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Understanding drug-drug interactions in the management of HIV disease

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Recent technologies within the last decade have resulted in our understanding a huge body of knowledge and information concerning the cytochrome P-450 isoenzymes present in the human body, and thus created an awareness of the many life-threatening interactions with such commonly prescribed drugs as the newer antihistamines and cisapride. A basic knowledge of the substrates, inhibitors and inducers of this enzyme system assists providers in predicting drug interactions that may become clinically significant. Apart from the processes of induction and inhibition, other factors that may affect microsomal drug metabolism include hepatic disease, state of nutrition, age, the presence of some endogenous chemicals, and genetic polymorphism. So far, as many as 30 human cytochrome isoenzymes have been identified. The major ones responsible for a majority of drug metabolism include CYP3A4, CYP2D6, CYP1A2 and the CYP2C subunits. This article, which will be continued in a later edition of this newsletter, will present fundamental concepts necessary for an appreciation of the role of these enzymes in drug-drug interactions as they relate to antiretroviral therapy.

Pharmacologically, there are two broad classes of drug interactions, namely the pharmacokinetic and pharmacodynamic drug interactions. Interactions are described as pharmacokinetic when the action of one drug alters the serum concentration of another drug by changing any of the following processes: drug liberation, absorption, distribution, metabolism and excretion. Pharmacodynamic interactions are described simply as those interactions that may alter the overall clinical response expected from use of the drugs by altering the efficacy and often toxicity of the drugs. It could be synergistic (mostly positive, i.e., the positive antiretroviral response seen when zidovudine is combined with lamivudine) or it could be negative (antagonistic, i.e., use of zidovudine and ganciclovir causing additive bone marrow suppression or concomitant use of d4T and ddI causing additive neuropathy).

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Inside

Medicine

Neurologic disease in HIV-1 infected children

April Palmer, MD

A Case Report

A 3-year-old black female was reported to be in good health until six weeks prior to her admission to the University of Mississippi Medical Center in Jackson. She initially presented with upper respiratory tract symptoms and was treated twice by her local pediatrician with oral antibiotics. Three weeks prior to admission to our facility, she began having difficulty walking, starting first as a limp which progressively worsened. She was referred to an orthopedic surgeon for evaluation. Physical examination, plain radiographs of the

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The majority of interactions do not require extensive changes

Interactions, continued from page 1

Defining pharmacokinetics: relationship to drug-drug interactions

Pharmacokinetics is simply defined as the study of the processes of drug action through the various processes of liberation, absorption, distribution, metabolism and excretion, often referred to as the LADME system. As a result of this broad definition and the involvement of several key processes, numerous possibilities abound for potential pharmacokinetic drug interactions. For instance, any circumstance that alters gastric pH can affect the absorption of many drugs. This is particularly important for patients receiving palliative care, many of whom may have hypochlorhydria which is common in advanced HIV disease and AIDS and may lead to suboptimal absorption of pH-dependent medications such as ketoconazole (Nizoral), itraconazole (Sporonox) and indinavir (Crixivan). Since fluconazole (Diflucan) is readily absorbed independent of gastric pH, it is often the azole of choice when an azole antifungal is indicated for the treatment of several opportunistic infections.

Drug-disease interactions

Drug interactions may arise because of changes due to HIV disease itself. As HIV-infected persons advance in their illness, often oral absorption of foods and drugs is compromised due to changes in gastric pH that accompany HIV enteropathy, a syndrome that describes the effect of advancing HIV disease on the gastrointestinal system. Diarrhea tends to be common in HIV disease and may result from a variety of causes, namely gastrointestinal disturbance following side effects of several of the most commonly used antiretroviral agents, and the presence of concurrent opportunistic organisms, bacterial, protozoal and viral infections that tend to be more common as the disease advances and the immune system weakens. The occurrence of diarrhea, especially if frequent and poorly controlled as in patients with cryptosporidiasis (a disease entity that is almost impossible to eradicate since none of the agents used for symptomatic treatment have shown persistent efficacy in clinical studies), may jeopardize absorption of all drugs because of the decreased transit time and may cause drug regimens to be less efficacious.

This will lead subsequently to less than optimal clinical outcomes and in some instances may predispose the patient to sub-therapeutic drug levels that may herald the emergence of resistant strains of the virus in patients still taking antiretroviral agents.

HIV-infected persons in palliative care are more likely to suffer from an increase in susceptibility to adverse events, such as a higher incidence of allergic reactions to sulfonamides and other drugs, than patients in the early stages of their disease. Other physiological components of advancing AIDS/HIV disease include the malabsorption which is the hallmark of enteropathy and predisposes the patient to changes in body weight that often reflect changes in volume as well as distribution of both fat and muscle tissue. This in turn may affect the dose-related efficacy of drugs, for example, the agents used in the treatment of tuberculosis and mycobacterial avium complex disease. Also frequently reported at this stage of illness are decreases in serum albumin, which in turn may alter the efficacy of drugs such as phenytoin when used in the management of patients with toxoplasmosis or sulfamethoxazole when used both as treatment and in the prophylaxis of patients with pneumocystis carinii pneumonia.

Other changes also occur in drug metabolism with advancing disease. These include changes due to hepatitis, frequently a co-infection in this population, especially those who were intravenous drug users (IVDUs), as biliary disease makes it necessary to adjust both the doses, and often the dosing intervals, of drugs that are mostly metabolized through the liver such as rifampin, isoniazid, ketoconazole, and to be selective in the choice of such medications. Changes in the renal elimination of drugs also occurs with advancing disease

and can be especially important for renally-cleared antiretrovirals such as zidovudine, lamivudine, didanosine, zalcitabine and stavudine, antiviral agents such as ganciclovir and cidofovir, antifungal agents such as amphotericin B, and antibacterial agents such as the aminoglycosides.

Changes in immune status that may affect drug responses to antimycobacterial medications (such as the tuberculostatics) or management of opportunistic infections (such as mycobacterium avium complex) have frequently been reported in patients with advancing disease. As a general rule, there is an increased incidence of drug toxicity as well as drug sensitivity, for example with use of the neuroleptics (chlorpromazine and prochlorperazine), which may necessitate a decrease in the usually recommended doses in order to avoid undue toxicity.

When to suspect a drug-drug interaction in a patient with HIV disease

As a general rule, patients experiencing exaggerated toxicities on usual doses of medications or manifesting treatment failure, in the absence of factors such as resistance or poor adherence/compliance, may be suffering from an unidentified drug-drug interaction. In order to monitor for such drug interactions, a careful review of the patient's medication profile is necessary. Clinicians should become familiar with the agents most often associated with significant drug-drug interactions and measures to circumvent them when necessary. Regimens with enzyme inducers such as rifampin or enzyme inhibitors such as ritonavir should be noted and checked against a list of other agents metabolized by those same enzyme pathways.

Fortunately, the majority of drug-drug interactions are minor in nature and do not require extensive changes to the patient's drug regimen. However, the minority population of drug interactions that can be clinically important may offset treatment goals and outcomes in patients when these remain unrecognized or unaddressed, leading to sub-optimal drug levels of various drugs and so to treatment failures, often due to emergence of drug resistant strains of the virus.

Drug-food interactions of clinical significance

It is well established that the presence or absence of food or certain beverages may significantly affect the bioavailability of a number of medications. A variety of mechanisms including changes in pH, formation of unabsorb-able cation complexes, increased solubility of drugs, interference with gut metabolism, as well as a decrease in the motility of the gut, may be at play. Table 1 (next page) lists some of the more common food-drug interactions and simple strategies to circumvent them.

Changes in the renal elimination of drugs also occur with advancing disease and HIV-associated nephropathy (HIVAN), which can disproportionately affect male African-Americans with a previous history of IV drug use. Such changes can be especially important for renally-cleared antiretrovirals such as zidovudine, lamivudine, didanosine, zalcitabine and stavudine; antiviral agents such as ganciclovir and cidofovir; antifungal agents such as amphotericin B; and antibacterial agents such as the aminoglycosides.

A second installment of this article will appear in a future issue of this publication. It will discuss interactions between antiretroviral agents, psychotropic agents and street drugs.❖

See next page for related tables.

