Therapeutic Cannabis (Marijuana) as an Antiemetic and Appetite Stimulant in Persons with Acquired Immunodeficiency Syndrome (AIDS)

Richard E. Bayer

SUMMARY. Acquired immunodeficiency syndrome (AIDS) is a common cause of death among young adults in the USA. AIDS wasting syndrome is the most common clinical presentation of AIDS. Antiretroviral drug therapy has improved the prognosis of persons with AIDS, but also contributed side effects, particularly nausea and anorexia. Case reports demonstrate persons with AIDS use cannabis as medicine to control nausea, anorexia, and pain, while noting improved mood. Recent clinical research comparing smoked cannabis to oral dronabinol (synthetic THC or Marinol) demonstrates no immune dysfunction in persons using cannabinoids and positive weight gain when cannabinoids are compared to placebo. Harm reduction research indicates that heating cannabis to temperatures well below combustion ("vaporization") yields active cannabinoids and a significant reduction or elimination of toxics (benzene, toluene, naphthalene, carbon monoxide, and tars) commonly found in smoked cannabis. More research is indicated but vaporizers appear to substantially reduce what is widely perceived as the leading health risk of cannabis, namely respiratory damage from smoking. In spite of a need for more rigorous scientifically controlled research, an increasing num-

Richard E. Bayer, MD, FACP, is board certified in internal medicine and a Fellow in the American College of Physicians–American Society of Internal Medicine. He lives in Portland, Oregon (E-mail: ricbayer@home.com).

[Haworth co-indexing entry note]: "Therapeutic Cannabis (Marijuana) as an Antiemetic and Appetite Stimulant in Persons with Acquired Immunodeficiency Syndrome (AIDS)." Bayer, Richard E. Co-published simultaneously in *Journal of Cannabis Therapeutics* (The Haworth Integrative Healing Press, an imprint of The Haworth Press, Inc.) Vol. 1, No. 3/4, 2001, pp. 5-16; and: *Cannabis Therapeutics in HIV/AIDS* (ed: Ethan Russo) The Haworth Integrative Healing Press, an imprint of The Haworth Press, Inc., 2001, pp. 5-16. Single or multiple copies of this article are available for a fee from The Haworth Document Delivery Service [1-800-342-9678, 9:00 a.m. - 5:00 p.m. (EST). E-mail address: getinfo@haworthpressinc.com].

ber of persons with AIDS are using cannabis to control nausea, increase appetite, promote weight gain, decrease pain, and improve mood.

KEYWORDS. Cannabis, marijuana, dronabinol, THC, Marinol , AIDS, HIV, harm reduction, immunodeficiency, vaporization, vaporizer, wasting, anorexia, nausea, appetite, pain

AIDS IN THE UNITED STATES

The history of acquired immunodeficiency syndrome (AIDS) began in 1981 when the first five cases of AIDS were reported in the United States. Shortly thereafter, the disease was categorized as an epidemic. In 1984, the etiology of AIDS was found to be an RNA virus called human immunodeficiency virus (HIV). In 1985, a sensitive enzyme-linked immunosorbent assay (ELISA) was developed, and clinical testing for antibodies to HIV became possible.

By 1993, the United States Department of Health and Human Services (DHHS) listed AIDS as the most common cause of death among men aged 25 to 44 years (US DHHS 1995). By the end of 1998, the United States Centers for Disease Control and Prevention (CDC) estimated that nearly one million Americans had contracted HIV infection, one-third of whom were unaware of their affliction (CDC 1999).

By the end of 1999, a total of 733,374 cases of affected persons with AIDS (PWAs) had been reported to the CDC. Demographics revealed that 82% were men, and 18% were women. Only 1% were children less than 13 years of age. Forty-three percent of persons with AIDS were white, 37% black, 18% Hispanic, < 1% Asians and Pacific Islanders, and < 1% American Indians and Alaska Natives. Forty-seven percent of persons with AIDS were men who have sex with men, 25% were injection drug users, 10% were persons infected heterosexually, and 2% were persons infected through blood or blood products (CDC 1999).

