

SEARCHLIGHT

QUARTERLY NEWS FROM AIDS RESEARCH ALLIANCE OF AMERICA

The National Leader in Fast-Track AIDS Research

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What's News—

Health Alert

Several LA-area medical practices have been seeing an unusually high incidence of the potentially serious condition avascular necrosis (AVN) in their HIV+ patient populations. It is important to determine whether these new cases represent a true rise in the incidence of AVN in the HIV+ population at large, and if so, what is causing this increase. We would like to hear from primary care physicians, treatment advocates and clinical trial investigators who know of HIV+ people diagnosed with AVN.

(Please see the article on page 6 for more details)

Clinical Research

AIDS Research Alliance of America is collaborating with Michael Poles, M.D. and his associates at UCLA on a study of HIV in gut tissue. This study will yield information on how HIV develops drug resistance. A related collaborative study underway with Peter Anton, M.D. at UCLA has focused on the use of gut viral measurements to quantify HIV reservoirs in individuals with undetectable plasma viral load.

(Article on page 3)

* * *

AnorMED, Inc. has selected AIDS Research Alliance of America to participate in a Phase I/II study of the experimental "Entry inhibitor", **AMD-3100**. This drug belongs to a new antiretroviral class, and is designed to prevent HIV from entering certain T cells. Volunteers for this study will be allowed to enroll in subsequent trials of AMD-3100.

(Article on page 12)

Skin Conditions in HIV Infection

Majority of HIV+ people are affected by some kind of dermatological problem; treatment requires careful diagnosis

A wide range of skin conditions affect HIV+ people. Careful diagnosis and treatment can greatly improve patients' quality of life, but for the dermatologist, discriminating between skin conditions with very similar symptoms can be challenging. Fortunately, for most skin disorders related to HIV infection, correct diagnosis is possible, and effective treatments are available.

Skin conditions have always been extremely common in HIV+ people, and this remains true today. Even though many of the complications associated with HIV infection have been declining in the U.S. since the advent of "cocktail" anti-HIV therapy (also known as HAART, for highly active antiretroviral therapy) several years ago, this has not been the case for skin disorders. One study from the pre-HAART era found that more than 90% of patients surveyed had some kind of dermatological problem. Another study from within the last year put that number at 86% of surveyed patients.

(Continued on page 4)

* * *

New Executive Director

AIDS Research Alliance of America is pleased to announce the appointment of Irl S. Barefield as Executive Director. Mr. Barefield, who has been Director of a San Francisco community-based HIV/AIDS research clinic, replaces Gregory S. Britt, who had been CEO for the previous 6 years.

(Article on page 19)

SEARCHLIGHT

quarterly news from AIDS RESEARCH ALLIANCE OF AMERICA

A National Leader in Fast-Track AIDS Research

ARAA envisions a future in which HIV and its effects are eliminated from infected individuals, and a vaccine preventing new cases eradicates the virus.

ARAA's mission is to find and accelerate the development of effective treatments for HIV and its complications. We do this by conducting cutting edge research and clinical trials in order to improve the longevity and quality of life for all people with immune deficiency.

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Message from the Chairman of the Board

The outlook for people living with HIV infection could be viewed with continued relative optimism. Although the hyperbolic proclamations of the "end of AIDS" have long since faded, death rates remain comparatively low in the U.S. as compared to several years ago. There are now 14 anti-HIV drugs approved for use by the FDA. AIDS Research Alliance of America is proud to have participated in the clinical research that contributed to the approval of several of these new drugs. Many individuals who initiated cocktail anti-HIV treatment continue to fare well—some in far better health than 3 years ago. The successes that have been gained in HIV treatment are in themselves testimonials to the tangible results that can be expected from dedicated biomedical research.

However, the downside of current therapeutic options have become apparent as well: cocktail anti-HIV therapy quite often fails to meet the goal of maintaining undetectable viral loads, and the toxic side effects of the drugs now often replace AIDS-related conditions in reducing the quality of life of infected individuals. Furthermore, people living with HIV face the troubling reality that even when their virus is well-suppressed by therapy, the virus remains ever-present in their immune cells, and could eventually become resistant to treatment. Already there are many with few or no remaining treatment options. Even worse, the vast majority of the world's HIV-infected population will never be able to afford these cocktail anti-HIV treatments at all.

Given the now universal recognition that current treatments simply fail to cure the infection, it behooves us not just to improve cocktail therapy, but to also develop novel therapeutic approaches. While current research findings suggest what these new approaches might be, we can state definitively what the goal must be—the long-term survival of as many HIV-infected people as possible, with the least detrimental effects on their quality of life.

New and better hope for those living with HIV will come from continuing the fervent pace of research into HIV/AIDS. We at AIDS Research Alliance of America will strive towards improving the treatment of HIV infection, until the day that a cure is found.

In continued partnership for the cure,

Cam Davis
Chairman, Board of Directors

Drug resistant HIV—

A prospective study to determine whether drug resistance develops faster in tissue than in blood

AIDS Research Alliance of America is collaborating with Dr. Michael Poles of the UCLA Center for HIV and Digestive Diseases in a study that will evaluate differences in the ability of HIV to mutate and develop resistance to antiviral medications in the human intestinal lining and in the blood. The hypothesis of this study is that the inflamed environment of the gut may enhance HIV replication and lead to more rapid development of drug resistance.

If this hypothesis is borne out, it will suggest that one therapeutic approach to treating HIV infection is to reduce inflammation in the gut while suppressing viral replication systemically with antiretroviral therapy.

The goal of anti-HIV therapy—commonly known as cocktail therapy or as HAART (highly active antiretroviral therapy)—is to completely suppress HIV replication throughout the patient's body. Recent studies have demonstrated, however, that even when patients are receiving "maximally" suppressive HAART, a small amount of residual viral replication continues in their bodies. When HIV continues to replicate—even to a minor degree—in the presence of anti-HIV drugs, the possibility exists that the virus will develop mutations in the genes encoding the reverse transcriptase and protease, and some of these

mutations could allow for drug resistance.

Unfortunately, this scenario is not uncommon, since there are many variables that lead to reduced drug levels—levels that are less than "maximally" suppressive within the patient's body. These variables include:

- ❖ Differences in the concentration of antiviral drugs between the blood and tissue

There is evidence to suggest that the inflamed environment of the gut may enhance HIV replication and lead to more rapid development of drug resistance. If so, it may be important to reduce inflammation in the gut while suppressing viral replication systemically with antiretroviral therapy.

compartments—such as the gut—where viral replication is rife,

- ❖ Poor absorption of medication into the body, especially for drugs with very strict dietary requirements, and
- ❖ Increased metabolism of medication, which can occur through metabolic interactions with other drugs. This can be particularly problematic for HIV infection, where patients might have to take many different concomitant medications, leading to complicated drug-drug interactions.

