

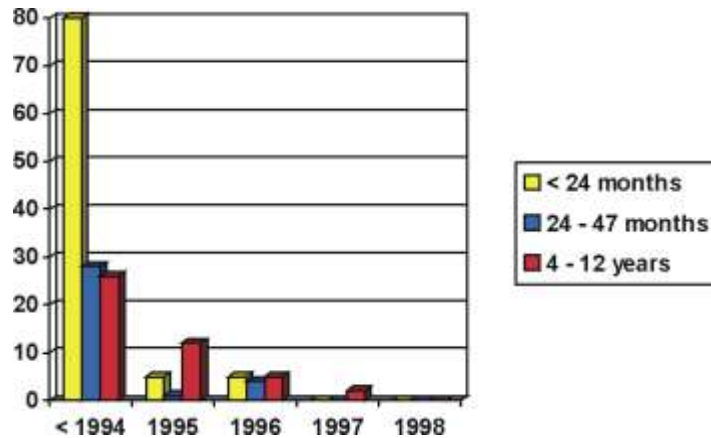
VIH/SIDA en Pediatría: Epidemiología Mundial, Transmisión Perinatal, Manejo Integral.

Juan Carlos Salazar, M.D. – Universidad de Connecticut, EE.UU.

End-1998 global estimates
Children (<15 years)

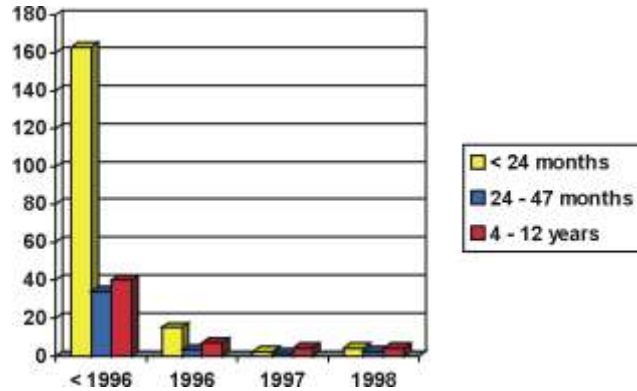
- | | |
|---|--------------------|
| • Children living with HIV/AIDS | 1.2 million |
| • New HIV infections in 1998 | 590 000 |
| • Deaths due to HIV/AIDS in 1998 | 510 000 |
| • Cumulative number of deaths due to HIV/AIDS | 3.2 million |
| • Cumulative number of children estimated to have been orphaned by AIDS* at age 14 or younger at the end of 1997 | 12 million |

Trends in Pediatric AIDS cases, by age at diagnosis and year of report, CT, 1981-98

