

Prevention and Treatment of HIV-infection in Children

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Outline

- Prevention of Vertical Transmission of HIV
- Treatment of HIV-infected Children
- Recent Important Advances

- 1981

- First launch of a space shuttle
- Prince Charles and Lady Diana wed
- First reports of homosexual men dying due to immunodeficiency

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1981 June 5;30:250–2

Pneumocystis Pneumonia – Los Angeles

In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal mucosal infection. Case reports of these patients follow.



HIV Early Milestones

- 1987-
 - FDA approved AZT (zidovudine, retrovir, ZDV); the first anti-retroviral agent
- 1989-
 - FDA approved ZDV syrup; could treat children.
- First studies showed that treatment with ZDV improved outcome in children; later studies showed treatment with 2 drugs was better than 1.
 - DDI, 3TC, d4T, ddC were licensed between 1990-1994.
- Still, outcomes poor and medications only slowed progression.

Challenges in Children

- Consistent delay between approval in adults and children
- Not always a pediatric formulation
- Pediatric formulation not always palatable
- ART resistance among young adults who were treated with sequential mono/dual therapy

What HAART meant

- Our 18 year old pre-pubertal, cachectic patient with no CD4 cells, had complete viral suppression and became an adult.
- Several of the younger children went from being sickly, wasted, and struggling infants to looking and acting like normal children.
- We could treat children soon after birth, when their HIV infection was first diagnosed, preventing the damage often caused by HIV.

Approach to treatment of HIV-infected children

- Diagnosis of Infection
 - Use RNA or DNA PCR if <18 months of age
 - Birth, 4-6 weeks, 4 months (if not breastfed)
 - Collect a confirmatory test if any positive
- Initiation of therapy
 - Treat as early as possible
 - Children treated at <3 months of life who remain suppressed often don't develop antibodies
- NVP vs Kaletra vs Raltegravir- based ART in infants (generally with ZDV and 3TC or FTC)

What HAART meant

- Once child can swallow tablets, and weights at least 25 kg, single tab combo are available



Genvoya



Biktarvy

Treatment limitations

- No cure (one, maybe two, cures)
- Therapy is lifelong
- Therapy is expensive
- The rate of increasing ART distribution does not keep pace with the number of new infections.

How Can We Prevent New HIV infections?

- Children
 - Prevention of MTCT
- Adolescents and Adults
 - Male circumcision
 - Progress in HIV vaccine
 - Pre-exposure prophylaxis
 - Treatment as prevention

Prevention of Vertical Transmission of HIV

- Given the availability of AZT, the known association of transmission with advanced HIV and viral load, and the high mortality of pediatric AIDS, pediatric and obstetric researchers proposed giving AZT to infected pregnant women to reduce MTCT.
- However, giving a potentially toxic drug to pregnant women was controversial; an FDA hearing was held prior to final FDA approval of the protocol.

POISONING OUR CHILDREN

AZT in pregnancy

Anthony Brink

Open books



One major advance in 1994

- 1994 the results of the study PACTG 076 were released.
- ZDV treatment to moms during pregnancy and intrapartum and to their infants for the first 6 weeks reduced transmission of HIV from 25% to 8%.
- When implemented in the field, results were the same or even a little better.
- Later studies showed that 2 doses NVP was almost as effective.



