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Acquired Immunodeficiency Syndrome: An Update

In June and July of 1981, investigators in the United States of America reported to the medical community the unusual occurrence of *Pneumocystis carinii* pneumonia and Kaposi's sarcoma among previously healthy homosexual men. Due to the underlying profound disturbance of the cellular immune system, these cases were referred to as the acquired immunodeficiency syndrome (AIDS). Over the past three years, over 7,000 cases of AIDS have been diagnosed in the United States, and the number of cases continues to increase by approximately 200 per week *(1)*. In addition, in preliminary surveillance reports it has been estimated that there are over 500 cases in the Americas outside of the United States, and approximately 600 in Europe *(2)*. With a case fatality rate of 80% two years after diagnosis, this outbreak now ranks as one of the most serious epidemics in the last several decades.

Until recently, the etiology of this syndrome was completely unknown, but its epidemiology reflected the transmission of an infectious agent. Within the past year medical scientists reported the recovery of a human retrovirus from AIDS patients and patients with prodromal signs and symptoms of AIDS *(3,4)*. While this virus, referred to as lymphadenopathy-associated virus (LAV) or human T-cell lymphotropic virus (HTLV-III), has not been definitively proven to be the cause of AIDS, all available evidence strongly supports an etiological role for it *(5)*. The virus has been cultured from T lymphocytes, lymph nodes, semen, and saliva from AIDS patients and from patients at high risk for AIDS. Antibody to this retrovirus is present in greater than 90% of such patients and in less than 1% of healthy individuals and patients with other immunosuppressive diseases. These virologic and serologic data, described in more detail in this report, provide rather convincing evidence for the etiologic role for this retrovirus in AIDS.

Epidemiology

Shortly after the recognition of *Pneumocystis carinii* pneumonia and Kaposi's sarcoma in homosexual men, a national surveillance system was formed in the United States and based at the Centers for Disease Control (CDC) in Atlanta, Georgia. An empirical clinical definition of AIDS, which is characterized by an unexplained deficiency in the immune system which renders persons susceptible to various opportunistic infections and malignancies, was formulated for purposes of surveillance. A case of AIDS is still clinically defined as "a reliably diagnosed disease that is at least moderately indicative of an underlying cellular immunodeficiency which occurs in a person who has no known underlying cause of cellular immunodeficiency or other cause of reduced resistance reported to be associated with that disease." As of 3 December

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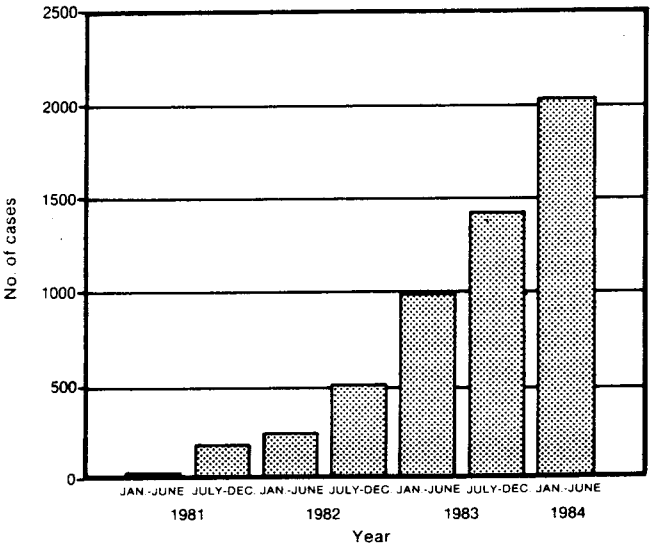
1984 physicians in the United States had reported 7,136 patients meeting this surveillance definition *(1)*. As shown in Figure 1, AIDS continues to spread in the United States and over 86% of the adult AIDS patients and 82% of the pediatric patients have been reported since January 1983 (Figure 1). Seventy-two cases (1%) have been diagnosed in patients under 13 years of age at the time of diagnosis and 7,064 (99%) have occurred in adults, and 3,391 (48%) of the reported patients are known to have died (48% of the adults and 69% of the children) including 73% of patients diagnosed before January 1983. Indeed, the cumulative incidence of cases from 1 January 1979 through December 1984 demonstrates that the case fatality rate increases dramatically two years from the time of diagnosis (Table 1). From such data it is estimated that the median survival for patients with Kaposi's sarcoma is 16.7 months and for those with opportunistic infections, 6.4 months.

Homosexual or bisexual men and intravenous drug abusers constituted the largest percentages of the adult AIDS patients, 73 and 17%, respectively, and remain at highest risk for developing AIDS (Table 2). The remaining 10% were in other groups with different or unknown risk factors. These include Haitians who had immigrated to the United States since 1978, hemophiliacs receiving factor 8 and factor 9 concentrates, heterosexual contacts of persons in an AIDS risk category, blood transfusion recipients, and patients who denied any of the above risk factors.

Figure 1. U.S. AIDS cases by half year of report through first half of 1984.



Source: MMWR 33(47):661, 1984.

Table 1. Reported cases and case fatality rates of AIDS in the United States by half-year diagnosis 1979 to June 1984.[a]

Half year of diagnosis	No. of cases	No. of deaths[b]	Case fatality rate (%)
1979			
1st half	1	1	100
2nd half	8	6	75
1980			
1st half	19	15	79
2nd half	27	27	100
1981			
1st half	82	71	87
2nd half	168	139	83
1982			
1st half	348	257	74
2nd half	629	424	67
1983			
1st half	1,145	685	60
2nd half	1,456	773	53
1984			
1st half	2,033	740	36

Source: Centers for Disease Control.

[a]Excluding seven cases with unknown dates of diagnosis and five cases diagnosed prior to 1979.

[b]Number of deaths among people diagnosed in the specific half year, regardless of year of death.

Among adult patients in the United States there is a 14:1 male to female ratio. White persons account for 59% of the cases; blacks for 25%; persons of Hispanic origen for 14%, and persons of other unknown race or ethnicity for 2%. Over 90% of AIDS patients are between the ages of 20 and 49 years and 47% are in the 30 to 39 year age group. A large proportion (75%) of the adults were reported to be residents of New York, California, Florida, or New Jersey while the remainder were reported to be from 41 other states, the District of Columbia, and Puerto Rico. Generally, the cities with the highest attack rates are those with large homosexual male populations.

The geographic distribution of AIDS among children with parents in high risk groups is similar to that seen for heterosexual adult AIDS patients; over 89% are from New York, California, New Jersey or Florida. "Twenty-nine (40%) of the 72 pediatric patients came from families in which one or both parents had histories of intravenous drug abuse; 17 had one or both parents who were born in Haiti; 12 had received blood or blood components before their onset of illness; four had hemophilia; one had a father who was bisexual; and one child's parent denied any risk factors. Risk factor information on the parents of the eight remaining patients is incomplete" *(1)* (Table 3).

Table 2. Adult AIDS patients by patient group in the United States through 3 December 1984.

