CAMFiC
societat catalana de medicina familiar i comunitària

Generalitat de Catalunya
Departament de Salut

CatSalut
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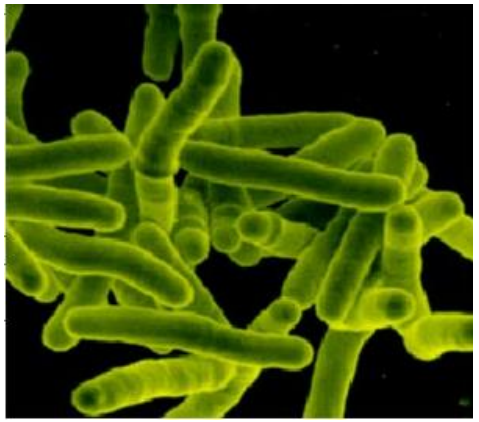
Update infeccioses 2016

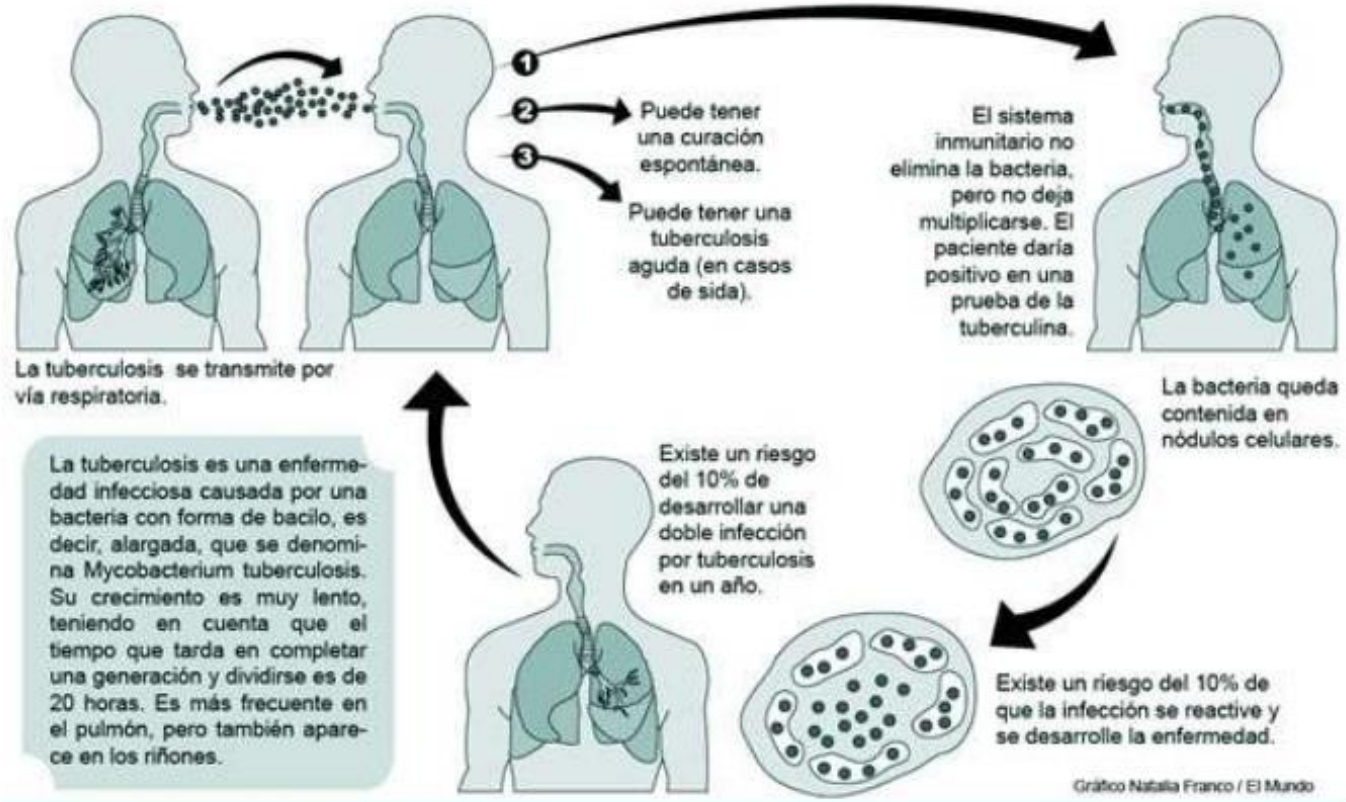
TUBERCULOSI



Docent : Anna Ferrer

Grup de Tuberculosi de la Camfic: Laura Clotet, Carmen Ros

La patología



Abstract Send to:

Int J Tuberc Lung Dis. 2010 Nov;14(11):1369-73.

Human tuberculosis caused by Mycobacterium bovis in the United States, Latin America and the Caribbean.

de Kantor IN[1], LoBue PA, Thoen CO.

Author information

Abstract

Human tuberculosis (TB) caused by Mycobacterium bovis appears to be rare in most of the region of the Americas, although some localities have reported an unusually high prevalence of M. bovis among human TB cases (e.g., San Diego, CA, USA; parts of Mexico). As surveillance data are lacking in many countries, there is substantial uncertainty regarding actual incidence. M. bovis is most often not identified, as the diagnosis of TB is made by smear microscopy alone or using egg-containing culture media lacking pyruvate. Where human M. bovis cases have been studied in the region, they appear to be associated with ingestion of unpasteurized dairy products, or with airborne acquired infection in animal keepers and meat industry workers from countries where bovine TB remains a problem. Human-to-human transmission of M. bovis does occur, but appears to account for a very small proportion of cases. Efforts to eradicate M. bovis in humans in the Americas should therefore be directed at eradicating the disease in cattle, increasing pasteurization of dairy products and providing education about the dangers of consuming unpasteurized dairy products.

PMID: 20937174 [PubMed - indexed for MEDLINE]

MeSH Terms

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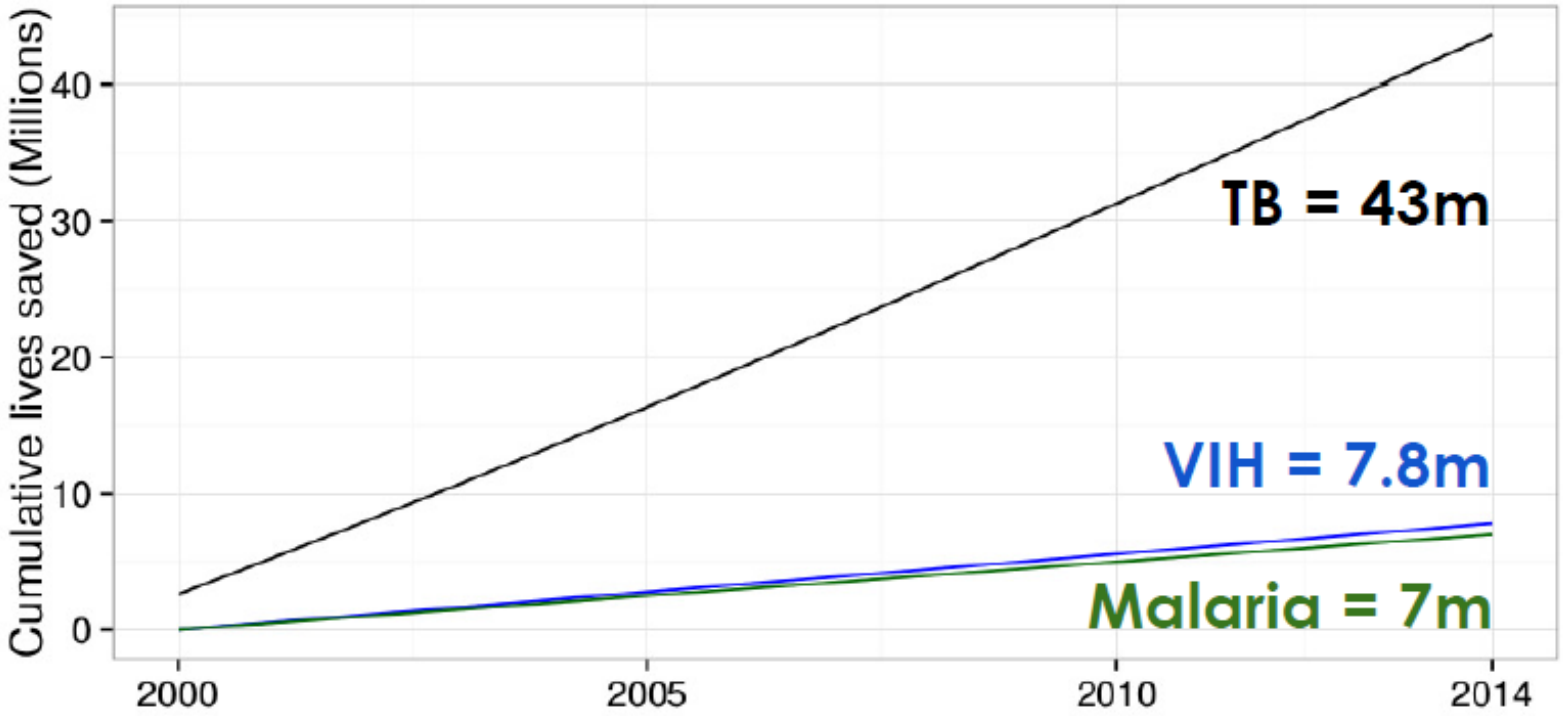
5 FACTS ON
TUBERCULOSIS
1.4 mln
TB is curable but still kills 1.4 mln people every year, with over 95% of deaths in low and middle income countries
SOURCE: WHO PHOTO: REUTERS/Finbarr O'Reilly
THOMSON REUTERS
FOUNDATION

