

Session 2
Experience with the
Immunogenicity and Efficacy of
Vaccines Licensed for Newborns

BCG and its Immunomodulatory Effects in the Neonate

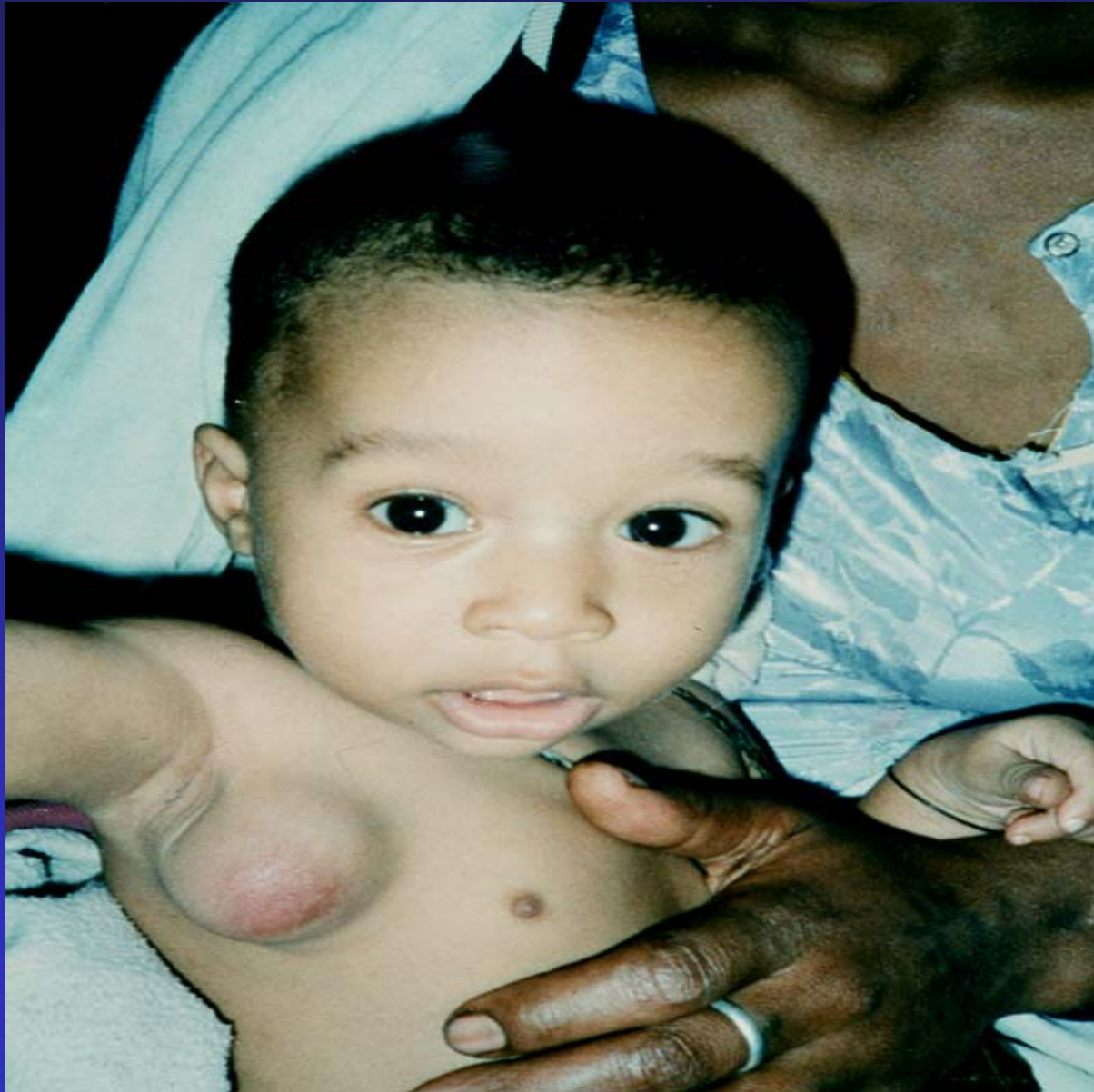
Martin Ota

BCG VACCINE

- Bacillus Calmette-Guérin
- Attenuated form of live *Mycobacterium bovis*
- Only licensed vaccine against tuberculosis
- Most widely used vaccine worldwide

BCG vaccine

- Many vaccine strains
- Variable vaccination schedule
- Variable efficacy
- Inability to control Tb epidemic
- Increased interest in novel Tb vaccines



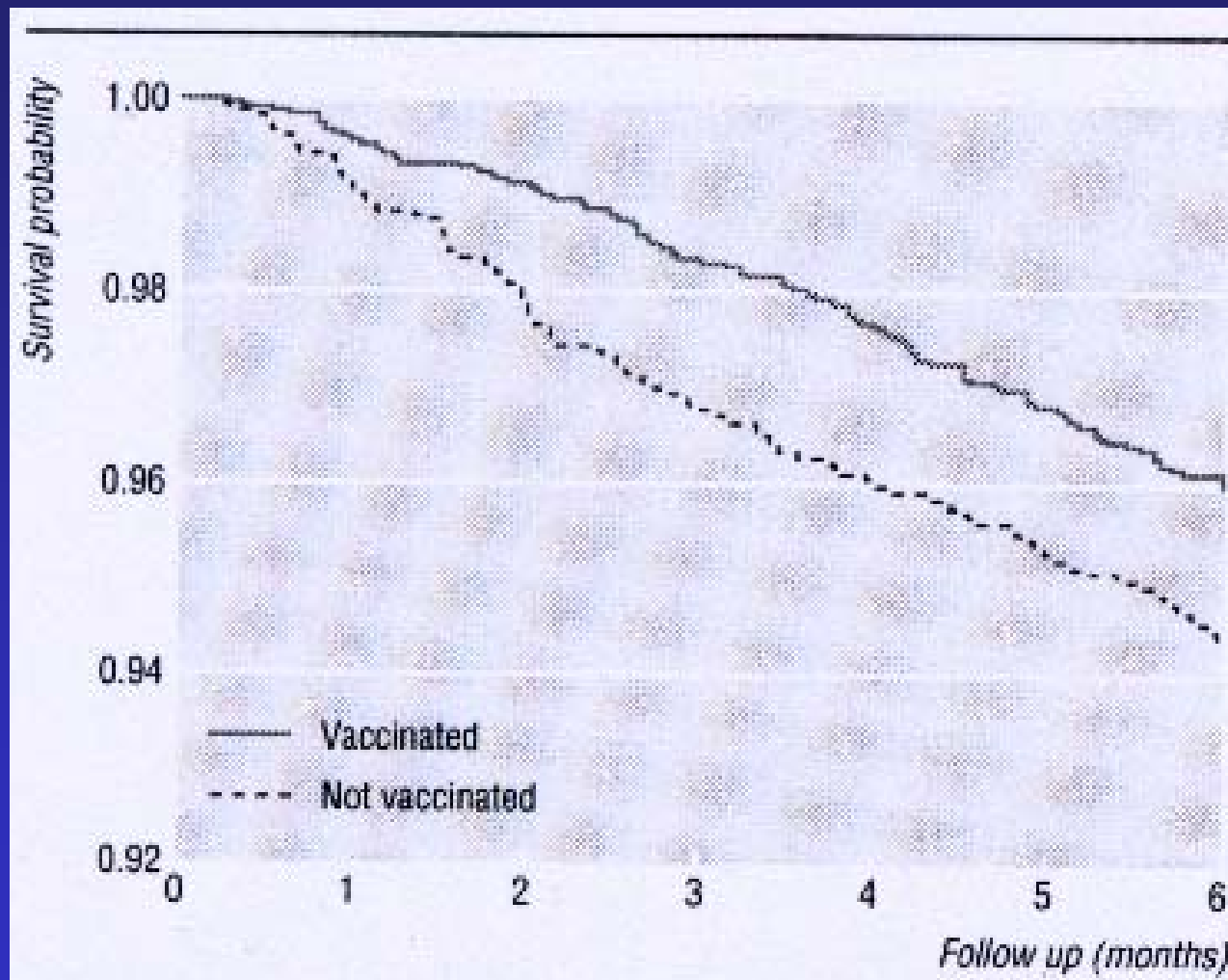
Immunogenicity of BCG vaccine

- BCG scar
- Postvaccination tuberculin skin test
- Potent Th1 response in adults

