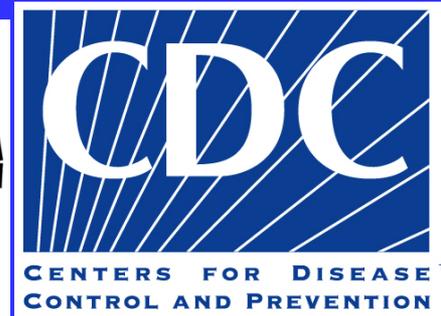


Measles, Mumps and Rubella Seropositivity in Children with Perinatal HIV Infection

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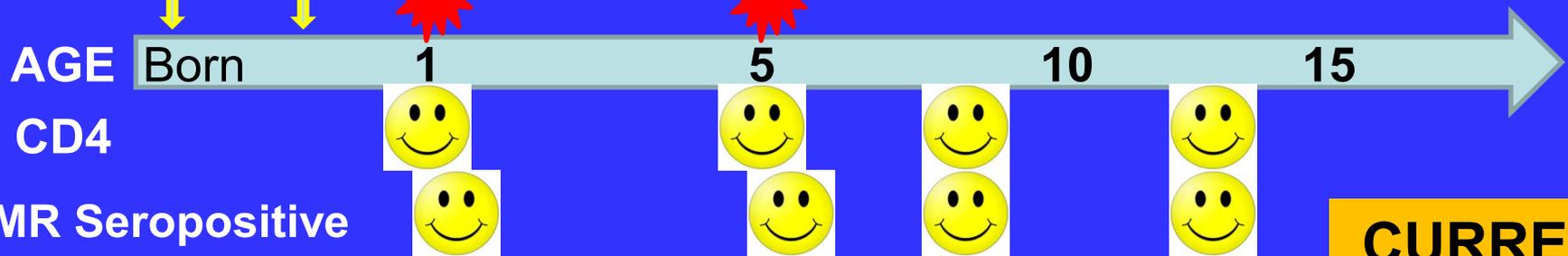
Background & Rationale

- Impaired response to measles vaccine in HIV-infected children not on ART Nair JID 2009
- Faster measles antibody loss in HIV-infected children not on ART Moss JID 2007
- ART does not reliably “restore” measles or rubella immunity from pre-ART immunizations Melvin 2003, Myers 2009, Aурpibul 2006, Farquhar 2009, Abzug 2012
- High response rate (83-90%) when measles vaccine repeated after ART but lower than in HIV-uninfected Melvin 2003, Aурpibul 2007, Abzug 2012
- When infants already on effective (good CD4) ART, ~Normal response to primary rubella vaccination Lima PIDJ 2004
- Should MMR be routinely repeated once stable, effective ART in place? Sutcliffe 2010

Timing of MMR and ART in Relation to Immunity in Adolescence

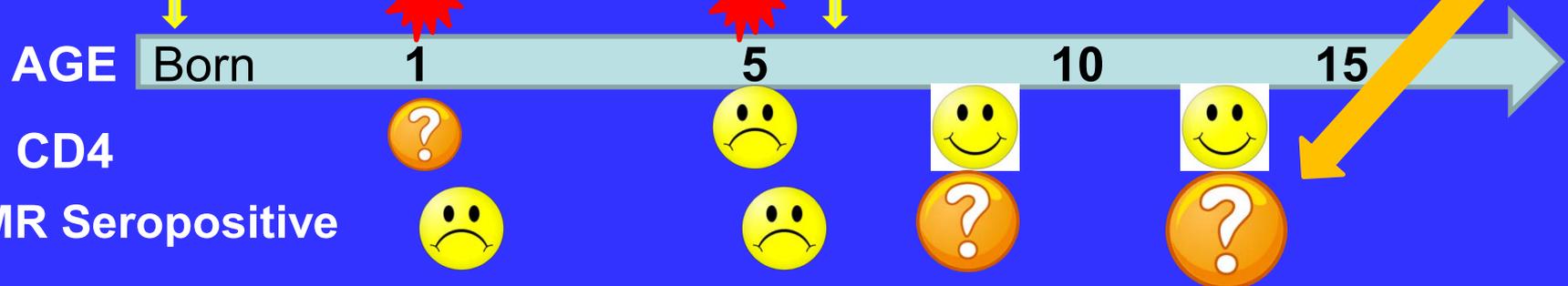
 = MMR

HIV ART



HIV

ART



Objectives

- Estimate rates of seropositivity to M-M-R among perinatally HIV-infected children and youth in the United States.
- Compare rates of seropositivity to M-M-R in HIV-infected youth and HIV-exposed, uninfected (HEU) controls
- Evaluate potential predictors of seropositivity to M-M-R

Pediatric HIV-AIDS Cohort Study (PHACS)

- **Adolescent Master Protocol (AMP) of PHACS** is a prospective cohort study recruiting perinatally HIV-exposed youth from 15 sites in US and Puerto Rico
- **AMP Population:**
 - Perinatally HIV-infected (HIV+) or HIV-exposed uninfected (HEU)
 - Age 7 to <16 years at study entry
 - Complete medical history, including ART, lab results and immunizations
 - Annual visits with exam, labs, repository blood
- **For present analysis:**
 - Most recent study visit with blood specimen available



Assessing serologic evidence of immunity

- Commercial enzyme-linked immunoassay (EIA) for measles, mumps and rubella antibody
 - Measles: EIA index ≥ 1.10
 - Rubella: EIA index ≥ 1.10 (≥ 10 IU/mL)
 - Mumps: Detectable
- Seropositivity vs Seroprotection
 - **Plaque reduction neutralization (PRN) for measles seroprotection** (commercial EIA often underestimates protective immunity). Seroprotection: ≥ 120 mIU/mL
 - Established correlation for rubella
 - No established correlate of immunity for mumps