43 millones de muertes por TB evitadas entre el 2000 y el 2014

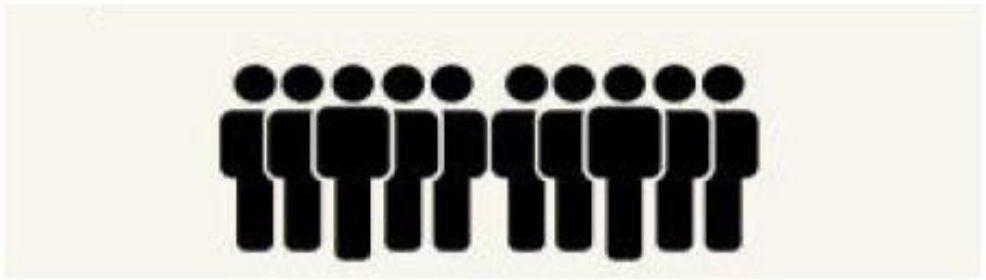


GLOBAL TB PROGRAMME

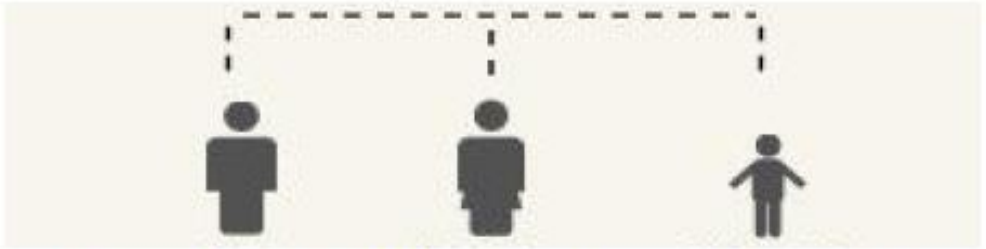
Ref: Global TB Control Report 2015

World Health Organization

9.6 millones caen enfermos con TB en el 2014

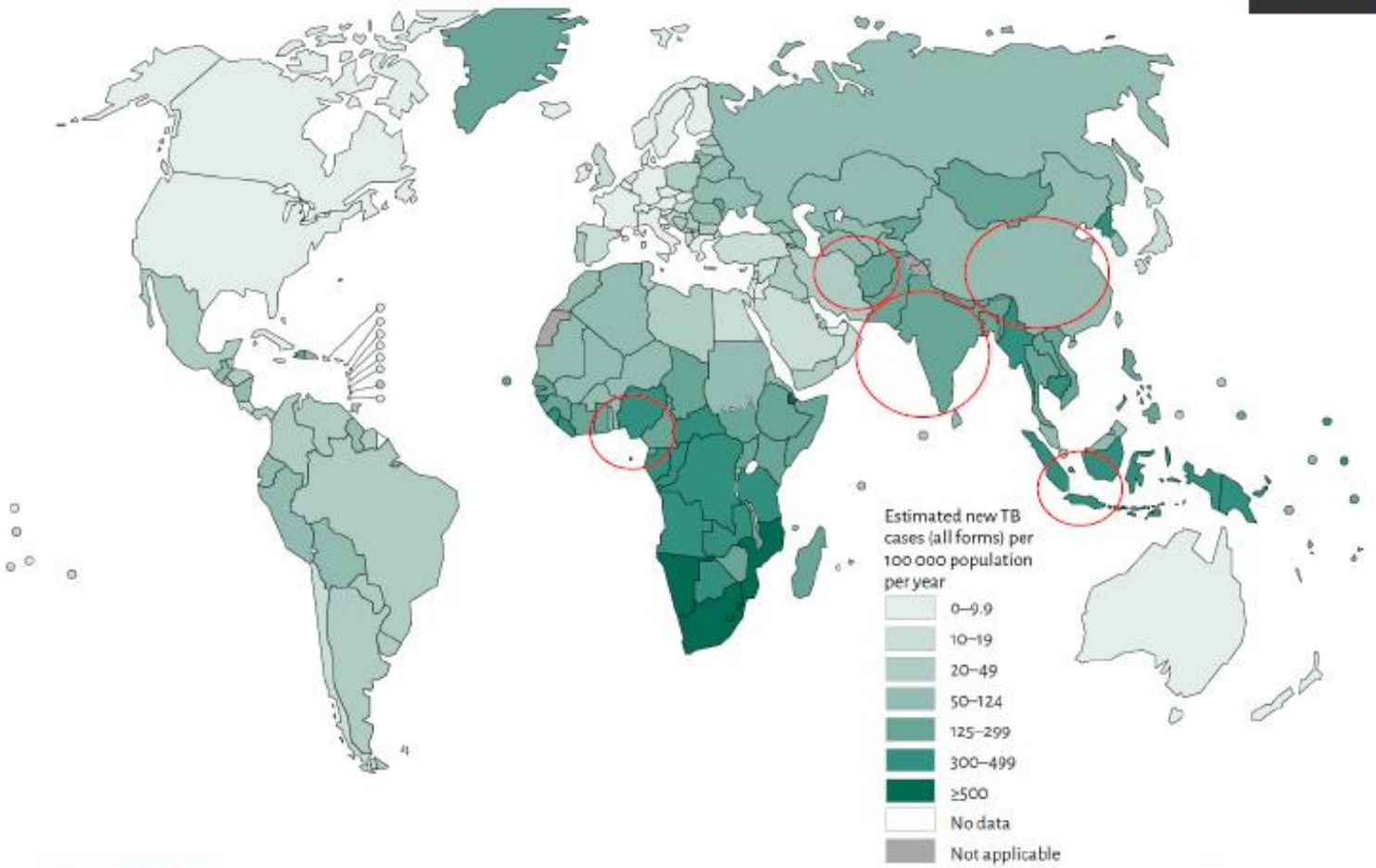


Casos de TB estimados y/o reportados



5'4 m hombres / 3'2 m* mujeres /*1m niños

Incidencia de TB: países y regiones



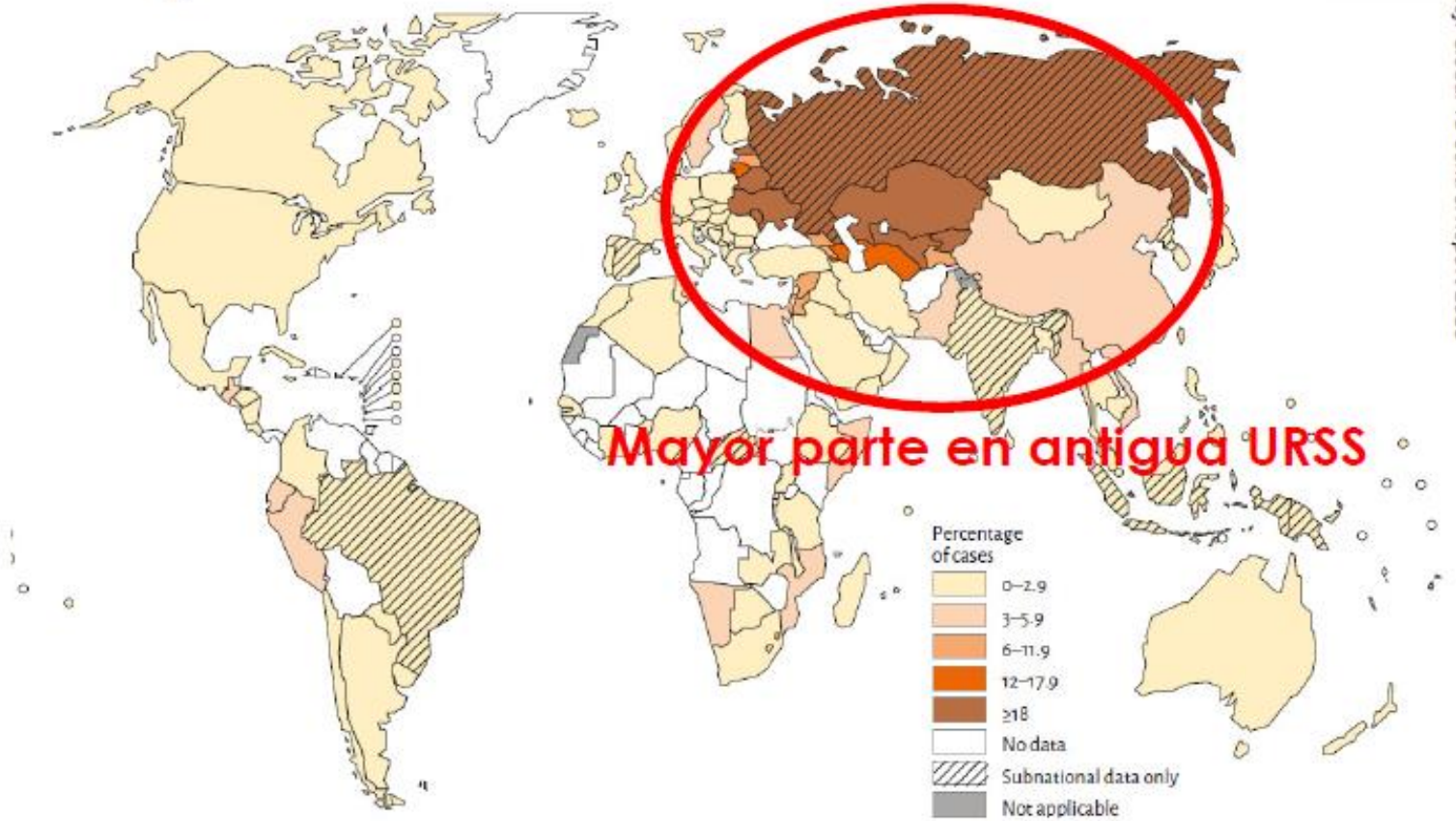
GLOBAL TB PROGRAMME

http://atlas.ecdc.europa.eu/public/index.aspx

World Health Organization

TB-MDR: 3% de los casos nuevos de TB

Porcentaje de casos nuevos de TB con TB-MDR



Ref. Global TB Control Report 2015

Mayor parte en antigua URSS

India, China, Russia, Pakistan y Ucrania tienen 62% de todos los casos

GLOBAL TB PROGRAMME

World Health Organization

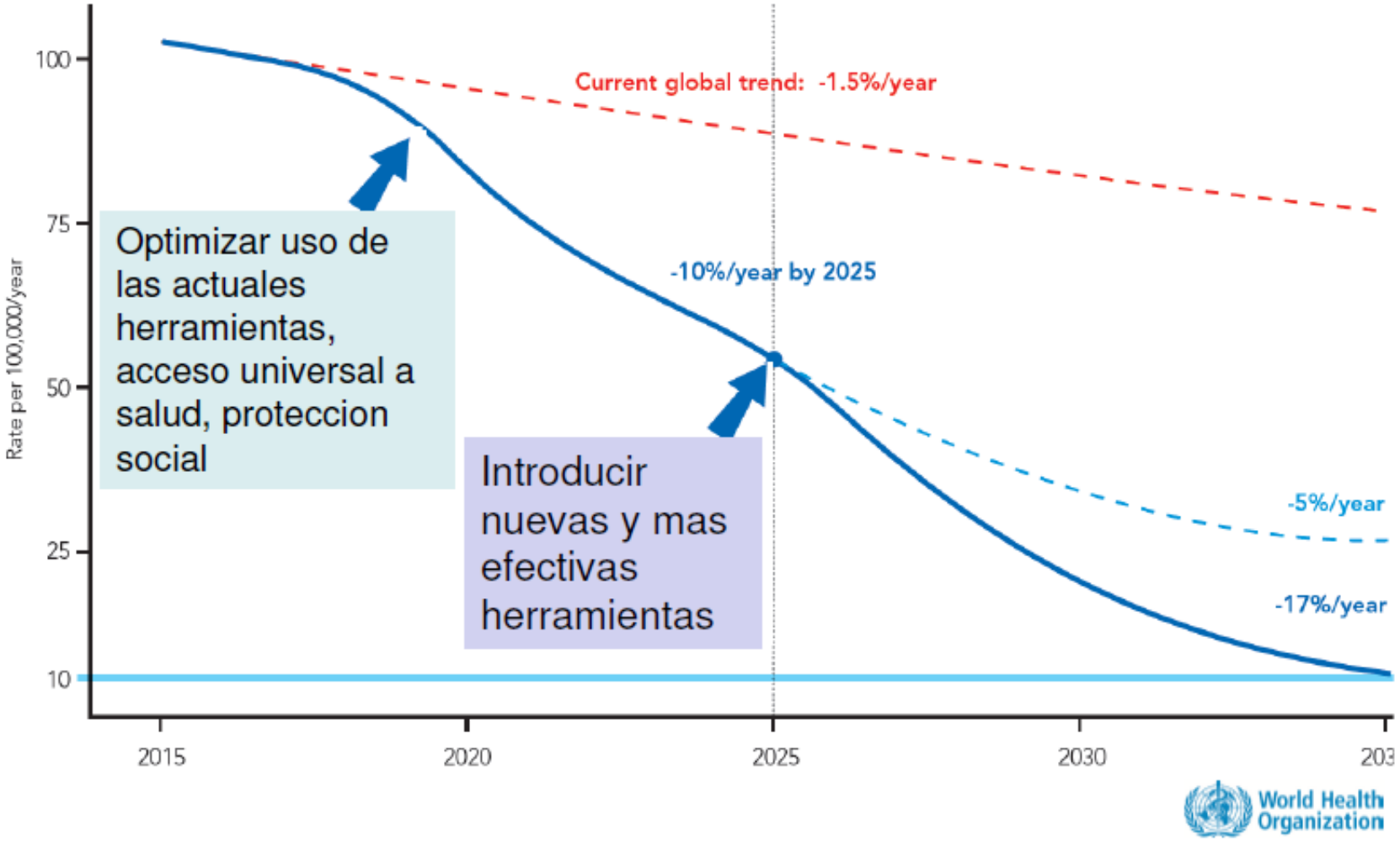
Aspectes generals del control de la TB
Objectius de l'atenció, prevenció i control

1. **Detectar tots els casos.**
2. **Diagnosticar el més aviat possible**
3. **Tractar i controlar tots els malalts.**
4. **Realitzar estudi de contactes**
5. **Seguir tots els contactes amb tractament.**

Pasemos de controlar la TB
a terminar la epidemia de TB en el 2030

- 80% reduccion en casos nuevos
- 90% de reduccion en mortalidad
- 100% de familias afectadas por TB sin gastos catastroficos debidos a la enfermedad y su tratamiento

Decliu incidència de TBC



Las ratas gigantes pueden detectar la tuberculosis

09 Apr 2015

Las ratas gigantes pueden detectar la tuberculosis. Foto AFP.

