

DEVELOPING ^{NEW}
TUBERCULOSIS VACCINES
FOR THE WORLD

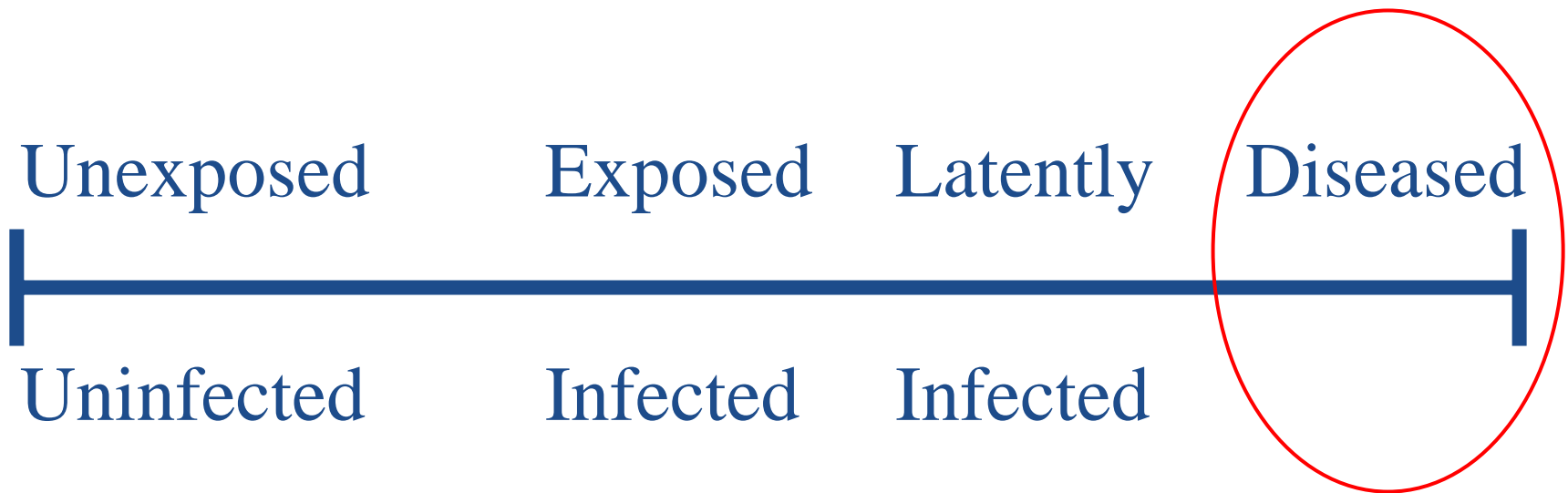
Rethinking the Epidemiology of Tuberculosis Infection

Public Health Implications of Studies with
Assays that Use Highly Specific TB Antigens