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Table 1: Important food-drug interactions and strategies to circumvent them

- Ketoconazole (Nizoral) and itraconazole (Sporonox): Increase in gastric pH due to agents such as antacids, H_2 blockers, proton-pump inhibitors and non-enteric-coated formulations of ddI impairs absorption of ketoconazole, absorption is optimal at gastric pH. Take 2 hours apart or use alternative antifungal agent (MMWR 1999: 48:[RR-10]:47); rifampin decreases activity of both drugs, INH decreases effect of ketoconazole; terfenadine and cisapride (both now removed from the market) lead to ventricular arrhythmias and concurrent use should be avoided
- Administration of acidic beverages such as 240mls of orange juice, tomato juice, ginger ale, grapefruit juice or cola drinks in the presence of achlorhydria of advanced HIV disease will enhance azole bioavailability especially for ketoconazole. When hypochlorhydria is severe, each 200mg of ketoconazole should be dissolved in 4ml of 0.2N hydrochloric acid. A straw should be used to avoid contact with teeth.
- Oral fluoroquinolones: Avoid dairy products, elemental minerals and heavy nutritional supplements: take fluoroquinolones 2 hours before or 6 hours after these items.
- Interactions with Protease Inhibitors (PIs) and the Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs): (As a general rule, use of ketoconazole with these agents is not advised due to a large number of potentially significant drug-drug interactions, fluconazole is preferred) (see tables 2 and 3).
- Indinavir: levels increased 68%—reduce indinavir dose to 600mg q 8h; SQV levels increased 3-fold—no dose change required; RTV increases ketoconazole levels>3 fold—use < 200mg ketoconazole/day. APV levels increased 31% and ketoconazole levels increased 44%—dose implications not clear; NFV—no dosage change, NVP levels increase 15%-30% and ketoconazole levels decreased by 60%, combination is not recommended. The interactions between ketoconazole and efavirenz have not been studied and so no recommendations can be made at the present time (for more detailed information consult the most recent package inserts of ketoconazole and the various drugs).

Table 2: Common Inducers of Cytochrome P450 Enzyme System

Enzyme	Known Inducers
CYP3A4	Carbamazepine (Tegretol), rifampin (Rifadin), Phenobarbital, phenytoin (Dilantin), efavirenz (Sustiva), nevirapine (Viramune), prednisone, rifapentine, troglitazone (Rezulin)
CYP1A2	Cigarette smoke, ritonavir (Norvir), omeprazole (Prilosec), charcoal-smoked foods, cruciferous vegetables
CYP2C9	Carbamazepine (Tegretol), ethanol, phenytoin (Dilantin), rifabutin (Mycobutin), ritonavir (Norvir), rifampin (Rifadin)
CYP2C19	Rifabutin (Mycobutin), rifampin (Rifadin)
CYP2D6	Pregnancy
CYP2E1	Ethanol, ritonavir (Norvir), isoniazid (INH)

Table 3: Common Inhibitors of Cytochrome P450 Enzyme System

Enzyme	Known Inhibitors
CYP3A4	Ritonavir (Norvir), nelfinavir (Viracept), Amprenavir (Agenerase), Indinavir (Crixivan), propoxyphene (Darvon), saquinavir (Fortovase), ketoconazole (Nizoral), itraconazole (Sporonox), erythromycin, grapefruit juice, nefazodone (Serzone), fluvoxamine (Luvox), fluoxetine (Prozac), diltiazem (Cardizem), verapamil (Calan), clarithromycin (Biaxin), omeprazole (Prilosec)
CYP1A2	Ciprofloxacine (Cipro), grepafloxacin (Raxar), fluvoxamine (Luvox), fluoxetine (Prozac), nefazodone (Serzone), Enoxacin (Penetrex)
CYP2C9	Amiodarone (Cordarone), clopidrogel (Plavix), fluvastatin (Lescol), fluvoxamine (Luvox), fluoxetine (Prozac), fluconazole (Diflucan), miconazole (Monistat), metronidazole (Flagyl), trimethoprim/ sulfamethoxazole (Bactrim/Septra)
CYP2C19	Ticlopidine (Ticlid), fluvoxamine (Luvox), fluoxetine (Prozac)
CYP2D6	Ritonavir (Norvir),* sertraline (Zoloft), fluoxetine (Prozac), paroxetine (Paxil), quinidine, thioridazine (Mellaril), cimetidine (Tagamet), amiodarone (Cordarone), diphenhydramine (Benadryl), haloperidol (Haldol), ticlopidine (Ticlid)
CYP2E1	Cimetidine (Tagamet), isoniazid (INH), watercress

* the only PI with CYP2D6 inhibitory activity

Table 4: Common substrates of 3A4 and 2D6 isoenzymes

3A4 Substrates	2D6 Substrates
Benzodiazepines	Beta blockers
Cisapride (Propulsid)	Tricyclic antidepressants
Macrolides	SSRIs
Methadone	Haloperidol
Risperidone	Lovastatin (Mervacor)
Quinidine	Simvastatin (Zocor)
Slidenafil (Viagra)	Atorvastatin (Lipitor)
	Cerivastatin (Baycol)
	Fluvastatin (Lescol)
	Pravastatin (Pravachol)

Medicine

HIV in children may affect brain through many mechanisms

Children, continued from page 1

lower extremities and a technetium bone scan failed to demonstrate bone or joint abnormalities. She was then referred to our facility for further evaluation. On her admission, she was noted to have normal growth parameters with a head circumference measuring 49.5 cm (50%). Examination of the mouth revealed mild chelosis at the left angle of the mouth and moderate oral thrush. On neurologic examination she was noted to have a wide-based gait, symmetric hypertonia of lower extremities and mild hyperreflexia in left lower extremity. Motor strength in the upper extremities was normal and no sensory defects were found. The rest of the physical examination was unremarkable. Magnetic resonance imaging (MRI) of the spine, and computed tomagraphy (CT) of the head was normal. Later in the evaluation, HIV-1 antibody was detected by ELISA and confirmed by Western blot. The patient's initial CD4 count and viral load measurements were 0 mm^3 and 131,456 copies/ml respectively. The patient was later started on a combination antiretroviral therapy, in addition to physical and occupational therapy.

Her hypertonic diplegia progressed rather rapidly over the first month after her diagnosis to the point of constant toe walking and spontaneous clonus in both ankles. Her symptoms changed very little until a year after diagnosis, when her viral load came under control. At that point she showed some improvement in her lower extremity tone and in her gait. She originally required ankle/foot orthotics but eventually began walking flat-footed and lost her spontaneous clonus. She still has a wide-based gait as well as increased tone and hyperreflexia in the lower extremities. Botulism toxin therapy was given twice without effect. She is doing well in school. Wechsler Intelligence Scale for Children revised (WISC-R) was done in December 1998 and showed performance IQ of 82, verbal IQ of 81 and full scale of 80. Repeat in May 2000 showed performance of 82, verbal of 86 and full scale of 83. Serial head MRI's were normal.

The patient was initially treated with zidovudine (ZDV) and lamivudine (3TC) alone. On this combination her viral load ranged between 15,000-50,000 copies/ml and her CD4 count steadily rose to 15%-18%. In June 1998, about 11 months after diagnosis she was put on highly active antiretroviral therapy (HAART) therapy and her viral load fell to <400 copies/ml by week 12. It has remained <400 copies/ml. Her CD4 also increased rapidly on HAART and has run 30%-34% since November 1998.

