HIV-1A, C, D, E....Researchers have identified new subtypes of the deadly virus in Asia and Africa. Now we must assess

The new AIDS risk for American women

by John Sedgwick photos: Josef Astor

From her corner office at the eucalyptus-shaded Naval Health Research Center overlooking San Diego Harbor, Captain Stephanie Brodine, M.D., can see the destroyers and aircraft carriers sail in from every corner of the globe. First just specks on the horizon, they emerge into massive gray ships that pass through the wide channel at the foot of Point Loma and follow the curve of the bay to their berths. Tens of thousands of sailors, having frolicked in ports around the world, pass through San Diego every year. A prominent Navy epidemiologist, albeit one with a taste for the Eagles on her office boom box, Dr. Brodine has the job of trying to keep those sailors from returning to the U.S. with infectious diseases—especially HIV—and she helps monitor them to see how well she has succeeded. It was the monitoring that led her to a little-publicized 1994 discovery that, despite the recent encouraging reports about improved treatments, may seriously darken both the perception and reality of Americans' risks of HIV infection.

Fully aware of the temptations that Navy men face in foreign ports after weeks at sea, the U.S. Department of Defense has long had a rigorous education campaign about the perils of sexually transmitted diseases. "In the military, there are a lot of young, single individuals," Brodine points out. "This is, by and large, a risk-taking population." Yet, like most surveillance organizations, the Navy for a long time merely tested for the presence of HIV, unaware of—or unconcerned with—emerging distinctions between different strains of the virus. In 1985, for example, researchers from the Harvard School of Public Health found that there was a slower-developing class of the virus, HIV-2, in West Africa. In 1990, researchers at the Los Alamos National Laboratory in New Mexico determined that the standard variety of the virus, HIV-1, has a number of geneticall-ly distinct subtypes. The list of major subtypes now runs from A to J, of which A through E are the most common. (Another strain of HIV-1, an extremely rare one, was dubbed *O* for "outlier" or "outgroup"; it is so distinct genetically, it sometimes doesn't show up on HIV blood tests, much to the dismay of blood banks and public-health authorities.) The most common subtypes seem to correspond with the geographic locations where they are most prevalent: B in North and South America, the Caribbean and Western Europe; A, C and D in sub-Saharan Africa; C in India; and E in Southeast Asia, especially Thailand. All of them are deadly, gradually suppressing the immune system to the point where the sufferer is unable to fight off infection. About 14 million people are believed to carry the virus in sub-Saharan Africa; India is now thought to have 2 to 5 million HIV infections, more than any other country, and some experts predict the number may grow to as much as 55 million by the year 2000; and in Thailand, 1 million out of the population of 60 million are now estimated to carry the virus.

Researchers were also struck by the different subtypes' patterns of sexual transmission. In the U.S., where subtype B is most firmly entrenched, gay/bisexual men and intravenous drug users account for more than 83 percent of all AIDS cases for individuals over age 12 reported to date; in Thailand, India and sub-Saharan Africa, where the major pockets of HIV infection are located, 90 percent of the cases are contracted heterosexually, with women taking a disproportionate share of the risk. Researchers naturally wondered if the fact that non-B subtypes were transmitted primarily through heterosexual sex revealed a characteristic of the virus. Are there, in short, strains of HIV in the developing world that are more easily transmitted by vaginal intercourse than the strain in North America? Could one of those HIV strains come to the U.S. and create a heterosexual epidemic to match—or exceed—the one among gay/ bisexual men and IV drug users? Would all Americans then face the same odds of exposure to HIV?

In the United States, these remained merely academic questions through 1994, for no non-B subtype had ever been identified among the nearly 1 million Americans believed to be HIV-positive. But then, no one had ever looked. In screening for HIV, few laboratories are geared up for the expensive and time-consuming process of distinguishing between subtypes. As part of the Department of Defense's surveillance effort, however, Brodine thought it important to go further to see if any non-B subtypes had made it to our shores. At the very least, such data would be useful for determining which subtypes a future vaccine would have to cover; for now, it would be good to know what we are dealing with. Her first thought was to use the Navy's extensive database on HIV-positive personnel throughout the country, and match those sailors with ports of call where non-Bs were most common, to see if she could come up with any non-B carriers, but that technique proved insufficient. So in 1993 she decided to also look at an outpatient population that was considerably closer at hand: the HIV clinic at the large Naval Medical Center near downtown San Diego. By targeting the individuals who were coming in for treatment and counseling, and matching them with the last ports visited before testing positive, she suspected she might find some non-Bs.