HIV destroys CD4+ T lymphocytes, and laboratory measurements of "T Cells" indicate immune system damage. More recently, the technology of polymerase chain reaction has allowed the actual measurement of HIV RNA blood levels or "viral load" and this parameter is increasingly utilized clinically to help determine when to initiate and modify antiretroviral therapies (Saag et al. 1996).

The surveillance conditions for diagnosis of severe HIV disease or AIDS were originally defined by the CDC prior to the identification of HIV as the etiologic agent. Although surveillance criteria have changed over the years, the clinician should view HIV disease as a spectrum of illness that ranges from a primary infection, to the asymptomatic infected, to advanced disease or AIDS, which causes marked morbidity and mortality (Fauci et al. 2000).

For surveillance purposes, AIDS is defined by indicator diseases such as the AIDS wasting syndrome, *Pneumocystis carinii* pneumonia, or Kaposi's sarcoma in young adults. AIDS is identified in asymptomatic persons by laboratory tests such as CD4+ T lymphocyte counts of less than 200/mcl or a CD4+ T lymphocyte percent of total lymphocytes less than 14 (CDC 1992). Since 1992, scientists have estimated that about half the people with HIV develop AIDS within 10 years after infection, but this time varies greatly from person to person (CDC 2000).

AIDS wasting syndrome is an AIDS-defining condition, identified when a patient manifests involuntary weight loss of more than 10% associated with intermittent or constant fever and diarrhea or fatigue for more than 30 days in the absence of a non-HIV explanation. It is the initial AIDS-defining illness in 9% of patients with AIDS in the United States and thus is currently the leading initial clinical indication of AIDS (Fauci et al. 2000).

Standard antiretroviral treatments for HIV infection, such as zidovudine (AZT or ZVD) or lamivudine (3TC) can cause significant nausea. Treated patients often have difficulty maintaining baseline weight. In 1996, the United States Food and Drug Administration (FDA) approved the use of protease inhibitors, which when taken in combination with standard antiretroviral drugs can reduce viral load and markedly slow the progression of HIV/AIDS disease (CDC 1998).

A concern for many who take protease inhibitors is that the side effects can be more severe than those associated with standard antiretroviral drugs. As occurs with some persons receiving chemotherapy for cancer, patients with AIDS often find that the medicines they need to sustain their lives can produce side effects so intolerable that they become reluctant to maintain their treatments, or fail to take treatment regularly. This can be dangerous, for failure to maintain a regular medication schedule can lead to the development of treatment-resistant strains of HIV (CDC 2000).

CANNABINOIDS AS ANTIEMETIC AND APPETITE STIMULANT IN AIDS WASTING SYNDROME

Ethnobotany documents important medical uses of herbs, including cannabis (Russo 2000), but the first modern placebo-controlled trial that demonstrated efficacy of THC as an antiemetic in cancer chemotherapy was published

in 1975 (Sallan et al. 1975). In the 1970's and 1980's, six American states engaged in clinical trials of smoked cannabis and oral THC to control nausea and emesis from cancer chemotherapy. These trials involved 748 persons who smoked cannabis and 345 patients who used oral THC capsules, and demonstrated that smoked marijuana can be a very successful treatment for nausea and vomiting following cancer chemotherapy (Musty and Rossi, 2001). A synergistic relationship of the combination of THC and the antiemetic prochloperazine was more effective than either drug alone, as suggested by past studies (Hollister 2001). These are important findings, because our most efficacious modern antiemetics, including well-tolerated serotonin antagonists like ondansetron (Zofran), promise only about 80% efficacy (Zofran package insert). In other words, in one out of every five treatment episodes, our best antiemetics demonstrate no efficacy. Although no studies have been done comparing ondansetron to cannabis, patients would be well served by studying efficacy of cannabinoids alone, or in combination with other antiemetics in persons who currently cannot control nausea and emesis with modern serotonin antagonists like ondansetron.

