

FRIENDS OF NICHD COALITION

**The Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health**

Friends of NICHD Webinar:

NICHD's Pediatric, Adolescent, & Maternal AIDS Branch



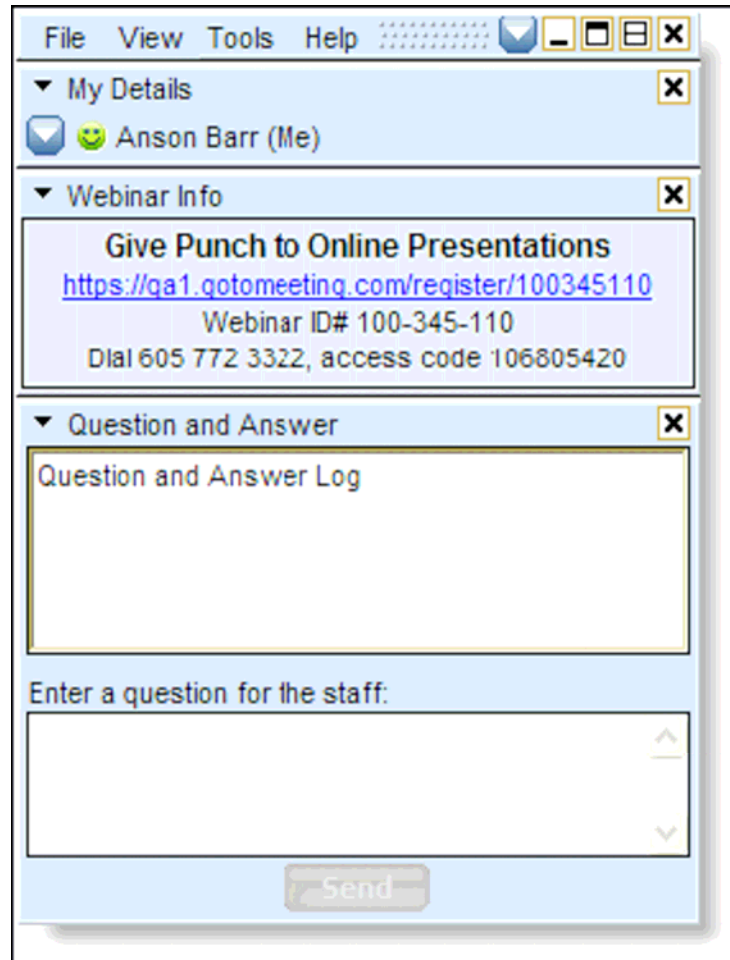
Lynne Mofenson, MD Branch Chief

December 19, 2008

Please call in-Dial: 888-517-2197

Code:7080363

Webinar Guidelines



Sample webinar screen

- All participants lines will be MUTED during the presentation
- Operator will facilitate the Q&A session
- Participants may submit questions online during presentation through Go To Webinar text box at any time

BIOGRAPHICAL SKETCH: Lynne M. Mofenson, M.D.

Dr. Mofenson is an infectious disease specialist and Board-Certified pediatrician. Dr. Mofenson received her medical degree from Albert Einstein College of Medicine (Alpha Omega Alpha) in 1977, followed by a pediatric residency at Boston Children's Hospital, and a pediatric Chief Residency and joint adult/pediatric infectious disease fellowship at the University of Massachusetts Medical School. She is currently Chief, Pediatric, Adolescent & Maternal AIDS Branch at the National Institute of Child Health and Human Development, National Institutes of Health, where she has worked since 1989 and been Chief since 2000. Dr. Mofenson is responsible for program planning and the development and scientific direction of research studies and clinical trials in domestic and international pediatric, adolescent and maternal HIV infection, disease and AIDS. She has published and lectured extensively on issues related to perinatal HIV transmission and prevention and on treatment of pediatric HIV infection, and is involved in clinical trials of HIV treatment in children and women and prevention mother-to-child HIV transmission in the United States and internationally.



