HIV transmission during paediatric health care in sub-Saharan Africa – risks and evidence

David Gisselquist, John J Potterat, Stuart Brody

Health care systems in sub-Saharan Africa are challenged not only to improve care for the increasing number of HIV-infected children, but also to prevent transmission of HIV to other children and health care workers through contaminated medical procedures and needlestick accidents. HIV-infected children aged to 1 year typically have high viral loads, making them dangerous reservoirs for iatrogenic transmission. Most vertically infected children experience HIV-related symptoms early, though many survive beyond 5 years. This leads to high HIV prevalence among inpatient and outpatient children. In nine African studies, HIV prevalence in inpatient children ranged from 8.2% to 63%, roughly 1 - 3 times the prevalence in antenatal women.

Investigations of large iatrogenic outbreaks in Russia, Romania, and Libya demonstrate efficient HIV transmission through paediatric health care. Unexplained HIV infections in African children are not rare – studies published through 2003 have recorded more than 300 HIV-infected children with HIV-negative mothers. In addition, several studies have reported much higher HIV prevalence in children 5 - 14 years old than could be expected from mother-to-child transmission alone. Research is required to determine the extent of iatrogenic HIV infection among African children as well as to identify high-risk procedures and settings. Such research can motivate and direct prevention efforts.

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Paediatric health services in sub-Saharan Africa are burdened by increasing numbers of HIV-infected children.[1,2] With progressive improvement in treatment for opportunistic infections and an emerging consensus to provide antiviral treatment, African health services face the challenge to extend and improve health care to the large and growing number of HIV-infected children. Meeting this challenge, however, brings with it an additional challenge, viz. to prevent horizontal HIV transmission to other children and health care workers through medical procedures and needlestick accidents. In this communication we review the published evidence on HIV prevalence in paediatric health care settings in Africa, risks for horizontal transmission to other patients, and non-vertical HIV infections in African children. We conclude with recommendations to assess and prevent HIV transmission in health care settings.

HIV infections in children in African health care settings

Robust estimates of the number of African children with HIV infection are not available, because few random-sample surveys have included children.[3] The overwhelming majority of HIV-infected African children are never tested for HIV. Although some symptoms such as nonspecific generalised dermatitis, ear discharge, lobar pneumonia, and tuberculosis are associated with HIV in African children,[4] most infected children die with symptoms such as failure to thrive, malnutrition, and respiratory infections that are common to all children, so that parents and health care workers may suspect but do not know if a child is infected.[5] Nevertheless, an approximate picture of the number of infected children and HIV prevalence in paediatric health care settings can be derived from available information.

HIV prevalence among all children

In the absence of representative paediatric serosurveys, WHO and UNAIDS estimate numbers of paediatric HIV infections from HIV prevalence in pregnant women (from antenatal surveys), observed rates of vertical (intra-uterine, perinatal, and breast-feeding) transmission, and assumed paediatric survival with HIV. In Africa, vertical transmission is assumed to infect 35% of children born to infected mothers[6] (circa 20% at birth and 15% from breast-feeding). Fifty per cent of vertically

29 West Governer Road, Hershey, Pennsylvania, USA
David Gisselquist, PhD

301 South Union Boulevard, Colorado Springs, USA
John J Potterat, BA

Institute of Medical Psychology and Behavioural Neurobiology, University of Tübingen, Germany
Stuart Brody, PhD

infected children in Africa are assumed to survive to 2 years old and 40% to 5 years old, with subsequent low mortality for an undetermined period.[7]

Given the above parameters and assumptions, HIV prevalence in children at birth would be roughly one-fifth of the HIV prevalence in mothers. In children aged 2 years old — with additional infections through breast-feeding offset by higher mortality among infected children — HIV prevalence would be roughly one-sixth of the HIV prevalence in antenatal women 2 years previously (i.e. in the children's birth year). This ratio falls as children age, so that the ratio of prevalence in children 0 - 14 years old to prevalence in mothers at birth would be much lower. Also, if we compare HIV prevalence in children with current HIV prevalence in antenatal women rather than with antenatal women in the children's birth years, the ratio would be lower in a growing epidemic (reflecting higher HIV prevalence in current antenatal women than when children were born).