Thirty-four individuals agreed to donate blood for her study. Several anxious months passed before Brodine heard back from the Army laboratory where tests were conducted. The head researcher called to say they had identified a 21-year-old sailor who had been in a Thailand port in May of that year. During the following months, two other subtype Es were identified: a 29-year-old and a 30-year-old, both of whom had spent time in Thailand. There were also a 35-year-old with subtype D from Kenya and a 24-year-old with subtype A from Uganda. "We expected these non-Bs would come sometime," says Brodine, careful not to exaggerate the importance of her results. Shortly afterward, one of the Es went on to infect his wife, bringing the total of known non-Bs in the U.S. to six. "That's the history of the HIV epidemic," Brodine says regretfully. "It's what we are all working so hard to combat."

The first report of the five original non-Bs in the U.S. was published on November 4, 1995, in *The Lancet*, together with an article on 11 Uruguayan military personnel who contracted HIV on foreign deployment, five of whom acquired E in Cambodia. The articles received scant attention in the popular press.

Then, on March 1 of this year, *Science* published a study by Max Essex, D.V.M., Ph.D., the widely respected chairman of the Harvard AIDS Institute, that put the news in a considerably more frightening context. Dr. Essex had been one of the first to suggest that AIDS was caused by a retrovirus, which works by integrating itself into the host's genetic material, and he had led the Harvard School of Public Health team that identified HIV-2. Now he the-

orized that subtype E was more easily transmitted by vaginal intercourse for a clear biological reason, and he set up an experiment with his colleagues to prove it. His laboratory study revealed that subtype E grows much faster (and in larger amounts) than subtype B in Langerhans' cells, which are found in the vagina. Normally, the spiky Langerhans' cells act as guardians of the vaginal lining, transporting any intruding viruses to local lymph nodes for destruction by immune cells. Essex theorizes that subtype E enters the Langerhans' cells more easily than B, then multiplies at higher rates as it rides the cells to other body fluids, creating a greater chance of infection. The paper closed with a carefully worded warning: "If introduced in the West, viruses such as HIV-1 E might pose a greater threat for heterosexual transmission than does HIV-1 B."

And, of course, now they're here.

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Despite Essex's professional stature, precious few HIV researchers have rushed to join him in sounding an alarm over the possible hazards of a non-B subtype like E. "Max Essex's Langerhans' cells hypothesis is still very much a hypothesis," says Francine McCutchan, Ph.D., director of global molecular epidemiology at The Henry M. Jackson Foundation/Walter Reed Army Institute of Research, who helped with the initial genetic analysis of the different subtypes. "It's too soon to know. It's a great leap from a laboratory observation to a change in public-health strategy, and we are not ready for that leap yet." Harold Jaffe, M.D., associate director for HIV/AIDS at the Centers for Disease Control and Prevention's (CDC) National Center for Infectious Diseases, takes a harder line: "No one thinks it's impossible that subtype E behaves differently from B. But right now, Max Essex is the only one saying that viral variation will be the driving force of a heterosexual epidemic."

Scientists are generally disinclined to make the kinds of extreme statements that might cause a panic, especially in a matter as inflammatory as AIDS. In the first six hours after Magic Johnson announced that he had contracted HIV from heterosexual intercourse, the National AIDS Hotline received more than 35,000 phone calls from terrified individuals, sure that they were now going to die because they had had unprotected sex. Researchers are also reluctant to get caught up in the touchy question of whether most heterosexuals need to worry about HIV in the U.S., which is heavily politicized on both sides of the issue.

That said, most HIV researchers have at least three significant reservations about Essex's theory. First, Essex's results from the Langerhans' cells experiments have not yet been reproduced in other laboratories, although several have reportedly been trying. Second, subtype B appears to have spread widely among heterosexuals in such Caribbean islands as Haiti, Trinidad and Jamaica, which casts doubt on the idea that subtype E has a propensity for vaginal transmission that B doesn't, and indicates that there may be reasons for E's spread among heterosexuals besides the nature of the virus. Third, the social environment in Thailand is so completely different from that of an industrialized country like the United States that it may not necessarily require a different virus to account for the different nature of the epidemic there.