Pediatric, Adolescent, and Maternal AIDS Branch

Research focus areas: Epidemiology, clinical manifestations, pathogenesis, transmission, treatment, and prevention of HIV infection and its complications in:

Infants, Children, Adolescents, and Pregnant/Non-Pregnant Women

PAMAB has Long History of Successful Collaborations with Multiple Groups



National Institute of Allergy
and Infectious Diseases

NICHD co-funding Leadership group:

IMPAACT
MTN

Collaboration with NICHD Networks:

IMPAACT
AACTG
MTN
HVTN

NICHD cofunding:

WIHS
leDEA
Predict

NIAID cofunding:

PHACS



NIMH cofunding:

ATN
PHACS



National Institute on Deafness and
Other Communication Disorders

NIDCD cofunding: PHACS



National Heart, Lung and Blood
Institute

NHLBI cofunding: PHACS



PAMA BRANCH



WHO

NICHD/CDC cofunding:
WHO breastfeeding trial



PENTA

Collaboration with NICHD Network



PEPFAR

Grant supplements
Staff on committees



CDC

NICHD cofunding:
Breastfeeding trials

What Progress Has Been Made?

What Challenges Remain?

**How is PAMAB Addressing
These Challenges?**



Prevention of Mother-to-Child HIV Transmission in the U.S.





Progress on Reducing Mother-to-Child HIV Transmission (MTCT) in the U.S.

- **About 9,000 HIV-infected women give birth each year in the U.S.**
- **NIH-funded research has identified interventions that have reduced mother to child transmission to <2% in the U.S.**
- **The number of infected infants born each year in U.S. has decreased from 2,000 before 1994 to under 200 currently.**

Consequences of Successful Prevention of Mother to Child Transmission in the U.S.



- Dramatic reduction in annual new perinatal infections in U.S.
- However thousands of infants who are now uninfected have *in utero* exposure to multiple drugs with limited data on long-term safety.



- Decrease in new infections and availability of potent therapy results in a cohort of HIV-infected children now aging into adolescence.
- HIV has become a chronic disease with all its challenges such as adherence to therapy, psychosocial challenges.



Pediatric HIV/AIDS Cohort Study

- Unique trans-Institute effort led by NICHD in collaboration with NIAID, NIMH, NIDA, NIDCD, NHLBI, and NCI collaboration.

- Addressing 2 major domestic questions:

- Evaluation long-term safety of fetal/neonatal exposure to antiretroviral prophylaxis in HIV-exposed uninfected children:



Surveillance Monitoring for ART Toxicities
Study [SMARTT Study]

- Evaluation of the effects of perinatally-acquired HIV infection and its treatment and treatment complications in adolescents:



Adolescent Master Protocol [AMP Study]



Prevention of Mother-to-Child HIV Transmission Internationally





Progress on Reducing Mother-to-Child HIV Transmission Globally

- **2,000 infants become infected each day, most in developing countries.**
- **Preventive regimens used in U.S. are too expensive and complex to use in many low-resource developing country settings.**
- **NIH research has identified shorter, less expensive regimens that reduce *in utero* and intrapartum transmission by 41-63%.**

Challenge: The Dilemma of Breastfeeding and HIV



➤ Breastfeeding provides optimal nutrition for first 6-12 months and is associated with significantly decreased infant morbidity and mortality over the 1st year of life.