According to recent WHO estimates, 900 000 children worldwide contracted HIV from vertical transmission in 2001,[8] and 3.2 million children 0 - 14 years old were living with HIV infections in 2002.[9] If we accept these estimates, and assume that 80% of incident and prevalent paediatric HIV infections worldwide are found in Africa (compared with 70% of total infections),[8-10] and assume as well that numbers of HIV infections in children parallel HIV infections in adults, then approximately 9% of total prevalent infections in Africa have been in children, and the number of new vertical infections each year has been roughly 2.7% of total adult and child prevalence (Table I). From these estimates, more than 5 million children in Africa have been infected via vertical transmission during the past decade.

HIV prevalence among outpatient and inpatient children

Like other children, HIV-infected children visit clinics and other health care settings for vaccinations and treatment of common childhood diseases such as diarrhoea and malaria. In addition, most HIV-infected children, including many who survive for years, experience HIV-related health problems from their first year, continuing intermittently. In an early study of vertically infected children in Europe (i.e. before multidrug antiviral treatment), more than 60% experienced an HIV-related sign or symptom by 9 months of age and about 75% by 16 months.[14] In several studies of children followed to ages 10 - 15 months in the Democratic Republic of Congo (DRC), vertically infected children were more likely than uninfected children to have episodes of acute diarrhoea (170 versus 100 episodes per 100 child-years) and were more likely to suffer persistent diarrhoea, fever, and dehydration.[15,16] In a study that followed Malawian children of HIV-positive mothers, only 1% of HIV-infected children did not experience HIV symptoms during the first 3 years of life.[17]

Hence, virtually all HIV-infected children interact with formal and informal health care systems for routine paediatric care and/or HIV-related symptoms. However, there are no comprehensive data on number of outpatient visits and inpatient days. The best information to describe the intensity of their interaction with health care providers comes from studies of HIV prevalence among inpatient and to a lesser extent outpatient children.

In 9 studies, the proportion of paediatric patients with HIV infections ranged from one to three times the proportion of HIV-infected women in antenatal settings within the same communities (Table II). This is considerably higher than HIV prevalence among children from vertical transmission, which is estimated above to be less than one-sixth the HIV prevalence in antenatal women. In the DRC, for example, 11% of a sample of paediatric inpatients aged 2 - 14 years were HIV-positive during 1984/85 compared with 5.9% of antenatal women (Table II). Similarly, in a hospital in Durban in 1998, 62.5% of paediatric inpatients were HIV-infected compared with 19.2% of urban antenatal women nationally. The proportion of inpatient children infected is generally higher for infants than for older children, but the difference is often not very great. For example, in Tanzania, 17 - 25% of inpatient children aged 0 - 12 months were HIV-infected compared with 19% of children aged 4 - 7 years. In three studies in South Africa, the mean duration of hospital stay for HIV-infected children was similar or greater than for other children: 8.9 days for both in Durban,[28]

Table I. Estimated number of African children with HIV infection from vertical transmission (millions)

Category of prevalent or incident infections	Year			
	1988	1994	1998	2002
Total prevalent infections in adults and children[9,11-13]	2.5	12*	21	29
Prevalent infections in children[†]	0.23	1.1	1.9	2.6
Incident infections in children[‡]	0.07	0.3	0.6	0.8

*WHO estimated 11.2 million infected adults;[12] this figure adds 1.1 million children.
[†]Estimated as 9% of prevalent infections in adults and children.
[‡]Estimated as 2.7% of prevalent infections in adults and children.

