

Perinatal Transmission of the Human Immunodeficiency Virus

JEAN W. PAPE¹ & WARREN JOHNSON, JR.¹



Vertical transmission of human immunodeficiency virus (HIV) from an infected mother to her fetus or infant can occur in utero and probably during labor and delivery. Transmission via breast milk has also been documented. Because of limitations of conventional HIV testing in infants, it is difficult to determine the rate of transmission from an infected mother to her fetus or infant, but it is probably between 20% and 60%, depending on the mother's health status. Perinatal HIV infection is a significant problem particularly in "Pattern II" countries, where HIV is spread primarily by heterosexual contact. In "Pattern I" countries, where HIV predominantly affects homosexual and bisexual men, children are infected by mothers who acquired the infection through I.V. drug abuse or sexual contact with an infected partner.

Two years after the first adult patients with the acquired immunodeficiency syndrome (AIDS) were reported, cases of a similar syndrome in infants and children were described (1-6). Since these early reports, the number of cases of pediatric AIDS has continued to increase worldwide at the same rate as that of AIDS cases in adults (7, 8). However, underreporting of AIDS cases probably occurs more frequently among infants and children than among adults because the clinical presentation of human immunodeficiency virus (HIV) infection is more subtle and serologic tests are less reliable in this population.

Like adults, children can acquire AIDS by transfusion of infected blood or blood products (9-11); as indicated in Table 1, up to 30% of the infected children may acquire their infections by this route (7, 8, 12). Another potential mode of HIV transmission in developing countries is

by "medical" injections with contaminated syringes or needles (12, 13). However, by far the most important risk factor for AIDS in children is vertical transmission from an infected mother to her fetus or infant (13-19). Casual transmission of HIV between adults and children has not been documented, even in crowded housing with unsanitary conditions where there have been two or more infected people per family (14, 15).

VERTICAL HIV TRANSMISSION

Vertical transmission of HIV occurs transplacentally during pregnancy and probably during labor and delivery as a result of contact with contaminated blood or body fluids. In addition, postpartum transmission via infected breast milk has been documented.

Because the transmission mechanisms have not been fully elucidated and serologic methods commonly used to diagnose HIV infection in infants are unreliable, it is difficult to determine the precise rate of transmission. Mothers infected

¹Division of International Medicine, Cornell University Medical College, 1300 York Avenue, New York, New York 10021, USA.

Table 1. Known and suspected routes of pediatric HIV transmission, showing reported percentages of transmission by those routes in developed and developing countries.

| Route of transmission | Developed countries | Developing countries |
|--|---------------------|----------------------|
| Vertical (perinatal) transmission ^a | 70-80% | 80-100% |
| Transfusions | 20-30% | 0-20% |
| "Medical" injections | Not reported | Suspected |
| Casual transmission | Not reported | Not reported |

^aIncluding transmission of HIV during delivery and by infected breast milk.

with HIV produce IgG antibodies that are transferred to the fetus transplacentally, resulting in cord blood being positive for antibody when tested by enzyme-linked immunosorbent assay (ELISA) or the Western blot (WB) technique.

As many as 25% of the infants seropositive at birth will continue to have maternal antibody beyond one year of age, while a similar percentage of those infected may not be identified by ELISA anti-HIV screening alone (20). Because neonates are not fully immunocompetent, they produce a less vigorous antibody response to HIV infection (21). Indeed, fetal synthesis of specific IgM antibody is not a useful marker of infection in utero because it is short-lived and because of nonspecific binding of IgM (22).

Demonstration of virus by the method of *in situ* hybridization is promising but is technically difficult and not always successful (16). Viral culture is the definitive method for confirming infection in the neonate. For these reasons, there is a wide range in the apparent rate of transmission from an infected mother to her fetus or infant, available studies having reported transmission rates that range from 0% to 70% (4-6, 23-37). The true transmission rate is probably between 20% and 60%, depending on the health status of the mother. In general, the transmission rate appears higher among women with more advanced disease (6, 20, 32).

Intrauterine Transmission

A substantial number of reports support the occurrence of intrauterine transmission (1-3, 38, 39). Intrauterine HIV infection selectively affecting one monozygotic twin and not the other has also been reported (40). The exact period at which HIV infection of the fetus occurs is not yet known. However, HIV has been detected in fetal tissues at 15 and 20 weeks of gestation (41, 42). In addition, studies of AIDS patients' sex partners have shown that seropositive women have twice as many miscarriages as seronegative ones, with most of these miscarriages occurring during the first trimester of pregnancy (43). In utero HIV infection could also account for the rare occurrence of a dysmorphic syndrome in children born to seropositive mothers (44).