Natural history of HIV disease in children

The natural history of HIV-1 infection in children is rapid clinical progression resulting in severe immune suppression and early death in approximately 20 percent of vertically infected children (rapid progressors) and slower progression in the other 80 percent (long-term progressors). Neurologic disease similarly manifests variably in HIV-infected children with severe progressive encephalopathy (PE) seen in rapid progressors and less severe disease seen in the long-term progressors. PE occurs in conjunction with immunologic (CD4 counts <750 mm^3 before age 1 and < 500 mm^3 between ages 1-5 years) and clinical AIDS defining conditions. Timing of HIV-1 infection may explain the differences in disease progression, including neurologic symptomatology. In rapid progressors, early detection of HIV by culture and/or polymerase chain reaction (PCR), typically at birth or within the first two weeks of life, reflects in-utero transmission. HIV infection of the fetal brain may explain the early and severe nature of neurologic impairment in the small group of rapid progressors. For the majority of HIV-1 infected children, those with slower onset of HIV disease progression, detection of HIV occurs after the first few weeks of life and largely reflects intrapartum (and to a lesser extent postpartum) transmission. Typically this group of children have normal neurologic development for years before manifesting neurologic symptoms consisting mainly of mild to moderate cognitive impairment. [1-4]

Clinical presentation

PE classically presents as a triad of symptoms: impaired brain growth; lack of acquisition, plateau or loss of neurodevelopmental milestones; and progressive motor dysfunction. PE has been compared to the AIDS dementia complex (ADC) described in adults, since both are seen at a time when severe immune dysfunction occurs. Both diseases can lead to motor deterioration with cognitive decline and have signs of brain atrophy. However, ADC occurs in a mature brain after horizontal infection whereas PE occurs in an immature brain after vertical infection. Unlike ADC, in HIV-infected children with PE, neurologic symptoms develop rapidly after infection, the peripheral nervous system is rarely affected, and cerebrovascular disease events and seizures are uncommon. Patients with PE and ADC are both at risk for opportunistic infections (OIs) but CNS OIs occur more frequently in ADC than PE. Other symptoms such as vacuolar myelopathy and psychiatric symptoms are described more frequently in ADC than in PE. Learning and attention disorders instead are seen primarily with PE. With both PE and ADC, CSF findings are generally nonspecific.[1,2]

Impaired brain growth in PE can be determined by serial head circumference measurements in infants with open fontanels. Poor growth is defined by no increase in head circumference, by crossing two percentiles in two months or, in children after one year of age, by loss of one standard deviation from baseline. Once fontanel closure has occurred, than assessment of brain parenchymal volume loss can be made with head CT or MRI.[1]

Motor dysfunction can dramatically present with hyper- or hypotonia and spasticity. Typically, fine motor dysfunction precedes gross motor dysfunction. Extrapyramidal symptoms (EPS) such as rigidity, dysarthria, hypomimetric facies and gait disturbances are occasionally seen.

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The most common finding on CT or MRI is brain atrophy

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Cranial nerve findings and/or focal neurologic symptoms are not typically associated with PE and should raise the clinician's suspicion of a mass lesion due to a neoplasm or secondary infection.[1-3]

In order to meet criteria for diagnosis of PE, an HIV-infected child should have evidence of progression of disease. Showing progression in one out of three symptoms in children who are neurologically normal at birth, or two out of three symptoms in children who are neurologically abnormal at birth, is required for diagnosis of PE.[2]

Pathogenesis

HIV infection in children may affect the brain through many mechanisms. Direct viral infection is seen in brain macrophages (microglial cells), monocytes, lymphocytes and to a lesser extent, astrocytes. Fetal astrocytes may be more susceptible to HIV-1 infection than mature astrocytes, thereby allowing in-utero infection of these cells. Cytokines contribute to HIV-1 infection of the CNS by activation of most microglial cells and astrocytes. In addition, cytokines such as tumor necrosis factor may have a direct toxic effect on brain cells. Through toxin release, cytokines can then indirectly cause neuronal death resulting in white matter lesions. Free radicals such as $NO^{\cdot}$ and $O2^{-}$, released by activated cells, may lead to further neuronal death. Finally, HIV-1 viral products may be directly toxic to neuronal cells by inducing programmed cell death, apoptosis, or by influencing intracellular calcium homeostasis.[3]

Differential diagnosis

Many other factors need to be considered during evaluation of CNS disease in HIV-infected children. Nutritional deficiencies, pain, environmental deprivation as well as maternal drug use, can contribute to neurologic problems in HIV-1 infected children.[1,2] Other infections should not be overlooked. Congenital toxoplasmosis can present with progressive neurologic deterioration, especially in the first year of life. Obstructive hydrocephalus and chorioretinitis should alert the clinician to this diagnosis. Similar to toxoplasmosis, cytomegalovirus (CMV) can affect brain development after in-utero infection. CMV infection acquired before or after birth may also act as a co-factor with HIV in progression of overall disease and neurologic impairment.[5] A mass lesion such as a neoplastic or focal infectious process should be suspected in any child presenting with focal neurologic signs.[2]

Diagnostic tests

Radiographic. The most common finding on cranial CT or MRI is brain atrophy. Calcifications, seen easier with CT, can be found in the basal ganglia, thalamus, and frontal grey/white matter. Calcifications are associated with severe neurologic disease and may also occur after congenital infection from toxoplasmosis or CMV. CNS neoplasms (primarily non-Hodgkin's lymphoma) or focal inflammatory processes present as hyperdense enhancing lesions on contrast enhanced cranial CT or MRI, although this radiographic finding is nonspecific. MRI is best for detecting demyelinating conditions such as progressive multifocal leucoencephalopathy (PML). PML, a disease linked to the papovirus JC SV40, is rare in HIV-1 vertically infected children. Cranial ultrasound may show vascular changes prior to calcification, as well as detect frank aneurysms.[6] Functional brain imaging such as positron emission tomography (PET), single photon emission tomography (SPECT), or proton magnetic resonance spectroscopy (PMRS) has detected abnormalities in a small number of tested HIV-infected children and may prove useful in the future but further research into these techniques is needed.[1]

CSF. CSF changes, when they occur, are generally nonspecific. Mild pleocytosis and protein elevation can be seen. HIV antibodies are present in the CSF of all HIV-1 infected children but cytokine production in CSF occurs only in children with PE. Myelin basic protein detection in CSF occurs in demyelinating conditions.[1]

Neurodevelopmental. Regular neurodevelopmental screening is important for all HIV-infected children. Complete testing involves both neurologic and psychomimetric testing. Intervals for testing are more frequent in the younger aged children: every three to four months in infants less than one year, every six months for children between one and three years, yearly for children between three and ten years, and then every two years thereafter. Children who display progressive neurologic decline need to be followed more closely. Psychomimetric testing involves evaluation of both motor and cognitive function and should be performed by a licensed psychologist. Scales for evaluating motor function include the Bayley and Peabody Scales. Language can be assessed with the Peabody Verbal Fluency test. Different scales are used based on age of patient, type of function assessed and degree of disability. In-depth discussion of various tests is beyond the scope of this article and is reviewed elsewhere.[1,2]

Intensive case management is required for families of HIV infected children with severe CNS disease.

Prognosis

Without antiretroviral therapy, children in the rapid progressor group typically die within one to three years after birth, whereas disease in the majority of HIV-1 infected children progresses much slower, with death occurring later, sometimes into the second decade. Children who develop PE fall into the rapid progressor group and have a poor outlook for neurologic development and survival.[1-3]

Treatment

Supportive care. Rehabilitation is essential for children with PE. Children with spasticity may benefit from physical, speech and occupational therapy in order to increase flexibility and perform activities of daily living.

Clinicians should vigilantly look for any signs of nutritional deficiencies. Failure to gain weight appropriately may be secondary to organic disease (e.g. chronic malabsorption, anorexia), nonorganic disease (maternal deprivation) or a combination of both. Specific nutrient deficiencies may lead to encephalopathy. Thiamin deficiency, as seen commonly in alcoholics, can cause Wernicke's encephalopathy. L-carnitine deficiency is linked to zidovudine (ZDV) associated myopathy but not PE. Specific nutrient deficiencies, when detected, should be treated, although few nutrient deficiencies (e.g. B12) are associated with PE. Infectious, metabolic, gastrointestinal or psychosocial causes of poor weight gain should be addressed. For children with inadequate oral intake, aggressive measures to obtain adequate weight gain, such as gastrostomy tube placement, may be necessary.

