Pain Management in Terminal Disease

Robert V. Brody, MD

In the past two decades, dramatic progress has been made in the successful treatment of pain in patients with terminal diseases. The sources of these advances include research laboratories which are sorting out the mechanisms of pain, and the consumer-based hospice movement, which has insisted that health professionals pay as much attention to symptom management as they do to disease management. In addition, pharmaceutical companies have made available new preparations of analgesic agents, and anesthesiologists and neurosurgeons have attempted to define the role of invasive procedures for pain control.

As the AIDS epidemic has grown, care strategies developed for other terminal patients have been successfully adopted for those with manifestations of the new syndrome. This is especially true for plans of care for cancer patients, individuals who often show the same protracted downhill course with increasing debility and dependence over time as seen in AIDS patients. Thus, approaches to pain management in AIDS have grown out of approaches to pain management in cancer, and it is these that I will discuss.

The Experience of Pain in AIDS

Bonica has estimated the prevalence of pain in cancer patients as 40% in those with intermediate disease and 60-90% in those with advanced disease. No such proportion has been determined for AIDS patients, but the intensity and prevalence of pain in AIDS is probably less than with cancer (J. Martin, Hospice of San Francisco, personal communication). In fact, other symptoms in AIDS patients are often more debilitating and difficult to control than pain, especially behavioral changes and diarrhea. This latter devastating symptom actually makes treatment of pain easier because the patient can tolerate high doses of narcotics without the otherwise universal constipation. Nevertheless, pain does occur in AIDS patients; and when it does, it must be addressed in a comprehensive and aggressive manner.

Pain is always more than a distressing sensation, or even the perception of a distressing sensation. It is useful to think of pain as a person's emotional experience of a distressing sensation; thus, morale and mood can be as important as the intensity of the feeling itself in determining the degree of pain.

Factors which can decrease the threshold of suffering pain include any type of discomfort, such as insomnia, fatigue, anxiety, fear, anger, sadness, depression, and especially memory and expectation of pain. On the other hand, the threshold can be raised by the relief of other symptoms, especially depression and anxiety. In addition, sleep, rest, sympathy, understanding, diversion, and analgesic agents can have a beneficial effect. This broader view is especially important in controlling the chronic pain of terminal disease, since chronic pain does not serve the protective or warning function of acute pain.

Treatment Approaches

How, then, should one approach a patient in pain? As with other medical complaints, a careful history and physical examination are indicated. Assessment instruments have been developed to help the physician or nurse gather necessary information, which falls into several dimensions:

(a) Pain location, intensity (perhaps objectified on a linear scale of one to ten), quality, onset, and duration all describe the sensory dimension.

(b) The physiological dimension can be described with laboratory or radiological data.

"Pain is always more than a distressing sensation. It is useful to think of pain as a person's emotional experience of a distressing sensation; thus, morale and mood can be as important as the intensity of the feeling itself in determining the degree of pain."

(c) The affective dimension notes the presence or absence of anxiety or depression or other alterations in mood.

(d) Aggravating or ameliorating factors are important behavioral data.

(e) The cognitive dimension describes the meaning which the patient attributes to the pain or the diagnosis.

Assessment must include past experiences with pain, and experiences with both effective and ineffective therapies should be documented. The functional status of the patient is also important. Physical examination should use the clues gained in history-taking to search for as specific a cause for the pain as can be defined.

What is the cause of pain in terminal disease? Pain may result from the disease process, the therapy for the disease, or it can be unrelated to the underlying disease. Thus a tumor may invade bone, compress a nerve, infiltrate a blood vessel, obstruct a hollow organ, or cause swelling in a structure with a tight

continued on page 2
Pain Management . . .

continued from cover

capsule. In addition, surgical, chemo therapeutic, or irradiation manipulations may result in pain. Finally, the patient dying of cancer or AIDS may have a heart attack or broken bone unrelated to the terminal disease.

It is best to attempt local, specific therapy for the process causing pain before relying on systemic analgesia. For instance, a boney metastasis may be irradiated for pain control, while at the same time a non-steroidal anti-inflammatory drug may be administered to antagonize the prostaglandins released at the periphery of the lesion. (Prostaglandins are a group of fatty acid derivatives present in many tissues). Tumors or other space-occupying lesions in the head may produce severe headache for which prednisone or other adrenal corticosteroid may be used; these agents are also useful for pain caused by nerve infiltration. The potential deleterious changes in the immune system induced by steroids are far outweighed by the relief from suffering the patient experiences.