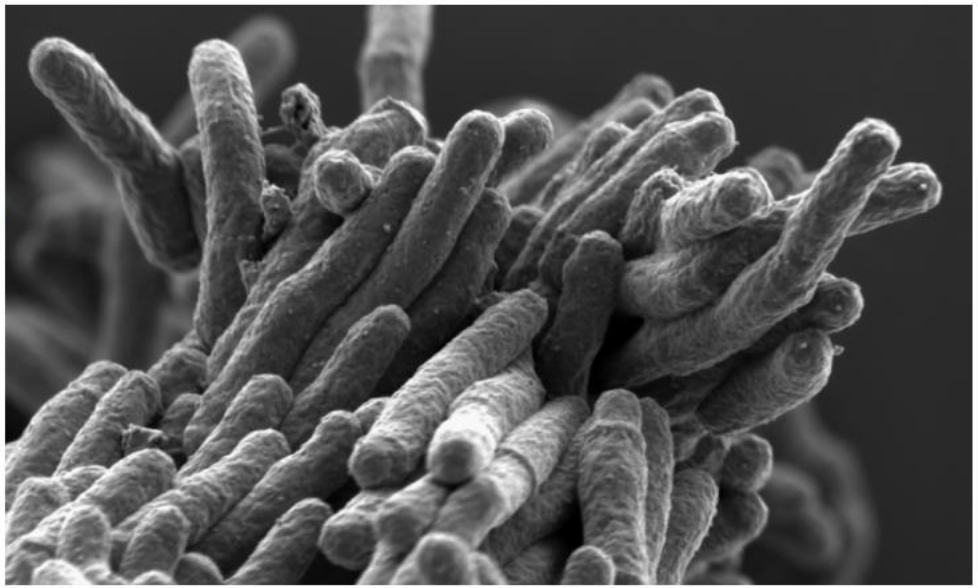
"Las ratas que utilizamos se llaman ratas de Gambia. Son endémicas de África y adaptadas a este entorno. Pesan entre 1 kilo y un 1,5 y miden cerca de 30 centímetros de largo. Son amigables, dóciles, fáciles de entrenar y tienen muy buen sentido del olfato, que las hace capaces de identificar esta partícula de olor de la tuberculosis", informó Emilio Valverde, Director del programa sobre tuberculosis de la ONG Apopo.

El ministerio de salud de Mozambique sigue de cerca la investigación. El país registró entre 2013 y 2014 un aumento del 10% en el número de casos y 20.000 personas murieron de tuberculosis en 2014.

- http://informaciona.com/video/ratas-gigantes-que-detectan-la-tuberculosis_x2m7da0

The next anti-tuberculosis drug may already be in your local pharmacy

July 7, 2015



A scanning electron micrograph of *Mycobacterium tuberculosis* bacteria. Credit: Stewart Cole/EPFL

Testing thousands of approved drugs, EPFL scientists have identified an unlikely anti-tuberculosis drug: the over-the-counter antacid lansoprazole (Prevacid).

Tuberculosis continues to be a global pandemic, second only to AIDS as the greatest single-agent killer in the world. In 2013 alone, the TB bug *Mycobacterium tuberculosis* caused 1.5 million deaths and almost nine million new infections. Resistance to TB drugs is widespread, creating an urgent need for new medicines. EPFL scientists have now identified lansoprazole, a widely used, over-the-counter antacid, as an excellent candidate against tuberculosis. The study is published in *Nature Communications*.

It takes well over ten years for a new tuberculosis drug to complete these trials and be approved for human use.

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more »

NATURE COMMUNICATIONS | ARTICLE OPEN

Lansoprazole is an antituberculous prodrug targeting cytochrome bc_1

Jan Rybniker, Anthony Vocat, Claudia Sala, Philippe Busso, Florence Pojer, Andrej Benjak & Stewart T. Cole

Affiliations | **Contributions** | **Corresponding author**

Nature Communications **6**, Article number: 7659 | doi:10.1038/ncomms8659
Received 08 January 2015 | Accepted 29 May 2015 | Published 09 July 2015

Abstract

Better antibiotics capable of killing multi-drug-resistant *Mycobacterium tuberculosis* are urgently needed. Despite extensive drug discovery efforts, only a few promising candidates are on the horizon and alternative screening protocols are required. Here, by testing a panel of FDA-approved drugs in a host cell-based assay, we show that the blockbuster drug lansoprazole (Prevacid), a gastric proton-pump inhibitor, has intracellular activity against *M. tuberculosis*. *Ex vivo* pharmacokinetics and target identification studies reveal that lansoprazole kills *M. tuberculosis* by targeting its cytochrome bc_1 complex through intracellular sulfoxide reduction to lansoprazole sulfide. This novel class of cytochrome bc_1 inhibitors is highly active against drug-resistant clinical isolates and spares the human H^+K^+-ATPase thus providing excellent opportunities for targeting the major pathogen *M. tuberculosis*. Our finding provides proof of concept for hit expansion by metabolic activation, a powerful tool for antibiotic screens.

PILLAR 1: INTEGRADA, ATENCION CENTRADA EN EL PACIENTE, CON PREVENCION

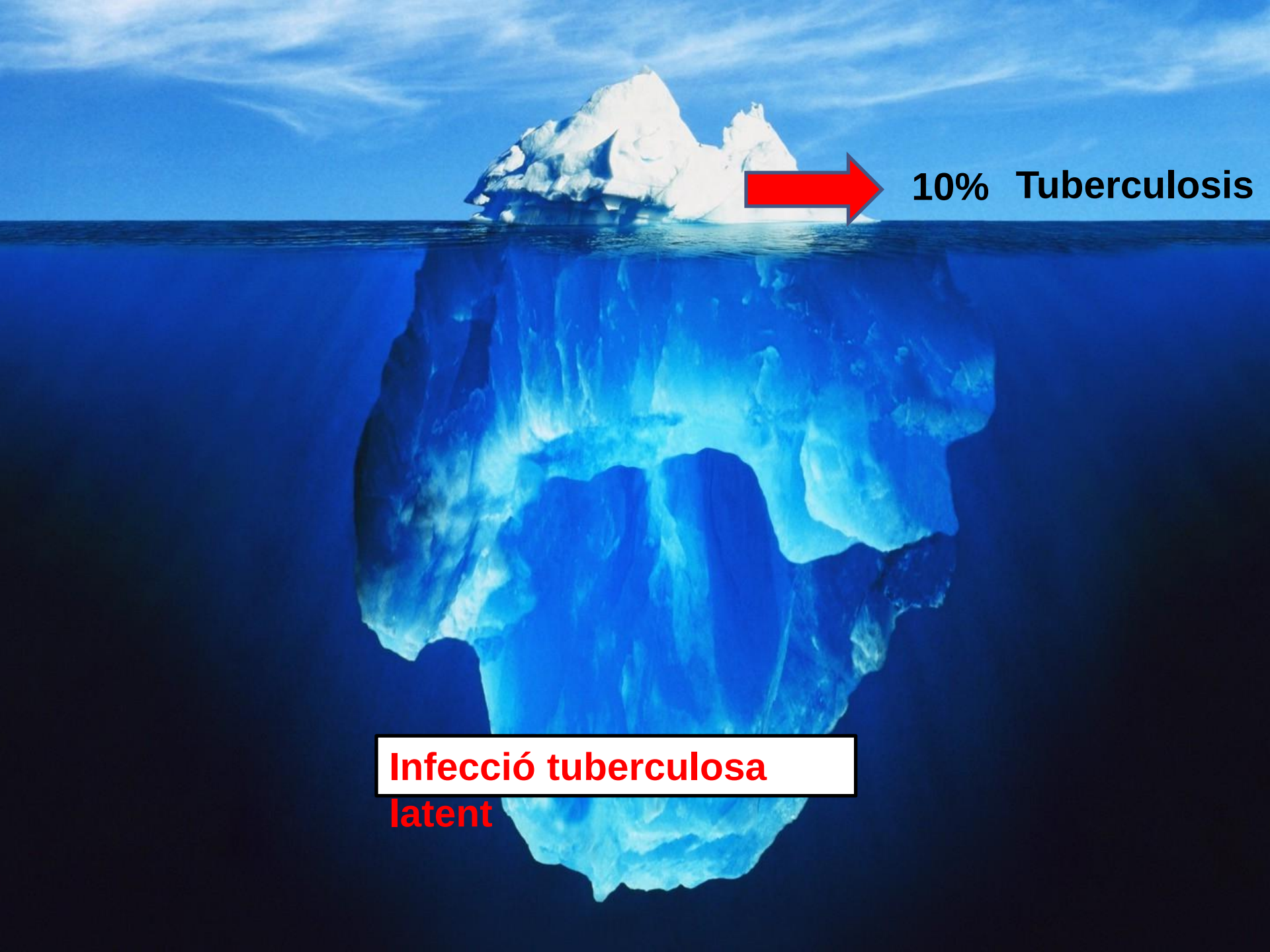
A. Early diagnosis of TB including universal drug-susceptibility testing, and systematic screening of contacts and high-risk groups

B. Treatment of all people with TB including drug-resistant TB, and patient support

D. Preventive treatment of persons at high risk; and vaccination against TB

C. Collaborative TB/ HIV activities; and management of co-morbidities

END TB


10% Tuberculosis
Infecció tuberculosa latent

Management of latent Mycobacterium tuberculosis infection: WHO guidelines for low tuberculosis burden countries

Latent tuberculosis infection (LTBI) is characterised by the presence of immune responses to previously acquired *Mycobacterium tuberculosis* infection without clinical evidence of active tuberculosis (TB). Here we report evidence-based guidelines from the World Health Organization for a public health approach to the management of LTBI in high risk individuals in countries with high or middle upper income and TB incidence of <100 per 100 000 per year. The guidelines strongly recommend systematic testing and treatment of LTBI in people living with HIV, adult and child contacts of pulmonary TB cases, patients initiating anti-tumour necrosis factor treatment, patients receiving dialysis, patients preparing for organ or haematological transplantation, and patients with silicosis. In prisoners, healthcare workers, immigrants from high TB burden countries, homeless persons and illicit drug users, systematic testing and treatment of LTBI is conditionally recommended, according to TB epidemiology and resource availability. Either commercial interferon-gamma release assays or Mantoux tuberculin skin testing could be used to test for LTBI. Chest radiography should be performed before LTBI treatment to rule out active TB disease. Recommended treatment regimens for LTBI include: 6 or 9 month isoniazid; 12 week rifapentine plus isoniazid; 3–4 month isoniazid plus rifampicin; or 3–4 month rifampicin alone.

Guidelines on LTBI for low TB incidence countries – essential element of the @WHO #EndTB strategy and TB elimination http://ow.ly/RW8xn

Management of latent *Mycobacterium tuberculosis* infection: WHO guidelines for low tuberculosis burden countries

"Systematic testing and treatment of LTBI should be performed in people living with HIV, adult and child contacts of pulmonary TB cases, persons initiating anti-TNF-alpha treatment, receiving dialysis, preparing for organ or haematological transplantation, or with silicosis. Either IGRA or Mantoux TST should be used to test for LTBI. (Strong recommendation, low to very low quality of evidence.)"

http://erj.ersjournals.com/content/46/6/1563.long

Management of latent *Mycobacterium tuberculosis* infection: WHO guidelines for low tuberculosis burden countries

"Systematic testing and treatment of LTBI should be considered for *prisoners, healthcare workers,immigrants from high TB burden countries, homeless persons and illicit drug users*. Either IGRA or Mantoux TST (Conditional recommendation, low to very low quality of evidence.)"

http://erj.ersjournals.com/content/46/6/1563.long

Management of latent *Mycobacterium tuberculosis* infection: WHO guidelines for low tuberculosis burden countries

"Systematic testing for LTBI is not recommended in people with diabetes, people with harmful alcohol use, tobacco smokers, and underweight people unless they are already included in the above recommendations. (Conditional recommendation, very low quality of evidence.)"

http://erj.ersjournals.com/content/46/6/1563.long

SYMPTOMS OF TUBERCULOSIS

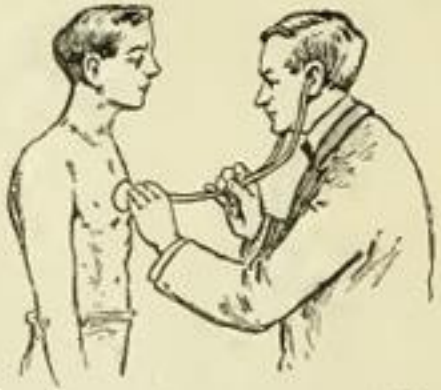
BE EXAMINED IF YOU HAVE ONE OR MORE OF THESE

Loss of weight or Tiring easily suggests tuberculosis

A cough lasting longer than three weeks is very suspicious

A continued temperature of 98.° or less in the morning and an afternoon temperature of 99.5 or more are strong indications of tuberculosis.