Patient group	Male		Female		Total	
	No.	%	No.	%	No.	%
Homosexual/bisexual	5,153	78	0	0	5,153	73
Intravenous drug user	958	14	251	55	1,209	17
Haitian residents in U.S.	214	3	37	8	251	4
Hemophiliac	46	1	0	0	46	1
Transfusion with blood	45	1	37	8	82	1
Heterosexual contact[a]	5	0	50	11	55	1
None of the above	190	3	78	17	268	4
Total	6,611	100	453	100	7,064	100

Source: Centers for Disease Control.
[a]With a person with AIDS or at risk for AIDS.

Table 3. AIDS cases among pediatric patients in the United States: relationship to risk factor.

Risk factor	Male		Female		Total	
	No.	%	No.	%	No.	%
Parent with AIDS or at increased risk for AIDS	23	54	24	80	47	65
Hemophilia	4	10	0	0	4	6
Transfusion with blood	10	24	2	7	12	17
None of the above	5	12	4	13	9	12
Total	42	100	30	100	72	100

Source: Centers for Disease Control, 3 December 1984.

"Eighty-one adults (1% of adult patients) and 12 children (17% of pediatric patients) with transfusion-associated AIDS have no other risk factors although they were transfused with blood components within five years of illness onset" *(1)*. Patients with transfusion-associated AIDS received blood from one to 75 donors (median 16 donors); and the time from transfusion to diagnosis was four to 62 months (median 29 months for adults; 14 months for children). In general, the adult patients with transfusion-associated AIDS tended to be older (median 53; range 19-81 years), and they received their transfusions in states and cities where the syndrome had been most commonly reported. Most adults received transfusions associated with surgery, while most infants with transfusion-associated AIDS (median age at diagnosis 14 months; range four to 46 months) were transfused for medical problems associated with prematurity.

In the adult patients in the United States, *Pneumocystis carinii* pneumonia is still the most common opportunistic infection, present in 54% of patients. Among the rest of the patients 23% have had Kaposi's sarcoma without *P. carinii* infection, 6% have had both Kaposi's sarcoma and *Pneumocystis* infection, and 17%, opportunistic infections (Table 4). Oroesophageal candidiasis, chronic ulcerative herpes simplex virus infection, disseminated cytomegalovirus infection, disseminated *Mycobacterium avium intracellulare* infection, cryptosporidia enteritis, and central nervous system toxoplasmosis are among some of the common opportunistic infections frequently seen in AIDS patients.

The proportion of adult patients with AIDS but without identified risk factors has remained relatively stable. These patients, classified as non-characteristic, are a rather heterogeneous group in which 71% are male and 29% are female *(6)*. Some patients had Kaposi's sarcoma and normal immunologic studies, and consequently may not have had AIDS even though they met the surveillance definition. Investigations of other male non-characteristic patients have identified 17 of 65 men (26%) who have had a history of sexual contact with female prostitutes. Five of the 17 gave a history of over 100 heterosexual partners within the

Table 4. Reported cases of AIDS in the United States: Distribution of cases and case fatality rate by disease category through 3 December 1984.

Disease category	Cases		Deaths	Case fatality rate (%)
	No.	%		
Pneumocystis carinii	3,882	54	1,968	51
Kaposi's sarcoma	1,634	23	488	30
Both *P. carinii* and Kaposi's sarcoma	433	6	287	66
Other opportunistic infections	1,187	17	648	55
Total	7,136	100	3,391	48

Source: Centers for Disease Control.

Table 5. Reported AIDS cases in the Americas excluding the United States, through June 1984.

Country	No. of cases
Argentina	8
Brazil	78
Canada	94
Colombia	4
Grenada	2
Guadeloupe	3
Haiti	287
Mexico	10
Suriname	2
Trinidad	16
Uruguay	3
Total	507

Source: Pan American Health Organization.

Table 6. Reported AIDS cases in 12 European countries as of 15 October 1984.

Country	No. of cases
Denmark	28
Finland	4
France	221
Federal Republic of Germany	110
Greece	2[a]
Italy	10
Netherlands	26
Norway	4
Spain	18
Sweden	12
Switzerland	33
United Kingdom	88
Total	559

Source: World Health Organization, *Weekly Epidemiological Record* 60(3):17, 1985.
[a]Data as of 15 July 1984.

past five years. In addition, one of the nine non-characteristic women interviewed claimed to be a former prostitute. Besides these preliminary reports of heterosexual transmission of AIDS in the United States, there have also been reports of such transmission in Haiti and in Africa. In the United States such transmission appears to be uncommon, but in Africa early reports have documented that heterosexual transmission appears to be the predominant mode of spread of AIDS *(7,8)*. In Kinshasa, Zaire, where the incidence of the disease is comparable to that in New York City, the male to female ratio has been reported to be 1.1 to 1 *(7)*. Transmission from male to females and female to males has been reported in Zaire as well as in Rwanda and Burundi, neighboring central African countries. In Rwanda, among 24 adults diagnosed as having AIDS, 12 of 17 men were reported to have had contact with prostitutes and three of the seven women were prostitutes *(8)*. These preliminary reports from Africa, Haiti, and the United States certainly suggest that women could be exposed to the AIDS virus through sexual contact, use of intravenous drugs, or transfusion and that these women may be capable of transmitting the virus to men through sexual contact. However, it is not known if such women will be as efficient as heterosexual or homosexual men in transmitting the AIDS virus. Further studies are needed to fully assess the risk of heterosexual transmission in different parts of the world in association with immunologic disturbances and infection with HTLV-III/LAV.

Surveillance of the occurrence of AIDS has also been established in the Americas through coordination of the Pan American Health Organization (Table 5), and in Europe through the World Health Organization collaborating center on AIDS in Paris, France (Table 6). From 11 countries in the Americas excluding the United States, 507 cases have been reported. In Europe, 559 cases of AIDS have been reported up to 15 October 1984 *(2)*. Estimates of the number of AIDS cases per million population vary considerably from one country to another. However, uneven geographic case distribution was found within individual countries and also in other parts of the world. Europeans accounted for 86% of the cases reported in Europe; among the rest of the cases some patients were from countries in the Caribbean region including 19 from Haiti and one from Dominica; one from Jamaica, 45 patients were from Africa; and 13 came from continental America including nine from the United States, one from Argentina, one from Canada, one from Nicaragua, and one from Peru (Table 7).

Table 7. Distribution of European AIDS cases by identified risk group and origin of patients, as of 15 October 1984.

Risk group	Europe (12 countries)	Caribbean	Africa	Other	Total
Male homosexuals	418	2	4	13	437
Intravenous drug users	7	–	–	–	7
Hemophiliacs	17	–	–	–	17
Transfusion recipients	3	–	–	–	3
No known risk					
Male	21	15	26	1	63
Female	12	4	15	–	31
Not known	1	–	–	–	1
Total	479	21	45	14	559

Source: World Health Organization, *Weekly Epidemiological Record* 60(3):18, 1985.

