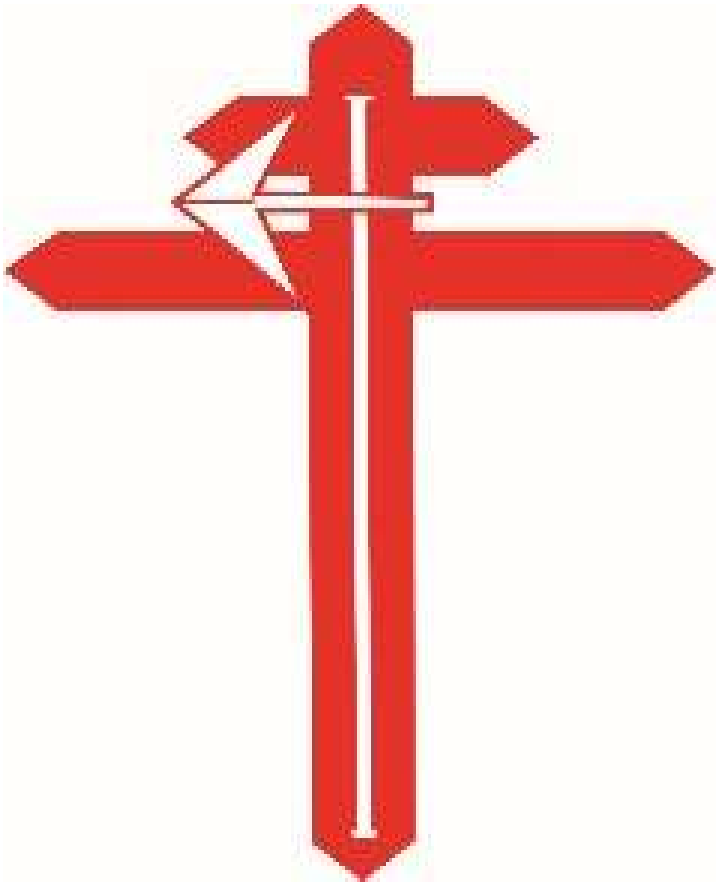
Tuberculosis pediátrica

Dr Pascual Caballero

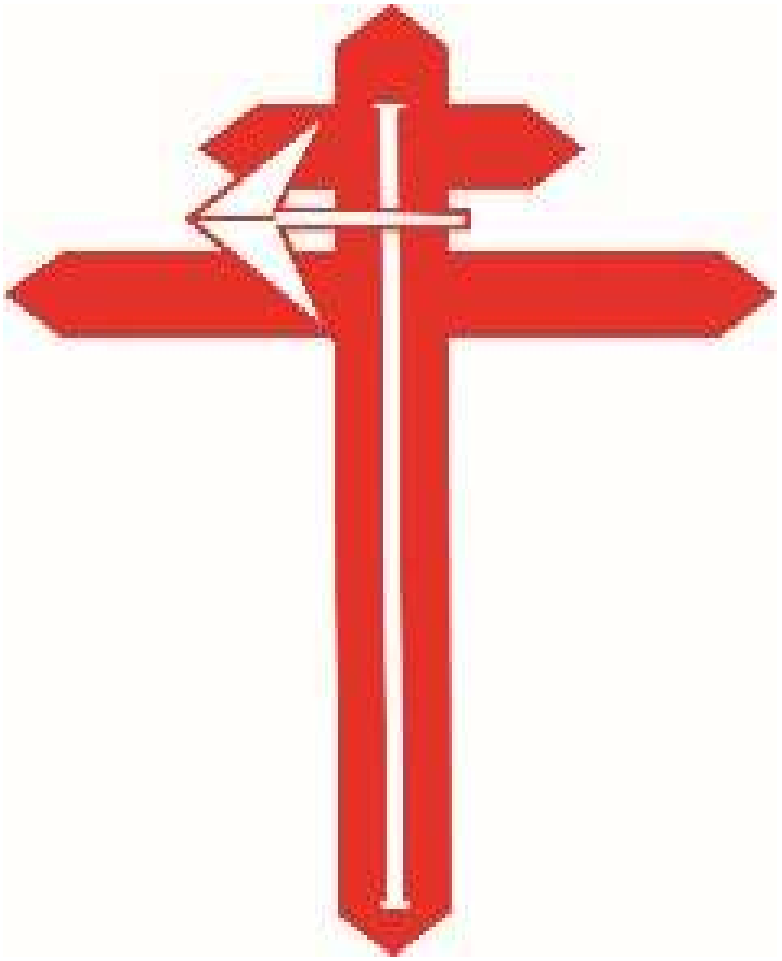
Pediatra

Noviembre 2018

MEDECINS SANS FRONTIERES
DOCTORS WITHOUT BORDERS



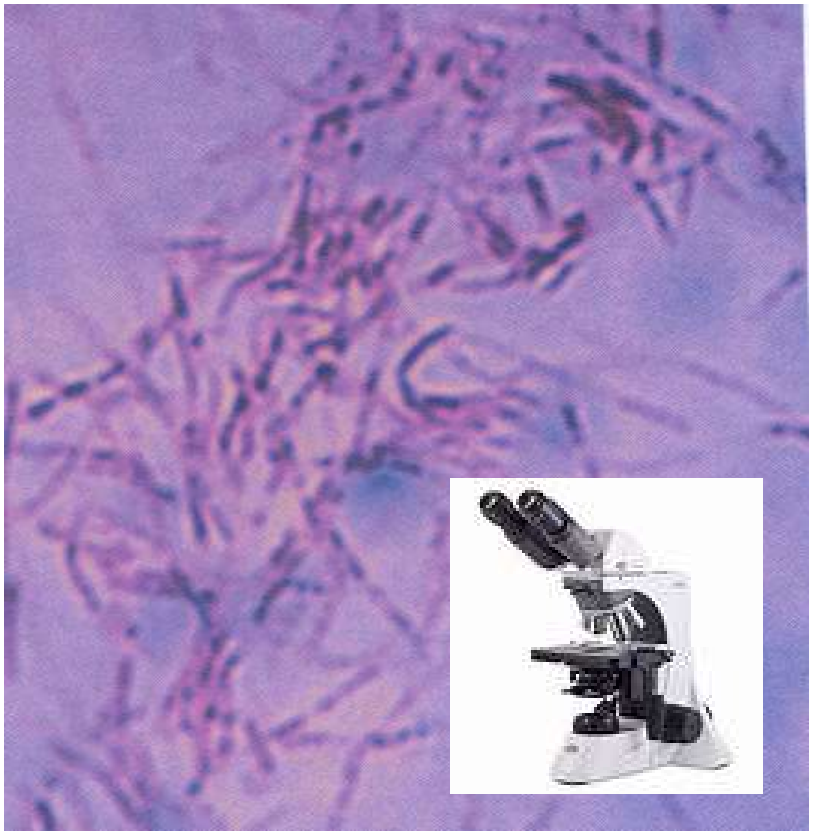
¿ Conoces el significado de estos símbolos ?

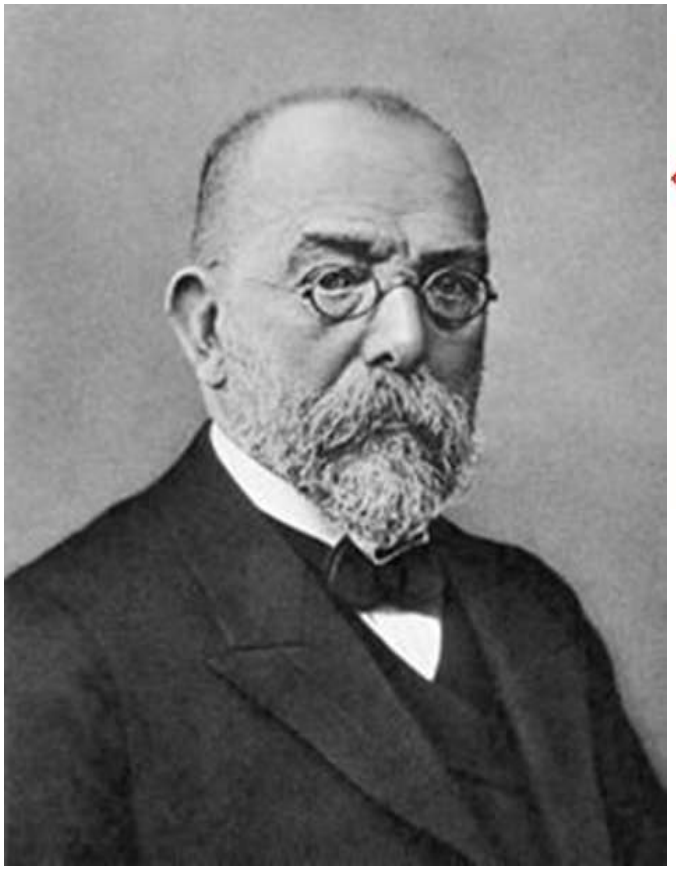


¿ Conoces el significado de estos símbolos ?

¿ Cuándo se celebra el día mundial de la **lucha contra el SIDA** ?

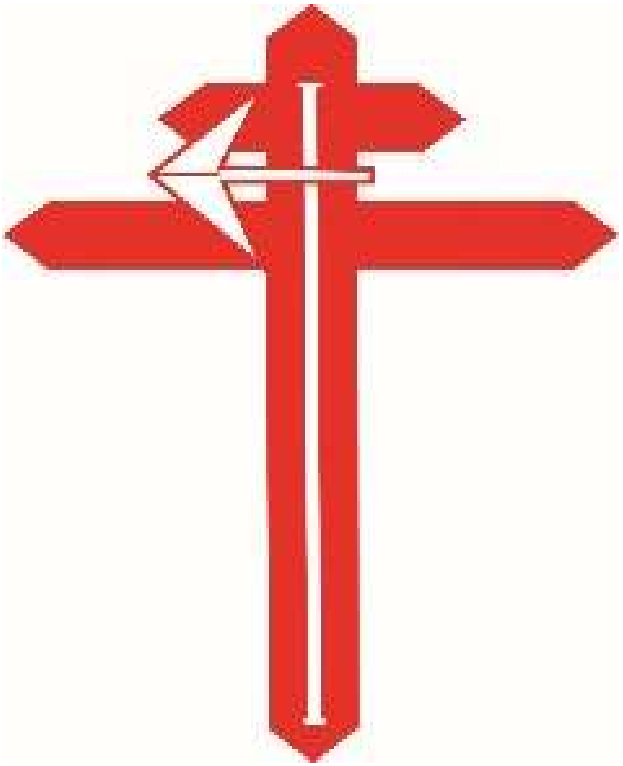
¿ Conoces a estos individuos ?





Dr Robert Koch describe
el **bacilo causante de la Tuberculosis**
en el Hospital de la Caridad en Berlín,
24 de Marzo de 1882


WORLD
TUBERCULOSIS
DAY 24 MARCH

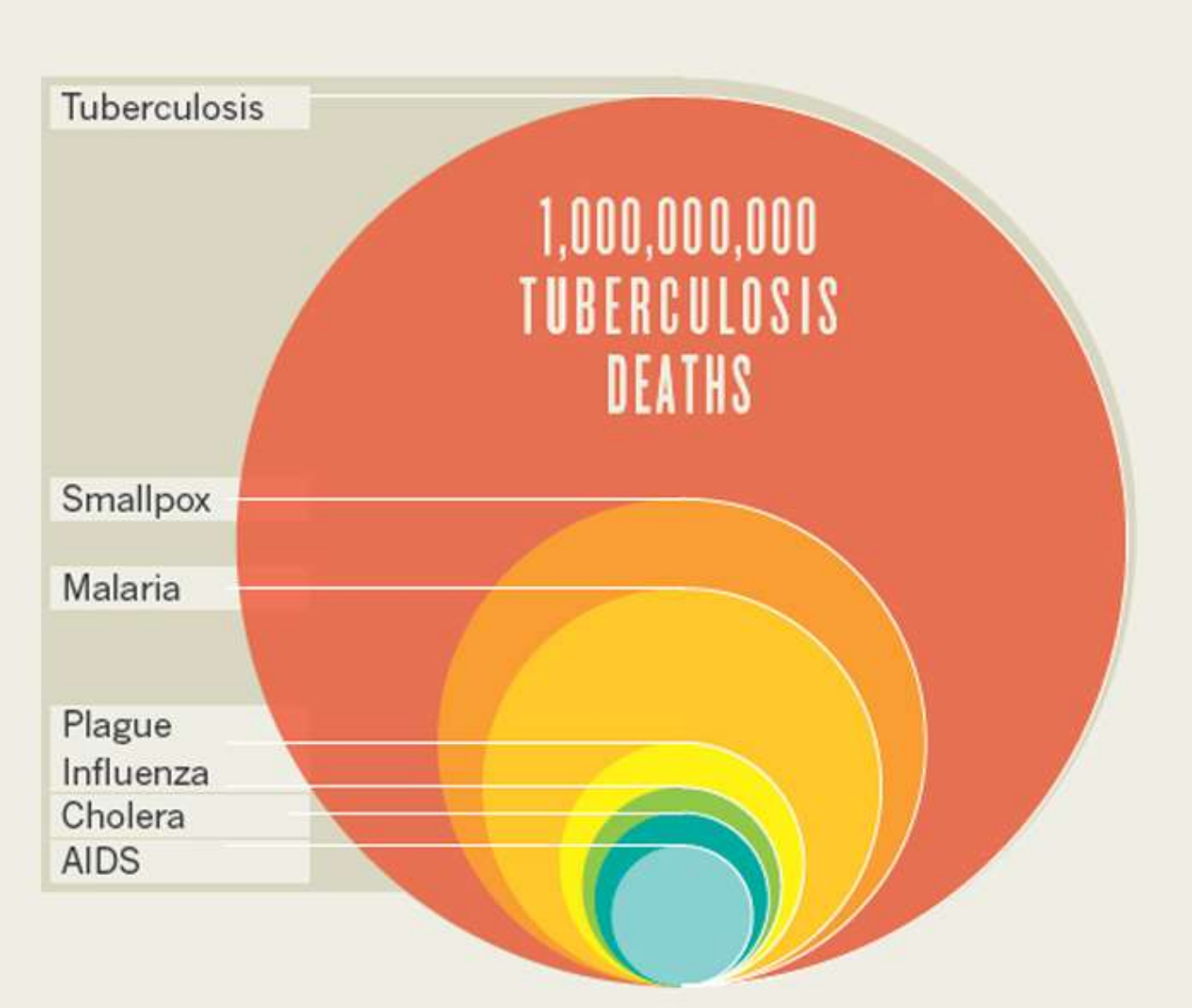


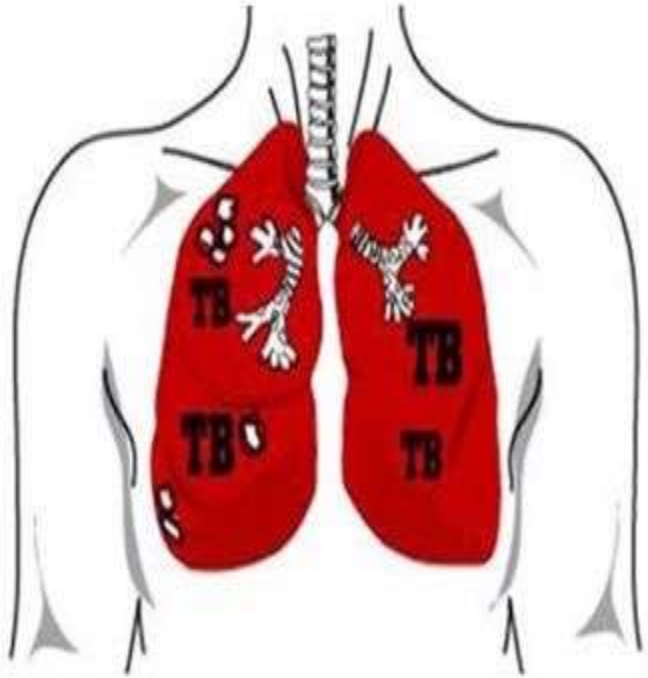
Pese a su **gran relación con el HIV SIDA**,
la Tuberculosis es una **enfermedad olvidada entre las olvidadas**
(incluso por los profesionales sanitarios)

