

# Update on significant recent research papers

Childhood Tuberculosis Sub-Group

27 October 2014

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[High-Dose Rifapentine with Moxifloxacin for Pulmonary Tuberculosis.](#)

1. Jindani A, Harrison TS, Nunn AJ, Phillips PP, Churchyard GJ, Charalambous S, Hatherill M, Geldenhuys H, McIlerron HM, Zvada SP, Mungofa S, Shah NA, Zizhou S, Magweta L, Shepherd J, Nyirenda S, van Dijk JH, Clouting HE, Coleman D, Bateson AL, McHugh TD, Butcher PD, Mitchison DA; the RIFAQUIN Trial Team.  
N Engl J Med. 2014 Oct 23;371(17):1599-1608.  
PMID: 25337749 [PubMed - as supplied by publisher]  
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[Serum Human Epididymis Protein 4 \(HE4\) in the Differential Diagnosis of Peritoneal Tuberculosis: A Report of Two Cases.](#)

Kabaca C, Dolgun ZN, Telci A, Karateke A.  
Balkan Med J. 2014 Sep;31(3):270-1. doi: 10.5152/balkanmedj.2014.13326. Epub 2014 Sep 1. No abstract available.  
PMID: 25337429 [PubMed]  
[Related citations](#)

[Alarming Levels of Drug-Resistant Tuberculosis in HIV-Infected Patients in Metropolitan Mumbai, India.](#)

3. Isaakidis P, Das M, Kumar AM, Peskett C, Khetarpal M, Bamne A, Adsul B, Manglani M, Sachdeva KS, Parmar M, Kanchar A, Rewari BB, Deshpande A, Rodrigues C, Shetty A, Rebello L, Saranchuk P.  
PLoS One. 2014 Oct 21;9(10):e110461. doi: 10.1371/journal.pone.0110461. eCollection 2014.  
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[World health dilemmas: Orphan and rare diseases, orphan drugs and orphan patients.](#)

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[Looking beyond the obvious: an unusual cause of iron deficiency anaemia.](#)

