AIDS

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General:

1) There is no disease AIDS! AIDS is a medico-legal construct that includes patients who are HIV positive AND who have a CD4 lymphocyte count less than 200 or a CD4 percent of total lymphocytes of less than 14% or who have one or more of a long list of diseases. Why is this important? In the US if a patient fulfills the definition of AIDS, then he or she is afforded certain state and federal protections against discrimination, access to low cost or free medical insurance and other social benefits. Especially during the early years, HIV+women who were dying of such diseases as rapidly progressive cervical cancer, did not fulfill the early definitions of AIDS and thus were denied these benefits.
2) AIDS is worldwide but especially common in Africa, with some of the coutries having up to 15% of their citizens HIV+, and is also rampant now in Thailand and India. The first cases were noted in the US in the mid 1970's and indeed blood stored from some of those patients has been documented to be HIV+, though the syndrome itself was not appreciated until the early 1980's. In the US there are about 1,000,000 HIV+ patients, though the incidence of AIDS is dropping. Nevertheless in 1996 there were about 60,000 new cases of males with AIDS and 10,000 new cases of females with AIDS, and about 40,000 deaths from AIDS.
3) HIV is a retrovirus, a large one, over 100nm in size. It is not the first retrovirus known to infect humans; in the early 1600's apparently the Portuguese brought the HTLV 1 virus from Africa to Southern Japan, where it remains ednemic. It is associated with leukemia and hypercalcemia, though many Japanese have antibodies to this virus yet are asymptomatic. There are actually two HIV viruses, HIV 1 and HIV2, though the latter is seen almost exclusively in West Africa. It seems to be relatively benign, and closely related to a simian retrovirus. Subtypes of HIV 1 do exist, and infection with more than one subtype seems to lessen survival.
4) The major modalities for contracting the HIV virus are sexual, both homo and heterosexual, intravenous drug use (IVDU) and blood transfusions, and oral transmission, by a bite and by deep kissing, has been reported. While blood transfusions are still a significant risk in the third world, unprotected sex and IVDU are the most common events associated with a high risk of becoming HIV positive. Taking care of HIV+ patients is actually of low risk, though every year a few medical personnel do become HIV+, usually through needle sticks, though it is much less likely than contracting Hepatitis B. We'll talk more about this later.
5) Other than a flu like syndrome, sometimes associated with a typical viral like exanthem, patients may be asymptomatic, but infectious, for years. For example, in one study in men 16 to 25, in San Francisco, 25% of HIV+ men did not know they were positive for the virus.
6) The virus reproduces prodigiously, up to 10

billion a day, with a plasma ½ life of 6 hours, so the chances for mutations, and drug resistant mutations, are tremendous.

7) The tests for the HIV virus include antibody or ELISA test; false positives occur and in the first 9-12 weeks, before antibodies develop, a patient can be infectious with a negative ELISA type test. A positive ELISA or antibody test should always be followed by a more specific Western Blot test, to rule out a false positive. Today one can look for actual viral RNA in the blood, using PCR methods, and it is now standard to measure the number of particles per ml. One fascinating, relatively inexpensive and very safe, quick and accurate method is the Orasure technique, where a tooth brush like device is put between the gums and buccal mucosa and then sent to the lab for analysis.
8) Before we discuss skin diseases associated with AIDS, please understand the best therapy is not to develop AIDS. If a patient is HIV+, then the standard of care today is HAART, that is, Highly Active Anti Retroviral Therapy. This almost always includes the use of two nucleoside analog reverse transcriptase inhibitors and one protease inhibior, used simultaneously, but I'll leave you to the latest articles on therapy of HIV+ patients for the details, which in any case change almost monthly. One good review article is "Antiretroviral Therapy for HIV infection in 1997" by Carpenter et. al. in JAMA June 25, 1997, Vol. 277 #24. There is at least one school of thought, that if you get enough anti-viral medication quickly enough, in several years all the virus would be killed and the patient would be cured. One other possibility is to be born with a genetic CCR5 cellular abnormality, that renders the body cells fairly immune to the HIV virus penetration!

Dermatological Manifestations of AIDS:

1) Many patients have as their presenting signs and symptoms dermatological problems. All diseases are made worse by the lack an intact immune system, so that every skin disease known to mankind, including Basal Cell Carcinomas, Squamous Cell Carcinomas, Kerato-Acanthomas and even Melanomas are seen in AIDS patients. Nevertheless, certain skin diseases are almost hallmarks of AIDS. In every disease that we will discuss, lowering the virus level, especially below 500/ml, and elevating the CD4 cells will always be the best therapy.

2) Seborrhea:
   a) Clinical - Severe seborrhea, in the usuall areas, such as central facial, axillary and groin. This is often the first marker for AIDS and can be a 'walk-in´ diagnostic element. It is quite common, found in up to 80% of HIV patients.
   b) Therapy - Topical corticosteroids and topical and oral anti pityrosporum therapy, such as Nizoral shampoo and cream or Itraconazole.