Transmission during Labor and Delivery

HIV has been isolated from cervical secretions (45, 46), which suggests that they could be a source of infection. Transmission by this route is commonly seen in other diseases caused by vertically transmitted agents such as cytomegalovirus and herpes simplex. To reduce this risk, it has been suggested that seropositive women should be delivered by cesarean section (26). However, there is no convincing evidence that cesarean section reduces the risk of HIV transmission to newborns.

Transmission via Breast Milk

HIV is present at high titers in cell-free breast milk and in the cellular fraction of colostrum (47). Transmission of another retrovirus, human T-cell leukemia virus type I (HTLV-I), via breast milk has been reported (48). In addition, five cases of HIV transmission by infected breast milk have recently been documented (49-52). In all cases the nursing mother was either symptomatic or recently infected by transfusion with HIV-contaminated blood.

Breast-feeding during the period of maternal seroconversion may carry more risk of transmission (50). However, in the usual situation of an infected mother breast-feeding her infant, the risk of transmission appears to be low (53). Forty-eight infants less than one year of age became HIV-seronegative or remained seronegative while being breast-fed by HIV-seropositive mothers. These children who remained seronegative or became seronegative were breast-fed for at least as long a period as those who remained seropositive.

In industrialized countries it may be appropriate to follow U.S. Centers for Disease Control guidelines that recommend that infected women stop breast-feeding their infants. However, in developing countries a major cause of infant death is diarrheal disease, which can be directly linked to artificial feeding. Until more information is available, infected women from impoverished areas of the world are better advised to continue breast-feeding.

THE IMPORTANCE OF PERINATAL INFECTIONS

The actual numbers of pediatric AIDS cases and of HIV-infected children is unknown. However, an indirect way to determine the importance of pediatric AIDS

is to analyze the pattern of transmission of HIV in heterosexual adults and particularly in women of childbearing age. In general, the situation in most countries corresponds to one of two recognized patterns.

Pattern I

In North America, Western Europe, parts of South America, Australia, and New Zealand, AIDS is primarily a disease of young homosexual and bisexual men. This is reflected by a large difference in the sex ratio (the male to female ratio is approximately 8:1 in Western Europe and 11.5:1 in the United States). These regions exhibit the "Pattern I" type of HIV distribution (54).

Under these circumstances, children are less likely to be infected. In the United States and Western Europe, respectively, only 1.5% and 2.5% of all AIDS cases occur among children under 13 years of age (7, 8). Underscoring this point, 70% of the children with AIDS in the United States and 68% of those with AIDS in Western Europe come from families in which the mother has AIDS or is infected with HIV.

It is also true that in the industrialized countries perinatal transmission usually occurs among women who belong to one of the following high-risk groups: intravenous drug abusers, women originally from regions where heterosexual transmission of HIV is common (Central Africa, the Caribbean), and women who have received a blood transfusion or who have an infected sex partner.

Actually, in Pattern I countries intravenous drug abuse has been the source of most AIDS cases contracted through heterosexual contact and the indirect source of most perinatally acquired AIDS cases. In the United States, women account for notably high percentages of the patients infected through intravenous drug abuse

and heterosexual contact. Specifically, while they account for only 8% of all AIDS cases in the United States, 19% of all cases acquired through intravenous drug abuse and 52% of those acquired by heterosexual contact have occurred in women. HIV transmission by these two routes is particularly important among black and Hispanic women, who account for 71% of all female AIDS cases. As a result of the large number of AIDS cases acquired in this manner by women in these minorities, 75% of all children with AIDS, 80% of those under five years of age, and 85% of all those infected perinatally are black or Hispanic youngsters.

HIV seroprevalence rates in the sexually active heterosexual population have direct consequences for perinatal infections. As could be expected, HIV seropositivity rates tend to be highest among risk groups living in geographic locations with the largest numbers of reported AIDS cases. As Table 2 indicates, seroprevalence rates among intravenous drug abusers have been found to range from 1% in Dallas, Texas, to 61% in New York City. Similarly, HIV seropositivity rates for female prostitutes in the United States have been found to vary from 0% to over 45%, with the highest rates occurring among prostitutes who are also intravenous drug abusers (55).

HIV seropositivity rates among women

of childbearing age tend to be highest in populations served by inner-city hospitals located in places reporting large numbers of AIDS cases. Hence, rates found among women of childbearing age served by inner-city hospitals in Massachusetts and New York were respectively 0.8% and 1.6%; rates were lower and comparable in both states (0.13%) among women using hospitals in nonmetropolitan areas (56, 57).

HIV seropositivity rates over 3% have been found among parturients in New York City. It is estimated that 1,620 to 4,800 HIV-infected infants are born each year in the United States (57), 900 in New York State alone. The seropositivity rate among newborns in New York State is 0.83%, while rates as high as 2.29% have been recorded in the Bronx, New York City (58).

Pattern II

In Pattern II regions, heterosexual contact with an infected person is the predominant mode of HIV transmission. Such regions include Central, East, and West Africa, as well as the Caribbean. The overall male to female ratio of AIDS cases in these regions is 1.5 to 1.