5. Jyotirmanju CS, Mallya P, Rau A, Rau AT.  
Indian J Hematol Blood Transfus. 2014 Sep;30(Suppl 1):183-5. doi: 10.1007/s12288-013-0321-9. Epub 2014 Jan 22.  
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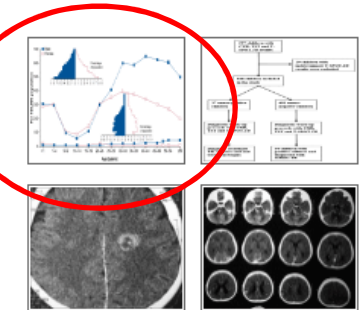
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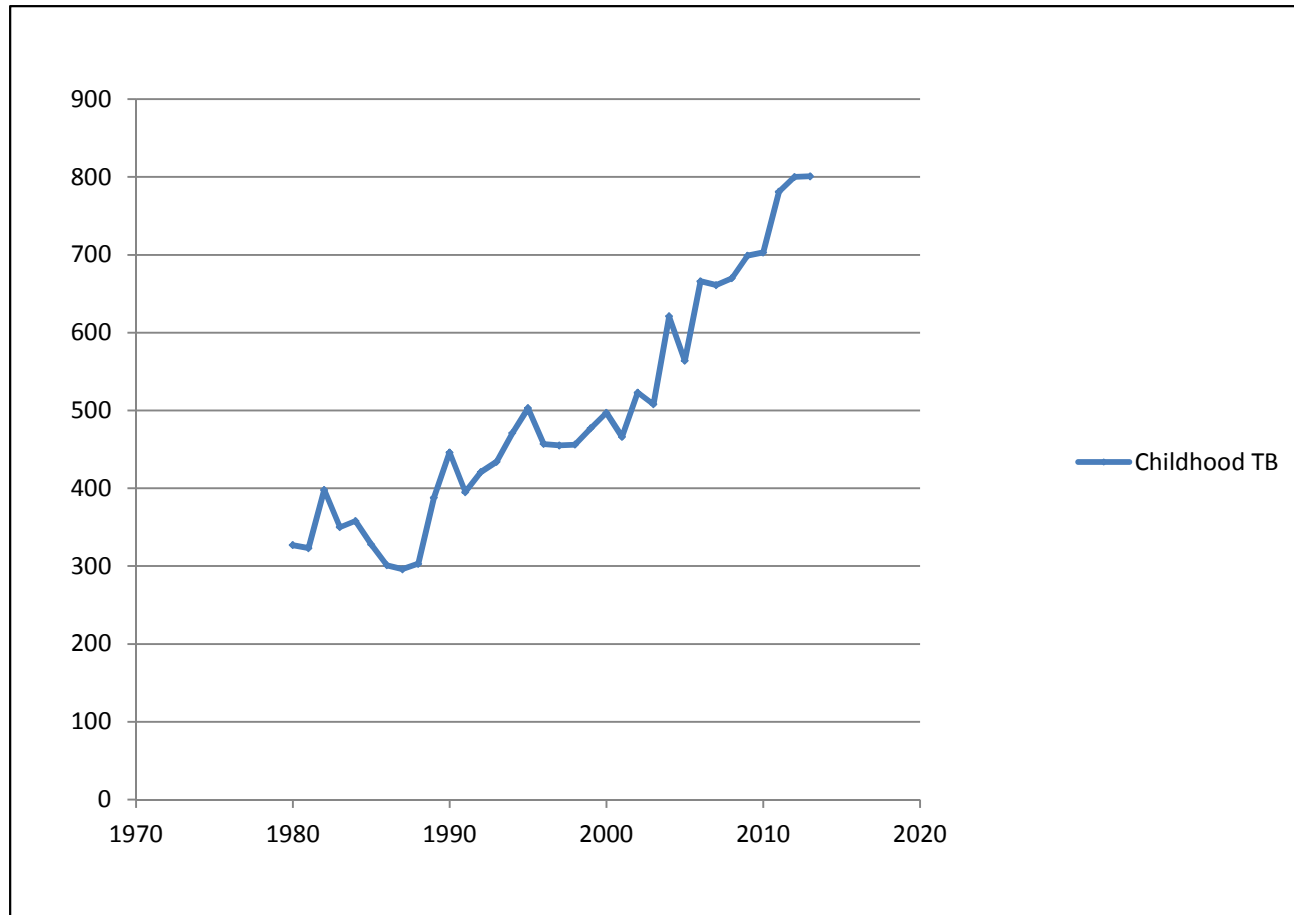
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Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010 [Lancet. 2012]  
The history of tuberculosis. [Respir Med. 2006]

Global, regional, and national incidence and mortality for HIV, tuberculosis, and [Lancet. 2014]

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[Current status of Paragonimus and paragonimiasis in Ecuador.](#)

1. Calvopiña M, Romero D, Castañeda B, Hashiguchi Y, Sugiyama H.  
Mem Inst Oswaldo Cruz. 2014 Oct 14;0:0. [Epub ahead of print]  
PMID: 25338151 [PubMed - as supplied by publisher]  
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[Rheumatoid Arthritis Increases the Risk of Nontuberculosis Mycobacterial Disease and Active Pulmonary Tuberculosis.](#)