3) Herpes Simplex:
   a) Clinical - Like an initial attack of Herpes Simple, the lesions are usual widespread, not grouped vesicles on an erythematous base. The ulcers may be quite deep, painful and persistent. Hepes simple lesions in an HIV negative patient, with open ulcers, apparently puts them at increased risk for contracting the HIV virus, and once HIV+, herpes infections somehow assists HIV replication, with concomitant lowering of the CD4 count and elevation of viral particle counts in the blood stream.
   b) Therapy-Large doses of oral or occasionally intravenous acyclovir, or now valcyclovir, for prolonged periods of time, is the treatment of choice. AIDS patients, more than anyone else, develop herpes viruses resistant to acyclovir, in which cases IV Foscarnet can be used. While Famcyclovir is an excellent agent for herpes simplex, it should not be used in patients with AIDS, as there can be hematological side effects.

4) Molluscum Contagiosum:
   a) Clinical-A double stranded DNA member

of the pox virus family, this can be a horrible problem with huge matted masses of Mollusca covering the face, genitals and anal areas. The differential, and there is always a long differential for all clinical conditions in people with AIDS, includes Cryptococcosis and Histoplasmosis, and can be quite difficult to tell apart.

b) Therapy - The usual treatment of curettage is not helpful, given the large numbers of huge lesions. Topical 5FU, Retin A, liquid nitrogen spray, laser therapy, and oral griseofulvin have been used without excellent results. A recent article documented that IV and even topical Cidofovir had excellent results, and probably should be tried, especially the topical therapy. Cidofovir is a nucleotide analog of deoxycytidine monophosphate, and is also active against the herpes simplex and zoster viruses, the Ebstein Barr virus, adenoviruses, CMV and Vaccinia. I might also try the new Imiquimod cream, an immuno-adjuvant meant for condylomata, as it is readily available in the US.

5) Kaposi's Sarcoma:

a) Clinical - unlike the 'classic' Kaposi's Sarcoma, which occurs mainly on the legs of elderly Jewish and Italians, 'epidemic' Kaposi's can and does occur all over the body, and along any and all blood vessels inside the body. It is the most common tumor in AIDS patients. While rarely a cause of death it is quite disfiguring and socially disabling. It is seen primarily in homosexuals and was initially thought to be somehow related to the use of amyl nitrate, a vasodilator, used as a sexual stimulant. We now know that it is caused by a virus, the Herpes Virus type 8, HHV-8. For some reason, perhaps the increasing habit of 'safe sex' the incidence of KS is decreasing markedly. It is rare in other HIV+ patients, but has been documented in a wide variety of immuno-suppressed patients, including transplant patients.

b) Therapy - Individual lesions can be treated with liquid Nitrogen therapy and larger lesions, like their classical counterparts, are sensitive to X-ray therapy. Intravenous and intralesional bleomycin have also been used, but the lesions often recur. Spontaneous cure is not uncommon as CD4 counts rise. Interferon alpha has also been used, with some success.

6) Bacillary Angiomatosis:

a) Clinical - This was first diagnosed about 14 years ago, and is characterized by the presence of many small and large vascular papules and plaques that can cover a fair amount of the body and also occur in the GI tract and internal organs. The differential diagnosis is of course Kaposi's Sarcoma, but also includes pyogenic granuloma, angiosarcoma and epitheliod hemangioma. A Warthin-Starry stain uncovered a bacterial cause, small gram negative bacteria, and for various arcane reasons they were named first Rochalimea henselae and are now called Bartonella henselae. If the name Bartonella sounds familiar, its because Bartonella bacilliformis causes verruga peruana. Incidentally the same B.henselae causes Cat Scratch disease; the differing clinical presentation may be due to different immune responses. It usually is associated with a cat that harbors the virus; fleas can carry it too.

b) Therapy-This otherwise frightening appearing infectious disease is fairly easily treated with oral erythromycin, vibramycin or anti-tuberculous drugs, though they may need to be continued for a long period of time.

7) Condylomata Acuminata:

a) Clinical-These venereal warts can not only cover the genitals but also totally obstruct the anus and vagina and fill the lower anal canal. HPV Types 16,18, 31 and 33 have also been associated with actual anal and

cervical cancers or cancer-like Bowenoid Papulosis.

b) Therapy-Liquid Nitrogen, podophylotoxin, laser therapy, topical 5FU, ED&C surgery, and now Imiquimod are all possibilities. I think I'd start with the patient applying podophylotoxin, either gel or liquid, BID for 3 days, 4 days off for 4 cycles, and if that didn't work, topical Imiquimod cream every other day. Large obstructing lesions will need a surgical approach.