Among the Europeans, 87.3% were male homosexuals, 3.5% were hemophiliacs and 1.5% drug abusers, while none of the known risk factors could be found for 6.9% of patients of both sexes (Table 7). In contrast, none of the known AIDS risk factors were found in any of the patients from the Caribbean and Africa reported in Europe. Indeed, subsequent studies in Africa and in the Caribbean have confirmed that many of the patients do not have any of the known risk factors for AIDS and that heterosexual transmission appears to be a major mode of spread of the disease *(7,8)*.

In summary, the vast majority of cases within the United States continue to occur among persons in the major identified risk categories, while cases occurring in tropical countries appear to lack previously recognized risk factors and heterosexual transmission appears to be a major mode of transmission. The cause of AIDS now certainly appears to be an infectious agent, probably a retrovirus described below which can be transmitted by intimate sexual contact or by percutaneous inoculation of infectious blood, through contaminated needles, or through blood products. At the present time there is no evidence to suggest airborne transmission of AIDS. Furthermore, the failure to identify cases among friends, relatives, and co-workers of AIDS patients and health care personnel with direct contact with such patients provides further evidence that casual contact offers little or no risk.

AIDS and the Immune System

AIDS is a distinctive disease of the immune system in which the common denominator is a profound immunosuppressed state based on defects of the cell-mediated immune system with secondary effects of the humoral immune system *(9)*. Indeed, AIDS has provided a unique insight into the function of our immune system including interaction between the cellular and humoral immune systems by which T lymphocytes, B lymphocytes, macrophages, biologically active molecules (lymphokines), and antibodies regulate together the magnitude, intensity, and duration of the immune responses to an invading pathogen or antigen.

Under evolutionary pressures, the immune system has divided into two separate but cooperating systems. The humoral (antibody-mediated) immune system consists of B lymphocytes, polymorphonuclear cells, and complement which are involved primarily in the defense against bacterial pathogens. In the humoral system immunoglobulins circulate and interact with bacterial antigens resulting either in lysis of the bacterial cell wall or in opsonization by macrophages which identify the attached antibody molecules on the pathogen.

The cell-mediated immune system, which consists of T lymphocytes, monocytes, basophils, and eosinophils, is primarily involved in countering viral, fungal, and intracellular bacterial infections. This system appears to be most profoundly affected by AIDS and this is reflected in the appearance of disseminated viral, fungal, and parasitic infections in AIDS patients. In the cell-mediated system, the T lymphocytes circulate and directly react with antigens via specific membrane receptors. Although T-cells are produced in the thymus, the population of these cells is heterogeneous. Several antigenically identifiable subpopulations with discrete functions have been described and these fall into three subsets of broad functional categories.

One specific subpopulation of T lymphocytes which plays a vital role in the early phase of all immune re-

sponses is that of the "helper T-cell" which is also known as the T4 lymphocyte because of the T4 antigen present on its membrane. T4 antigens are now readily identifiable due to the introduction of monoclonal antisera which are specific for this moiety. While this cell has multiple functions, it is primarily responsible for the recognition of self and foreign antigens, whereby it may activate a series of humoral and cellular events essential to immobilization of invading pathogens by B lymphocytes and effector T-cells to produce an effective immune response. This cell population appears to be most severely affected by AIDS, as manifested by a marked depletion in the circulation of T helper cells and by the lack of effector T-cell function which is dependent upon the initial signals produced by the helper T-cells.

There are two distinct cooperating forms of effector T lymphocytes which are present in our immune system. Both carry receptors for specific antigens on their cell membranes, and both can detect antigens after physically interacting with them or receiving help through the soluble factors released by the helper T-cells described above. One type of effector T lymphocyte stimulates monocytes to form macrophages and to produce the delayed type hypersensitivity reaction readily elicited by intradermal injection of antigens into a sensitized individual. The second type of effector T-cell is directly cytotoxic and thus is termed a killer T-cell. It has the capacity through the release of preformed molecules contained within its cytoplasm to kill viruses, tumor cells, fungi, and parasites. Both types of effector T-cells are essential in our host defense against many of the opportunistic infections which are seen in AIDS patients, implicating the loss of this effector T-cell function.

Another subpopulation of T lymphocytes consists of the suppressor or immunoregulatory T-cells frequently referred to as T8 lymphocytes. These lymphocytes control the information produced by the effector T-cells, control antibody production by the B-cells and block activation of T- and B-cell clones which might be reactive to self antigens, thus inhibiting autoimmune reactions.

In AIDS all of these populations of T-cells appear to be affected, but the most severe effects are evident in the depletion of the T helper lymphocytes or T4 cells. Clinically, patients will initially present with leukopenia and an absolute lymphopenia (total lymphocyte count less than 1,500 cells/mm^3). As mentioned above, the most characteristic laboratory aspect of AIDS is the depletion of both the relative and absolute number of circulating T helper lymphocytes. In normal individuals, there are usually two to three times as many T helper cells as T supressor cells. In AIDS patients, however, the ratio of T helper to T supressor cells is usually less than one due to this specific depletion of T helper cells. This lack of T helper cells is reflected *in vivo* as the absence of cutaneous skin test reactivity or anergy (depressed delayed type hypersensitivity), and as depressed natural killer cell activity both *in vitro* and *in vivo*, as manifested by increased susceptibility to intracellular pathogens including viruses, fungi, bacteria, and parasites. Essentially all *in vitro* measurements of T lymphocyte function with respect to nonspecific as well as specific antigens or mitogens are decreased in patients with AIDS, due to this lack of T helper cell function. In addition, AIDS patients exhibit abnormal B lymphocyte function as manifested by the finding of polyclonal hypergammaglobulinemia and a failure of B-cells to mount a *de novo* response to antigen, such as vaccine with a previously unexposed antigen. Suppressor cell function also appears to be directly affected by this disease as demonstrated by the findings of autoimmune phenomena such as the thrombocytopenic purpura and hemolytic anemia identified in many AIDS and suspected AIDS patients.

Thus, it appears that AIDS induces both quantitative and qualitative defects in T lymphocyte subpopulations, and consequently, on B lymphocyte function. In addition to the above described defects, other investigators have also commented on a reduction in the production of certain lymphokines and other chemical mediators of inflammation. For example, antigen-activated monocytes release a molecule termed interleukin-1 which triggers the proliferation of thymocytes and antigen-stimulated peripheral T-cells. After antigen and interleukin-1 triggering, T-cells synthesize and secrete other peptides including interleukin-2 which is essential for clonal expansion of the antigen-triggered T-cell. It has been proposed by many investigators that a defect in the synthesis or secretion, or both, of interleukin-2 is associated with AIDS. In fact, it has been shown *in vitro* that the addition of interleukin-2 to cell cultures can restore some immune functions *in vitro*. On the basis of these studies, treatment with interleukin-2 as well as with other immunomodulators is being administered to AIDS patients to enhance the immune system's attack on opportunistic infections.