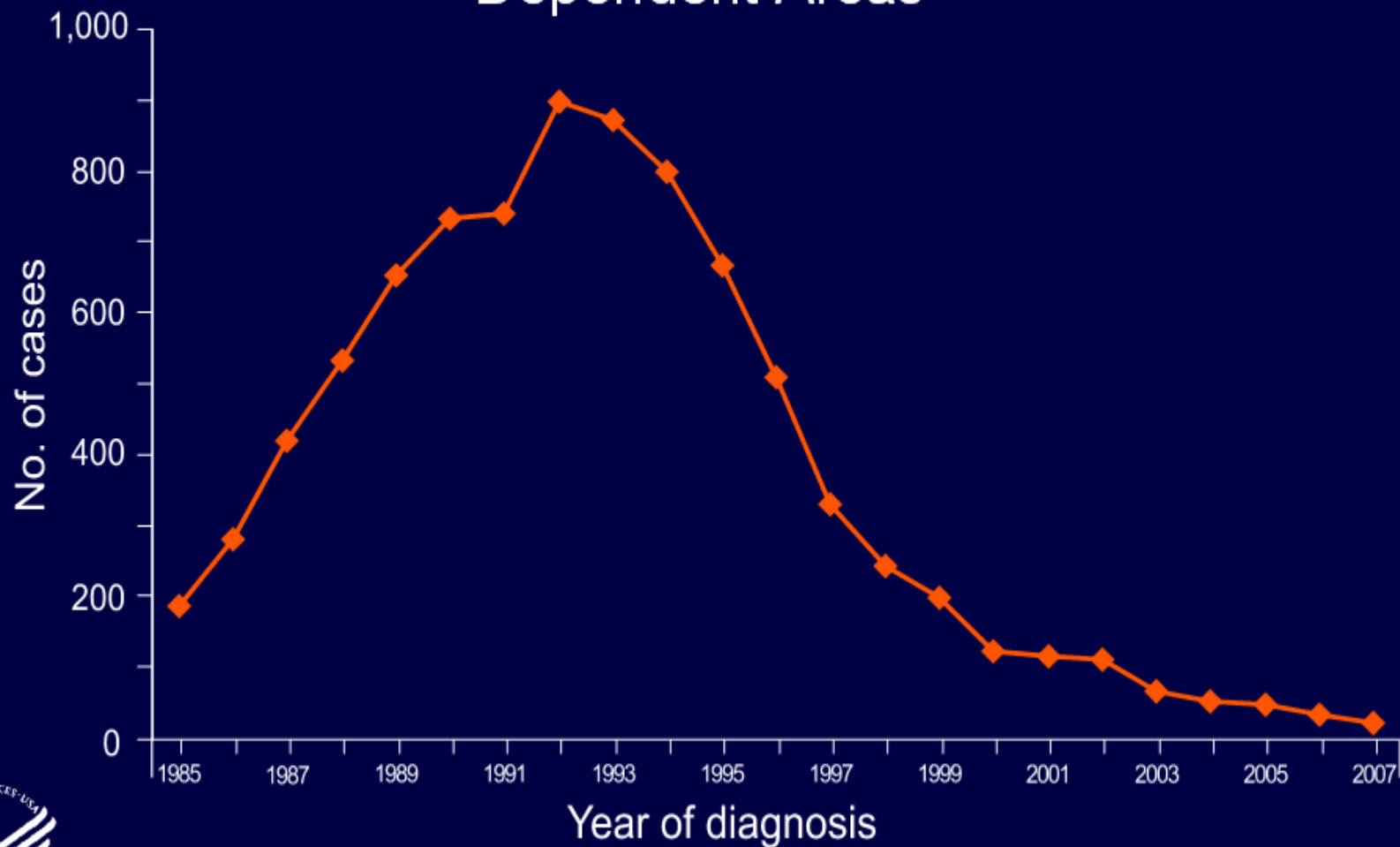
1999 initiated “Call to Action”- a program designed to bring HIV testing to pregnant women and provide treatment to prevent mother to child HIV transmission to those women found to be infected.

Over subsequent years, this program expanded through private donations and then through PEPFAR to provide support in 17 countries.

Prevention of Vertical HIV transmission

- Developed countries-
 - Combination ART to mom
 - AZT to baby, no breastfeeding
 - C-section if detectable virus.
 - All efforts combined- transmission <1%
- Developing countries-
 - Combination ART through pregnancy and breast feeding or for life
 - Generally, exclusive breastfeeding through 6 months
 - NVP to infant if mom not on HAART
 - Transmission risk reduced but variable

Estimated Numbers of Perinatally Acquired AIDS Cases by Year of Diagnosis, 1985–2007—United States and Dependent Areas