A low blood pressure may mean tuberculosis.



If you have any one or more of these symptoms be examined by a careful physician at once.

Management of latent *Mycobacterium tuberculosis* infection: WHO guidelines for low tuberculosis burden countries

TABLE 2 Performance of different screening strategies to rule out active tuberculosis (TB) before latent TB infection treatment based on a hypothetical cohort population of 1000 at a baseline TB prevalence of 0.5% [21]

Screening strategy	Sensitivity %	Specificity %	Negative predictive value %	False negatives at screening n	False positives at screening n
Cough for more than 2–3 weeks alone	35	95	99.6	3	53
Presence of cough for more than 2–3 weeks followed by CXR	90	56	99.7	3	23
Any TB symptom alone#	77	68	99.8	1	321
Presence of any TB symptom followed by CXR	90	56	99.8	1	141
TB specific abnormality on CXR	87	89	99.9	0.6	105
Any abnormality on CXR	98	75	99.9	0.1	244
Any abnormality on CXR plus presence of any TB symptom	100	61	100	0	385

CXR: chest radiograph. #: includes any one of: cough, haemoptysis, fever, night sweats, weight loss, chest pain, shortness of breath and fatigue.

http://erj.ersjournals.com/content/46/6/1563.long

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The impact of migration on tuberculosis epidemiology and control in high-income countries: a review

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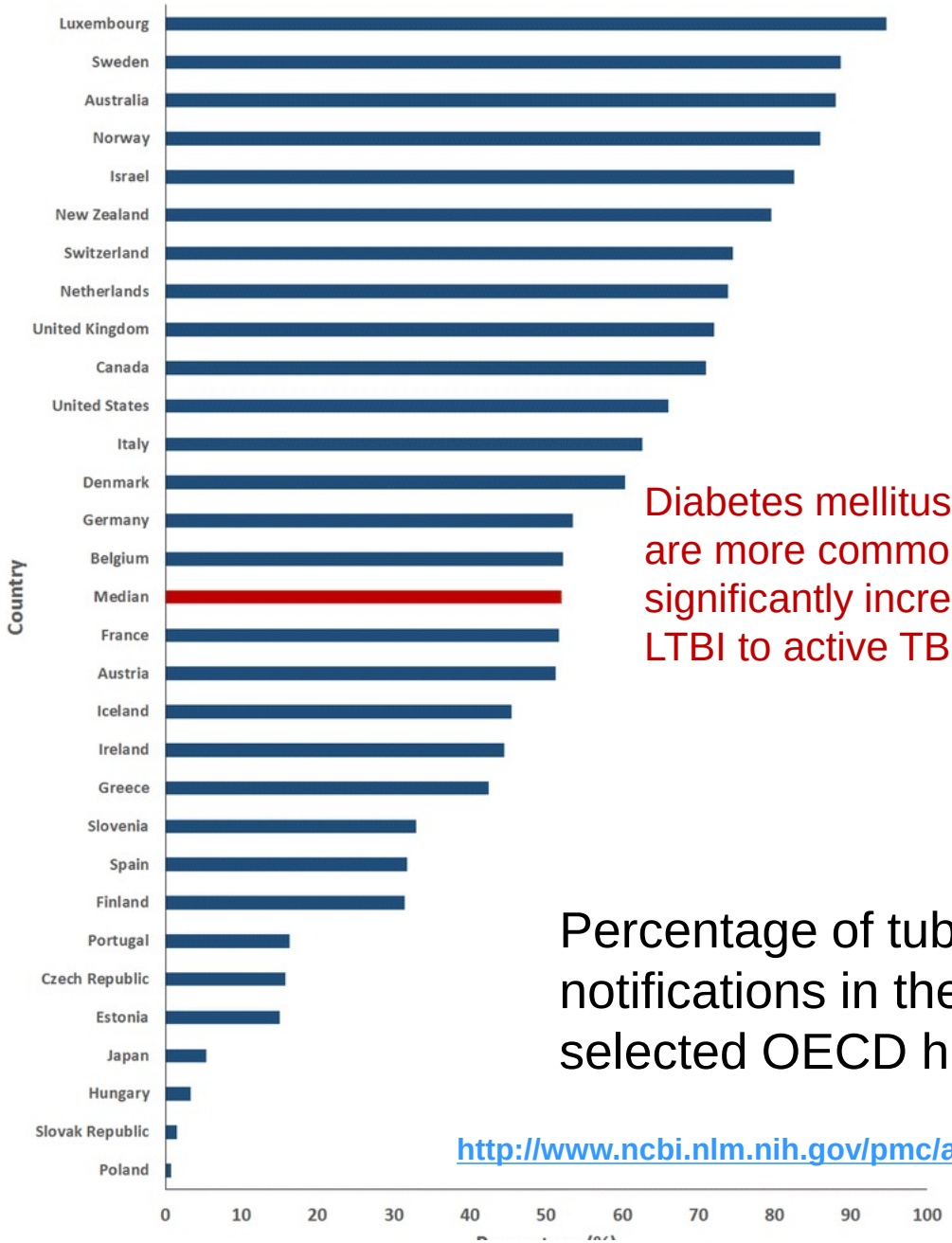
Received 2016 Feb 2; Accepted 2016 Mar 8.

Abstract

Tuberculosis (TB) causes significant morbidity and mortality in high-income countries with foreign-born individuals bearing a disproportionate burden of the overall TB case burden in these countries. In this review of tuberculosis and migration we discuss the impact of migration on the epidemiology of TB in low burden countries, describe the various screening strategies to address this issue, review the yield and cost-effectiveness of these programs and describe the gaps in knowledge as well as possible future solutions.

Fig. 1



Diabetes mellitus and chronic kidney disease are more common in migrant populations and significantly increase the risk of reactivation from LTBI to active TB

Percentage of tuberculosis notifications in the foreign-born for selected OECD high-income countries

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4804514/

“Although health-economic analyses have shown that TB control in high income settings would benefit from providing targeted LTBI screening and treatment to certain migrants from high TB burden countries, implementation issues and barriers such as sub-optimal treatment completion will need to be addressed to ensure program efficacy”.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4804514/

Eur Respir J 2010; 36: 925–949
DOI: 10.1183/09031936.00201609

SERIES "UPDATE ON TUBERCULOSIS"
Edited by C. Lange, M. Raviglione, W.W. Yew and G.B. Migliori
Number 1 in this Series

Tuberculosis contact investigation in low prevalence countries: a European consensus

C.G.M. Erkens*, M. Kamphorst*,#, I. Abubakar[¶], G.H. Bothamley[+], D. Chemtob[§], W. Haas[ƒ], G.B. Migliori**, H.L. Rieder[#,¶¶], J-P. Zellweger[++] and C. Lange[§§,ƒƒ]

ABSTRACT: **Contact investigation to identify individuals with tuberculosis and latent infection with *Mycobacterium tuberculosis* is an important component of tuberculosis control in low tuberculosis incidence countries. This document provides evidence-based and best-practice policy recommendations for contact tracing among high- and medium-priority contacts in a variety of settings. It provides a basis for national guidelines on contact investigation and tuberculosis outbreak management, and should support countries and tuberculosis control managers in evaluating and revising national policies. A review of existing guidelines, a literature search, several meetings and consultation with experts were used to formulate and grade recommendations for action during contact investigation.**

Available tests to identify individuals with latent infection with *M. tuberculosis* are designed to identify immune response against mycobacterial antigens and have variable predictive value for the likelihood to develop active tuberculosis in different populations. Contact investigation should therefore be limited to situations with a clear likelihood of transmission or to those with a higher probability of developing active tuberculosis, for instance, young children and immunocompromised persons. A risk assessment-based approach is recommended, where the need to screen contacts is prioritised on the basis of the infectiousness of the index case, intensity of exposure and susceptibility of contacts.

KEYWORDS: **Active case finding, contact investigation, consensus statement, latent tuberculosis infection, preventive chemotherapy, tuberculosis**

The primary objective of any tuberculosis control activity is prompt identification and adequate treatment of newly emerging tuberculosis cases. Timely identification and adequate treatment of those with transmissible tuberculosis reduces the risk of exposure of community members. As a result, the future incidence of tuberculosis is diminished, as the prevalence of infection with *Mycobacterium tuberculosis* declines in the cohort with the passage of time. The Stop TB Strategy and World Health Organization (WHO) guidelines for effective tuberculosis control [1] provide a framework for tackling tuberculosis, largely for countries with a high tuberculosis incidence.

Low-incidence countries in the European region have, in addition, addressed the goal of tuberculosis elimination [2–5], requiring a substantially broader approach. In particular, in addition to case identification among contacts of newly identified potential sources of infection, emphasis is also given to adequate preventive therapy or, as a minimum if the latter is contraindicated, follow-up of persons with recent *M. tuberculosis* infection. Identification of infected contacts thus targets an important subset of the prevalently infected who had escaped the focus on the prevention of infection. Contact investigation is the most readily available intervention to identify recently infected individuals and has been

For editorial comments see page 714.