Clinical Features

Although immunologic dysfunction is a common factor among all of the AIDS patients, the clinical spec-

trum has been quite diverse. There is usually a two to eight month symptomatic prodromal period which is frequently characterized by unexplained fever, night sweats and chills, lymphadenopathy, diarrhea, weight loss, dysphagia, fatigue, apathy, depression, and/or occasional diminished libido and impotency. There is usually a prolonged delay in diagnosis, and symptoms may vary depending on the development of either Kaposi's sarcoma or *Pneumocystis carinii* or other opportunistic infections. In tropical regions, *Pneumocystis* has not been commonly identified in AIDS patients, whereas other parasitic infections, such as cryptosporidia, toxoplasmosis, and fungal infections, such as oroesophageal candidiasis and central nervous system cryptococcosis, have been more frequently reported. It is as a consequence of their immunosupressed cell-mediated response that AIDS patients have an unusual susceptibility to such a wide variety of opportunistic infections, which may occur sequentially or simultaneously. Laboratory tests in most of these patients will reveal lymphopenia, leukopenia, anergy, reversed T helper to supressor cell ratio (less than 1.0), and a polyclonal hypergammaglobulinemia.

Other illnesses which may be related by a common etiology to the AIDS agent but which do not fulfill the clinical definition of AIDS include an unexplained lymphadenopathy syndrome, a diarrheal wasting syndrome, and autoimmune states including autoimmune thrombocytopenic purpura and hemolytic anemia. With the aid of serologic tests for identification of HTLV-III/LAV, we have now recognized that infection with this virus is associated with a broad clinical spectrum of diseases, of which AIDS only represents a more severe and fatal form of infection. Prospective cohort studies of populations at risk for AIDS will eventually establish the natural history and implications of the various immunologic abnormalities seen in other patients infected with HTLV-III/LAV.

Etiology

The finding of a profound and thus far irreversible cellular defect resulting in the depletion of T4 or T helper lymphocytes suggested to investigators that a lymphotropic virus with an affinity for the T helper lymphocyte may be involved in causing AIDS. The resulting investigations eventually culminated in the recovery of an unusual retrovirus from a patient with AIDS-related lymphadenopathy syndrome in May 1983 by Montagnier and colleagues at the Pasteur Institute *(3)*. This virus was named lymphadenopathy-associated virus (LAV) and it could be propagated *in vitro* in cultures of T lymphocytes which had been activated by interleukin-2, thus demonstrating its tropism for T lymphocytes. In May 1984, Gallo and colleagues reported the detection, isolation, and production of a group of closely related cytopathic retroviruses referred to as human T-cell lymphotropic viruses (HTLV-III) from lymphocytes derived from patients with AIDS and pre-AIDS *(4)*. These retroviruses are RNA viruses which contain a reverse transcriptase which produces a DNA copy of their viral genome. This DNA copy integrates into the genome of the host cell, and in the cases of HTLV-I and II, the viruses induce T-cell proliferation resulting in T-cell leukemia or lymphoma. In AIDS, the retrovirus preferentially infects the T helper cell population eventually causing cytolysis and thus T helper cell depletion, and consequently, immunosuppression of the cell-mediated immune system as described above.

As indicated in the first reports, this retrovirus was isolated from 18 to 21 patients with lymphadenopathy, from three to four women who were mothers of children with AIDS, from 26 of 72 AIDS patients, and from only one of 137 control patients. This one control patient later went on to develop AIDS. Antibodies to these viruses have been found in 88% of pre-AIDS patients, in 92% of AIDS patients, and in less than 1% of the control population in selected studies.

Serologic studies utilizing an enzyme-linked immunosorbent assay (ELISA) have provided a unique insight into the rapid propagation and transmission of this virus. In a recent study *(10)*, antibody to LAV in serum from homosexual men attending a sexually transmitted diseases clinic in San Francisco was found in only 1% of the samples in 1978, 25% in 1980, and 65% in 1984. Antibody was present in 55% of the above men tested in 1984 who had no symptoms or clinical signs of AIDS or AIDS-related conditions. Similarly, in New York City where the AIDS cases among intravenous drug abusers are concentrated, 75 out of 86 (87%) recent heavy intravenous drug users without AIDS had antibody to LAV. Among hemophiliacs 18 (82%) of 22 had antibody to LAV present. Similar studies have also demonstrated serologic evidence of infection by this virus in European and Zairian AIDS patients. In one study in Kinshasa, Zaire, 94% of 80 AIDS patients were found to be seropositive for HTLV-III/LAV, whereas less than 30% of the general population were seropositive *(11)*.

In vitro assays have demonstrated that HTLV-III/LAV is cytopathic and preferentially tropic for the T4

or T helper lymphocyte subset which are the cells most severely affected in AIDS *(9)*. Most recently, HTLV-III/LAV has been shown to be transmissible from mother to fetus during pregnancy and through blood product transfusion *(12, 13)*. In both instances infection and the later development of AIDS occurred in the absence of other known microbial pathogens. In summary, these studies clearly provide convincing evidence that HTLV-III/LAV is the etiologic agent of AIDS. However, they also demonstrate that exposure to the virus is much more common than AIDS itself among populations with increased incidence of the disease. Indeed, if AIDS were to follow the pattern of other infectious diseases, host response to infection would be expected to range from subclinical to severe. Milder disease states than AIDS have been suspected since the reported frequency of lymphadenopathy and immunologic abnormalities often associated with AIDS have also been reported in patients at risk for AIDS. Seroepidemiological studies have demonstrated that HTLV-III is associated with an asymptomatic carrier state, with a mildly symptomatic state with transient immunologic abnormalities, with a chronic lymphadenopathy state, and with other malignancies in addition to AIDS. Identification of these patients is extremely important since HTLV-III/LAV infection is frequently transmitted by asymptomatic carriers. In one study, the annual incidence of developing AIDS in seropositive homosexual men was estimated at 6.9% *(14)*. If we extrapolate the prevalence rate of HTLV-III infection from the above limited studies to the entire high risk population, an extremely large number of individuals have already been exposed to HTLV of which a definite, but unknown number will progress to AIDS.

Prospective studies of the natural history of AIDS using the serologic and virologic markers of HTLV-III/LAV will, it is hoped, determine which factors are responsible for host response to infection. In these studies genetic susceptibility, the site of inoculation and viral titer of inoculation, coinfection with other pathogens, immunologic status prior to and during infection, and virulence factors present within the genome of HTLV/LAV, a rather heterogeneous group of retroviruses, need to be examined. In studies in tropical and subtropical regions of the world the transmission of this virus should be examined carefully since many of the patients with AIDS lack other recognized risk factors for infections. The high degree of heterosexual activity in AIDS patients in the tropics as compared to developed countries may represent unique susceptibility factors which may be genetic, virological, or cultural, or may represent a predisposed, altered immunological status at the time of infection due to exposure to other immunosuppressive diseases such as viral infections and chronic parasitic infections common in tropical countries. Early studies suggest that coinfection or prior immunological alteration may result in accumulation of effects which are additively or synergistically effective in activating T lymphocytes required for infection and continued viral replication of HTVL/LAV. These immunological perturbations need to be assessed and studies of the risk of heterosexual transmission in tropical countries will be required to further explain these epidemiological differences.