2. Yeh JJ, Wang YC, Sung FC, Kao CH.  
PLoS One. 2014 Oct 22;9(10):e110922. doi: 10.1371/journal.pone.0110922. eCollection 2014.  
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3. Kärki T, Napoli C, Riccardo F, Fabiani M, Dente MG, Carballo M, Noori T, Declich S.  
Int J Environ Res Public Health. 2014 Oct 21;11(10):11004-11014.  
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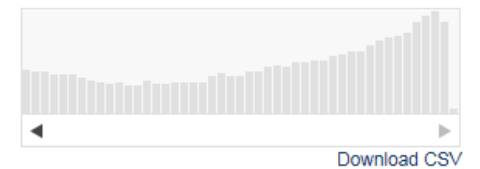
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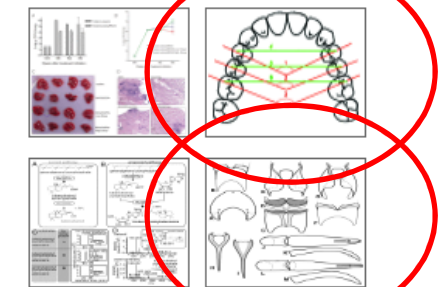
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Accidental condom inhalation. [Indian J Chest Dis Allied Sci. 2004]  
Anatomy of the anterolateral ligament of the

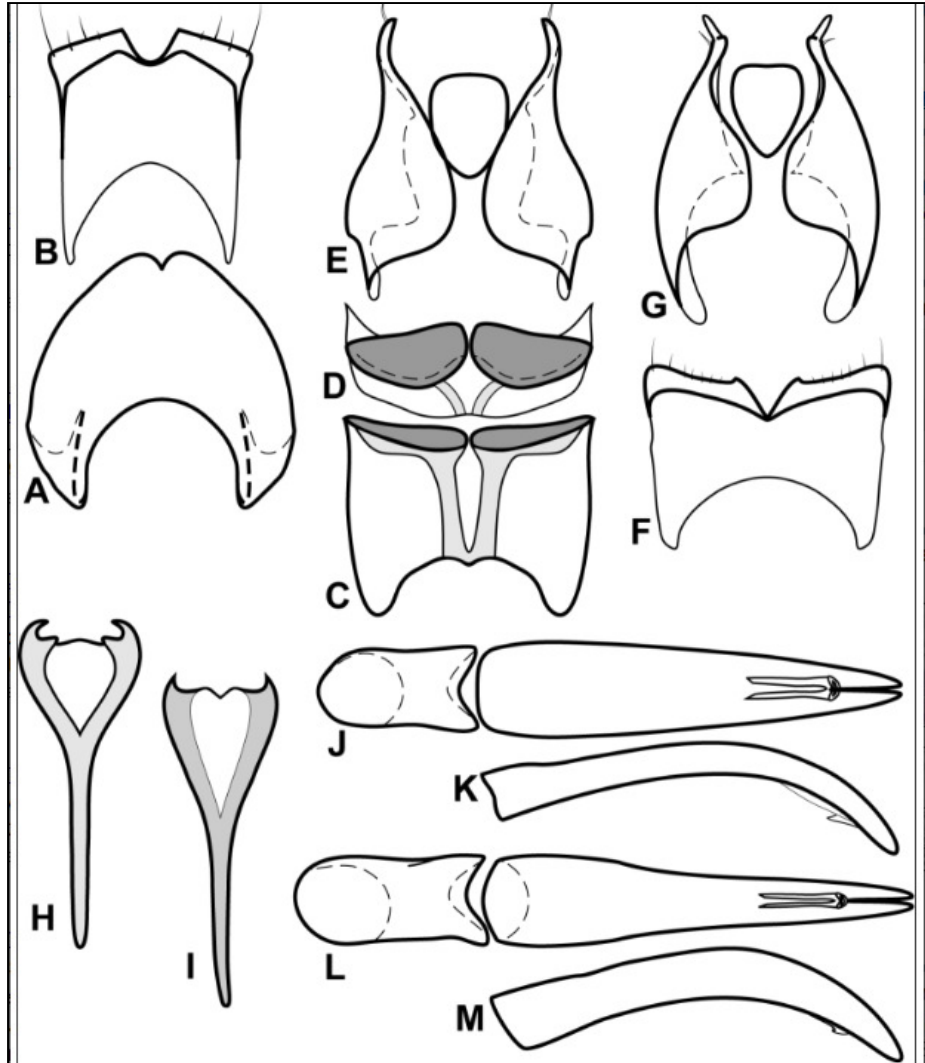


Figure 57.