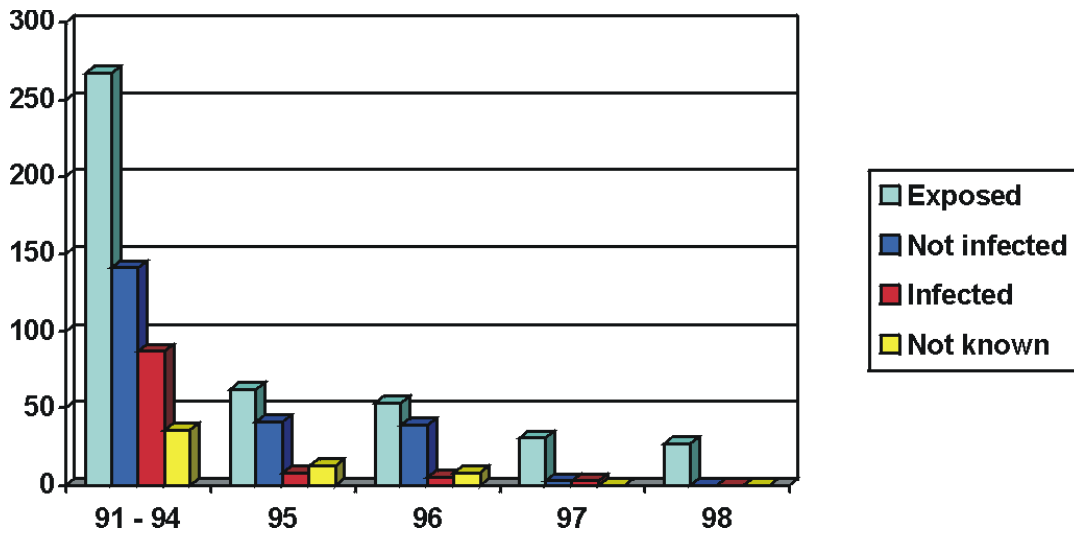


Source: HIV/AIDS annual report, 1997, CDPH

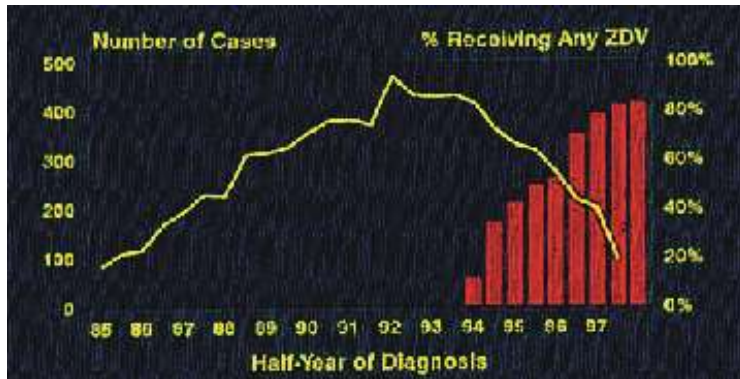
Trends in Pediatric HIV - AIDS cases, by age at diagnosis and year of report, CT, 1981-98



Connecticut Children Reported With a Perinatal HIV Exposure, by Year of Birth and Current HIV Status (83-98)

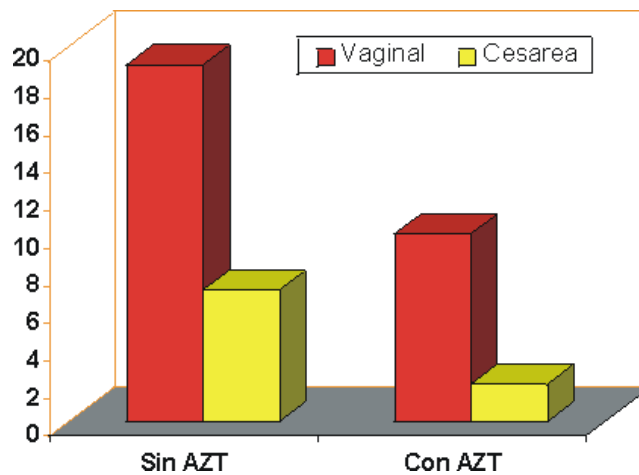


**No. Perinatally-Acquired AIDS by Half-Year Dx & Receipt of Any ZDV
 (prenatal, intrapartum, neonatal) Lindgren ML, et al, 6th Retro Conf,
 1999 Abs 228**



Among HIV + women, diagnosed before birth, 29 States, USA

**Perinatal Transmission, Vaginal vs C-section.
 Read J, NEJM, April 1, 1999**



8,533 pairs

Pediatric HIV: Diagnosis

- HIV DNA PCR:

— 48 hrs: **38% (90% CI; 29 - 46%)**

— **2 weeks: 93% (90% CI; 76 - 97%)**

- Other methods

- **HIV RNA PCR**

- **Viral culture**

- **Ag: p24 (poor specificity before age 1 m.)**

- When to test?

- **48 hrs, 2 weeks - 2 months, 3 - 6 months.**

Pediatric HIV: Clinical Classification

Immunologic Compromise	Clinical Manifestations			
	N	A	B	C
None	N1	A1	B1	C1
Moderate	N2	A2	B2	C2
Severe	N3	A3	B3	C3

If the infection is not confirmed, add the letter E (exposed)

Immunologic – Classification

Clinical Manifestations

- **Rapid progressors** (in utero infection)
 - Disease in the first year of life
 - Failure to thrive
 - Progressive encephalopathy
 - PCP pneumonia
 - Death at age three
- **Slow progressors** (intrapartum 70%)
 - manifestations at 2 - 5 years of life
 - LIP< lymphadenopathy
 - Recurrent bacterial infections
 - Death after five years
- **Long term progressors** (<1%)
 - Clinical manifestations after 10 years