Women in Pattern II countries usually acquire the infection from infected heterosexual or bisexual men. However,

Table 2. HIV seroprevalence rates found among selected U.S. populations.

| Group | Place | % seropositive | Year(s) | Source |
|------------------------------|--|-------------------|-----------|--------|
| I.V. drug abusers | Dallas, Texas | 1 | 1987 | 57 |
| | New York City | 61 | 1986 | 57 |
| Prostitutes | Las Vegas, Nevada | 0 | 1986-1987 | 56 |
| | New Jersey | 45 | 1986-1987 | 56 |
| Women of childbearing age | Inner-city hospitals, Massachusetts | 0.8 | 1988 | 58 |
| | Inner-city hospitals, New York | 1.6-3 | 1988 | 58 |
| | New York State | 0.8 | 1988 | 59 |
| Newborns | Bronx, New York City | 2.3 | 1987 | 59 |

rapid risk-factor changes from bisexual contact to heterosexual contact have occurred in Haiti and other Caribbean countries, resulting in a doubling of the percentage of female AIDS patients within a five-year period (59-61). Indeed, while the roles of risk factors in Haiti such as bisexuality and receipt of blood transfusions have progressively decreased, the percentages of patients having a spouse with AIDS or admitting to prostitution have tripled within the same period.

This shift from a primarily bisexual mode of transmission to a heterosexual mode of transmission could occur in countries that now fit Pattern I, resulting in more women and children being infected. In Pattern II countries, blood transfusion is the second most important risk factor, particularly among women (59, 62).

In contrast to the picture in Pattern I countries, intravenous drug abuse is rarely reported in Africa and is only found among 1% of the Caribbean AIDS patients outside Bermuda and Puerto Rico, where intravenous drug abuse is important. The possible role of "medical" injections in the transmission of HIV by contaminated needles or syringes has been raised in Pattern II countries but is difficult to assess (12, 13).

As a result of the important role of heterosexual transmission in Pattern II countries, prostitutes are both the victims and the prime reservoir of HIV. However, the seropositivity rate among prostitutes varies according to their geographic location, socioeconomic status, and associated sexually transmitted diseases (59, 62-66). In Africa, HIV seropositivity among prostitutes is much higher in Central and East African countries (27-88%) than in West and North Africa (1-20%) (see Table 3).

Though prostitution plays a significant

Table 3. HIV seroprevalence rates among prostitutes of four Pattern II countries, as determined by ELISA with Western blot or radioimmunoassay confirmation.

| Country and region | % seropositive | Year |
|--------------------------------------|-------------------|------|
| Rwanda (Butare), East Africa | 88 | 1984 |
| Kenya (Nairobi), East Africa | 67 | 1985 |
| Zaire (Kinshasa), Central Africa | 27 | 1985 |
| Haiti (Port-au-Prince), Caribbean | 66 | 1987 |

role in the spread of HIV (67-69), the seroprevalence rate among apparently healthy women of childbearing age reveals that a surprisingly large proportion of those living in urban areas are infected with the virus (Table 4). Overall, 3% to 7% of the apparently healthy women in some parts of Africa and the Caribbean may be seropositive (59, 62, 70-74). These rates are much higher than those generally reported in the United States

Table 4. Seroprevalence of HIV among women of childbearing age in certain African, Caribbean, and North American localities, as indicated by ELISA with Western blot or radioimmunoassay confirmation.

| City/country and region | % seropositive | Year |
|--|-------------------|------|
| <i>Africa:</i> | | |
| Kinshasa, Zaire (Central Africa) | 5 | 1980 |
| Dar es Salaam, United Republic of Tanzania (East Africa) | 3.6 | 1986 |
| Malawi (Southern Africa) | 4 | 1986 |
| <i>North America:</i> | | |
| Bronx, NY, USA | 2.6 | 1986 |
| New York, NY, USA | 3 | 1987 |
| Jacksonville, Florida, USA | 0.7 | 1986 |
| <i>Caribbean:</i> | | |
| Port-au-Prince, Haiti | 8 | 1987 |
| San Juan, Puerto Rico | 1.7 | 1986 |

(25, 55, 57). Rates are usually higher in urban than in rural areas.

Perinatal transmission is a significant problem in Pattern II countries. Up to 35% of all AIDS cases occur among children (75, 76), with more than 80% and up to 100% of all pediatric subjects with AIDS being born to seropositive mothers (12, 15, 17, 77). However, even the large number of pediatric AIDS cases reported in Pattern II countries underrepresents the real problem.

