Tice, AD. Infectious Diseases. 1990 Medical and Health Annual, Encyclopaedia Britannica. Chicago, Encyclopaedia Britannica Inc. Bernstein E.

Infectious Diseases

The worldwide epidemiological patterns of infectious disease continue to evolve and change. In the U.S. there has been a recrudescence of some long-known diseases, among them tuberculosis and syphilis, and a growing recognition of relatively new infectious agents, such as human T-cell lymphotropic virus, type 1 (HTLV-1), and anisakis, a parasite transmitted in raw fish. Advances in technology have brought about new types of infection; infections of artificial joints, for example, are now an increasing problem. Medical science continues to find new ways to treat infections—creating more potent antibiotics and better antiviral agents—but the development of organisms resistant to medication poses a continuing challenge.

TB: old health threat renewed

Despite the advances that have been made in the treatment of tuberculosis (TB), approximately eight million new cases are reported annually around the world, and three million people die of the disease each year. The incidence of TB in the United States is less than in most countries—and until just a few years ago was declining steadily. Recently, however, the incidence of TB has been rising. The 22,768 new cases reported to the U.S. Centers for Disease Control (CDC) in 1986 represented a 2.6% increase over the 1985 number. Slightly fewer cases were reported in 1987 (22,517), but this was hardly indicative of any appreciable decline. Twenty-four percent of the new cases reported in 1987 were in persons born outside the U.S., an especially high prevalence being reported in Asian immigrants. A factor of even more concern to public health officials, however, was the increasing incidence of TB among certain populations of native-born Americans—including prison inmates, homeless people, migrant farm workers, intravenous drug abusers, and minorities. The proportion of TB cases in nonwhites rose from 24% in 1953 to 49% in 1987. The tuberculosis bacillus is particularly suited to transmitting the disease among the poor, especially people living under crowded conditions.

Several reports published in 1988 and 1989 attributed the recent increase in TB to intravenous drug abuse and concomitant infection with HIV (human immunodeficiency virus), the AIDS virus. One such report focused on TB incidence in a population of current and former drug abusers enrolled in a methadone program in the Bronx, N.Y. Of those who were infected with the AIDS virus, 23% also carried tuberculosis bacteria. Another 20%, who tested negative for the AIDS virus, were shown to be TB carriers. Two years later active TB had developed in eight of the HIV-infected people but in none of the others. The authors of the report noted that people whose immune systems are weakened by HIV usually develop TB as a result of activation of a long-standing infection rather than new exposure to the disease. They recommended that intravenous drug abusers who carry the AIDS virus be treated prophylactically with the antituberculous drug isoniazid.

Minority groups and drug addicts are particularly difficult populations for public health efforts to reach; prevention and even treatment of infections are problematic in these groups. The situation is further complicated by the fact that tuberculosis must be treated for a much longer time than most other infections. In the past, treatment regimens consisted of two antituberculous drugs to be taken for a year. Recent studies of newer medications indicate that a shorter course of therapy may be effective, but a six-month course is the minimum. This is a long time in a transient population such as the homeless or migrant workers or in a population that is known to have difficulties complying with a medical regimen. Because of inadequate or intermittent treatment, it is not unusual for persistent infectious tuberculosis to develop in some people. Drug-resistant organisms also develop. As a result of the increasing number of cases of tuberculosis in U.S. inner-city populations, the disease has spilled over to other urban dwellers; there has been, for example, a clear increase in incidence of TB in children in some major metropolitan areas.

The AIDS virus undermines the body's immune system, thus making the treatment of TB much more diffi-

A tuberculosis patient is examined at Harlem Hospital in New York City. The disease, in decline until a few years ago, is now on the rise; at greatest risk are the homeless, minorities, and persons infected with the AIDS virus.

Mario Ruiz

Grev Villet—Black Star

Drug abuse—especially the use of crack, which is often the object of sex-for-drugs barter—accounts in large measure for the rising incidence of syphilis in the United States. Public health officials also see evidence of a possible link between syphilis and AIDS: sexually transmitted diseases that cause genital ulcers may facilitate the transmission of the AIDS virus.

cult. Because of the immune defect, the TB organism is seldom eradicated. Treatment may be necessary for life, and the infection is often fatal despite the use of multiple antituberculous drugs.