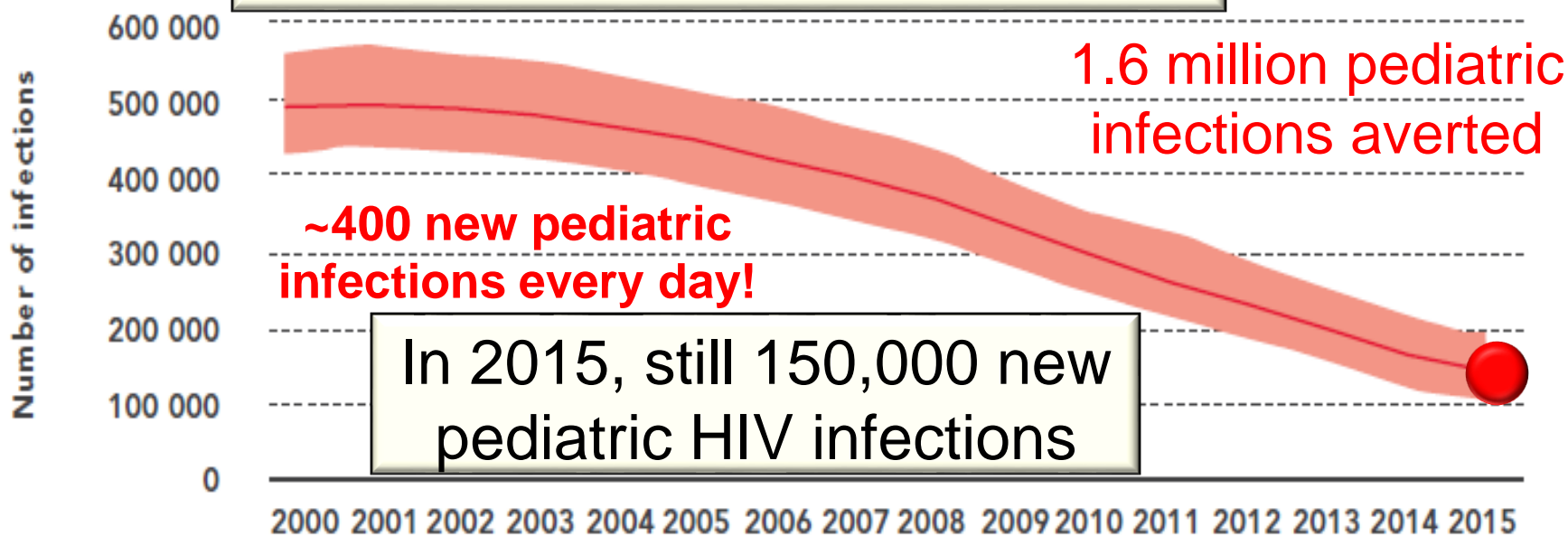
Note. Data have been adjusted for reporting delays and missing risk-factor information.



Where are We in the Plan to Eliminate New Pediatric HIV Infections?

Major Progress in Preventing Perinatal Infection Since 2000

But we have not yet reached the goal of global elimination of MTCT



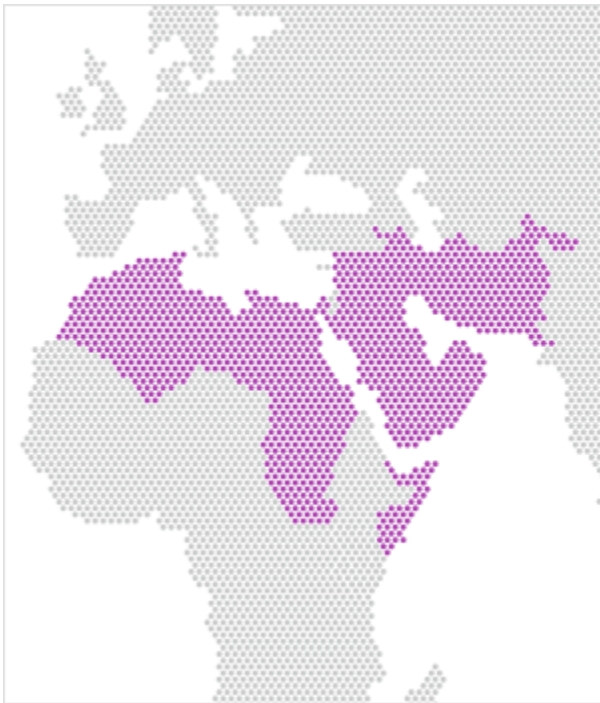
In 2015, still 150,000 new pediatric HIV infections

70% decrease in new pediatric infections since 2000



Towards an AIDS-free world for children
A global push to end pediatric AIDS

HIV in the Middle East



Middle East & North Africa (2017)

220,000 people living with HIV

<0.1% adult HIV prevalence (ages 15-49)