Drug therapy is warranted in some cases. EPS symptoms can be treated with levodopa. Children with psychiatric or attentional disorders may require specific psychomimetric medication. Pain is being increasingly recognized as contributing to poor overall function in chronic disease. Children with HIV infection face pain in a number of ways, from multiple painful procedures to drug associated neuropathies. Treating pain in children improves quality of life and ability to function in society. During venupuncture, distraction therapy may work in older children but younger children need topical anesthesia (e.g.EMLA® cream) when possible. Chronic pain requires a step-up approach from non-opioid to opiod medications until pain is controlled.[2]

Finally, intensive case management is usually required for families of HIV-1 infected children with severe CNS disease. Case managers can coordinate medical care, in addition to providing referrals for family and individual counseling. Case managers can also identify and address poor social conditions contributing to or exacerbating CNS disease.

Antiretrovirals. Ultimately, treatment of HIV neurologic disease requires suppression of viral infection. Early trials showed regression of neurologic symptoms and improved brain growth with ZDV. This response was short-lived, however, probably secondary to development of resistance. Later, in a trial comparing ZDV, ZDV and didanosine (ddI), and ddI alone, both ZDV alone and the combination therapy improved neurologic outcome but the combination arm was more effective at preventing neurologic deterioration after 24 weeks of therapy. Not all antiretroviral drugs cross the blood-brain barrier. But agents like ddI, which penetrate the CNS poorly, probably affect neurologic outcome by reducing viral load systemically.[7] Highly active antiretroviral therapy (HAART) reduces viral load and restores immune cells (CD4 cell count) in HIV-1 infected children. Hopefully, ongoing studies into the long-term neurologic effects of HAART will show improvement in neurologic outcome as well.❖

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Plan ahead to attend HIV conferences...

▲ June 13-15, 2002
12th International Symposium on HIV and Emerging Infectious Diseases
Toulon, France
E-mail: bettina.albine@wanadoo.fr

▲ June 19-22, 2002
Neuroscience of HIV Infection
Düsseldorf, Germany
E-mail: bwigdahl@psu.edu

▲ July 2-5, 2002
XI International HIV Drug Resistance Workshop: Basic Principles & Clinical Implications
Seville, Spain
E-mail: info@informedhorizons.com

▲ July 7-12, 2002
XIV International AIDS Conference
Barcelona, Spain
E-mail: aids2002@aids2002.com

▲ September 19-22, 2002
Sixth Annual United States Conference on AIDS
Anaheim, California
E-mail: pwoods@nmac.org

▲ September 22-25, 2002
4th International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV
San Diego, California
E-mail: lipodystrophy@us.intmedpress.com

▲ October 24-27, 2002
40th Annual Meeting of the Infectious Diseases Society of America
Chicago, Illinois
E-mail: info@idsociety.org

▲ November 17-21, 2002
6th International Congress on Drug Therapy in HIV Infection
Glasgow, UK
E-mail: HIV6@gardiner-caldwell.com

▲ December 1-3, 2002
Second International Conference on Substance Abuse and HIV
Mumbai, India
E-mail: yusufmerchant@sanskritiindia.com

▲ April 2003
5th International Conference on Nutrition and HIV Infection
Cannes, France
E-mail: hivcannes@wanadoo.fr

Legal

Will Louisiana's new consent statutes be helpful to clinicians?

Linton Carney, JD

In the last few years, the changing demographics of the HIV/AIDS pandemic in the United States have become readily apparent. Clinicians who once treated a largely homogenous population of gay white men now see clients of every ethnicity, background and gender. As the baby boomer generation has gotten older, the number of people infected with HIV who are over 50 has increased, while at the other end of the spectrum the number of infected minors has remained steady. In addition, as the advances in therapy have lengthened the life expectancy of the infected population, many more people living with HIV/AIDS are facing dual diagnoses: HIV and some variety of cancer, for example. At AIDSLaw of Louisiana, we have begun to see many more clients who may be eligible for Social Security disability benefits on grounds that seem unrelated to HIV, particularly mental disorders. Responding appropriately to these changes is an important goal for everyone who provides services to the affected population.

As of January 31, 2002, there were 247 people under the age of 18 who were infected with HIV in Louisiana.[1] Although Louisiana law permits minors (people under 18) to consent to their own medical and surgical treatment,[2] the preferred course is to receive authority from a parent or from an adult who is considered to be standing in loco parentis (in the place of the parent).[3] Moreover, in the case of young children, they may be too young to give consent or be deemed too young for their consent to be considered meaningful. Certainly no practitioner would want to rely on the consent of a six year old to a serious and complicated course of treatment.

In response to this and other issues concerning minors, the Louisiana legislature passed Act 410 of 2001,[4] to create a non-legal custodian affidavit for adults who are taking care of a minor but who have not been legally appointed as the minor's guardian. By executing the affidavit, the adult may have authority to make certain decisions on the minor's behalf, including giving consent for the minor's medical treatment.

The affidavit form (which is available by calling AIDSLaw at 504-568-1631) provides a section for the custodian to indicate either that he or she has received the consent of the parent(s) to act on the minor's behalf, or that the custodian is unable to locate the parents to receive their consent (or both if one parent can be located and the other cannot be found). There is also a section for comments which can be used to explain the particular situation. An example might be when one parent cannot be found and the other is incarcerated.

Although the prior law permitted "any person standing in loco parentis [in the place of the parent] whether formally serving or not"[5] to authorize medical treatment for the child under his or her care, the law left undefined what constitutes being in loco parentis in particular situations. Medical practitioners had to make that judgment call. Was it sufficient that the adult appeared to exercise authority over the minor? What if the minor protested that the adult was not empowered by the parents to make such decisions? In addition, the old law[6] only permitted the person standing in loco parentis to consent if the parent was not "reasonably available, willing, and competent to act." Once again, clinicians were left to determine whether they should try to contact the parents. What was the clinician to do if the minor protested that his parents were readily available, despite the representations made by the adult? To a large extent, the new law removes these burdens from the clinician and instead places them on the party executing the affidavit. Moreover, the new law specifically provides that third parties can rely on the affidavit unless they have actual knowledge that it is false; under the old law, the courts had absolved medical providers from liability if they acted in good faith, which is arguably a slightly higher standard. And of course now clinicians will have an actual document in their file to rely on rather than merely a notation in medical records that could be challenged at a later date.

Nevertheless, the ultimate decision for children's medical care still rests with their parents, and the new statute specifically provides that parents may override the custodian's decisions. Thus the situation could arise in which the custodian authorized treatment, such as antiretroviral therapy, and the parent subsequently appeared to countermand the decision. Despite the practitioner's concerns that interrupting treatment would be dangerous for the minor, the parent's wishes would have to be followed, since a competent parent is generally empowered to consent to medical treatment for his or her children. Although the courts will scrutinize the parent's decision carefully, courts generally recognize the right of a competent parent to make medical decisions for their children, even if the decisions do not seem to be in the child's best interests. At least one court has upheld a parent's decision not to have a child undergo antiretroviral therapy.[7]

Clinicians in Louisiana, therefore, should be familiar with the new affidavit form. (AIDSLaw can provide the form on disk or by e-mail.) If it is properly executed and the guardian can identify him/herself through some mechanism such as a driver's license or a state-issued identification card (it is a good idea to make a copy of this for your files, too), clinicians can rely on the affidavit unless they have actual knowledge of its falsity. Supervisors may want to consider requiring such an affidavit in certain cases (when the guardian is not related to the minor, or in a situation involving life-threatening procedures), and the new form can be used for on-site execution, provided there is a notary public available.