In addition to *Mycobacterium tuberculosis*, there is another form of tuberculosis—called *Mycobacterium avium intracellulare*—that often infects persons with AIDS. Although it is a common environmental organism, it is found only rarely in people whose immune systems are not compromised. When the organism establishes itself in AIDS patients, it can often be recovered at random from the bloodstream because there is no immune response to counteract it. While *M. avium intracellulare* is not usually fatal in itself and is not communicable, it undoubtedly contributes to the debility of the individual who is infected with it. Unfortunately, the antituberculous medications presently available are not very effective against this organism and are generally not used, as their toxicity outweighs their benefit.

In 1987 the Department of Health and Human Services established an advisory committee for the elimination of tuberculosis in order to develop a strategic plan for the U.S. as a whole. The goal is to reduce the incidence of TB to less than one case per million population by the year 2010, with an interim target of 3.5 cases per 100,000 by the year 2000. It is the hope of the advisory committee that advances in biotechnology will produce better diagnostic and therapeutic measures than those now existing. A second step will be aggressive application of these new methods to clinical practice and public health. If this plan is to succeed, it will require the cooperation of local health departments and practitioners throughout the entire country and improved methods of reaching the more problematic populations, especially the indigent and drug abusers.

Incidence of syphilis in California, 1988*

population group	number of cases	percentage
white males	601	9
white females	289	4
black males	2,002	30
black females	1,658	25
Hispanic males	1,448	22
Hispanic females	432	7
other	191	3

*provisional data

Source: California Department of Health Services, Sexually Transmitted Disease Section

Syphilis, drugs, and "unsafe sex"

Syphilis has been recognized since the 16th century. Its spread has been facilitated by military conquest, increasing international travel, and a gradually more sexually permissive society. Penicillin injections, which can cure the disease, have been available since the 1940s. Despite this therapeutic advance, syphilis persists and is now increasing in incidence. In fact, the rate of incidence of syphilis in the U.S. now equals that of 1982—the highest rate since 1950. In 1987 there were 35,241 cases of primary and secondary syphilis reported in the U.S. This represents a 25% increase over the previous year and a rate of 14.6 cases per 100,000 population.

The greatest part of the increase seems to be concentrated in urban areas, with cities in California, Florida, and New York accounting for more than 50% of the total number of cases and about 80% of the increase. Minority groups are disproportionately af-

fected; black males, for example, have an incidence rate of 145 cases per 100,000—ten times the national rate. This recent rise in syphilis is strongly linked to heterosexual transmission. In contrast, there has been a clear decline in the incidence of syphilis (as well as gonorrhea) in the homosexual population, presumably due to the institution of "safe sex" practices because of the threat of AIDS.

According to CDC reports, the increase in heterosexual transmission of syphilis is associated with prostitution and drug abuse, particularly the abuse of crack, which is often the object of sex-for-drugs barter. Prostitutes, drug abusers, and their sexual contacts are now major risk groups. Some of the increase may be attributed to the use of spectinomycin to treat penicillin-resistant gonorrhea. While this drug is effective against gonorrhea, it is not able to kill the syphilis spirochete as penicillin does. Recent recommendations by the CDC have suggested that the antibiotic ceftriaxone be used instead for gonorrhea because it also can kill incubating syphilis. Public health officials are concerned that the increased incidence of syphilis may be due in part to the diverting of health resources from medical treatment of persons with syphilis and tracing of their sexual contacts to the prevention of AIDS. From a public health perspective, however, the two diseases—AIDS and syphilis—are related. Several studies published in 1988 suggested that sexually transmitted diseases that cause genital ulcers (syphilis and herpes simplex, type 2) increase the likelihood of the transmission of AIDS. When syphilis does occur with AIDS, the immune deficit makes it harder to treat. Earlier in the AIDS epidemic, some physicians had speculated that syphilis might be responsible for some of the clinical manifestations of AIDS, but this does not appear to be the case.