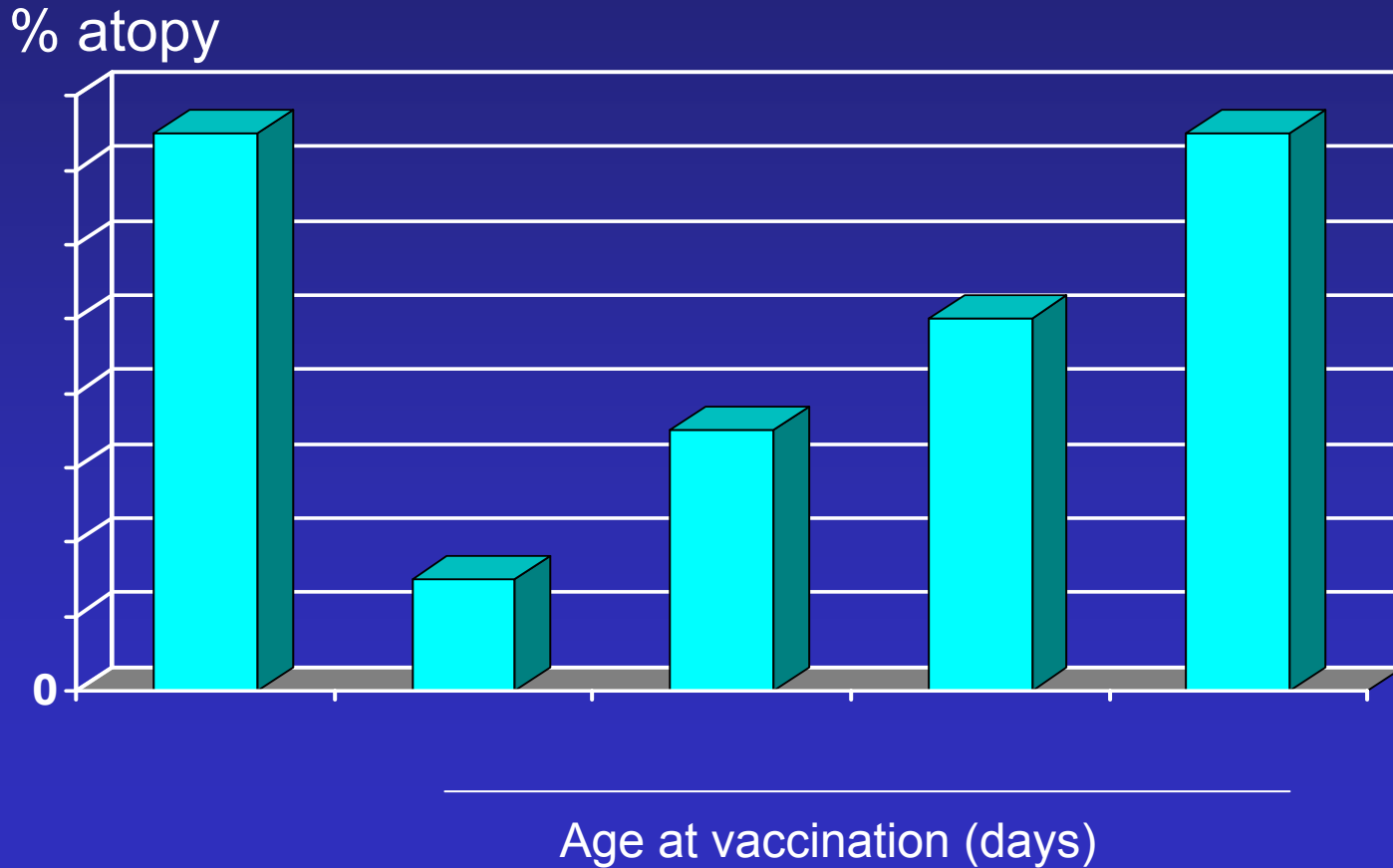
Immune response in targeted cohort?

Non specific effects of BCG vaccination in early life

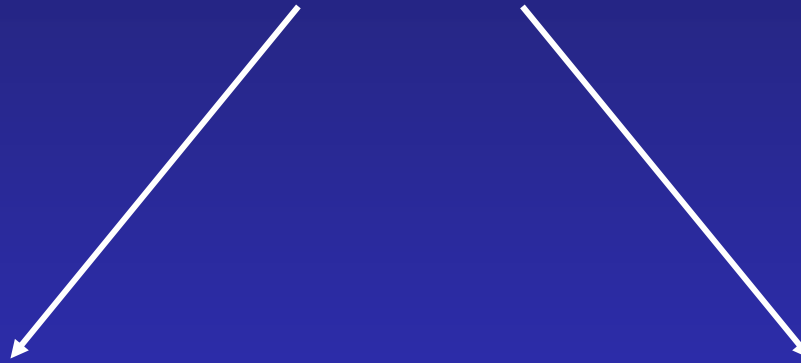
Child survival following BCG immunisation



Early BCG vaccination and atopy in Guinea-Bissau



BCG vaccination in early life



**Type of immune
response in newborns**

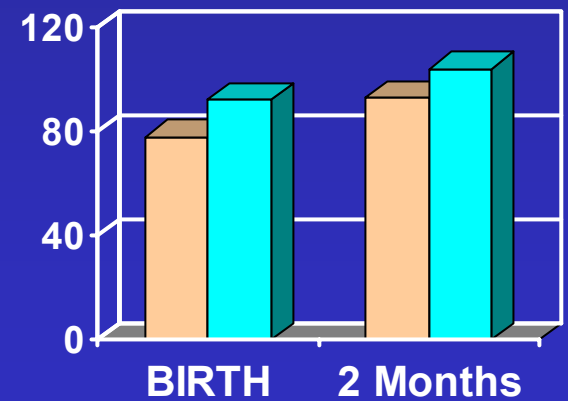
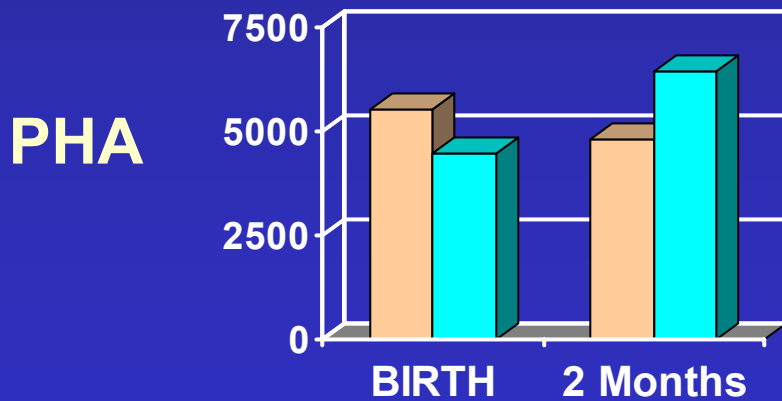
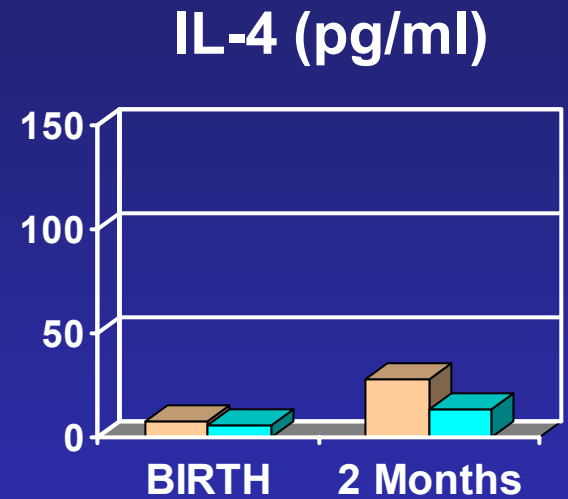
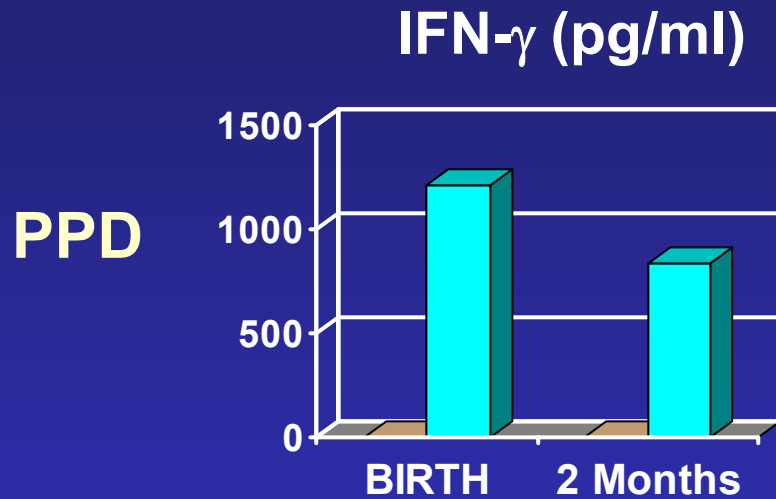
**Influence on unrelated
antigens in childhood**