Among other things, because of the high infant mortality from diarrheal and respiratory infections, the full impact of HIV in the pediatric population is not well-defined. Seropositive women in Haiti and parts of Africa have reported having lost at least twice as many infants prior to their current pregnancy as had seronegative women (6, 43). One-third of the children with diarrhea who died after discharge from a rehydration unit in Port-au-Prince had antibody to HIV (78). Therefore, it appears that a majority of the children in the developing countries who are infected with HIV may not live long enough to develop clinical AIDS. It has been found that the mortality rate among children 0-5 years old born to HIV seropositive mothers is 99 deaths per thousand person-months, as compared to one death per thousand person-months among seronegative children (15).

Severe malnutrition is also common among seropositive children (15, 78), and may be a presenting manifestation of HIV infection (79). Forty-five percent of children 2 to 29 months old who were hospitalized consecutively for severe malnutrition in pediatric wards in Bujumbura, Burundi, were HIV seropositive (80). Most of these children were expected to die, since severe malnutrition is a major determinant of death among children in developing countries.

PROBLEMS ASSOCIATED WITH CONTROL OF PERINATAL INFECTIONS

Control of perinatal infection depends on effective measures to prevent HIV transmission in women.

Transfusion of infected blood and blood products is an important mode of HIV transmission in countries where mandatory screening procedures are not in effect. Although present blood screening procedures for HIV appear simple, their cost is prohibitive in most developing countries. The present cost of the ELISA test used by most blood banks for screening blood and blood products may be the equivalent of three to ten times the amount many developing countries are spending for health care per person annually. In addition, the necessary infrastructure for adequately performing the test is not available in remote villages. The best approach at present may be to use rapid and simple methods for HIV testing that do not require complicated equipment (81-83). Some of these tests appear to have good specificity but more variable sensitivity (84).

Even more important than blood screening are control measures designed to prevent HIV transmission involving women who are I.V. drug abusers or who have acquired the infection by heterosexual contact. This target population can be more readily identified in Pattern I countries, where a significant proportion of infected women are I.V. drug abusers or sex partners of I.V. drug abusers. In countries where such drug abuse is important, information campaigns directed at adolescents should pay particular attention to education on drug abuse.

In contrast to the situation in Pattern I countries, most women in Pattern II countries may not belong to any high-risk group or recall any high-risk expo-

sure to HIV. One possible approach for identifying potentially infected men and women in Pattern II countries would be to screen the following groups:

1. Those with symptoms, signs, or infections associated with the presence of HIV;¹
2. Sex partners of seropositive individuals and of patients with AIDS or suspected AIDS;
3. Those with other sexually transmitted diseases;
4. Those having children with AIDS or suspected AIDS;
5. Those who have received a blood transfusion within the last 10 years;
6. Pregnant women early in the course of pregnancy;
7. Women with previous miscarriage or death of a child 0-5 years old within the last 10 years;
8. All male and female prostitutes (85).

Like blood screening for HIV, identification of potentially infected individuals is a continuing process that will require funds not readily available in countries where it would be most appropriate.

Once seropositive women are identified, information and counseling to prevent heterosexual spread and perinatal transmission should be initiated. Also, women should be informed about their risk of sexually acquiring HIV and should be encouraged to have only one lifetime sexual partner. In addition, women who have more than one regular sexual part-

ner and those who have sexual contact with HIV-infected men should be told to reduce their risk by insisting that their partners always use condoms during intercourse.

It is also true, however, that in many developing countries where women depend on men for support, they may have no choice regarding whether or not their sexual partners use condoms. In addition, the target population in both developed and developing countries may not be very responsive to health education strategies. The high illiteracy rates prevailing in Pattern II countries and the lack of motivation of I.V. drug abusers in Pattern I countries are not conducive to health interventions. Contraceptive methods including condoms are available and often free in many developing countries, and yet less than 5-10% of the women of childbearing age actually use them.

Infected women already pregnant should be made aware of the high rate of vertical transmission and the likelihood of manifest disease in their offspring. In addition, infected pregnant women should be informed of the high probability that they may develop AIDS and die before their child is five years old. If possible, termination of pregnancy should be offered to women who desire it; however, in many countries elective abortion is illegal.

Serosurveys in almost all countries have shown a higher HIV seropositivity rate in urban than in rural areas. This difference is probably related to the greater sexual promiscuity, particularly sexual contact with prostitutes, existing in large cities.

Health education should be directed at all sexually active individuals. Ongoing educational interventions have been successful in convincing prostitutes to use condoms (86, 87). In male-dominant societies, another approach is to convince

¹Common signs and symptoms or infections associated with HIV in Pattern II countries include the following: (1) chronic diarrhea with severe weight loss ($\geq 10\%$ of body weight in three months), (2) prurigo, (3) persistent or intermittent fever, (4) unexplained lymphadenopathy, (5) thrush, (6) herpes zoster, (7) genital herpes, and (8) nontyphoid salmonellosis.

men to use condoms when practicing "risky sex." In Haiti, women who become infected usually have one male sex partner who in turn has had many other sex partners and contact with prostitutes. Hence, the control of the infection in women and children in Haiti is dependent upon control of the infection in men. Within this context, it should be noted that a limitation on the number of sex partners may not be easily accepted in societies where polygamy is common.