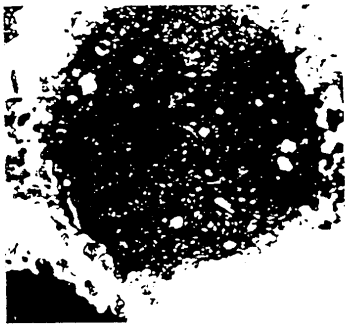
There are three reasons why the new outbreak of syphilis is of particular concern. First, because of the prominence of heterosexual transmission, the chances that the disease will spread to the fetus of an infected woman, producing congenital syphilis and its associated deformities, are much greater. In fact, there has already been an increase in the number of cases of congenital syphilis reported in New York City. Second, the increase in syphilis among heterosexuals also suggests an increasing level of unsafe sex practices associated with drug abuse and prostitution in inner-city neighborhoods. This creates an ideal setting for transmission of HIV. Finally, the presence of syphilis in this segment of the urban population may facilitate the transmission of HIV through syphilitic genital ulcers, which are usually painless but, as noted above, are believed to provide a ready path for transmission of the AIDS virus.

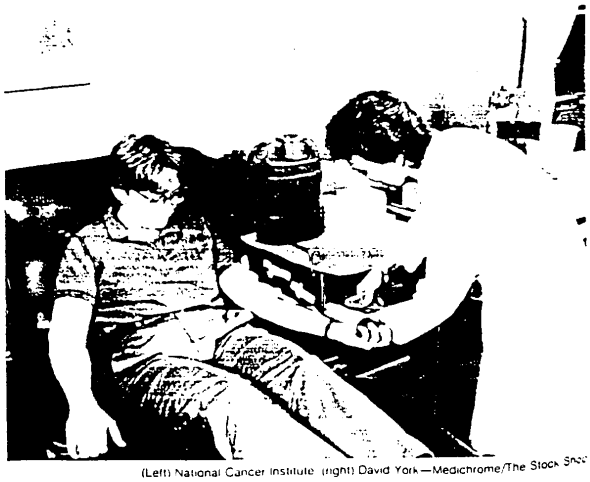
It is not clear what exactly is to be done about this recrudescent disease. The Public Health Service had to abandon its goal of reducing the incidence of primary and secondary syphilis to 7 cases per 100,000 by 1990. It appears that more specific plans to deal with the inner-city and minority populations are needed. It is also apparent that there will be no lessening of syphilis transmission without a reduction in drug abuse and prostitution.

Concerns about the human retrovirus HTLV-I

The first human retrovirus discovered was given the name human T-cell lymphotropic virus, type I (HTLV-I). It was first isolated in 1978 but was not reported until 1980. Since that time HTLV-II and HTLV-III (the latter now called human immunodeficiency virus, type 1, or HIV-1—or simply HIV) have been identified. The discovery that AIDS is caused by HIV launched a massive

Although the human retrovirus HTLV-I (shown in photomicrograph below) is relatively rare in the U.S., the country's blood banks now screen donated blood for it as well as for the viruses that cause hepatitis-B and AIDS.





(Left) National Cancer Institute (right) David York—Medichrome/The Stock Shot

international research effort that has already brought some insight into the workings of retroviruses. Still, much remains to be learned, and new retroviruses continue to be discovered.

HTLV-I, while clearly a human retrovirus, is quite different from HIV in that it does not produce AIDS and does not inevitably result in fatal illness. Instead, it causes an unusual type of blood disease called T-cell leukemia or lymphoma. It has also been associated with a progressive neuromuscular disease, called tropical spastic paraparesis, in which nerve damage usually causes a progressive weakness and spasticity of the leg muscles and often loss of bowel or bladder control. The disorder has also been reported in Japan and the Caribbean. Like HIV, HTLV-I is believed to have originated in Africa, although in a different area. Presumably it then spread to and became endemic in areas in the Caribbean and Japan.