With an average annual per capita income of just $2,965, Thailand has about 2.5 percent of the wealth of the United States and an impoverished health care system to match. Prostitution is relatively widespread and accepted, and it is common for young Thai men to have their first sexual experience in a brothel before entering marriage. Thus, one infected Thai prostitute can pass the virus to scores of young Thai men, who then return to their villages to give it to their wives and, potentially, children. (Once the public-health message about the importance of condoms went out in 1990, the rate of new infections in Thailand began to decline markedly.) Further, the rates of ulcerative STDs like syphilis, herpes and chancroid are considerably higher in Thailand than in the U.S.; such STDs, by literally perforating the genital tract, can dramatically increase HIV susceptibility.

Essex's office at the Harvard School of Public Health is adorned with African sculptures that he acquired during his numerous trips to that continent and a massive world map that attests to his global perspective. Right now, he sits impatiently at his conference table. A small, gray-haired fireplug of a man, Essex has heard the counterarguments a thousand times and is completely unmoved by them. "Let me state this as simply and as emphatically as I can," he says. "Subtype B was present in Thailand before the heterosexual epidemic took off. With all the STDs and the prostitutes in Thailand, why couldn't our B cause a heterosexual epidemic there? I'm amazed by that. I really am. I can't explain that. And I would ask anyone who disputes me, why didn't it?" To Essex's way of thinking, the fact that B was present at the beginning of the epidemic, but E was the subtype that proved dominant, means that E outdoes B when the major available route of transmission is vaginal intercourse.

His critics have no good answers to that, but they counter with a question of their own—about the reports from the Caribbean, where B does appear to spread widely among heterosexuals. How does Essex explain that? "Very easily," he replies. "Number one, the rates of expansion in the Caribbean are definitely not what they are in India, Africa and Thailand. And number two, everyone I've heard says there is significantly more homosexual contact in the Caribbean than in Thailand or India or Africa." Asked to name any researchers he knows who claim this, he cites only one, Luis E. Soto-Ramirez, M.D., lead author of the Langerhans' cells study and chief of the molecular biology lab at Mexico's National Institute of Nutrition. "It's not the sort of thing that people like to talk about," Essex explains. "It's politically awkward to accuse a population of higher rates of rectal sex." He adds that it reminds him of the early days of the AIDS epidemic when physicians would whisper about certain sexual practices of homosexual men but de-

cline to mention them in print—even though they proved to have a significant impact on the disease. "I don't know what to do about it," Essex concludes unhappily. "I feel boxed in on this one."

As for the fact that other labs have not yet been able to repeat his results, Essex and other researchers say it's too soon for any tests to be completed. Besides, he states, "I haven't heard of other people who have done the exact same transmission efficiency experiments as we have." He can't imagine that he is wrong, for, to him, the Langerhans' cells hypothesis is the only one that makes any sense. "There are no Langerhans' cells in the wall of the rectum," he points out. "And there are no lymphocytes or monocytes"—the cells generally targeted by any HIV strain—"in the surface of the vagina. Langerhans' cells are the only ones there, unless you think the epithelial cells are important," he adds, with a tone that conveys that he can't imagine why anyone would (since studies show that the virus doesn't infect them). Regarding the primary reason for E-subtype epidemics among heterosexuals, Essex says, "Those people who disagree with me have no other hypothesis for what is important in heterosexual transmission." What's more, he cites evidence from Africa that may demonstrate the role of the Langerhans' cells in the transmission of subtype C, which he believes works the same way. The Langerhans' cells are present in foreskins, which may explain studies showing that the rates of infection were lower for African men who were circumcised than for those who were not.

Essex suspects that all the HIV subtypes were originally spread heterosexually, and that the B subtype, which like all HIVs is known to mutate rapidly, reduced its ability to infect via vaginal intercourse in the U.S. and Western Europe because it adapted to transmission where blood was present and the populations were more contained. "It makes more sense to me in an evolutionary, logical model to think that B transmitted better heterosexually once and lost that capability, than to think that E somehow gained it," he says.

Either way, it is important to emphasize that B and non-B subtypes are still essentially the same organism. Neither E nor B transmits exclusively by one sexual mode or another. The difference may only be a matter of degree. "It's like Russian roulette," explains Essex's colleague, Harvard AIDS Institute executive director Richard Marlink, M.D. "For heterosexual transmission with subtype B, you put one bullet in the chamber. With E, you put in two or three. You still might not get it, but you are more likely to."

