

**Resources for
Child Health**
REACH

PN-ABE-478
64976



**IS THERE A DEMONSTRABLE OR POTENTIAL RELATIONSHIP BETWEEN EPI AND
TRANSMISSION OF HUMAN IMMUNODEFICIENCY VIRUS (THE AIDS VIRUS)?**

Bert Hirschhorn

**Presented at NCII Conference
May, 1988**

AID Contract No: DPE 5927-C-00-5068-00

IS THERE A DEMONSTRABLE OR POTENTIAL RELATIONSHIP BETWEEN EPI AND TRANSMISSION OF HUMAN IMMUNODEFICIENCY VIRUS (THE AIDS VIRUS)?

This paper examines the evidence and potential for HIV transmission through the Expanded Programme on Immunization (EPI) and discusses the implications for EPI. All conclusions about AIDS, however, are subject to rapid change as new data emerge.

To date there has been no evidence of any child becoming HIV-positive due to vaccination by EPI. Virtually all instances have been related to maternal transmission from an HIV-positive mother (before or during delivery); or to blood transfusion with HIV-positive blood; rarely by breast-feeding [3 likely cases to date (1,2)], and perhaps by multiple unsterile injections.

The issue of EPI and AIDS is important, nonetheless, because the perception exists that EPI has the potential to transmit HIV, and this could discourage people from vaccination. It is true that contaminated needles and syringes used by intravenous drug-takers readily transmit HIV. One assumes, therefore, that if EPI needles and syringes are not sterilised they too could transmit HIV. A recent issue of WORLD HEALTH advises on the need for sterile injections that, "there has been, particularly, the risk of hepatitis transmission, and now the risk of passing on the HIV virus (sic) that causes AIDS."(3)

The failure so far to demonstrate HIV transmission by EPI comes from several studies:

In Zambia (4), 2,300 children aged 5-12 were screened for HIV antibodies. All but 5 were seronegative and these 5 were asymptomatic. Three of these seropositive had received blood transfusions and the other two, girls aged 11 and 12 years, were thought to have acquired the infection as a result of heterosexual activity. It is likely that about half of the children would have been immunized, which would have happened to some of the younger ones at the time HIV was first recorded in Zambia in 1982. None appear to have acquired HIV as a result of immunization.

In December, 1986, a national community-based serosurvey was conducted throughout Rwanda in a large cohort of children. The preliminary results of this survey indicate children are not at risk from HIV infection as a result of immunization during the first year of life (5).

In some central African cities (6), children with AIDS make up 20% or more of recorded AIDS cases. All have either HIV infected mothers, and/or a history of blood transfusion, and/or multiple medicinal injections. None detected to date has a history of EPI vaccinations alone.

Nevertheless, this evidence should not discount the risk of multiple unsterile injections, particularly as there is no evidence that any unsterile injections were, in fact, given in these programs.

Mann and coworkers (7) examined 16 seropositive children in Zaire for risk factors whose mothers were seronegative (C+M-) and compared them to 222 seronegative children whose mothers were also seronegative (C-M-): (OH#1)

	SEROPOSITIVE CHILDREN (C+M-) N=16	SERONEGATIVE CHILDREN (C-M-) N=222
-mean age (months)	10.6	11.4
-average no. of lifetime medical injections	44	23
-previous blood transfusion	5 (31%)	15 (7%)
-vaccinations, mean no. received	2.8	3.2
-scarification	1 (6%)	33 (15%)

Multiple medical injections, transfusions and hospitalizations were significant risk factors differentiating the two groups; EPI vaccinations were similar in both groups. Among seropositive children with seronegative mothers (C+M-) who were neither transfused, nor admitted to hospital, the median number of medical injections was 34.5 compared to 14.5 in seronegative children (C-M-) (P = 0.0006). C+M- children still had significantly more medical injections than C+M+ children (P = 0.03), even though the disease burden should have been comparable in each group. The data do not allow for estimation of attributable risk for medical injections, neither are ranges of the number of injections given for the averages.

The study indicates that multiple, presumably unsterile medical injections constitute a risk factor for HIV transmission, albeit not the principal one.

The question then is, what is the attributable risk of a normal EPI series of vaccinations? For in respect to sterility many EPIs perform inadequately: practitioners not sterilizing needles and syringes, or reusing unsterile syringes with a sterilized needle for each child. We can only give a crude estimate of this risk. The analysis depends on several variables, none of which is known accurately, or are derived from situations not strictly analogous to an EPI. (OH#2)