Male genitalia of *Baconia gibbifer* group. A T8 of *Baconia tenuipes* B S8 of *Baconia tenuipes* C S8 of *Baconia tuberculifer* D S8 (apical view) of *Baconia tuberculifer* E T9 & T10 of *Baconia tuberculifer* F S8 of *Baconia globosa* G T9 & T10 of *Baconia globosa* H S9 of *Baconia tenuipes* I S9 of *Baconia tuberculifer* J Aedeagus, dorsal view of *Baconia tenuipes* K Aedeagus, lateral view of *Baconia tuberculifer* L Aedeagus, dorsal view of *Baconia tuberculifer* M Aedeagus, lateral view of *Baconia tuberculifer*.

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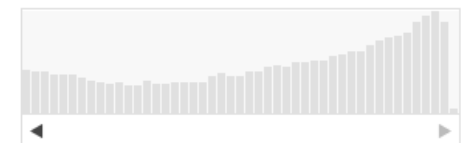
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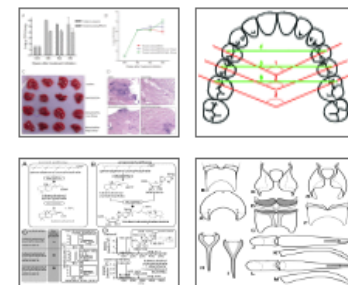
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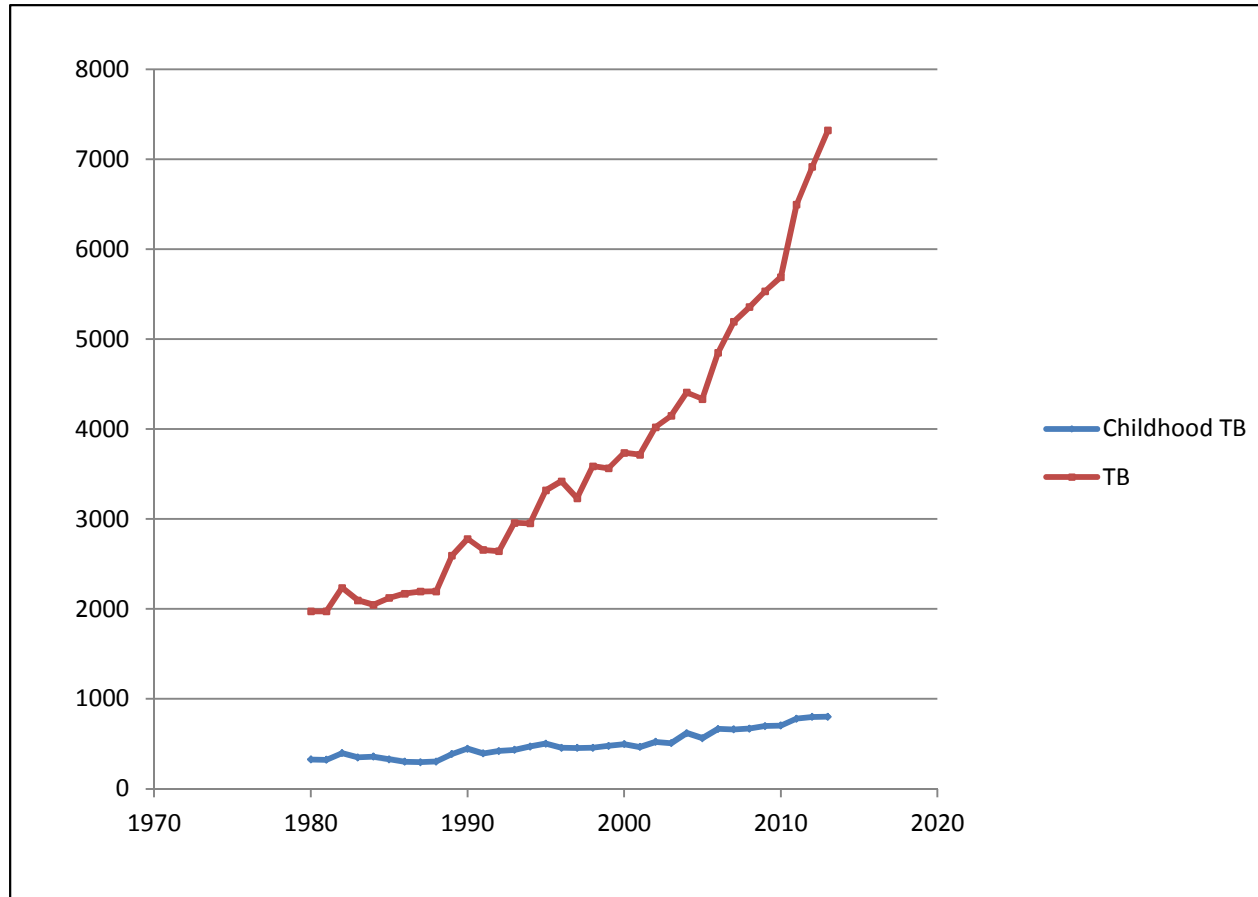