➤ However, prolonged breastfeeding is associated with a 10-15% increased risk of HIV transmission and erodes the efficacy of antiretroviral prophylaxis.¹³



Recently Completed PAMAB-Funded Studies on Breastfeeding and HIV Transmission

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

JULY 10, 2008

VOL. 359 NO. 2

Effects of Early, Abrupt Weaning on HIV-free Survival of Children in Zambia

Louise Kuhn, Ph.D., Grace M. Aldrovandi, M.D., Moses Sinkala, M.D., M.P.H., Chipepo Kankasa, M.D., Katherine Semrau, M.P.H., Mwiya Mwiya, M.B., Ch.B., Prisca Kasonde, M.D., Nancy Scott, M.P.H., Cheswa Vwalika, M.B., Ch.B., Jan Walter, Ph.D., Marc Bulterys, M.D., Ph.D., Wei-Yann Tsai, Ph.D., and Donald M. Thea, M.D., for the Zambia Exclusive Breastfeeding Study

Zambia: Early weaning at age 4 months did not improve HIV-free survival of infants of HIV+ mothers compared to continued breastfeeding, **demonstrating importance of breastfeeding to infant survival in Africa.**

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

JULY 10, 2008

VOL. 359 NO. 2

Extended Antiretroviral Prophylaxis to Reduce Breast-Milk HIV-1 Transmission

Newton I. Kumwenda, Ph.D., Donald R. Hoover, Ph.D., Lynne M. Mofenson, M.D., Michael C. Thigpen, M.D., George Kafulafula, M.B., B.S., Qing Li, M.Sc., Linda Mipando, M.Sc., Kondwani Nkanaunena, M.Sc., Tsedal Mebrahtu, Sc.M., Marc Bulterys, M.D., Ph.D., Mary Glenn Fowler, M.D., M.P.H., and Taha E. Taha, M.D., Ph.D.

Malawi: Extended antiretroviral prophylaxis with nevirapine to the breastfeeding infant for 14 weeks reduced breast milk transmission by over 50% age 9 months, **giving an intervention to allow safer, more prolonged breastfeeding.**



Pediatric HIV Treatment





Progress in Treatment of HIV-Infected Children

- **Clinical trials have led to incremental improvements in health of the estimated 15,000 children living with HIV in the US.**
- **Some new drugs are being simultaneously approved for adults and children.**
- **Combination therapy now standard treatment for children.**
- **Cases of pediatric AIDS and mortality have significantly decreased.**



Challenges Remain

- **Still limited availability of newer drugs and drug classes for children.**
 - **Increased recognition of adverse long-term effects of treatment (metabolic, lipodystrophy, osteoporosis).**
 - **Need to evaluate drug effect on growth, sexual maturation, metabolism, neurodevelopment.**
 - **Studies of treatment and response to treatment in children in developing countries are needed.**
- Critical component of PAMAB portfolio are clinical trials to identify treatment for HIV and its complications in infants, children, adolescents and women.**

NICHD International and Domestic Pediatric and Maternal HIV Clinical Trials Network

collaboration with NIAID Networks



International Maternal, Pediatric, Adolescent AIDS Clinical Trials Network

- **NICHD co-funds the IMPAACT Leadership**
- **NICHD independently supports 31 clinical trials sites (21 domestic, 10 international in Latin America)**
- **Collaboratively develop and conduct IMPAACT clinical trials**

Multiple New Approvals of Antiretroviral Drugs in Children in 2008: Protease Inhibitors

Drug	Pediatric label	Liquid formulation	Neonate/ infant dose	
Amprenavir	Yes (>4 yrs)	Yes	No	
NEW Atazanavir	Yes (>6 yrs)	No	No	
Darunavir	No	No	No	
NEW Fos-amprenavir	Yes (>2 yrs)	Yes	No	
Indinavir	No	No	No	
Lopinavir/ritonavir	Yes (>14 d)	Yes	Yes	NEW
Nelfinavir	Yes (>2 yrs)	Powder	No	
Ritonavir	Yes (>1 mo)	Yes	No	
Saquinavir	No	No	No	
NEW Tipranavir	Yes (>2 yr)	Yes	No	



Cohort Studies in Children

- **Pediatric HIV/AIDS Cohort Study**

- **Domestic**

- Effect perinatal HIV and its treatment in adolescents



- **NICHD International Site Development Initiative**

- **Latin America**

- Addresses issues of drug safety in pregnancy, pediatric HIV treatment



- **International Epidemiologic Database for Evaluation of AIDS (NICHD cofunds NIAID)**

- **Global: NICHD funds pediatrics Asia/Africa**

- Global collection of standardized information on children on response to therapy at time treatment and care rollout being initiated





Adolescents and HIV Infection





Adolescents and HIV Infection in U.S.