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EContactes

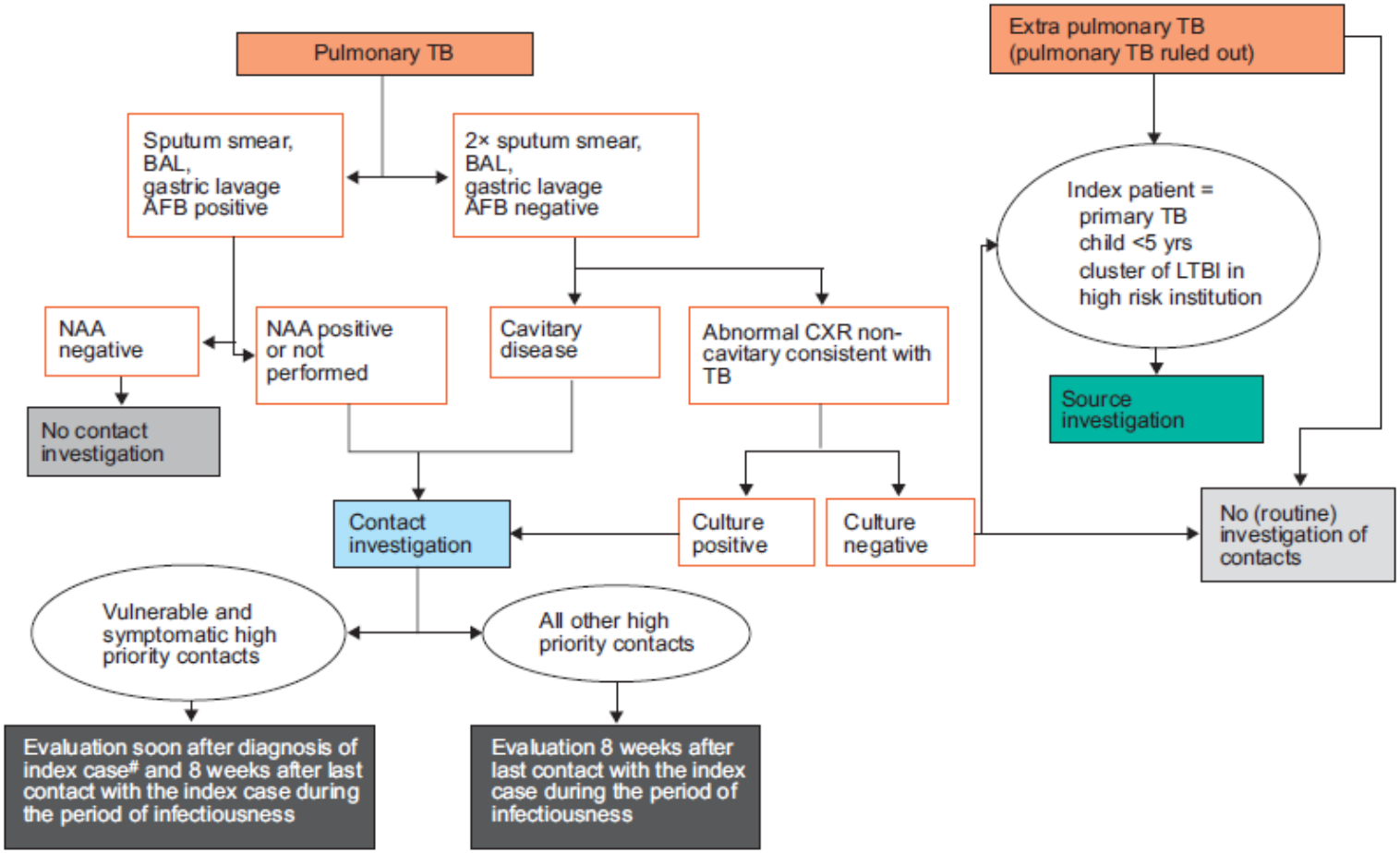


FIGURE 1. Need and timing of contact investigation. TB: tuberculosis; BAL: bronchoalveolar lavage; AFB: acid-fast bacilli; NAA: nucleic acid amplification; CXR: chest radiograph; LTBI: latent TB infection. #: first evaluation, other priority or vulnerable medium-priority contacts optional.

Recomanacions per a la realització d'Estudis de Contactes de malalts amb Tuberculosi a Catalunya

Subdirecció General de Vigilància i
Resposta a Emergències de Salut Pública
Departament de Salut

3.2.Indicacions de la realització d'Estudi de contactes

3.2.1. Tuberculosi Pulmonar / laríngia

Bacil·loscòpia d'esput positiva: **realitzar sempre EC.**

Bacil·loscòpia negativa i cultiu positiu: realitzar sempre EC

Bacil·loscòpia d'esput negativa o no realitzada:

Radiografia de tòrax compatible amb TBC *amb* imatge cavitària : **realitzar sempre EC.**
Radiografia de tòrax compatible amb TBC *sense* imatge cavitària: **realitzar sempre EC.**
Radiografia de tòrax dubtosa compatible amb TBC: realitzar EC en circumstàncies excepcionals No s'inclouen les petites cavitats parenquimatoses que solament són detectables per TAC o ressonància magnètica

En el cas d'altres mostres respiratòries (broncoaspirat, rentat bronquial, aspirat gàstric), existeix l'acord de considerar-les com l'esput

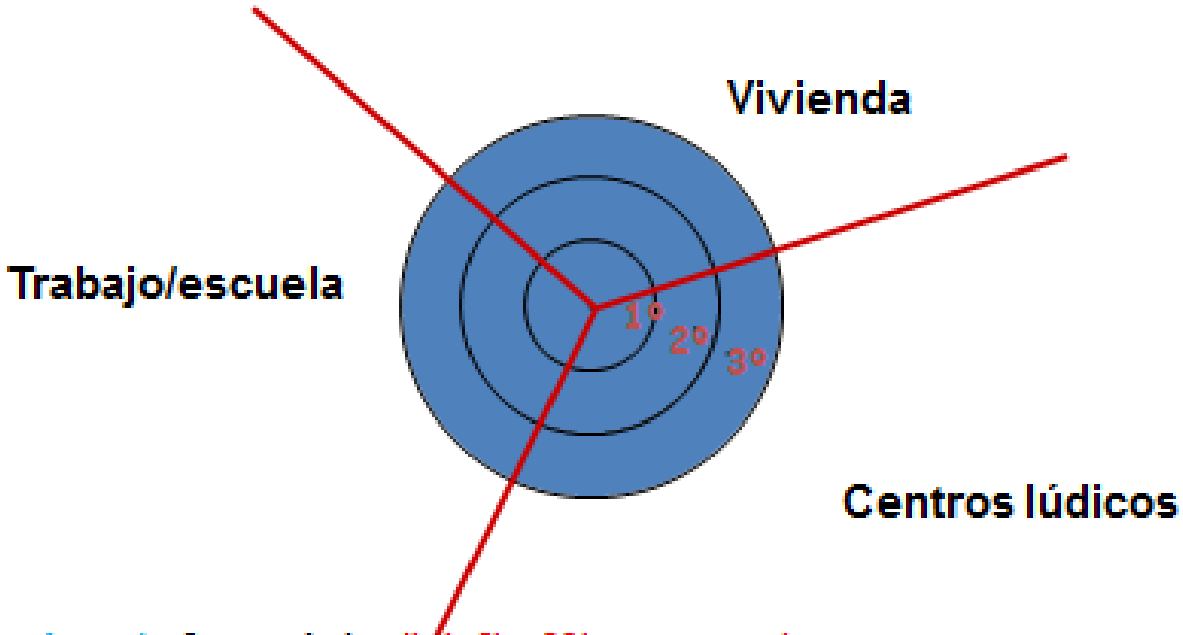
Taula 2. Paràmetres per establir la contagiositat del cas índex

Característica
Localització anatòmica: Pulmonar i/o laríngia
Símptomes: Producció d'esput/ Data inici símptomes
Microbiologia de mostres respiratòries: Bacil·loscòpia positiva
Lesions a la radiografia de tòrax: Cavitacions
Símptomes: Tos

Es recomana estudiar els contactes en els 3 mesos abans d'inici dels símptomes en pacients tuberculosos amb tos i bacil·loscòpia positiva.

El període seria d'1 mes en aquells pacients amb bacil·loscòpia negativa i cultiu positiu

Classificació contactes. Sistema dels cercles concèntrics



1r cercle: Contacte intim: diari >6h o 30 hores setmanals

2n cercle. Contacte freqüent: diari <6h

3r cercle. Contacte esporàdic: no diari

1st circle of contacts (inner circle)	Description
Close household contacts	Those who live in the same household as the infectious case. Household contacts are considered, by definition, to share breathing space on a daily basis with the source case.
Close nonhousehold contacts	Close nonhousehold contacts may include those persons with short exposure times to direct face-to-face streams of air with a particularly high density of infectious droplet nuclei, such as may occur during bronchoscopy or otorhinolaryngeal examination of patients with hence untreated sputum smear-positive tuberculosis, and similar situations. For all other close nonhousehold contacts, an arbitrarily defined cumulative exposure time of 8 h, if the index is sputum smear-positive, or 40 h, if only sputum culture-positive has been recommended as a guiding principle [18]. This group also includes contacts with regular, prolonged contact with the source case, who share breathing space but do not live in the same household or who have spent time with the source case in a confined space, such as a car, sweatshop or prison cell. These may also include contacts, such as close friends and colleagues.
2nd circle of contacts (middle circle)	
Casual contacts	Those who spent less time with the infectious case. These may include frequent visitors to the home, friends, relatives, school or class mates, colleagues at work or leisure contacts, members of a club or team, or passengers in adjoining seats during aircraft travel of >8 h [201].
3rd circle of contacts (outer circle)	
Community contacts	Those living in the same community or attending the same school, sports club or workplace who may have had sporadic contact.

Taula 4. Factors de risc de progressió d'infecció fins a malaltia tuberculosa.	OR/RR
Característica	
Càncer hematològic (limfomes, leucèmies). Càncer de cap, coll o pulmó.	16 2.5-6.3
Immunosupressió VIH positiu i prova de la tuberculina positiva SIDA Transplantaments amb tractament immunosupressor Tractament amb TNF- α Tractament amb prednisona>15 mg durant 2-4 setmanes	 50 - 110 110 - 170 20 - 74 1,5 - 17 4,9
Gastrectomia	2,5
Bypass ili jejunal	27-63
Silicosis	30
Insuficiència renal crònica o hemodiàlisi	10-25
Diabetis mellitus	2-3,6
Tabaquisme	2-3
Consum excessiu d'alcohol	3
Baix pes	2,0-2,6
Edat <5 anys Font : Erkens, modificat	2-5

Grups de contactes de casos de TBC segons grau de prioritat per al seu estudi.

Contactes de alta prioritat

- Contactes del primer cercle amb risc alt de desenvolupar TBC si resulten infectats.
- Altres contactes del primer cercle.
- Contactes del segon cercle amb risc alt de desenvolupar TBC si resulten infectats.
- Contactes de TBC multiresistent.

Contactes de prioritat mitjana

- Contactes del segon cercle
- Contactes del tercer cercle amb risc alt de desenvolupar TBC si resulten infectats

Contactes de baixa prioritat

- Contactes del tercer cercle o de fora dels cercles

3.6. Avaluació dels contactes de mitjana prioritat

Es recomana iniciar l'estudi després del període de finestra de *12 setmanes* per tal de no repetir la prova de la tuberculina en els negatius. Tanmateix, en certs àmbits com els centres educatius o els centres sanitaris, serà difícil posposar l'estudi durant 12 setmanes degut a situacions d'alarma i preocupació. En el cas que s'hagi detectat altes prevalences de la infecció en els contactes d'alta prioritat s'ha d'iniciar l'estudi d'aquests contactes el mes aviat possible

- **5.1. Tractament d'infecció probable (TIP)**
- El TIP s'iniciarà en pacients no infectats (PT negativa) que han tingut un contacte d'alt risc. Actualment està indicat en nens menors de 5 anys, persones infectades per VIH i es pot valorar en persones que prenen

  tractaments immunosupressors
- **5.2 TITL**

Taula 14. Indicacions del Tractament de la Infecció Tuberculosa latent (TITL).

Persones infectades amb la PT>=5 mm independentment de l'edat.

A tots els contactes infectats (PT positiva) que es trobin fent l'estudi de contactes delimitat correctament i en els que s'ha descartat malaltia estaria indicat valorar el TITL, especialment els contactes menors de 65

Persones VIH positives amb la PT negativa, que pertanyin a col·lectius d'alta prevalença d'infecció.

TITL

Opcions terapèutiques per al TITL de la tuberculosi sensible a fàrmacs de primera línia.

Isoniazida: 6 o 9 mesos (la pauta més eficaç és la de 9 mesos i seria la recomanable en nens).

Isoniazida més rifampicina durant 3 mesos (3RH).

Rifampicina sola durant 4 mesos.