Additionally, in different parts of the body HIV very likely replicates to varying degrees, and so the rate of development

of drug resistance would be expected to vary as well. This is essentially because the ability of HIV to replicate is dependent in part on the activity of the cell populations that it infects; the more activated the cell, the more HIV replicates.

The lining of the gastrointestinal tract contains predominantly activated cells that function to protect the interior of the body from harmful microbes that line the gut surface. These activated CD4+ T cells are highly susceptible to HIV and, once infected, permit a high level of viral replication. This difference in HIV replication in the gut lining would permit more rapid develop-

ment of drug resistance. Furthermore, the gut lining is a highly metabolic environment which may be characterized by decreased penetration of antiviral drugs and greater breakdown and inactivation of the drugs contained therein.

To study the differences in the development of antiviral resistance in the gastrointestinal lining and the blood, we will obtain blood samples and small biopsy specimens from the gut lining over the course of a year, and examine the resistance/susceptibility of virus in these sites to 15 antiviral drugs.

Patients and procedures

10 - 12 patients will be enrolled for this study. In order

continued on page 12

Skin Conditions in HIV Infection—

continued from page 1

Although similar rates of dermatological complaints have been seen before and after HAART became the standard of care, some of the problems dermatologists see have since been replaced with others. For example, Kaposi's sarcoma (KS), the purple lesions that were once considered the "Scarlet letter" of AIDS, is rarely seen in people successfully treated

and inflammation of the skin surrounding the nails (sometimes including ingrown nails). Other HIV medications can cause rashes to develop. Each of these conditions is treatable.

Some dermatological complications of HIV infection can have many causes. Folliculitis—inflammation of the hair follicles—is an example. Folliculitis

Table 1. Medication-related effects on the skin (drug eruptions)

Condition	Cause	Symptoms	Treatment
Lipodystrophy syndrome	HAART, especially associated with protease inhibitor use	"Sunken cheek" appearance	Injection of collagen under the skin
"C.A.P.E."	Use of protease inhibitors	Syndrome with several symptoms, including dryness of lips or skin, and inflamed skin surrounding the nails, ingrown nails	Low- to-mid potency topical cortisone
Rash	Sensitivity to HIV/AIDS drugs, particularly: nevirapine (Viramune), efavirenz (Sustiva), amprenavir (Agenerase), abacavir (Ziagen), and Bactrim	Rash. With some drugs the rash is accompanied by fever and other symptoms	In some cases, discontinuing or changing the dose of the medications is indicated; in other cases antihistamines or cortisone may be used.

with HAART. On the other hand, some of the very medications that have been extending the lives of many HIV+ people have also been responsible for other kinds of skin problems not seen before these drugs became available.

As Table 1 illustrates, the medications used in HAART therapy can cause several effects on the skin. The so-called "lipodystrophy" syndrome—thought to be associated with the protease inhibitors used in some HIV cocktails—includes hollowed cheeks. Protease inhibitors also cause a syndrome known as "C.A.P.E.", with symptoms including dry lips and skin,

can occur when microbes that are normally held in check by a healthy immune response overgrow within the follicles. However, folliculitis can also be a side effect of steroid use (steroids are often used in treating other aspects of HIV infection). A dermatologist can correctly distinguish between these types of folliculitis, and treat it appropriately.

Other dermatological complications of HIV infection are also related to immune suppression. Scientists are becoming more aware of how a healthy immune system can counteract the growth of cancers. KS is one example of a cancer that is allowed to grow

Table 2. *Viral infections of the skin.*

Virus	Condition caused by virus	Treatment
Human papilloma virus (HPV)	Warts	Multiple treatment options, including "destructive" therapy (freezing or burning the wart), or medications
Molluscum contagiosum	Papule (small raised spot on the skin), usually on face or groin	Curettage (a controlled scraping technique) under local anesthesia
Human herpes virus-8 (HHV-8)	Kaposi's sarcoma (KS)	Highly-active antiretroviral therapy (HAART); local treatment may be necessary
Herpes simplex virus (HSV)	Cold sores, genital herpes	Acyclovir (Zovirax), famcyclovir (Famvir), or valacyclovir (Valtrex)
Herpes zoster virus (HZV)	Chicken pox, shingles	Same as HSV, but with higher doses
Epstein-Barr virus (EBV)	Oral hairy leukoplakia	Oral acyclovir (Zovirax)

when HIV suppresses immune function. Often, the restoration of immune health by HAART therapy is sufficient to control KS.

Many people are infected with viruses that usually do little or no harm, such as Epstein-Barr virus, or some herpes viruses. The immune suppression caused by HIV can also permit these viruses to grow, leading to skin disorders (see Table 2). These conditions too are treatable.

Awareness of the skin problems that affect HIV+ people—by both physicians and their patients—is the key to ensuring healthy skin.



This issue of Searchlight features an article by Los Angeles-area dermatologist Derek Jones, M.D. on skin conditions in HIV infection (article begins on page 7). This article, "HIV Dermatology 2000", reviews the scope of HIV dermatology at the present time, and is intended for health-care professionals. Dr. Jones serves on both the ARAA Board of Directors and the Medical Executive Committee.

AVN: a potentially serious complication of HIV infection—
Is the number of cases increasing?

AIDS Research Alliance has learned that unusually high numbers of the potentially serious condition avascular necrosis, or AVN, have been seen recently in HIV+ individuals at several Los Angeles-area medical practices.

Throughout the epidemic, AVN has only rarely been seen in HIV-infected individuals. As one index of the rarity of AVN in this population, only 23 cases had been reported in the medical literature before 1996. With such a sporadic incidence, clinicians have not been able to solidly identify the associated cause(s) or risk factor(s) for the HIV+ patient, although hyperlipidemia (high fats and cholesterol in the blood) and steroid use might be involved.

AVN occurs when the blood supply to the bone is diminished. Bone is living tissue, and without proper blood supply, it can become brittle and susceptible to breakage. Thus, with time, AVN sufferers can require hip replacement surgery. One unusual aspect of the AVN cases reported to us is that other joints have been affected, such as ankles and knees.

Patients suffering from AVN will experience joint pain. Joint pain, of course, can have many causes. An MRI scan is required to diagnose AVN, because X-rays will not detect the problem.