	NOT TRANSFUSED NOT HOSPITALIZED	
	C+M-	C-M-
MEAN MEDICAL INJECTIONS	34.5	14.5

.21

For instance, the risk of acquiring HIV from a contaminated needle by pricking is about 0.5% [4 cases among 870 exposures (8)]. But a vaccination pushes the inoculum into the body and may, therefore, pose a higher risk. Then again, the intravenous route --a very high risk exposure among drug addicts and persons receiving transfusions-- is sure to be far more efficient than inocula under the skin or into the muscle. Also, in the former situation residual blood in an unsterile syringe came directly from the bloodstream; in the latter --as in EPI-- the reused unsterile needle has picked up extracellular fluids from under the skin or within muscle. Although HIV particles may be present in such juices (9), they are probably, similar to saliva, fewer there than in blood. The size of the infecting dose may account for the difference in the rates of infection by needle stick between Hepatitis B [(20-40% when the contaminated blood is Hepatitis B virus e antigen positive, 10-15% if e antigen negative (10)] and HIV. A carrier of Hepatitis B may have 10^8 infectious particles per ml of blood (11), while HIV infected blood has less than 1 (12). However, the biology and pathogenesis of Hepatitis B virus and HIV differ markedly (even though routes of transmission are virtually identical) and no data exist on ID50 of either. Nonetheless, the data of Mann, et al (7) suggest that if just one of the 44 unsterile injections sufficed to transmit HIV then the 0.5% infectious rate by pricking is too low an estimate by nearly five-fold.

The risk of HIV transmission by EPI requires also that the unsterilised needle and syringe have been used in a previously inoculated child who has HIV infection. This risk varies widely between countries and even within countries otherwise highly endemic for AIDS. In Kinshasa, Zaire, for instance, about 1-2% of healthy children, 9-20 months old, are HIV positive (7) but in rural areas of Zaire the figure is perhaps indistinguishable from zero (13). A worst-case estimate may be obtained for 1984-1986: 8.6% of child-bearing age women (20-39) in Kinshasa were HIV positive (7), compared to 2.2% of pregnant women in rural Zaire (13). If maternal transmission occurs in 60% of pregnancies (7), a high estimate (14), then about 5% of urban infants and 1% of rural infants are currently potential HIV transmitters (although up to 25-33% may expire within the first year of life and some positive infants may have a lag time before becoming infectious).

Let us now assume that in a poorly-run EPI 85% of the needles and/or syringes are non-sterile, and the transmission rate is 0.5% if the needle comes HIV from an HIV+ previous inoculee. If a child gets the required vaccinations in the first year of life a crude upper bound estimates of HIV transmission by EPI in Central and parts of East Africa are: (OH#3)

RISK OF NEEDLE-STICK TRANSMISSION

VACCINATION PUSHES INOCULUM:	RISK (?)
DIRTY NEEDLE CAME FROM SKIN/MUSCLE:	RISK (?)

HOW MANY HIV PARTICLES NEEDED FOR TRANSMISSION?

(OH#4)

0.005 X 4.25 X 0.01 = .00021 (21/100,000
(transmission rate per inoculation coming from an HIV-positive previous inoculee) (contaminated inoculations in series of 5 shots) (rural prevalence in children) rural vaccinees getting full EPI)

X 0.05 = .00106 (106/100,000
(urban prevalence in children) urban vaccinees getting full EPI)

If infected injected transmission is really five times as great as suggested by Mann's data these figures are 105 and 530/100,000 vaccinees rural and urban respectively. Against the background of other coincidental exposures to HIV among children, these cases may be epidemiologically undetectable; that is, we are unlikely to be able to calculate the attributable risk of EPI; but the risk is not zero. Currently --and for some time to come-- only about 30% of all African newborns are completely immunized in infancy, about 6 million children. If pan-African HIV prevalence in infants is on the order of rural Zaire --surely that is too high-- EPI could currently account for about 1260-6300 annual transmissions of HIV in Africa (needle prick vs. Mann data). Compare to potential Hepatitis B virus (HBV) transmission: (OH#5)

0.30 X 4.25 X 0.25 = 0.31875
(transmission rate per inoculation coming from an HBV-positive previous inoculee) (contaminated inoculations in series of 5 shots) (prevalence in children under 1) (31,875/100,000 vaccinees)

Since the majority of Hepatitis B transmissions are probably pre- and perinatal, before EPI vaccinations are started, the actual HBV transmission by EPI is less than the potential, but still several 100-fold greater than HIV transmission by EPI.

This comparison of potential HIV and HBV transmission is oversimplified. In the former, mortality comes within a few years of an infant infection, and may be close to 100% in Africa. In HBV about 30% of children infected after the neonatal period, but before age 5, by needle sticks, become chronic carriers (15), of whom up to 40% may die of cirrhosis or liver cancer over 3-4 decades (16). This means that we may see, per 100,000 vaccinees, 7 deaths per year from HIV [(21 X 1.0) over 3 years] and 96 deaths per year from HBV [(31,875 X .3 X .4) over 40 years]. However, HBV carriers are efficiently infectious to others over a much longer time, through all routes of transmission, and therefore HBV is a substantial public health hazard whenever unsterile injection equipment is used. (OH#6 - following page)

(OH#6)