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[Serum Human Epididymis Protein 4 \(HE4\) in the Differential Diagnosis of Peritoneal Tuberculosis: A](#)

1. [Report of Two Cases.](#)

Kabaca C, Dolgun ZN, Telci A, Karateke A.

Balkan Med J. 2014 Sep;31(3):270-1. doi: 10.5152/balkanmedj.2014.13326. Epub 2014 Sep 1. No abstract available.

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[Alarming Levels of Drug-Resistant Tuberculosis in HIV-Infected Patients in Metropolitan Mumbai,](#)

2. [India.](#)

Isaakidis P, Das M, Kumar AM, Peskett C, Khetarpal M, Bamne A, Adsul B, Manglani M, Sachdeva KS,

Parmar M, Kanchar A, Rewari BB, Deshpande A, Rodrigues C, Shetty A, Rebello L, Saranchuk P.

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Indian J Hematol Blood Transfus. 2014 Sep;30(Suppl 1):183-5. doi: 10.1007/s12288-013-0321-9. Epub 2014 Jan 22.

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adult intensive care unit in fiji: [J Trop Med. 2014]

Acute febrile encephalopathy in children and  
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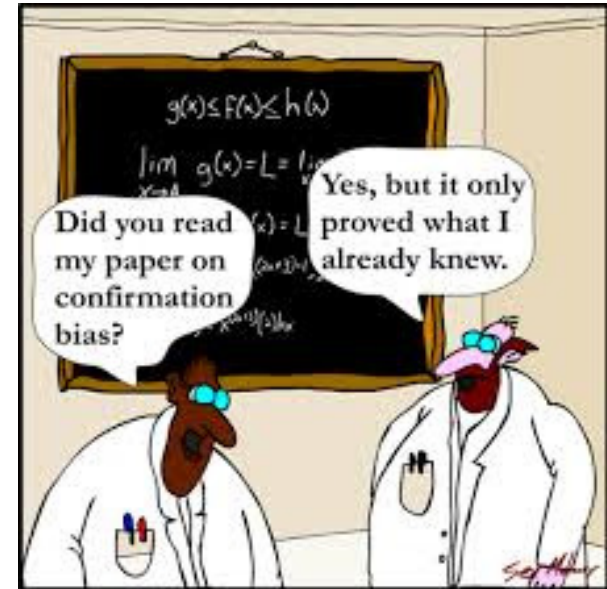
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# My biases

- 746 studies identified on PubMed
- On review of title I selected 28 that I thought were pretty interesting
  - Based on my own clinical and research interests
  - Slightly biased towards clinical/epi studies
  - Slightly biased towards drug resistance
- Broadly divided into five categories



# Findings

- Epidemiology/natural history
- Diagnostics
- Treatment
- Prevention
- Vaccines

# Findings

- Epidemiology/natural history
- Diagnostics
- Treatment
- Prevention
- Vaccines

# Incidence of multidrug-resistant tuberculosis disease in children: systematic review and global estimates

Helen F. Jenkins, Aislinn W. Tolson, Courtney M. Yuan, Jonathan B. Rose, Solomon Kachur, Carlos M. Pérez-Velazquez, Rebecca Merce...