Most experts insist that, even if subtype E is everything that Essex claims it is, the basic HIV prevention strategy in this country would be no different. "Would the public-health strategy change?" asks Dr. Jaffe. "No." In his view, HIV remains a disease that is completely preventable: Individuals need only avoid risky sex and stay away from infected needles or contaminated blood.

Soothing as this mantra may be, it demonstrates a certain blindness to contemporary attitudes toward HIV that have stemmed from the infection statistics. This spring, *The Wall Street Journal* ran a much-publicized story headlined "AIDS Fight Is Skewed by Federal Campaign Exaggerating Risks" that argued that the public-education campaign should be directed almost exclusively at homosexuals and IV drug users since they bear the greatest odds of exposure to HIV. The story asserted that when this campaign began in 1987, "for most heterosexuals, the risk from a single act of sex was smaller than the risk of ever getting hit by lightning," reflecting an emerging consensus among the general public that AIDS in America isn't their problem.

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Certainly, they're not behaving as if they were afraid of contracting the disease. Despite all the warnings about the importance of wearing condoms, only 31 percent of people who had five or more sex partners in the past year—the highest-risk group—did so the last time they had vaginal intercourse, according to a University of Chicago survey published in *The Social Organization of Sexuality*. This may explain why there are 13 million new cases of STDs in the U.S. every year.

And because they aren't being careful, heterosexuals are contracting HIV. As homosexual AIDS cases have decreased, heterosexuals have become the fastest-growing group of new AIDS patients. Between 1989 and 1990, the number of heterosexual AIDS cases increased 41 percent, while other risk-behavior categories increased just 8 percent. Last year, 2,840 male and 5,253 female cases of AIDS from heterosexual contact were reported. Women, it is important to remember, now bear the brunt of any heterosexual HIV transmission. It is significantly more likely that a woman will receive HIV from a man than it is that a woman will give the disease to a man. Nineteen percent of all new adult and adolescent AIDS cases are now female.

And that's with subtype B, as far as we know. But suppose the predominant subtype is E, and suppose further that Essex is right and the resulting risk of vaginal transmission is markedly greater? *The Lancet*, after all, reported that the risk of HIV transmission in a single act of intercourse was 31 to 56 times higher in Thailand than in the United States, although no one would attribute the entire increase to the virus alone. Essex has predicted that we'll eventually get epidemics of a non-B subtype here. The transformation, however, would certainly not happen overnight. He points out that in epidemiology there is an important relationship between prevalence (the total number of cases) and incidence (the number of new cases each year). For the incidence to rise markedly, the prevalence has to reach the point where the disease is fairly common: The more people have it, the more people get it. And E is certainly not common here now.

But, for all anyone knows, E's prevalence may be growing quietly. One of the most disturbing hallmarks of an HIV infection has always been its invisibility, and currently the invisibility is being compounded by spotty research on the part of the CDC. While it is good at tracking AIDS cases from hospital reports, the CDC has remarkably little idea how many HIV infections are actually occurring, and it still has no reliable information whatsoever *Continued on page 212*

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on subtypes, although speedier ways of subtyping are being developed. "The system is in evolution," Jaffe admits.

It's the invisibility that makes HIV so diabolical. "The virus stays silently in the body for years and years," says Essex, "and it's capable of being spread all the while." Without a massive public-health effort, it is not hard to imagine the initial course of a C- or E-strain epidemic, if Essex is correct about them and one does occur. It would, most likely, not immediately develop in the suburbs of middle-class America, but rather establish a foothold within those segments of American society that are already suffering the highest rates of heterosexual HIV and other STDs. Cheryl Healton, D.P.H., an AIDS specialist who is associate dean at the Columbia University School of Public Health, lists Miami, Los Angeles, San Antonio, New York City and Washington, DC, as prime candidates for the disease. (The fact that it is the dispossessed who are at greatest risk in these cities may contribute to society's relative indifference to the threat.) Overlapping social/sexual networks could bring these strains to *any* sexually active segment of society.

There are cheerier scenarios, however. Thailand is now the testing ground for two possible HIV vaccines, produced by Biocine and Genentech. If the vaccines prove effective against E, they might help limit any outbreak here. Also, AIDS researchers hold out hope for certain antimicrobial gels that could provide women with an extra line of defense against an HIV infection if condoms fail or aren't used. "It's a belt-and-suspenders kind of thing," explains Kenneth Mayer, M.D., director of the AIDS program at Brown University. Or, of course, it may be that nothing comes of these non-Bs at all, and the great shrug of the scientific community and the country at large at their discovery will have been entirely justified.

