BCG: What have we learnt about vaccination of the newborn

Thomas J. Scriba
Global BCG vaccination policy

- Unknown
- Universal BCG Vaccination
- BCG no longer recommended
- Never universally recommended

BCG-induced protection against pulmonary TB is variable

BCG protects against disseminated forms of TB in infants

Polymorphisms in TLR6 are associated with different inflammatory profiles and T cell responses

C745T


*Soluble cytokine measured following BCG incubation in whole blood for 7 hours.
Age and the pro-inflammatory monocyte response

**Box plots**

- **TNF-α**
  - Unstimulated: p=0.3
  - BCG: p=0.0005, p=0.04
  - LPS: p=0.1

- **IL-6**
  - Unstimulated: p=0.01
  - BCG: p=0.0008, p=0.4
  - LPS: p<0.0001

- **IL-12**
  - Unstimulated: p=0.2
  - BCG: p<0.0001
  - LPS: p<0.0001

**Graphs**

- Cytokine expression vs. Age (weeks)
Responses by innate cells

- Pro-inflammatory cytokine response
- Co-stimulatory response
- Anti-inflammatory cytokine response

Age (weeks)
At which age should BCG be given?

South Africa

BCG-response at 1 year of age,
Kagina et al, Vaccine 2009
At which age should BCG be given?

Uganda

BCG-response at 9 months of age, Lutwama et al, unpublished
Heterologous prime-boost
At which age should boost be given?

Prime
Birth

Boost
6, 10, 14 weeks

Boost
Adolescence

BCG
(Whole Bacteria)

Specific antigens, delivered in viral vectors, or with adjuvants
When is the best time to boost the BCG-primed immune response?

- Infant 1: Birth, 3 weeks, 6 weeks, 10 weeks, 14 weeks, 27 weeks, 40 weeks, 52 weeks
- Infant 2: Birth, 3 weeks, 6 weeks, 10 weeks, 14 weeks, 27 weeks, 40 weeks, 52 weeks
- Infant 3: Birth, 3 weeks, 6 weeks, 10 weeks, 14 weeks, 27 weeks, 40 weeks, 52 weeks
- Infant 4: Birth, 3 weeks, 6 weeks, 10 weeks, 14 weeks, 27 weeks, 40 weeks, 52 weeks

33 participants/time point
The magnitude of BCG-specific cells peaks at 10 weeks of age.
BCG-specific cells are highly activated and express low levels of BCL-2 during the effector response.
BCG-specific CD4 T cells develop a central memory phenotype

![Graph showing the proportion of BCG-specific cytokine+ CD4+ T cells with and without CD45RA and CCR7 markers at different ages (6 and 27 weeks).]
Proliferation of BCG-specific cells peaks at 10 weeks of age and then wanes.
Questions for discussion

Environment

How do we assess effects of co-infections, environmental mycobacteria, climate, on BCG efficacy?

Host

How do we best harness maturation of infant immunity to improve BCG efficacy?

Vaccine

When is the best time to boost with heterologous vaccines?

- Probably best to boost the BCG response after 14 weeks, after the peak Th1 response
Funders and partners