8) Eosinophilic Folliculitis:

a) Clinical-Multiple itchy small peri-follicular papules are present on the face, trunk, neck and extremities. A peripheral eosinophilia is usually not present in patients with AIDS but a biopsy shows intra and peri-follicular mixed infiltrate with many eosinophils, similar to what is seen in Ofuji's syndrome. While the clinical picture of Eosinophilic Folliculitis in AIDS patients and classic Ofuji's syndrome is quite different, it may be because of the different immune response to the same cause? Organism?

b) Therapy - Topical and systemic steroids do help the itch and systemic steroids are dramatically effective in typical Ofuji's syndrome. All of the 'neutrophilolytic' drugs, such as erythromycin, dapsone, colchicine and niacinamide (short acting, not long acting) are potentially useful. UVB therapy, oral retinoids, various antibiotics and even topical Indocin have been used in individual cases.

9) Psoriasis:

a) Clinical-While the overall picture is not that of classic psoriasis, the thickened scaling plaques do look identical and the histological picture is similar to psoriasis. As psoriatic like lesions are so common in these immunosuppressed patients, does that tell us something about regular psoriasis'etiology? Is it a response to an infection? An altered immune state?

b)Therapy-While most therapy for classical psoriasis is immunosuppressive, either topically or systemically, for obvious reasons clinicians have tried to further avoid immuno-suppressing patients with AIDS. Topical steroids seem only marginally useful. UVB, while damaging to Langerhans cells, which are already infected with the HIV virus, still seems useful and not harmful, and tars, the Vitamin D3 analog calcipotriol, as well as the newer Vitamin A analogs may be useful. One exciting study, using one of my favorite drugs, Cimetidine, showed complete clearing of 3 patients with severe AIDS associated psoriasis. Histamine has been known to be immunosuppressive for many years (patients with TB will have a negative TB test if histamine is first injected into the skin) so maybe Cimetidine's H2 blocker activity may be at work here

10) Scabies:

a) Clinical-The usual pruritic papules are present in the finger webs, volar wrists, waist line and the head of penis. When it becomes widespread, as it often does, there can be scaling plaques all over the body, looking just like severe eczema and is then called "Norwegian Scabies" though it has nothing to do with Norway. Incidentally, it is only the female mite that gets under your skin!

b) Therapy - Gamma hexabenzene is a time honored therapy but theoretically poses certain risks to infants, pregnant mothers etc, and resistant mites are now not uncommon. The therapy of choice in the US is Elimite, containing the chrysanthemum based 'permethrin', which seems both safe and effective. In socalled Norwegian scabies, multiple treatments, with physical removal of debris under the nails, may be necessary. In certain recalcitrant cases oral ivermectin, which has been used in animals for a long time, about 12 mg for a 70 kg.

patient, seems extremely effective and quite safe.

11) Oral Hairy Leukoplakia:
   a) Clinical-This condition consists of white filiform plaques usually on the side of the tongue, occasionally associated with complaints of pain or burning. Biopsy shows parakeratosis, acanthosis and characteristic ballooning of the epithelial cells. Ebstein Barr virus seems to be the cause, and the presence of OHL is often associated with a guarded prognosis.
   b) Therapy -While there is no specific therapy for this disease, I would try the acyclovir family, as EB is in the Herpes grouping. Famvir is especially good, but can be associated with hematological abnormalities in AIDS patients. I might also try a gel based product with Cidofovir, as it seems to have some anti-EB capabilities. Why a gel? Creams would wash off before they had a chance to penetrate into the mucosa.

11) Other: The category `other´ covers a lot of territory, including lymphomas, other infections such as histoplasmosis, coccidioidomycosis, blastomycosis, alternaria and especially atypical mycobacterial infections, such as mycobacteria avian-intracellulare complex (MAC attack) infections-almost every infectious organism known to mankind has been reported, usually with severe manifestations, in patients with AIDS.

Summary: In a patient with AIDS, you don't know what you're looking at! All of our clinical experience depends on a healthy immune system giving a relatively standard response to a given insult. When the immune system is defective, the picture changes radically, so I have always approached the patient with AIDS with an "A to Z" workup. If the picture is somewhat classical, I treat accordingly, otherwise the patient gets a biopsy for microscopic examination and a biopsy culture for virus, deep fungus, bacterial infections etc. I remember one patient who had a round, doughnut shaped dermal nodule, with no epidermal component, that on culture proved to be Herpes Simplex and responded well to oral acyclovir. While "Universal Precautions" are now the law throughout the US, accidents do happen and medical workers do get exposed to the HIV virus. While there is no standard approach, the Centers for Disease Control in the US has issued a document describing a stratified approach to exposure, depending on the level of risk. I highly recommend that you read this document and it can be found in JAMA July 10, 1996, Volume 276 # 2. I personally have triple therapy immediately available and would start on it ASAP if the risk warranted it, as there is some suggestion that this may indeed preclude chronic HIV infection.