Enfermedades olvidadas, endémicas y epidémicas

Cólera, sarampión, fiebres hemorrágicas, VIH/sida, malaria, tuberculosis, Chagas, Kala Azar, enfermedad del sueño, desnutrición

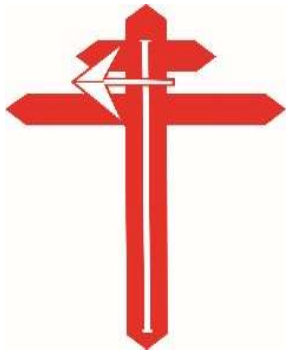
Muertes atribuibles a nivel global en los últimos 2 siglos





TB

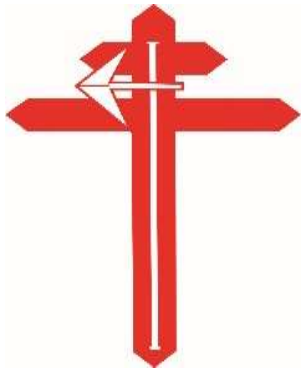
HIV



Todo paciente TB (niño o adulto) debe ser testado para HIV

Todo paciente HIV (niño o adulto) debe ser testado para TB

(historia clínica, examen físico)



STOP

TB in Children

Strive

to raise healthy children...

Children are at high risk of suffering from TB

* their immunity is not strong enough
* they are too young to protect themselves from TB
* they cannot provide themselves with healthy nutritious meals

Immunize your child
Cover your cough
Finish your medication
Open windows

MEDECINS SANS FRONTIERES

MSF REFERENCE BOOKS By ITC

Medical references

MSF Medical Guidelines website is now online. Guides are going to be available as one goes along on the platform. We updated the links on *Refbooks* when the guidelines are available on Medical Guideline.

Essential drugs - 2016
English / Français / Español / Arabic

Refugee health - 1997
English

Rapid health assessment of refugee or displaced populations - 2006
English

Tuberculosis - 2014
English / Français

Clinical guidelines - 2016
English / Français / Español

Essential obstetric and newborn care - 2015
English / Français / Arabic

Public health engineering - 2nd edition 2010
English / Français

Measles - 2013
English / Français

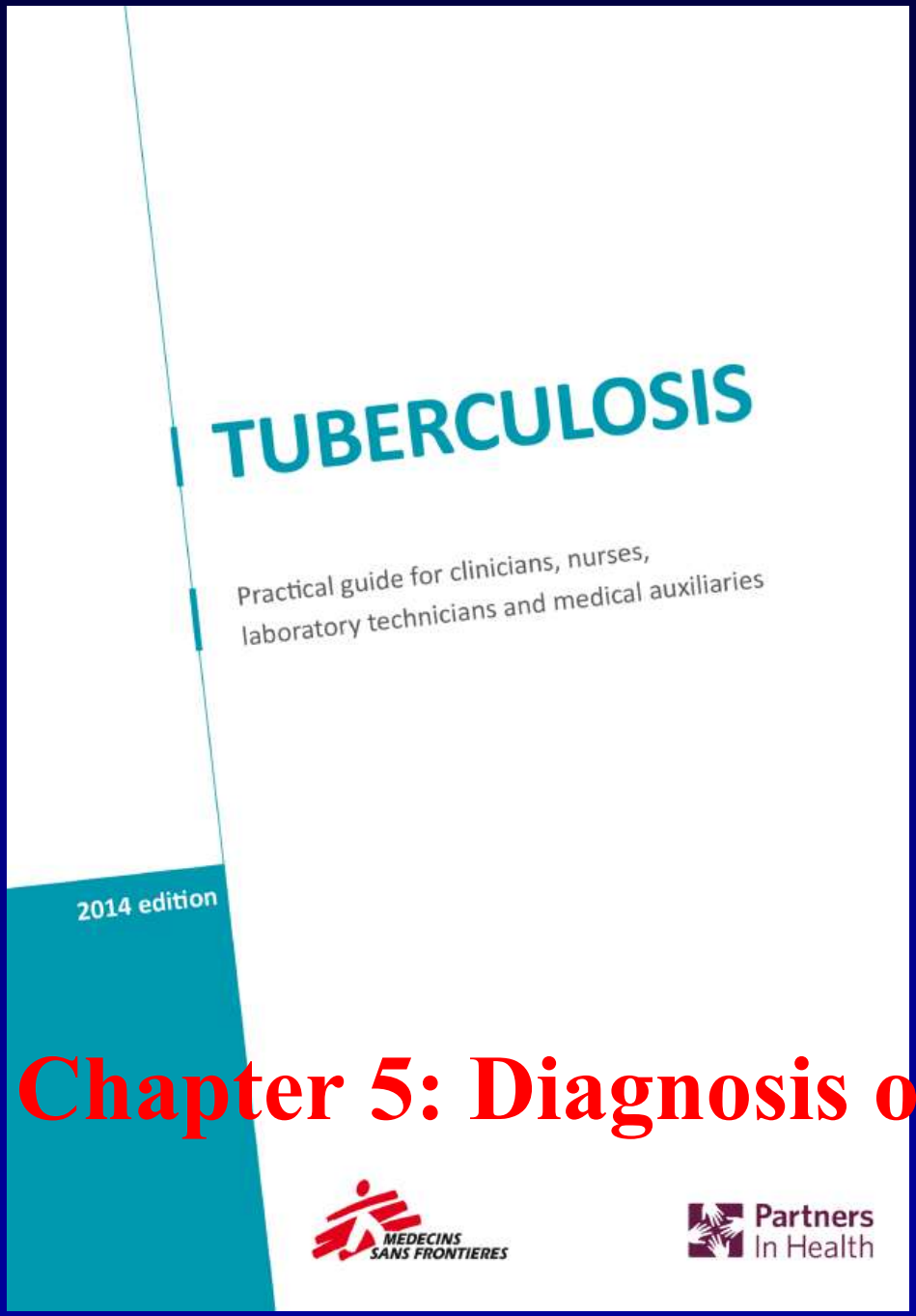
Other links

To purchase MSF Reference Books

Français

Adobe Get Adobe Reader

Updated on November 15th, 2018



MSF

2014

Guía TB

Chapter 5: Diagnosis of TB in children

www.who.int/tb/publications/global_report/en/

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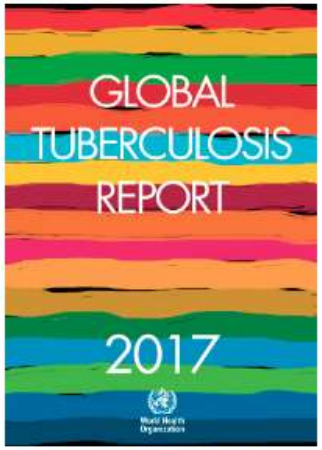
Tuberculosis (TB)

- Tuberculosis
- The End TB Strategy
- Areas of work
- TB publications
- TB data
- News, events and features
- About us

Global tuberculosis report 2017



WHO has published a global TB report every year since 1997. The main aim of the report is to provide a comprehensive and up-to-date assessment of the TB epidemic, and of progress in prevention, diagnosis and treatment of the disease at global, regional and country levels. This is done in the context of recommended global TB strategies and targets endorsed by WHO's Member States and broader development goals set by the United Nations.

The data in this report are updated annually.

Global TB reports from previous years are available from the WHO Institutional Repository for Information Sharing (IRIS) and can be found here.

Please note that direct comparisons between estimates of TB disease burden in the latest report and previous reports are not appropriate. The most recent time-series of estimates are published in the 2017 Global TB Report.

Note 1 December 2017: TB mortality estimates were updated for China.

Download

Full report
pdf, 8.2Mb

Executive summary
pdf, 288kb

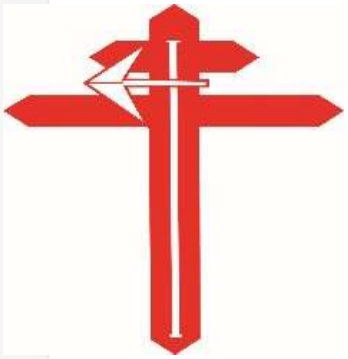
Main text
pdf, 7.49Mb

WHO press release

WHO report signals urgent need for greater political commitment to end TB

Video

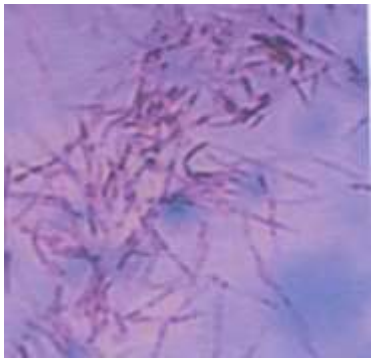
Emma Thompson, the British actress and Mayor of London's TB Ambassador, speaking out on the importance of joining WHO and its partners to end tuberculosis, which kills over 4,000 people each day.



http://www.who.int/topics/tuberculosis/es/

Tuberculosis pediátrica

1. Patogénesis y manifestaciones de la enfermedad en lactantes, niños y adolescentes
2. Epidemiología: ¿ es la TB un problema ?
3. Diagnóstico: retos y posibilidades
4. Tratamiento & monitorización
5. Actitudes preventivas
6. Conclusiones



Mycobacterium tuberculosis

Evidencia de Mal de Pott (tuberculosis vertebral) en necropsias de momias egipcias de hace 4.000 años.

Características de esta enfermedad :

- Baja infectividad.
- Periodo *latente*:

  sobrevive dentro del cuerpo.
- Crecimento lento.
- Sol puede matar a esta bacteria.

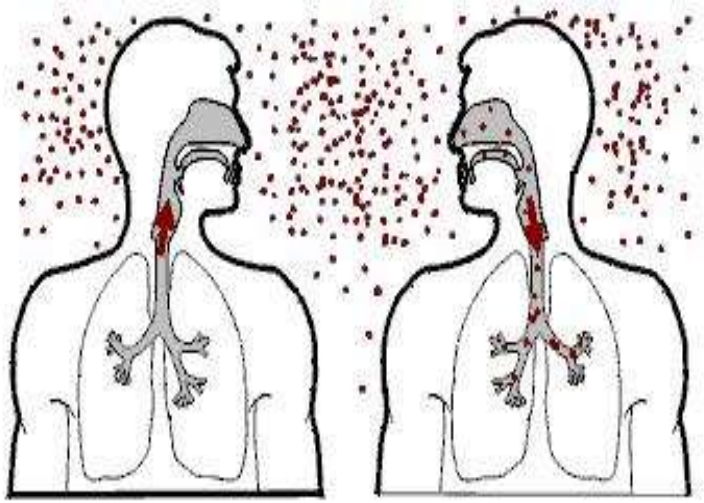
Otros nombres: Germen tuberculoso, bacilo acido-alcohol resistente (BAAR), Bacilo Koch

Transmisión respiratoria de TB

Enfermo de TB emite microgotas infecciosas :

- **Tos** (0 - 3.500 microgotas)
- Estornudo (4.500 - 1.000.000)
- Hablando o cantando (0 – 200)

Transmisión cuando otra persona inhala microgotas con bacilo Koch



Tuberculosis en niños

Los niños expuestos suelen permanecer latentes durante décadas

Las cavernas pulmonares son frecuentes en niños

En niños las formas de enfermedad extrapulmonar son más habituales que la forma pulmonar

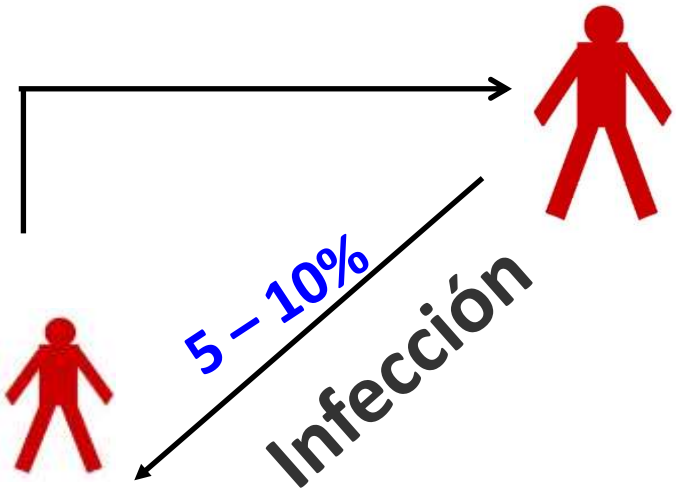
La baja inmunidad de los lactantes no focaliza la carga bacilífera, y por tanto pueden hacer TB miliar y/o meningitis tuberculosa