HIV:	$\frac{(21)}{100,000}$	(100%)	-	3 years	=	7/100,000
	transmissions	mortality		duration of illness	=	mortality rate
HBV:	$\frac{31,875}{100,000}$	(30%)(40%)	-	30-40 years	=	96/100,000
						per cohort per year

Discussion

The potential impact of transmission of HIV from vaccine has raised concern among EPI program planners and AIDS control programs. Our estimates show EPI can yield some epidemiologically undetectable instances of HIV transmission. Even though no EPI-related cases would arise if EPI followed the proper rule of one sterile needle and one sterile syringe per injection, those who escape EPI-induced HIV would still be susceptible to infection by multiple medical injections or blood transfusions. Vaccination has its own competing risks: The risk of vaccine-induced encephalopathy from DPT is as high as 1/30,000 per vaccination or about 9/100,000 for the full series (17).

The consequences of not immunizing, however, are too well known. If, in Africa, there are 20 million new infants each year, tetanus, pertussis and measles alone --in the absence of immunization-- will kill 1.6 million during their first year of life: (OH#7)

IMMUNIZABLE DISEASES: MORTALITY IN FIRST YEAR OF LIFE, AFRICA

0.4 million	tetanus (20/1000 live births)
0.2 million	pertussis
1.0 million	measles (acute and late)
1.6 million children dying	

The known risk to children of dying from these diseases is thus anywhere from 250 to over 1000 times greater than the potential risk of acquiring HIV infection through immunizations. Therefore, given the magnitude of EPI-preventable diseases, it is essential that political and financial commitment to EPI continues even in the face of the AIDS epidemic.

Major changes in current injection practices will, however, be required in many countries to ensure one sterile needle, one sterile syringe per injection.

EPI, with international support, has developed reusable steam-sterilizable syringes and needles, and pressure cookers fitted with appropriate racks. Some advocate disposable equipment instead; disposable syringes and needles are, in fact, susceptible to reuse by less scrupulous

practitioners. More recently, several prototype single-use automatic self-destructing syringes have been developed and will be tested in field trials to determine their feasibility as direct replacements of traditional syringes. It is hoped that this would make it impossible to transmit any infection by EPI.

More important, however, is that EPI is a leader in preventive health care and in respectful application of technology. No mother would care to have her child inoculated with contaminated needles if she knew the facts. Close attention to sterile equipment will encourage health workers and families to demand the same of all injections.

--Norbert Hirschhorn. M.D.
Project Director
Resources for Child Health (REACH)

--Cynthia D. Rawn
Senior Technical Officer, REACH

--Anne Martin
Health Economist
Family Health International

NOTES

1. Ziegler, et al. "Postnatal Transmission of AIDS Associated Retrovirus From Mother to Infant." *Lancet* 1, 1985, pp. 896-897.
2. Thiry, et al. "Isolation of AIDS Virus From Cell-free Breastmilk of Three Health Virus Carriers." *Lancet* 2, 1985, pp. 891-892.
3. Newsbriefs: World Health. March, 1988, p. 31.
4. Zambia AIDS Control Program, Donor Meeting, March 1988.
5. Family Health Institute ("AIDSTECH"), personal communication.
6. Personal communication via Family Health Institute with Dr. Wilson Carswell, Public Health Advisor, Rubagu Hospital, Kampala, Uganda.
7. Mann, et al. "Risk Factors For Human Immunodeficiency Virus Seropositivity Among Children 1-24 Months Old in Kinshasa, Zaire." *Lancet* 2, 1986, pp. 986, 654-657.
8. Morbidity and Mortality Weekly Report 37, April 22, 1988, p. 231.
9. Kolata, G. "Where is the AIDS Virus Harbored?" *SCIENCE*, pp. 232, 1986, 1197.
10. "Feedback." National Centers for Disease Control, International Health Programs Office, 1986.
11. Hoofnagle, J.H. and Shafer, D.F. "Serologic Markers of Hepatitis B Virus Infection" in Seminars on Liver Disease 6, Number 1, 1986, pp. 1-20.
12. Harper, M.H. et al. *Proc. National Academy of Sciences*, 83, 1986, p. 772.
13. Nzilambi, N. et al. "The Prevalence of Infection With Human Immunodeficiency Virus Over a 10-Year Period in Rural Zaire." *New England Journal of Medicine*, 318, 1988, pp. 276-279.
14. "AIDS - A Public Health Crisis." *Population Reports*, Series L, No. 6, 1986.
15. Seeff, L.B. and Koff, R.S. "Evolving Concepts of the Clinical and Serologic Consequences of Hepatitis B Virus Infection." in Seminars on Liver Disease 6, Number 1, 1986, p. 11.
16. Beasley, R.P. "Hepatitis B Immunization Strategies." WHO/EPI unpublished position paper, November, 1987.
17. Clements, C.J. Risks of Infection Using Non-Sterile Equipment or Contaminated Vaccine in the Expanded Programme on Immunization. WHO/EPI/Geneva/1986/5.