M.A., Ph.D., J.D., MBA

Abstract
A recent decision from the Oregon Supreme Court casts a new light on state laws authorizing the use of medical marijuana, particularly in the workplace. Its helpful discussion includes a warning that state laws that put themselves on a collision course with federal law are invalid from the outset.

Oregon’s medical marijuana law was introduced by voter initiative in 1998. It established a state registry program intended to protect eligible users who are resident in the state from state criminal prosecution for the production, possession or delivery of marijuana. Applicants must have a qualifying debilitating medical condition verified by an attending physician; conditions can be objective or subjective including “severe pain.”(1) The statute is codified at DRS 475.300-345, and administrative rules appear at OAR 333-008-0000 to 333-08­0120. Over the decade from April 2000 to April 2010 the number of authorized cardholders grew from 500 to 32,929, with an additional 16,922 cards issued to caregivers as of April 2010. (2)

At first blush the law did not appear to require employers to adjust their substance abuse policies. Under federal and state disability law,(3) employers are generally required to adjust policies to accommodate employees with disabilities to the extent such adjustments can be made without undue hardship. Under federal disability law, however, accommodation of marijuana use or users could not be required because marijuana is a Schedule I drug under the federal Controlled Substances Act, 21 USC 812(c), and therefore wholly illegal. Federal law permits adverse actions taken against employees or applicants based on their current illegal use of drugs. State law, however, was apparently not as clear as it initially seemed to employers.

The Oregon Medical Marijuana Act (ORS 475.340) provides that nothing in the law shall be construed to require “an employer to accommodate the medical use of marijuana in any workplace.” However, “use” is defined to mean production, possession, delivery, or administration. In the first appellate decision that attempted to define an employer’s obligation, the Oregon Court of Appeals concluded that an employee who used the drug outside of the physical workplace was not using it in the workplace, and therefore an employer might be obligated to accommodate the user by adjusting its substance abuse policies (Washburn v. Columbia Forest Products, Inc. 197 Or.App. 104, 112, 104 P.3d 609, 613 (2005)). Washburn was later overturned by the Oregon Supreme Court, but on a conclusion that the employee did not have a disability in the first place. To be sure, the Court of Appeals recognized that the issue of accommodating a possibly impairing drug presented some issues for employers:

“However, whether defendant must accommodate plaintiff in these circumstances remains a matter for the trial court. ORS 475.340(2) makes clear that employers are not required to accommodate certain specified things. That the medical use of marijuana in the workplace need not be accommodated under ORS 475.340(2) does not per se establish, however, that, under all circumstances, an employee’s medical use of marijuana must be accommodated by an employer. In other words, our conclusion that ORS 475.340(2) does not apply here does not mean that plaintiff is automatically entitled, under Oregon disability law, to the accommodation that he requested. That question remains to be resolved by the trial court, applying pertinent aspects of Oregon disability law to the particular facts. Although we express no opinion on the matter, we note that defendant’s concern about employees coming to work under the influence of marijuana might provide, under some circumstances, justification for not accommodating plaintiff given various provisions of Oregon disability law, including the concepts of reasonable accommodation, undue hardship, and qualification for a position.” Washburn v. Columbia Forest Products, Inc. 197 Or.App. 104, 116-117.

Because the Supreme Court overruled the Court of Appeals on the issue of whether the employee had a disability, the analysis of whether an employer was required to accommodate users remained intact. That set the stage for Emerald Steel Fabricators, Inc. v. Bureau of Labor and Industries, 345 Or. 157 (2010).

Emerald Steel does structural and mechanical steel fabrication and machining. In 2003 the company hired a temporary employee who was an authorized user under the state program. He used the drug daily, though never on the company’s premises. The question of his drug use arose when, after several weeks of satisfactory employment, he was about to be offered regular employment. That, however, would require him to pass a drug test so he disclosed his drug use and was discharged; the employer did not discuss possible accommodations with him. (4) The case had a complicated procedural path from the
administrative agency, Oregon's Bureau of Labor and Industries, to the Oregon Supreme Court but the state's highest court did not permit claimed procedural irregularities to get in the way of issuing a dispositive ruling on the state's marijuana law. Two other states, California and Washington, had ruled that employers are not required to accommodate users under those state laws, but in both cases the decisions were made by interpreting the text of those state laws. The Oregon court focused its analysis not on the structure of the state law, but instead on how the state could not have such a law in light of contrary federal drug policy. That requires a Constitutional analysis.