Treatment

The treatment of patients with AIDS has been unrewarding since the patients are often infected with multiple opportunistic infections for which no therapy may be available. Even if initial treatment is successful in controlling an opportunistic infection or in altering the progression of Kaposi's sarcoma, the immunological defect is persistent. Consequently, the patient frequently has recurrences of the same opportunistic infection or succumbs to a different opportunistic infection. Guidelines for therapy consist of aggressive specific therapy for each opportunistic infection and avoidance of any further immunosuppressive drugs. Immunomodulators such as interferon, interleukin-2, and thymus transplantation, and bone marrow transplant have all been tried but without significant success. Since the identification of HTLV/LAV as the most likely candidate etiologic agent of AIDS, drugs are being rapidly screened *in vitro* for effectiveness against this retrovirus. One drug, surmin, has been shown to inhibit the reverse transcriptase of HTLV-III/LAV *in vitro* and human studies are presently being evaluated. However, until a vaccine is developed or a successful treatment is identified, it is likely that the number of cases of AIDS and related diseases will continue to increase in epidemic numbers throughout the world.

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(Source: Thomas C. Quinn, M.D.; Senior Investigator, National Institute of Allergy and Infectious Diseases, National Institutes of Health, U.S.A.)

Editorial Note

Dr. Quinn's report updates previous articles published in the *Epidemiological Bulletin* 4(2 and 5), 1983 and succinctly summarizes current knowledge about AIDS. The Centers for Disease Control recently published additional recommendations for prevention of transmission *(MMWR* 34(1), 1985). Until satisfactory treatment or preventive measures are developed, nothing further can be recommended.

AIDS remains a major concern for researchers and public health workers in developed countries in Europe and North America. As more information is collected, AIDS may prove to be a bigger problem in developing countries than heretofore suspected. Early evidence from African studies indicates that the epidemiology of AIDS may be quite different especially with respect to transmission mechanisms. In some situations heterosexual transmission may predominate.

PAHO requests all countries in the Americas to report AIDS cases and deaths every six months for trend analysis. Summaries of reported data are available from PAHO's Epidemiology Unit.

Tuberculosis in Chile

Chile's tuberculosis control program was evaluated at a seminar during the XVII annual course on the epidemiology and control of tuberculosis held in Santiago in August 1984. During the seminar, consolidated national data up to 1983 were presented and the operational aspects of the program in the health services of two areas of the Santiago metropolitan region were examined in detail. Some of this information is presented below for analysis of the tuberculosis situation in Chile.

Mortality

The tuberculosis mortality rates from 1964 to 1983, given in Table 1, reveal a gradual decline, from 45.8 to 8.1 deaths per 100,000 population, equivalent to a reduction of about 8.7% a year.

Figure 1 shows the mortality curves by age group in 1966 and 1983. A comparison of the age structures of the mortalities in 1983 and 1966 indicates that the decline of mortality was much sharper in the younger

groups, in which it dropped more than 90%. This was partly an effect of the different measures taken under the program. In addition to the reduction of the risk of death of patients afforded by proper diagnosis and treatment, the enhancement of the individual's defenses by vaccination and, above all, the reduction of the risk of infection resulting from fewer sources of contagion in the community have been extremely important for young people. In older age groups, only a small proportion of the cases are due to primary tuberculosis or exogenous reinfection; the majority are produced by the multiplication of bacilli acquired many years earlier. Hence reducing the risk of infection in this group has less impact. Consequently, the average age of patients and the average age at death due to the disease rise as the tuberculosis problem decreases in the community.

Despite the sharp reduction observed in recent years, mortality from reported cases of tuberculosis may still be considered high. However, it should be noted that statistics in Chile include deaths from late effects of tuberculosis (ICD-137), which are not included in the figures of other countries. Moreover, the administration of short-duration, highly effective treatments throughout the country warrants the expectation that this downtrend will hold and even accelerate.

Morbidity

Figure 1 also illustrates the incidence, as reported in 1981, for all forms of tuberculosis by age group. It can be seen that the higher rates are no longer among young adults, as they usually are in areas where the tuberculosis problem is greatest, but the curve still rises most sharply between the ages of 10 and 20 years.

Table 1. Annual mortality rates from tuberculosis[a] in Chile, 1964-1983.

Year	Rate[b]	Year	Rate[b]	Year	Rate[b]	Year	Rate[b]
1964	45.8	1969	30.8	1974	19.5	1979	15.4
1965	43.4	1970	27.4	1975	18.9	1980	12.2
1966	40.9	1971	23.9	1976	19.2	1981	9.4
1967	37.8	1972	24.7	1977	18.4	1982	8.6
1968	34.9	1973	20.8	1978	16.0	1983	8.1

[a]Codes 010-018 and 137 of the *International Classification of Diseases. 1975 Revision*. Scientific Publication No. 353. Washington, D.C., Pan American Health Organization, 1978.
[b]Deaths per 100,000 inhabitants.

Table 2 shows the distribution of 6,941 tuberculosis cases reported in 1982, by site and mode of diagnostic confirmation. A high proportion of the pulmonary cases (77.5%) were confirmed by bacilloscopy; 87.2% of the cases at this site were confirmed.

The proportion of confirmed cases of extrapulmonary forms is high for a developing country and betokens diagnosis of good quality. In turn, the total proportion of cases that were of extrapulmonary form (22.5%) detected in a country in which there is active case-finding of pulmonary cases by bacilloscopy suggests good coverage by services capable of diagnosing these sites.

The 4,168 smear-positive cases are equivalent to about 36 cases per 100,000 inhabitants, which amounts to an annual risk of infection of 0.6 to 0.7% (based on an annual incidence of 50-60 smear-positive cases per 100,000 inhabitants for every 1% of annual risk of infection). In 1976, 6,185 smear-positive cases (59 per 100,000 inhabitants) were reported, which was at the peak of the curve in the last decade. Since that year, despite a steady rise in the number of sputum smears done for diagnosis, which increased 21% between 1979 and 1983, the rate of pulmonary tuberculosis cases with positive smears has been decreasing about 6% per year.

One consequence of this and of the decline in tubercu-

Figure 1. Age-specific death rates for tuberculosis in 1966 and 1983 and incidence rate as reported in 1981, in Chile.