Given the stakes, it is distressing that no one knows for sure how many carriers of non-B subtypes there are in this country. If Brodine hadn't decided to shine her statistical flashlight where she did, we might still be waiting for the first confirmed reports. After Brodine published her results, Kathleen Irwin, M.D., a medical epidemiologist at the CDC's division of HIV/AIDS Prevention, led a study of patients at Bronx-Lebanon Hospital Center in New York City. While Brodine concentrated on likely non-B carriers, Dr. Irwin's survey was considerably broader. Of the 828 people tested, 43 proved to be HIV-positive. Of them, eight individuals, or nearly 20 percent, had blood screening test results that differed from those typical of patients infected with the U.S. B-strain, including two confirmed subtype A cases so far. From May to August of this year, 73 cases of subtype E were diagnosed in Britain. Since Brodine did her work, thousands more ships have arrived in San Diego, of course, to say nothing of all the planes that have landed in New York and Los Angeles and hundreds of airports in between. As time passes, there will be other cases of non-B subtypes. That is guaranteed. What happens after that, God only knows.

JOHN SEDGWICK has been SELF's national correspondent for three years.

BEAUTY DETAILS

Editors' choice Page 70 Here's where to find these must-have items: Kim Lépine's Modular Hair Care System is available at the Kim Lépine Salon in NYC, or call 888-750-4247; Dermatone's Sunblock Creme can be found at Eastern Mountain Sports, L.L. Bean and other sporting-goods stores, or call 800-225-7546 to order; Tommy Girl Cologne Spray is available at Macy's, Bloomingdale's and Dillard's; Sarah Michaels' Bath Oil Pearls are sold at drugstores and mass-merchandise stores nationwide.

On the ball: a new therapy for tension Page 74 For more information on ball therapy, call 800-649-6846.

Not just for babies Page 74 To order Kiehl's products, call 800-KIEHLS-1; for information on where to buy Autumn Harp's Hot Spots for Tots, call 800-LIPS-367; to order Burt's Bees products, call 888-50-ORDER; for Mustela products, call 800-927-7882; to order Phytotherathrie products, call 800-55-PHYTO. Other children's products that are great for adults include Jacadi's Le Lait (for stores, call 800-469-6133) and Baby Guess and Guess Girls' body lotion and hair-care products (call 800-91-GUESS to order).

Crash course: coloring your hair at home Page 199 All of the major at-home haircolor manufacturers have 24-hour hotlines to help you with everything from shade selection (bring a cellular phone along while you shop) to application tips. Keep this handy directory with you for quick reference: Clairol, 800-223-5800; Revlon, 800-4-REVLON; L'Oréal, 800-631-7358; and Laboratoires Garnier, 800-4-GARNIER.

Some product suggestions: If you want a temporary color change, try Clairol's Glints No Commitment Conditioning Color Enhancer. For semipermanent color, look for L'Oréal's Exuberance 7-Day Color Foam; L'Oréal's Advantage; Clairol's Loving Care; Revlon's Rev Up Conditioning Color Enhancer; or Dark and Lovely's Reviving Colors for African American hair (for more information, call 800-442-4643). Some good long-lasting semipermanent products are L'Oréal's Casting Tone-on-Tone Gentle Colorant; Clairol's Natural Instincts; and Revlon's Shadings Tone-on-Tone Colorant. Here are more permanent haircolors to try: Clairol's Nice 'n Easy; Clairol's Hydrience; Clairol's Ultress; L'Oréal's Preference Fade Resistant Formula; L'Oréal's Excellence Creme; L'Oréal's Excellence Creme Blonde Supreme. For subtle highlights, try L'Oréal's Creme Frost. The Color Gone Haircolor Stain Remover cleans semipermanent and permanent haircolor stains off skin (to order, call 800-651-7921). To help your at-home color last, try Senscience's True Hue after-shampoo treatment (to order, call 800-22-VITAL); Schwarzkopf's Igofleur Prescription Color Shampoos (to order, call 800-234-4672); or Angela Cosmai's Color Protective Hair Care System (to order, call 800-992-9585).