- **25% of all new HIV infections in the U.S. occur in youth 13-19 years old, and half of all new infections are in young adults age 20-24 years.**
- **New infections among adolescent females, primarily sexually acquired, equal or surpass new infections in young men.**
- **Resurgence of HIV among young gay men is of concern.**



ADOLESCENT **T**RIALS **N**ETWORK
for HIV/AIDS Interventions
Prevention and Care for Today's Youth



Mission: To study treatment, adherence, and clinical management in **HIV-infected youth**, and primary prevention, including HIV vaccines and microbicides in **HIV at-risk youth**, independently and in collaboration with existing research networks.



Adolescent Issues in Community: Preparation for Trials

CONNECT TO PROTECT

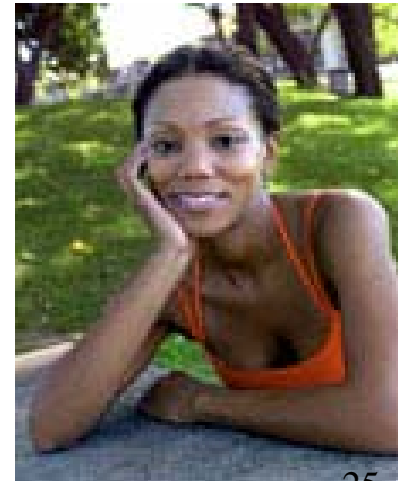
Developing partnerships that build on the diverse insights and skills of researchers and the community to select culturally responsive and research-based interventions to meet the needs of the community's youth



HIV in Women



**Women, Girls,
HIV and AIDS**
World AIDS Campaign 2004





Women and HIV

- Women are at the forefront of the HIV epidemic globally; globally, **50 percent of new infections are in women.**
- HIV infection rates in some low-resource countries are up to **six times higher** than among adolescent males.
- These data underscore the need for prevention strategies, such as microbicides, that are controlled by women.



Women-Specific HIV Activities



- **Women's Interagency HIV Study (WIHS):**

- Longest and largest cohort study in women in U.S., 80% minority women
- Natural history of HIV in treated women
- \$10 million/year in >30 R01/P01 grants



- **NICHD Network**

- Enrollment from NICHD sites into adult ACTG women-specific protocols

- **New microbicide activities**

- Collaborations with the Microbicide Trials Network (pregnancy)
- Investigator-initiated portfolio



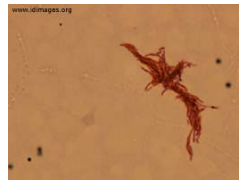
Studies to Begin in New Research Areas Focused on HIV & Co-Infections in Developing Countries

- **MALARIA**



- **Kenya:** Program project for 3 clinical trials related to HIV treatment and malaria in pregnant HIV+ women and children.

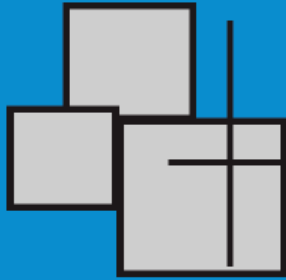
- **TUBERCULOSIS**



- **South Africa, Ethiopia, Kenya:** Studies to evaluate diagnosis of tuberculosis in HIV-infected children; impact of malnutrition on TB immune reconstitution syndrome in children; pharmacokinetics of anti-HIV and anti-TB drugs/drug interactions in children

Pediatric, Adolescent and Maternal AIDS Branch Staff

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FRIENDS OF NICHD COALITION

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