In 1992, the FDA approved the use of Marinol (dronabinol or synthetic THC) for the treatment of AIDS wasting syndrome. Dronabinol has been shown to stimulate appetite, promote weight gain and improve mood in persons with AIDS in short term studies (Beal et al. 1995), while maintaining effectiveness and safety over during a longer (12 month) study (Beal et al. 1997). Marinol is usually prescribed at a dose of 2.5 mg by mouth 2 to 3 times daily before meals to improve appetite (Roxane Labs 1999). Although the Drug Enforcement Administration (DEA) originally listed dronabinol as a Schedule II drug, it was recently moved to Schedule III, which may increase the likelihood of American physicians prescribing it.

While dronabinol is the only cannabinoid that physicians can legally prescribe in the USA, it remains extremely expensive (often $600 to $1200 US each month), has a slow onset of action because it can only be taken orally, and has a relatively high incidence of side effects (particularly dysphoria), so that many patients prefer herbal cannabis. As is the case in many cancer patients, people with AIDS frequently expressed a preference for smoked cannabis over dronabinol because it provides results with smaller doses and fewer undesirable side effects. In addition, some persons report better symptom control consuming cannabis rather than dronabinol, which may be related to the additional cannabinoids, such as cannabidiol, that are found in cannabis but not in dronabinol (Grinspoon et al. 1997).

Other agents used to treat AIDS wasting include anabolic steroid hormones such as the progesterone megestrol acetate (Megace), tested alone and in combination with dronabinol (Wright et al. 1997), and androgenic steroids such as oral oxandrolone (Berger et al. 1996), or intramuscular testosterone

enanthate (Grinspoon et al. 1998). More extreme options include human growth hormone, which can cost over $150 daily, and total parenteral nutrition, which is expensive, invasive, and medically risky (Krampf 1997). The above treatments have shown some successes, but all have drawbacks, and thus treatment must be individualized to meet each patient's needs.

For a more comprehensive discussion of cannabis as antiemetic and appetite stimulant, readers are referred to Leo Hollister's review, "Marijuana (Cannabis) as Medicine." in the charter issue of *Journal of Cannabis Therapeutics* (Hollister 2001). For a comprehensive clinical discussion of HIV disease, readers are referred to an internal medicine textbook such as *Harrison's Principles of Internal Medicine* (Fauci et al. 2000).

CASE REPORTS (THE PATIENTS' PERSPECTIVE)

There are many case reports from persons with AIDS who benefit from adjunctive use of cannabis to stimulate appetite, control pain, and improve quality of life (Zimmerman et al. 1998; Grinspoon et al. 1997; Krampf 1997).

Patient S.C. describes:

> Within eight months, beginning in 1995, I was hospitalized three times for pneumonia and sinus infection. I'd been feeling pain and congestion in my chest, and then I began having trouble breathing. I was still taking AZT and they put me on antibiotics and prednisone for the pneumonia. It was so difficult for me to swallow the pills. Almost immediately after taking them, a violent nausea would set in. I couldn't eat or hold down any food. After a few weeks of this, my weight dropped down from 150 to 115 pounds.
>
> I did what I could during that time to get relief. That's when I realized, almost coincidentally, that marijuana alleviated my nausea. When I took a few hits of marijuana, I felt better within five to fifteen minutes. It also gave me back my appetite. In a short time, I gained back almost all my weight, and I began feeling much healthier.
>
> Just as importantly, my marijuana use would help me deal with the new drugs I'd soon be taking. They began combining AZT and another anti-viral drug, called 3TC, with a protease inhibitor called Crixivan . I did notice a gradual improvement in my health, and my T-cell count started coming up. But the nausea I experienced was worse than anything I had felt with AZT alone. It was indescribable. It didn't seem like I had many choices though. I knew I needed these medicines to stay alive, even though the nausea they caused me was unbearable. So, I kept taking them, along with marijuana to control the nausea.