18,000 new HIV infections

9,800 AIDS-related deaths

29% adults on antiretroviral treatment*

35% children on antiretroviral treatment*

*All adults/children living with HIV

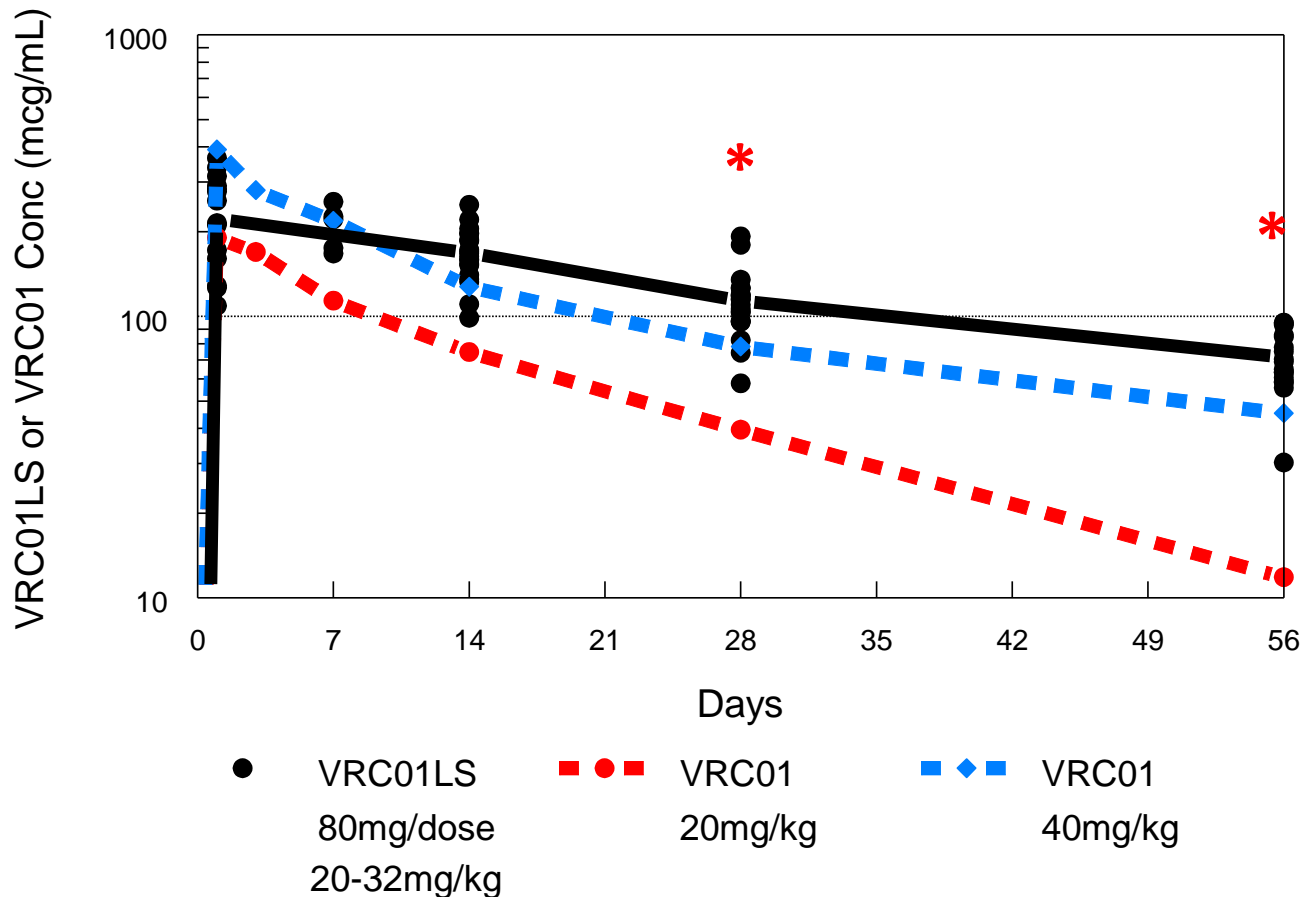
Source: UNAIDS Data 2018

Prevention of Vertical Transmission of HIV

- Universal testing of pregnant women
- ART for all infected women, especially those who are pregnant
- If mother not virologically suppressed, then C- section for delivery
- Antiretrovirals for the infant, ZDV or NVP alone, if low risk, combination therapy, if high risk
- Additional therapies are needed.....

Infants receiving VRC01LS (Dose Group 4) achieve significantly higher levels than those receiving VRC01

* VRC01LS vs. VRC01 40mg/kg p < 0.002



Take home messages

- If diagnose HIV infection in woman, please test all her children.
- Treat infected children as early as possible.
- Test all women during pregnancy, treat with ART starting early, and aim for RNA “undetectable” before delivery.
- Continue ART in mom, if breastfeeding
- Treat infant for 4-6 weeks post delivery
- Keep your eye out for new developments in long acting agents