(= palma abierta) Todas son ciertas

(= puño cerrado) Todas son falsas

Enfermo no tratado (esputo positivo)
con tuberculosis pulmonar

Tuberculosis
Ciclo de infección



1 enfermo suele transmitir hasta 10 – 15 nuevos casos por año

5 – 10%

Infección

90%

Infección

Tuberculosis Activa

Reactivación

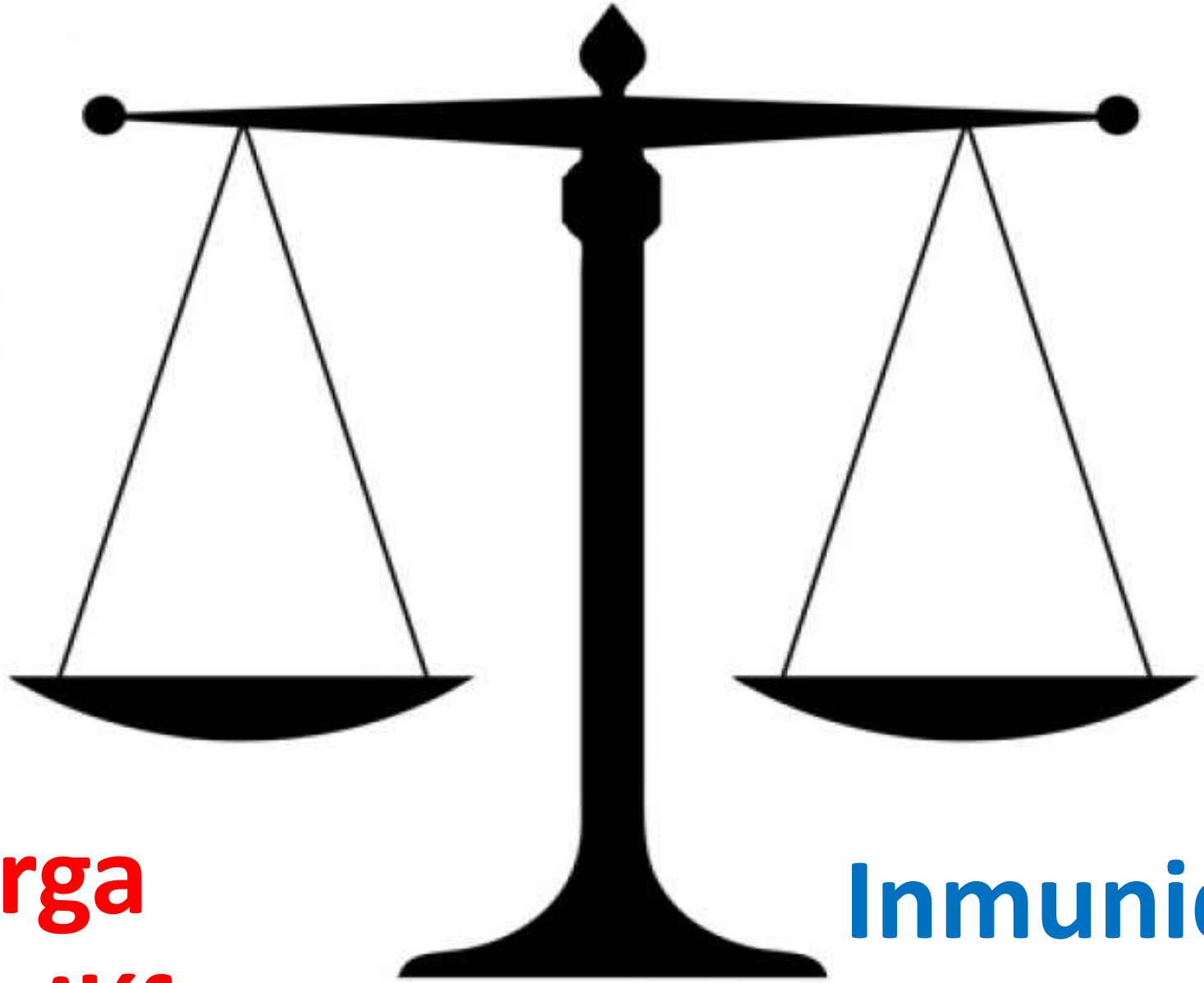
5 – 10 % durante la vida

Tuberculosis Latente

10.4 millones **nuevos casos** por año

➔ 1.8 millones **muertes** al año

Prevalencia estimada 2.000 millones
= Un tercio de la población mundial !!



Carga bacilífera

Inmunidad

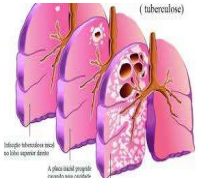
Tuberculosis pediátrica

Los niños tienen

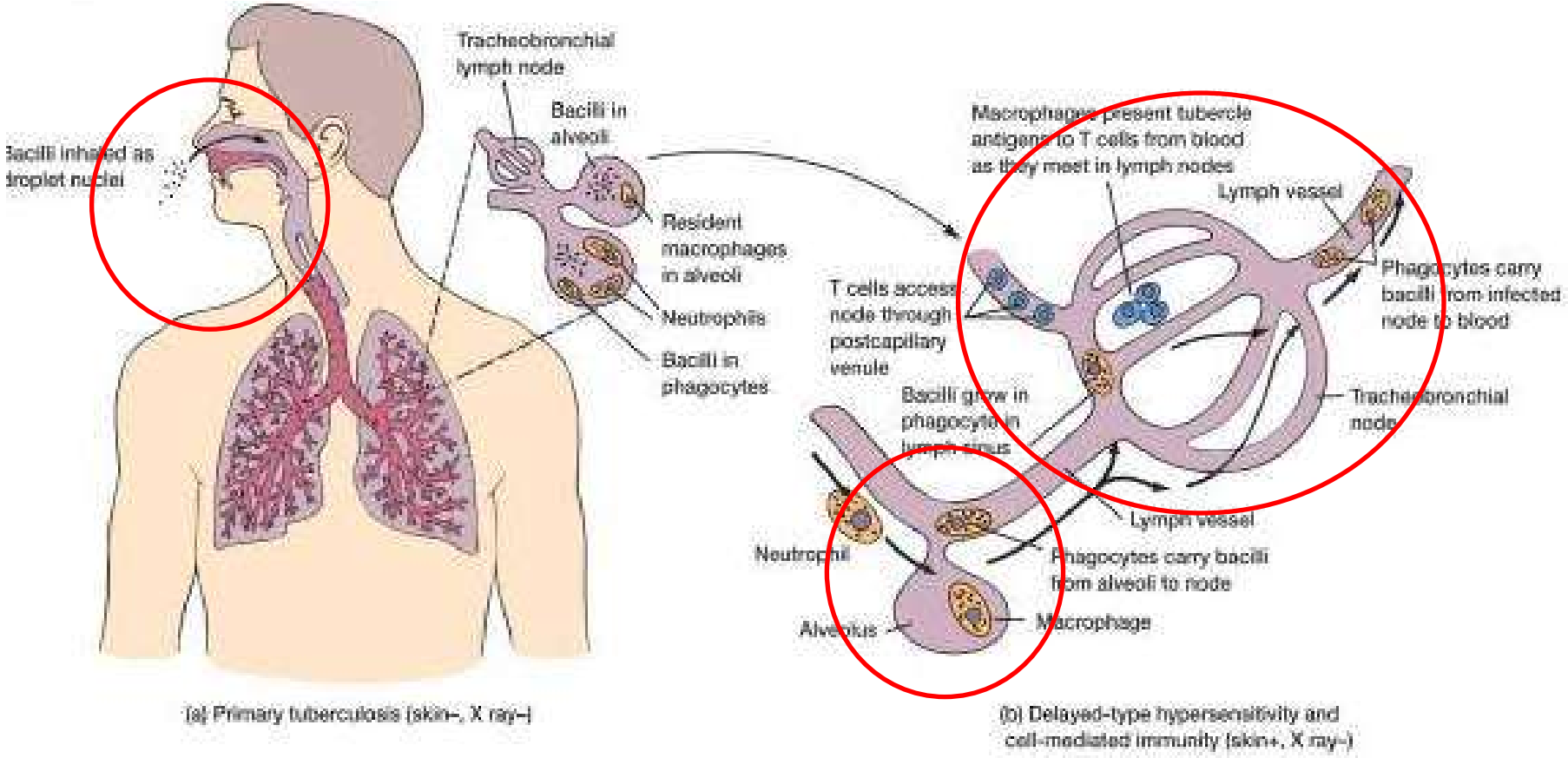
menos inmunidad que los adultos,

por tanto **pocos bacilos** (= *paucibacilar*)

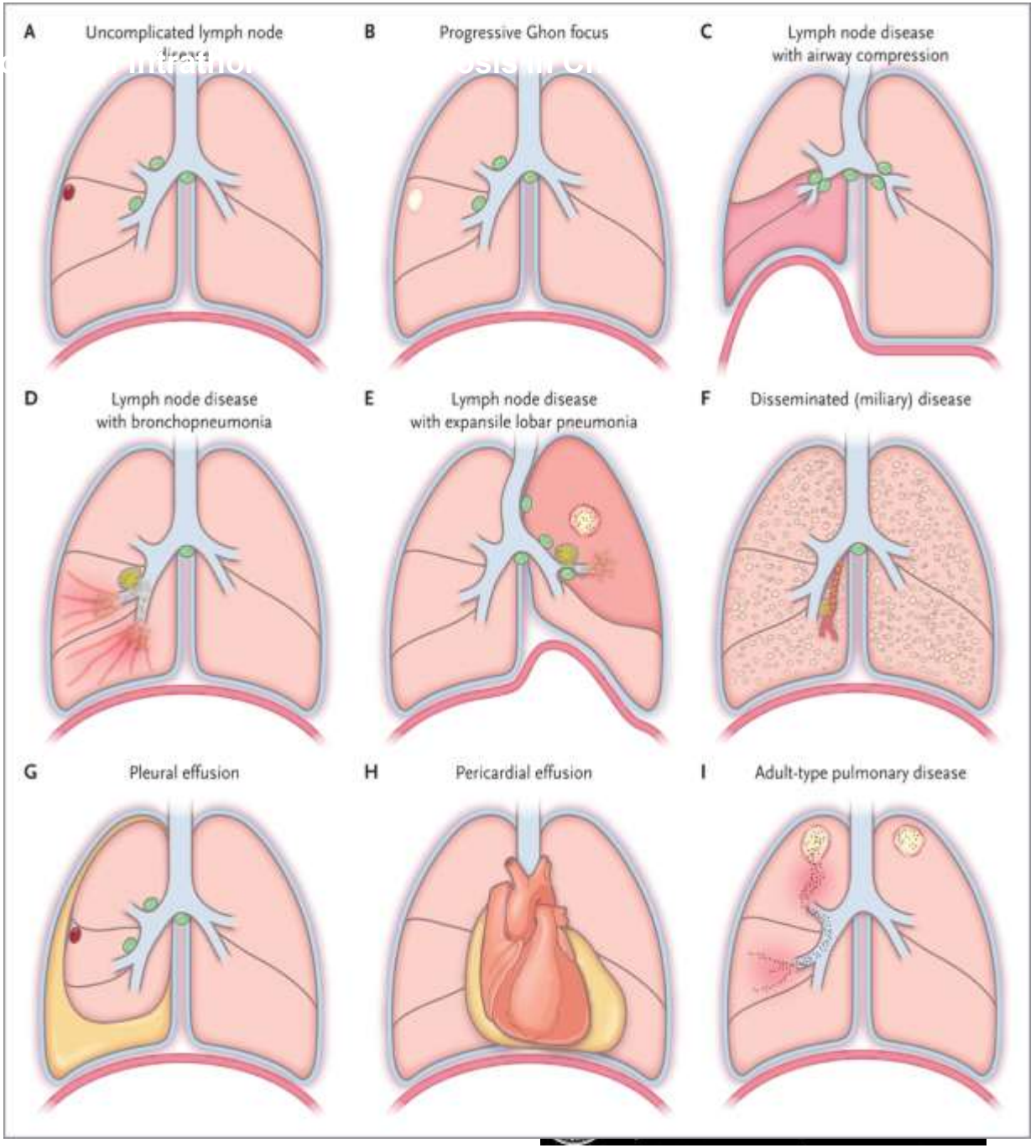
pueden producir infección activa ☹



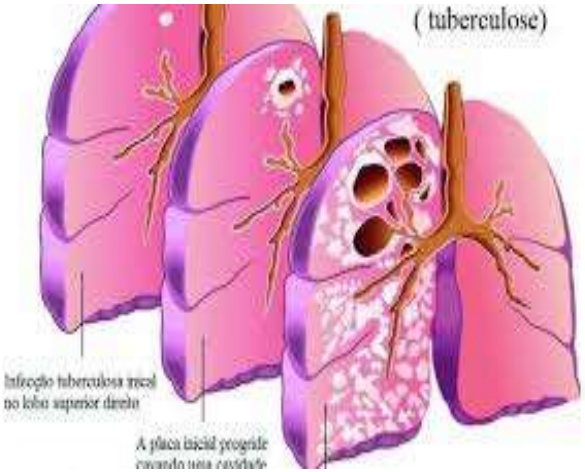
Patogénesis de la tuberculosis

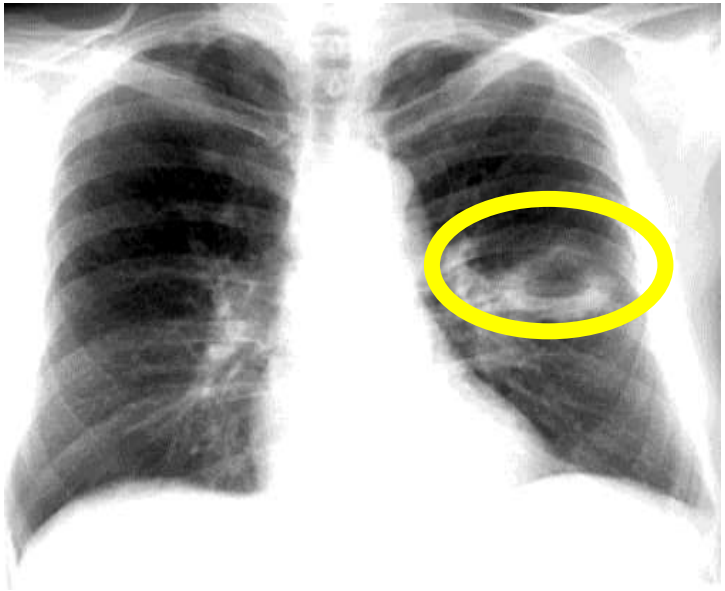


Múltiples formas de **tuberculosis intratorácica pediátrica**



Perez-Velez CM, Marais BJ. N Engl J Med 2012;367:348-361.