> I have to tell you that I sincerely doubt I could have continued the treatment without marijuana. This is very important because, while there is no cure for AIDS, I believe these medications have actually reversed my disease and saved my life. What marijuana did, aside from making me feel better, was make these drugs tolerable for me.
>
> Right now, my weight is up to 148 pounds. I take 16 pills a day, and I smoke marijuana before each meal to quell the nausea and stimulate my appetite. About one-half hour before I want to eat, I take three or four puffs. Usually, in about 20 minutes, I get the munchies and then I want to eat. It's still a struggle sometimes, but I'm healthier, stronger, and I enjoy living. (Zimmerman et al. 1998, pp. 48-49)

Patient G.S. summarizes his experience:

> Even if I was not recovering [from AIDS], the relief would have been worth any bad effect the marijuana might have had. I could keep down food, and I could stop the aching. Also, I'm convinced that one of the worst things for my immune system was the stress my sickness caused me. Marijuana reduced my stress and it calmed my soul. It made me not worry so much about the difficult regimen of pills I had to take, or how I was going to get to the grocery store because I didn't think I'd be able to walk. Marijuana allowed me to accept the possibility that I might die, and yet, I believe, because I smoked marijuana, I lived. (Zimmerman et al. 1998, p. 53)

In the US, many persons with AIDS use cannabis daily to control nausea, increase appetite, decrease pain, and improve mood. Although case reports like those above are frequent, the federal drug bureaucracy has kept a virtual stranglehold on all clinical research into the safety and effectiveness of cannabis (Doblin 2000).

RECENT CLINICAL RESEARCH ON CANNABINOIDS, IMMUNITY, AND WEIGHT GAIN

After an Byzantine ordeal that lasted the better part of a decade (Doblin 2000), University of California-San Francisco (UCSF) researcher, Donald Abrams, MD, was finally able to do a study to compare the effectiveness of dronabinol (Marinol) versus smoked cannabis versus placebo in persons with AIDS.

The results of Dr. Abrams's study, "Marijuana does not appear to alter viral loads of HIV patients taking protease inhibitors," were released July 13, 2000 by UCSF (Abrams 2000). The study found that patients with HIV infection

taking protease inhibitors do not experience short-term (3 week) adverse virologic effects from using cannabinoids.

Of the 62 subjects who completed the inpatient study, values for 36 with undetectable HIV RNA levels remained unchanged through the trial. All 26 subjects with detectable HIV RNA levels experienced declines in those levels. Of those, the subjects who smoked cannabis or took oral dronabinol experienced slightly greater decreases in HIV RNA levels than did subjects who took the placebo, but there was no statistical difference between the three groups.

All three groups gained weight, thanks to regularly scheduled meals and available snacks. However, the subjects in the placebo arm gained an average of 1.30 kg, while those who took oral dronabinol gained an average of 3.18 kg, and those who smoked cannabis gained an average of 3.51 kg. These results should alleviate some concerns about the effects of THC as dronabinol and smoked herbal cannabis on immunity,

CANNABIS AND HARM REDUCTION STRATEGIES FOR PERSONS WITH AIDS

There is concern about risk of potential respiratory and lung infection in immunocompromised persons from smoking cannabis because underground market sources may be contaminated with bacteria or fungal spores. Some patients minimize this risk by cultivating their own cannabis, while others are careful to obtain cannabis only from trusted sources. Some persons heat the cannabis in a toaster oven for several minutes to reach the temperature used to pasteurize milk, 71°C (160°F), but keep the heat much lower than the 140°C to 190°C (284°F to 374°F), at which temperature the cannabinoids "vaporize" or "volatize" causing significant degradation of source material (Rosenthal et al. 1997; Gieringer 2001).

These are descriptions of some patients' strategies, but there are no controlled trials demonstrating increased risk for infection in cannabis-only smokers versus nonsmokers among persons with AIDS or any documented clinical benefit from attempting to sterilize the cannabis as described above.

Some patients try to reduce the risk of using contaminated cannabis by alternately smoking cannabis and cooking it in food. Some books on medical use of cannabis contain recipes (Rosenthal et al. 1997), or alternatively, patients may use a standard search engine on the Internet. Patients sometimes rely on smoked cannabis when the symptoms of nausea are so severe they are incapable of oral intake, but at other times, bake it into brownies or put in other food. In this way, the patient may get the immediate and effective relief that smoking provides, but when the need is less pressing, minimize the risk of smoking potentially contaminated cannabis through oral intake.