Clinical Manifestations

- **Inmunopathogenesis (Rapid progressors)**
 - High viral replication (1 billion particles per day)
 - Persistently high viral load (>100,000 copies)
 - Severe immunologic compromise
 - Marked decrease in CD4 + t-lymphocytes
 - Alteration of CD8 lymphocytes + (cytotoxicity)
 - Alter lymphokine production (IL-2, interf, etc.)
 - Absent or diminished cellular immunity
 - Alteration in B lymphocyte function

Clinical Manifestations

- Lymphadenopathy
- Organomegaly
- Chronic parotitis
- Chronic rinorrhea
- Exanthems
 - candida
- eczematoid

Clinical Manifestations

- Growth
 - Drop in Height and Weight.
 - Drop is symmetric.
 - Differences can be seen by the 4th month.

Clinical Manifestations

- **Opportunistic Infections**
 - PCP is most common
 - Candidiasis (thrush)
 - Esophagitis
 - Others (MAI/MAC, CMV, Cryptosporidium)
- **Recurrent Bacterial Infections**
 - Otitis media, pneumonia, bacteremia/sepsis
- **Neoplasias (rare)**

Natural History of HIV in Children

- Developed Nations
 - 1983 - 1993
 - 1993 - 2000+
- Developing Nations
 - Africa
 - Latin America

Natural History Developed Nations 1983 – 1993

- **1983 - HIV discovered as cause of AIDS**
- **1983 - Literature reports of children with AIDS**
 - Children born to women with AIDS
 - Children with hemophilia
 - Associated with transfusions
- **1984 - Vertical Transmission Documented**
 - Three children infected - same mother with 3 diff partners
- **1985 - ELISA becomes available**
- **1988 - CDC reports 1346 pediatric AIDS cases**
 - Transfusion (14%), Perinatal (76%), Hemophilia (4%)

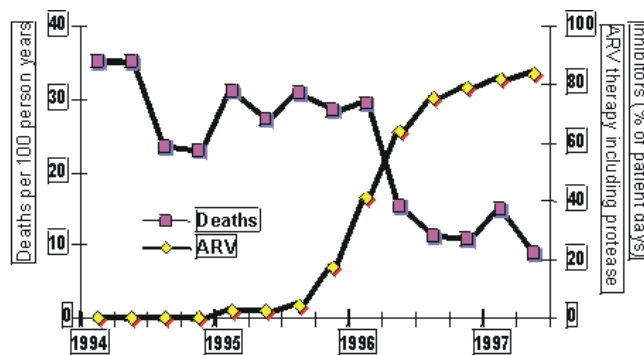
Natural History Developed Nations 1983 – 1993

- Monotherapy with nucleoside analogues
 - Zidovudine (ZDV, Retrovir)
 - Alters progression of HIV encephalopathy (Pizzo, et al. NEJM, 1988;319:889-896.)
 - FDA approves AZT to be used in children
 - Didanosine (ddI, Videx)
 - Zalcitabine (ddC, Hivid)
- Quality of life improves in general, weight gain, slows down progression of the disease.
- Limited effect because of rapid emergence of resistance
- ACTG 152 (ddI + AZT vs ddI): combined therapy is better

Natural History Developed Nations > 1993

- Prevention in perinatal transmission (ACTG 076)
- Early diagnosis (HIV DNA PCR and HIV RNA PCR)
- Improvements in understanding, pediatric HIV pathophysiology.
 - CD4 cell count normograms, appropriate for age.
 - Viral load in children.
- Advances in therapy
 - Combined therapy (HAART)
 - New preparations in pediatric HIV therapy.