Once health education interventions are developed, the most pressing need is to monitor their efficacy in leading to fewer sexual partners, reduced contact with prostitutes, and increased utilization of condoms. A multisectoral approach should be used in every community to mobilize all members in an open crusade against what has become a challenge for society, a challenge for the world.

REFERENCES

- Oleske, J., A. Minnefor, R. Cooper, Jr., et al. Immune deficiency syndrome in children. *JAMA* 249:2345-2349, 1983.
- Scott, G. B., B. L. Buch, J. G. Leterman, et al. Acquired immunodeficiency syndrome in infants. *N Engl J Med* 310:76-81, 1984.
- Rubinstein, A., M. Sicklick, A. Yupta, et al. Acquired immunodeficiency syndrome with reversed T4/T8 ratio in infants born to promiscuous and drug-addicted mothers. *JAMA* 249:2350-2356, 1983.
- Blanche, S., C. Rouzioux, F. Veber, et al. Prospective Study on Newborns of HIV Seropositive Women. Paper presented at the III International Conference on Acquired Immunodeficiency Syndrome, held in Washington, D.C., on 1-5 June 1987. Book of Abstracts, Abstract TH.7.4, p. 158.
- Braddick, M., J. K. Kreiss, T. Quinn, et al. Congenital Transmission of HIV in Nairobi, Kenya. Paper presented at the III International Conference on Acquired Immunodeficiency Syndrome, held in Washington, D.C., on 1-5 June 1987. Book of Abstracts, Abstract TH.7.5, p. 158.
- Nzilambi, N., R. W. Ryder, F. Behets, et al. Perinatal HIV Transmission in Two African Hospitals. Paper presented at the III International Conference on Acquired Immunodeficiency Syndrome, held in Washington, D.C., on 1-5 June 1987. Book of Abstracts, Abstract TH.7.6, p. 158.
- Centers for Disease Control. Update: AIDS worldwide. *MMWR* 37 (18):286-295, 1988.
- Centers for Disease Control. *AIDS Weekly Surveillance Report*. United States AIDS Program, Center for Infectious Diseases, June 20, 1988, pp. 1-5.
- Curran, J. W., D. N. Lawrence, H. J. Jaffe, et al. Acquired immunodeficiency syndrome (AIDS) associated with transfusions. *N Engl J Med* 310:69-75, 1984.
- O'Duffy, J. F., and A. F. Isles. Transfusion-induced AIDS in four premature babies. *Lancet* 2:1346, 1984.
- Wykoff, R. F., E. R. Pearl, and F. T. Saulsbury. Immunologic dysfunction in infants infected through transfusion with HTLV-III. *N Engl J Med* 312:294-296, 1985.
- Mann, J. M., H. Francis, F. Davachi, et al. Risk factors for human immunodeficiency virus seropositivity among children 1-24 months old in Kinshasa, Zaire. *Lancet* 2:654-657, 1986.
- Pape, J. W., B. Liautaud, F. Thomas, et al. The acquired immunodeficiency syndrome in Haiti. *Ann Intern Med* 103(5):674-678, 1985.
- Friedland, O. H., H. R. Saltzman, M. F. Rogers, et al. Lack of transmission of HTLV-III/LAV infection to household contacts of patients with AIDS or AIDS-related complex with oral candidiasis. *N Engl J Med* 314:344-345, 1986.
- Pape, J. W., R. I. Verdier, S. Jean, et al. Transmission and Mortality of HIV Infection in Haitian Children. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 2, Abstract 6581, p. 292.
- Pyun, K. H., H. D. Ochs, M. T. Dufford, and R. J. Wedgwood. Perinatal transmission with HIV virus. *N Engl J Med* 317(10):611-614, 1987.