Oral ingestion of cannabis resolves the issues of smoking toxicity, but the harm-reduction issue is complicated by the United States' War on Drugs, which causes a "prohibition tariff" and increases cost by a factor of about 10. Estimates are that without cannabis prohibition, production costs would be $30 to $40 per ounce (Grinspoon 1997), but current street prices are about $300 to $400 per dry ounce for high-quality female flowers ("bud"). Eating cannabis, or making tea is expensive, and as for dronabinol, it has a slower onset of action. Oral THC also produces lower blood levels, and is less effective in controlling nausea when compared to smoked THC cigarettes (Chang 1979).

Inhalation of therapeutic drugs, such as treatment of asthma using metered dose inhalers, provides rapid onset of action and dose titration using the minimum effective dose (which minimizes drug side effects). Medical inhalation of cannabis provides similar advantages, but without vaporization, carries the risk of inhaling smoke. Therefore, one method to reduce harm from smoking is for patients to use only high medical quality cannabis, so there is a greater concentration of therapeutic cannabinoids per mass ingested.

Promising initial results from a study by California NORML (National Organization to Reform Marijuana Laws) and the Multidisciplinary Association for Psychedelic Studies (MAPS) demonstrate that patients may be able to protect themselves from harmful toxics in cannabis smoke by inhaling their medicine using an electric vaporizer (Gieringer 2001). Vaporization involves releasing cannabinoids by heating cannabis to temperature short of combustion, thereby eliminating or substantially reducing harmful toxics that are present in cannabis smoke. Gieringer reports traces of THC appearing at temperatures as low as 140°C (284°F) while significant amounts of benzene did not appear until 200°C (392°F) and combustion did not appear until around 230°C (446°F) or above. An aromatherapy device called the Volatizer (*www.volatizer.com*) consisting of an electric heating element similar to an automobile cigarette lighter on a metal wand produces a temperature of 185°C (385°F) and is placed over the bowl of cannabis that sits inside the top of a 0.5 liter side-arm Erlenmeyer flask. Vapors are inhaled through a rubber tube connected to the side-arm of the flask. The Volatizer reduced measured toxics (benzene, a known carcinogen, plus toluene and naphthalene), carbon monoxide, and tars when compared to combusting the cannabis by flame. More research is indicated, but vaporizers appear to substantially reduce what is widely perceived as the leading health hazard of cannabis, namely respiratory damage from smoking. Drawbacks to vaporization include cost (a complete Volatizer unit costs $250 US), and portability. Competing aromatherapy devices include using a thermocouple heat gun blown across the cannabis and collecting vapors in a chamber or bag (*www.mystifier.com*) or placing cannabis in one end of a small (pencil size) glass tube with the other end of the glass tube connected to a

plastic tube for inhalation. The glass end with cannabis is then inserted in an "oven" that looks like an automobile oil filter and vapors are inhaled through the plastic tube (*www.vaportechco.com*). These two units are less expensive (about $150 US) than The Volatizer but have not yet been laboratory tested. Other units are available, but until paraphernalia laws are relaxed and mass production of vaporizers is possible (e.g., using small batteries), vaporization remains an attractive but expensive harm reduction tool.

Simpler devices such as water pipes or "bongs" that combust the cannabis and draw the smoke through water before inhalation serve to cool the inhaled smoke, but there is no evidence that they reduce the ratio of tar and particulate matter to therapeutic cannabinoids (Gieringer 1994). There may be undiscovered health advantages from cooling the inhaled smoke or filtering out certain gases, but any advantage of a water pipe or bong over a joint to deliver smoked cannabis remains undocumented.

A medical records review of 452 daily cannabis smokers who never smoked tobacco showed a slight increase in clinic visits for colds, flu, and bronchitis over a 2 year period when compared to demographically similar group of non-smokers of either substance (Polen 1993). Although heavy cannabis smokers report "smokers' cough" (chronic bronchitis), there is no evidence that cannabis smokers who do not smoke tobacco will develop small airways disease, such as emphysema (Tashkin et al. 1997).

Patients should be advised to stop holding one's breath after inhaling smoke for this technique does not increase benefits from cannabis, but rather appears to increase risks of potentially dangerous deposits in the airways. Probably because the lifetime quantity of smoke consumed by cannabis smokers is typically far less than for tobacco smokers, there exists no clinical evidence that typical cannabis smokers have higher rates of respiratory cancer (Zimmer et al. 1997). However, recent reports from the United States (Zhang et al. 1999) and Europe (Carriot et al. 2000) suggest heavy cannabis smokers may increase risk of head and neck cancer with a strong dose-response pattern.