Analyses

- **Prevalence estimates** of measles and rubella seroprotection and mumps seropositivity rates in HIV+ and HEU
- Seroprotection/seropositivity predictors
 - HIV-infected vs HEU
 - Demographics, Time since MMR, #MMR doses
 - HIV+: CD4, VL, ART, MMR doses after ART
- Multivariate* modeling of potential predictors of seroprotection/seropositivity among HIV+ only

Baseline Characteristics

	PHIV	HEU	Total	P value
Number	428	221	649	
Age (range)	11.5 (7-15)	9.9 (7-15)	10.9 (7-15)	<0.01
Male sex	46%	52%	48%	0.163
Black race	75%	64%	71%	0.003
Mean BMI-Z	0.32	0.76	0.47	<0.001
≥ 1 MMR	98%	92%		<0.001
≥ 2 MMRs	91%	75%		<0.001
VL < 400	68%	-		
CD4 > 500	77%	-		
CD4 % ≥ 25	77%			
CDC Class C	24%	-		
On ART	93%			

Measles and Rubella Seroprotection and Mumps Seropositivity Rates

	HIV Status	
	HIV-Infected	HEU
Measles (PRN)	245/428 = 57% (52%,62%)	218/221 = 99% (96%,100%)
Mumps	254/428 = 59% (55%,64%)	215/221 = 97% (94%,99%)
Rubella	279/428 = 65% (61%,70%)	217/221 = 98% (95%,99%)

MEASLES SEROPROTECTION (PRN)

PHIV only	Positive	Negative	Total	P value
Number	244	183	427	
Mean age(range)*	13.8 (8-19)	15.4 (8-20)	14.5 (8-20)	<0.001
Male sex	46%	46%	46%	0.978
Black race	77%	73%	75%	0.302
Mean BMI-Z	0.27	0.40	0.33	0.300
≥ 2 vaccine doses	91%	93%	92%	0.138
Mean yrs since vaccine	9.2	10.7	9.8	<0.001
VL < 400*	71%	55%	64%	<0.001
CD4 > 500*	82%	62%	73%	<0.001
CD4 % ≥ 25*	81%	68%	75%	<0.001
Nadir CD4% (mean)	18.7%	15.7%	17.4%	<0.001
CDC Class C*	24%	27%	26%	0.170
Mean Age at 1 st HAART**	3.16 y	4.66 y	3.80 y	<0.001

*At time serum was obtained. **Among 413 who received on HAART.

RUBELLA Seroprotection

PHIV only	Positive	Negative	Total PHIV	P value
Number	279	149	428	
Mean age(range)*	13.9 (8-20)	15.6 (8-20)	14.5 (8-20)	<0.001
Male sex	45%	49%	46%	0.408
Black race	77%	71%	75%	0.157
<u>Mean BMI-Z</u>	0.23	0.49	0.32	0.027
≥ 2 vaccine doses	91%	93%	91%	
Mean time (yrs)since vaccine	9.1	11.1	9.8	<0.001
VL < 400*	69%	56%	65%	0.056
CD4 > 500*	76%	69%	74%	0.009
CD4 % ≥ 25*	77%	70%	75%	0.004
<u>Nadir CD4% (mean)</u>	17.7%	17.1%	17.5%	0.401
<u>CDC Class C*</u>	24%	29%	25%	0.004
Mean Age at 1st HAART**	3.1 y	5 y	3.8 y	<0.001

*At time serum was obtained. **Among 413 who received HAART.

Seropositivity Among Youth with Well-controlled HIV

	VL < 400 copies/mL	CD4 count ≥ 500 cells/mm³
Measles	71%	78%
Rubella	69%	78%
Mumps	69%	76%

Poor seropositivity/seroprotection rates even among youth who currently have their HIV infection well controlled

M-M-R results (HIV+ only) by number of vaccine doses received after on HAART for ≥ 3 months

Number of vaccine doses received after on HAART ≥ 3 months					
	0 (N=188)	1 (N=141)	2* (N=99)	Total (N=428)	P-Value (a)
Measles (PRN)					
Protected	84 (45%)	77 (55%)	83* (84%)	244 (57%)	<.001
	1 missing				
Mumps					
Seropositive	99 (53%)	79 (56%)	76 (77%)	254 (59%)	<.001
Rubella					
Protected	98 (52%)	97 (69%)	84 (85%)	279 (65%)	<.001

(a) Fisher's Exact Test *Includes one subject who received 3 MMRs after ≥ 3 months of HAART.

- Reminder: 91% HIV+ had ≥ 2 MMR doses
- No effect of total # MMR doses on M-M-R serology result

Ongoing Work

- Asking sites to verify immunization records for all subjects (HIV+ and HEU) with < 2 MMRs
- Multivariable analysis and modeling
 - Relative contributions of univariate predictors
 - For ex: HIV/ART status at time of MMR vaccine vs at time of serologic testing

Summary & Implications

- Largest cohort PHIV+ children and youth on ART assessed for M-M-R immunity
- Large numbers of PHIV youth in the US may not be protected against measles, mumps and rubella
- Despite current use of ART, virologic suppression and high CD4 values
- Benefit of MMR after ART (Abzug 2012)
- No evidence that HEU lack protection
- ***Evidence supporting recommendation for MMR reimmunization in PHIV who have not received MMR immunization while on effective ART***

THANK YOU!

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