There comes a point for many terminal patients when local therapy will not control pain, and systemic analgesia is needed. I think it is important to remember that not all terminal patients in pain require narcotics. Aspirin, acetaminophen, non-steroidal agents — all are perfectly appropriate to use and are preferred for their lower side effect and abuse potential. However, these, like all analgesics, must be used on the proper schedule. No chronic pain syndrome should be treated with medication on a p.r.n. (as circumstances require) or as-necessary basis; this dosing requires the patient to suffer pain before the next dose is administered. Rather, the drugs should be administered around-the-clock to abolish the memory and expectation of pain and therefore raise the pain threshold.

Behavioral therapy for pain in terminal disease can be very helpful for selected patients. Among the methods in common use are hypnosis, biofeedback, and psychotherapy. Other modalities include accupuncture, physical therapy, heat, ice, massage, and transcutaneous electrical nerve stimulation (affecting the nerves that provide sensory pathways for stimuli to the skin).

Narcotic Interventions

Behavioral therapy and conventional analgesics, including codeine and oxycodone or Percodan, are insufficient to control pain, then a shift to the narcotic analgesics is indicated. That these agents are under-utilized is well documented. Some physicians are afraid of the sedation and respiratory depression induced by morphine and other narcotics. However, if the amount of the drug is carefully titrated against the pain in increasing doses, this central nervous system depression is minimal, especially after the first 48-72 hours.

Professionals, patients, families, partners, or friends may fear that the patient may become addicted to morphine. Certainly persons taking more than a minimal amount of narcotic for more than ten days are likely to show an abstinence syndrome upon withdrawal of the drug, but the drug-seeking behavior that marks the true addict is never seen in terminal patients who take the narcotic to allow themselves to function as normally as possible in the world. Finally, some observers worry that patients will use narcotics to commit suicide. However, hospice workers report that if care-givers successfully address the two fears of dying people, the fear of abandonment and the fear of suffering, then suicide ceases to be an issue.

Morphine is the most useful narcotic for the severe chronic pain of terminal disease. Demerol is rarely used because of its short duration of action. Dilaudid is useful for those who find the small pills easier to take than the sometimes nauseating morphine elixir, and it is available in rectal suppository form if oral dosing is not possible for a short period. Heroin and morphine are equally potent when proper doses are compared, and the only advantage of heroin seems to be its increased solubility so that a smaller volume can be used for intramuscular injection. Oral preparations of the narcotics are preferred as they are effective and are easy for patients and others to administer. Morphine should be given in an oral dose about two times the intramuscular, intravenous, or subcutaneous dose. Caregivers should note the duration of relief to ensure the abolition of the memory and expectation of pain. With the introduction of long-acting preparations of morphine which can be administered every eight or even every twelve hours, nighttime dosing can be eliminated. Methadone is less useful because of its propensity to accumulate in the body. The concentrated oral solution of morphine is useful in patients no longer able to take normal amounts of fluid by mouth.

"Behavioral therapy for pain in terminal disease can be very helpful for selected patients. Among the methods in common use are hypnosis, biofeedback, and psychotherapy. Other modalities include accupuncture, physical therapy, heat, ice, massage, and transcutaneous electrical nerve stimulation (affecting the nerves that provide sensory pathways for stimuli to the skin)."

Side effects of narcotics can be anticipated and aggressively managed. Nausea may be handled with pre-treatment with a phenothiazine, like Compazine and others; sedation, as mentioned, resolves after several days. The side effect usually most troublesome, and which must be anticipated with an adequate therapeutic regimen, is constipation, but for many AIDS patients even morphine cannot slow the constant diarrhea.

Adjunctive pharmacological analgesia is useful when treating with narcotics. The non-steroidal agents may allow the use of lower narcotic doses with fewer side effects. Tricyclic agents, especially imipramine, amitriptyline, and doxepin, block serotonin uptake and have an analgesic effect which occurs earlier and at a lower dose than that seen when treating depression. Finally, anxiolytic or antidepressant medications are helpful as analgesics when anxiety and depression lower the pain threshold.