"Rates of progression from LTBI to active disease are reduced by around 70–90% in those who complete daily isoniazid (H) monotherapy for 6–9 months (9 months [9H] is the current standard) or daily combination therapy with rifampicin and H for 3 months" *Treatment of latent infection with Mycobacterium tuberculosis: update 2010. 2010. Eur Respir J 2011; 37: 690–711.*

Management of latent *Mycobacterium tuberculosis* infection: WHO guidelines for low tuberculosis burden countries

TABLE 3 Standard random effects meta-analysis comparison of efficacy and hepatotoxicity among various treatment regimens for treatment of latent tuberculosis (TB) infection

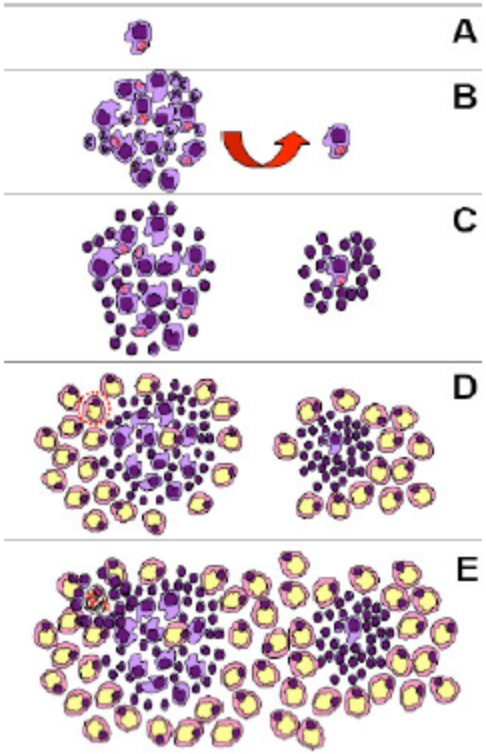
Comparator	Intervention	Development of incident TB	Hepatotoxicity
Placebo	Isoniazid 6 months	0.61 (0.48–0.77)	0.99 (0.42–2.32)
Placebo	Isoniazid 12–72 months	0.53 (0.41–0.69)	0.59 (0.23–1.55)
Placebo	Rifampicin 3–4 months	0.48 (0.26–0.87)	
Placebo	Rifampicin and isoniazid 3–4 months	0.52 (0.33–0.84)	
Isoniazid 6 month	Rifampicin 3–4 months	0.78 (0.41–1.46)	0.03 (0.00–0.48)
Isoniazid 6 month	Rifampicin and isoniazid 3–4 months	0.89 (0.65–1.23)	0.89 (0.52–1.55)
Isoniazid 6 month	3 month weekly rifapentine plus isoniazid#	1.09 (0.60–1.99)	1.00 (0.50–1.99)
Isoniazid 9 month	3 month weekly rifapentine plus isoniazid	0.44 (0.18–1.07)	0.16 (0.10–0.27)

Data are presented as odds ratios with 95% confidence intervals. #: exclusively among people living with HIV.

http://erj.ersjournals.com/content/46/6/1563.long

IMMUNODEPRIMITS

Inmunopatogenia de la Tuberculosis



- Inhalación del bacilo y fagocitosis por los macrófagos pulmonares
- Inmunidad celular (Linfocitos T helper $CD4^+$)
- Reclutamiento y Activación de los macrófagos mediada por citocinas (TNF-α, IFN γ, IL-12)
- Formación de los Granulomas que contienen al microorganismo y previenen su diseminación

Tractaments biològics

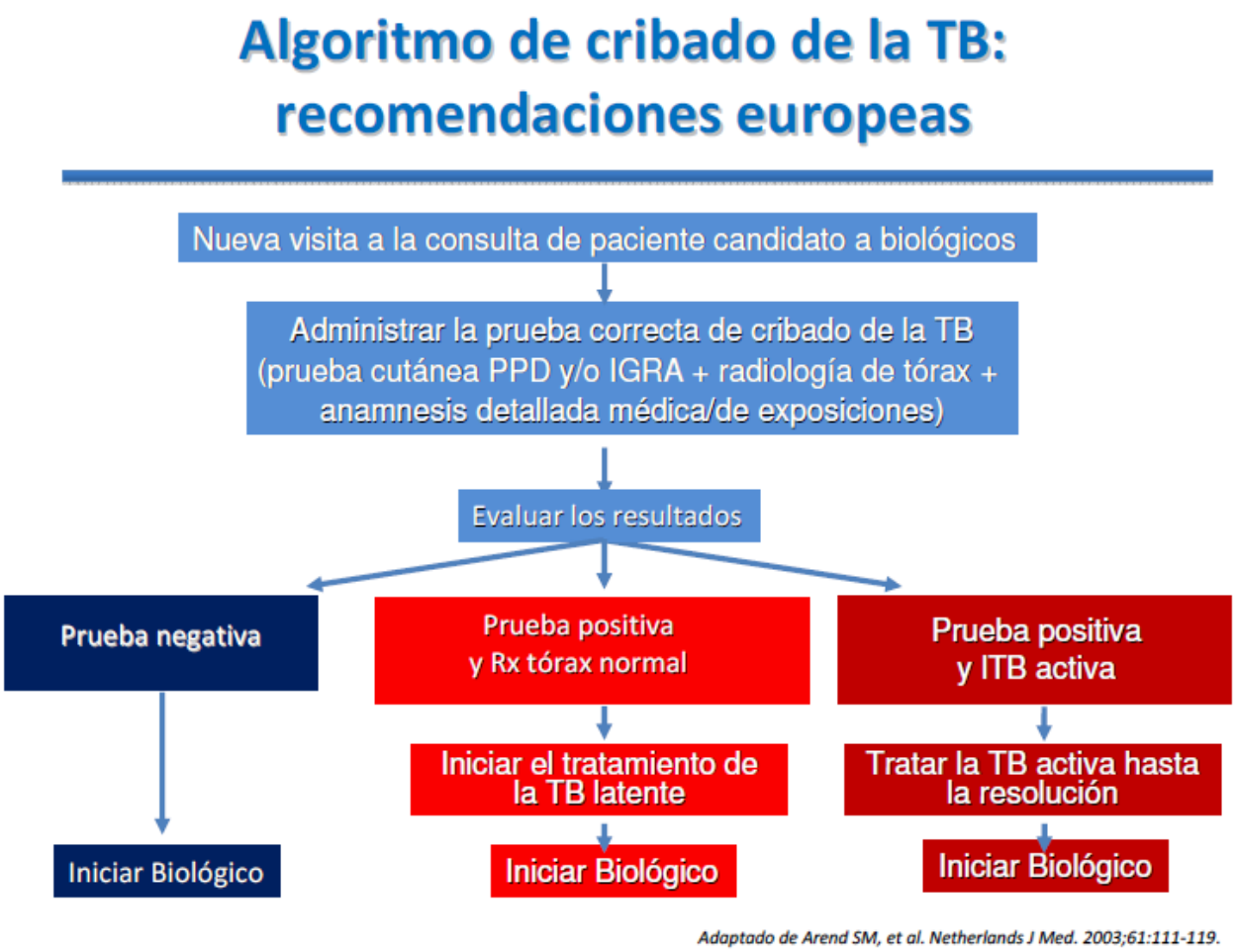
- Terapias que bloquean la acción de las citocinas:
- - TNF-α
- - Interleukinas: IL-1, IL-2, IL-6,IL-12/IL-23
- - B-LyS (BAFF)
- Terapias que actúan sobre receptores linfocitarios:
- - CD 20
- - CD 22
- - CD 80/86
- - LFA1

TB risk during anti-Tumor Necrosis Factor (TNF) therapy

Incidence (x100,000) / Country	TB general population	TB in Rheumatoid Arthritis	TB in Rheumatoid Arthritis with anti-TNF
USA	5.8	6.2	**52.5**
Spain	21	95	**1,113**
Korea	67.2	257	**2,558**
Peru	122	216	

Wolfe et al. A&R, 2004; Gomez-Reino et al, A&R, 2003; Seong et al, J Rheum, 2005; Gamboa, et al A&R, 2007

Què fer


Algoritmo de cribado de la TB: recomendaciones europeas
Nueva visita a la consulta de paciente candidato a biológicos
Administrar la prueba correcta de cribado de la TB (prueba cutánea PPD y/o IGRA + radiología de tórax + anamnesis detallada médica/de exposiciones)
Evaluar los resultados
Prueba negativa
Prueba positiva y Rx tórax normal
Prueba positiva y ITB activa
Iniciar Biológico
Iniciar el tratamiento de la TB latente
Tratar la TB activa hasta la resolución
Iniciar Biológico
Iniciar Biológico
Adaptado de Arend SM, et al. Netherlands J Med. 2003;61:111-119.

Què diuen les guies?

Guías Nacionales para el cribado de TB en pacientes candidatos a biológicos

País	Evaluación de riesgo y Rx tórax	PPD	Retest	PPD (+)	Tratamiento	Referencia
UK	Todos	No si en tratamiento inmunosupresor	No	5mm (15 mm si BCG+)	INH 6 meses	BTS
USA	Todos Rx tórax si PPD+	Todos	No	5 mm (ignorar BCG)	INH 9 meses	MMWR
España	Todos	Todos	Sí	5 mm	INH 9 meses	*Gómez-Reino*
Francia	Todos	Todos	No	10 mm	RIF-PZA 2 meses	*Mariette and Salmon*
Irlanda	Todos	Todos	No	5 mm (ignorar BCG)	INH 9 meses	*Kavanagh et al*
Suiza	Todos	Mejor IGRA	Mejor IGRA	IGRA	INH 9 meses	*Beglinger et al*

Tratamiento de la ITbL
Recomendaciones (CDC-ATS)

Fármaco	Duración	Intervalo	Recomendación (Evidencia)	
			VIH-	VIH+
Isoniacida	**9**	**Diaria**	A (II)	A (II)
Isoniacida	9	Intermitente	B (II)	B (II)
Isoniacida	6	Diaria	B (I)	C (I)
Isoniacida	6	Intermitente	B (II)	C (I)
Rif + Pz	2	Diaria	C (II)	A (I)
INH + RF	3	Diaria	B (III)	B (I)
Rifampicin	4	**Diaria**	B (II)	B (III)

a

A: preferida; B: alternativa aceptable; C: ofrecer si A y B no posibles
I: ensayos clínicos randomizados; II: datos de ensayos clínicos no randomizados o realizados en otras poblaciones; III: opinión de expertos

UNIVERSITY of York
Centre for Reviews and Dissemination

PROSPERO International prospective register of systematic reviews

Screening, diagnosing and prophylaxis for latent tuberculosis in immunosuppressed individuals: systematic review of clinical practice guidelines

Tasnim Hasan, Germaine Wong, Allison Tong, Sharon Chen

Citation
Tasnim Hasan, Germaine Wong, Allison Tong, Sharon Chen. Screening, diagnosing and prophylaxis for latent tuberculosis in immunosuppressed individuals: systematic review of clinical practice guidelines. PROSPERO 2016:CRD42016036516 Available from http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016036516

Review question(s)
Review the rationale, quality, scope and consistency of national and international clinical practice guidelines on the screening for, and diagnosis of LTB infection

Review the rationale, quality, scope and consistency of national and international clinical practice guidelines on the treatment options for prophylaxis against TB in immunosuppressed individuals.

Searches
MEDLINE, EMBASE, PsycINFO, and guideline registries will be searched using MeSH terms and text words for "tuberculosis, immunosuppressed, and immunocompromised" will be combined with terms relating to waiting lists and clinical practice guidelines and consensus statements.

Types of study to be included
Evidence-based clinical practice guidelines (defined as "systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances" and consensus statements (defined as documents containing clinically-relevant suggestions or recommendations based on the collective opinion of an expert panel)

Condition or domain being studied
Tuberculosis

Immunosupressed individuals

INT J TUBERC LUNG DIS 19(9):1002

http://dx.doi.org/10.5588/ijtld.15.0599

EDITORIAL

Tuberculosis preventive chemotherapy: the times they are a-changin'

LATENT INFECTION with *Mycobacterium tuberculosis* is defined by a positive tuberculin skin test or interferon-γ release assay in the abscence of active disease.[1] Without an intervention that is more effective than childhood vaccination with *M. bovis* bacille Calmette-Guérin, tuberculosis prevention relies on infection control measures and identification of individuals with latent tuberculous infection (LTBI) from groups at risk for the future development of tuberculosis.[2] Treating such individuals with preventive chemotherapy is an effective intervention. Rates of progression from LTBI to active disease are reduced by around 70–90% in those who complete daily isoniazid (H) monotherapy for 6–9 months (9 months [9H] is the current standard) or daily combination therapy with rifampicin and H for 3 months.[3]

However, taking daily tablets for 6–9 months for infectious disease prevention is an unusually long period. Adherence and completion rates for treatment of LTBI are low, negating some of the benefit of this intervention, and hepatotoxicity also limits completion rates.

The results of the PREVENT TB study[4] have clearly documented that 12 weekly supervised doses of rifapentine (P) and H ($3HP_1$) are as effective as 9H in preventing progression from LTBI to tuberculosis. The study also found higher rates of completion in the

Not all regimens for tuberculosis preventive chemotherapy are equal. The findings from this study and the main PREVENT TB study are very important, and have implications for future guideline developments. Although trial conditions are very different from operational situations, extrapolations can be made. $3HP_1$ is as effective as 9H in the treatment of LTBI and is safer with regard to hepatotoxicity. Measuring AST at baseline is helpful in identifying who may develop hepatotoxicity with LTBI treatment. The risk factors for hepatotoxicity identified in this study could be usefully included in operational guidelines on whom to monitor during LTBI treatment. Wide implementation of the findings of this study will hopefully lead to more people being safely treated for LTBI.