Immune response to neonatal BCG vaccination

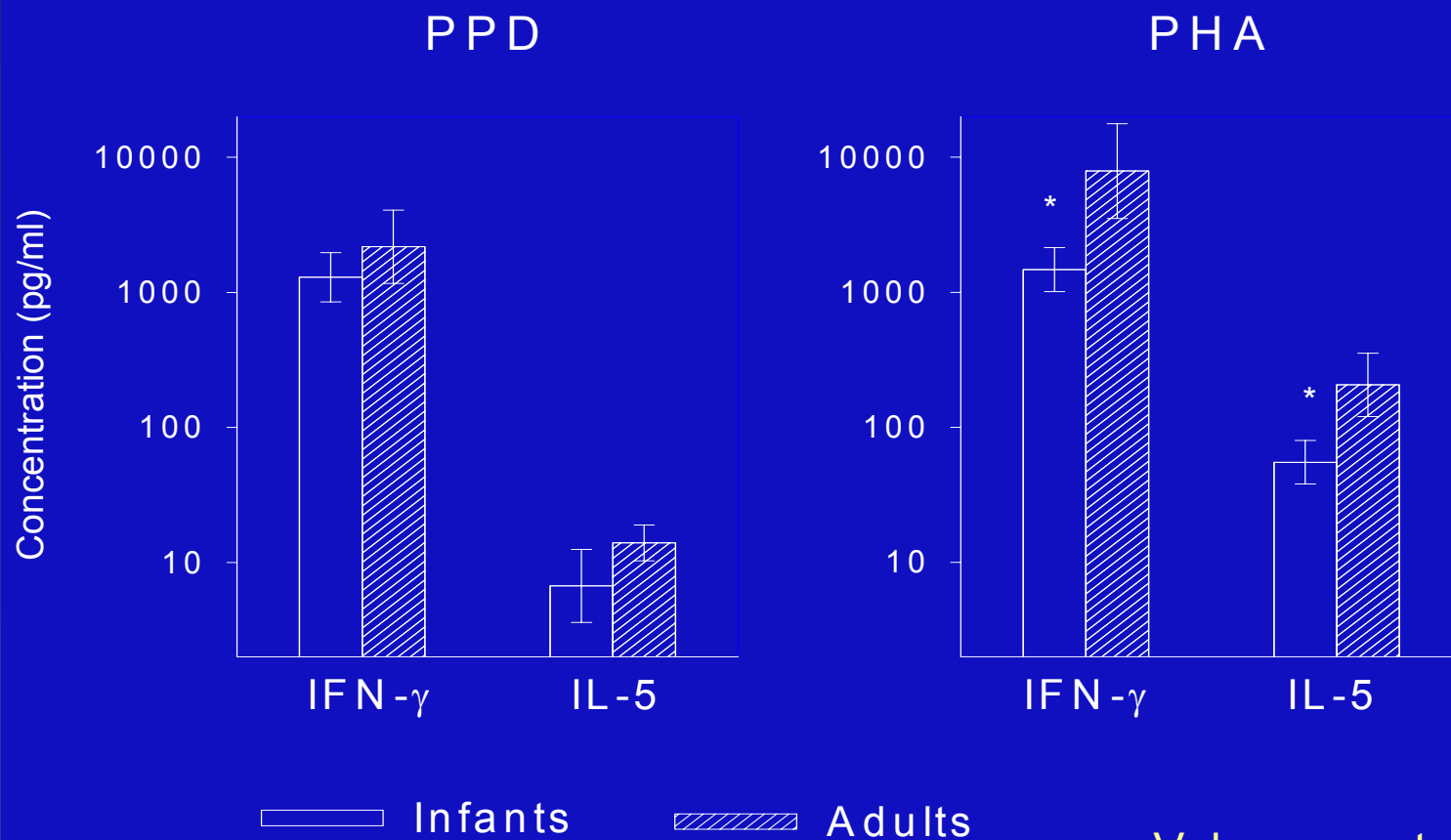


Group I	BCG	Post Imm	Memory	
Group II		Pre Imm BCG	Post Imm	Memory
Group III			Pre Imm BCG	Memory