A second new law enacted by the Louisiana legislature, Act 755 of 2001,[8] establishes ground rules for advance medical directives for mental health treatment. Under the new law, a person may designate another to make these decisions, and may specify what sort of treatment he/she wants or doesn't want. These acts (which must be notarized before two witnesses) will be good for up to five years. There are some particular requirements: the directive must be "accompanied by a written mental status examination performed by a physician or psychologist attesting to the principal's ability to make reasoned decisions concerning his mental health treatment."[9] The agent must also accept the power of attorney in writing.[10] The treating physician, care provider, their employees, or the owner or operator of

the patient's facility cannot be the agent unless they are related to the patient by blood, marriage or adoption.[11] The law also prohibits the treating physician, care provider, their employees, or the owner or operator of the patient's facility from being witnesses, as well as anyone related by blood, marriage or adoption.[12]

While the new law has some evident advantages for people with a history of mental problems, it raises some troubling questions for clinicians who work with the HIV/AIDS population. An initial question is whether dementia is covered by the new law. The law defines "mental health treatment" to include "electroshock therapy, treatment of mental illness with psychoactive medication, admission to and retention in a treatment facility [up to 15 days], and outpatient services."[13] Although most people with AIDS do not get dementia[14] and the advances in treatment have reduced further that number, a substantial number of persons with HIV may get dementia, either from cytomegalovirus, toxoplasmosis, or HIV-associated dementia (HAD). (There are also 380 people over 60 who have HIV in Louisiana, a population susceptible to non-HIV related forms of dementia like Alzheimer's.[15]) If dementia is covered, many of the protocols and treatments may also be covered since the new law even covers outpatient services. If this proves to be the case, a patient who has executed a Medical Power of Attorney may not be covered for dementia-related services. Most forms that are presently used for Medical Powers of Attorney do not comply with the new law; it is rare for the medical agent to accept in writing, and the attestation of the physician or psychologist is a completely new requirement.

One solution to this problem is to offer the new document to all clients. However, there may be some problems with such a blanket approach. For some clients, discussing dementia is simply too depressing. In addition, since the majority of clients will have no history of mental health treatment, they are unlikely to be familiar with the options that the new law provides. Spending the time to make coherent decisions about mental health treatment may seem like "overkill" to these clients (and some clinicians). For many people without a history of mental health problems, the detailed options set forth in the new law may seem confusing or just too much information to take in. Many people in this situation may want simply to appoint their medical agent as their mental health agent with no other details, but the new law is unclear whether such a "lite" power of attorney will be acceptable. (The statute provides that the Mental Health Advocacy Service and the State Department of Health and Hospitals will develop a form[16] which should be available this spring.) Clinicians must strike a delicate balance. On the one hand, they risk overloading their clients (who are already getting lots of relevant HIV/AIDS information) with information about mental health treatment that most clients won't need. On the other hand, no one can predict who will get dementia, and the document has to be executed before dementia sets in.

For clients who decide that they want an advance directive for mental health treatment, there are some requirements that could pose problems. The agent has to accept in writing, but the law is unclear whether the acceptance has to be part of the actual document or can come later. If the agent is present when the client signs, the agent should sign an acceptance on the spot. If the agent is not present when the client signs, the clinician needs to make sure that the client understands that the whole document is ineffective until the agent accepts, and in writing. Once the written acceptance is obtained, it should be kept with the advance directive.

Another stumbling block is the new requirement that the document be accompanied by the attestation of mental health competency by a physician or psychologist. The new law is unclear whether the attestation has to be part of the notarial act (probably not), but even if the attestation can be on a separate piece of paper, it should be substantially contemporaneous with the act. Getting the attestation may be relatively easy for patients who have had mental health problems, and particularly so if they are presently in treatment. But the majority of patients with HIV/AIDS will not have been in treatment, and they may not have ready access to a psychologist or physician who feels competent to attest to the patient's mental competency.

Conclusion

These new statutes make important changes in health care law and can affect clients living with HIV/AIDS. Clinicians can use the non-legal custodian affidavit in ambiguous situations, or for serious procedures and therapies. The new law on advance mental health directives is more problematic, particularly the new requirement that a physician or psychologist attest to the patient's mental health.❖

FOOTNOTES

1. Surveillance Report, State of Louisiana, Department of Health and Hospitals, Office of Public Health, HIV/AIDS Program, January 31, 2002.
2. La. R.S. 40:1095
3. La. R.S.40:1299.53.
4. Now found at La. R.S. 9:975. There is no similar statute in Arkansas or Mississippi.
5. La. R.S. 40:1299.53
6. La. R.S. 40:1299.53
7. In Re Nikolas E., 720 A.2d 562, 563 (Me. 1998).AD.H. v. State Dept. of Human Resources, 640 So.2d 969 (Ala.Civ.App. 1994). See LaFleur-Spawn,"Clinicians Faced with More HIV+ Women of Child-bearing Age," HIV Clinician, Vol.13, No.4 (Fall 2001).
8. Now found at La. R.S. 28:221 et seq.
9. La. R.S. 28:224.
10. La. R.S. 28:223.
11. La. R.S. 28:233.
12. La. R.S. 28:234.
13. La. R.S. 28:236.
14. La. R.S. 28:221 (5).
15. Surveillance reports from 2000 indicate that 4% of persons with AIDS in Louisiana developed dementia.
16. Surveillance Report, State of Louisiana, Department of Health and Hospitals, Office of Public Health, HIV/AIDS Program, January 31, 2002.
17. La. R.S. 28:236.

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Nursing

Depression can be a serious problem for HIV infected

Deborah J. Konkle-Parker, PhD FNP, ACRN

M.C. was recently diagnosed with HIV after giving blood at her university's blood drive. She appeared young and healthy, there were no signs of opportunistic infections, and it appeared that her immune status was most likely very adequate and probably early stage disease. Her depression, however, was debilitating, and she became quite tearful early in the interview. "They told me that this isn't seen as a terminal disease anymore, and I know that I am not about to die, but it is so hard. I can't sleep and I haven't had any appetite ever since they told me. I don't think I can make it! I'm so scared."

R.S., was diagnosed three years ago, and had excellent viral control of his AIDS. Despite his healthy appearance, however, he reported little activity in his life, and confessed that he had been missing doses of his medicines recently "because I just couldn't get myself to take them. It brings my AIDS right into my face, and that makes it hard."

These are two of the many faces of depression in the setting of HIV disease, and brings to the forefront some of the problems that depression causes that make it an urgent problem in HIV. Inability to cope, suicidal ideations, a diminishing of quality of life, and poor adherence to medications make depression a serious problem in the lives of those infected with HIV.

Major depression and dysthymic disorder are two types of depression that are classified by the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV). One of these depression disorders is very common in those diagnosed with HIV disease (Penzar, Reddy, and Grimsley, 2000). As opposed to minor depression, which is usually fairly short-term and precipitated primarily by circumstances, these disorders are affected by a combination of genetic, biochemical and environmental factors. Various studies estimate the lifetime prevalence of depression in HIV-infected individuals anywhere from 22% to 45%, depending on the type of methodology used to determine depression. This appears to be a higher rate than the general population, where it affects 13 to 20% of the population (Penzar, Reddy, and Grimsley). The psychological stress of an HIV diagnosis appears to be influential in these high rates of depression.

Major depression is defined in the DSM-IV as five of the following symptoms for at least two consecutive weeks. One of the first two symptoms must be present:

1. Depressed mood most of the day almost everyday;
2. Decreased interest and pleasure in nearly all activities;
3. Changes in appetite or weight without dieting;
4. Disruptions in sleep patterns nearly every day;
5. Psychomotor retardation or agitation;
6. Feelings of worthlessness or inappropriate guilt;
7. Diminished ability to concentrate; and
8. Recurrent thoughts of death or suicide.

Depression clearly affects quality of life in any individual by decreasing the pleasure in life, the ability to sleep, and feelings about self. Many of the symptoms of HIV can exacerbate symptoms of depression, making it even more damaging to quality of life. Stress and depression can also affect disease status through direct effects on the immune system, as well as decreased ability to cope with the disease. According to Penzar, Reddy, and Grimsley (2000), stress and depression can decrease immune function through reductions in the number of natural killer cells and CD8 cells. These cells are important in controlling viral replication, so depression may theoretically negatively impact the course of HIV disease.

Ability to cope with HIV disease can also be decreased because of the apathy, self-neglect, and forgetfulness that can occur in depression. Adherence to HIV medications can be adversely affected, making control of viral replication more difficult and emergence of resistant virus more likely. In several studies, depression has been shown to be associated with decreased adherence to antiviral medications (Singh, et al, 1996; Paterson, et al, 2001).