The fact that physicians at several practices have been seeing more AVN cases recently might indicate that there is an increasing incidence of this condition in the HIV+ population at large. If the number of new cases of AVN in HIV-infected individuals is in fact increasing, that would suggest that these cases are related to treatment choices available only recently, rather than a direct consequence of HIV infection itself.

At the 6th Conference on Retroviruses and Opportunistic Infections, held in February 1999, a group from Georgetown University Medical Center also reported a high incidence of AVN in their HIV patient population, and suggested a link between some cases of AVN in HIV+ individuals and the use of protease inhibitors. However, this suggestion was based on data from only 5 patients. This link cannot be proven without further study of larger numbers of affected patients.

Patients experiencing unusual joint pain should consult a physician. No one should consider discontinuing their medication without first consulting their doctor.

Given the importance of determining whether there has been a true increase in AVN in the HIV+ population, and identifying the risk factor(s) underlying such an increase, AIDS Research Alliance requests that primary care physicians, treatment advocates, and clinical trial investigators who are aware of HIV+ individuals diagnosed with AVN to contact us at the following e-mail address: avn@aidsresearch.org.

As of press time, ARAA is scheduled to sponsor a meeting of Los Angeles area healthcare practitioners to discuss this issue on April 27.

We will evaluate whether to express our concerns to the FDA based on the responses that we receive.

(The internet contains good resources for learning about AVN, for both lay people and health care professionals. Performing a search for "AVN" on the site orthopedics.about.com/health/orthopedics will yield links worth exploring).

New Skin Challenges in the HAART era—

HIV Dermatology 2000

By Derek H. Jones, M.D.

Diplomate, American Board of Dermatology

Clinical Assistant Professor of Medicine, UCLA

In the era of Highly Active Antiretroviral Therapy (HAART), the scope of HIV-dermatology has changed dramatically. In this article I will review the most common skin problems affecting HIV-infected individuals today, and discuss the causes and treatment options.

I. VIRAL INFECTIONS OF THE SKIN

A. Human Papilloma Virus

Human papilloma virus (HPV) causes warts. Over 70 different distinct types of human papilloma virus have been identified, with preferences for infecting different body parts. The virus is passed primarily through skin to skin contact, although skin-object transmission may occur (it is common to contact plantar warts on the feet from shower floors). Certain subtypes of HPV are also considered oncogenic (cancer causing), and HPV is implicated in many cases of cervical cancer and in many cases of squamous cell carcinoma (a form of skin cancer), especially in genital areas. HPV is ubiquitous and with sensitive molecular techniques (such as PCR), the virus can frequently be detected in human skin in the absence of visible warts. An intact immune system is required to keep warts at bay.

HPV infections are one of the more frequent and challenging dermatologic problems facing the HIV patient in the HAART era. Multiple warts often occur on the beard area, fingers, feet and genital region, frequently despite relatively high (>500) CD4 T-cell counts. With lower CD4 counts, warts become more frequent, more numerous, and more difficult to treat. Warts in the beard area are common and are spread by shaving. Diffuse mucosal warts in the mouth or anus occur frequently. When anal warts are detected, the internal anal mucosa should be visualized with anoscopy and the internal warts should be treated with local destruction or excision. Genital warts and mucosal (oral, vaginal, anal) warts should always be biopsied prior to treatment and the tissue should be analyzed for the presence of oncogenic subtypes of HPV, including subtypes 16, 18, 31, 33 and 51. The presence of any of these subtypes dictates close follow up exams for detection of squamous cell carcinoma, such as Bowen's disease (squamous

This article is intended for health-care professionals, due to its scope and detail. A lay person-friendly summary of skin complications in HIV infection begins on page 1.

cell carcinoma in situ.) Bowen's disease is very common around the anus in HIV patients where it presents as a velvety red patch or erosion, and on the penis, where it frequently presents as a benign-looking brown or red papule (raised lesion) or patch. Bowen's disease rarely progresses into invasive squamous cell carcinoma, even in the most immunocompromised patients. However, Bowen's should still be treated. I usually treat limited Bowen's with electrodesiccation. Extensive Bowen's may be treated with topical 5-fluorouracil (Effudex) or imiquimod (Aldara) used every other night.

Destructive therapy for warts includes freezing with liquid nitrogen, desiccating the wart with an electric device called a hyfercator, or application of podophyllum or a strong acid such as trichloroacetic acid (TCA). Destructive treatments frequently need to be repeated in 4-6 week intervals, especially in the HIV patient. I favor electrodesiccation over freezing for warts on locations other than the fingers, palms and soles, as liquid nitrogen is often toxic to melanocytes, the cells that give the skin its color, and may leave white scars. Warts on the feet (plantar warts) are very difficult to treat. Two effective therapies for plantar warts include injection of Bleomycin directly into the wart or treatment with the pulsed dye laser, both of which I use frequently. Topical cantharone applied by the physician is also useful in selected cases. Topical therapies for at-home wart treatment include salicylic acid (available over the counter and usually not very effective), tretinoin (Retin-A, which is occasionally helpful for diffuse facial or flat warts), 5-fluorouracil (Effudex, which is useful for diffuse facial or flat warts), condylox (for genital warts), and imiquimod (Aldara). Imiquimod (Aldara) deserves special mention, as it is one of the more effective treatments for HPV infections

continued on page 8

HIV Dermatology 2000—

continued from page 7

associated with HIV. It is an immune modulating topical agent that increases levels of interferon in the skin, which augments the local immune response to HPV. I frequently use it on any non-mucosal area where warts are recurrent, along with intermittent destructive treatments. Aldara should be used three times weekly (such as Monday, Wednesday, and Friday) applied at bedtime. It may cause irritation at the site of application and a therapeutic response may not be evident for weeks. It is expensive, but is on many managed-care formularies, including Medi-Cal.

B. Molluscum Contagiosum

Molluscum contagiosum is a skin virus that causes white to gray dome-shaped papules that have a predilection for the skin on the face and groin, although they may occur anywhere on the body. Molluscum was a much bigger problem before the age of HAART, and HIV patients were not uncommonly covered with hundreds of lesions. It is still often seen however, especially if the CD4 count is less than 200. The best treatment is curettage (a controlled scraping technique) with a small ophthalmologic curette under local anesthesia. I avoid liquid nitrogen therapy for the reason mentioned earlier. Electrodessication is a good therapy, and topical 5-fluorouracil (Effudex), tretinoin (Retin A) or imiquimod (Aldara) are beneficial in some cases. I have seen dramatic responses to topical cidofivir (Vistide), but a topical preparation is not commercially available and must be compounded by a cooperative and knowledgeable pharmacist. Vistide is expensive and not usually covered by insurance companies for this indication. There is also a recent report of superficial radiation therapy clearing diffuse, intractable facial molluscum.