Cavidad, caverna

Alta cantidad Mycobacterium Tuberculosis

➔ **contagioso (en vida)** ☹

Relativamente frecuente en adultos

Algunos casos en adolescentes

Excepcional en niños

Tuberculosis pediátrica

Progresión rápida de la enfermedad

(especialmente por debajo de 2 años de edad)

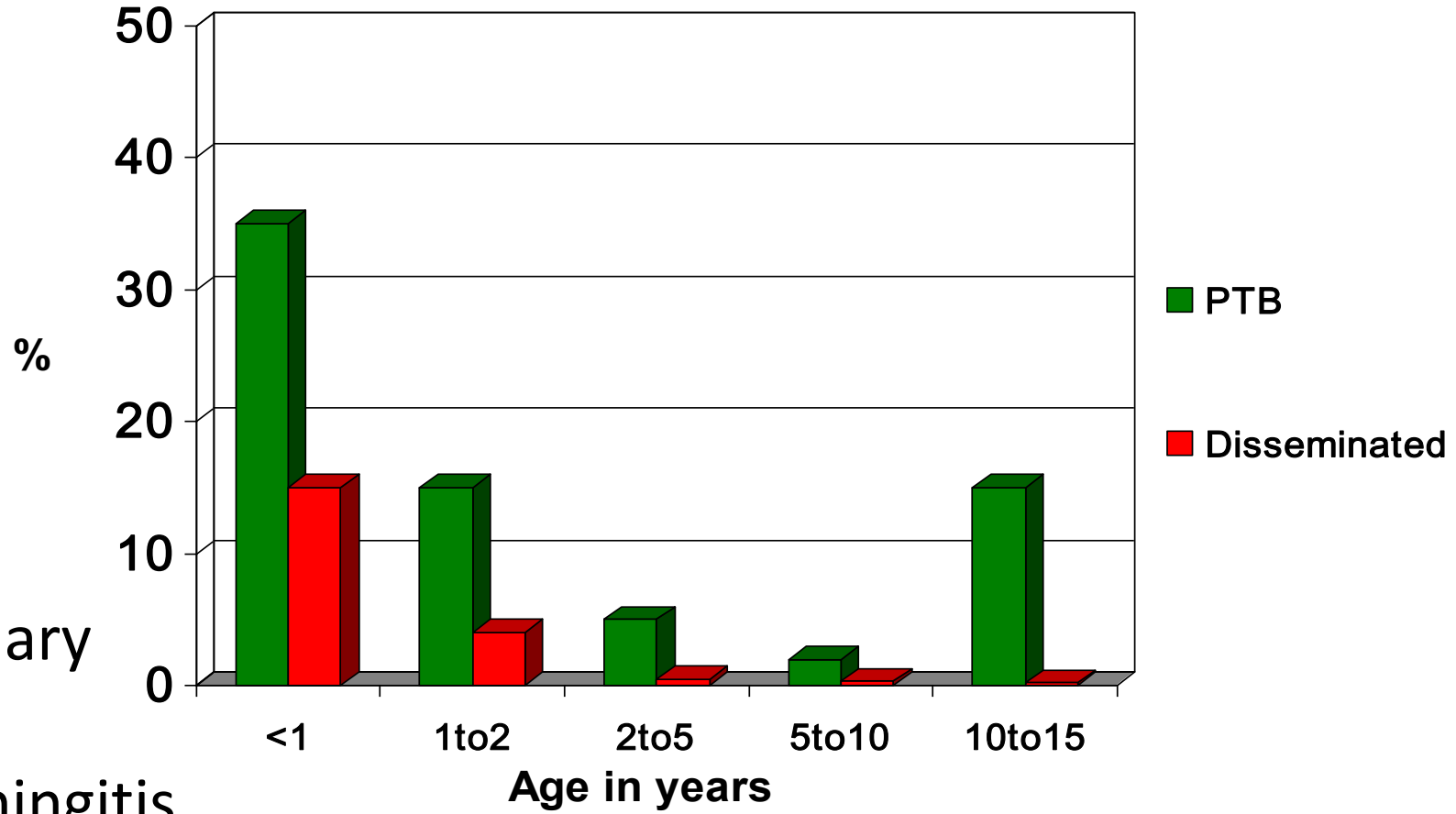
90% enfermos 1er año tras exposición

Además, mayor riesgo
de **enfermedad extrapulmonar**

Pathogenesis : Age-specific risk to progress to disease after primary infection with *M.tb* in children

Age at primary infection	Risk to progress to disease	
< 1 year	No disease	50%
	Pulmonary disease	30-40%
	Disseminated (miliary) disease or TBM	10-20%
1 - <2 years	No disease	75-80%
	Pulmonary disease	10-20%
	Disseminated (miliary) disease or TBM	2-5%
2 - <5 years	No disease	95%
	Pulmonary disease	5%
	Disseminated (miliary) disease or TBM	0.5%
5 – 10 years	No disease	98%
	Pulmonary disease	2%
	Disseminated (miliary) disease or TBM	<0.5%
>10 years	No disease	80-90%
	Pulmonary disease	10-20%
	Disseminated (miliary) disease or TBM	<0.5%

Pathogenesis : Age-specific progression to PTB / EPTB disease after primary infection with *M.tb* in children



Milliary & Meningitis in infants & < 2 years old

Skin, lymphnodes, ostearticular in older children

Tuberculosis pediátrica

En niños la forma de TB
más frecuente es la **pulmonar**

Pero tienen más **enfermedad extrapulmonar** que los adultos

< 2 años (lactantes): **TB miliar, meningitis TB**

10 – 15 años (adolescentes): **piel, ganglios, articular**

Tuberculosis extrapulmonar EPTB

Linfadenitis TB

Ascitis TB

TB espinal (= mal de Pott)

Tuberculosis extrapulmonar cutánea

Escrofuloderma

Lupus vulgaris

TB papulonecrótica

Nodular

Erythema induratum

Patogénesis TB pediátrica

Rápida progresión a enfermedad,

especialmente < 2 años edad

90% de enfermos en el 1er año tras exposición

Implicaciones:

- **Periodo de vigilancia** tras exposición
- Indicador de **transmisión reciente** en la comunidad → búsqueda activa de casos !!!

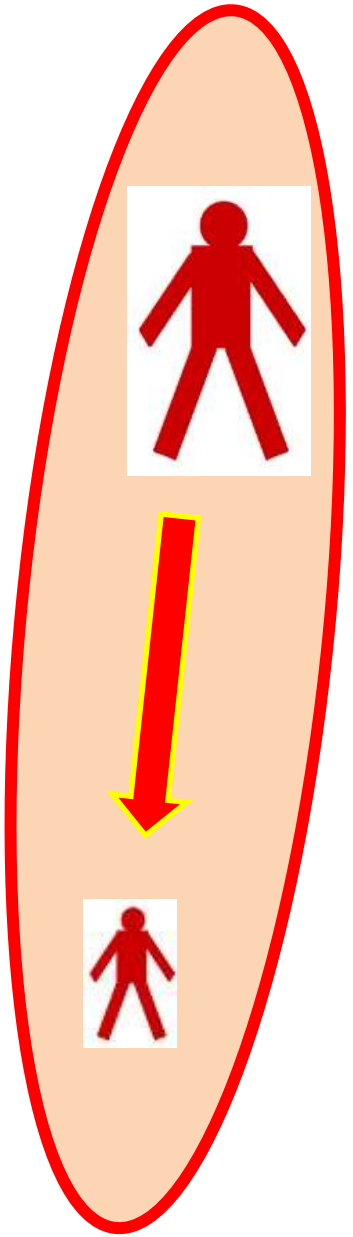
Patogénesis TB pediátrica

Ante un niño enfermo de tuberculosis, debemos buscar un **adulto tosedor**

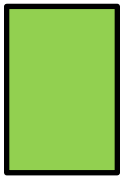
(= caso índice)

Generalmente familiar o conviviente

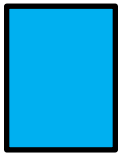
Contagio TB por exposición continuada en lugares con poca ventilación



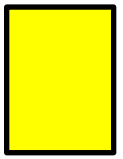
Tuberculosis en niños



Los niños expuestos, si desarrollan enfermedad lo suelen hacer en el primer año tras exposición

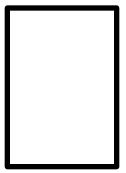


Las cavernas pulmonares son excepcionales en niños

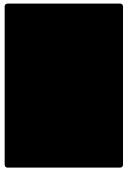


La enfermedad pulmonar es la más habitual en niños

Las formas extrapulmonares son más frecuentes en niños que en adultos



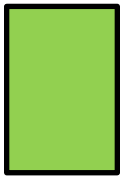
Los lactantes desarrollan TB miliar y meningitis tuberculosa más que ningún otro grupo de edad



(= puño cerrado)

Todas son ciertas

Tuberculosis en niños



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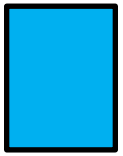

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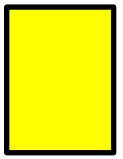

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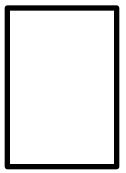

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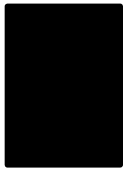
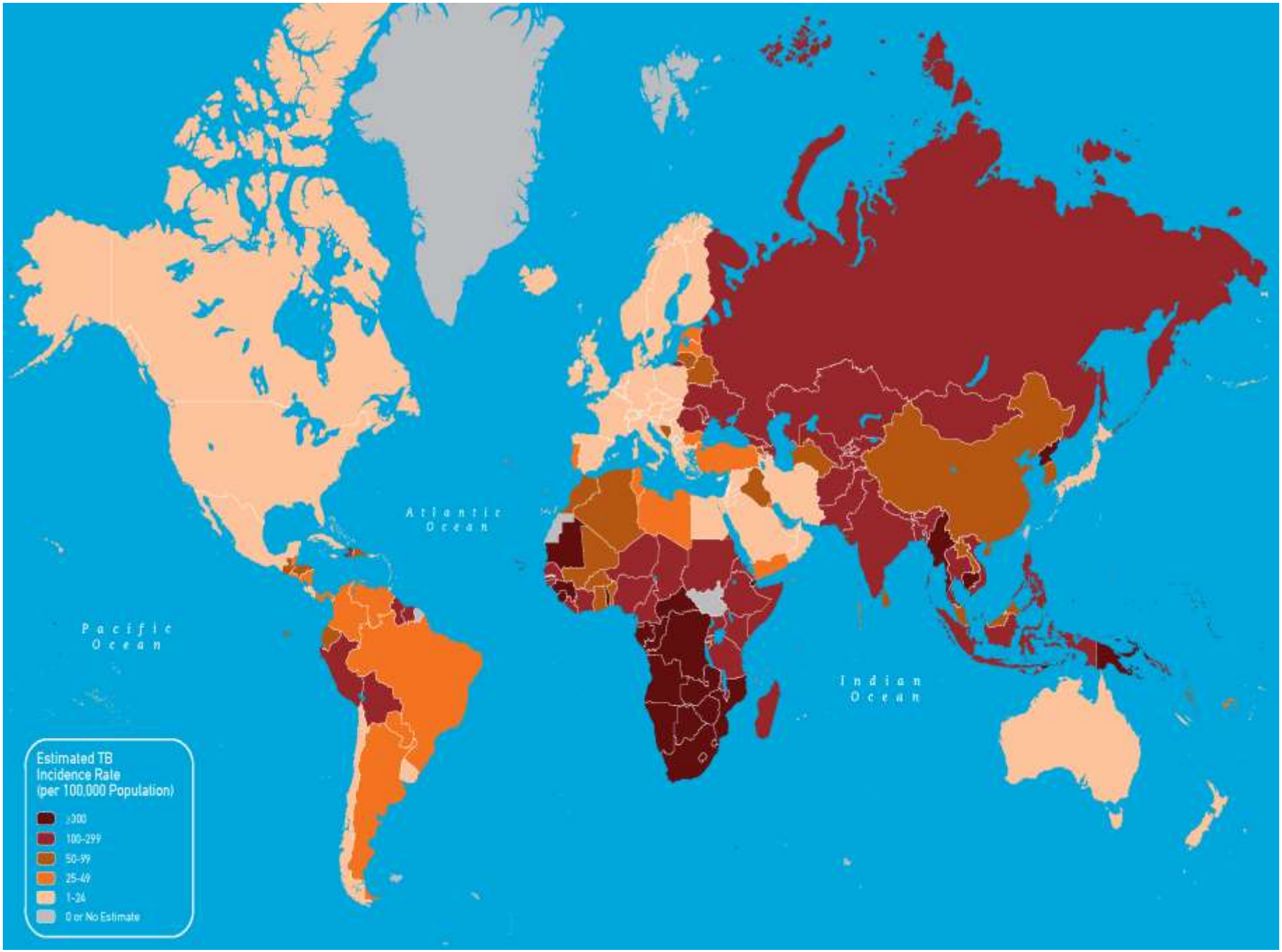


(= puño cerrado)