Immune response to neonatal BCG vaccination

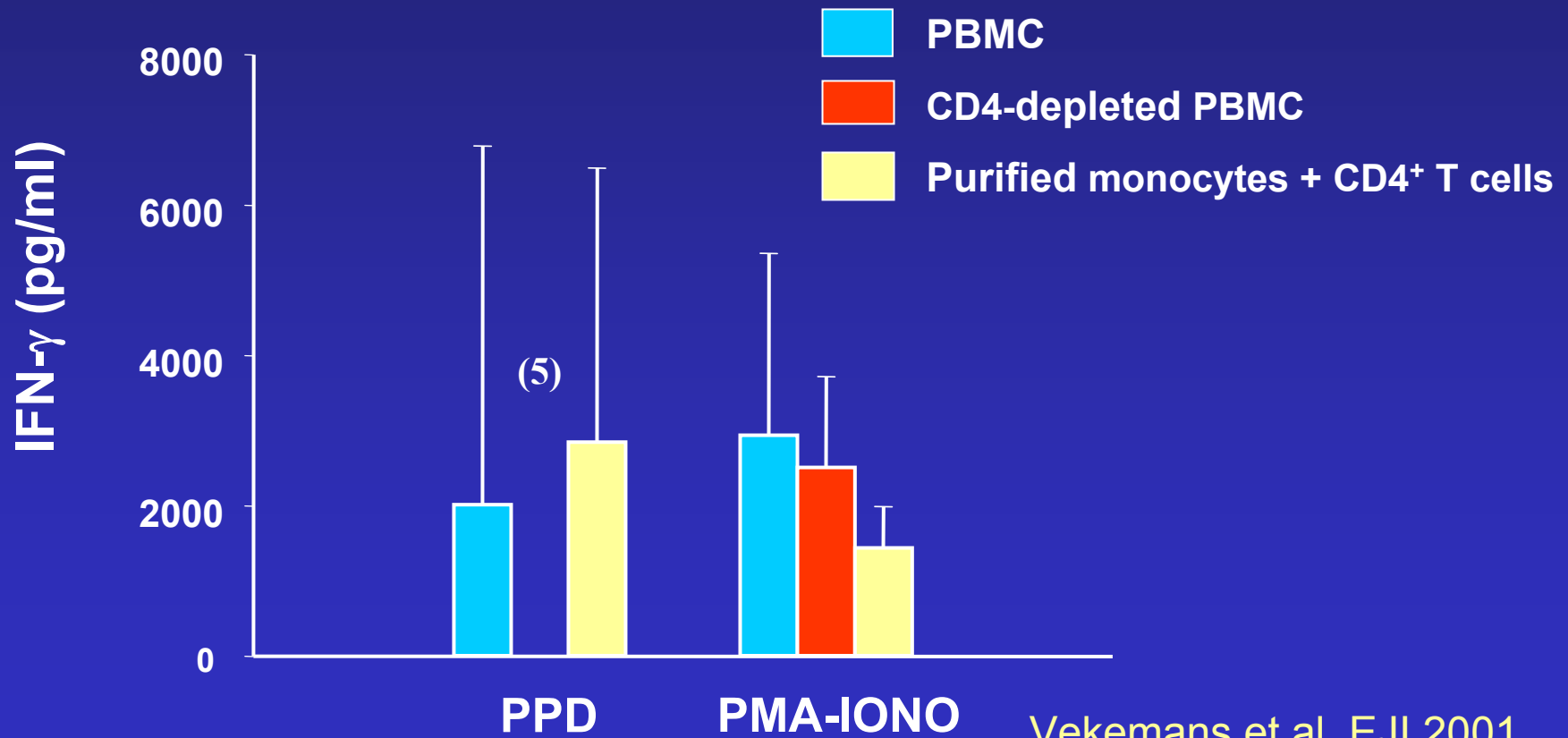


Cytokine response to PPD in BCG vaccinated infants and immune adults



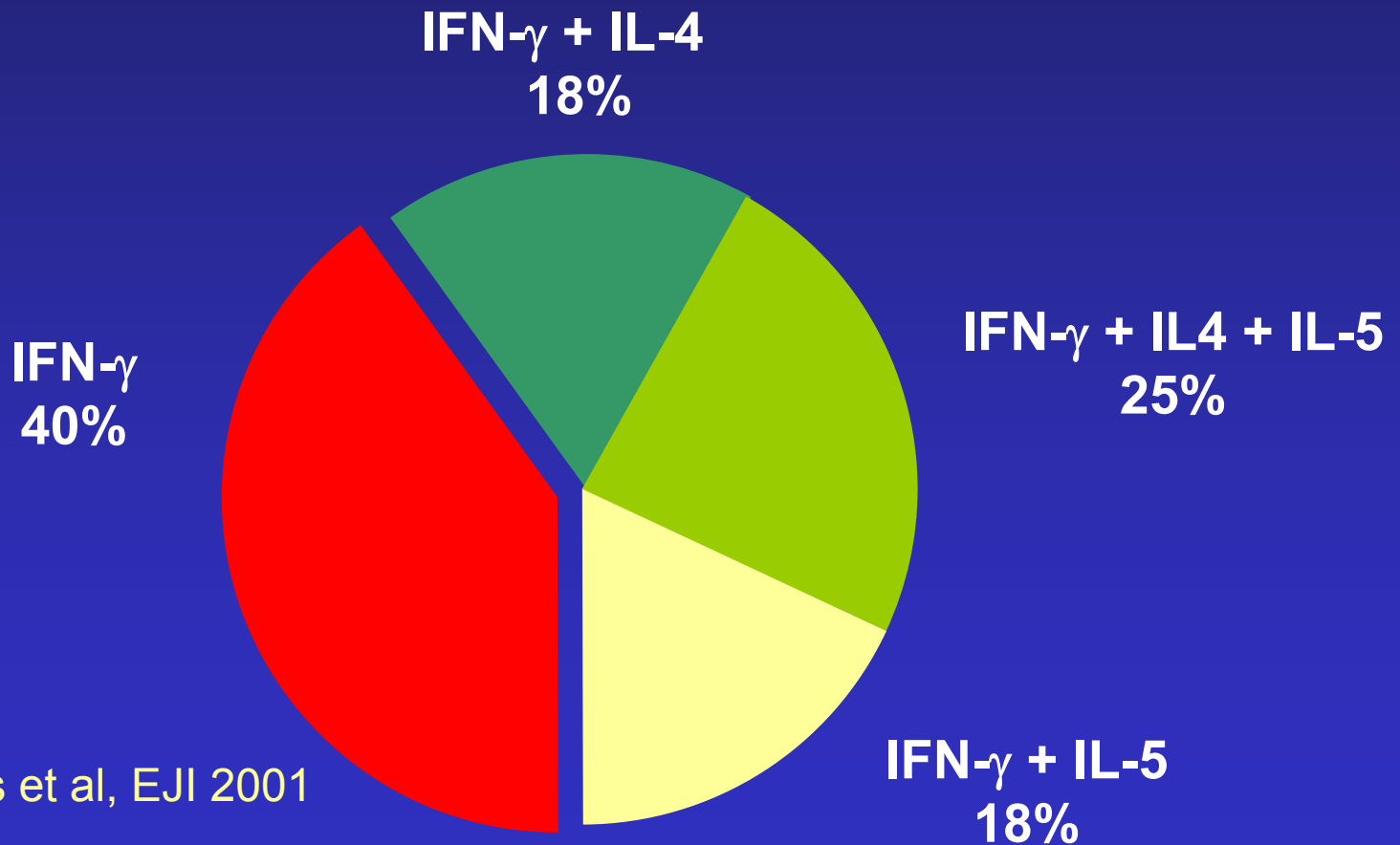
Vekemans et al, EJI 2001

CD4⁺ cells are necessary and sufficient for IFN- γ secretion



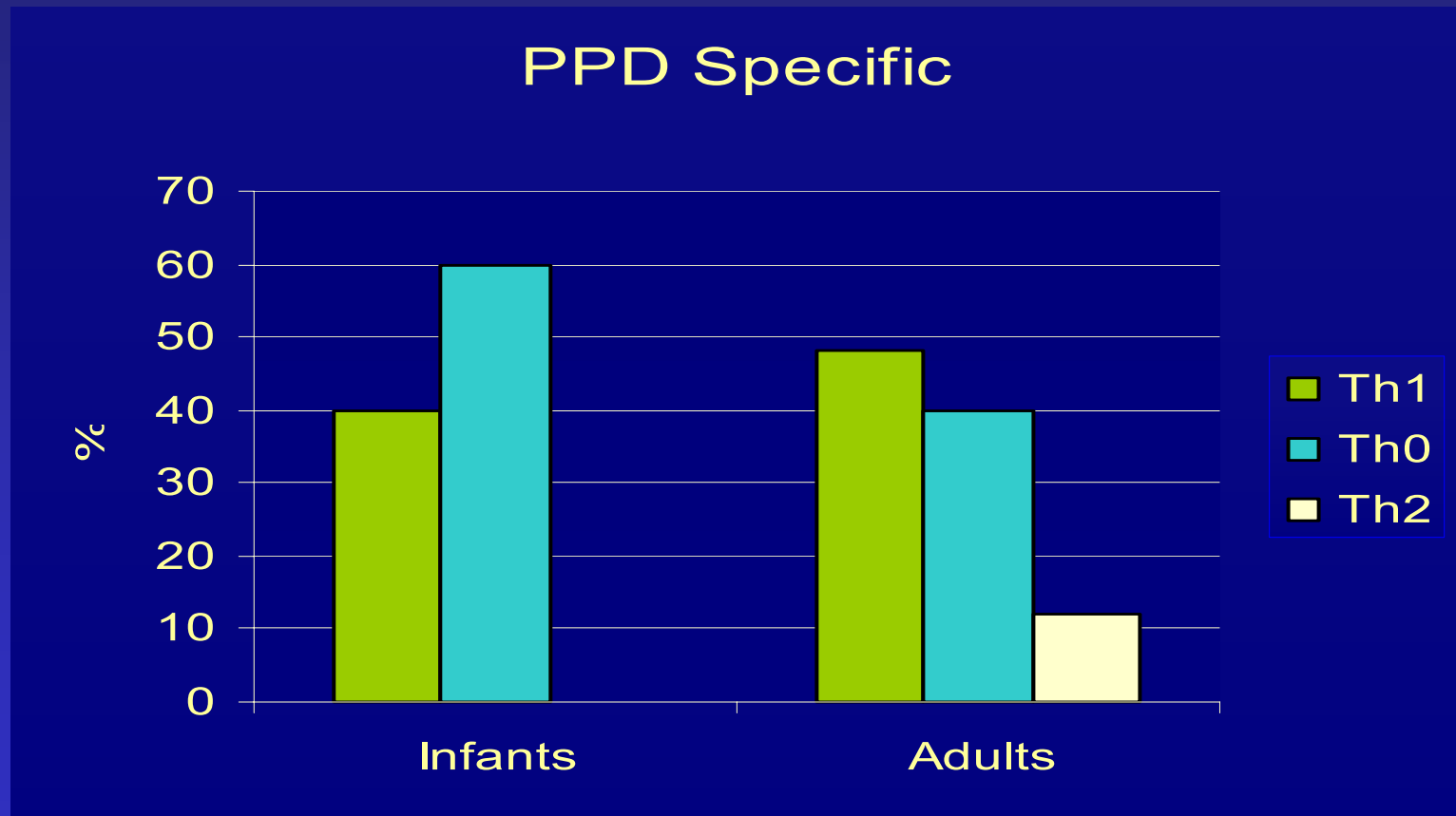
Vekemans et al, EJI 2001

Cytokine production by PPD specific CD4⁺ T cell clones

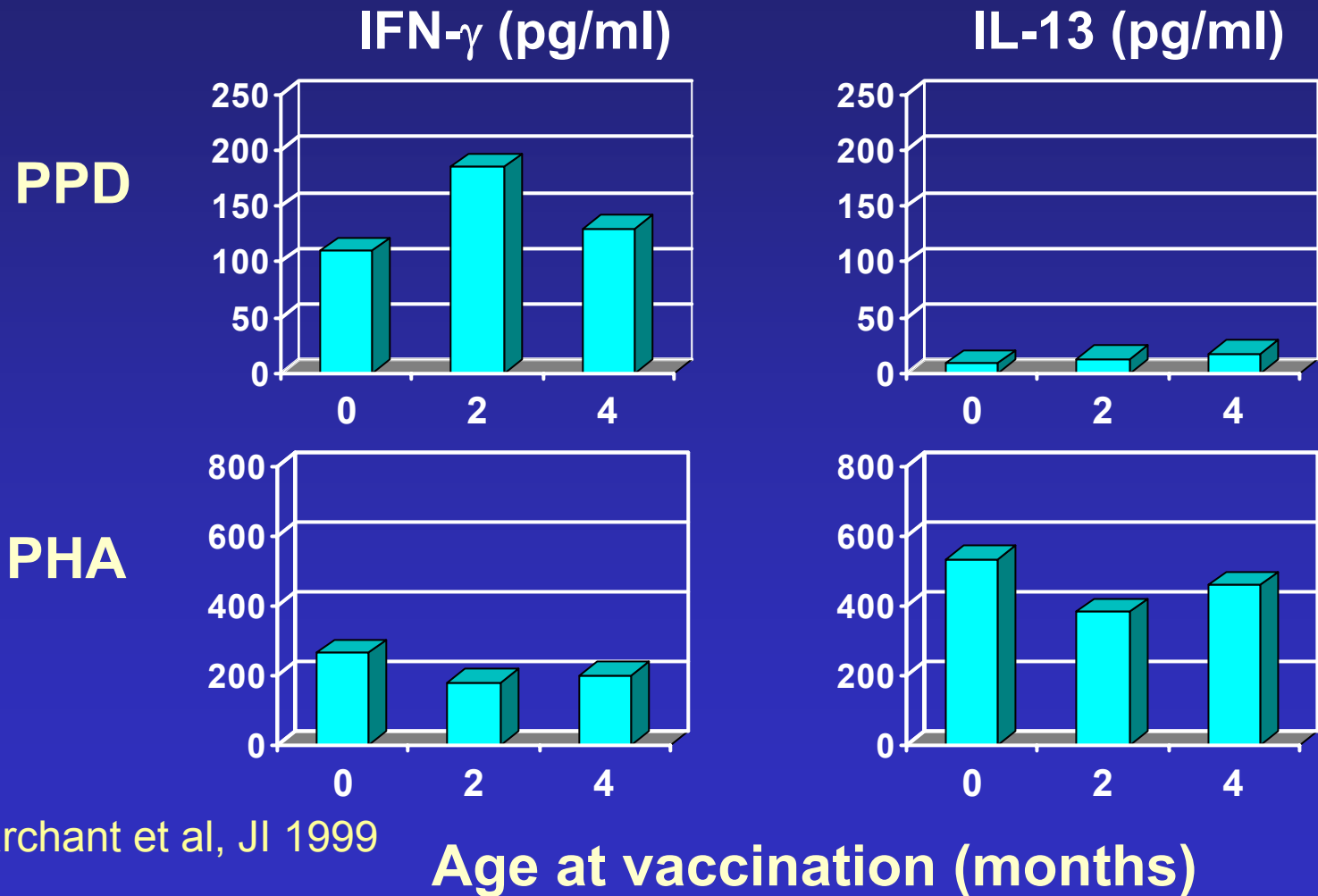


Vekemans et al, EJI 2001