## Risk for Tuberculosis in Child Contacts

Development and Validation of a Predictive Score

Pei-Chun Chan<sup>1,2,3</sup>, Steven Shinn-Fong Peng<sup>4,5</sup>, Mei-Yu Chiou<sup>1</sup>, Du-Lin Ling<sup>6</sup>, Luan-Yin Chang<sup>3</sup>, Kwei-Feng Wang<sup>1</sup>, Chi-Tai Fong<sup>2,7\*</sup>, Li-Min Huang<sup>3\*</sup>

Naranbhai et al. *BMC Medicine* 2014, 12:120  
<http://www.biomedcentral.com/1741-7015/12/120>



Medicine for Global Health



RESEARCH ARTICLE

Open Access

## The association between the ratio of monocytes: lymphocytes at age 3 months and risk of tuberculosis (TB) in the first two years of life

Vivek Naranbhai<sup>1,2</sup>, Soyeon Kim<sup>3</sup>, Helen Fletcher<sup>4</sup>, Mark F Cotton<sup>5</sup>, Avy Violari<sup>6</sup>, Charles Mitchell<sup>7</sup>, Sharon Nachman<sup>8</sup>, George McSherry<sup>9</sup>, Helen McShane<sup>4</sup>, Adrian VS Hill<sup>1,4\*</sup>, Shabir A Madhi<sup>10\*</sup> for the IMPAACT P1041 team

## National and international guidelines

Elettra Berti, Luisa Galli, Elisabetta Venturini, Maurizio de Martini, Elena Chiappini\*

# Findings

- Epidemiology/natural history
- **Diagnostics**
- Treatment
- Prevention
- Vaccines

## Assessment of the novel T-cell activation marker-tuberculosis assay for diagnosis of active tuberculosis in children: a prospective proof of concept study

Damien Portevin, Felicien Moukambi, Frederick Haraka, Andrea Rachow, Elma Claudia Daubenberger, Klaus Reither\*

## Safety and efficacy of induced sputum in young children hospitalised with suspected pulmonary tuberculosis

N. S. Planting,\* G. L. Visser,\* M. P. Nicol,† L. V. Visser

\*Erasmus Medical Centre, Rotterdam, The Netherlands, †Department of Paediatrics and Respiratory Medicine, University of Cape Town, Cape Town, South Africa

## Xpert MTB/RIF assay for diagnosis of pulmonary tuberculosis in children: A prospective, multi-centre evaluation

Klaus Reither<sup>a,b,c,\*</sup>, Christina Manyama<sup>d</sup>, Petra Clowes<sup>d,e</sup>, Andrea Rachow<sup>e,f</sup>, Daniel Mapamba<sup>d</sup>, Andreas Steiner<sup>a,b</sup>, Amanda Ross<sup>a,b</sup>, Elirehema Mfinanga<sup>c</sup>, Mohamed Sasamalo<sup>c</sup>, Martin Nsubuga<sup>g</sup>, Francesco Aloisi<sup>g</sup>, Daniela Cirillo<sup>h</sup>, Levana Jugheli<sup>a,b,c</sup>, Fred Lwilla<sup>c</sup>