Todas son ciertas

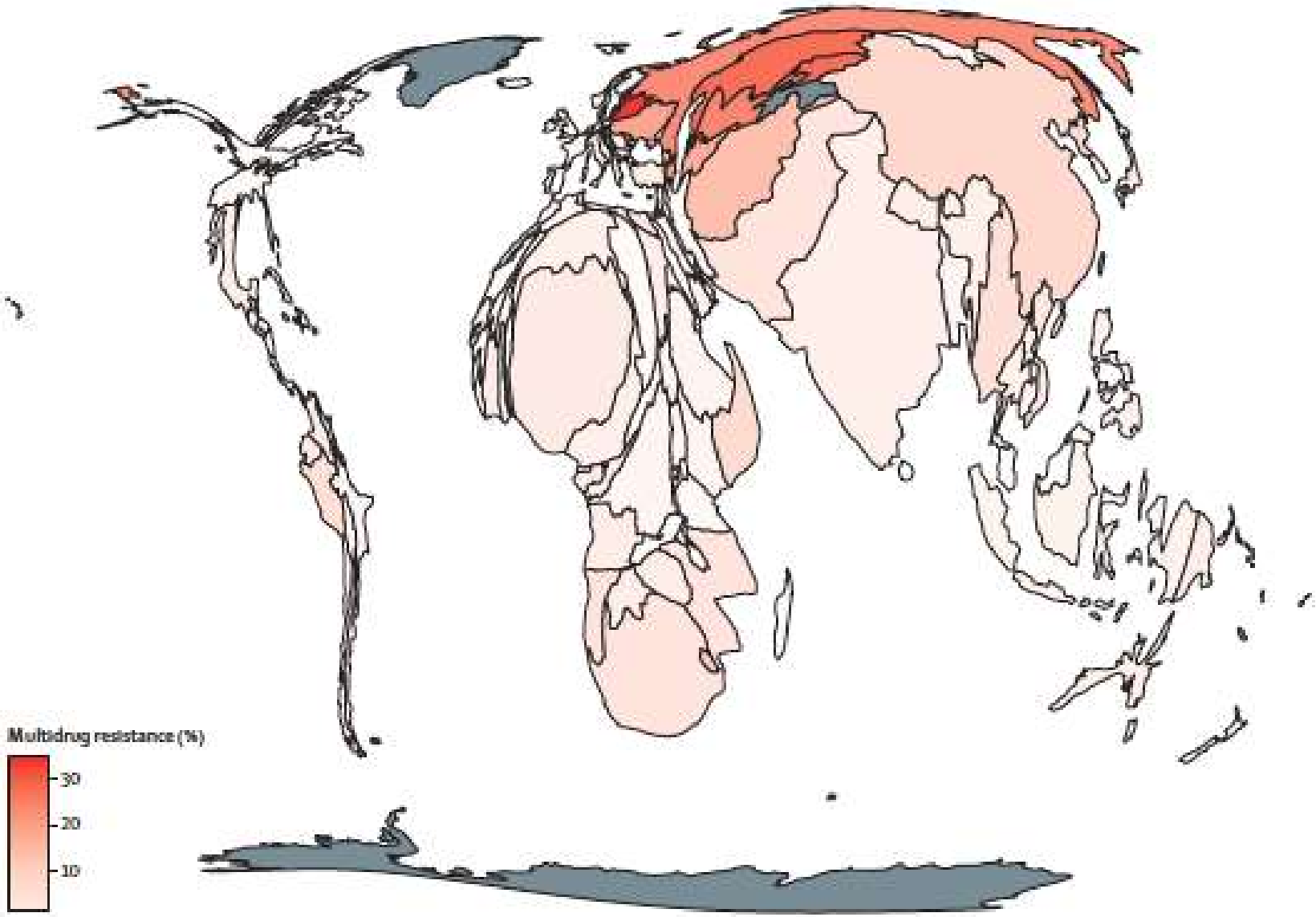

Atlantic Ocean
Pacific Ocean
Indian Ocean
Estimated TB Incidence Rate (per 100,000 Population)
≥300
100-299
50-99
25-49
1-24
0 or No Estimate

Epidemiología de la TB pediátrica

- 10% de la carga de enfermedad TB[1]
- Variabilidad basada en la carga de enfermedad y de la demografía de cada contexto [2]
  - Developed countries: children <5% of TB cases
  - High-burden resource-limited countries: 15-20% or more
- WHO Global TB report 2016
  - 950.000 nuevos casos casos en niños (10% del total)
  - 180.000 muertes en niños (10% del total)

1. Nelson, L. J. and C. D. Wells (2004). "Global epidemiology of childhood tuberculosis." *Int J Tuberc Lung Dis* 8(5): 636-647.
2. Donald, P. R. (2002). "Childhood tuberculosis: out of control?" *Curr Opin Pulm Med* 8(3): 178-182.

Global burden of incident TB in **children**



Diagnóstico de tuberculosis en niños

Si hay un niño sospechoso de tuberculosis, debemos preguntar, buscar y encontrar un adulto tosedor

Con los adelantos tecnológicos actuales, es fácil demostrar presencia de bacilos Koch en niños con TB

El Mantoux y los IGRA son de gran utilidad en LRS

No podemos evaluar la respuesta al tratamiento según la evolución clínica de los niños, es muy inespecífica

(= palma abierta) Todas son ciertas

(= puño cerrado) Todas son falsas

Caso clínico: Kevin

Infant 11 months old, HIV negative, male

- 4 weeks of cough, fever, weight loss
- Not improved after 7 days of antibiotics
- Father recently diagnosed with MDR-TB, lives in same house, sleeps in same room
- Chest X Ray: clear right hilar and paratracheal lymph nodes, Right Upper Lobe and Rigth Lower Lobe opacification

- Does this child Kevin have TB disease?
- Any other diagnostic tests you would do?
- 3 gastric aspirates come negative. What do you do?
- Would you give treatment?

  If so, what?

Diagnóstico de Tuberculosis

Historia clínica,

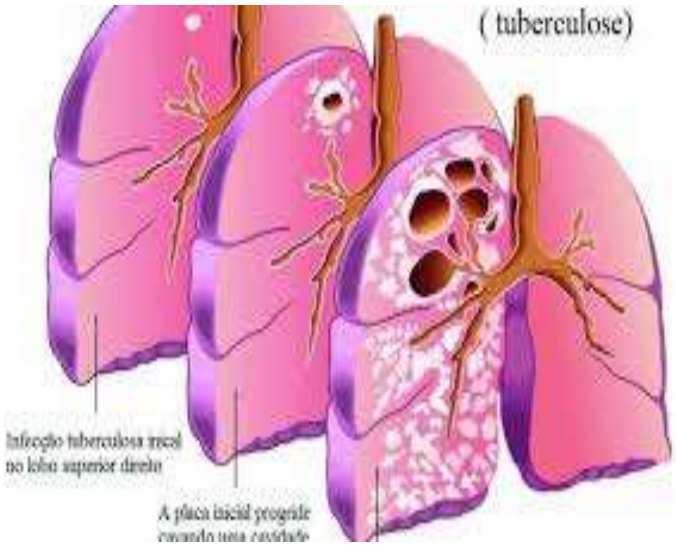
examen físico

&

Pruebas complementarias

Diagnóstico de Tuberculosis activa

1. **Historia clínica** (=síntomas)
2. **Examen físico** (=signos)
3. Pruebas complementarias



   - **Radiografía de tórax**
   - Tests de **laboratorio**, para confirmación microbiológica, y detección de resistencias (DSTB vs DRTB)

Historia clínica (=síntomas):

1. **Fiebre**: No / Sí. Desde cuándo ? Días / semanas / meses
2. **Tos**: No / Sí. Desde cuándo ? Días / semanas / meses
3. *Otra persona con tos en casa ??* Dias / semanas / meses
4. **Apetito** : Bueno / Medio / Malo / Ninguno

   ➔ **pérdida peso, retraso ponderal**
5. Vómitos : Desde cuándo ? Cuántas veces hoy ??
6. Orina: Normal / Po ca / Ausente. Color ??
7. Heces: Normal / Diarrea / Mucoide / Con sangre ??
8. **Dolores:** Dónde ??? Desde cuándo ? Dias / semanas / meses

Presentación clínica TB activa en adultos

Pulmones afectos

- Tos prolongada
  (> 2 semanas)
- Produción esputo
- Hemoptisis
  (= esputo sanguinolento)
- Falta de aire
- Dolor torácico

Síntomas constitucionales:

- Fiebre / febrícula
- Sudores nocturnos
- Pérdida de peso
- Falta de apetito
- Fatiga, cansancio

Síntomas específicos de TB extrapulmonar

Síntomas pueden ser atípicos en paciente **HIV positivo**

Presentación clínica TB activa en niños

Pulmones afectos

Tos prolongada

(> 2 semanas)

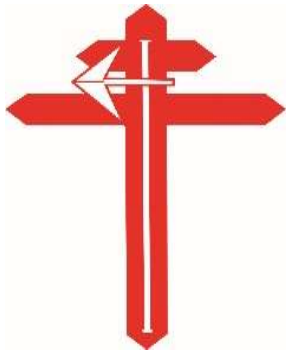
que no mejora tras tratamiento antibiótico convencional

Síntomas constitucionales:

- Fiebre / febrícula
- Menor actividad
- Falta de apetito
- Estancamiento ponderal (= no ganancia de peso ni de altura)

Síntomas específicos de TB extrapulmonar

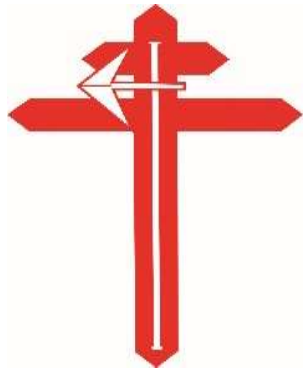
Síntomas pueden ser atípicos en paciente **HIV positivo**



Todo paciente TB (niño / adulto) debe ser testado para HIV

Todo paciente HIV (niño / adulto) debe ser testado para TB

(historia clínica, examen físico)



Diagnóstico de Tuberculosis en niños

No hay diferencia en la presentación clínica entre DS-TB y MDR-TB

- Historia de exposición a TB, síntomas
- Examen físico
- Prueba (¨*trial*¨) de antibioticos
- Radiografía de tórax
- Confirmación microbiológica; difícil

Making a diagnosis is not challenging in most cases; confirming a diagnosis can be challenging

Muestras Tuberculosis pediátrica

En niños es difícil conseguir muestras de esputo (tos poco productiva, no cavernas)

Lavado gástrico, esputo inducido

Enfermedad extrapulmonar

➔muestras por punción

meningitis TB, piel, ganglios, articular

Muestras Tuberculosis pediátrica

1.- Dificultad técnica de **obtención de las muestras**

2.- Condición *paucibacilar* (pocos bacilos) disminuye considerablemente la rentabilidad diagnóstica de las pruebas

➔ difícil confirmación microbiológica

Bacteriología en niños con Tuberculosis:

Esputo positivo ??	10-15%
Gene Xpert ??	75%
Cultivo positivo ??	30-40%

Implicaciones:

- Diagnóstico más subjetivo; el reto es **confirmar**
- Difícil monitorizar objetivamente la respuesta a tratamiento

GeneXpert

1. Sputum liquefaction and inactivation with 2:1 sample reagent

2. Transfer of 2 ml material into test cartridge

3. Cartridge inserted into MTB-RIF test platform (end of hands-on work)

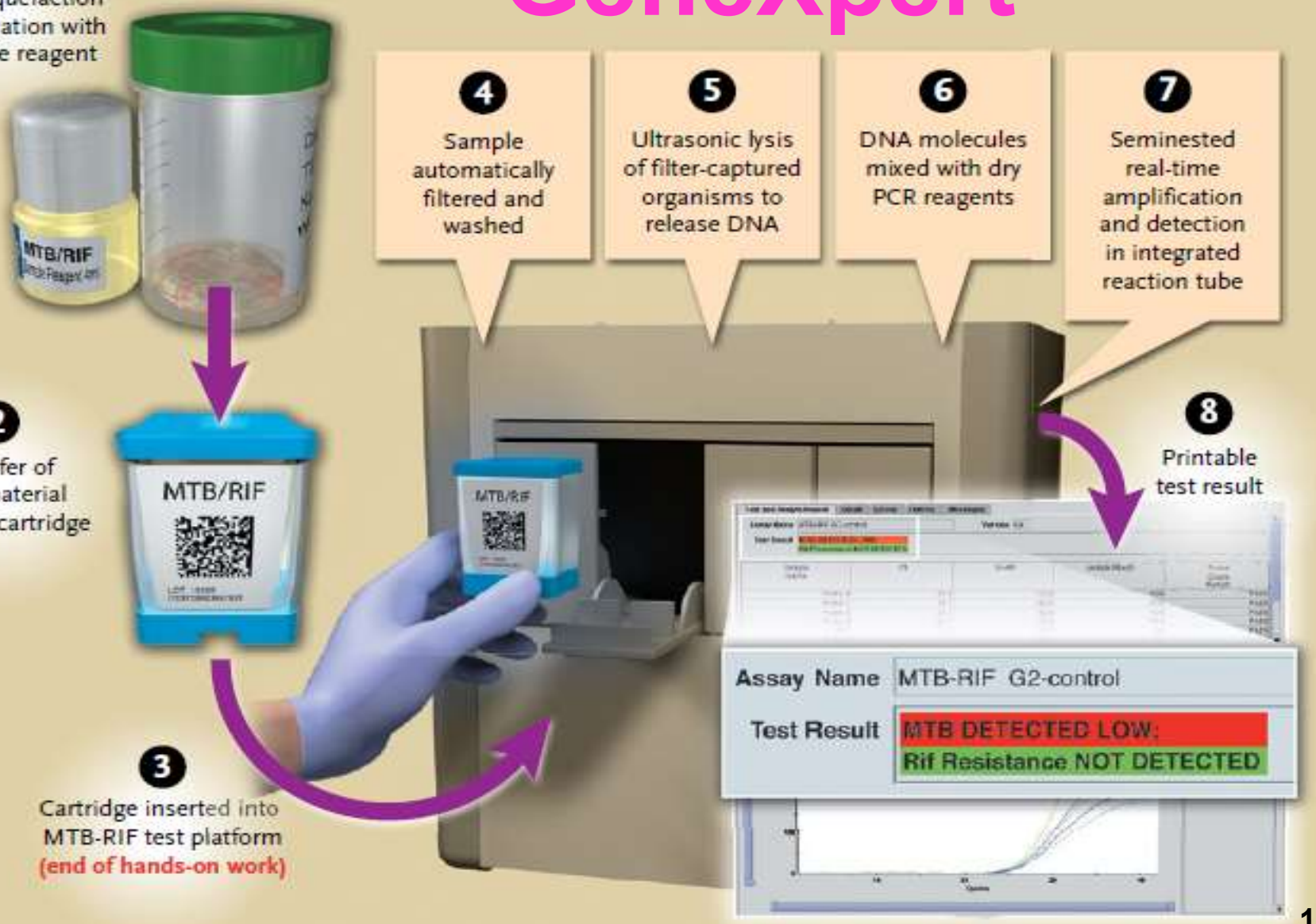
4. Sample automatically filtered and washed