CD4 clones following BCG vaccination



Memory immune response to neonatal BCG vaccination



Marchant et al, JI 1999

Conclusions

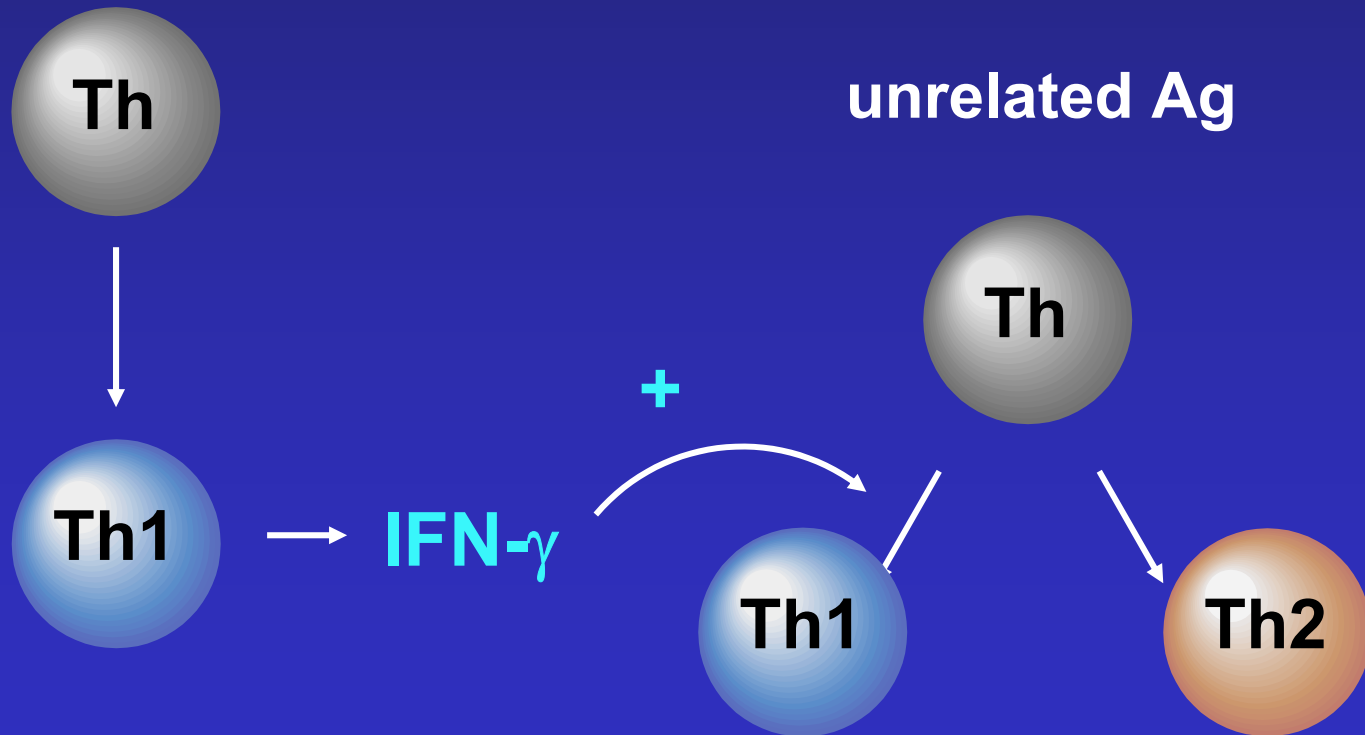
- Newborns develop a type 1 response to BCG vaccination
- Clonal studies show that IFN- γ is produced by both Th1 and Th0 cells

Could neonatal BCG vaccination influence the immune response to unrelated antigens ?

Would this include the inhibition of Th2 type and the promotion of Th1 type responses ?