Depression is important to recognize, in order to be able to use appropriate interventions for improved health. This author uses a pneumonic, SIGECAPS, to remind of the seven cardinal signs (source unknown):

- S sleep
- I interest
- G guilt
- E energy
- C concentration
- A appetite
- P psychomotor activity
- S suicide

It is important to keep in mind that an affected individual may not have a change in the same direction as others: for example, a tendency to eat in an uncontrolled fashion may be as much of a symptom of depression as decreased appetite. In the same way, agitation may be as much of a symptom as decreased psychomotor activity. When one recognizes the condition, then interventions directed at the particular issue can be effectual. Antidepressant medications are an important focus, as well as psychological therapy.

Nonpharmacological issues that may be important in affecting depression can be identified by the factors that appear to be more likely to predict depression. Factors that were associated with depression in a study by Kelly et al (1993) were the number of illness symptoms, social support, health locus of control, substance use, and high-risk sexual behavior. By knowing this information, nurses can be particularly vigilant in those who are symptomatic, those who appear to be isolated, and those who are actively using substances. Support groups, peer support, or empathic listening by the nurse can affect low perceived social support. Instructing and encouraging clients to be active in their health care, thus gaining a sense of control in their health status, can also assist in improving and/or preventing depression. Actively encouraging and facilitating individuals to receive treatment for substance abuse can also be effective.

A goal of preventing or improving depression symptoms is a worthy goal for a nurse in HIV care, as depression appears to be implicated in decreased health status, quality of life, and potentially risky sexual behavior. As nurses know, quality of life matters a great deal in health care, particularly in relation to depression in the setting of HIV disease.❖

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Research

Study: HIV+ people often don't disclose status to sex partners

Megan O'Brien, MPH
Patty Kissinger, PhD

Disclosure of HIV serostatus is a complex and difficult issue both for individuals with HIV and for clinicians. Disclosure to friends and family, if successful, may open up opportunities for social and material support for an individual with HIV. This support can lessen feelings of isolation and despair. Supportive persons can provide assistance with reminders for medication dosing, help with transportation, childcare, and financial burdens of illness. Disclosure to potential sexual partners is a key component for transmission reduction if it results in safer sex practices. However, disclosure can also put the seropositive individual at risk for rejection, stigma, and loss of privacy. Although disclosure behaviors were the subject of several studies in the early 1990s, there has not been much in the recent literature regarding disclosure. However, the advent of highly active retroviral therapy has lengthened the life of HIV-infected persons and has made it easier to hide the disease for a longer period of time. This may have significant impact on disclosure behavior.

In a recent study among individuals diagnosed with HIV in the last five years and receiving outpatient care in New Orleans, our team from the Epidemiology Department of the Tulane University School of Public Health and Tropical Medicine asked about disclosure to friends, family, and sexual partners.

The 269 persons interviewed had disclosed to: main sex partner (74%), casual sex partner (25%), immediate family (70%), other relative (27%), friend (26%), co-worker (15%), and stranger (10%). Younger respondents (aged 18-22) were less likely than older respondents to disclose to a main partner, someone in their immediate family, and a friend. Compared to others, respondents with low CD4 cell counts were more likely to disclose to a main partner, someone in their immediate family, and another relative. Those who reported complete non-disclosure to significant others were more likely to be aged 18-22 and to have acquired HIV through heterosexual contact or intravenous drug use. Among the 101 individuals who reported having both a main and a casual sex partner, 58% disclosed to their main partner, but only 23% disclosed to any of their casual sex partners.

Among the 205 individuals who were sexually active since their diagnosis, only 50% of respondents disclosed to their most recent partner and 37% used a condom. Those who disclosed to a partner were approximately five times more likely to have used a condom with that partner. Their reports on these most recent encounters indicate that in 41% of the encounters, the respondents did not disclose to their partner and did not use a condom. The respondents withheld disclosure but did use a condom in only 10% of the encounters.

How can we explain such low rates of disclosure? There are several possible explanations. One is that optimism about HIV treatment options has reduced both fear of contracting and transmitting HIV. Individuals with HIV live longer, healthier lives with an improved quality of life. They remain active and participate in "normal" social lives. Advertisements for antiretroviral therapies foster this image and many individuals who have achieved an undetectable viral load falsely believe that they cannot transmit the virus to others. Some point to a fatigue with the safe sex message. Years of bombardment and scare tactics have left some "stressed out" with worrying about safe sex and longing for spontaneous intimacy. For some individuals with HIV, the stigma of the disease is disincentive for disclosure, and this fear is certainly warranted. In our study, an understanding reaction was the most prevalent reaction to disclosure among the partnerships where the respondent disclosed (53%), but respondents also reported reactions of their partner becoming upset (28%), violent (17%), and ending the relationship (24%). Finally, clinicians and public health practitioners may have overlooked the need to counsel and educate patients about the need for safer sex. Advances in treatment have lured us all toward the optimistic focus on treatment and away from the more difficult task of prevention. Conversations about disclosure and safe sex practices may seem awkward and paternalistic.

However, the results of this study suggest that disclosure needs renewed attention. The implications of HAART need to be explained both to seropositive individuals and their partners, as well as to the population at large. We need to clarify the misconception that HAART is a cure for HIV, instead of a treatment. We need to focus on ways to improve counseling and education of individuals with HIV, so that we can teach our patients to decide to whom to disclose and ways to disclose that minimize unwanted reactions and maximize support and understanding for the seropositive individual. Although disclosure and safe sex may be addressed in initial counseling sessions, we may need to reinforce the message with ongoing counseling and education. Patients with recurrent sexually transmitted infections should be targeted for counseling about the risks of unsafe sex. Finally, we need to revive the message that HIV is a chronic illness and that the only way to prevent it is to insist on condom use all the time, every time.❖

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Nutrition

How should nutrition goals change in end-of-life care?

Ginger Bouvier, MEd, LDN, RD

Dietitians and other health care providers working in the field of HIV/AIDS are often challenged with patients who have experienced severe weight loss. As a dietitian at MCLNO's HIV Outpatient Program, I often hear a patient say, "How can I gain my weight back?" or hear a family member say, "If he would only gain weight, he'd get better."

The use of nutritional supplements, anabolic steroids, growth hormone, and treatments for symptoms such as anorexia, nausea and diarrhea have assisted many HIV-infected individuals in regaining lost weight and muscle mass, and achieving good nutritional status. For patients with advanced AIDS and a high viral burden, such interventions may only provide temporary "quick fixes" or may be futile unless the HIV disease can be effectively treated.

Wasting syndrome or cachexia often occurs in patients with end-stage AIDS as a result of multiple factors, including chronic hypermetabolism, malabsorption, and altered metabolic processes. When patients with wasting syndrome are unable to achieve virologic improvement, they are often unable to attain nutritional improvement. The wasting patient's inability to gain weight can be frustrating for the patient, his or her family, and the health care providers. It is important to determine if weight gain, especially back to a healthy weight, is a realistic goal. The patient's prognosis should be a major consideration. Refractory weight loss in a patient with prolonged, advanced HIV disease and poor virologic control is a significant symptom that can assist in identifying the need for hospice/palliative care.

Nutritional care does not end when a patient is receiving palliative and/or hospice care. However, we must remember that when the overall goals of medical care are palliative, not curative, the nutritional goals will also be palliative. Nutritional care will typically focus on alleviating unpleasant symptoms and providing comfort rather than on achieving weight gain and nutritional improvement.

Food for Thought

Food provides the energy and nutrients necessary for life. Food is therefore often equated with life. Among the issues that families and caregivers have to resolve for themselves, in the context of a dying patient, is the powerful symbolic meaning of food. The intake of food and fluids often becomes the center of a struggle between a terminally ill patient and caregiver. Foods have different meanings to each of us. Certain foods may remind us of holidays, childhood, family, pleasant events, or unpleasant ones. Food may give comfort ("Homemade chicken soup always makes me feel better"), or pain ("My mouth sores burn when I eat anything"). Food can provide hope ("He ate good today, he must be getting well"), or despair ("He won't eat, he's giving up"). When patients are allowed to determine their own food and beverage intake, they often feel a sense of relief, as well as a sense of control over this aspect of their lives. Decisions concerning nutrition in palliative care should be patient-centered, individualized, and open to change if the patient's condition improves.