## Diagnosis of Tuberculosis and Host Immune Response in Children

Suzanne T. Anderson, Ph.D., M.R.C.P.C.H., Myrsini Kaforou, M.Phil., Andrew J. Brent, Ph.D., M.R.C.P., Victoria J. Wright, Ph.D., Claire M. Banwell, Ph.D., George Chagaluka, M.B., B.S., Amelia C. Crampin, F.F.P.H.M., Hazel M. Dockrell, Ph.D., Neil French, F.R.C.P., Ph.D., Melissa S. Hamilton, Ph.D., Martin L. Hibberd, Ph.D., Florian Kern, M.D., Paul R. Langford, Ph.D., F.S.B., Ling Ling, M.B., B.S., Rachel Mlotha, F.C.P. (Paeds) (SA), Tom H.M. Ottenhoff, M.D., Ph.D., Sandy Pienaar, M.Sc., Vashini Pillay, M.B., Ch.B., J. Anthony G. Scott, F.R.C.P., Hemed Twahir, M.Med., Robert J. Wilkinson, F.R.C.P., Ph.D., Lachlan J. Coin, Ph.D., Robert S. Heyderman, F.R.C.P., Ph.D., Michael Levin, Ph.D., and

## Urine lipoarabinomannan testing for diagnosis of pulmonary tuberculosis in children

Mark P Nicol, Veronica Allen, Lesley Workman, Washiefa Isaacs, Jacinta Munro, Yonas Ghebrekristos, Heather J Zar

## Enhancing TB Case Detection: Experience in Offering Upfront Xpert MTB/RIF Testing to Pediatric Presumptive TB and DR TB Cases for Early Rapid Diagnosis of Drug Sensitive and Drug Resistant TB

Neeraj Raizada<sup>1\*</sup>, Kuldeep Singh Sachdeva<sup>2</sup>, Sreenivas Achuthan Nair<sup>3</sup>, Shubhangi Kulsange<sup>1</sup>, Radhey Shayam Gupta<sup>2</sup>, Rahul Thakur<sup>1</sup>, Malik Parmar<sup>3</sup>, Christen Gray<sup>4</sup>, Ranjani Ramachandran<sup>3</sup>, Bhavin Vadera<sup>1</sup>, Shobha Ekka<sup>1</sup>, Shikha Dhawan<sup>2</sup>, Ameet Babre<sup>1</sup>, Mayank Ghedia<sup>3</sup>, Umesh Alavadi<sup>1</sup>, Puneet Dewan<sup>3</sup>, Mini Khetrapal<sup>5</sup>, Ashwini Khanna<sup>6</sup>, Catharina Boehme<sup>4</sup>, Chinnambedu Nainarappan Paramasivan<sup>1</sup>

# Findings

- Epidemiology/natural history
- Diagnostics
- **Treatment**
- Prevention
- Vaccines

# Treatment outcomes of childhood tuberculous meningitis: a syste

Silvia S Chiang\*

## Intermittent versus daily therapy for treating tuberculosis in children (Review)

Bose A, Kalita S, Rose W, Tharyan P



ELSEVIER

REVIEW

Linezolid for the  
A review and re

Anthony J. Garcia-Pr

Desmond Tutu TB Centre, Departme  
Cape Town, South Africa

## Tuberculosis Immune Reconstitution Inflammatory Syndrome in Children Initiating Antiretroviral Therapy for HIV Infection

*A Systematic Literature Review*

Ruth Link

Centers for Disease Control and Prevention

**MMWR**

Morbidity and Mortality Weekly Report

Recommendations and Reports / Vol. 62 / No. 9

October 25, 2013

ch, MD, MPH,†

**Provisional CDC Guidelines for the Use  
and Safety Monitoring of  
Bedaquiline Fumarate (Sirturo)  
for the Treatment of  
Multidrug-Resistant Tuberculosis**

**s Consilium**

**assistance with extensively drug-resistant  
tuberculosis management in a child: case  
study of compassionate delamanid use**



# Findings

- Epidemiology/natural history
- Diagnostics
- Treatment
- **Prevention**
- Vaccines

# Contact Investigation for Active Tuberculosis Among Child Contacts in Uganda

Devan Jaganath,<sup>1</sup> Sa  
Christina Lancioni,<sup>4</sup>  
and Ezekiel Mupere,

INT J TUBERC LUNG DIS 18(9):1057–1061  
© 2014 The Union  
<http://dx.doi.org/10.5588/ijtld.14.0286>