Immune consequences of neonatal BCG vaccination

BCG



Influence of BCG on antibody and cytokine responses to vaccination in early life



Group I	BCG					
Group II	BCG					
Controls	BCG					
	HBV		HBV		HBV	
	OPV	OPV	OPV	OPV		
			DTP	DTP	DTP	
	Imm		Imm		Imm	

Influence of BCG on antibody and cytokine responses to vaccination in early life

Study population

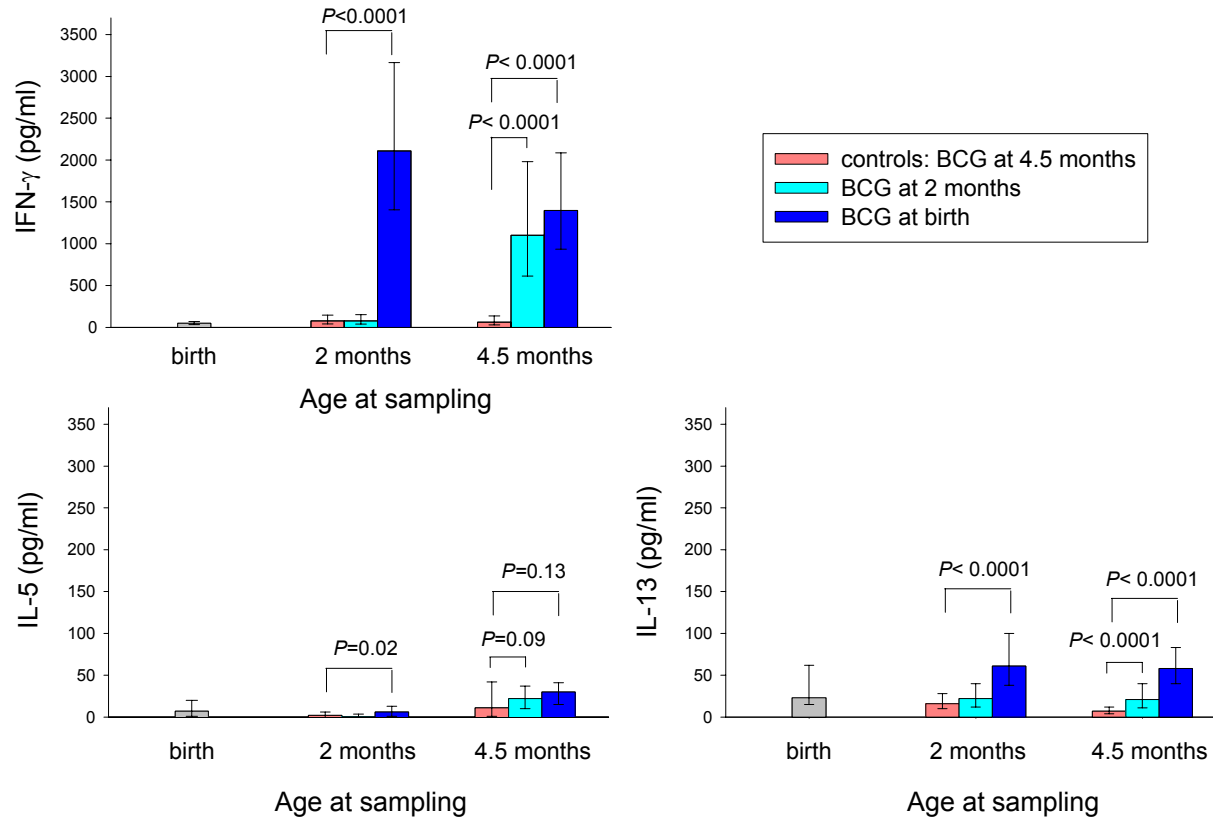
- 4.5 months old infants:

Group I	n= 27
Group II	n= 29
Group III (controls)	n= 28

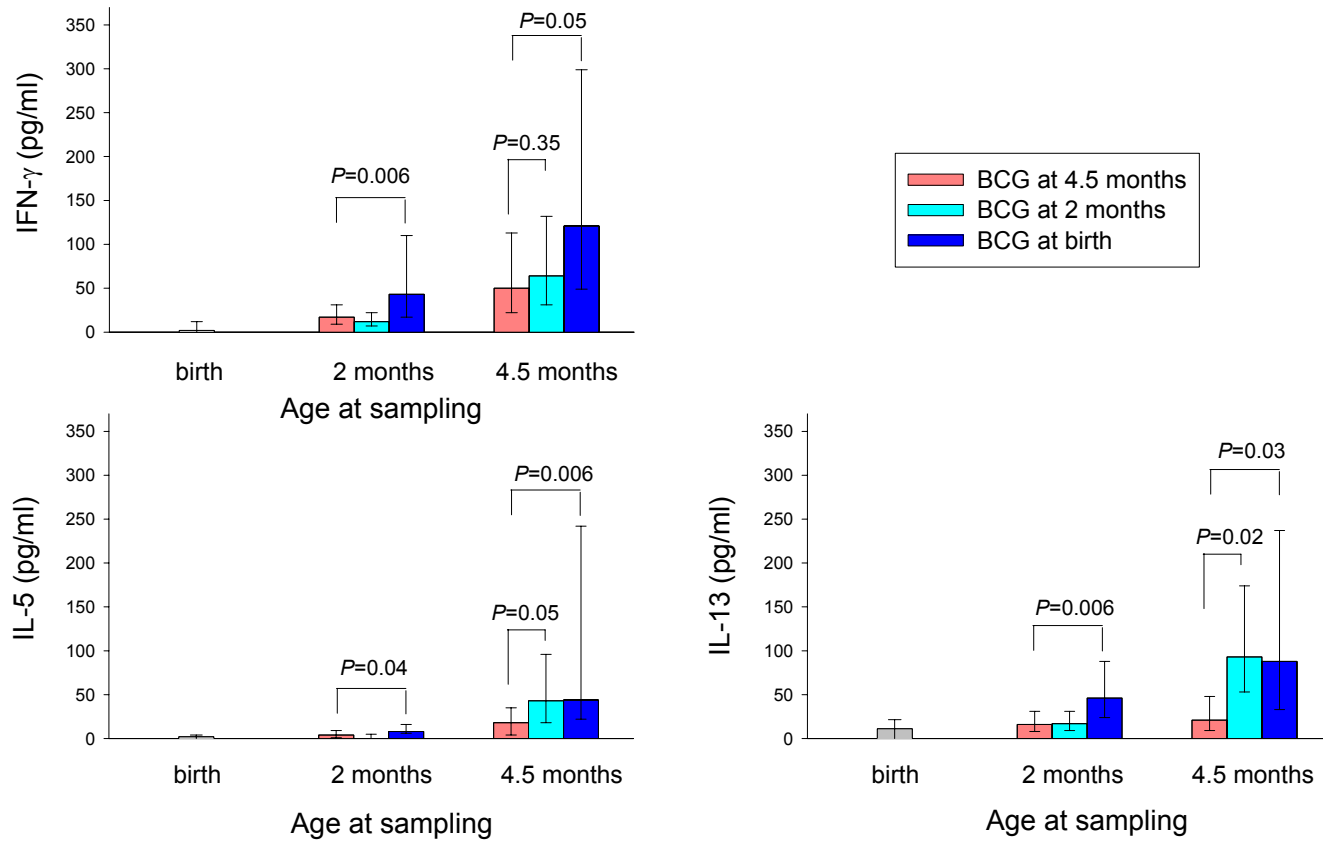
Immune responses to vaccines

- Serology: HBV, TT, DT (ELISA)
OPV (neutralisation assay)
- Cytokines: PBMC + Ag (HBs, TT)
day 6: IFN- γ , IL-5, IL-13 (ELISA)