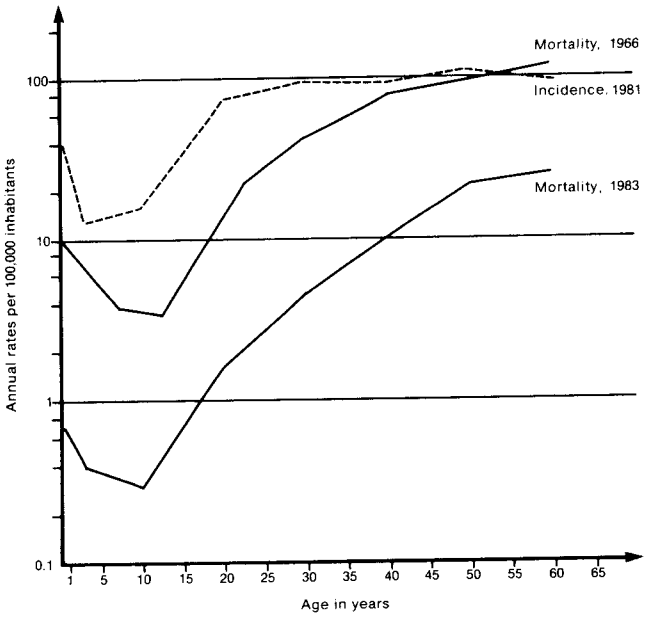

Table 2. Distribution of 6,941 reported cases of tuberculosis by site and mode of diagnostic confirmation in Chile, 1982.

Site	Total cases	Confirmed by: Bacilloscopy No.	Bacilloscopy %	Culture No.	Culture %	Biopsy No.	Biopsy %	Unconfirmed No.	Unconfirmed %
Lungs	5,377	4,168	77.5	462	8.6	59	1.1	688	12.8
Meninges	76	10	13.2	15	19.1	1	1.3	50	65.8
Others	1,488	225	15.1	174	11.7	697	46.8	392	26.3

losis in the community is that fewer cases are detected by bacilloscopy among persons with respiratory symptoms coming to health facilities. The proportion of positive sputum smears in the country as a whole was 10.2% in 1973, 4.5% in 1979, and 2.8% in 1983. Another indicator of the quality of the program is bacterial resistance to drugs in individuals with no history of treatment (primary resistance), which decreased from 12.8% in 1970 to 7.9% in 1981, as a result of greater adherence to treatment and better therapeutic regimens.

Unfortunately, no data were available on the age distribution of confirmed cases for a comparative analysis of 1982 with earlier years; rates in the 15-19, 20-24, and 25-29 age groups convey the trend of tuberculosis in that population and, resulting as they do from recent infections, generally parallel the trend of the risk of infection in the community.

Conclusions

According to the available information, Chile's tuberculosis control program has considerably improved the values of the epidemiological indicators for that disease. This is attributed to active case-finding and effective treatment, low dropout rates, and integration of the activities into a health structure with extensive population coverage and the resources needed for basic laboratory procedures and for treatment of all detected cases free of charge.

(Source: Maternal and Child Health Program, PAHO, based on: Ministry of Health of Chile. Epidemiología de la Tuberculosis en Chile. *Boletín de Vigilancia Epidemiológica* 11(8), 1984.)

Diseases Subject to the International Health Regulations

Cholera, yellow fever, and plague cases and deaths reported in the Region of the Americas up to 31 March 1985.

Country and administrative subdivision	Cholera Cases	Yellow fever Cases	Yellow fever Deaths	Plague[a] Cases
ECUADOR	–	–	–	*3*
Loja	–	–	–	3

[a]Note: Since the publication of the last issue of the *Epidemiological Bulletin* in 1984 (Vol. 5, No. 6), *Brazil* reported an additional 10 cases of plague, 5 in the State of Ceará and 5 in the State of Bahía, for a partial total of 36 cases in 1984. *Peru* reported an additional 27 cases of plague, all in the Department of Piura, for a partial total of 415 cases in 1984.

Calendar of Courses and Reports on Meetings

National Tuberculosis Courses, 1985

The following courses on the epidemiology and control of tuberculosis, organized by the Governments with PAHO collaboration, will be offered in 1985:

Venezuela: 28 May - 30 June
Person in charge: Dr. Manuel Adrianza, Jefe
Departamento de Tuberculosis y Enfermedades Pulmonares
Ministerio de Sanidad y Asistencia Social
El Algodonal-Antímano
Caracas 1100

Mexico: 5 - 6 September
Person in charge: Dr. Calderón Jaimes
Director General de Medicina Preventiva
Masaryk 490
México 5, D.F.

Chile: 5 - 31 August
Person in charge: Dr. Edgardo Carrasco, Director
Instituto Nacional de Enfermedades Respiratorias y Cirugía Toráxica
Casilla de Correos 9634
Santiago

Cuba: 7 October - 1 November
Person in charge: Dr. Rodolfo Rodríguez Cruz, Director
Departamento de Epidemiología
Ministerio de Salud
La Habana

Argentina: 10 October - 1 November
Person in charge: Dr. Eduardo Balestrino, Director
Instituto Nacional de Epidemiología
Casilla de Correos 106
Santa Fe 3000

Brazil: 5 weeks, October - November
Person in charge: Dr. Germano Gerhardt, Director
División Nacional de Pneumología Sanitaria
Rua do Resende 128
Rio de Janeiro

The courses on the bacteriology of tuberculosis for professionals, listed below, will also be offered:

Mexico: 1 - 30 August
Person in charge: Dr. Lamberto Blancarte
Laboratorio Referencia Nacional Tuberculosis
Lago Pátzcuaro 55, Col. Anahuac
Delegación Miguel Hidalgo
México, D.F. 11320

Canada: 5 August - 13 September
Person in charge: Dr. Adalbert Laszlo
Laboratory Centers for Disease Control (LCDC)
Tunney's Pasture
Ottawa, Ontario, K1A 0L2

Summer Courses in Epidemiology in the United States

The Johns Hopkins University School of Hygiene and Public Health will sponsor the third annual Graduate Summer Program in Epidemiology, to be conducted from 24 June to 13 July 1985. The program includes design and conduct of clinical trials, epidemiological methods for evaluating health services, epidemiological and preventive aspects of cancer, epidemiology of infectious diseases, introduction to biostatistics, methods in epidemiology, occupational epidemiology, environmental epidemiology, and principles of epidemiology. Proficiency in the English language is required.

Further information is available from: Mr. Steven G. Warm, Program Coordinator, Graduate Summer Program in Epidemiology, School of Hygiene and Public Health, The Johns Hopkins University, 615 North Wolfe Street, Baltimore, Maryland 21205, U.S.A.

The School of Public Health of the University of Minnesota will offer its 20th summer session for graduates from 23 June to 13 July 1985. The program will include: fundamentals of epidemiology and biostatistics, clinical epidemiology, epidemiology of infectious diseases, hospital epidemiology and infection control, epidemiology of cancer, epidemiology of cardiovascular diseases, environmental and occupational epidemiology, and advanced statistics courses. Addi-

tional advanced courses which will be offered may include: surveillance and control of communicable diseases, epidemiology and health policy, diseases due to drugs, epidemiology of injuries, analysis of categorical data and statistical regression, nutritional epidemiology, epidemiology of alcoholism, clinical trials, international epidemiology, and epidemiology of aging. A sound knowledge of English is required.