The Constitution's Supremacy Clause makes clear that in the case of conflict between federal law and state law, federal law prevails or preempts state law. That can happen, for example, in the case of a federal law that expressly displaces inconsistent state law, or in the case of a federal law intended to "occupy the field," or in a case of actual conflict resulting in the physical inability of a person to comply with both federal and state law. Or, preemption can be implied where state law stands as an obstacle to the accomplishment and execution of the full purpose and objectives of Congress. In such a case, state law must fall so that the Congressional objectives can be met. The Oregon court resolved the preemption analysis on that point, stating that "affirmatively authorizing a use that federal law prohibits stands as an obstacle to the implementation and execution of the full purposes and objectives of the Controlled Substances Act" by affirmatively authorizing the very conduct that federal law prohibits. That means that any state provision that attempts to authorize the use of marijuana is preempted and without effect. This is so-called "obstacle preemption."

The employee's arguments shattered against that analysis because he was utterly dependent on arguing that he was not engaging in the illegal use of drugs, for which he had to argue that he was affirmatively authorized to use marijuana, something a state cannot do. As a result, no Oregon employer is required to accommodate a medical marijuana user regardless of where he uses the drug, and no Oregon employer is required to engage in an interactive process about modifying a substance abuse program.

The decision is broader than the employment context however, and it bears consideration in looking at the legality of medical marijuana laws generally. A state is not required to apply its criminal laws to marijuana. That follows from a Constitutional principle that makes clear that Congress lacks the authority to criminalize conduct that a state chooses to leave unregulated by state law. So, under this reasoning, any state could decide not to criminalize marijuana under state law. That is not, however, the same thing as telling individuals they are permitted to use the drug.

Much of the Emerald Steel opinion is based on the thought that the Oregon state law attempted to authorize or permit medical marijuana use (and is therefore subject to obstacle preemption); the question it leaves is whether the law can be rewritten to avoid obstacle preemption and additionally impose accommodation obligations on employers. Though it seems unlikely, this has been an area in which proponents have shown themselves to be astonishingly creative.

Oregon has, in its own way, been ground zero for the battle to legalize marijuana. One result of Emerald Steel v. Bureau of Labor and Industries may be that the battle moves to other states. In that case, the decision is a primer on the force of obstacle preemption. The real question may still be whether Congress can be persuaded to reschedule the drug.

Author Information
Paula A. Barran, A.B. M.A., Ph.D., J.D., MBA, is a founding partner of the Oregon based labor and employment law firm Barran Liebman LLP which represents employers in labor and employment matters. She is admitted to practice before the state and federal courts in Oregon and Washington, and is admitted to the U.S. Supreme Court. Ms. Barran has provided legal advice and training for employers and has written extensively on legal issues related to substance abuse in the workplace. She filed a brief amicus curiae in the Oregon case Emerald Steel v. Bureau of Labor and Industries which is the subject of this article.

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1. OAR 333-008-0010.
3. The accommodation obligation is imposed by the federal Americans with Disabilities Act, 42 USC §12112 and by Oregon state law at ORS 659A.112 and 659A.118.
4. State and federal disability law generally interpret the accommodation requirement to include an obligation to engage in a meaningful interactive process to discuss a reasonable accommodation for qualified employees with a disability.
The Cost of Failure
Ian Oliver

Abstract
Failure to deal with the Afghan opium trade appropriately and urgently will have a severe and lasting impact on most people in ways that may not be immediately apparent to them and will almost certainly diminish the quality of life for many.

Addiction Crime and Insurgency
UNODC(1) published an important document late in 2009(2) which received little media attention but which contains a significant analysis of the global consequences flowing from the Afghan opium trade. Failure to deal with that trade appropriately and urgently will have a severe and lasting impact on most people in ways that may not be immediately apparent to them and will almost certainly diminish the quality of life for many. Regrettably, numerous politicians and journalists have failed to grasp the significance of this report which has some parallels in other drug producing areas such as Colombia and Mexico which also have been described as Narco-States, but in the case of Afghanistan in particular they have chosen to focus on the counter-insurgency almost to the exclusion of the failure to follow adequate counter-narcotics policies in a comprehensive and coordinated manner.