C. Kaposi's Sarcoma

Kaposi's Sarcoma (KS) is the purple skin cancer that was frequently the "scarlet letter" of HIV infection in the pre-HAART era. With HAART, it is thankfully much less common as immune systems become reconstituted. It is rare with CD4 counts above 200-300, but I have seen many cases present soon after HIV seroconversion when CD4 counts are high. We now know that the causative agent is human herpes

virus-8 (HHV-8), a member of the human herpes virus family. KS is more common in gay men with HIV than in heterosexuals with HIV, which suggests that specific sexual practices among gay men such as oral-fecal contact may increase the probability of transmitting this infectious agent. Blood transmission is unlikely, as KS is rare in HIV-infected IV drug users and hemophiliacs. The detection of HHV-8 DNA sequences in the semen of many healthy subjects is consistent with the idea that HHV-8 infects a large portion of the general population and could be transmitted by infected semen. It has been detected in saliva, and mucosal transmission may play a role, as with other human herpes viruses. HHV-8 is probably a ubiquitous virus that is reactivated in immunosuppressed conditions.

The best treatment for KS is HAART therapy. As the immune system reconstitutes, KS lesions frequently fade away. For aggressive or rapidly spreading KS associated with HIV unresponsive to HAART, systemic chemotherapy is frequently indicated. Daunorubicin, bleomycin, vinblastine, doxorubicin, and paclitaxel are all effective, but are limited by systemic side effects, with myelosuppression being common. Doxorubicin is used most commonly. High-dose interferon alpha is successful in 25-50% of cases with higher T-cell counts. However, its use is limited by systemic toxicity, which includes malaise, fatigue, weight loss, and neutropenia.

For localized KS that is not rapidly spreading but still remains present despite HAART therapy, local treatment may be considered. Local treatment includes excision, destruction with liquid nitrogen, photodynamic therapy, electrodestruction, injection of intralesional vinblastine (Velban), localized radiation, and the pulsed dye laser. Topical retinoids such as Panretin (alitretinoin) are useful in fading the color and decreasing nodular infiltration, but slow therapeutic response, high cost and infrequent complete remission limit their use. In my experience, these localized treatments frequently result in pigmentary changes in the skin, most notably darkening of the treated skin or hyperpigmentation. I have treated several patients with the Nd:YAG frequency-doubled laser at 532 nm, which in many cases clears the lesions with minimal to no hyperpigmentation.

Retrospective studies have shown that the antiviral

continued on page 13

Safety and clinical trials—

How Phase I dose escalation study designs can reduce the risk to participants

Although drugs are thoroughly tested in animals before clinical trials can begin, introducing any new compound into people for the first time always carries an element of risk. The risk comes as much from the fact that animals cannot tell investigators how a drug makes them feel as from the chance that the human body could respond differently to a drug. The clinical testing process for an experimental compound is designed to reduce this risk as much as possible, and to minimize

piled for that compound. For this reason, the effectiveness of an experimental drug—which requires a relatively large number of participants—is determined in the last phase of testing (Phase III).

The other strategy that is commonly applied to reduce the risk for clinical trial participants is the use of a dose-escalation design for the Phase I study. The first participants in a Phase I study are usually given very small doses of an experimental compound. Although this means that the first

establishes the maximum tolerated dose.

Subsequent clinical investigation can then proceed using doses of the compound that other participants can be expected to tolerate. This does not mean that adverse effects will not be seen in later studies. (Sometimes, adverse effects only happen to a small percentage of people using a drug; if this percentage is very low for a given side effect, it may not even be seen by doctors until the drug is marketed. There are many examples of this.). The point,

The three phases of clinical testing

Phase	# participants	Goal
I	10 - 30	Detection of harmful drug effects, and the dose(s) at which they occur.
II	20 - 300	Some efficacy information, as well as additional safety information.
III	200 - 5,000	Determine whether the drug is both safe and effective enough to warrant approval for marketing.





the number of people who are asked to accept this risk.





Two strategies are used to accomplish this. The first is to divide clinical testing into three phases. With each phase, more participants may be recruited into studies. Safety risks are less for participants in the later phases of clinical trials, because safety data would already have been com-

tested dose carries less risk of safety concerns, it also is usually too small a dose to be effective as a drug (assuming that the compound actually is effective). The purpose of Phase I studies, then, is to test subsequently higher doses of the compound for safety, increasing the dose until a dose is reached where side effects begin to be seen. This process

rather, is that by incorporating dose-escalation methods, Phase I trials are routinely designed to reduce the risk of participating for study volunteers.



STUDY	SPONSOR	DESCRIPTION	STATUS
Tipranavir™	Pharmacia & Upjohn	An open-label, randomized study comparing combination therapy (tipranavir and ritonavir vs. saquinavir and ritonavir) used with two nucleoside reverse transcriptase inhibitors in single protease inhibitor-experienced HIV-1 patients.	Currently enrolling
Remune™ + HAART	Agouron Pharmaceuticals 	A randomized, double-blind, adjuvant-controlled, multicenter study to compare the virologic and immunologic effect of Highly Active Antiretroviral Therapy (HAART) plus REMUNE™ versus HAART plus Incomplete Freund's Adjuvant (IFA) on antiretroviral-naïve patients infected with HIV-1.	Currently enrolling
Zerit® (Stavudine)	Bristol-Myers Squibb 	Evaluation of the safety and antiviral activity of stavudine <u>extended release</u> formulation as compared to stavudine <u>immediate release</u> formulation, each as part of potent antiretroviral combination therapy.	Enrollment complete
Anticort™	Steroidogenesis Inhibitors, Inc. 	A pharmacokinetic and safety study of Anticort™ (an oral procaine formulation) in HIV-infected patients.	Currently enrolling
Hydroxychloroquine (in combination with hydroxyurea and didanosine)	AIDS Research Alliance of America 	An open-label, Phase I/II study of the safety and antiviral efficacy of hydroxychloroquine in combination with hydroxyurea and Videx® (ddl or didanosine) in HIV-1 infected patients.	Currently enrolling