Mortality in patients with CD4<100 of antiretroviral (ARV) therapy including a protease inhibitor among those patients, USA, 1994–1997



Source: Palella et al., *New England Journal of Medicine*, 1996 Mar, 26:336-60

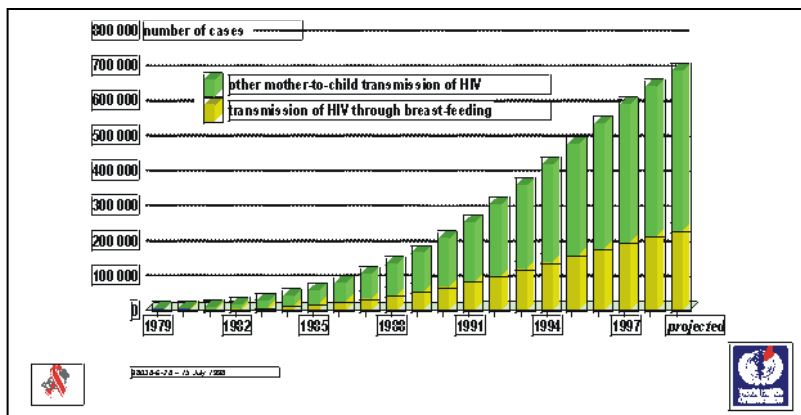


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Natural History Developing Nations

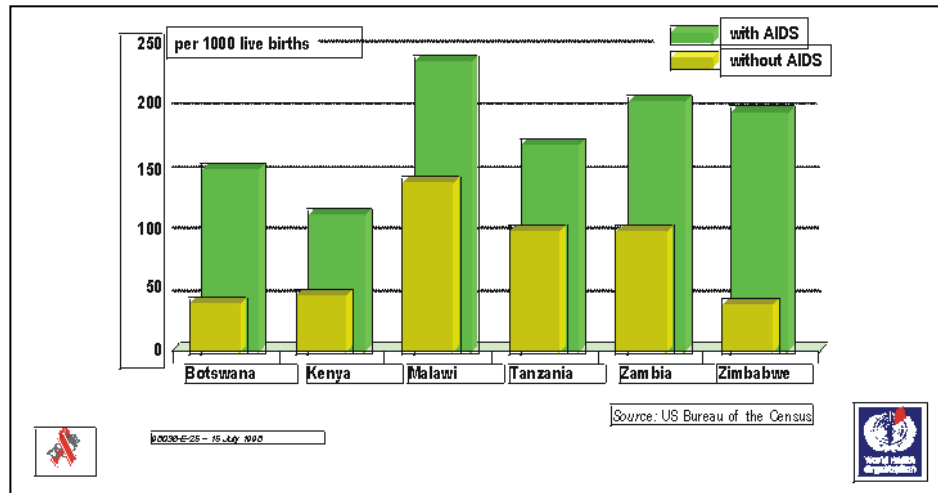
Mother-to-child transmission of HIV
Estimated number of children newly infected in the world



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Estimated impact of AIDS on under-5 child mortality rates – Selected African countries, 2010



Pediatric HIV: AFRICA

- Heterosexual transmission in adults
- HIV1 and HIV2, both prevalent.
- Vertical transmission is common, breast feeding adds risk.
- ACTG 076 hard to implement because of cost
- Shortened protocols beneficial (Thailand)
- Most frequent cause of death:
 - IRA, Desnutrición
 - Anemia, Malaria
 - EDA, Meningitis

Pediatric HIV: AFRICA

- Definition (WHO guidelines)
 - Major manifestations
 - Weight loss
 - Chronic diarrhea
 - Fever > 1 month
 - Recurrent pneumonia
 - Minor manifestations
 - Generalized lymphadenopathy
 - Oral candidiasis
 - Recurrent common infections
 - Confirmed maternal infection

Latin America / Caribbean

Pediatric HIV: Latin America / Caribbean

- Simone SJ, et al. Natural history of human immunodeficiency virus 1 infection in Haitian infants. *Pediatr Infect Dis J*, Jan, 1999
 - Prospective study 81 HIV exposed children and 88 controls.
 - Followed for two years (no therapy).
 - 27% (22) infected (Dx with p24)
 - Mortality < 6 months
 - Exposed/ Infected: 60% (14/22)
 - Exposed not infected: 4% (2)
 - Controls - 6% (5)
 - 6/19 deaths - failure to thrive + gastroenteritis = sepsis, meningitis, pneumonia.
- Conclusions
 - High mortality in first 6 months of life
 - Factors independent from HIV contributed to the high mortality

Clinical findings at the last visit before death in Haitian children