CONCLUSION

Many patients report that cannabis helped prolong their lives by enabling them to cope with some of the difficult symptoms and treatments associated with AIDS. In spite of a need for more rigorous scientifically controlled research, an increasing number of persons with AIDS are using cannabis because they find it controls nausea, increases appetite, promotes weight gain, decreases pain, and improves mood.

REFERENCES

Abrams, D. 2000. Marijuana does not appear to alter viral loads of HIV patients taking protease inhibitors. University of California at San Francisco press release. 1999 Regents of the University of California. Alice Trinkl, News Director. Source: Jeff Sheehy (415) 597-8165. *http://www.ucsf.edu/pressrel/2000/07/071302.html*

Beal, J. R., L. Olson, J. Laubenstein, J. Morales, P. Bellman, B. Yangco, L. Lefkowitz, T. Plasse, and K. Shepard. 1995. Dronabinol as a treatment for anorexia associated with weight loss in patients with AIDS. *J Pain Sympt Manag* 10(2):89-97.

Beal, J.R., L. Olson, L. Lefkowitz, L. Laubenstein, P. Bellman, B. Yangco, J. Morales, R. Murphy, W. Powderly, T. Plasse, K. Mosdell, and K. Shepard. 1997. Long-term efficacy and safety of dronabinol for acquired immunodeficiency syndrome-associated anorexia. *J Pain Sympt Manag* 14(1):7-14.

Berger J., L. Pall, C. Hall, D. Simpson, P. Berry, and R. Dudley. 1996. Oxandrolone in AIDS-wasting myopathy. *AIDS* 10(14):1657-62.

Carriot, F. and Sasco, A. 2000. Cannabis and cancer. *Revue d'Épidémiologie et de Santé Publique* 48(5):473-83.

Centers for Disease Control and Prevention. 1992. 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *MMWR Morb Mortal Wkly Rep* 41(51):961-962. *http://www.cdc.gov/mmwr/preview/mmwrhtml/00018179.htm*

Centers for Disease Control and Prevention. 1999. CDC guidelines for national human immunodeficiency virus case surveillance, including monitoring for human immunodeficiency virus infection and acquired immunodeficiency syndrome. *MMWR Morb Mortal Wkly Rep* 48(RR-13). *http://www.cdc.gov/mmwr/PDF/RR/RR4813.pdf*

Centers for Disease Control and Prevention. National Center for HIV, STD, and TB Prevention, Divisions of HIV/AIDS Prevention. 1998. *Trends in the HIV and AIDS Epidemic*, *1998*. *http://www. cdc.gov/hiv/stats/trends98.pdf*

Centers for Disease Control and Prevention. National Center for HIV, STD, and TB Prevention, Divisions of HIV/AIDS Prevention. 1999. *HIV/AIDS Surveillance Report* 11(2):5. *http://www.cdc.gov/hiv/stats/hasr1102.htm or www.cdc.gov/hiv/stats/hasr1102.pdf*

Centers for Disease Control and Prevention. National Center for HIV, STD, and TB Prevention, Divisions of HIV/AIDS Prevention. 2000. *Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents*. *http://www.cdc.gov/hiv/treatment.htm*.

Chang, A. 1979. Delta-9-tetrahydrocannabinol as an antiemetic in cancer patients receiving high-dose methotrexate. *Ann Intern Med* 91(6):819-824. *http://www.teleport.com/~omr/omr chang.html*

Doblin, R. 2000. Multidisciplinary Association for Psychedelic Studies (MAPS) website with additional references: *http://www.maps.org/mmj/mjabrams.html*

Fauci, A.S. and H.C. Lane. 2000. *Harrison's Principles of Internal Medicine*. *Harrison's Online Edition*. New York City: McGraw Hill, Inc.