Many caregivers fear that the patient will experience discomfort due to hunger, or suffering from the lack of food and fluids. In contrast, the general impression among hospice clinicians is that starvation and dehydration in the dying patient may actually contribute to a gentle and comfortable death. It is important for caregivers and family to understand that decreased intake of food and fluids is a predictable physiological change as death approaches, and that lack of food and fluids is not painful to the patient. Force-feeding and artificial nutrition support, however, may cause or exacerbate painful conditions, such as fluid overload, vomiting, or aspiration, in a dying patient. Only if the prognosis of a patient in palliative treatment or hospice care is improving contrary to expectations are strategies of medical nutritional therapy indicated.❖

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Dentistry

Some dental professionals still reluctant to treat HIV patients

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As with any medical condition, persons with HIV/AIDS (PWH/A) have special needs for dental care. This includes many of the oral lesions and medical conditions, such as thrombocytopenia, that may alter dental treatment plans. These oral conditions can be painful and life-threatening. Dental health care professionals are showing an increased willingness to treat PWH/A, but in some cases there is still a great reluctance to treat them.[1-5] Education of dental professionals about the special needs of PWH/A and transmission of HIV infection should allay the fears of treating this patient population. According to past studies with surveys, more than just education is needed.

A 1988-89 survey of 319 students in the medical, dental, nursing, and allied healthcare professions revealed that over one-third had some reservations about treating acquired immunodeficiency syndrome (AIDS) patients. Most of those surveyed also believed that health care workers had the right to refuse care to AIDS patients. In this study, unwillingness to treat AIDS patients was strongly associated with homophobic attitudes and concerns that patients with AIDS posed a risk to health professionals. The authors recommended AIDS education for health professionals should emphasize methods for the prevention of HIV infection among health workers. They also said that "teaching strategies designed to deal with the irrational feelings that AIDS often engenders need to be addressed."[1]

Even in 1992, many dental health care workers (DHCW) in one study felt they were not equipped or willing to treat PWH/A in a private practice situation, and thought that many should be referred. In a random sample from Minnesota, more than 50% of DHCWs said they did not have sufficient information to safely and effectively provide care for HIV+ patients. Nearly twice as many DHCWs said offices have an ethical versus a legal duty to treat HIV infected patients. Only a small percentage of DHCWs believed the private practice dental office is the best place to treat HIV patients, and only 50% said they would provide care. Seventy-six percent said staff had been uncomfortable treating HIV+ patients, 14% said staff had refused to treat, and 10% said referrals were difficult. The authors suggested that additional cognitive and behavioral changes are necessary to ensure that all DHCWs provide care with the highest technical, legal, and ethical standards for all patients.[2]

One 1995 study showed that 83% of dental professionals agreed "that they had tender feelings for HIV+ patients," but over one-third reported it was "hard to be sympathetic." Only 68% would treat an HIV+ patient even if the possibility of legitimate referral exists.[3]

An anonymous postal questionnaire survey studying the knowledge, attitudes, beliefs and practices on human immunodeficiency virus (HIV) infection was conducted among all registered medical and dental practitioners in Singapore in 1996. The level of knowledge regarding transmission and prevention was generally good, although there were a number who believed that HIV could be transmitted by the respiratory and oral routes. However, knowledge regarding diagnosis and medical management was unsatisfactory. Although a large majority felt they had the ethical obligation to treat HIV patients, only half of them indicated their willingness to do so if they were given the choice. Dentists seemed more sensitive to issues involving transmission in the workplace, although 95% of them practiced universal precautions.[4]

In a 1999 article, researchers from the University of Western Ontario conducted a survey of dentists in Canada to assess the percentage of care providers who refuse to treat HIV-infected patients. Of 4,107 respondents, 16 percent said they would refuse treatment to HIV-positive patients. These responses were most strongly associated with lack of belief in an ethical responsibility to treat infected patients. Staff fears, patient loss, cost of infection control, and safety concerns also played a role. Eighty-one percent of dentists said they would treat HIV-positive patients[5].

Education on the transmission of HIV infection should reduce the fears or affect attitudes for dentists treating PWH/A. One study used a training seminar, "At Ease with AIDS," at a dental school. This involved role playing and seminars to measure empathy and willingness to treat persons with PWH/A. They found that this training for those with weak skills in the treatment of PWH/A was slightly more affective than those with moderate or high levels. The responses of those individuals who may not have a positive response towards treating PWH/A, and who previously were educated in treating PWH/A, did not change significantly. This study was conducted on academic dentists who have different interests than their private practice counterparts. Other forms of communication such as touch, tone of voice, and facial expression were not measured.[6]

Some studies have shown that in dental and medical education, the further along the dental and medical students are in school, the more reluctant they are to treat PWH/A. In a 1989–1991 study of medical students' attitude toward treating PWH/A, the class of students studied indicated that as they progressed through medical school over the two years of the study, they became more restrictive in their attitudes toward HIV-positive patients, felt less personal obligation toward caring for these patients, and were less likely to use appropriate infection-control methods to ensure their own safety.[7]

In another study, the two most important predictors of students' ideas of treatment of PWH/A were the degree to which respondents perceived a personal risk of HIV exposure and their sense of professional obligation to treat all patients. Furthermore, knowledge levels were unrelated to desire to treat PWH/A. Results suggest that educational interventions aimed simply at increasing a provider's knowledge of HIV may not be effective in changing behavior.[8]

In one study involving dental students, the best predictors of belief in the right to refuse treatment of PWH/A were non-professional attitudes, low optimism scores, low levels of comfort with homosexuality, and gender. Neither knowledge of HIV, year in dental school, or fear of contagion reliably predicted belief in the right to refuse treatment.[9]

Apparently more than education is needed to allay the fears and stigma associated with treatment of PWH/A. "The advice of counselors, social scientists and behavioral modification experts must be sought if dental personnel wish to provide care to HIV+/AIDS patients in an atmosphere of mutual trust, confidence and respect."[10] There are those dentists who express a desire to treat PWH/A. In one publication, twelve dental students interested in Oral Medicine as a career expressed an increased willingness to care

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for medically compromised patients. These students anticipated an increase of this type of patient in their future practice whether they were PWH/A or had other medical problems. These students wanted to treat PWH/A because they found "personal and academic satisfaction from working in a clinic which provides care to individuals with specific medical needs."[11]

I believe Dr. Sol Silverman of the University of California correctly summed up the need for dental education and the status of treating PWH/A in an abstract; "There is no end in sight for the HIV/AIDS pandemic. Therefore, with or without knowledge of their own serologic status, HIV-infected patients will be seeking dental care in increasing numbers in the decade ahead. Additionally, the diagnosis and management of frequently occurring HIV-associated oral lesions will add to dental responsibilities. By following infectious disease guidelines for blood-borne pathogens, dental clinicians, office workers and patients will have an extremely low risk for HIV transmission."[12] Dr. Silverman's statement is excellent, but more is needed for many dentists to have this attitude.

Because of HAART making HIV infection a chronic long term disease, dentists will see an increase in PWH/A. Additionally, the baby boomer generation is aging and more patients with HIV infection and other medical conditions will present to the dental office. Although very important, education for treating PWH/A is not enough. Dentists need to genuinely care for these patients and other patients with medical conditions. How to best teach empathy and change attitude towards treating these patients is a challenge. Can this be accomplished? Legally all health care workers including dentists are obligated to treat PWH/A. As the years have progressed, more dentists, actually now the majority of dentists, are gaining a more willing attitude towards treating PWH/A. I believe "baby-step" progress is occurring among dentists who do not feel obligated or comfortable to treat PWH/A.❖

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syntonic reading. Much of the information is common sense, practical, straightforward advice and probably isn't new. So what? Yalom writes in a style that makes the reader feel as though the book was written only for him or her. There are no doubt countless textbooks that cover much of the material presented, but do you really remember anything you've read in a dry, boring textbook? Yalom writes with the same warm, personal style that I imagine he uses in his therapy sessions. He also never hesitates to share his own insecurities and feelings of doubt in his work with clients, showing strength in humility. Both beginning and seasoned therapists will find useful and memorable information in this book. For excerpts, visit the author's website at www.yalom.com.