HTLV-I appears to be more easily spread than HIV, at least in southwestern Japan, where in some areas up to 30% of the population have antibodies to the virus; women are infected as frequently as men. Sexual transmission is likely, and there is a clear association of the virus with blood transfusions. Unlike HIV, however, HTLV-I does not appear to be transmitted by infusion of blood plasma or serum factors (the liquid fraction of the blood), probably because it is more closely associated with blood cells.

In the U.S. the incidence of antibodies to HTLV-I is less than one in 1,000 and is often associated with prior residence in the Caribbean or intravenous drug abuse. Despite this low prevalence of HTLV-I antibodies, however, there has been concern about contracting the virus through blood transfusion. Recent studies of more than 20,000 transfusions suggest that the possibility of receiving blood contaminated with HTLV-I (0.024%) may now be higher than the risk of contracting HIV-1 (0.003%), as all donated blood in the U.S. has been tested for HIV-1 since March 1985. To combat the potential for further HTLV-I transmission via transfusions, broad-scale epidemiological studies are being conducted to determine the incidence of the disease in the U.S.; in 1988 the Food and Drug Administration (FDA) licensed tests for the antibody to the virus, which are now being used in most blood banks. The test is similar to the ones used to detect antibodies to HIV and also requires duplication of a positive result (*i.e.*, any blood sample found to contain antibody must be tested a second time and produce the same result) and confirmation with a backup test before a positive result is confirmed. Blood donors who test positive for the virus will be notified of the result, but it is not clear yet what the next step will be.

Parasitic infections from raw fish

Parasitic disease occurs in every form of life. Parasites afflict a large part of the world's human population—particularly in less developed countries, where poor sanitation and primitive methods of sewage disposal are common. Ascariasis, schistosomiasis, hookworm disease, and other intestinal parasitic infections account for much more human disease than cancer, heart disease, and stroke in most countries of Africa and Asia. In North America the spread of these organisms has virtually been eliminated by modern methods of sanitation.

Over the past few years, with increasing consumption of fish in the United States and a growing taste for sushi and other Japanese delicacies has come an increased incidence of parasitic infection. Human infection may occur as the result of eating either raw or insufficiently cooked, smoked, or marinated fish. The fish parasite that most often affects humans is the roundworm called anisakis. Common parasites in marine mammals, the worms live in the bowels of seals and walruses, where they lay their eggs. The eggs pass out into water and are then taken up by fish or squid and become encysted in muscle tissue or body cavities. When the fish is eventually eaten, the larvae migrate out of the cyst and, if ingested by humans, can develop into adult worms in the individual's stomach or become attached to the bowel wall. Symptoms of anisakiasis may include nausea, stomach pain, and indigestion. If the larvae perforate the bowel wall, peritonitis can develop. In some cases the worms migrate up from the stomach to the mouth and are regurgitated or coughed up—often as quite a surprise to the unknowing "host." Anisakis worms in the stomach can be removed by means of an endoscope passed through the mouth.

Another relatively common fish parasite that infects humans is eustrongylides. Like anisakis, it is associated with saltwater fish, but fish-eating birds rather than mammals are its usual host. This parasite has been previously reported in fishermen who inadvertently ate bait fish; there have also been reported cases of bowel perforation after the eustrongylides larva was ingested with sushi.

Fish parasites are so common that there is virtually no way to avoid eating them. The way to prevent human disease is to make certain that the parasite in the fish is not ingested alive. Either cooking a fish for ten minutes at 65° C (149° F) or freezing it at less than −20° C (−4° F) for five days is an effective measure. Supermarket fish have usually been frozen long enough that the parasites are not viable by the time the fish is sold. However, fresh fish are sometimes flown directly from the site of the catch to major distribution points. If the consumer does not plan to cook fish immediately, it should be frozen.