STUDY	SPONSOR	DESCRIPTION	STATUS
PMPA Prodrug	Gilead Sciences, Inc. 	A Phase II, randomized, double-blind, placebo-controlled study of the safety and antiviral activity of the addition of PMPA Prodrug to combination anti-retroviral regimens in treatment-experienced HIV-infected patients.	Enrollment complete, study ongoing
AIDSVAX™ B/B	VaxGen, Inc. 	A double-blinded, placebo-controlled, Phase III trial to evaluate the efficacy of the AIDSVAX™ B/B vaccine in adults at risk of sexuality transmitted HIV-1 infection.	Enrollment complete, study ongoing
Ziagen™ (abacavir): combination	Glaxo Wellcome 	A Phase III, randomized, double-blind study to evaluate the safety and efficacy of 3TC/AZT/1592U89 vs. 3TC/AZT/Crixivan in HIV-infected antiretroviral-naïve subjects.	Enrollment complete, study ongoing
Nelfinavir™ (viracept)	Agouron Pharmaceuticals 	A Phase II/III placebo-controlled study of Nelfinavir™ in combination with AZT+3TC versus AZT+3TC alone.	Long-term extension phase continuing

For information about enrolling in any of our studies, contact Corie Castro at (310) 358-2429. Transportation to our clinical research facility is available upon request. For priority notification of new/enrolling clinical trials, sign-up for our Priority Notification Program.

Experimental "Fusion Inhibitor"— AnorMED's AMD-3100

This trial is a Phase I/II antiviral, safety and pharmacokinetic study of AMD-3100, the first in a new class of entry (fusion) inhibitors. Currently, HIV medications work against HIV that has already entered the cells. AMD-3100 is designed to prevent HIV from entering T-cells by blocking one of the cellular proteins to which HIV attaches.

This is a 12-day, in-patient study at Midway Hospital. Participants will receive a continuous intravenous infusion of AMD-3100. In order to participate, volunteers have to be infected with the type of HIV that scientists call "SI." SI is associated with rapid progression of HIV and is present in 10-40% of the HIV+ population. All prospective participants will be tested for SI prior to being accepted into the study.

Participants will be compensated for volunteering their time in this study.

Requirements

- HIV+ male or female, 18-55 years old
- Must be on stable antiretroviral therapy for 4 weeks prior to beginning study OR not taking any antiretrovirals
- Viral load greater than 5000
- SI type of HIV (ARA will test for this)
- T-cell count greater than 50 (this may change to only 10)
- If female, not pregnant and willing to use contraception throughout the study

Patient Slots

Up to 6

Principal Investigator

Stephen J. Brown, M.D.

For more information about participation in this study, contact Corigan Castro at (310) 358-2429.

AnorMED Inc. is a publicly traded company based in Langley, British Columbia engaged in the discovery and development of drugs based on metal and metal-binding compounds. The company is focused on discovering and developing therapeutic applications of small molecule metal complexes and metal binding compounds with emphasis on life threatening disease and acute treatments. The Company currently has a number of compounds in clinical trials including two in Phase III and two in Phase II.

A prospective study to determine whether drug resistance develops faster in tissue than in blood—

continued from page 3

to maximize our ability to examine the changes in antiviral resistance over time, patients will be enrolled who are ready to initiate, but who have not yet begun, HAART therapy (i.e., "naive" to anti-HIV drugs) or patients who are receiving HAART but are about to stop therapy for greater than 2 months (drug holiday).

Blood samples and gut biopsies—involving a procedure known as flexible sigmoidoscopy—will be obtained at the first visit for a baseline measure, and then at week 1, week 2, week 4, week 8, month 6 and 1 year following the baseline visit. Flexible sigmoidoscopy is a simple 10 minute pro-

cedure in which a flexible tube is inserted into the rectum that contains a light source to allow the physician to examine the rectum and collect biopsy samples. From these small pieces of tissue (about 8 mm in diameter), HIV RNA and DNA are extracted and used both to quantify the HIV viral load and for drug resistance tests. Antiviral resistance testing will be performed in collaboration with Virco N.V. of Belgium; both "genotypic" and "phenotypic" resistance tests will be performed. Genotypic tests look for genetic mutations in HIV that are known to be associated with drug resistance. Phenotypic tests are more direct tests of resis-

tance. In these tests, HIV is extracted from blood or tissue samples and exposed to antiviral drugs, and the ability of these drugs to suppress the virus is measured.

Results of the resistance tests will be made available to each study participant's primary care physician.

Treatment

The primary care physician for each participant will be responsible for treatment decisions while the participant is on-study.

For more information, call Marie Fuerst, R.N., at the UCLA Center for HIV and Digestive Diseases, at (310) 825-9254.

HIV Dermatology 2000—

continued from page 8

compounds ganciclovir and foscarnet, but not acyclovir, decrease the risk of development of KS in HIV infected individuals not yet afflicted with KS. Small studies also have shown that patients with KS sometimes improve with Foscarnet therapy. These antiviral compounds inhibit viral DNA polymerization. HHV-8 is thought to be able to persist in forms not dependent on viral DNA polymerase, which would explain the incomplete efficacy of these compounds.

Novel approaches for the treatment of KS may in the future include compounds that inhibit cytokines and stimulating factors that control angiogenesis. Hormonal therapy may also be promising, in the form of beta-chain human chronic gonadotropin (beta-hCG), which has shown activity against KS cell lines. Sensitization of KS cells to Fas-mediated apoptosis may be a possible approach to treatment, as one recent study showed that KS cells are resistant to Fas-mediated apoptosis.

D. Herpes Simplex Virus and Herpes Zoster Virus

Herpes simplex virus (HSV) is the causative agent of recurrent sores around the mouth (cold sores) or around the genitals (genital herpes). It is more frequent and aggressive in HIV-infected individuals, especially if the CD4 count is less than 200. Perianal HSV is common with CD4 counts less than 200, and presents as tender perianal erosions with scalloped borders.

Prophylactic therapy is recommended in patients with a CD4 less than 200 or in patients who are having more than 3 or 4 outbreaks in a given year. Treatment is with acyclovir (Zovirax), famcyclovir (Famvir) or valacyclovir (Valtrex). Viral culture studies are always recommended to aid in the diagnosis. HSV resistance to these drugs is common, so clinical failure should prompt sensitivity studies, a change to a different drug, and consideration of possible problems with absorption of medication taken by mouth.

HSV should not be confused with herpes zoster virus (HZV), another member of the human herpes virus family, and the causative agent of chicken pox and shingles. Shingles is a recurrence of the chicken pox virus (HZV) that has laid dormant for years in the sensory nerve ganglia of the spine. As immunity wanes, the virus is able to infect sensory nerves, with a resultant painful blistering rash that usually is distributed along the path of the sensory nerve involved, called a dermatome. The characteristic rash usually involves only one side of the body with a sharp cut-off at the midline, and is distributed in bands characteristic of the sensory dermatome affected. HIV-infected individuals are more prone to shingles, particularly with CD4 counts less than 200. Treatment is with the same medications used for HSV infection, typically at higher doses. Severely immunocompromised patients may be prone to

recurrent outbreaks of shingles, or disseminated shingles, which is a severe, frequently life-threatening infection requiring IV antiviral therapy.