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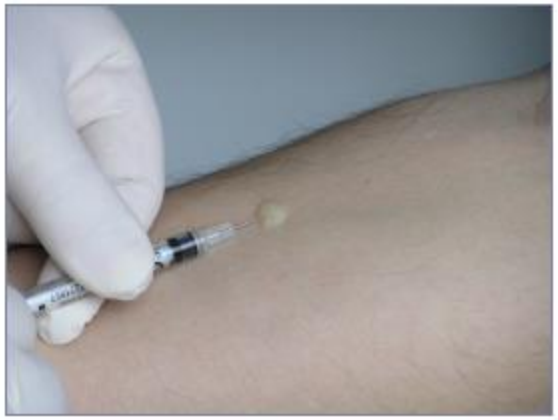
§German Center for Infection Research, Clinical Tuberculosis Center, Borstel
¶International Health / Infectious Diseases

DIAGNÒSTIC D'INFECCIÓ TUBERCULOSA LATENT

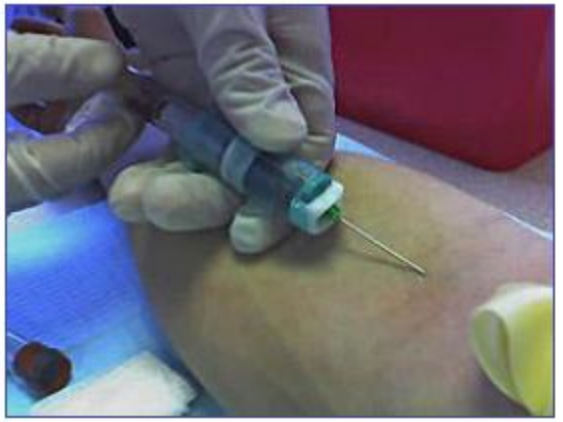
LTBI diagnosis

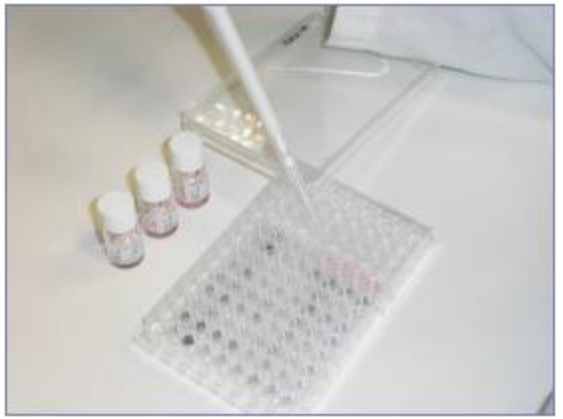
Tuberculin skin testing



2002

IGRAs



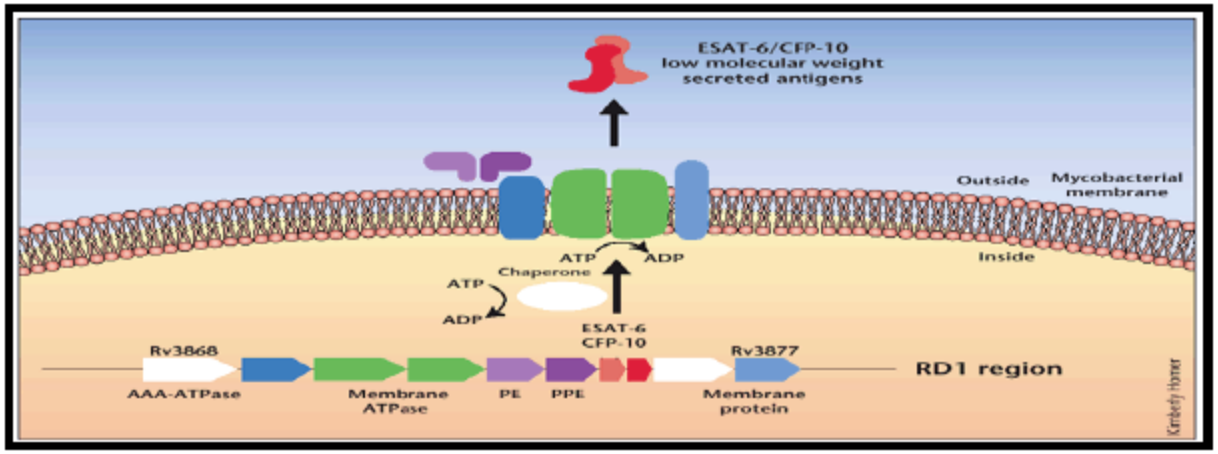


Moving LTBI diagnosis from clinical departments to laboratory.
A more accurate diagnosis.

LTBI diagnosis: IFN-γ assays
Specific antigens

ESAT-6, CFP-10 and TB7.7

Proteins coded in the region of difference 1 and 11, which are present in *M. tuberculosis* but not in any BCG strain nor in the majority of NTM.



IGRAs

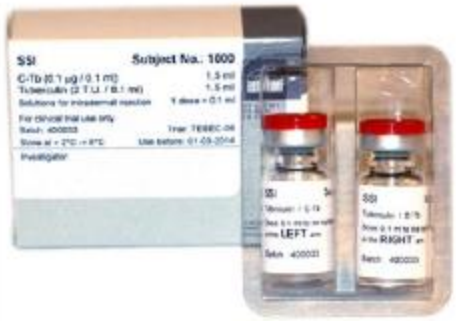
- Exposure and risk factor association
- Higher specificity (no affected by BCG). Reduce unnecessary prophylaxis.
- PPV higher/similar than TST and very good NPV
- Less afected by immunosuppressor treatments

- Improve positive predictive value: differentiate between those persons who will develop TB and those who will not.
- Remote vs. recent infection
- Infection vs. active TB
- Monitoring of the treatment
- Severe immunosuppression

Waiting for the next generation…

- C-Tb is a novel skin test for Mtb infection
- Phase II results show
  - Superior specificity to PPD
  - Similar performance as QFT
- Currently in phase III in Spain and South Africa
- TESEC-06: Large multi-center study ongoing in Spain

STATENS SERUM INSTITUT



Diaskintest®

Product description
Diagnostic test for detection of *Mycobacterium tuberculosis* infection by means of a specific immune reaction using the recombinant protein CFP-10- ESAT-6

Active substance
Recombinant protein CFP-10- ESAT-6, produced in *Escherichia coli* bacteria by recombinant DNA technology

Probl Tuberk Bolezn Legk. 2009;(2):11-6.

[Clinical trials of the new skin test Diaskintest for the diagnosis of tuberculosis].

[Article in Russian]

Kiselev VI, Baranovskiĭ PM, Rudykh IV, Shuster AM, Martʹianov VA, Mednikov BL, Demin AV, Aleksandrov AN, Mushkin AIu, Levi DT, Slogotskaia LV, Ovsiankina ES, Medunitsin NV, Litvinov VI, Perel'man MI, Pal'tsev MA.

INT J TUBERC LUNG DIS 19(5):504–516

http://dx.doi.org/10.5588/ijtld.15.0048

STATE OF THE ART SERIES
New tools in the management of tuberculosis
Series editors: Wing-Wai Yew and Martien Borgdorff
NUMBER 1 IN THE SERIES

Advances in the diagnosis of tuberculosis: current status and future prospects

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Center for Tuberculosis Research, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

SUMMARY

Lack of diagnosis and diagnostic capacity remain barriers to tuberculosis (TB) control. This review describes recent advances in TB diagnostics, the current TB diagnostic landscape, and some of the key challenges in the quest for accurate, simple diagnostic tests that have meaningful impact on the health of individual patients and on TB epidemiology.

KEY WORDS: tuberculosis; diagnostics; review

Diagnosis is not the end, but the beginning of practice. – Martin Henry Fischer

THERE HAS BEEN RECENT PROGRESS in the development of new diagnostic tests for tuberculosis (TB) (Appendix Table A.1).[1–10] There has also been progress in the programmatic rollout of new tests, assessment of their impact, and modeling of diagnostic strategies to understand how they might best be used. Despite these advances, however, an estimated one third of all TB cases are missed (either not diagnosed or not reported), and fewer than one in four cases of multidrug-resistant tuberculosis (MDR-TB) is detected.[11] Sputum smear microscopy, the susceptibility testing (DST). Radiographic imaging and the diagnosis of latent tuberculous infection (LTBI) are not covered for reasons of space; the reader is referred to recent publications on these topics.[13–19] Outside the scope of this review are the role of implementation science in integrating diagnostic research findings into sustainable practice that improves health; the role of mathematical modeling in informing public health decision-making about optimal diagnostic strategies; and the needs for laboratory and human capacity building as well as strengthening of health systems.[20–25]

Bibliografia

- **WHO 2015.Global Tuberculosis Report.Disponible a: http://www.who.int/tb/publications/global_report/en/**
- **Management of latent *Mycobacterium tuberculosis* infection: WHO guidelines for low tuberculosis burden countries. http://erj.ersjournals.com/content/46/6/1563.long**
- **Tuberculosis surveillance and monitoring in Europe 2016** : **http://ecdc.europa.eu/en/publications/_layouts/forms/Publication_DispForm.aspx?List=4f55ad51-4aed-4d32-b960-af70113dbb90&ID=1452#sthash.m748iVhv.dpuf**
- **Erkens CGM.Tuberculosis contact investigation in low prevalence countries: a European consensus. Eur Respir J 2010; 36: 925–949 http://erj.ersjournals.com/content/36/4/925.long**
- **AlsedàGraells,Miquel Il.JansàiLópezdel Vallado, Josep Maria, ed. Ill. Catalunya. Departament de Salut IV. Col·lecció: Documents de vigilància epidemiològica ; 13 1. Tuberculosi – Prevenció http://canalsalut.gencat.cat/web/.content/home_canal_salut/professionals/recursos/protocols i_recomanacions/21_tuberculosi/documents/protocolserie.pdf**
- **Grupo de trabajo de la Guía de Práctica Clínica sobre el Diagnóstico, el Tratamiento y la Prevención de la Tuberculosis. Centro Cochrane Iberoamericano, coordinador. Guía de Práctica Clínica sobre el Diagnóstico, el Tratamiento y la Prevención de la Tuberculosis. Plan de Calidad para el Sistema Nacional de Salud del Ministerio de Sanidad, Política Social e Igualdad. Agència d´Informació, Avaluació i Qualitat en Salut (AIAQS) de Cataluña; 2009. Guías de Práctica Clínica en el SNS: AATRM No 2007/26.**
- **Eines de consulta ràpida sobre el diagnòstic,prevenció I tractament de la tuberculosi. http://www.guiasalud.es/egpc/traduccion/catalan/herramientas_tuberculosis/preguntas.html**
- **Recomanacions per a la realització d'Estudis de Contactes de malalts amb Tuberculosi a Catalunya. Subdirecció General de Vigilància i Resposta a Emergències de Salut Pública.Departament de Salut 2016**

GRÀCIES PER LA VOSTRA ATENCIÓ!