Table II. HIV prevalence and symptoms among paediatric inpatients in Africa

| Country, city, hospital, reference | Year | HIV prevalence (%)* | | | Common diagnoses and categories of symptoms in HIV-positive children (%) |
| | | Antenatal women[†] | Inpatient children | | |
			Age	Prevalence	
Cote d'Ivoire, Abidjan, three university hospitals[18,19]	1991/92	11	< 15 mo. 15 - 23 mo. 2 - 4 yr ≥ 5 yr Total	8.5[‡] 11.2[‡] 11.1[‡] 4.6[‡] 8.2[‡]	Malnourished: 26 Acute respiratory infection: 26
DRC, Kinshasa, Mama Yemo Hospital[20,22]	1984/85	5.9	2 - 4 yr 5 - 7 yr 8 - 10 yr 11 - 14 yr Total	11 12 10 8 11	Malnutrition Pneumonia Anaemia
DRC, Kinshasa, Mama Yemo Hospital[21,22]	1985	5.9	< 9 mo. 9 - 24 mo.	12 13	Gastrointestinal: 59 Malnutrition: 38 Anaemia: 34
DRC, Kinshasa, Mama Yemo Hospital[22,23]	1986	5.6	1 mo. - 12 yr	13	Weight loss/slow growth: 65 Fever > 1 mo.: 59 Hepatomegaly: 59 Persistent cough/pneumopathy: 53
South Africa, Johannesburg, Chris Hani Baragwanath Hospital[24,25]	1992 1993 1994 1995 1996	1.75 3 5.95 9 13.45	Paediatric Paediatric Paediatric Paediatric Paediatric	7.1/3.2*[§] 14/5.6*[§] 23/7.5*[§] 31/11*[§] 42/19*[§]	Pneumonia: 55 Gastroenteritis: 12 Septicaemia: 9.2 Meningitis: 3.4
South Africa, Hlabisa Hospital[25,26]	1996/97	16.3	Paediatric	26*	Diarrhoea: 51 Malnutrition: 18 Acute respiratory infection: 13
South Africa, Soweto, tertiary care hospital[25,27]	1996	11.8	0 - 5 yr	29*	Pneumonia: 81 Malnourished: 66 Gastroenteritis: 32
South Africa, Durban, King Edward VIII Hospital[25,28]	1998	19.2	Paediatric	63*	Acute pneumonia Gastrointestinal Neurological
Tanzania, Dar es Salaam, Muhimbili Medical Center[29,30]	1995/96	12.2	1 - 3 mo. 4 - 6 mo. 7 - 9 mo. 10 - 12 mo. 13 - 18 mo. 19 - 24 mo. 25 - 36 mo. 37 - 48 mo. 48 - 84 mo. Total	25* 21* 17* 19* 20* 21 16 14 19 19	Acute respiratory infections: 39 Malnutrition: 38 Tuberculosis: 19 Malaria: 18 Diarrhoea: 12

*Prevalence determined by antibody test except for marked estimates, where PCR or other tests or procedures were used to determine HIV infection in young children with possible antibodies from their mothers.
[†]The table shows HIV prevalence in antenatal women from the WHO's Epidemiological Fact Sheets, as follows: Abidjan in 1991; in 1985 only for DRC children 1984/85; for South African studies, median for urban or rural antenatal clinics for the year (or first year) of each study; median for Dar es Salaam in 1995.
[‡]Includes HIV-1 and HIV-2.
[§]Not all children were tested for HIV. The first number gives the percentage of HIV-positive children among tested children; the number after the slash reports the percentage who tested HIV-positive among all children admitted, including children not tested.
DRC= Democratic Republic of Congo.

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8 versus 6 days in Soweto,[27] and 18.5 versus 11.9 days in the Western Cape in 1996.[1]

In outpatient settings, routine medical care — such as vaccinations — draws children equally, whether infected or not. Hence, HIV prevalence in outpatient children should be intermediate between prevalence in inpatient children and in all children. In Kinshasa in 1986, 12 outpatient children (3%) aged 9 months - 12 years old were HIV-positive,[31] roughly half of 5.6% HIV prevalence in antenatal women.[22] In South Africa in 2002, 29% of outpatient children aged 2 - 59 months seen at a district hospital in KwaZulu-Natal were HIV-infected,[32] which is somewhat more than the 24.8% prevalence reported nationally for women in 2001.[33] From this admittedly sparse information, HIV prevalence among paediatric outpatients may be estimated very roughly to range from 0.5 to 1 or more times the HIV prevalence in women seen for antenatal services in the same community.

Risks of HIV transmission to other children and to health care workers

The risk of HIV transmission from infected children to others exposed to the health care system depends on the viral load, the specific procedures involved, and the care taken to implement infection control and universal precautions.