E. Epstein-Barr Virus

Epstein-Barr virus is implicated in many different human diseases, including infectious mononucleosis. It is important in HIV as it may cause a condition called oral hairy leukoplakia. Oral hairy leukoplakia presents as white patches and plaques on the sides of the tongue. The plaques are not easily scraped off as are the similar-appearing plaques of oral candidiasis or thrush, which is caused by the candida yeast. Oral hairy leukoplakia is more common with CD4 counts less than 200, and responds to oral acyclovir (Zovirax) therapy. Topical podophyllum may also be beneficial. I see less oral hairy leukoplakia now in the HAART era as immune systems are better functioning and many patients take prophylactic acyclovir.

II. FOLLICULITIS

Folliculitis—inflammation of the hair follicle—presents as red papules or pustules (pus bumps) located perifollicularly (around the hair follicle). It is extremely common in HIV and represents a common endpoint for a variety of different causative pathways. Misdiagnosis regarding the cause is common. Appropriate diagnosis is essential in order to tailor therapy appropriately.

continued on page 14

HIV Dermatology 2000—

continued from page 13

A. Eosinophilic Pustular Folliculitis (EPF)

Eosinophilic pustular folliculitis (also called itchy red bump disease, papular dermatitis, Ofuji's disease) clinically presents with itchy red perifollicular papules or papulopustules on the face, trunk or extremities. The clinical hallmark is intense pruritis (itching) which is frequently unbearable, leading to scratching, excoriation and formation of thickened papules named prurigo nodularis. It is more common with CD4 < 200, but I have several patients with higher CD4 counts and good response to HAART who nevertheless continue to get outbreaks. EPF is definitively diagnosed with skin biopsy, which shows folliculitis, usually with a predominance of eosinophils. The cause appears to be related to an aberrant Th2-type immune response to a hair follicle antigen. No one antigen has been identified, and culture results and special stains on skin biopsy usually fail to reveal an antigen. However, responses to different antimicrobials suggest that fungi, mites or bacteria may play a role. Responses to itraconazole (Sporonox, an antifungal), pyrimethrin (Elimite, an anti-scabidical or anti mite lotion) and Ivermectin (an anti-parasite) are reported, suggesting that EPF is an HIV-induced type of hypersensitivity reaction to normal cutaneous flora such as pityrosporum species (a yeast) or human mites such as demodex. Responses to metronidazole and minocycline suggest that the follicular antigen may in some cases be a bacteria. Therapy aimed at altering

cytokine production and reducing inflammation has proven effective. Specifically, UVB phototherapy, high dose topical cortisone, systemic cortisone, and interferon gamma are all useful.

In my practice, I frequently start to treat EPF with Elimite applied three nights weekly to affected areas and a Class I topical cortisone to individual lesions. If response is not noted within 3 weeks, I often use Sporonox if no contraindications are present. In more severe cases, intramuscular Kenalog with Celestone frequently produces immediate and long-lasting relief (often for many months) with a minimum of systemic side effects. Low-dose Accutane (10-20 mg daily) is frequently very helpful, even as first-line therapy. However, serum lipids should be carefully monitored, especially if the patient is on protease inhibitor therapy.

B. Anabolic Steroid Folliculitis

Many HIV-infected patients are now being treated with anabolic steroids such as Testosterone, Oxandrin or Decadurabolin. The main effects of anabolics on the skin are increased sebum production, cutaneous vascular flushing (resulting in a red-purple skin hue), and telangiectasia (spider vein) formation. Each hair follicle is associated with an oil-producing gland called a sebaceous gland, which produces an oily product called sebum. Sebum exits through the hair follicle opening on the skin. Increased sebum production causes blockage and inflammation of the hair

follicle. Steroid acne is therefore a form of folliculitis. Clinically, steroid acne may not become apparent until months after introduction of anabolic therapy, and presents as non-itchy papules and papulopustules on the face and trunk. Culture studies are negative, and biopsy usually shows a necrotizing folliculitis with no increase of eosinophils and negative staining for fungi or other organisms. The only effective treatments are retinoids such as Retin-A or Accutane. Topical or oral antibiotics or benzoyl peroxide are of little use. The best treatment for steroid acne is discontinuation of the steroid. Many of my patients who are unable to discontinue anabolic steroids for a variety of reasons are frequently well controlled on low-dose Accutane. However, Accutane may have long-term side effects and the risk to benefit ratio must be carefully considered. Again, blood lipids should be carefully monitored especially if the patient is on protease inhibitor therapy.

C. Pityrosporum Folliculitis

Pityrosporum is a yeast and a normal inhabitant of human skin, and requires oil to survive. As mentioned before, each hair follicle is associated with an oil producing sebaceous gland, which may create an optimal oily milieu for the overgrowth of pityrosporum. Pityrosporum folliculitis results when pityrosporum becomes overgrown within the hair follicle. In my experience, patients on anabolic steroid treatment have an increased risk of pityrosporum folliculitis, due to

increased oil or sebum production. *Pityrosporum folliculitis* clinically presents as an acute eruption of papulopustules, which frequently have a red halo, distributed on the trunk and shoulders. Culture studies are negative, and biopsy with PAS staining show characteristic fungal elements within the hair follicle. Treatment is with Sporonox. Diflucan is less effective and Lamisil does not appear to be of benefit. Topical antifungal preparations are also therapeutically disappointing. Accutane has been shown to decrease *pityrosporum* counts on the skin, probably related to its inhibitory effect on sebum production, and it is a good treatment for severe cases of *pityrosporum folliculitis*.

D. Demodex Folliculitis

Demodex is a human mite and is considered to be a normal inhabitant of human skin. In rare cases, especially in the immunocompromised host, it may become overgrown and lead to folliculitis. Skin biopsy is diagnostic, showing demodex organisms within the hair follicle. Treatment is with anti-scabidals such as Elimite or Lindane.

E. Bacterial Folliculitis

Bacterial folliculitis results when bacteria become overgrown within the hair follicle structure. Usually the causative bacteria is *Staphylococcus aureus*. Staph folliculitis is common. Bacterial culture studies and drug sensitivity studies of pustule contents are recommended to isolate the bac-

terial pathogen and differentiate this entity from other forms of folliculitis, which may appear similar.