In those very few patients for whom oral or other systemic narcotics cannot control pain, nerve blocks, narcotics to affect the intrathecal (within the spinal canal) or epidural (the area above the membrane covering the spinal cord) areas, or even neurosurgical procedures may be considered. The indications for these must be individualised.

In summary, the aims of pain control in dying patients are (a) to identify and address the cause of pain, (b) to prevent chronic pain, (c) to erase the memory of pain in order to diminish anxiety, (d) to allow the patient to remain alert, (e) to allow the patient to function as normally as possible, (f) to permit the patient to have a normal affect, to have feelings, and to express them, and (g) to do this with greatest ease for the staff and family caring for the patient.

Robert V. Brody, MD is an Assistant Clinical Professor of Medicine at UCSF and the Assistant Chief of Medical Clinics at San Francisco General Hospital. He is a member of the Board of Directors of VNA of San Francisco, the parent organization of Hospice of San Francisco, and he serves as chair of the Hospice Committee and Program Committee for the new Coming Home Hospice Residence.
Diagnosis/Treatment

Hemophilia and AIDS

Michael Helquist

People with hemophilia speak of their disbelief and disillusionment when the serious impact of AIDS upon their community became apparent in 1982. Many adults with the blood disorder had achieved a certain normality in their daily lives; they were able to control their bleeding problems with infusions of Factor VIII or Factor IX; both blood clotting components developed in the late 1960s. Reconstructive orthopedic surgery to correct the arthritis that often results from the disorder had become available, and many hemophiliacs could anticipate a nearly normal life-span.

When AIDS was first linked to blood clotting products, the recently-attained degree of autonomy, well-being, and stability of health among hemophiliacs was threatened. People with AIDS and hemophilia reported that once again they encountered the misunderstanding, prejudice, and ostracism of society that they had long endured as a result of their blood disorder. Now they faced renewed discrimination plus a new life-threatening illness.

A Blood Disorder

Hemophilia is the medical term applied to congenital disorders that disrupt coagulation of the blood. These disorders leave hemophiliacs susceptible to bleeding that cannot be stopped without special treatments. The treatments essentially replace the proteins that are deficient in the different types of hemophilia. Thus, people with hemophilia A have a deficiency of the protein Factor VIII and must use manufactured treatments of Factor VIII to control their bleeding. Those with hemophilia B lack the protein Factor IX and must replace it with Factor IX products. Both types of hemophilia are sex-linked disorders, transmitted from asymptomatic mothers to sons; thus both hemophilia A and B are found in males only. The disorder is usually diagnosed either at birth due to family history or during the first year of life.

Symptoms of hemophilia can range from the mild to the severe. Unlike the popular conception, hemophiliacs do not risk bleeding to death due to a minor cut. Instead, the major problem results from internal bleeding into the joints, muscles, and organs. Often pain is a constant companion as a result of the arthritis and crippling that may develop after bleeding into joints.

Hemophilia and AIDS in the U.S.

The Centers for Disease Control (CDC) notes a total of 156 cases of AIDS among hemophiliacs in the United States as of April 7, 1986. (San Francisco has had only two reported cases of persons with hemophilia and AIDS). The individuals have all developed the disease as a result of receiving clotting factor concentrates contaminated with the AIDS virus. The incidence rate of AIDS is higher in persons with hemophilia A, although a few individuals with hemophilia B have also developed AIDS.

People with hemophilia A are more likely to have a severe deficiency of the blood clotting factor and thus receive more clotting concentrate than those with hemophilia B. This difference likely places the former group at a much greater risk for exposure to viral agents, including the AIDS virus. In addition, people with severe clotting deficiencies are at a greater risk than those with mild to moderate deficiencies.

An estimated 75 to 80% of the heavily-treated Factor VIII patients in the United States are seropositive to the AIDS virus. Health workers estimate that there are 1700 seropositive hemophiliacs in California and more than 20,000 in the United States. Heat treatment of the clotting factor components has been shown to kill the AIDS virus. The process was initially developed in hopes of decreasing the risk of contamination with non-A or non-B hepatitis virus present in some blood products, but heat treatment apparently has no effect on this additional threat.