Viral load in children

Infected infants characteristically have HIV viral loads 10 - 100 times higher than those found in adults. High viral loads are associated with efficient HIV transmission. In a study of HIV-infected children in the USA with little or no experience with antiretroviral therapy, the mean reported viral load for 164 children aged from 3 to less than 12 months was $6.0 \log_{10}$ RNA copies/ml in plasma, falling to $5.2 \log_{10}$ copies/ml for children aged 12 to under 30 months.[34] In a similar study of HIV-infected children in the USA and Puerto Rico, the geometric mean RNA virus load in serum for children aged less than a year was $5.6 \log_{10}$ copies/ml; this mean did not fall below $5.0 \log_{10}$ copies/ml until 3 years of age.[35] A study of African children reported geometric mean RNA titres of $5.3 - 5.5 \log_{10}$ copies/ml (from dried blood spots) in the first year for those infected *in utero*, at birth, or from early breast-feeding.[36] These rates can be compared with viral loads in HIV-infected adults of $6 - 7 \log_{10}$ copies/ml during primary infection (the most infectious period), after which the load drops to a plateau with characteristically slow growth.[35,37] In Uganda, the mean serum viral load among 415 rural HIV-infected adults was $4.02 \log_{10}$ RNA copies/ml.[38]

Health care prodedures to treat HIV-infected children

The most common symptoms and diagnoses for HIV-infected

children in Africa include failure to thrive, malnutrition, gastrointestinal disorders, and acute and chronic respiratory symptoms. Injections of antibiotics to treat respiratory illness and childhood fevers are common in Africa, as is administration of intravenous saline for rehydration of patients with diarrhoea. In addition, many febrile children are treated for suspected malaria with drugs delivered through intravenous catheters.
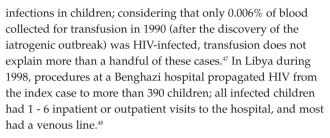
For all children in Africa, home, traditional, or outpatient care are more common for rural and poorer children[39] and in countries with less developed public health systems. HIV-infected children from wealthier families and in urban communities and countries with more developed public health systems are more likely to be treated as inpatients. Hence, risk for horizontal transmission in health care settings may well vary directly according to wealth and development of the community and country unless adequate care is taken to implement universal precautions.

Frequency of unsterile procedures

From observation of injections in formal and public health settings several recent WHO studies have estimated that 50%[40] and 17 - 19%[41] of medical injections in Africa are administered with equipment re-used without sterilisation. Adherence to universal precautions in private and informal settings and for other procedures – such as minor surgery and dental care – may be more or less common. Many clinics and hospitals in Africa lack working sterilisers, fuel or electricity, disinfectants, and other supplies to facilitate sterile procedures.[42,43] Transfusion of untested blood poses an additional risk for African children, although in this instance HIV transmission would be from adult donors rather than from other children. The WHO's Regional Office for Africa estimates that 25% of blood transfused regionally during 2001 was not screened for HIV.[44]

Transmission efficiency through unsterile procedures in paediatric health care

Documented outbreaks of iatrogenic HIV infection among children in three countries provide some sense of HIV transmission efficiency in paediatric settings. Medical procedures at two hospitals in Elista, Russia, were implicated in the propagation of HIV from the index child to 90 other children during an 11-month period in 1988, during which time the number of infections doubled, on average, in less than 2 months. Because, presumably, many HIV-infected children returned home, the true average time for an infected, hospitalised child to transmit to another may have been closer to weeks than months. Overall, an investigation of the outbreak in 1988/89 found 250 children in Elista and elsewhere in the region with linked nosocomial infections.[45,46] In Romania during 1989/91, physicians identified more than 1 000 iatrogenic

infections in children; considering that only 0.006% of blood collected for transfusion in 1990 (after the discovery of the iatrogenic outbreak) was HIV-infected, transfusion does not explain more than a handful of these cases.[47] In Libya during 1998, procedures at a Benghazi hospital propagated HIV from the index case to more than 390 children; all infected children had 1 - 6 inpatient or outpatient visits to the hospital, and most had a venous line.[48]

Although the risk for HIV seroconversion in health care workers after a single contaminated needlestick injury has been estimated at 0.3%,[49] a case control study[50] in the USA and Europe reported an adjusted odds ratio (OR) of 15 for deep needlesticks (with the berm of the needle penetrating the skin, so that the lumen is buried). Based on this finding, the risk for seroconversion after an average deep needlestick is estimated to be 2.3%.[46] Because unsafe injections are comparable to deep needlesticks — followed by washing the inside of the syringe and needle into the wound — this is a better but still uncertain estimate of the risk from unsafe medical injections. The same case control study reported adjusted ORs of 5.6 for terminal illness in source patient (read: high viral load), and 0.19 for post-exposure prophylaxis. High viral load in the source patient and absence of post-exposure prophylaxis for children unknowingly exposed to contaminated procedures are likely conditions for amplified HIV transmission risk during paediatric health care in Africa. Moreover, HIV can survive drying at room temperature for days, and for weeks in wet conditions, allowing delayed transmission through unboiled and unwashed syringes, multidose vials, or rinsing pans.[51-54]