17. Lesbordes, J. L., S. Chassignol, E. Ray, et al. Malnutrition and HIV infection in children in the Central African Republic. *Lancet* 2:337-338, 1986.
18. Centers for Disease Control. Update, acquired immunodeficiency syndrome Europe. *MMWR* 35:35-46, 1986.
19. Centers for Disease Control. Recommendations for assisting in the prevention of perinatal transmission of human T-lymphotropic virus type III/lymphadenopathy associated virus and acquired immunodeficiency syndrome. *MMWR* 34:721-732, 1985.
20. Mok, J. G., A. De Rossia, A. E. Ades, et al. Infants born to mothers seropositive to HIV. *Lancet* 1:1164-1168, 1987.
21. Harnish, D. G., O. Hammerberg, J. R. Walken, and K. L. Rosenthal. Early detection of HIV in a newborn. *N Engl J Med* 316:272-273, 1987.
22. Johnson, J. P., P. Nain, and S. Alexander. Early diagnosis of human immunodeficiency virus infection in the neonate. *N Engl J Med* 316:273-274, 1987.
23. Semprini, E. A., A. Vucetian, G. Pandi, and M. M. Cossu. HIV infection and AIDS in newborn babies of mothers positive for HIV antibody. *Br Med J* 294:610, 1987.
24. Scott, G. B., M. T. Mastrucci, S. C. Hutto, and W. P. Parks. Mothers of Infants with HIV Infection: Outcome of Subsequent Pregnancies. Paper presented at the III International Conference on Acquired Immunodeficiency Syndrome, held in Washington, D.C., on 1-5 June 1987. Book of Abstracts, Abstract THP.91, p. 178.
25. Luizi, G., B. Ensoli, G. Turbessi, et al. Transmission of HTLV-III infection by heterosexual contact. *Lancet* 2:1018, 1985.
26. Chiodo, F., E. Ricchi, P. Costogiolia, et al. Vertical transmission of HTLV-III. *Lancet* 1:739, 1986.
27. Thomas, P. A., M. J. Lubink, J. Milberg, et al. Cohort comparison study of children whose mothers have AIDS. *Pediatr Infect Dis* 6:247-251, 1987.
28. Scott, G. B., M. A. Fischl, N. Klimar, et al. Mothers of infants with acquired immunodeficiency syndrome: Evidence for both symptomatic and asymptomatic carriers. *JAMA* 253:363, 1985.
29. Rubinstein, A. Pediatric AIDS. *Curr Probl Pediatr* 16:365-409, 1986.
30. Andiman, W. A., J. Simpson, L. Dember, et al. Prospective Studies of a Cohort of 50 Infants Born to Human Immunodeficiency Virus Seropositive Mothers. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 2, Abstract 6590, p. 294.
31. Weintrub, P. S., C. Rumsey, D. Wara, et al. Prospective Evaluation of Infants of HIV Antibody Positive Women. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 2, Abstract 6593, p. 295.
32. Mok, J., R. Hague, L. MacCallum, et al. Perinatal Transmission of HIV: Prospective Study. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 2, Abstract 6580, p. 291.
33. Levy, J., F. Puissant, G. Soumenkoff, et al. Prospective Study of Vertical Transmission of HIV. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 2, Abstract 6582, p. 292.
34. Willoughby, A., H. Méndez, J. Hittelman, et al. Epidemiology of Perinatal Transmission of Human Immunodeficiency Virus. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 2, Abstract 6588, p. 293.
35. Ryder, R. W., W. Nsa, F. Behets, et al. Perinatal HIV Transmission in Two African Hospitals: One-year Follow-up. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 1, Abstract 4128, p. 291.
36. Terragna, A., A. De Maria, F. Sampietro, et al. Perinatal HIV Infection: Evaluation of the Risk for the Mother and Child. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 1, Abstract 4028, p. 266.
37. Grosch-Wörner, I., S. Koch, M. Vocks, et al. Newborns of HIV-positive Mothers: Berlin Follow-up Experience. Paper presented at the IV International Conference