III. MEDICATION RELATED EFFECTS ON THE SKIN (DRUG ERUPTIONS)

HIV appears to predispose patients to multiple hypersensitivity reactions, including exaggerated reactions to bug (arthropod) bites, photosensitivity and hypersensitivity to a variety of drugs. The predisposition is thought to be related to the altered immunologic state, with a thy-2 shift of T-lymphocytes and production of a cytokine profile which promotes cutaneous hypersensitivity.

Many drug-related eruptions may present as symmetric, perifollicular papules resembling folliculitis. History, clinical suspicion, and skin biopsy which frequently shows specific findings aid in the diagnosis. Specific drug eruptions are discussed in further detail in the following section.

A. The Lipodystrophy Syndrome

Protease inhibitor therapy for HIV is associated with hyperglycemia and diabetes mellitus, elevated serum lipids (mainly cholesterol and triglycerides), and abnormal body fat distribution (the lipodystrophy syndrome). The lipodystrophy syndrome includes wasting of fat under the skin (subcutaneous fat) in the arms, legs, trunk and face. It also includes peculiar growths of fat on the back of the neck ("buffalo hump") and deep in the connective tissue surrounding the

intestines, resulting in increased abdominal girth (the "protease paunch"). Buffalo humps have been successfully treated with liposuction. Whether lipodystrophy is 100% related to protease inhibitor therapy has been recently contested and debated in the scientific community. Nevertheless, protease inhibitors certainly seem to play a role.

One of the more distressing aspects of lipodystrophy is the "sunken cheek" appearance that results from loss of subcutaneous fat in the cheeks. Many patients feel that hollowed cheeks have replaced Kaposi's sarcoma as the "scarlet letter" of HIV, and understandably want to do something to correct the problem. In the early days of the lipodystrophy syndrome, I performed many fat transfer procedures to correct the problem. The procedure involves a modified liposuction technique that removes subcutaneous fat from the abdomen or buttocks. The collected fat is then injected into the cheek hollows. In my experience, the resulting correction was excellent in most cases. However, the injected fat tended to fade away over a few months. More recently, I have been using bovine-derived collagen (a natural connective tissue component of skin) injected into the hollowed cheek areas to restore a normal contour to the cheeks. Although the hollows are dramatically improved in most cases, the correction tends to fade over a few months, necessitating repeat injections. Collagen is relatively expensive, and is not reimbursed by insurance plans, even for

continued on page 16

HIV Dermatology 2000—

continued from page 14

lipodystrophy. Today, there are several alternatives to bovine collagen for soft tissue augmentation, but none seem to have any distinct advantage over collagen in terms of cost or longevity. A human-derived connective tissue product called Fascian has recently received attention within the HIV community as a possible filler substance for lipodystrophy-associated cheek wasting. However, there are no studies that have carefully evaluated Fascian for this indication, and the current claims made in favor of Fascian at this point may appear more theoretical than real. A group of dermatologists and I are currently designing a study to evaluate potentially more promising injectable soft-tissue augmenting substances for the treatment of lipodystrophy, including Dermalogen, micronized Alloderm, Fascian, and Artecoll.

B. The Protease Inhibitor "C.A.P.E." Syndrome

Like a group of drugs called retinoids, which include the drug Isotretinoin (Acutane), protease inhibitors have all-trans-retinoic acid signaling function *in vitro*. As a result, the two groups of drugs share similar side effects, including frequent elevation of serum triglycerides and numerous skin side effects. The acronym "C.A.P.E." syndrome refers to a constellation of dermatologic retinoid-like side effects associated with protease inhibitors. "C" stands for cheilitis, which refers to an extreme dryness of the lips which frequently results in splitting and peeling of the lips. "A"

stands for asteatosis, which is a diffuse dryness of the skin, which compromises the skin's barrier function. "P" stands for paronychia, which refers to infection or inflammation of the folds of skin surrounding the nails. Both retinoids and protease inhibitors may cause a general thinning of the epidermis or outer layer of the skin, which may be especially pronounced on the hands and feet. In my view, this thinning of skin makes it easier for the sharp edges of the nailplate to cut or become ingrown into the nailfold skin, resulting in inflammation and a predisposition to bacterial infection. Many of my patients on protease inhibitors experience repeated paronychia infections requiring antibiotic therapy, and many require partial nail avulsion (removal), most frequently on the toenails. Finally, "E" stands for eczema, which presents as dry, scaly, red and sometimes itchy patches on the skin. It frequently occurs on the skin around the groin and buttocks, and is often confused with tinea cruris (jock itch). However, appropriate diagnostic tests fail to reveal the skin fungus associated with tinea cruris. Treatment for protease-inhibitor related dryness and eczema includes emollients and low to mid potency topical cortisone. Patients must be urged to use caution with topical cortisone preparations, especially when used under the arms or in the groin. Over long periods of time, these compounds may cause atrophy (thinning of the skin) which only exacerbates the protease inhibitor-related thinning of the

skin. Furthermore, mid to high potency topical cortisone cause local immune suppression, which increases the predisposition to viral infections (HPV, molluscum, HSV-8) in the areas they are used. I have seen several cases of stretch marks on the buttocks and upper inner thighs (caused by skin thinning), or cases of diffuse molluscum, warts or recurrent Kaposi's caused by overzealous local use of topical cortisone—especially Lotrisone (which contains a mid-potency topical cortisone combined with the antifungal clotrimazole).

Thinning of the hair on the scalp and body, thinning of the nails, and development of subcutaneous angioliomas are also frequent side effects of protease inhibitors.

C. Other Drug Eruptions

Viramune, a non-nucleoside reverse transcriptase inhibitor (NNRTI), is frequently associated with a skin rash. The rash usually occurs during the first three weeks after initiation of therapy, and frequently presents as a symmetrically distributed red, morbilliform (measles-like) rash on the trunk and extremities. Primary care physicians are accustomed to diagnosing and managing these rashes. If the drug is initiated and continued at one-half of the usual dose for the first two weeks of therapy, the incidence of rash decreases from greater than 50% to less than 10% of cases. A small percentage of the patients who react to Viramune (3-6%) progress to full blown Stevens Johnson Syndrome, with occasion-

al fatal outcomes. Viramune may also be responsible for a diffuse redness of the skin, which usually appears within the first few months of therapy and may be difficult to distinguish from a similar redness caused by anabolic steroids.