La reacció tuberculínica (RT)

La RT és l'exploració que permet detectar la infecció tuberculosa

Infecció pel *Mycobacterium tuberculosis*

Sensibilitat al micobacteri

Antígens tuberculina → ↓

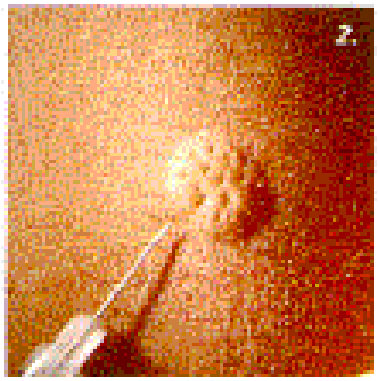
Reacció d'immunitat

- **Tuberculina PPD-RT 23**
- **Dosi 2UT/0.1ml**

  (bio equivalent a 5 UT de PPD-S)

Tècnica de Mantoux

Punció intradèrmica



Formació d'una pàpula

Maneig i conservació

- **Estabilitzador antiabsorbent → permet utilitzar-la d'un mateix envàs fins esgotar-lo.**
- **Agitar flascó**
- **Conservació en un frigorífic 4º**
- **Protecció llum**

Indicacions de la RT I

Ajuda diagnòstica de malaltia tuberculosa

Clínica:

- **febre**
- **suor nocturna**
- **pèrdua de pes**
- **tos i expectoració**
- **esgotament constant**
- **pèrdua de la gana**

Indicacions de la RT II

Ajuda diagnòstica de la infecció tuberculosa

- **Contactes recents de pacients amb TB pulmonar**
- **Persones que tenen malalties que cursen amb immunosupressió o han d'iniciar fàrmacs immunosupressors**
- **Residents i empleats de centres d'alt risc: presons, residències, centres geriàtrics i crònics, hospitals.**
- **Treballadors de centres educatius...**

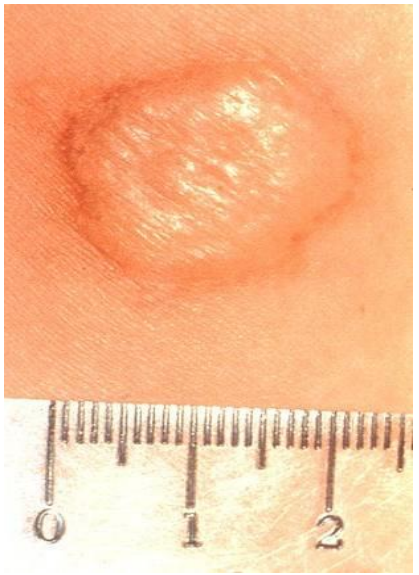
Indicacions de la RT III

- Personal laboratori mico bacteriologia de països amb alta prevalença de TB.
- Indigents, Toxicomanies, HIV +
- Pacients amb les següents malalties: silicosi, malalties hematològiques (leucèmia, limfoma), altres tumors..
- Canvis fibrosis a Rx suggerents TB no tractada

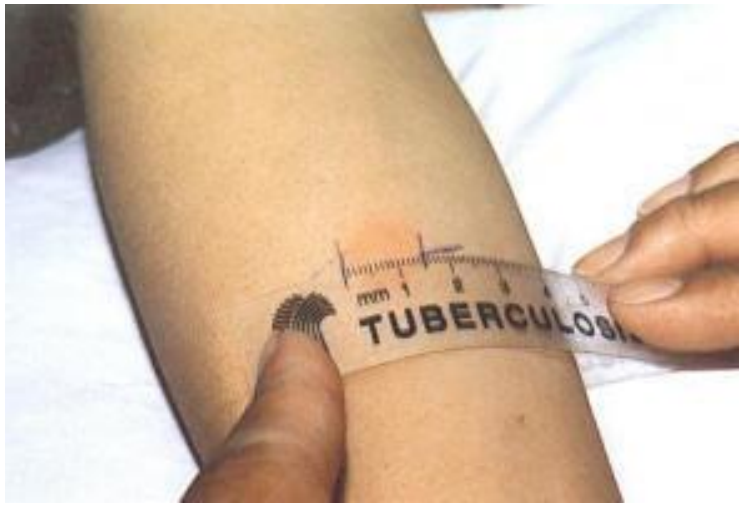
Característiques de la RT

- La RT no té contraindicacions
- La repetició no sensibilitza
- Si antecedent positivitat no es repeteix

INTERPRETACIÓ



- Lectura a les 72hores
- Induració, diàmetre transversal
- Eritema no valor
- Expressa en mm



INTERPRETACIÓ RT

Persones amb alt risc de desenvolupar TB o amb molt alta prevalença d'infecció.	**RT + si ≥ 5 mm** **(no valorar BCG)**	• **Contactes íntims o freqüents de malalts TB.** • **Pacients portadors del VIH.** • **Pacients portadors de lesions fibròtiques.** • **Immunodeprimits per fàrmacs o transplantaments.**
Persones amb risc moderat-alt de desenvolupar TB o amb alta prevalença d'infecció.	**RT + si ≥ 10 mm** **(no valorar BCG)**	• **Nens i adolescents.** • **UDVP.** • **Persones amb malalties debilitants.** • **Personal laboral i residents de centres de risc per la propagació de la TB.** • **Personal de laboratoris de micobacteriologia.** • **Immigrants de països amb alta prevalença de TB.**
Persones amb baix risc de desenvolupar TB i amb baixa prevalença d'infecció.	**RT + si ≥ 15 mm** **(≥ 20 mm en els vacunats amb BCG)**	**Persones no incloses en els grups anteriors.**

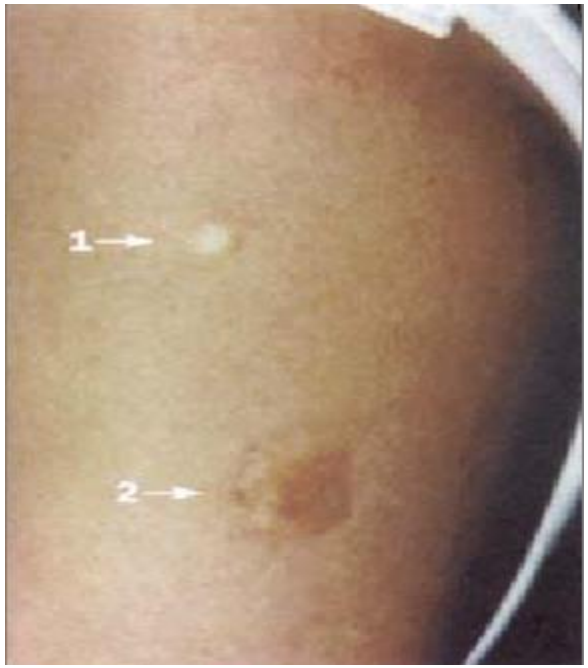
INTERPRETACIO RT: VACUNATS BCG

Cicatriu a la part superior dels braços

A Espanya entre 1965 i 1974 es va posar BCG a 14 milions de persones

(6-14 anys)

A Marroc, Europa de l'est i països de sud-americà es continua vacunant.



1. BCG
2. Verola

THE BCG WORLD ATLAS

A DATABASE OF GLOBAL BCG VACCINATION POLICIES AND PRACTICES.

Welcome to the World Atlas of BCG Policies and Practices.

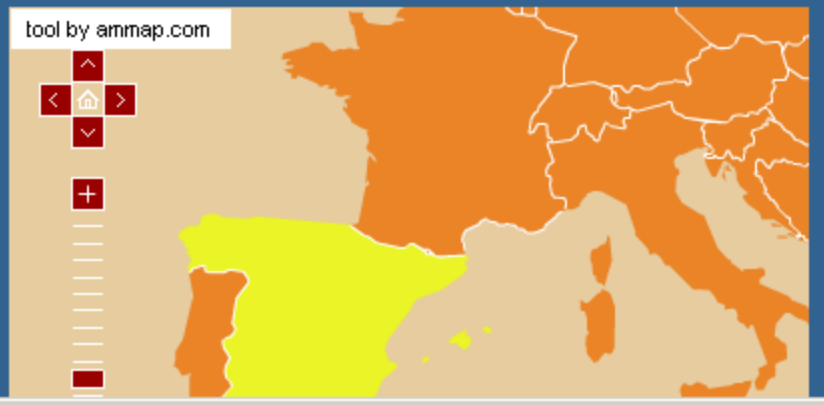
This interactive website provides detailed information on current and past BCG policies and practices for over 180 countries. The Atlas is designed to be a useful resource for clinicians, policymakers and researchers alike, providing information that may be helpful for better interpretation of TB diagnostics as well as design of new TB vaccines.

The rationale and methodology for this Atlas is described in a paper in PLoS Medicine.

Please select a Country from the drop down box, or use the map to select a country to view all available information concerning that country's BCG policies and practices.

Spain

Country	Spain
Region	..
TB Incidence (per 100 000 per year) * †	17
TB Incidence (Count) * †	7500
TB Prevalence (per 100 000 per year) * ‡	19
TB Prevalence (Count) * ‡	8600

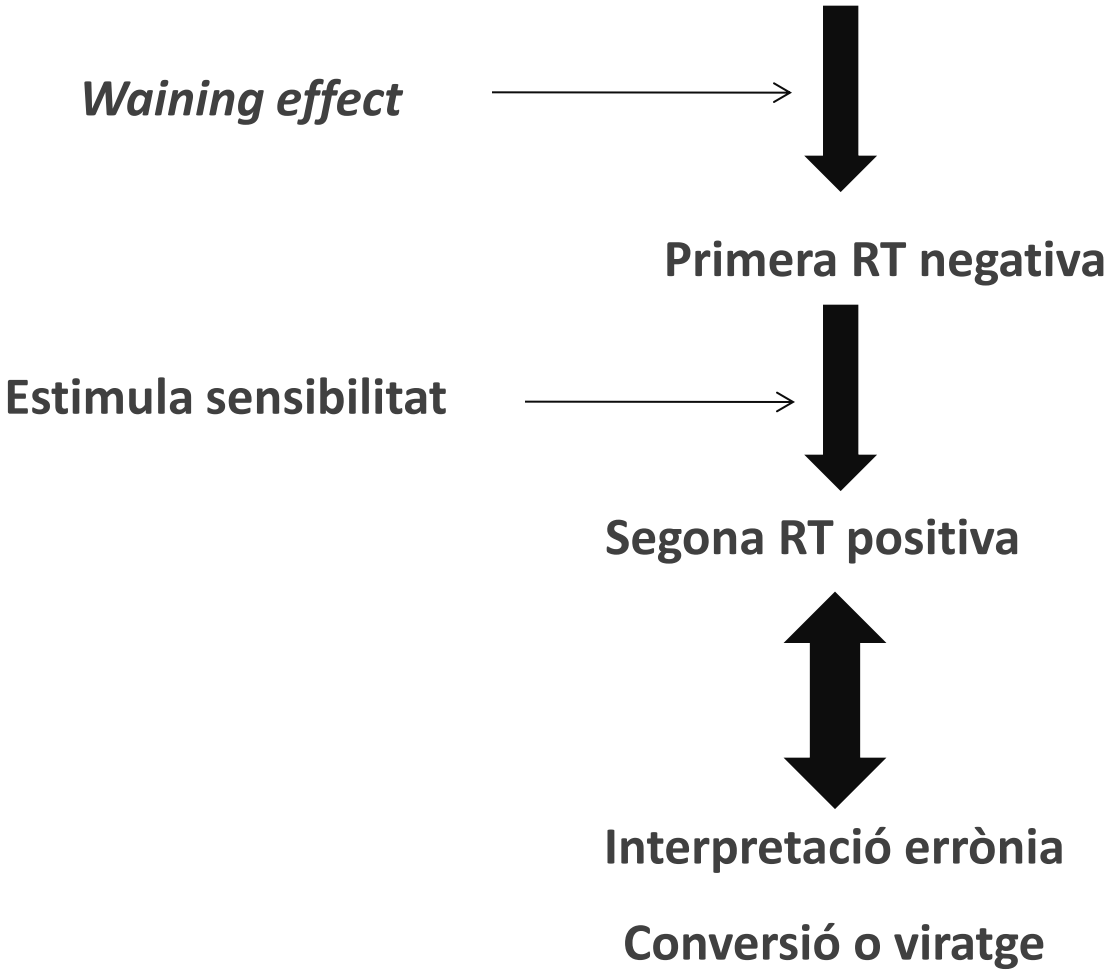


BOOSTER EFFECT

- **La pràctica repetida de la RT mai indueix sensibilitat**

- **La RT sí que estimula una sensibilitat tuberculínica preexistent → Efecte d'empenta o de reforç**

RT en > 55 o en vacunats BCG



Com evitar aquesta interpretació errònia ?

>55 no vacunats o vacunades qualsevol edat amb RT negatiu

Repetir RT als 7 dies

Acceptar com a vàlid 2ª RT

CAMFiC
societat catalana de medicina familiar i comunitària

Generalitat de Catalunya
Departament de Salut

CatSalut
Servei Català de la Salut