It is extremely difficult to gain accurate statistics relating to the consequences of the illicit drug trade and many of the figures published can only be described as “informed guesstimates”. However, the following information in the UNODC report is significant and alarming and must not be ignored:

An annually more people die from Afghan opium and its derivatives than from any other drug; 10,000 die from heroin overdoses annually in NATO countries = 5 x the number of military deaths in Afghanistan since 2001. (Military action has been responsible for an untold but extremely high number of civilian deaths described as ‘collateral damage’.)

In the Russian Federation addiction has multiplied by 10 in the last decade; 75-80 tons of Afghan heroin is consumed annually. More Russian people die from drugs estimated at 30-40,000 p.a. than the total number of Red Army soldiers killed during the 7 year Soviet campaign in Afghanistan.

Iran, one of Afghanistan’s immediate neighbours, has at least 1 million addicts despite major efforts to combat trafficking and faces the world’s most serious opiates addiction problem.

Central Asia is now a major consumer of Afghan heroin that has resulted in an HIV epidemic caused by injecting drug use. Central Asia is also extremely vulnerable to the activities of terrorist groups funded by drugs money.

Why Is There an International Presence in Afghanistan?
Afghanistan produces over 90% of the world’s heroin supply and that yields approximately 52% of the country’s GDP; it is severely dysfunctional and beset by problems relating to weaknesses in both Central and Provincial Government which are compounded by systemic corruption at all levels and in almost all aspects of society. The insurgency by the Taliban has intensified to such an extent that military experts are indicating that it is of a type that cannot be won in the same way as a conventional war(3).

Questions that are often posed but seldom answered in a comprehensive manner are: “Why are we in Afghanistan?” and “Is that country worth the cost in terms of lives and expense?” There are many nations represented in Afghanistan under NATO as part of the ISAF (International Security Assistance Force) but not all have the same commitment and some are seeking an exit strategy that will enable them to leave without losing face.

There is a growing loss of public confidence which has resulted in a widespread call to abandon the mission and to “bring the troops home”; in the UK a public opinion poll in October 2009 indicated that 56% of those questioned wanted an end to military involvement in Afghanistan(4); in the US the statistics were similar to those of the UK. Unfortunately, many of those who expressed an opinion did not appear to have a comprehensive knowledge of the situation upon which to base a judgement.

Other pressing questions that politicians must address if defeat and disaster in that part of the world are to be avoided is: Why has this been allowed to happen? Why are the wealthiest and most powerful nations failing to deal with a problem that has the potential to become a global disaster and why are the ordinary
Afghan nationals being exposed to such chaos and failure? It is apparent that NATO allies have failed to conduct themselves in a meaningful and effective manner.

A “Good and Just War”

After the tragedy of 9/11 the US attacked Afghanistan because it was the haven of Al Q’aeda and Osama bin Laden, and thus posed a serious global terrorist threat; this was perceived to be a ‘good and just war’. However, the ‘good war’ has come to be regarded as a much more complex situation that is haemorrhaging both lives and support and is seen to be a prop for a barely credible Government that is universally regarded to be weak, self-serving and corrupt(5). Bin Laden and his cohorts are thought to have crossed the Pakistan border and are believed to be sheltering and conducting their lethal operations from the Federally Administered Tribal Areas (FATA) which are difficult to access and are virtually ungoverned. Nevertheless, Al Q’aeda could just as easily operate from a dozen other locations around the world and is suspected of running terrorist franchises in Sudan, Yemen, Somalia and Eritrea for example. At any time and with little difficulty Al Q’aeda could relocate.

The vague reason given for the presence in Afghanistan is usually that it is part of the war on terror and that a military effort is necessary to defeat the Taliban and thus make the likelihood of terror attacks less likely. We read of the need for more troops and the difficulty of fighting an enemy that is not easily recognised and operates in an unconventional and non-military manner. The distinction between terrorism and insurgency is often blurred, and the reasoning behind a war on terror and counter-insurgency is seldom explained. The need for effective counter-narcotics policies is rarely mentioned in the popular media.

Simply put, counter terrorism is a policy of identifying and eliminating known terrorists by either killing them or detaining them so that they are unable to continue as a threat. Counter-insurgency is more complex and has more to do with supporting a legitimate Government and ensuring that it is able to provide good governance, abide by the rule of law and progress to democracy. Failure to address insurgency risks the fall of the Government and eventual anarchy with all of the dangers that this can pose to the region. In the case of Afghanistan this could result in a return of Al Q’aeda or more likely, the destabilisation of Pakistan and its eventual collapse. Pakistan is a nuclear state with between 25-50 warheads, and the risk that these could fall into the hands of terrorists is unlikely but unthinkable. A significant problem is that the Afghan Government is not seen to be legitimate, and thus the NATO ‘support’ for a corrupt regime diminishes any respect that local nationals may have for the intervention; this is compounded by the tragedy of “collateral damage”. ISAF is perceived by some to be pursuing self-interest and not supporting the innocent nationals who are as much victims as beneficiaries.