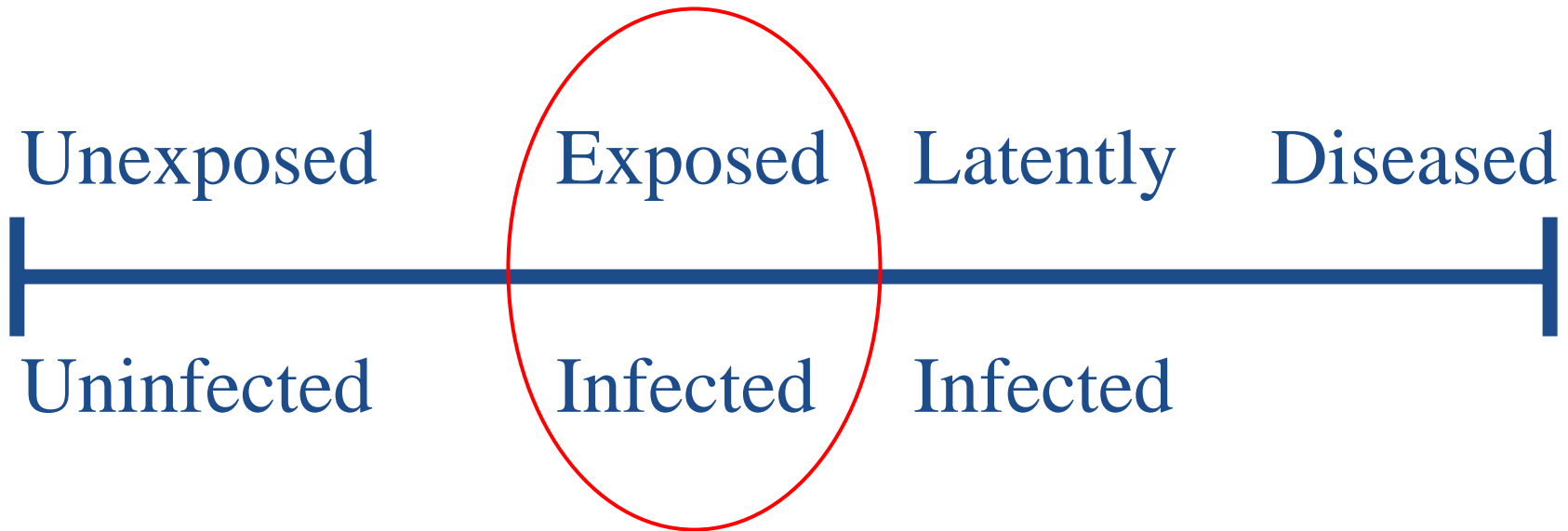
February 21, 2007

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Diagnosis of Tuberculosis Infection in Vaccine Studies



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Diagnosis of Tuberculosis Infection in Vaccine Studies



Uses of IGRA in High Burden Countries

- **Diagnosis of Active Disease**
 - Diagnosis in infants and young children
- **Diagnosis of Latent Infection**
 - Diagnosis in infants and young children
 - Increase efficiency of treatment of LTBI

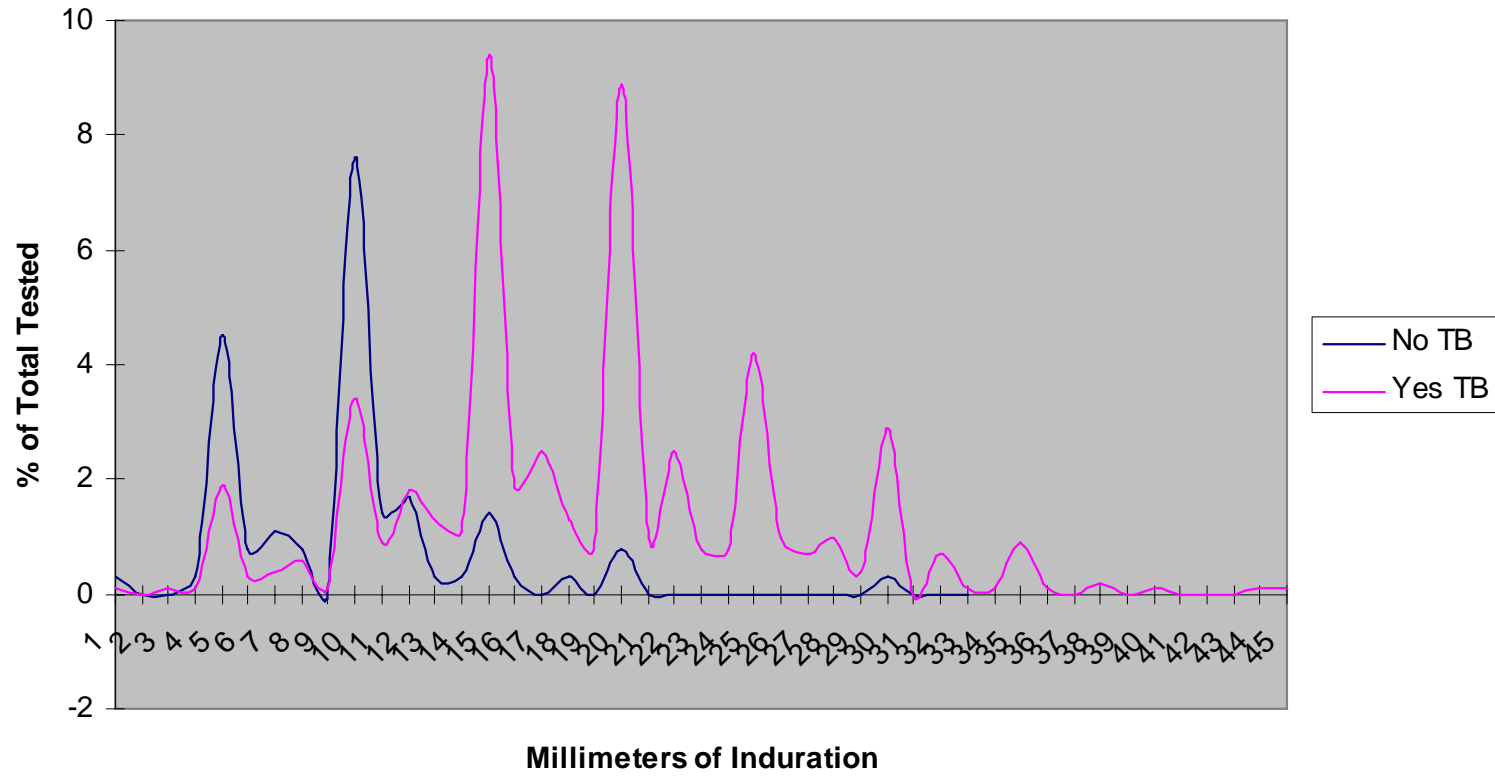
Diagnosis of TB Disease in Infants and Young Children

- SATVI BCG Trial
 - 1,751 infants admitted to case verification ward
 - 736 infants diagnosed with definite, probable or possible tuberculosis
 - 34% of definite cases, 48% of probable and possible cases had 0 mm induration
- 91% QFT + compared to 71% TST + in adolescent study
- SATVI/FIND/Aeras MOU to evaluate IGRA in a second cohort of neonates at this site



Diagnosis of TB Disease in Infants and Young Children

TST Reactions for Infants with and without TB



Data from SATVI BCG Trial: G. Hussey PI.