Evidence for iatrogenic HIV infection in African children

From 1984 through early 2003, at least 312 African children with non-vertically transmitted HIV infection have been reported in medical articles, conference abstracts, and other publications (Table III). Several of these publications reported results from case control studies showing that HIV-positive children with HIV-negative mothers had more and/or more frequent medical injections than HIV-negative children with HIV-negative mothers.[21,67,68] In a study in South Africa,[71] most infected children with HIV-negative mothers had been hospitalised and had had an intravenous line. Although 124 (40%) of 312 children with anomalous HIV infections were reported to have received blood or blood products, few studies traced donors to confirm epidemiological linkage.

In addition to iatrogenic exposures, several other explanations have been supposed and/or demonstrated to account for non-vertical paediatric infections including transmission by an HIV-infected wet nurse, accidental switching of babies at birth, sexual abuse,[71,75] and precocious sexual activity. Considering the low efficiency of HIV transmission through sexual exposure — even for child rape[3,78,79] — sexual abuse and premature sexual activity cannot explain more than exceptional cases; similarly, infected wet nurses and the switching of babies are unlikely to account for more than rare cases. In many studies (Table III), more than 10% of HIV-infected children had HIV-negative mothers, suggesting that non-vertical infections are common in many communities; hence, iatrogenic transmission would seem to be the best explanation for most cases.

Other evidence suggestive of iatrogenic HIV transmission to African children comes from the limited number of random sample surveys that have sought HIV markers in African children aged 5 - 14 years (Table IV). HIV prevalence contributed by vertical transmission in that age interval is not likely to be common. For example, in South Africa during 2002 the 5.6% HIV prevalence reported in children aged 2 - 14 years in a national household survey is several times greater than expected from vertical transmission.[3] Similarly, 4.2% HIV prevalence in urban Rwandan children 6 - 15 years old in 1986 is much greater than could be expected from vertical transmission. On the other hand, some African studies have reported low HIV prevalence in children – for example, 0.4% of children aged 5 - 12 years in a rural community in Uganda,[75] suggesting that, at least in those communities, non-vertical HIV transmission to children has been uncommon.

In 1992, Quinn and colleagues[10] estimated that '15% [of HIV-infected children worldwide, of which 80% are in Africa] acquired infection parenterally from unscreened blood transfusions or through exposure to blood-contaminated needles and syringes'. The evidence supporting this estimate is not clear. The true figure could be higher or lower, and presumably varies across countries and communities.

Discussion

Our review of the published evidence for the presence and provenance of paediatric HIV infection in Africa is limited by the inadequate attention paid to the phenomenon by physicians and researchers in the region. Yet sufficient data exist to suggest that non-vertical and non-sexual transmission to children may be a common event. This review focuses on HIV infection only, and so underestimates the iatrogenic burden, which includes illness from hepatitis B and C viruses and other pathogens transmissible through health care procedures.

Importantly, the large number of recorded HIV-infected children in Africa whose mothers test negative for HIV suggests that a much larger number of untested African children may have been infected through health care procedures than previously realised. In Russia in 1988/89, the investigations that found 250 iatrogenic HIV infections in children were triggered by an unexplained infection in a single

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Table III. Reported HIV-positive African children with HIV-negative mothers