- on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 1, Abstract 7255, p. 441.
38. Cowan, M. J., D. Hellmann, D. Chudwin, et al. Maternal transmission of AIDS. *Pediatrics* 73:382-386, 1984.
 39. Wilmer, E., A. Fischer, C. Griscelli, et al. Possible transmission of human lymphotropic retrovirus (LAV) from mother to infant with AIDS. *Lancet* 2:229-230, 1988.
 40. Menez, B. R., S. M. Kikrig, and S. Pahwa. Monozygotic twins discordant for the acquired immunodeficiency syndrome. *Am J Dis Child* 140:678-679, 1986.
 41. Lapointe, N., J. Michaud, D. Pekovic, et al. Transplacental transmission of HTLV-III. *N Engl J Med* 312:1325-1326, 1985.
 42. Jovaisas, E., M. A. Koch, A. Schaefer, et al. LAV/HTLV-III in 20-week foetus. *Lancet* 2:1129, 1985.
 43. Pape, J. W. Outcome of Offspring of HIV Infected Pregnant Women in Haiti. In: R. F. Schinazi and A. J. Nahmias (eds.). *AIDS in Children, Adolescents and Heterosexual Adults*. New York, Elsevier Science Publishing Co., Inc., 1987, pp. 216-219.
 44. Marion, R. W., A. A. Wiznia, R. G. Hutcheon, et al. Human T-cell lymphotropic virus type III (HTLV-III) embryopathy: A new dysmorphic syndrome associated with intrauterine HTLV-III. *Am J Dis Child* 140:638-640, 1986.
 45. Vogt, M. W., D. J. Witt, D. E. Craven, et al. Isolation of HTLV-III/LAV from cervical secretion of women at risk for AIDS. *Lancet* 1:525-527, 1986.
 46. Wofsy, C. B., J. B. Cohen, L. B. Haver, et al. Isolation of AIDS-associated retrovirus from genital secretions of women with antibodies to the virus. *Lancet* 1:527-529, 1986.
 47. Thiry, L., S. Sprecher-Goldenberger, T. Jonckheer, et al. Isolation of AIDS virus from cell-free breast milk of three healthy virus carriers. *Lancet* 1:891-892, 1985.
 48. Hino, S., K. Yamaguchi, S. Katamine, et al. Mother to child transmission of human T-cell leukemia virus type I. *Jpn J Cancer Res* 76:474-480, 1985.
 49. Ziegler, J. B., D. A. Cooper, R. O. Johnson, and J. Gold. Postnatal transmission of AIDS-associated retrovirus from mother to infant. *Lancet* 1:896-898, 1985.
 50. Ziegler, J. B., G. J. Stewart, R. Penny, et al. Breastfeeding and Transmission of HIV from Mother to Infant. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 1, Abstract 5100, p. 339.
 51. Weinbreck, P., V. Loustaud, F. Denis, and F. Liozon. Breastfeeding and HIV-1 Transmission. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 1, Abstract 5102, p. 340.
 52. Colebunders, R. L., B. Kapita, W. Nekwei, et al. Breastfeeding and Transmission of HIV. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 1, Abstract 5103, p. 340.
 53. Stanback, M., J. W. Pape, R. I. Verdier, et al. Breastfeeding and HIV Transmission in Haitian Children. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 1, Abstract 5101, p. 340.
 54. Piot, P., F. Plummer, S. Mhalu, et al. AIDS: An international perspective. *Science* 239:573-579, 1988.
 55. Centers for Disease Control. Supplement, human immunodeficiency virus infection in the United States: A review of current knowledge. *MMWR* 36(Suppl. 5,6):1-48, 1987.
 56. Hoff, R., V. P. Berardi, B. J. Weiblen, et al. Seroprevalence of human immunodeficiency virus among childbearing women. *N Engl J Med* 318(9):525-530, 1988.
 57. Sperling, R., H. S. Sacks, L. Mayer, and R. Berkowitz. Serosurvey of an Obstetrical Population in a Voluntary Hospital in New York City. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 1, Abstract 4030, p. 267.
 58. Novick, L. F., D. Berns, R. Stricof, and R. Stevens. HIV Seroprevalence in Newborn Infants in New York State. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 1, Abstract 7221, p. 433.
 59. Pape, J. W., and W. D. Johnson, Jr. Epidemiology of AIDS in the Caribbean. In: P. Piot and J. Marn (eds.). *Bailliere's Clinical Tropical Medicine and Communicable Dis-*

eases, *AIDS and HIV Infection in the Tropics*, 1988 (in press).