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Psychosocial

Yalom's book attempts to mentor new generation of therapists

Danny Sansovich, LCSW

By the time this article appears, I will have attended a workshop titled "The Art of Psychotherapy" featuring psychiatrist Irvin Yalom, M.D.

Dr. Yalom is the author of *The Theory and Practice of Group Psychotherapy and Existential Psychotherapy*, perhaps his most widely read professional texts, in addition to a number of other books and novels related to the practice of psychotherapy.

If you're like me (get help immediately!!), rarely do you find that the fantasy of how you imagine an author to be matches the reality. Dr. Yalom is an exception. I had the chance to hear him speak at a conference of the Milton Erikson Institute and to meet with him after his session ended. I imagined he would be outgoing, warm, sincere, empathic, nurturing, and the reality far exceeded expectations. If you missed this chance to hear him, I would suggest the next best thing is to read his latest book *The Gift of Therapy: An Open Letter to a New Generation of Therapists and Their Patients*.

The Gift of Therapy is Yalom's attempt to mentor therapists, fulfilling what Erik Erikson identifies as the life stage known as "generativity," the stage in an individual's life cycle when he/she becomes genuinely altruistic. In his introduction, he points out how problematic this might be in view of the state of managed care and the emphasis on brief psychotherapy or psychopharma-cology in a market driven by low-cost, fast-results treatment algorithms. This clearly is a hint that what is to follow in the rest of the book is contrary to the current managed care mindset.

The book contains 84 chapters, though before you panic and think this is longer than *War and Peace*, each chapter is like a letter on a specific psychotherapy theme, with most only two or three pages in length. The chapters are divided into five thematic sections. The first section (1- 40) focuses on the therapist-patient relationship. The second (41-51) focuses on content. The third (52-76) addresses what Yalom feels are issues that frequently occur in therapy. The fourth (77-83) focuses on the use of dreams in therapy. The final section (84-85) discusses the "hazards and privileges" of being a therapist. The introduction also provides excellent brief introductions to his theories of group and existential psychotherapy.

Yalom believes that "therapy should not be theory driven, but relationship driven." The idea that the therapist-patient relationship is the primary vehicle of change is not a new concept. (Carl Rogers certainly devoted volumes to this process.) However, perhaps nowhere is this concept so eloquently described in such a succinct manner as in chapters' 1- 40. Yalom starts by describing how his task is to "remove obstacles to growth," a concept he credits to Karen Horney in her book *Neurosis and Human Growth.*" Yalom believes that given the opportunity, patients want their lives to improve and would accomplish this growth on their own once obstacles to growth are removed, a task that he accepts as his responsibility. He goes on to emphasize the importance of avoiding DSM-IV diagnosis. He points out that this is difficult in a managed care environment, but challenges the reader to consider how the initial diagnosis might change significantly, once the therapist gets to know the patient better as the therapist-patient relationship is nurtured. He also suggests that therapists seeking their own therapy consider how they might be diagnosed with a DSM-IV diagnosis! He doesn't completely discount DSM-IV, recognizing that there are situations in which the diagnosis is useful for working with the seriously mentally ill.

The most predominant theme in the first section addresses conducting therapy in the here and now. The therapy session, be it group or individual, serves as a microcosm for the real world outside of therapy. The patient will often exhibit patterns of behavior, emotions, or relationship difficulties in the therapy session that brought the client to therapy in the first place. In Yalom's view, this is the essence of the importance of the patient-therapist relationship. Thus, the patient who had difficulty being intimate with others will likely have trouble being intimate with the therapist (intimate in terms of exposing thoughts, feelings, etc.). Likewise, any growth in intimacy in the therapy session is likely to be mirrored in the "real" world. The second section focuses on the existential issues that Yalom frequently describes in his sessions with clients, such as death and death anxiety, meaning of life questions, life enhancement. He also writes in this section about the importance of having the client assume responsibility for his/her problems, suggesting that perhaps the most significant change only occurs once this therapeutic task is accomplished. He further emphasizes this theme by also saying that it is not the responsibility of the therapist to make decisions for the client, but that the therapist can facilitate the decision making process by challenging the patient to consider the process used to reach a decision.

The third section is perhaps the most enlightening in terms of revealing what it must be like to have Yalom as a therapist. He covers a lot of personal ground here, describing what he thinks works in the therapy session. He raises some points that at first glance seem controversial but upon further consideration can only be described as the essence of what Yalom must be as a therapist. He recognizes a time and place for touching patients (literally...holding hands, hugging) with appropriate caveats, such as being aware of and respecting boundaries, and almost is vehement in his condemnation of a sexual relationship with clients. He does believe that it can be helpful to discuss sexual feelings the patient may feel towards the therapist, or the therapist towards the patient, with a great deal of cautionary consideration of the impact on the therapeutic relationship. He even recognizes the usefulness of occasional home visits. All of his tasks are done with an emphasis on the here and now described earlier and how these tasks contribute to the therapist-client relationship. The fourth section addresses the use of dreams in therapy. Yalom encourages exploration of dreams and recognizes that dreams can provide "grist" for the therapy mill. He stresses that therapists shouldn't let their fear of using dream work prevent them from exploring this option. The last section does an eloquent job of emphasizing the importance of caring for self, and the privilege given to therapists of caring for others.

I once attended a conference where the speaker started his presentation by asking the audience to practice "syntonic listening." He defined this as listening to the information he presented and simply accepting it as true. What he wanted us to do was avoid the mental debates in which listeners often engage while listening to a speaker, debates that are usually one sided and detract from "hearing." I would suggest that readers of Yalom's book practice

See Psychotherapypage 14

Stay current with the latest HIV/AIDS journal articles

▲ Structured Treatment Interruptions for the Management of HIV Infection [Lori F and Lisziewicz J *JAMA* 2001;286:2981]

▲ Postexposure Prophylaxis for Human Immunodeficiency Virus Infection after Sexual or Injection Drug Use Exposure: Identification and Characterization of the Source of Exposure [Roland ME et al. *JID* 2001;184:1608]

▲ Residual HIV-1 Disease in Seminal Cells of HIV-1-Infected Men on Suppressive HAART: Latency Without On-Going Cellular Infections [Nunnari G et al. *AIDS* 2002;16:39]

▲ Focal Neurological Disease in Patients with Acquired Immunodeficiency Syndrome [Skiest DJ. *CID* 2002;34:103]

▲ Ischemic Cardiovascular Disease in Persons with Human Immunodeficiency Virus Infection [David MH et al. *CID* 2002:34:98]

▲ Pulmonary Complications of HIV Infection [Beck JM et al. *Am J Respir Crit Care Med* 2001;164:2120]

▲ Emergence of Resistance to Fluconazole as a Cause of Failure during Treatment of Histoplasmosis in Patients with Acquired Immunodeficiency Disease Syndrome [Wheat LJ et al. *CID* 2001;33:1910]

▲ Rates of Disease Progression by Baseline CD4 Cell Count and Viral Load After Initiating Triple- Drug Therapy [Hogg RS et al. *JAMA* 2001;286:2568]

▲ Update: Fatal and Severe Liver Injuries Associated With Rifampin and Pyrazinamide for Latent Tuberculosis Infection, and Revisions in American Thoracic Society/CDC Recommendations - United States, 2001 [*Am J Respir Care Med* 2001;164:1319]

▲ Correlation Between Reduction in Plasma HIV-1 RNA Concentration 1 Week After Start of Antiretroviral Treatment and Longer-Term Efficacy [Polis MA et al. *Lancet* 2001;358:1760]

▲ New Insights Into Transmission, Diagnosis, and Drug Treatment of Pneumocystis carinii Pneumonia [Kovacs JA et al. *JAMA* 2001;286:2450]

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▲ Many HIV Patients Carry Mutated Drug-Resistant Strains [Susman E. *Lancet* 2002;359:49]

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▲ Impact of Discontinuation of Initial Protease Inhibitor Therapy on Further Virological Response in a Cohort of Human Immunodeficiency Virus-Infected Patients [Le Moing V et al. *CID* 2002;34:239]

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▲ Evaluation and Management of HIV-Infected Women [Levine AM. *Ann Intern Med* 2002;136:228]

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