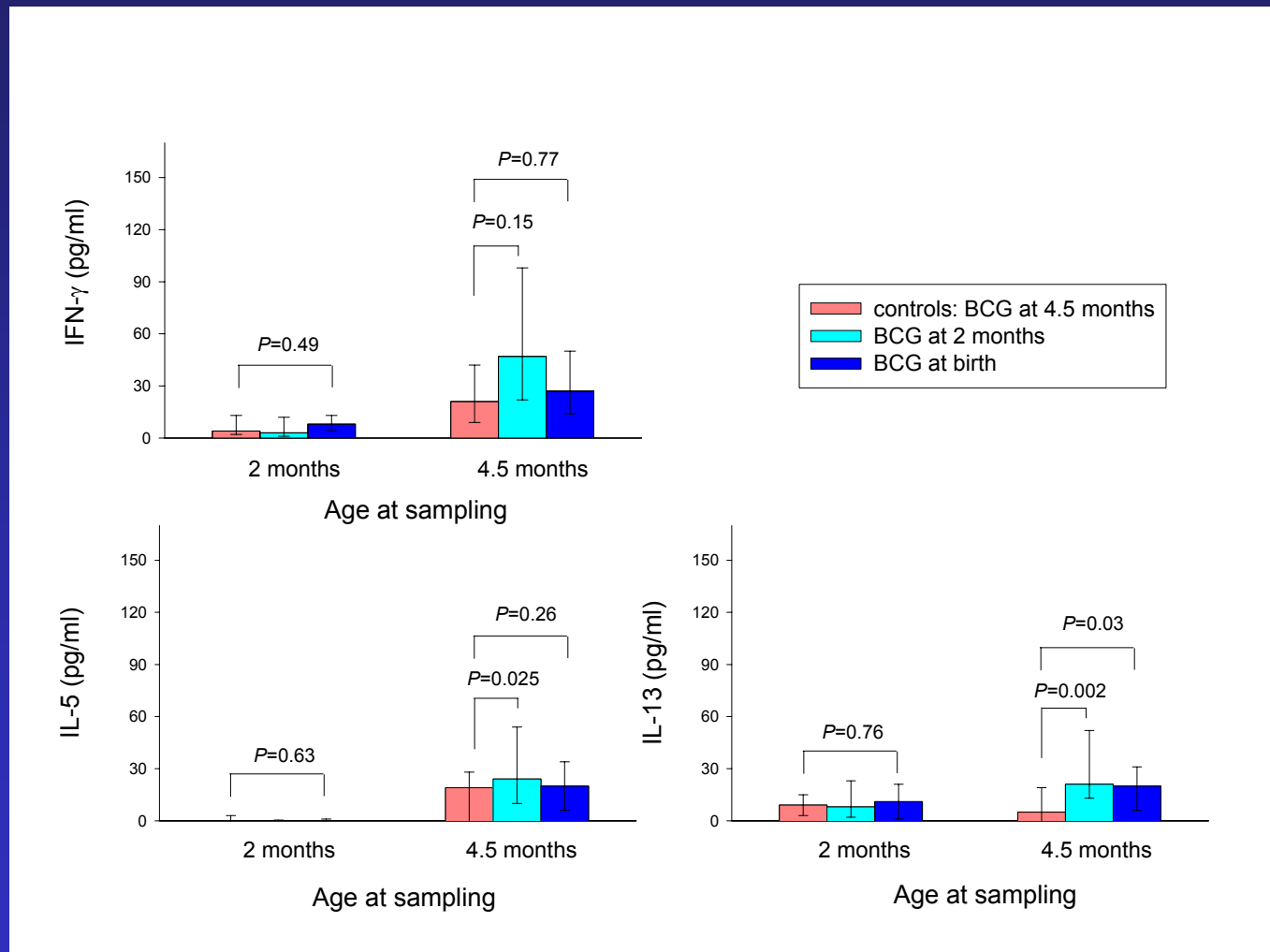
Cytokine response to PPD



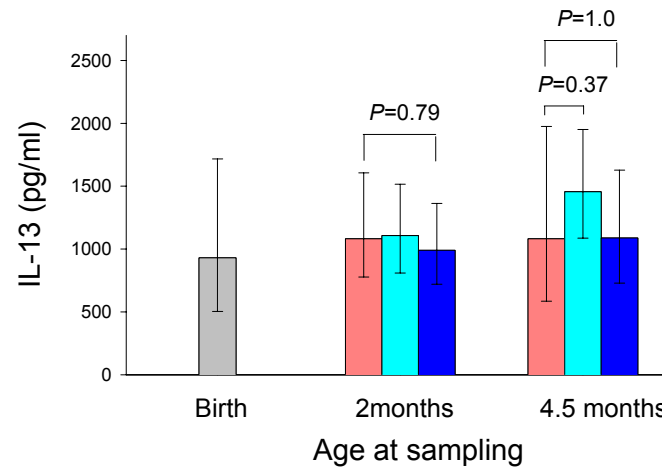
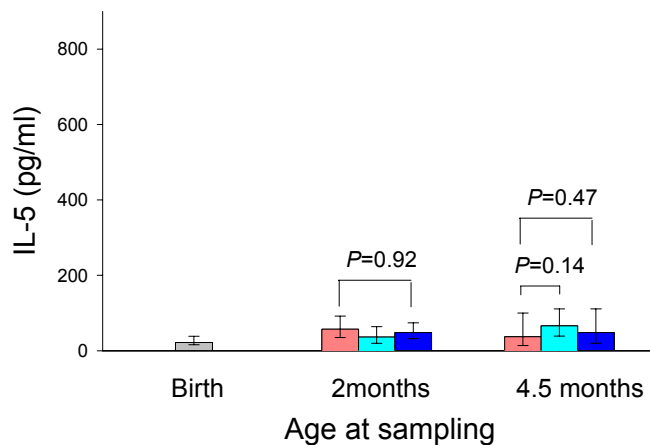
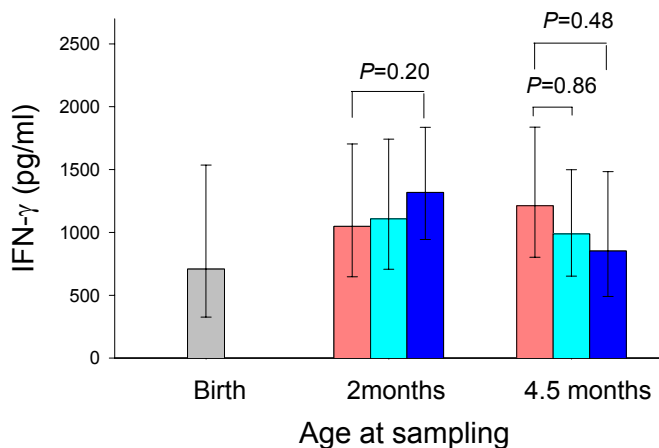
Influence of BCG on cytokine response to HBV



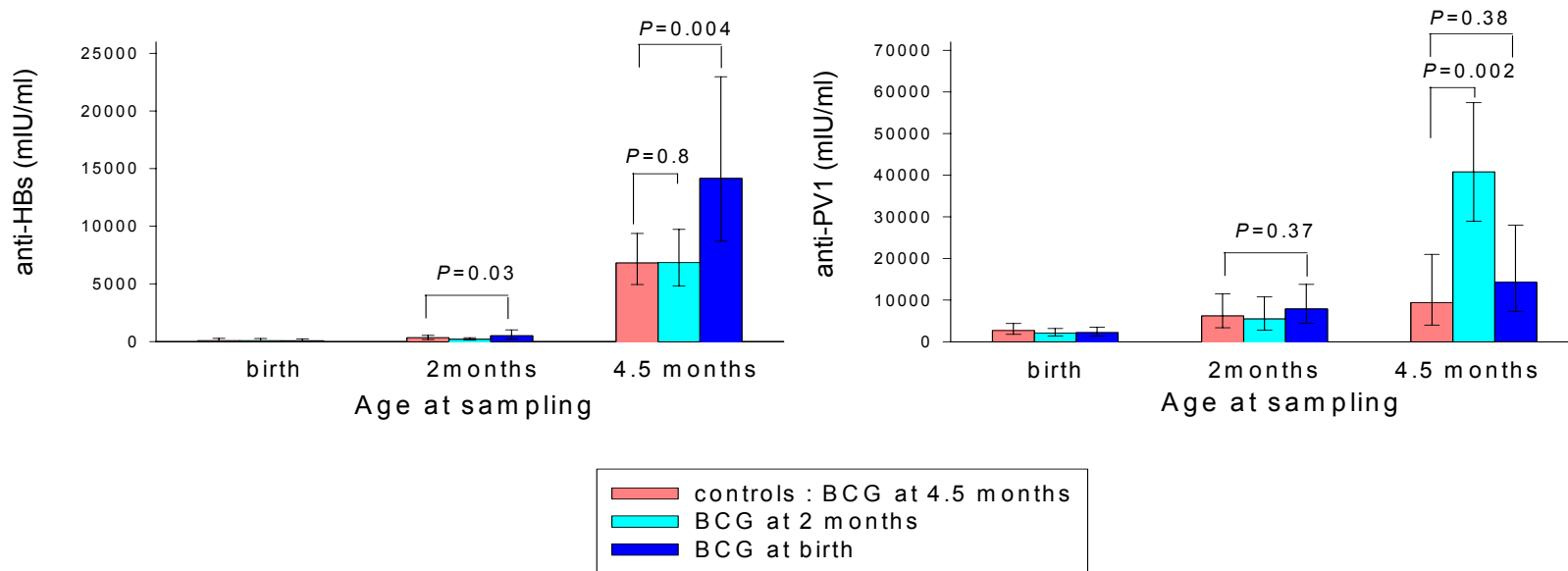
Influence of BCG on cytokine response to TT