60. Hospedales, C. J. The Epidemiology of AIDS in the Caribbean and Action to Date. Paper presented at the First International Conference on the Global Impact of AIDS, held in London, 1988. Book of Abstracts, Abstract 529.
61. Guerrero, E., E. A. De Moya, I. Garris, et al. Predominance of Heterosexual Transmission of HIV Infection in the Dominican Republic. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 2, Abstract 5502, p. 239.
62. Quinn, T. C., J. M. Mann, J. W. Curran, and P. Piot. AIDS in Africa: An epidemiologic paradigm. *Science* 234:955-963, 1986.
63. Neequaye, A. R., J. Neequaye, J. A. Mingle, and A. D. Ofari. Preponderance of females with AIDS in Ghana. *Lancet* 2:978, 1986.
64. Mann, J. M., T. C. Quinn, H. Francis, et al. Sexual Practices Associated with LAV/HTLV-III Seropositivity among Female Prostitutes in Kinshasa, Zaire. Paper presented at the II International Conference on AIDS, held in Paris, France, on 23-25 June 1986.
65. Van de Perre, P., and M. Carael. HIV Infection in Prostitutes in Africa. In: R. F. Schinazi and A. J. Nahmias (eds.). *AIDS in Children, Adolescents and Heterosexual Adults*. New York, Elsevier Science Publishing Co., Inc., 1987, pp. 166-167.
66. Van de Perre, P., N. Clumeck, M. Carael, et al. Female prostitutes, a risk group for infection with human T-cell lymphotropic virus type III. *Lancet* 2:524-527, 1985.
67. Simonsen, N., P. Plummer, N. Gakinya, et al. Longitudinal Study of a Cohort of HTLV-III/LAV Infected Prostitutes in Nairobi. Paper presented at the II International Conference on AIDS held in Paris, France, on 23-25 June 1986.
68. Van de Perre, P., D. Rouvroy, P. Lepage, et al. Acquired immunodeficiency syndrome in Rwanda. *Lancet* 2:62-65, 1984.
69. Kreiss, J. K., D. Koech, F. A. Plummer, et al. AIDS virus in Nairobi prostitutes: Spread of the epidemic to East Africa. *N Engl J Med* 314(7):414-418, 1986.
70. Clumeck, N., M. R. Guroff, P. Van de Perre, et al. Seroepidemiological studies of HTLV-III antibody prevalence among selected groups of heterosexual Africans. *JAMA* 254:2592-2602, 1985.
71. Koenig, E. R., J. Pittaluga, M. Bogart, et al. Prevalence of antibodies to the human immunodeficiency virus in Dominicans and Haitians in the Dominican Republic. *JAMA* 257(5):631-634, 1987.
72. Gürtler, L. G., G. Zoulek, G. Frösner, et al. Prevalences of HIV-1 and HIV-2 Antibodies in a Selected Malawian Population. Paper presented at the III International Conference on Acquired Immunodeficiency Syndrome, held in Washington, D.C., on 1-5 June 1987. Book of Abstracts, Abstract THP. 93, p. 179.
73. Mhalu, F., E. Mbeni, U. Bredberg-Raden, et al. Prevalence of HIV Antibodies in Healthy Subjects and Groups of Patients in Some Parts of Tanzania. Paper presented at the III International Conference on Acquired Immunodeficiency Syndrome, held in Washington, D.C., on 1-5 June 1987. Book of Abstracts, Abstract TP.86, p. 76.
74. Boulos, R., N. Halsey, J. R. Brutus, et al. Risk Factors for HIV-1 Infection in Pregnant Haitian Women. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 1, Abstract 5119, p. 344.
75. Ndinuyeze, A., G. Bugingo, and A. Ntilyamundo. Adult and Pediatric AIDS and AIDS Related Syndrome in Rwanda. Paper presented at the Second International Symposium on AIDS and Associated Cancers in Africa. Naples, 1987. Book of Abstracts, Abstract 5-2-2.
76. Bartholomew, C., F. Cleghorn, B. Hull, et al. Transition from Homosexual to Heterosexual AIDS in Trinidad. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 2, Abstract 5505, p. 240.
77. Lepage, P., and P. Van de Perre. Strategies in the Identification and Control of HIV-infected Women in Africa. In: R. F. Schinazi and A. J. Nahmias (eds.). *AIDS in Children, Adolescents and Heterosexual Adults*. New York, Elsevier Science Publishing Co., Inc., 1987, pp. 214-215.
78. Oriol, L., J. W. Pape, J. Clarke, et al. Factors Associated with Mortality Post-discharge from a Rehydration Unit in

- Port-au-Prince, Haiti. (Manuscript in preparation.)
79. Scott, B. G., W. Park, and M. Jonas. Protein-calorie Malnutrition as a Presenting Manifestation of Human Retrovirus (HTLV-III) Infection in Infants and Children. Paper presented at the First International Conference on AIDS, held in Atlanta, 1985.
 80. Excler, J. L., B. Standaert, E. Ngendandumwe, and P. Piot. Malnutrition et infection à HIV chez l'enfant en milieu hospitalier au Burundi. *Pediatric* 42(9):715-718, 1987.
 81. Weisner, D., D. Taylor, A. Suarez, et al. Passive Hemagglutination Assay for HIV Antibody Screening. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 2, Abstract 5593, p. 262.
 82. Said, O. I., J. A. Hinda, S. Bygdeman, and L. Grillner. Evaluation of a Particle Agglutination Test for Detection of HIV Antibodies. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 2, Abstract 5596, p. 262.
 83. Rosenheim, M., M. Ritterband, F. Fish, et al. A Method for Anti-HIV Antibodies Testing in Developing Countries. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 2, Abstract 5600, p. 263.
 84. Kabeya, C. M., F. Spielberg, N. K. Kifuani, et al. Comparison of Rapid HIV Antibody Screening Assays, Mama Yemo Hosp. Kinshasa, Zaire. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 2, Abstract 5595, p. 262.
 85. Pape, J. W. Identification and Control of HIV Infected Pregnant Women. In: R. H. Schinazi and A. J. Nahmias (eds.). *AIDS in Children, Adolescents and Heterosexual Adults*. New York, Elsevier Science Publishing Co., Inc., 1987, pp. 257-260.
 86. Plummer, F., M. Braddick, W. Cameron, et al. Durability of Changed Sexual Behavior in Nairobi Prostitutes: Increasing Use of Condom. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 1, Abstract 5141, p. 350.
 87. Lampthey, P., A. Neequays, S. Weir, and M. Potts. A Model Program to Reduce HIV Infection among Prostitutes in Africa. Paper presented at the IV International Conference on AIDS, held in Stockholm on 12-16 June 1988. Book of Abstracts 1, Abstract 5149, p. 352.