5. Ultrasonic lysis of filter-captured organisms to release DNA

6. DNA molecules mixed with dry PCR reagents

7. Seminested real-time amplification and detection in integrated reaction tube

8. Printable test result



Time to result, 1 hour 45 minutes

WHO case definitions for TB & DRTB

Classifier	Types of TB	Notes / Explanation
Site of disease	Pulmonary	Lungs are affected (could be also other organs)
	Extra-pulmonary	Outside lung parenchyma
History of TB	**New cases**	Never treated with TB drugs
	Previously treated	Already treated with TB drugs (1st or 2nd line)
Resistance pattern	DSTB	Susceptible to First Line Drugs (=FLD)
	DRTB	Mono-resistance Poly-resistance Rifampicin Resistance INH Resistance Multi-drug Resistance Pre-extensive drug Resistance Extensive drug Resistance

DRTB = Drug Resistant Tuberculosis

- **Mono:**

Resistance to a single drug

- **Poly:**

Resistance to more than one drug, but not both R & H

- **MDR (Multi):**

Resistant to R (Rifampicin) and H (Isoniazid, INH)

- **Pre-XDR:**

Resistant to R and H and either an injectable ***or*** a fluoroquinolone

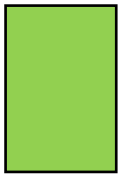
- **XDR (Extensively):**

Resistant to R and H and an injectable ***and*** a fluoroquinolone

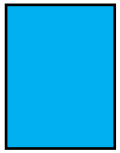
***Injectable* = Amikacin, Capreomycin, Kanamycin**

***Fluorquinolone* = Levofloxacin, Moxifloxacin, Gatifloxacin**

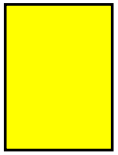
Diagnóstico de tuberculosis en niños



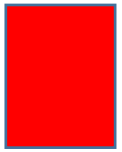
Si hay un niño sospechoso de tuberculosis, debemos preguntar, buscar y encontrar un adulto tosedor



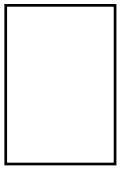
Los síntomas de TB sensible y TB resistente son iguales



El Mantoux y los IGRA no se usan en LRS



Los hallazgos radiológicos no permiten distinguir TB sensible de TB resistente, ni en adultos ni en niños

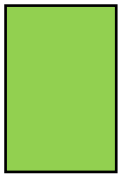


Pese a los adelantos tecnológicos actuales, no es fácil demostrar presencia de bacilos Koch en niños con TB

(= puño cerrado)

Todas son ciertas

Diagnóstico de tuberculosis en niños



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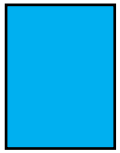
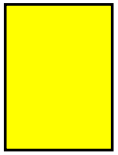


Los síntomas de TB sensible y TB resistente son iguales



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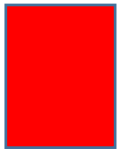

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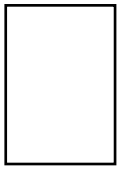


Pese a los adelantos tecnológicos actuales, no es fácil demostrar presencia de bacilos Koch en niños con TB

(= puño cerrado)

Todas son ciertas

Diagnosis of pediatric TB:

- Decide to treat for TB: **confirmed vs probable** TB
- If decide to treat for TB, decide on most appropriate regimen
  - Drug-susceptibility **DST**of child's isolate, if confirmed
  - According to the **DST**: of the **most likely source case**
  - Other risk factors: contact of source case with risk factors for DRTB, or the child has failed adherent first-line TB treatment

GeneXpert and culture: Negative result does not rule out TB.

Diagnosis: Probable vs confirmed DSTB

- ***Confirmed DSTB***: At least 1 of the signs and symptoms suggestive of TB disease, and detection of *M.tuberculosis* from the child, with demonstration (genotypic or phenotypic) of no resistance to drugs
- ***Probable DSTB:*** Diagnosis of clinical TB disease and confirmed DSTB contact, without microbiological detection of *M. tuberculosis* on the child

Diagnosis: Probable vs confirmed DRTB

- *Confirmed*: At least 1 of the signs and symptoms suggestive of TB disease and detection of *M.tuberculosis* from a child with demonstration of genotypic or phenotypic resistance
- *Probable:* Diagnosis of clinical TB disease *and* confirmed DRTB contact
- *Possible:* Diagnosis of clinical TB disease together with either
  - (a) contact of a source case with TB disease who has risk factors for drug resistance, or
  - (b) failure of adherent first-line TB treatment

Tuberculosis pediátrica es *paucibacilar*

= poca cantidad de bacilos

➔ **Baja positividad** de las pruebas de laboratorio

(difícil confirmación microbiológica) ☹

➔ niños **no son contagiosos** ☺

➔ mejor repuesta a tratamiento ☺

Tratamiento de TB sensible

2 meses

Rifampicin

Isoniazid

Pyrazinamide

Ethambutol

4 meses

Rifampicin

Isoniazid

Niños misma duración y régimen que los adultos

Tratamiento de TB sensible en adultos

2 meses

Rifampicina
Isoniacida
Pirazinamida
Etambutol

4 meses

Rifampicina
Isoniacida

FDC = *Fixed Dose Combination*

Tratamiento de TB sensible en niños

Body weight of TB patient	**Anti TB therapy tablets:** Fixed dose combination (Rifampicin 60 mg, Isoniazid 30 mg, Pyrazinamide 150 mg)
< 5 kg	1 tablet
6 - 9 Kg	2 tablets
10 – 14 Kg	3 tablets
15 – 18 Kg	4 tablets
19 - 20 Kg	5 tablets

& Ethambutol
100 mg tablets
(20 mg/kg/day)

Mejoras en presentaciones pediátricas para tratamiento de TB sensible

Soporte nutricional & vitamina B6

Monitorización de tratamiento TB en niños

1.- **Clínica:** Fundamental

Resolución de síntomas, mejoría general & ganancia ponderal

2.- **Radiológica**: Lenta, poco fiable

Algunos cambios pueden tomar tiempo (cicatrices Rx)

Rx de control cada 2-6 meses. Si buena evolución, demorar.

3.- **Microbiológica**: Difícil ; muchas veces no tenemos ni siquiera confirmación inicial !!!

- Seguir recomendaciones locales, muestras mensuales
- Pragmatismo: mejor no molestar con lavados gástricos a un niño que va bien, que arriesgarnos a perder su seguimiento.

- Does Kevin have TB disease?
- Any other diagnostic tests you would do?
- Would you give treatment?

  If so, what?
- 3 gastric aspirates come negative. What do you do?

Tratamiento de **TB resistente** en niños

- Deciding on a regimen
- Dosing second-line TB drugs
- Treatment outcomes
- Novel TB drugs :

  Delamanid & Bedaquiline

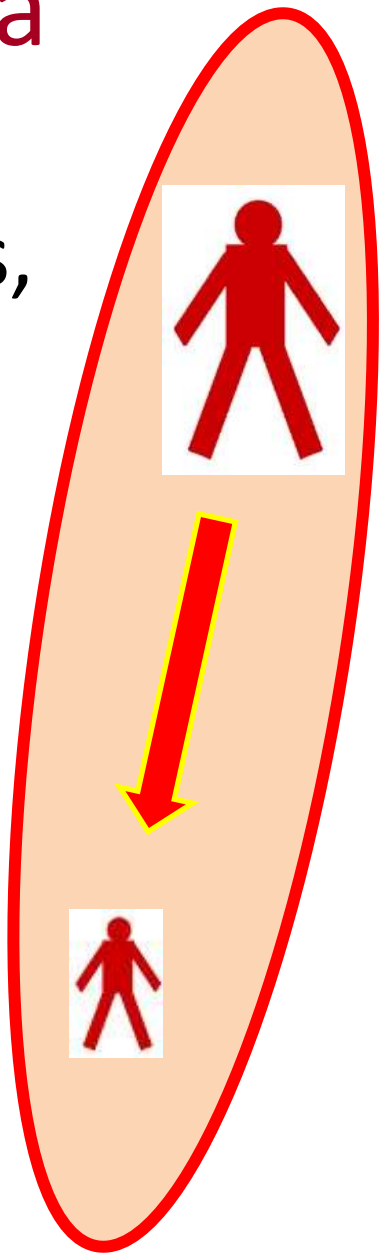
Patogénesis TB pediátrica

Ante un niño enfermo de tuberculosis, debemos buscar un **adulto tosedor**

(caso índice)

Generalmente familiar o conviviente

TB requiere exposición continuada en lugares con poca ventilación



Principles of MDR-TB treatment in children

Treat the child as you would the most likely **source case**, if no isolate for the child

- Standardised DR-TB treatment if empirical treatment for treatment failure
- Confirm the DR-TB in the child if at all possible

Principles of MDR-TB treatment in children

Generally, same regimens as in adults

- Shortened (9-12 month regimen), if eligible
- If not eligible, individualized regimen
  - Give 4 or more drugs to which the patient's isolate is susceptible and/or naïve
  - Never add one drug alone to a failing regimen
  - Be aware of the different drug groups and cross-resistance (and co-resistance) amongst these drugs

Tratamientos contra MDR TB

Tratamiento standar

20-24 meses

Short course regimen

Tratamiento corto

9-11 meses

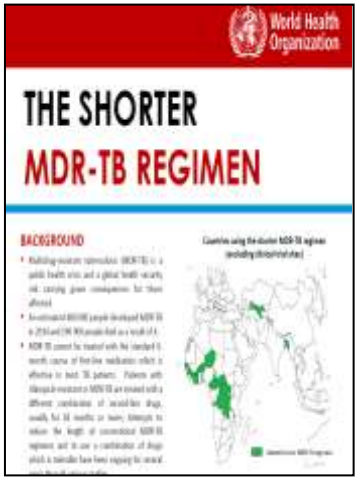
Z - E – Mfx - Pto - Cfz - H - Km

Z - E – Mfx - Pto – Cfz

Short Course Regimen MDR-TB

Intensive Phase	Continuation Phase
At least 4 mths and continue until sputum smears are negative.	For 5 months, starting after negative sputum smears
Seven drugs Monitoring for side effects Includes injectable, high dose Isoniazid	Fewer side effects Four drugs, Only oral drugs

Z–E–Mfx–Pto–Cfz–H–Km **Z–E–Mfx–Pto–Cfz**



Short course regimen. **Tratamiento corto (9-11 meses)**

MDRTB pediatric treatment regimens

SCR = Short course regimen (9 -12 months)

4-6 Km/Amk-Mfx-Cfz-Pto-HH-Pza-E

then 5 Mfx –Cfz – Pto – Pza - E

MDRTB long regimen (20-24 months)

8 Km/Amk - Lfx – Trd – Eth – Pza +/- PAS

then 12-16 Lfx –Trd –Eth –Pza +/-PAS

Challenges MDR-TB treatment in children

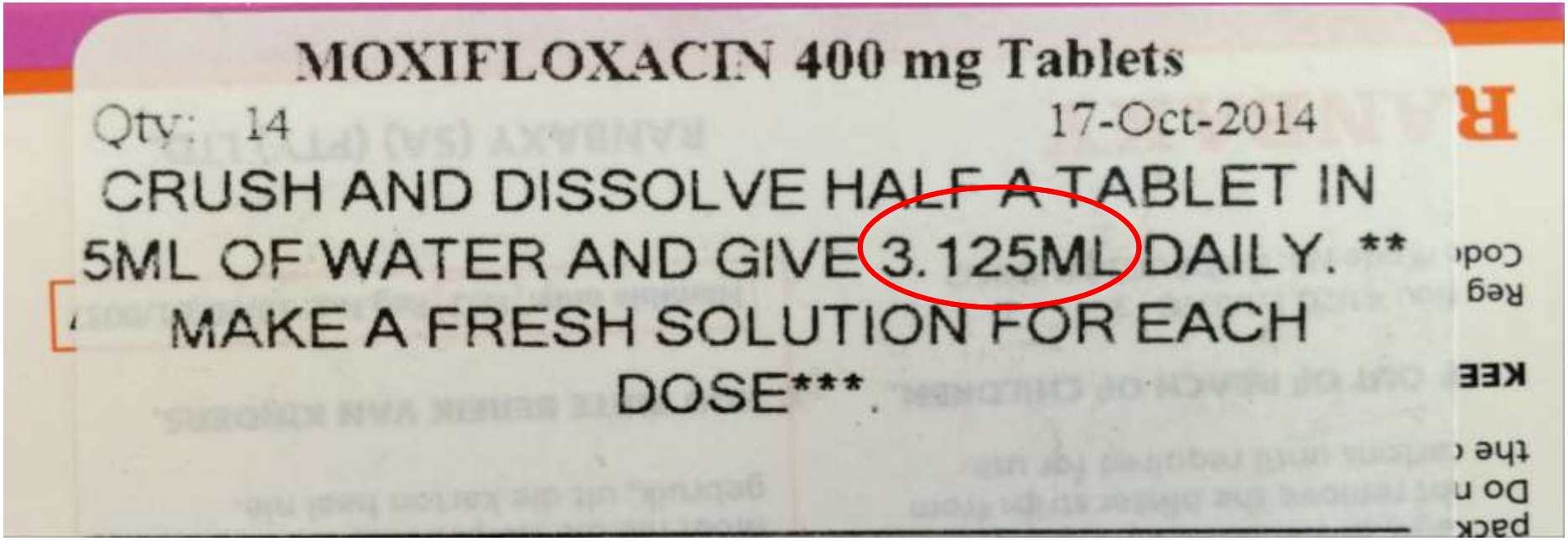
- Shortened regimen (9-12 months)
  - Fluoroquinolone – moxi vs levofloxacine ??
  - Clofazimine dosing
  - Issues, but likely to be effective regimen in children
- Individualized regimens: if non-severe
  - Can spare injectable agent
  - Often culture-negative (paucibacillary): 12-15 months treatment probably sufficient ??
  - Depends on lots of factors: 2^{nd} line DST, adherence, clinical and radiologic response, site of disease
- TB meningitis
  - Consider CSF penetration: FQNs, CS/TZD, Linezolid
  - Corticosteroids