REVIEW

## Safety and completion of a 4-month course of rifampicin for latent tuberculous infection in children

Systematic  
utility of interper  
diagnosis of *Myc*  
in children: a 201

A. T. Cruz,\*† J. R. S

S Sollai†, L Galli†, M

## Preventive Therapy for Child Contacts of Multidrug-Resistant Tuberculosis: A Prospective Cohort Study

**Bacillus**  
**Protect C**

James A. Seddon,<sup>1,3,4</sup> Anneke C. Hesselning,<sup>1</sup> Heather Finlayson,<sup>2,5</sup> Katherine Fielding,<sup>6</sup> Helen Cox,<sup>7</sup> Jennifer Hughes,<sup>7</sup> Peter Godfrey-Faussett,<sup>3</sup> and H. Simon Schaaf<sup>1,5</sup>

Jonathan L. Zelner<sup>1,2</sup>, Megan B. Murray<sup>3,4</sup>, Mercedes C. Becerra<sup>3,5,6</sup>, Jerome Galea<sup>5</sup>, Leonid Lecca<sup>5</sup>, Roger Calderon<sup>5</sup>, Rosa Yataco<sup>5</sup>, Carmen Contreras<sup>5</sup>, Zibiao Zhang<sup>6</sup>, Bryan T. Grenfell<sup>1,2</sup>, and Ted Cohen<sup>4,6</sup>

## Concordance of B in Households of Multidrug-Resista

<sup>1</sup>Department of Ecology and Evolutionary Biology, Princeton University, Princeton, New Jersey; <sup>2</sup>Fogarty International Center, National Institutes of Health, Bethesda, Maryland; <sup>3</sup>Department of Global Health and Social Medicine, Harvard Medical School, Boston, Massachusetts; <sup>4</sup>Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts; <sup>5</sup>Partners In Health, Boston, Massachusetts and Lima, Peru; and <sup>6</sup>Division of Global Health Equity, Brigham and Women's Hospital, Boston, Massachusetts

Jonathan B. Parr,<sup>1,2,3</sup> Carole D. Mitnick,<sup>1,2,3</sup> Sidney S. Atwood,<sup>1</sup>  
Katuska Chalco,<sup>3</sup> Jaime Bayona,<sup>3</sup> and Mercedes C. Becerra<sup>1,2,3</sup>

<sup>1</sup>Division of Global Health Equity, Brigham and Women's Hospital, <sup>2</sup>Department of Global Health and Social Medicine, Harvard Medical School, and <sup>3</sup>Partners In Health, Boston, Massachusetts

# Findings

- Epidemiology/natural history
- Diagnostics
- Treatment
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- Vaccines

## Protection by BCG Vaccination Against

Tuber  
Rando

Punam Mar  
Laura C. Ro

### IMMUNOLOGICAL ASPECTS

Safety and immunogenicity of the M72/AS01 candidate tuberculosis vaccine when given as a booster to BCG in Gambian infants: An open-label randomized controlled trial

Olubukola T. Idoko <sup>a,\*,1</sup>, Olumuyiwa A. Owolabi <sup>a,1</sup>, Patrick K. Owiafe <sup>a</sup>, Philippe Moris <sup>b</sup>, Aderonke Odutola <sup>a</sup>, Anne Bollaerts <sup>b</sup>, Ezra Ogundare <sup>a</sup>, Erik Jongert <sup>b</sup>, Marie-Ange Demoitié <sup>b</sup>, Opokua Ofori-Anyinam <sup>b,2</sup>, Martin O. Ota <sup>a,c,2</sup>

Causes of variation in BCG vaccine efficacy: Examining evidence from the BCG REVAC cluster randomized trial to explore the masking and the blocking hypotheses

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The novel tuberculosis vaccine, AERAS-402, is safe in healthy infants previously vaccinated with BCG, and induces dose-dependent CD4 and CD8T cell responses

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Page 1 of 11

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# Conclusions

- Exciting times for paediatric TB
- Lots of studies being published
- Lots more work to do...