Artificial joints: infection risk

The development of artificial joints represents a dramatic advance for people with severe, crippling arthri-

tis. Hips and knee surfaces can now be replaced, allowing a person to walk who might otherwise be confined to a bed or wheelchair. Even the joints of the fingers and toes can be replaced with joints made of metal or other material. While the outcome of joint replacement can be a dramatic improvement when all goes well, the risk of infection is significant. Approximately 1–2% of all artificial joints become infected with bacteria. These infections are particularly difficult to eradicate because of the presence of the implant itself—a "foreign body" within the body's own tissues, which provides an opportunity for bacteria to escape destruction by the body's normal defense mechanisms. Standard antibiotic therapy is not sufficient to reach and destroy bacteria hidden within the complex surface layers of the implanted material. The most frequent bacteria to cause infections in artificial joints are the staphylococci; the more virulent *Staphylococcus aureus* (a common cause of wound infections) and the more common *Staphylococcus epidermis* (a normal inhabitant of the skin that seldom causes infection without a foreign body) play a major role. The infection may be introduced at the time of surgery, when organisms from the skin enter the wound via the initial incision. The prosthetic joint can also be "seeded" by bacteria in the bloodstream that have not yet been filtered out by the liver and spleen. Bacteria may enter the bloodstream from skin sores, or they may be introduced during the course of dental work or diagnostic procedures such as colonoscopy.

Once an infection has become established, there are two treatment options: (1) removal of the infected joint, followed by fusion of the bones on either side, or (2) removal of the joint, aggressive intravenous antibiotic therapy for a period of weeks, and then replacement with a new joint. There is an ongoing debate among physicians about the value of prophylactic antibiotics—for example, the taking of penicillin before and shortly after dental work—for people with artificial joints.

Resistance to antiviral drugs

Developing effective medication for treating viral infections is a difficult task; viruses live within normal human cells, and anything that damages the virus is likely to harm the cell. Nevertheless, great strides have been made in the past decade with the development of acyclovir (Zovirax) to treat herpes simplex infections, zidovudine (also called azidothymidine, or AZT; Retrovir) to treat HIV infection; ribavirin (Virazole) for infection caused by respiratory syncytial virus; and ganciclovir (Cytovene) to treat cytomegalovirus infections. There have been encouraging studies of the use of interferons for a variety of viral illnesses and new antiviral agents foscarnet, dideoxyinosine, and dideoxycytidine for HIV infections. Other antiviral drugs are under active investigation.

With the increased use of antiviral agents, however, the potential exists for viruses to develop resistance mechanisms—just as many bacteria came to be resistant to penicillin. In fact, with viral infections the development of resistant strains is even more likely than it is with bacterial infections because the antiviral agents now available often are not able to eradicate the viruses but simply lessen the severity of the disease or suppress the infection. The herpesviruses, for example, persist within the body's cells despite antiviral therapy and may cause renewed infection at any time. Recurrent or prolonged use of antiviral agents such as acyclovir may contain the spread of disease, but it also applies selective evolutionary pressure in favor of mutant strains that are resistant to acyclovir. The development of drug-resistant viruses is particularly likely to occur in an immunosuppressed patient, such as one with AIDS.

During the past year there have been reports of herpes simplex viruses that are resistant to acyclovir and of cytomegalovirus resistant to ganciclovir. There have been indications that HIV may become resistant or refractory to zidovudine therapy. While many of the resistant mutant viral strains may not be as virulent as the original strains, they can still cause significant disease in an immunosuppressed person.

It is difficult to scientifically test the resistance of a given virus; usually simple clinical indications are all that is possible. At present most available antivirals still appear to be effective and useful. Unfortunately, the future of antiviral drugs is likely to follow a course like that of the antibiotics—a gradually escalating battle between the organisms and the drug developers. In the long term, the best way to deal with infection is to prevent its occurrence rather than to try to treat or manage it once it occurs. The eradication of smallpox through vaccination is perhaps the best example of how successful this approach can be.

—Alan D. Tice, M.D.

Medical Education

Currently in the United States persons 65 years of age and older represent more than 12% of the overall population; this percentage will rise to 20% by the year 2030, amounting to approximately 65 million persons. Until very recently most physicians in the United States were inadequately trained in geriatric medicine. With the current population trends, it has become increasingly essential that geriatrics be incorporated into the education of physicians. In response to these demographic changes, several educational efforts have been initiated to teach physicians how to best care for older persons.

Within the past few years, several notable events have indicated that the discipline of clinical geriatrics is "coming of age." Geriatrics is a relatively new specialty,