Corruption

The tragedy of Afghanistan is that the Government is weak, and its legitimacy, particularly after the farce of the 2009 election, is in question. Corruption is endemic, and its elimination is hugely difficult if not impossible; thus the confidence of the Afghan nationals is severely dented both in the so-called democratic government and in those NATO allies who are equally regarded with suspicion because of their support for it. In other words, the public trust is absent, and the winning of hearts and minds of the population which is a normal part of counter-insurgency campaigns has been neglected because of the emphasis on the war on terror(6). Without public confidence and support both counter-terrorist and counter-insurgency campaigns are vulnerable to failure for the reason that those who are able to identify the terrorists in their midst are reluctant to give this information because they do not trust ISAF to protect them and because they fear the Taliban reprisals. A democratic government is a meaningless concept when corruption and collateral damage from clumsy counter-terrorist actions prevail. More innocent Afghans are believed by the locals to be killed than terrorists or Taliban.

Global Problems

However, CT and counter-insurgency are only a part of the reason why Afghanistan is a global problem. The continuing production of the opium crop has presented the world with significant problems that are seldom mentioned but which are equally as important as “the war on terror” In 2006 Afghanistan produced 6100 tons of opium(7). Figures produced at the end of August 2007 indicated a significant increase (34%) in opium production compared with the previous year, with 193,000 hectares under opium poppy cultivation (+17%) resulting in 8200 tons of opium(8). In 2008 estimated production was slightly less at 7,700 tons(9). In 2009 it was estimated at 6900 tons. UNODC estimates that 2/3 of opium is transformed into heroin in country. In 2009 it was estimated that 12,000 tons of opium were stockpied, which represents two years’ supply, in unknown locations; only 10% is estimated with Afghan farmers, the rest is likely with criminal traffickers and insurgent groups. (10)

Such amounts represent an enormous social problem, for the abuse of opium and the derivative is directly connected to major global issues:

Public Health. The spread of HIV/AIDS, hepatitis C and other blood-borne diseases, which have been classified by the World Health Organisation as global pandemics, and the spread of associated sexually transmitted infections and chronic drug dependency arise from the abuse of drugs.
Organised crime. This includes, for example, trafficking in humans, arms smuggling and money laundering which has a profound impact on global economics. National police forces often indicate that between 50-70% of crimes committed worldwide are in some way drug related.

International terrorism. Many terrorist groups are thought to be in receipt of some of their funding from drug trafficking and associated crimes.

Transnational threat/International Security: The Afghan opiate trade represents a transnational threat not only to the countries on the trafficking routes and final destinations, but also as a factor of international insecurity. It threatens the stability of governments and financial systems, funds insurgency and the arms trade and undermines social stability.

One of the disturbing but equally neglected comments in the UNODC report refers to developing problems in Central Asia.

Drug money is funding insurgency; i.e., Islamic Movement of Uzbekistan (IMU), Islamic Party of Turkmensnistan, East Turkmen Liberation Organisation and other extremist groups.

The Silk Route is now the Heroin Route of death, destruction and violence in one of the world’s most volatile and strategic regions, and the “perfect storm” that has been swirling round the Afghan/Pakistan border for years is now heading for Central Asia, creating a huge threat to the massive energy reserves there, particularly in Turkmenistan.

The reality of the situation in all major drug producing countries is that the drug lords have become so powerful that they are able either to buy support from impoverished communities as has been the case in Colombia and Mexico, or they use extremely brutal methods to undermine government, corrupt officials and profit from massive tax free incomes that have to be weighed rather than counted. In Afghanistan the country is overwhelmed by weak and unreliable government, drug incentified warlords and the international presence is regarded as being ineffective and unlikely to succeed. The counter narcotics activities have thus far produced little in the way of supply reduction, and despite extravagant claims about the number of Provinces that are drug free, those in the South of the country continue to produce more than enough opium crops to meet global demand well into the foreseeable future. Opium reduction has not been the priority, and law enforcement agencies within Afghanistan and in the surrounding region have managed only to interdict less than 5% of production. The Afghan drug trade is thriving to great global detriment.