The drugs Sustiva (efavirenz) and Agenerase (amprenavir) may be frequently associated with maculopapular rashes, especially during the initiation of therapy. Most of these rashes resolve with continued therapy in association with aggressive oral hydration and systemic antihistamines. Ziagen (abacavir) may be associated with a syndrome of hypersensitivity, which may include fever, lymphadenopathy and increased liver function enzymes. The rash associated with Ziagen hypersensitivity is usually mild and somewhat less common than the associated systemic symptoms. The significance of the Ziagen hypersensitivity syndrome rests with reintroduction of the drug in the truly reactive individual if it has been previously discontinued. Following reintroduction of Ziagen, upwards of 3-5% of truly reactive individuals will experience a rapid rebound of hypersensitivity that may lead to cardiorespiratory collapse with a potentially fatal outcome.

Bactrim, a drug commonly used as prophylaxis against pneumocystis pneumonia, is frequently associated with varying degrees of a drug hypersensitivity rash in upwards of 50% of patients. This can be avoided almost 100% of the time by a gradual desensitization of the patient with titrated

dose increases over 2-4 weeks.

Hydroxyurea, another drug commonly used in HIV therapy, frequently causes pigmentation of the nails (as does AZT), and may also cause skin ulcers on the lower extremities. Oral ulcers may be associated with ddC.

The difficulty with drug rashes is recognizing when they are life-threatening. Almost all HIV drugs have been associated with cases of erythema multiforme (Steven's- Johnson Syndrome) or toxic epidermal necrolysis. Erythema multiforme is a severe, blistering rash that is frequently associated with ulcers or erosions in the mouth and conjunctiva of the eyes. In its' most severe form, it is life threatening. Toxic epidermal necrolysis is an extremely life-threatening drug reaction and is characterized by shedding of skin in large sheets, resulting in a "burn-victim" appearance. Patients initiating HIV therapy, especially with the aforementioned drugs, should be counseled to have any new rash evaluated as soon as possible by a physician knowledgeable with these conditions.

IV. SKIN CANCER

Non-Melanoma Skin Cancer

Non-melanoma skin cancer includes mostly basal cell and squamous cell cancer. Basal cell cancers and squamous cell cancers may have unusual presentations, and frequently go ignored or misdiagnosed. If left untreated, they may progress and cause significant tissue destruction. On the face, treatment of larger can-

cers may lead to significant cosmetic disfigurement. On the trunk or extremities, these cancers may present as small scaly patches that resemble eczema, but fail to resolve. Although no clear cut epidemiologic data exists, in my view basal cell and squamous cell carcinoma clearly have an increased incidence in the HIV population. I have many patients who develop several new cancers yearly. Treatment is usually best done with surgical excision, although several treatment modalities exist. For cancers on the face, Mohs surgery is usually indicated. Mohs surgery is a specialized form of microscopic skin cancer surgery performed by dermatologists and designed to remove only cancerous tissue while preserving as much normal tissue as possible. A recent study suggests that Aldara (imiquimod) cream may be useful in the treatment of some superficial basal cell cancers. Development of squamous cell cancer and basal cell skin cancer are definitely related to sun exposure, and are more common in fair-skinned individuals. Everyone, and especially those with HIV, are advised to avoid the sun as much as possible, wear sunblock, and receive yearly dermatologic examinations to detect for non-melanoma and melanoma skin cancer. Basal cell and squamous cell cancer should not be confused with melanoma skin cancer. Melanoma usually presents as a new or changing pigmented lesion, may rapidly spread (metastasize) to other parts of the body, and is frequently fatal. Squamous

continued on page 18


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HIV Dermatology 2000—

continued from page 17

and basal cell cancers rarely metastasize or cause death.

V. OTHER CONDITIONS

Seborrheic dermatitis or seborrhea (dandruff of the face and scalp) is very common and frequently more severe in HIV patients. It may be related to the overgrowth of pityrosporum yeast on the skin. Treatment is with topical cortisone preparations and anti-yeast compounds, such as Nizoral (ketoconazole) shampoo. Psoriasis, which presents as chronic scaling plaques on the scalp and body, is not found as frequently as is seborrhea, but it tends to be more persistent and recalcitrant to therapy.

A large spectrum of cutaneous fungal or bacterial infections (such as bacillary angiomatosis) are also seen more frequently in HIV patients, but their incidence is greatly reduced in the age of HAART. I have picked up several cases of secondary syphilis in HIV patients, many of whom had higher CD4 counts. Syphilis may appear atypical in HIV, and syphilis is known to mimic many other cutaneous conditions. Therefore it should be routinely

considered in any patient who has a diffuse, symmetric, papulosquamous rash with no clear-cut explanation.

Conditions such as alopecia areata, porphyria cutanea tarda, photosensitivity, and cutaneous lymphoma are also more frequent in the setting of HIV, but their occurrence in this population is still relatively rare.

An "immune reconstitution" phenomenon has recently been described whereby specific cutaneous conditions may appear in the HIV-infected individual with a low CD4 count after the initiation of HAART therapy. Granuloma annulare, cutaneous sarcoid, mycobacterial infections and molluscum contagiosum have all been reported to appear only after the initiation of HAART. The presumed mechanism is that as CD4 counts rise, the immune responses to previously unrecognized cutaneous antigens become apparent.



AIDS Research Alliance of America announces appointment of Executive Director—

Irl S. Barefield

ARAA is pleased to announce the appointment of Irl S. Barefield as Executive Director of the organization. He takes over the helm from Gregory S. Britt, who had served as Chief Executive Officer for 6 years until this winter.

Since 1996, Mr. Barefield has been Director of HIVCare & Clinical Research, a community-based clinical trials program for HIV and oncology that is affiliated with Saint Francis Memorial Hospital in San Francisco.

Prior to becoming Director of HIVCare, Mr. Barefield was an associate attorney at two different San Francisco law firms. In his law career, he litigated in defense of the rights of the mentally ill, the Sierra Club and clients living with HIV/AIDS. He received his J.D. from the University of California Boalt Hall School of Law, in Berkeley, in 1992.

In his tenure at HIVCare, Mr. Barefield achieved substantial success in widening outreach to women and minorities, and in providing a broader range of services to trial participants. Trial enrollment rates increased during this time as well.

"We are delighted to have Mr. Barefield join our team," said Kenneth C. "Cam" Davis, Jr., Chairman of the Board of Directors, "His energy, leadership, and experience in running a community-based HIV research clinic make him exceptionally qualified to lead ARAA. His concern for the HIV community will empower our research efforts to meet the demanding challenges of HIV disease."



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For further information on trial enrollment or joining the Priority Notification Program, please call Corie at 310/358-2429.

Para información en español, llame al 310/360.3876.

*ICCAC, abstract 1-179, 1997.