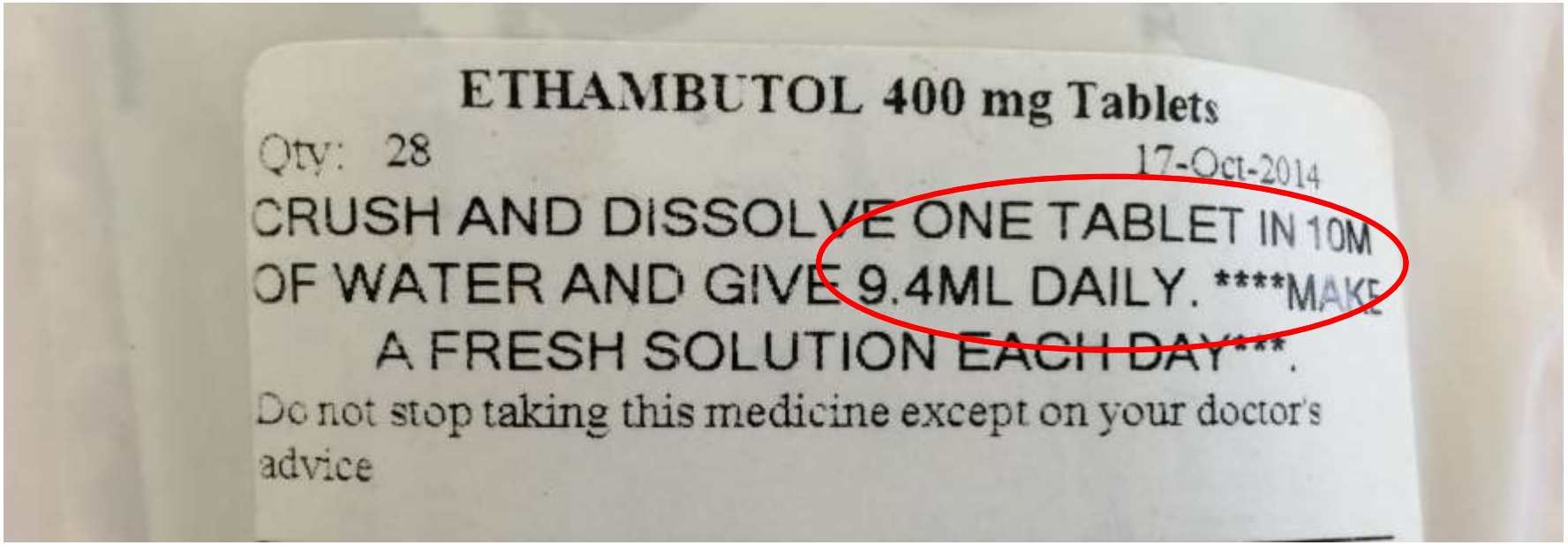
Dosing 2nd line TB drugs in children

Table 9.2. Paediatric dosing of second-line medications				
Drug	**Formulation**	**Daily dose mg/kg/day**	**Frequency**	**Maximum daily dose**
Streptomycin	Vials: 37.5, 250, 333, 500 mg/ml	20-40	QD	1g
Kanamycin	Vials: 37.5, 250, 333, 500 mg/ml	15 – 30	QD	1g
Amikacin	Vials: 50, 250 mg/ml	15 – 22.5	QD	1g
Capreomycin	Vials: 1g/ml	15 – 30	QD	1g
Ofloxacin	Tablets: 200, 300, 400 mg	15 – 20	BID	800mg
Levofloxacin	Tablets: 250, 500, 750 mg	7.5 – 10	QD	750mg
Moxifloxacin	Tablets: 400 mg	7.5 – 10	QD	400mg
Ethionamide	Tablets: 250 mg	15 – 20	BID	1g
Prothionamide	Tablets: 250 mg	15 – 20	BID	1g
Cycloserine Terizidone	Capsules: 250 mg	10 – 20	QD or BID	1g
PAS	PASER® 4 g packets	150	BID or TID	12 g

(Source: World Health Organization. Guidelines for the programmatic management of drug-resistant tuberculosis: Emergency update 2008 (WHO/HTM/TB/2008.402). Geneva, Switzerland: World Health Organization; 2008).

Challenges dosing 2nd line TB drugs in children


MOXIFLOXACIN 400 mg Tablets
Qty: 14
17-Oct-2014
CRUSH AND DISSOLVE HALF A TABLET IN 5ML OF WATER AND GIVE 3.125ML DAILY. **
MAKE A FRESH SOLUTION FOR EACH DOSE***.


ETHAMBUTOL 400 mg Tablets
Qty: 28
17-Oct-2014
CRUSH AND DISSOLVE ONE TABLET IN 10M OF WATER AND GIVE 9.4ML DAILY. ****MAKE A FRESH SOLUTION EACH DAY***.
Do not stop taking this medicine except on your doctor's advice

Dosing 2nd line TB drugs in children

Lack of child friendly formulations:

challenging to accurately dose,

and decreases palatability

- Provide anticipatory guidance to parents
- Follow-up dosing method, accuracy each visit
- Ultimately, child friendly formulations

Offer empathic support to child and caregiver

MDR-TB Weight-Based Dosing Chart for Children

	Group 1: Oral first-line anti-TB drugs				Group 2:	Group 3: Fluoroquinolones					Group 4: Oral bacteriostatis agents					Group 5:		
	Ethambutol		Pyrazinamide		Injectable anti-TB drugs (injectable agents or parental agents)	Levofloxacin		Moxifloxacin		Ofloxacin	Cycloserine/Terizidone		PAS		Protionamide/ Ethionamide	Anti-TB drugs with unclear efficacy or unclear role in MDR-TB treatment	Isoniazid High Dose	
Target Dose	(15-25 mg/kg)		(30-40 mg/kg)			(15-20 mg/kg)		(7.5-10 mg/kg)		(15-20 mg/kg)	(15-20 mg/kg)		(150-200 mg/kg)		(15-20 mg/kg)		(15-20 mg/kg)	Target Dose
Available Formulations	100 mg tablet	Suspend 400mg tab in 8 mL of water for a 50 mg/mL suspension	400 mg tablet	500 mg tablet		250 mg tablet	25 mg/mL suspension	400 mg tablet	20 mg/mL suspension	200 mg tablet	250 mg capsule	1 capsule in 10 mL water	Daily	Twice Daily	250 mg tablet		100 mg tablet	Available Formulations
Wt (kg)	Consult with a clinician experienced in pediatric MDR-TB prescribing for neonates (<28 days of age) and infants weighing <3 kg																	Wt (kg)
<3																		<3
3-3.9	1 tab	2 mL	.25 tab	.25 tab	To illustrate dose calculation, take the example of a child that weighs 6.9 kg. Both the low and high doses for the child's weight are calculated. For kanamycin: Low dose: 15 mg/kg x 6.9 kg = 103 mg High dose: 30 mg/kg x 6.9 kg = 207 mg A convenient dosing is then chosen between the two numbers. Select a dose between the two numbers and towards the higher number. In this case, choose: 200 mg per day, single dose. Calculate the number of mL to draw up in the syringe based on the mg/mL concentration of the preparation.	.25 tab	2.5 mL	not recommended	1.5 mL	.5 tab	.25 cap	2.5 mL	500 mg	250 mg	.25 tab	Group 5 drugs are not recommended by the WHO for routine use in MDR-TB treatment because their contribution to the efficacy of MDR regimens is unclear. Their role in pediatric MDR-TB treatment is even less clear. Most of these drugs are expensive, and some require intravenous administration, and/or have severe side effects. However, they can be used in cases where adequate regimens are impossible to design with the medications from Groups 1-4. They should be used in consultation with an expert in the treatment of DR-TB.	.5 tab	3-3.9
4-4.9									2 mL				1000 mg	500 mg				4-4.9
5-5.9			.5 tab	.5 tab		.5 tab	5.0 mL		2.5 mL		.5 cap	5 mL	1500 mg	750 mg	.5 tab		1 tab	5-5.9
6-6.9																		6-6.9
7-7.9																		7-7.9
8-8.9	2 tabs	4 mL	1 tab	1 tab		.75 tab	7.5 mL		5 mL	1 tab	.75 cap	7.5 mL	2000 mg	1000 mg	.75 tab		2 tabs	8-8.9
9-9.9																		9-9.9
10-10.9																		10-10.9
11-11.9																		11-11.9
12-12.9						1 tab	10 mL				1 cap	1 cap	2500 mg	1250 mg	1 tab			12-12.9
13-13.9	3 tabs	6 mL															3 tabs	13-13.9
14-14.9																		14-14.9
15-15.9			1.5 tabs	1 tab					7.5 mL	1.5 tabs								15-15.9
16-16.9	4 tabs	8 mL				1.5 tabs	15 mL	.5 tab			1.5 caps	15 caps	3000 mg	1500 mg	1.5 tabs			16-16.9
17-17.9																		17-17.9
18-18.9																		18-18.9
19-19.9																		19-19.9
20-20.9									10 mL	2 tabs			4000 mg	2000 mg			4 tabs	20-20.9
21-21.9			2 tabs	1.5 tabs														21-21.9
22-22.9																		22-22.9
23-23.9																		23-23.9
24-24.9																		24-24.9
25-25.9																		25-25.9
26-26.9						2 tabs	20 mL				2 caps	20 mL	5000 mg	5000 mg	2 tabs		5 tabs	26-26.9
27-27.9	5 tabs	10 mL	2.5 tabs	2 tabs					12.5 mL	2.5 tabs								27-27.9
28-28.9													6000 mg	6000 mg				28-28.9
29-29.9																		29-29.9

For preventive regimens, consult with experts regarding optimal regimen construction.
The doses of isoniazid, ethambutol, and fluoroquinolones for preventive regimens are the same as in this dosing chart.

Group 2	Streptomycin	Amikacin	Kanamycin	Capreomycin
Daily Dose	20-40 mg/kg once daily	15-20 mg/kg once daily	15-20 mg/kg once daily	15-20 mg/kg once daily
Maximum Daily Dose	1000 mg	1000 mg	1000 mg	1000 mg

Group 5	Cycloserine (CS)	Amoxicillin-clavulanate (AMX-CLV)	Meropenem (MPN)	Linezolid (LZD)	Clarithromycin (CLR)
Daily Dose	3-5 mg/kg once daily; if the child is >20kg, give 500mg every second day	80 mg/kg/d in two divided doses based on the amoxicillin component	20-40 mg/kg/d IV every 8 hours	10 mg/kg dose twice daily for children <10 years of age 300 mg daily for children >10 years of age (also give vitamin B6)	7.5 mg/kg twice daily
Maximum Daily Dose	250 mg	4000 mg amoxicillin and 500 mg clavulanate	6000 mg	600 mg	1000 mg

Sentinel Project on pediatric drug-resistant tuberculosis

http://sentinel-project.org

Chart developed by
Chelsie GawneMark

Clofazimine dosing in children

- Formulation: 50 mg and 100 mg gel capsules
- Unknown pharmacokinetics in children
- Recommended dosing: 2-4 mg/kg/day
- Pragmatic dosing

	5-10 kg	10-20 kg	>20 kg
50 mg caps	1 cap alt days	1 cap OD	2 caps OD
100 mg caps	1 cap every 3 days	1 cap alt days	1 cap OD

Novel TB drugs in children

Bedaquiline

- Children >12y :

  same indications as in adults

- Children < 12y : case-by-case basis

Delamanid

- Children 6-17 years old:

  same indications as in adults

- Children <6 y: case-by-case basis

Pediatric TB: www.sentinel-project.org

Sentinel Project
on pediatric drug-resistant tuberculosis

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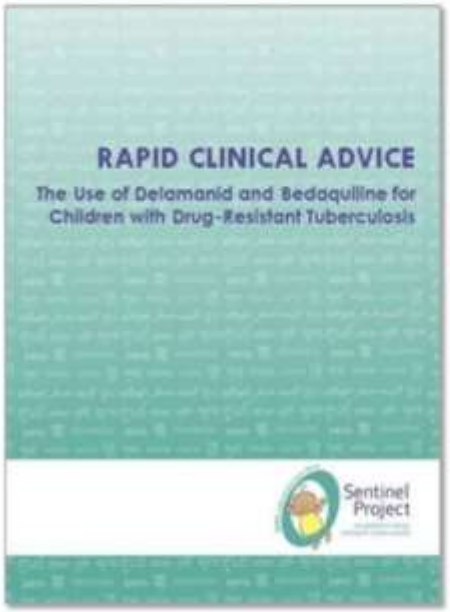


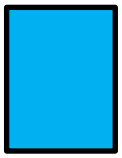
Advancing Access for New TB Drugs for Children

Read More...