Counter-Narcotics Policy

In terms of effective supply reduction the most efficient law enforcement agencies are able to interdict at best 20% of the product, and in most cases the percentage seizures are considerably lower than that. In Afghanistan seizures are below 2%,(12) and in the surrounding region the figures are not much better, not necessarily because there is not a willingness to address the problem but because there is little effective professionally competent coordination, unnecessary competition between some agencies, lack of funding, equipment and trained personnel, a considerable degree of corruption and a UN agency that is operating on a slender budget controlled by donors rather than an agreed internationally funded commitment to reduce the supply of drugs and diminish demand effectively. The UN policy is one of striking a balance between supply and demand reduction and seeking to diminish the harms that are associated with illicit drugs (13).

The question that must be answered is “How can the illicit drugs problem be addressed in a more positive and effective manner?” Despite the calls for legalisation that are heard more and more frequently, there is little doubt that over ‘00 years of anti-drug policies have been effective and that the global situation would have been much worse without the commitment and efforts of many dedicated agencies and individuals (14). There is a clear realisation that the illicit drug trade is hugely damaging, but it is equally clear that much more needs to be done in an internationally coordinated way to reduce the harm.

It is obvious that law enforcement alone is never likely to be able to deal with the problem and that education against the widespread demand for drugs must be a major priority combined with all of the other ancillary actions that help people to deal with dependency where it occurs. A decade ago, few would have anticipated the widespread reaction against smoking in some regions; similarly, although there are huge problems associated with the excessive consumption of alcohol, nevertheless there is a growing awareness of the need to counter that excess. For example, in the UK drink driving is regarded as anti-social in a way that was not apparent earlier. With properly coordinated education policies it is possible that a similar outcome against the misuse of drugs may occur.

Lack of Awareness

One of the reasons for much of the failure is that there is widespread public ignorance about the extent of the global problems. Most people are unaware of the ways in which they can be affected by drug trafficking unless they have the misfortune to be confronted with a family problem involving drugs. The fear of terrorism is much greater than the fear of being affected by drug trafficking. The recent example of the attempted destruction of an aircraft en route to Detroit by a suicide bomber with explosives sewn into his clothing has resulted in Governments’ promising costly body scanners at major airports, but there is little reaction to the demand for X-ray machines at border crossings where multi-ton shipments of drugs are transiting on a daily basis(15). The failure to interdict illicit drug and chemical shipments has just as
serious consequences as a suicide bomber, but the security priorities are loaded more in favour of the so-called ‘war on terror’, almost guaranteeing failure to combat the global drug problems.

**Time for a new UN Convention on Drugs**

Drug money has enabled organised criminals to finance the take over of whole regions and to bring about political paralysis, institutional weakness, widespread venality and corruption, leading to the failure of effective counter-narcotic policies with crippling global effects: the drug lords have dominated whole countries. Examples of these extremes are daily apparent in Latin America and Central Asia, and the impact and consequences beyond these regions are severe and devastating. Thus, a much more comprehensive international response is required. Not only is greater political and public awareness essential but also international collaboration on a scale not seen before must be developed. The world must address this problem with a similar passion to that which is applied to the dangers of global warming, for example, if any real progress is to be made. Where incompetence prevails, professional support must be supplied, and it is surely time to consider another International Convention to achieve more efficiency and cooperation in addressing this multi-faceted problem. It is no longer good enough to leave the initiative to an underfunded, donor driven organisation like UNODC. Greater support and guaranteed funding must be provided to accomplish greater efficiency and effectiveness for this organisation. Without a major change in priorities the world will suffer increased ravages caused by drug trafficking indefinitely.

**Author Information**

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5. For example see -The Guardian 10 01 2010 Karzai selects sacked minister for key post in Afghanistan’s new cabinet Zarar Ahmed Moqbel, accused of corruption and incompetence at interior ministry, offered anti-drugs role.

6. Assessments in January 2010 indicated a slight improvement in public attitudes towards the presence of ISAF but it was still lower than 50%, the Afghan Centre for Socio-Economic and Opinion Research.

7. World Drug Report 2007 (UN Publication, Sales No E.07.XII.5)


9. UNODC Afghanistan Opium Survey 2008


15. Christmas Day attempt to destroy plane bound from Amsterdam to Detroit by Umar Farouk Abdulmutallab.