Country	Year of blood samples	Population studied	HIV+ children with HIV- mothers		
			Number	As % of all HIV+ children (%)	Number who had received blood or blood products*
Rwanda, Tanzania, Belgium[56]	1990/91? NA	Inpatients 6 - 59 m Children in families immigrating from Africa	65[†] 7	NA 5.9	3 7
Angola[57]	1988/93	Children in Cabinda	26	NA	24
Burkina Faso[58]	1989/90	Inpatients > 1 yr with malnutrition	11	23	6
Cote d'Ivoire[59]	1987/88	Paediatric patients	26	14	NA
Cote d'Ivoire[60]	1989	Inpatient and healthy children 15 - 60 m	5	23	5
Cote d'Ivoire[61]	No date	Children of selected women	3[‡]	20	NA
DRC[21]	1985	Inpatients and outpatients 1 - 24 mo.	17	39	5
DRC[62,63]	1986	Inpatients 1 m - 12 yr in a malaria study	5[§]	NA	5*
Ethiopia[64]	1994	Children ≤ 5 yr in community-based survey	1	≥ 33	NA
Guinea-Bissau[65]	1987/89	Children in a community-based survey	1	≥ 50	NA
Nigeria[66]	1989/95	Children 0 - 16 yr seen at a hospital	50	79	30
Rwanda[67,68]	1984/86	Children 6 - 48 mo. with AIDS seen at hospital	15	20	6
Rwanda[69]	1984/90	Children with AIDS seen at hospital	39[¶]	5.7	16[¶]
South Africa[70]	2002	Case reported in a newspaper	1	NA	0
South Africa[71,72]	1996 - 2003	Children < 13 yr reported to a registry	15	NA	5*
Tanzania[73]	1988	Malnourished children 3 - 88 mo.	7	15	7
Uganda[74]	1985/90	Children seen at hospital	4	2	NA
Uganda[75]	1989/90	Children 0 - 14 yr seen in community study	5	18	1
Uganda[76]	1986/90	Children < 16 yr with Kaposi's sarcoma	4	24	4
Uganda[77]	1989/94	Children < 15 yr with Kaposi's sarcoma	5	19	NA
Total			312		124

*Few studies traced blood donors. In DRC 1986, 5 children seroconverted from before to after blood transfusion, but only 1 donor (the father of 1 child) could be traced. In South Africa 1996 - 2003, all blood donors were negative for all 5 case children transfused.
[†]Including 4 incident cases observed during follow-up.
[‡]Two children with HIV-1 negative mothers had HIV-1 infections; 1 with an HIV-negative mother was dually infected with HIV-1 and HIV-2 infections.
[§]For these 5 children, the HIV status of their mother is unknown; all 5 first tested HIV-negative, then HIV-positive after blood transfusions.
[¶]Excluding 15 HIV-positive children with HIV-negative mothers (including 6 children with transfusions) reported in 1984/86, although it is not clear from the text whether or not cases have been double-counted.
NA= not available or not applicable. DRC= Democratic Republic of Congo.

Table IV. HIV in children 5 - 14 years old

Country	Year	Population	HIV prevalence (%)
Rwanda[80]	1986	Urban, 5 - 16 years old	4.2
		Rural, 5 - 16 years old	1.7
Rwanda[81]	1997	National survey, 2 - 14 years old	4.2
South Africa[33]	2002	National survey, 2 - 14 years old	5.6
Tanzania[82]	1989	Rural boys, 10 - 15 years old	3.3
		Rural girls, 10 - 15 years old	3.7

child.[83] Similarly, the investigations that uncovered over 1 000 iatrogenic infections in Romanian children in 1989/91 were set in motion by 1 unexplained infection.[47] In documented iatrogenic HIV outbreaks in Russia, Romania, and Libya, paediatric HIV infections multiplied rapidly from a limited number of index cases. In Africa, most of the more than 5 million children vertically infected over the past decade have been treated as outpatients and/or inpatients for HIV-related symptoms. The extent to which these millions of vertically infected children transmitted HIV to others is unknown.

The evidence for widespread unsterile procedures in African medical settings and non-vertical infections in African children calls for new initiatives to strengthen infection control in formal and informal health care settings and to test transfused blood. Additionally, because health care workers in paediatric wards are at risk from needlestick accidents in settings with high HIV prevalence and high viral load among patients,[84] steps to protect health care workers – training and providing equipment for consistent implementation of universal precautions – are reasonable components of such initiatives.

Yet, more is necessary. Investigations of non-vertical HIV infections in children – tracing and testing other children who shared clinics and medical procedures with the infected child to determine the source of the infection and number of linked iatrogenic infections, if any – are required to determine the scale of the problem and to identify high-risk procedures and clinics for preventive interventions. Continuing failure to search for and to investigate anomalous HIV infections in children sends the message, to both patients and health care providers, that iatrogenic HIV transmission is 'acceptable' at some unknown level. Even with ambitious efforts to improve infection control in health care settings, it is unreasonable to ask that patients and parents of paediatric patients trust the safety of health care procedures without thorough investigations and public reports of anomalous HIV infections. Hence, investigations are necessary not only to motivate and guide prevention efforts but also to reassure the public that the medical establishment and civil authorities have a zero-tolerance policy for HIV transmission through health care.

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