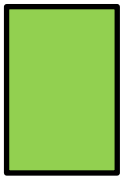
Medidas de control

Prevención de transmisión de TB

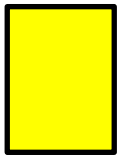
Prevención de transmisión de TB



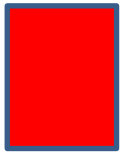
Vacuna BCG



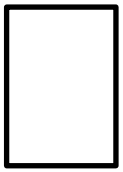
Buena ventilación de viviendas, edificios, transportes



Aislamiento de enfermos



Detección precoz y tratamiento oportuno de casos



(= palma abierta) Medidas de barrera, máscara

(= puño cerrado) Todas son falsas

Prevención de transmisión de TB

- Vacuna BCG
- Buena ventilación de viviendas, transportes, centros sanitarios, escuelas, …
- **Detección precoz** de casos
- **Tratamiento** dirigido, supervisado y mantenido
- Aislamiento de enfermos (adultos > niños)
- Medidas de barrera, máscaras y respiradores

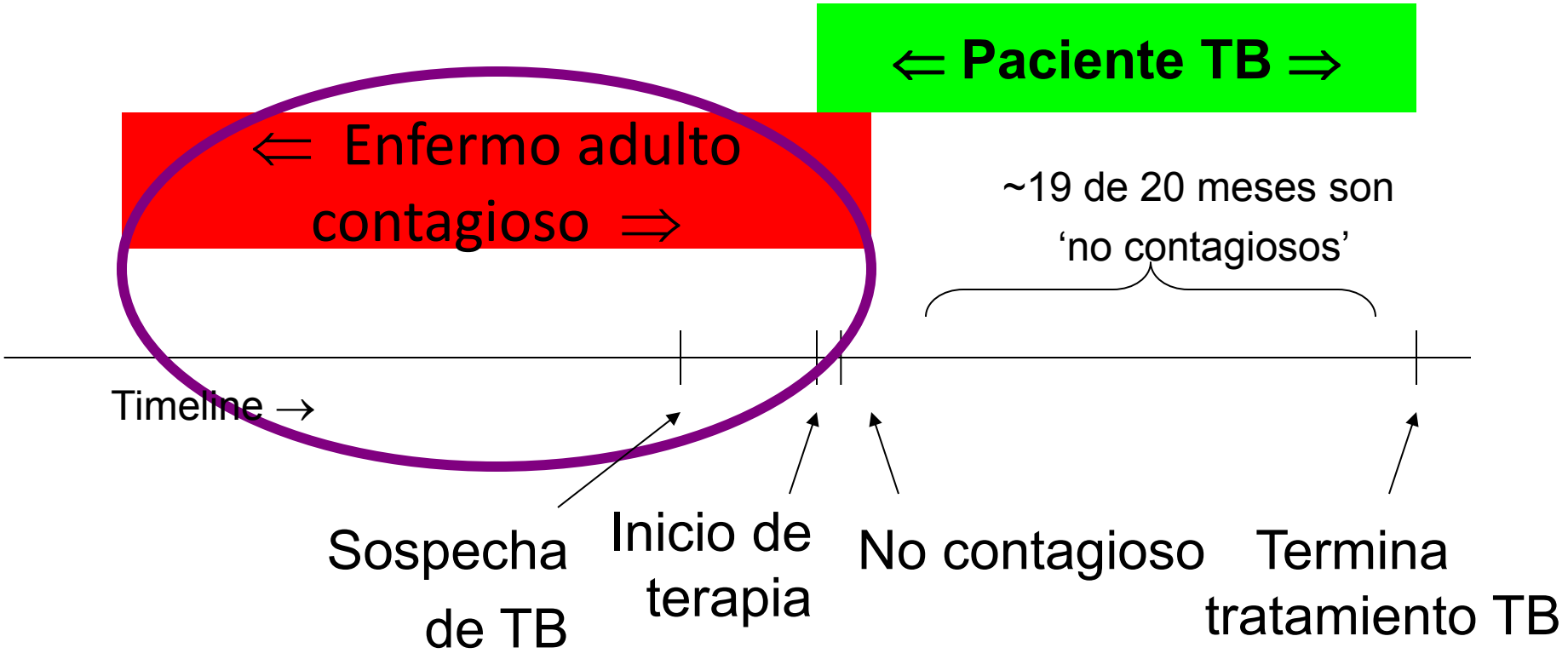
Tuberculosis pediátrica es *paucibacilar*

= poca cantidad de bacilos

➔ niños **no son contagiosos** ☺

➔ no precisan aislamiento ☺

Quiénes son los casos contagiosos ???



Adultos no diagnosticados o mal tratados son fuente de transmisión & contagio

Barreras físicas contra **exhalación & inhalación** de microgotas infecciosas

Enfermos usan **Máscaras**

Trabajadores de salud & familiares usan **Respiradores**

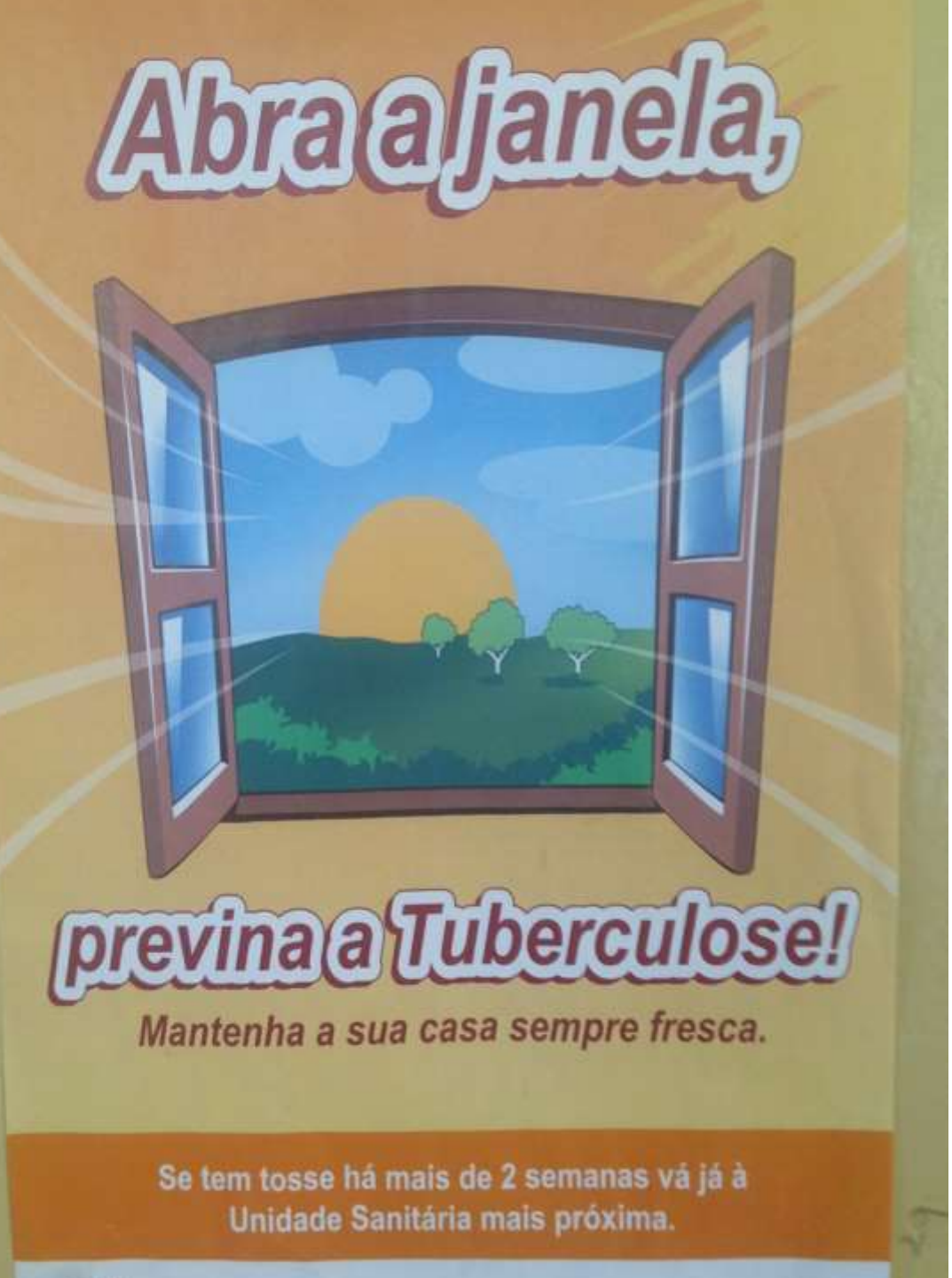
Respirador

Trabajadores de salud

Familiares sanos

Máscara

Pacientes



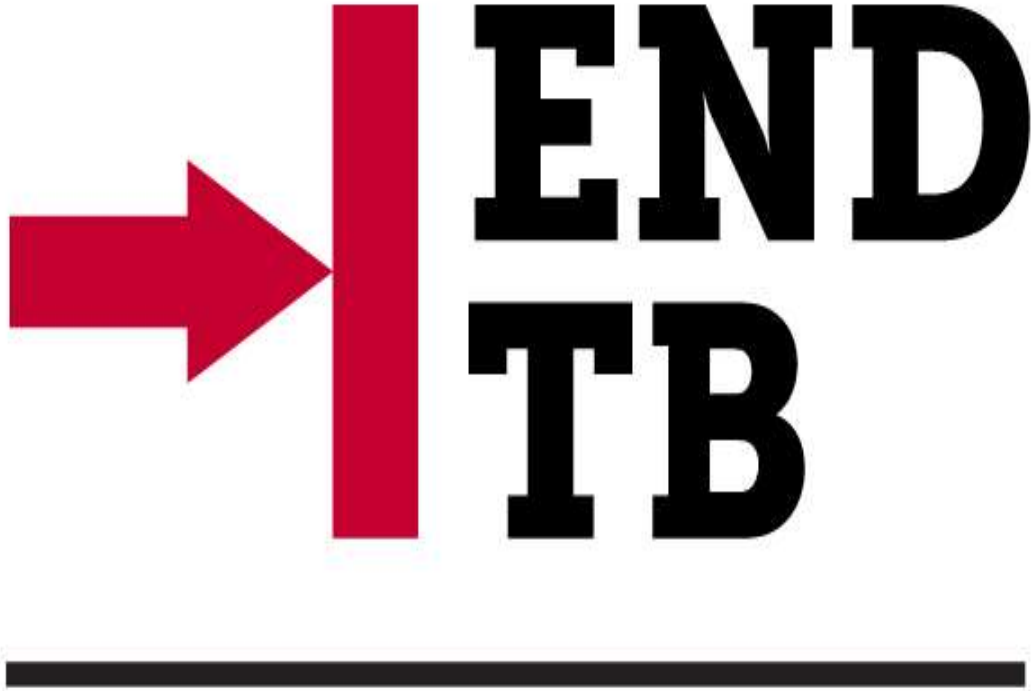
Buena ventilación remueve microgotas

General public: health education

Community sensitization:

IPC trainings

& awareness campaigns (IEC)



THE
END TB
STRATEGY

GLOBAL TB
PROGRAMME

World Health
Organization

Estrategia para terminar TB: Pilar 1

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

Estrategia para terminar TB: Pilar 2

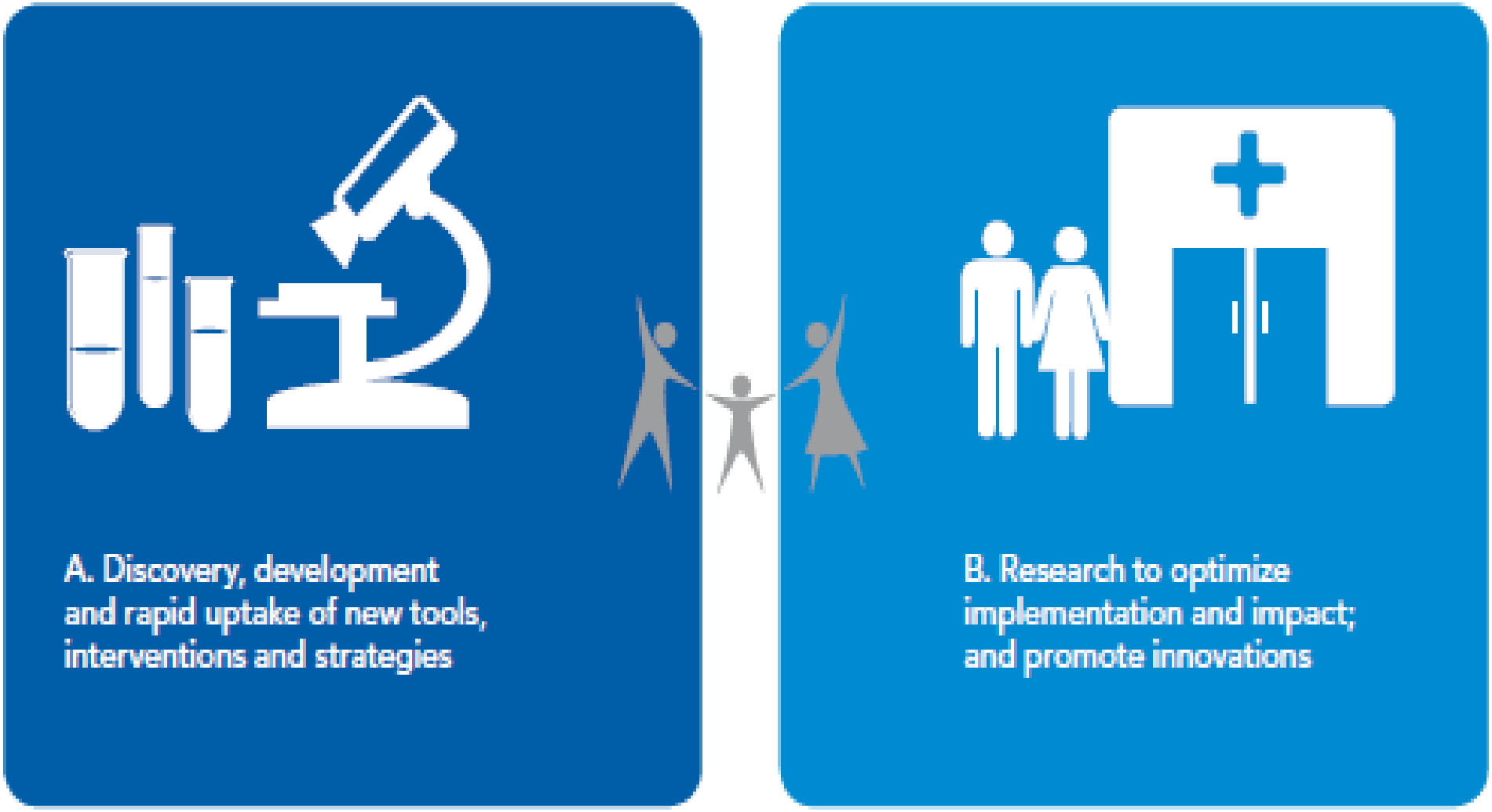
A. Political commitment with adequate resources for TB care and prevention

B. Engagement of communities, civil society organizations, and all public and private care providers

D. Social protection, poverty alleviation and actions on other determinants of TB

C. Universal health coverage policy, and regulatory frameworks for case notification, vital registration, quality and rational use of medicines, and infection control

Estrategia para terminar TB: Pilar 3



Tuberculosis pediátrica

1. Características y peculiaridades de la enfermedad en niños
2. Epidemiología: TB es un problema mundial
3. Retos diagnósticos
4. Avances en el tratamiento
5. Efectos adversos, monitorización
6. Búsqueda activa de contactos & terapias preventivas

- Agradecimientos
  - Dr Tony Garcia-Prats
  - Dra Elisa López Varela
  - Dr Alberto García –Basteiro
  - Dra Veronika Polcova

- Comentarios y preguntas a Pascual Caballero

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Médecins Sans Frontières (MSF) / Doctors Without Borders

Gracias !!

www.msf.org

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