Further information is available from: Dr. Leonard M. Schuman, Director, Graduate Summer Session in Epidemiology, School of Public Health, P.O. Box 197, Mayo Memorial Building, University of Minnesota, Minneapolis, Minnesota 55455, U.S.A.

The University of Massachusetts at Amherst and The New England Epidemiology Institute are sponsoring a course that will be offered from 28 July to 16 August 1985. The course will deal with the theory and practice of epidemiology; biostatistics; multivariate methods in epidemiological analysis; the epidemiology of cancer; reproductive, clinical, environmental, and occupational diseases; and the use of microcomputers. Knowledge of English is essential.

Further information is available from: The New England Epidemiology Institute, P.O. Box 57, Chestnut Hill, Massachusetts 02167, U.S.A.

Workshop on the Prevention and Care of Motor Vehicle Injuries in the Caribbean

In accordance with Resolution No. 20 of the 8th Meeting of the Conference of Ministers Responsible for Health in the Caribbean, a Workshop on the Prevention and Care of Motor Vehicle Injuries was held in Bridgetown, Barbados, from 12 to 15 June 1984. The workshop was sponsored by PAHO and the WHO Global Program for Accident Prevention, in collaboration with the Caribbean Community (CARICOM) and the Government of Barbados.

Twenty-one delegates from the Bahamas, Barbados, British Virgin Islands, Dominica, Grenada, Guyana, Haiti, Jamaica, St. Kitts/Nevis and Suriname attended the workshop, including epidemiologists, police and transport officials, and administrators. Consultants from the WHO Global Program for Accident Prevention and the PAHO Regional Program for Traffic Accident Prevention also attended.

The workshop participants adopted a standard form for data collection by the police at the scene of the accident. This form was developed from input from the police, health sector, and transport representation.

Among the conclusions reached by the group are the following:

- Road crashes and their toll of deaths, casualties and disabilities have become a major public health problem in the Caribbean, striking young people in the age group 15 to 25 years in particular.
- The improvement of road safety needs a political commitment at the highest level in order to ensure that protection of the transport system users is not subordinated to economic interests. This commitment should be long term, comprehensive, and consistent.
- The very strong economic impact of the road accidents including direct costs (damage to vehicles, roads and property, etc.) and indirect costs (especially those due to the loss of production by the victims). To illustrate the economic impact in just the health sector, the data reveal that in 1982 the average length of hospitalization of accident victims in Barbados was 18 days, and the average cost per day per patient was $145. The 5,424 hospital days in 1981 for traffic accident victims can thus be estimated to have cost $800,000.
- Without adequate collection, analysis and interpretation of accident data, it is difficult to establish efficient countermeasures, strategies and evaluation systems. It was agreed that the police records would be utilized as the data starting point.
- Use of alcohol and/or drugs is a significant cause of serious traffic injuries and fatalities, probably accounting for 40 to 60% of all fatalities. In all the participating countries but Suriname appropriate legislation to facilitate the testing of drivers for alcohol is lacking.
- The widespread use of seat belts and crash helmets can reduce car occupants' deaths and hospital admissions by 50 to 60%, according to the experience in many countries outside the Caribbean.
- Training courses on traffic accidents are needed for law enforcement and health professionals.
- Current legislation is generally inadequate to assure effective enforcement of traffic regulations.

The group recommended the following for action in the near term:

- Each country should establish a national road safety committee with executive power and appropriate funding to address the problem of road accidents. This agency should develop and implement policies in the field of transport safety and coordinate the activities in the health and transport sectors; it should have linkages with the law enforcement authorities.

- The Caribbean Epidemiological Centre (CAREC) should be designated the coordinating office for epidemiological, training and research activities of traffic accidents in the Caribbean. It should receive strong support from PAHO and WHO headquarters.
- National reporting systems should be established a) to monitor the overall national accident situation; b) to monitor changes over time; c) to provide information to the policymaking sectors; and d) to evaluate the effectiveness of the countermeasures.
- In relation to alcohol and/or drugs:

1. Clear, comprehensive laws should be enacted to make driving under the influence of such substances a punishable offense. A blood alcohol level of 0.08% has been adopted by many countries in the world to define "impairment" and is recommended for use in the Caribbean.
2. New legislation should specify that blood alcohol tests be performed on all persons in accidents where injury or death has occurred, permitting the analysis of information on alcohol in traffic fatalities.
3. Public awareness and involvement in the drunk driving problem should be increased through use of the media and existing community groups.
4. There must be increased certainty, severity and rapidity of punishment for drunk driving.

- The fitting of vehicles with lap and shoulder seat belts and their use should be made mandatory as soon as possible and certainly within the next three years.
- The mandatory use of crash helmets should be introduced in the countries as soon as possible. The Bahamas and Suriname have demonstrated effective enforcement even with the rental of motorcycles by tourists.
- PAHO and individual countries in the Caribbean should develop short-term training courses in traffic medicine, crash investigation and injury control. To supplement such courses appropriate educational material should be prepared for use in this area.
- Limitations for driving certain vehicles should be adopted. For passenger-carrying vehicles, e.g., large buses and large, heavy commercial vehicles, the minimum licensure age should be 21. In addition, 3 years of driving experience and more frequent medical evaluation after age 60 should be required. For motorcycles above 250cc the minimum licensure age should be 21.
- The development of national systems of emergency medical care should be promoted to assure the care, transport and treatment of the injured persons in accordance with the resolutions adopted by the PAHO Seminar on Emergency Medical Services held in Washington in September 1983.
- Limiting of the number of dangerous vehicles on the road should be encouraged through fiscal measures.

For action over the long term the group recommended the following:

- Information on vehicle design defects should be circulated throughout the Caribbean.
- Annual and spot inspection of vehicles for maintenance defects, covering types of vehicles, brakes, steering and lighting in particular, should be encouraged.
- Thought should be given to the use of speed governors on buses and other public service vehicles and the fitting of underrun guards on trucks should be introduced.
- Uniform specifications for the main safety-related features of new vehicles should be required. Standards adopted from the industrialized countries should be applied to laminated windscreens, steering wheels, head restraints, seat belts and anti-burst door locks as soon as possible.
- The mandatory use of headlights by motorcycles at all times of the day should be introduced soon.
- More effort should be made to identify roadside hazards. Better identification of black spots is required and to this end closer liaison between police and transport authorities is needed.
- In-person renewals for driver's licenses at 5-year intervals should be established. Vision screening by the licensing agency as well as completion of a brief self-reporting form on the presence or absence of medical conditions that have proven to be an undue safety risk, e.g., grandmal seizure disorders, should be required.
- The successful experiences of a number of countries with demerit point systems in licensing should be shared with a view toward regional adoption.