Retrospective studies of AIDS among hemophiliacs indicate initial exposure in 1979 with greater rates of exposure occurring in 1981 and 1982.

The natural history of AIDS infection among hemophiliacs remains unknown. Pneumocystis carinii pneumonia is the most common AIDS-related infection among hemophiliacs in the United States; few cases of hemophiliacs with Kaposi's sarcoma have been reported. The CDC also notes the incidence of AIDS Related Conditions in hemophiliacs, with cases of lymphadenopathy, thrombocytopenic purpura, and Burkitt's lymphoma.

Psychosocial Issues

Health care professionals who work with hemophiliacs have reported that several clients continue to fear using the clotting factors; some have discontinued their self-treatments, risking the pain and disability that may result from uncontrolled bleeding episodes. Although hemophiliacs diagnosed with AIDS experience the same complex set of emotions that confront others with AIDS, the diagnosis also leads to unique problems. People with hemophilia fear further misunderstanding and isolation from a public that still does not understand their bleeding disorder.

Many are quite angry about their exposure to AIDS, feeling that it could have been prevented. Those who also have AIDS are often troubled with the popular association of AIDS with homosexual activities and with I.V. drug use. This concern has led many to "become invisible" about their medical and physical status.

Some hemophiliacs view themselves as outcasts in light of the more stringent precautions taken by the health care providers who work with them. Many are frustrated that protocols for AIDS experimental drug trials often exclude patients with complicating health problems like hemophilia. There is confusion about the risk of transmitting AIDS to sexual partners, and some resentment exists about the lack of educational materials developed specifically to address the concerns of the hemophilia community.

On the other hand, public officials and funding agencies are finding that the hemophilia community is becoming more politically adept and more committed to obtaining funds for their own education needs. Several individuals with hemophilia have assumed positions of leadership to help guide their friends, families, and communities through this most recent challenge.

Although heat-treating processes and use of the AIDS antibody test to screen blood appear to have greatly reduced the risk of further spread of AIDS among hemophiliacs, the high proportion of seropositivity in this risk group will inevitably lead to rising numbers of cases of AIDS. The need for risk reduction information, education about hemophilia, counseling, natural history studies, and experimental therapies will only increase as AIDS continues to affect the hemophilia community.

Note: The Hemophilia Council of California is a non-profit organization functioning as a consortium of local hemophilia foundations and chapters in the state. The Council has established a statewide hemophilia AIDS Project to provide information, education, and psychosocial services related to the AIDS epidemic to members of the hemophilia community. The Project Coordinator can be contacted at the following address and phone number: 2206 K Street, Suite 4, Sacramento, CA; (916) 448-7444. The coordinator for the San Francisco and Monterey Bay Areas is Paul Murray, LCSW. He can be contacted at 2712 Telegraph Avenue, Berkeley, CA 94701. Telephone: (415) 548-8357.

References

Treatment Update: AZT

Azido-deoxynucleoside, or AZT, is the latest of several potentially effective antiviral drugs to be used as an AIDS treatment. First called Compound 5, AZT was tested with 19 AIDS and ARC patients by researchers at the National Cancer Institute. Their report, published in The Lancet (March 15, 1986), outlined the apparent benefits of the drug. Significantly, AZT was able to penetrate the cerebrospinal fluid — and thus pass the blood-brain barrier — an important function given the evidence that the AIDS virus is capable of infecting the nervous system.

The study involved 8 subjects with ARC including persons with symptoms of candidiasis, fevers, lymphadenopathy, night sweats, and weight loss. The other 11 subjects included 5 with Kaposi’s sarcoma and 6 who had recovered from a bout of Pneumocystis pneumonia. One of the 19 subjects was female. AZT was given intravenously for 2 weeks, then orally for 4 weeks at twice the intravenous dose. Side effects included headaches and depression of white blood cells.

Of the 19 patients, 15 had increases in their numbers of circulating helper-inducer T cells during therapy; 6 who were anergic (unable to mount an immune response) at entry showed positive skin test reactions; 2 had clearance of chronic fungal nailbed infections without specific anti-fungal therapy; and 6 others had evidence of clinical improvement. The groups as a whole experienced a weight gain of 2.2 kg. The researchers also reported that with the highest dose regimen cultures of peripheral blood mononuclear cells for HTLV-3 became negative.