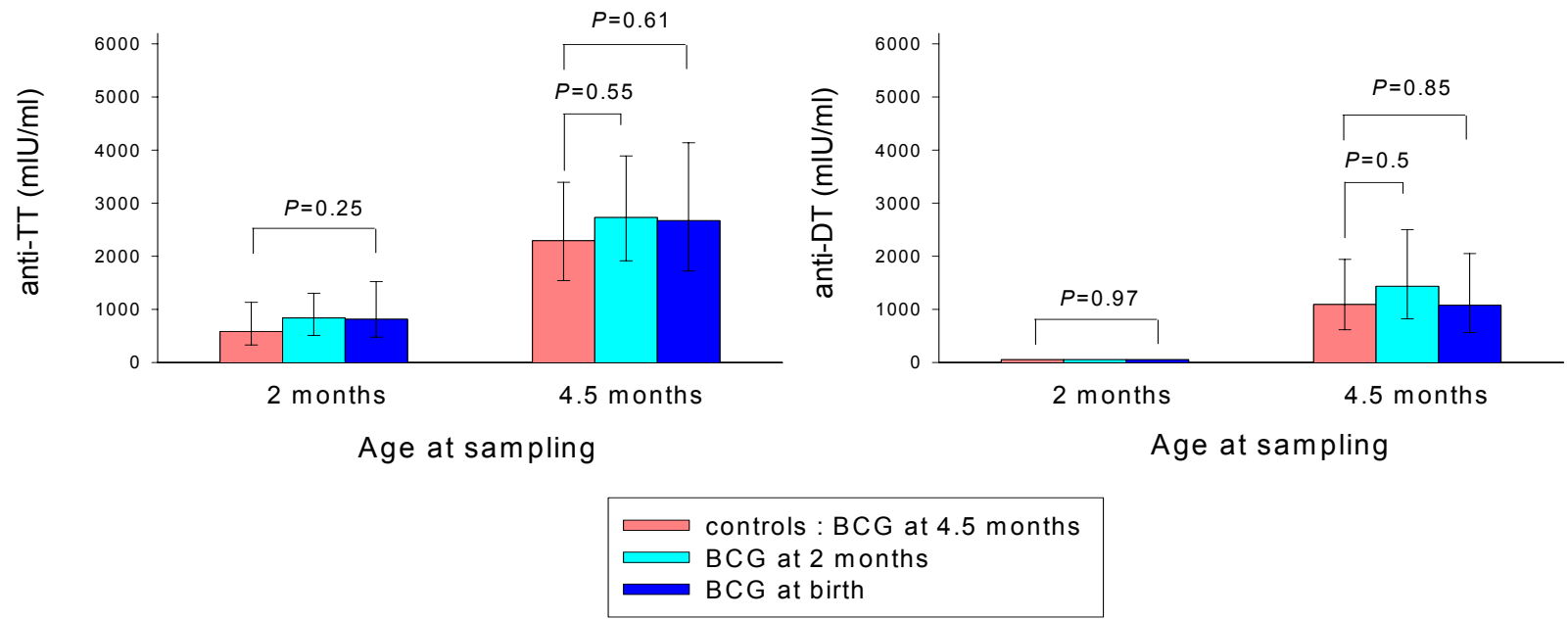
Influence of BCG on cytokine response to PHA



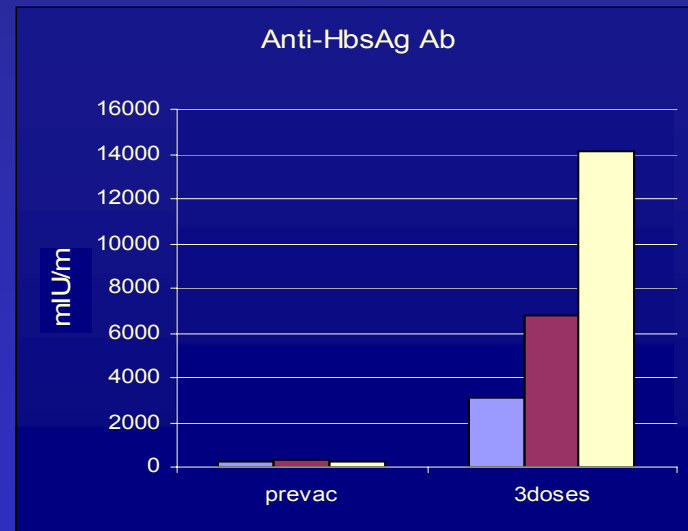
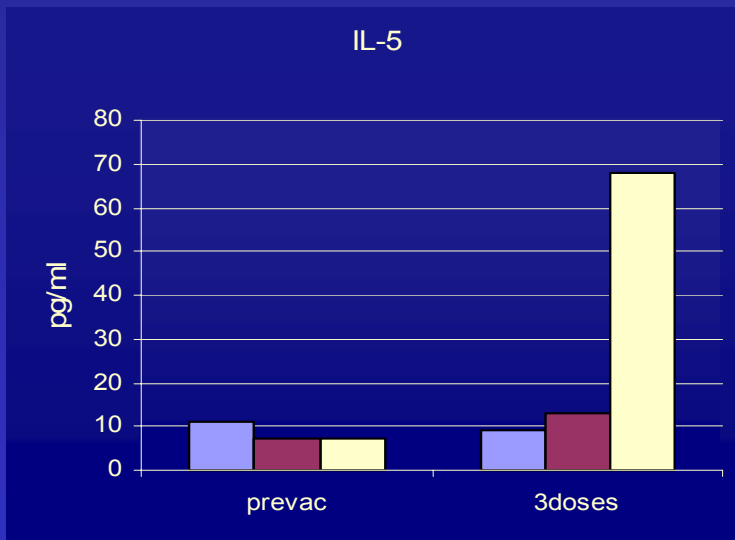
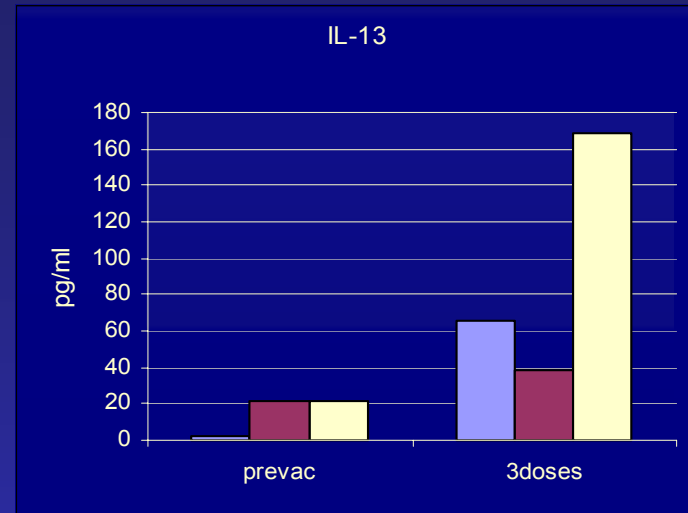
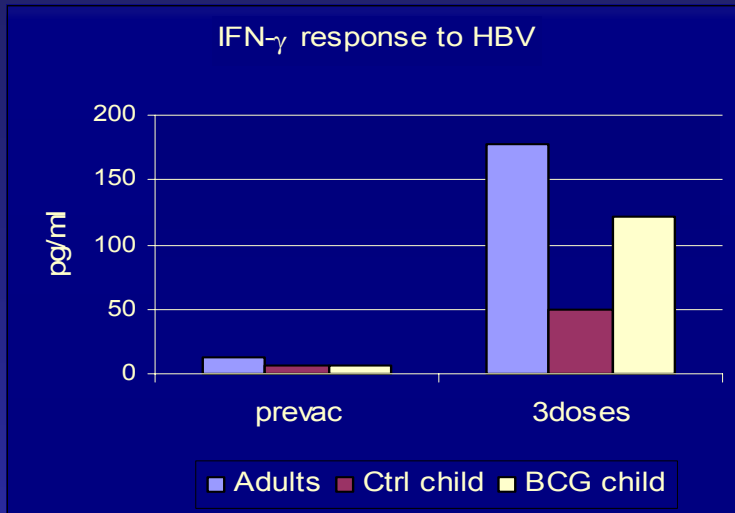
Influence of BCG on antibody response to HBV and OPV



Influence of BCG on antibody response to TT and DT



Response to HBV: Infants vs adults



Conclusions

- BCG promotes cytokine and antibody responses to unrelated vaccine antigens in infants
- Priming or boosting, effect depends on vaccine
- Both Th1 and Th2 cytokines
- Regional / Systemic effects

Implications

- BCG could be used to improve the immunogenicity of vaccines in early life
- BCG vaccination in early life could influence immune responses to unrelated infectious pathogens or allergens

Acknowledgements

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