Orientation Meeting on Health Care of the Elderly

An Orientation Meeting on Health Care of the Elderly in Latin American Countries was held at the headquarters of the Pan American Health Organization in Washington, D.C., from 15 to 19 October 1984.

Scientific, technological and administrative progress has brought about great increases in the population of 60 years and older in almost every region of the world. In Latin America, this population group will grow from

23.3 million in 1980 to 41.0 million in the year 2000 and to 78.2 million in 2030. Although these figures average out at 6.4%, 7.2% and 9.7%, respectively, of the population at large, these levels of aged population were reached by 1980 by some countries such as Uruguay, with 14.8%; Argentina, with 12.7%; Barbados, with 12.5%; and Cuba with 10.4%.

This relative and absolute increase of the elderly population has made it necessary for many countries to expand their health care systems and adapt them to meet the demands of this social group. These changes must necessarily be connected with the social, economic and cultural development of those countries and even with their policies on aging.

The purpose of the Washington meeting was to stimulate health planners and administrators of the countries participating in the first collaborative study on the needs of the aged and to inform them on intersectoral planning for the health of the elderly, one of the four specially targeted groups of the Plan of Action for the Implementation of Regional Strategies for the attainment of health for all by the year 2000.

The meeting participants heard descriptions of the experiences of some developed countries and had the opportunity to evaluate them as well as to identify critical aspects of policies related to care for the elderly. Demographic, scientific, economic, social, and psychological frameworks were provided. Presentations were made and discussed on aspects of public information, personnel training, alternatives in social security, the importance of self-care, the role of social health services with special emphasis on primary care and family and community participation, the role of nongovernmental organizations in the promotion of appropriate policies and collaboration with governments and initiatives for technical cooperation with specialized agencies and other countries.

The meeting was attended by 25 experts from Belgium, Canada, Costa Rica, Denmark, Mexico, the Netherlands, the United Kingdom, the United States of America and Venezuela, who shared their experience with delegates from Argentina, Barbados, Costa Rica, Chile, El Salvador, Guyana, Honduras, Jamaica and Uruguay. Other participants were representatives of the United Nations Center for Social Development and Humanitarian Affairs in Austria and of the International Center for Social Gerontology in France.

This meeting was cosponsored by the Global Program for Health of the Elderly of the World Health Organization and the International Program on the Elderly of the Kellogg Foundation.

Workshop on Trends in Health Services Research

This workshop was held in Cocoyoc, Mexico, from 16 to 20 July 1984 to analyze the findings of a study conducted in 15 Latin American and Caribbean countries. Its participants were the research workers responsible for collecting and analyzing the data on the countries included in the study.

On the basis of the results of analysis of 2,899 studies of health services done in the countries between 1974 and 1983, the situation was discussed in relation to the following major subjects:

- Research in health needs from the viewpoint of the delivery of services. Trends and gaps in research to detect the priority needs of population groups in different economic and social circumstances in urban and rural areas.
- Research on the organization and functioning of health services, including their accessibility and use, their technological appropriateness, and the utilization of human, material, and financial resources.
- Methodological aspects of health services research with special emphasis on the contribution of the different disciplines and on the difficulties of applying the theoretical principles in practice.
- Strategies for the development of health services research with respect to the foregoing subjects and in accordance with policies for the mobilization of national resources and intercountry cooperation.

The findings of the study are presented in a document that may be obtained from the Health Services Delivery Program, PAHO, at the Organization's headquarters in Washington, D.C.

Interagency Technical Meeting on Child Survival Programs, UNICEF-PAHO

In the framework of the Memorandum of Understanding signed by the Regional Director of UNICEF and the Director of PAHO in September 1983, a UNICEF-PAHO interagency technical coordination meeting on child survival programs was held in Bogotá from 15 to 26 October 1984.

The purposes of the meeting were to exchange information on the development of programs in the Region for the control of acute respiratory infections, diarrheal diseases, and child growth and development and to discuss priorities and strategies for interagency coordination in support of those country programs.

The two agencies agreed that, since the signing of the Memorandum, distinct progress had been made in the coordination of their activities. However, it was recognized that still greater emphasis was needed on the joint participation of the two organizations with the countries in analyzing the situation in regard to diagnosis as a first and basic step towards the joint programming of technical cooperation.

As part of the collaboration between UNICEF and PAHO in the Region, priority activities were established in connection with acute respiratory infections, diarrheal diseases, and child growth and development, and it was agreed to hold another interagency technical meeting on child survival programs in Washington, D.C. in May 1985.

First Mexican Congress on Epidemiology

This Congress, sponsored by the Mexican Association of Epidemiologists and the General Department of Epidemiology of the Ministry of Public Health and Welfare with the assistance of PAHO, was held in San Luis Potosí from 3 to 8 December 1984. It focused on the topic "Uses and Prospects of Epidemiology: A Mexican Approach."

In the presentations and discussions the role of epidemiology in the analysis of a health situation, in the planning and evaluation of services, and in the monitoring and control of diseases, and the impact of these approaches on the development of services, manpower training, and epidemiological research were examined.

Publications[1]

Epidemiology and Control of Falciparum Malaria in the Americas. PAHO Scientific Publication No. 471. 1984. 46 pages. ISBN 92 75 11471 4. US$6.00. Published also in Spanish (1984) as *Epidemiología y control de la malaria causada por* Plasmodium falciparum *en las Américas*. ISBN 92 75 31471 3.

This publication resulted from a workshop held in Albuquerque, New Mexico, 26 to 29 October 1982 and was sponsored by the University of New Mexico School of Medicine in cooperation with the Pan American Health Organization. It was supported by the Special Program for Research and Training in Tropical Diseases (UNDP/WORLD BANK/WHO), and the United States Agency for International Development.

The objectives of the workshop were to review the status of falciparum malaria in different parts of the Region of the Americas, to identify constraints to effective control of the disease, to review current knowledge regarding drug resistance in falciparum malaria, and to identify appropriate measures and research projects that would improve the epidemiological assessment and control of falciparum malaria in the various geographic areas.

Recommendations dealt with various issues grouped under the headings of epidemiology and epidemiological surveillance; monitoring of the drug susceptibility of *P. falciparum;* social behavior and attitudes; antimalarial drugs; and malaria control.

Las drogas, el conductor y la seguridad en el tránsito. PAHO Scientific Publication No. 475. 1984. 54 pages. ISBN 92 75 31475 6. US$6.00.

PAHO has just published a Spanish edition of WHO Offset Publication No. 78, the product of a meeting of experts convened to make recommendations on the problem of drug use in relation to traffic accidents. The publication is of timely and practical use to countries that for several years have been enacting legislation on drugs and driving but have lacked proper standardized instruments for evaluating the effectiveness of that legislation.

This work is being published at a time when a scientific approach is being taken regarding the problem of the occurrence and severity of traffic accidents and when the predominant fatalism toward their causes is being abandoned.

[1]Available at the listed price from the Distribution and Sales Service, PAHO, 525 Twenty-third Street, N.W., Washington, D.C. 20037.

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