The scientists cautioned that based on their study it cannot be determined “whether AZT can be tolerated over a long time, whether immunological improvements will be sustained, whether viral drug resistance will develop, or ultimately whether AZT will affect disease progression or survival in patients with HTLV-3 induced disease.” They concluded that these questions can only be answered by appropriately controlled long-term studies.

The Burroughs Wellcome Company, manufacturers of AZT, have begun a large multi-center trial of the experimental drug. Company representatives report that logistical demands of the trial and limit use of the drug to the major cities with AIDS. They further comment that the study design does not make it practical to follow patients away from the parent institution involved in trials, and the company has declined many requests to have patients followed at outside hospitals. (Private correspondence forwarded to FOCUS, February 1986). The spokesperson, Joan Drucker, MD, medical advise to the company’s infectious diseases unit, observed that there is great interest in a national trial of AZT with asymptomatic, antibody positive persons, but such an effort would have to await further experience with the drug.

Experimental trials with AZT began in late March in San Francisco. Protocols have established a trial with 20 subjects who have had pneumocystis pneumonia within the last 120 days or who have a combination of ARC symptoms (a 10% weight loss in three months, documented culture of thrush, plus other conditions related to AIDS viral infection).

The trials are being conducted at San Francisco General Hospital; protocols manager is Doug Beardslee. People with previous cases of pneumocystis pneumonia have been given preference in this initial trial. Beardslee explained to FOCUS that additional trials with AZT are expected this summer. People with ARC and those with Kaposi’s sarcoma will be eligible for these later trials. While news of the increased trials provide hope to many people with AIDS and ARC, local physicians and mental health professionals have observed that such news reports also cause anxiety for patients who worry that they won’t be included in the upcoming trial programs.

BRIEFS

RECENT REPORTS

The Impact of AIDS on Medical Residency Training. AIDS has had a profound effect on the workload, education, and day-to-day emotions of medical residents in major urban centers, according to Robert M. Wachter, MD of the University of California San Francisco. In a report published in the New England Journal of Medicine (Jan. 16, 1986), Wachter noted that residents find care of AIDS patients labor intensive due to the often exhaustive and invasive workups required to exclude a treatable infectious cause. In addition, residents find that a large proportion of teaching rounds, conferences, and Grand Rounds is devoted to the care of AIDS patients.

Residents must cope with their own fears of transmission, their frustrations with the limits of current therapies, and sometimes their discomfort with the lifestyles of patients with AIDS. Wachter observes, “For house officers involvement in this tragic scenario must exact a substantial psychological toll.”

The author does acknowledge that the care of patients with AIDS provides the resident with rewarding personal and professional opportunities, including involvement with a new infectious disease that promises to reveal many of the mysteries of the human immune system. Wachter concludes that the residents’ involvement with AIDS care will be “an indispensable attribute of a well-trained internist for the foreseeable future.”

The amount of research information now appearing in the medical and lay press staggers most AIDS health care and service providers. This newsletter represents an attempt to place much of the data and press reports in a context that will prove meaningful and useful to its readers. Suggestions and comments are welcome and encouraged. Please address correspondence to Editor, AIDS Health Project; 333 Valencia Street, 4th Floor; San Francisco, CA 94103. For information about other AIDS Health Project programs, call (415) 626-6637.

NEXT MONTH

The public and the media remain alert to each new report about the incidence and possible spread of AIDS to the heterosexual population. Questions abound: What relevance does the high ratio of AIDS among African heterosexuals have for Americans? Do prostitutes represent a high-risk group? Do natural history studies of men at risk for AIDS provide applicable information for women at risk?

In the June issue of FOCUS, Nancy Padian, MS, MPH, epidemiologist and project director of the California Partners Study, will outline the incidence of AIDS and ARC among women in the United States and throughout the world. Padian will also consider the risk for women of exposure to AIDS via sexual activities, artificial insemination, and needle-sharing I.V. drug use.

In addition, Paul Shearer, MSW, LCSW and Leon McKusick, PhD will discuss the impact on survivors of losing a loved one to AIDS. The grief experienced by families and lovers is often complicated by the special social context of AIDS. Shearer and McKusick will suggest approaches counselors might take to assist survivors cope with their loss.