Gieringer, D. 1994. The MAPS/California NORML marijuana waterpipe/vaporizer study. *MAPS Bull* 5(1):19-22. *http://www.maps.org/news-letters/v06n3/06359mj1.html*

Gieringer, D. 2001. *NORML-MAPS study shows vaporizers reduce toxins in marijuana smoke*. California NORML press release. 2001 California NORML. (415) 563-5858. *http://www.canorml.org/research/vaporizerstudy1.html*

Grinspoon, L. and J. Bakalar. 1997. *Marihuana*: *The forbidden medicine*. New Haven, CT: Yale University Press.

Grinspoon, L. 1997. Testimony of Lester Grinspoon, M.D. before the Crime Subcommittee of the Judiciary Committee, U.S. House of Representatives on October 1, 1997. *http://www.rxmarihuana.com/testimony.htm*

Grinspoon S., C. Corcoran, H. Askari, D. Schoenfeld, L. Wolf, B. Burrows, M. Walsh, D. Hayden, K. Parlman, E. Anderson, N. Basgoz, and A. Klibanski. 1998. Effects of androgen administration in men with the AIDS wasting syndrome. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 129(1):18-26.

Krampf, W. 1997. AIDS and the wasting syndrome. In M.L. Mathre (ed.), *Cannabis in medical practice*: *A legal*, *historical*, *and pharmacological overview of the therapeutic use of cannabis*. Jefferson, N.C: McFarland & Co.

Polen, M.R., S. Sidney, I. Tekawa, M. Sadler, and G. Friedman. 1993. Health care use by frequent marijuana smokers who do not smoke tobacco. *West J Med* 158(6): 596-601.

Rosenthal, E., D. Gieringer, and T. Mikuriya. 1997. *Marijuana medical use handbook*: *A guide to therapeutic use*. Oakland, CA: Quick American Archives.

Roxane Laboratories Package Insert with full prescribing information for Marinol brand of dronabinol. Revised 1999. *http://hiv.roxane.com/prodinfo/marinol.html*

Russo, E. 2000. *Handbook of psychotropic herbs*: *A scientific analysis of herbal remedies for psychiatric conditions*. Binghamton, NY: The Haworth Press, Inc.

Saag M.S., M. Holodniy, D. Kuritzkes, et al. 1996. HIV viral load markers in clinical practice: recommendations of an International AIDS Society-USA Expert Panel. *Nature Med* 2:625-629.

Summary at *http://www.hivatis.org/viral.html*

Sallan, S.E., N.E. Zinberg and E. Frei. 1975. Antiemetic effect of delta-9-tetrahydrocannabinol in patients receiving cancer chemotherapy. *New Eng J Med* 293:795-797.

Tashkin, D., M. Simmons, D. Sherrill, and A. Coulson. 1997. Heavy habitual marijuana smoking does not cause an accelerated decline in FEV1 with age. *Am J Respir Crit Care Med* 155:141-148.

Timpone, J., D. Wright, N. Li, M. Egorin, M. Enama, J. Mayers, and G. Galetto. 1997. The safety and pharmacokinetics of single-agent and combination therapy with megestrol acetate and dronabinol for the treatment of HIV wasting syndrome. *AIDS Res Hum Retroviruses*. 13(4):305-315.

United States Department of Health and Human Services. 1995. National Center for Health Statistics. *Health United States 1995*. *http:// www.cdc.gov/nchs/data/hus_95.pdf*.

Zhang Z.F., H. Morgenstern, M. Spitz, D. Tashkin, G. Yu, J. Marshall, T. Hsu, and S. Schantz. 1999. Marijuana use and increased risk of squamous cell carcinoma of the head and neck. *Cancer Epidemiol Biomarkers Prevent* 8(12):1071-1078.

Zimmer, L. and J.P. Morgan. 1997. *Marijuana myths*: *Marijuana facts*. *A review of the scientific evidence*. New York and San Francisco. The Lindesmith Center.

Zimmerman B., R. Bayer, and N. Crumpacker. 1998. *Is marijuana the right medicine for you? A factual guide to medical uses of marijuana*. New Canaan, CT. Keats Publishing, Inc.

Zofran , brand of ondansetron, package insert. 2000. Glaxo-Welcome Inc. *http://www.glaxowellcome.com/pi/zofran.pdf*