Uses of IGRA in Diagnosing LTBI

- Primary evidence
 - Improved correlation of IGRA with TB exposure
 - Improved correlation with recent exposure
- Problems
 - Inconsistent evidence (Gambia)
 - Problems in conducting tests in high volume laboratory
 - Lack of prospective data



Comparison and % agreement of Mantoux 15 mm and QuantiFERON tests

The two tests compared	Percentage agreement	Both positive	First positive, second negative	First negative, Second positive	Both negative	Kappa score
Mantoux15 mm vs QuantiFERON TB	60	129 (36%)	56 (16%)	86 (24%)	87 (24%)	0.20
Mantoux15 mm vs QuantiFERON Gold	56	82 (23%)	103 (29%)	55 (15%)	118 (33%)	0.12
Mantoux15 mm vs QuantiFERON Gold in-tube	64	128 (36%)	57 (16%)	73 (20%)	100 (28%)	0.27

QF=QuantiFERON®



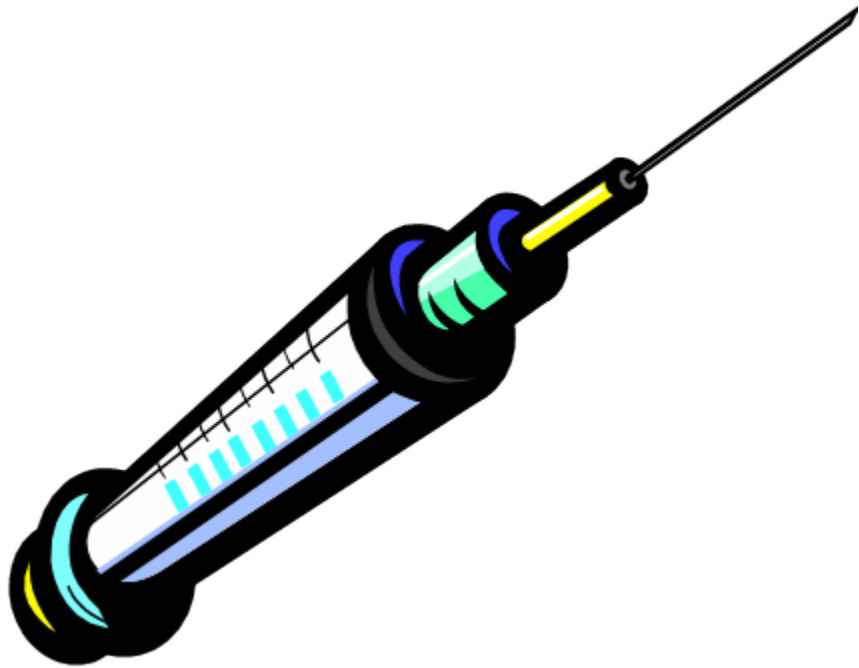
Comparison and % agreement of QuantiFERON tests

The two tests compared	Percentage agreement	Both positive	First positive, second negative	First negative, Second positive	Both negative	Kappa score
QuantiFERON TB vs QuantiFERON Gold	64	112 (31%)	103 (29%)	25 (7%)	118 (33%)	0.32
QuantiFERON TB vs QuantiFERON Gold in-tube	66	148 (41%)	67 (19%)	53 (15%)	90 (25%)	0.31
QuantiFERON Gold vs QuantiFERON Gold in-tube	74	123 (34%)	14 (4%)	78 (22%)	143 (40%)	0.50

QF=QuantiFERON®

Adolescent Cohort Studies

- Recruit cohorts of 8,000 adolescents 12 – 18 years of age and follow for two years
- TST and QuantiFERON® (IGRA?) test all subjects at baseline and at end of follow up
- For participants in active follow-up:
 - Every six months
 - Re-test 4,000 in active follow-up with QuantiFERON® (IGRA?) every six months
 - Bank PBMC's and Plasma



“Pure logical thinking cannot yield us any knowledge of the empirical world; all knowledge of reality starts from experience and ends with it. Propositions arrived at by purely logical means are completely empty as regards reality.”

Albert Einstein in praise of Galileo