excellent
kind
responsible
respectful

St George's University Hospitals NHS
NHS Foundation Trust

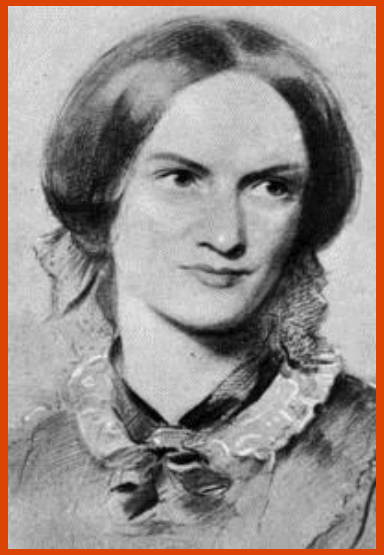
# Tuberculosis

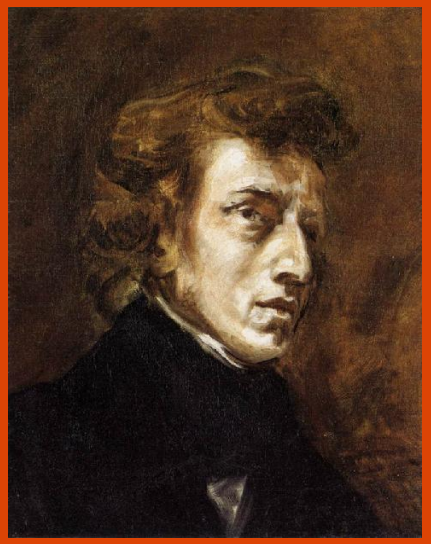
Anne Dunleavy

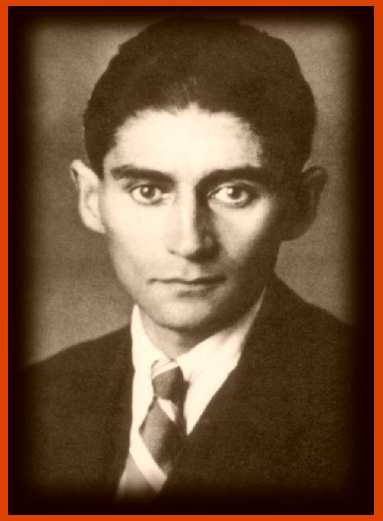
# Overview

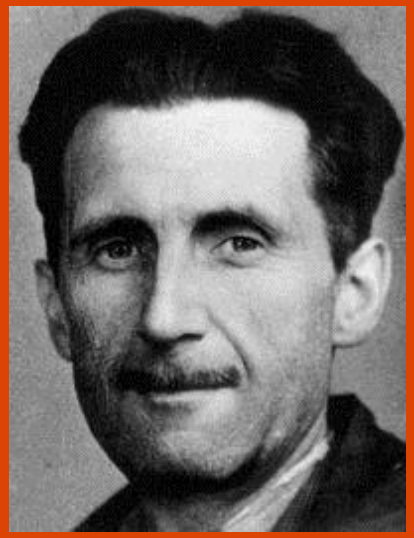
- Epidemiology
- Illustrative cases
- Treatment
- Priorities
- Conclusion

# The White Plague









# WHO 2016

- 1/3 infected (2 billion)
- 10.4 million new cases
- 1.8 million deaths

theguardian
website of the year

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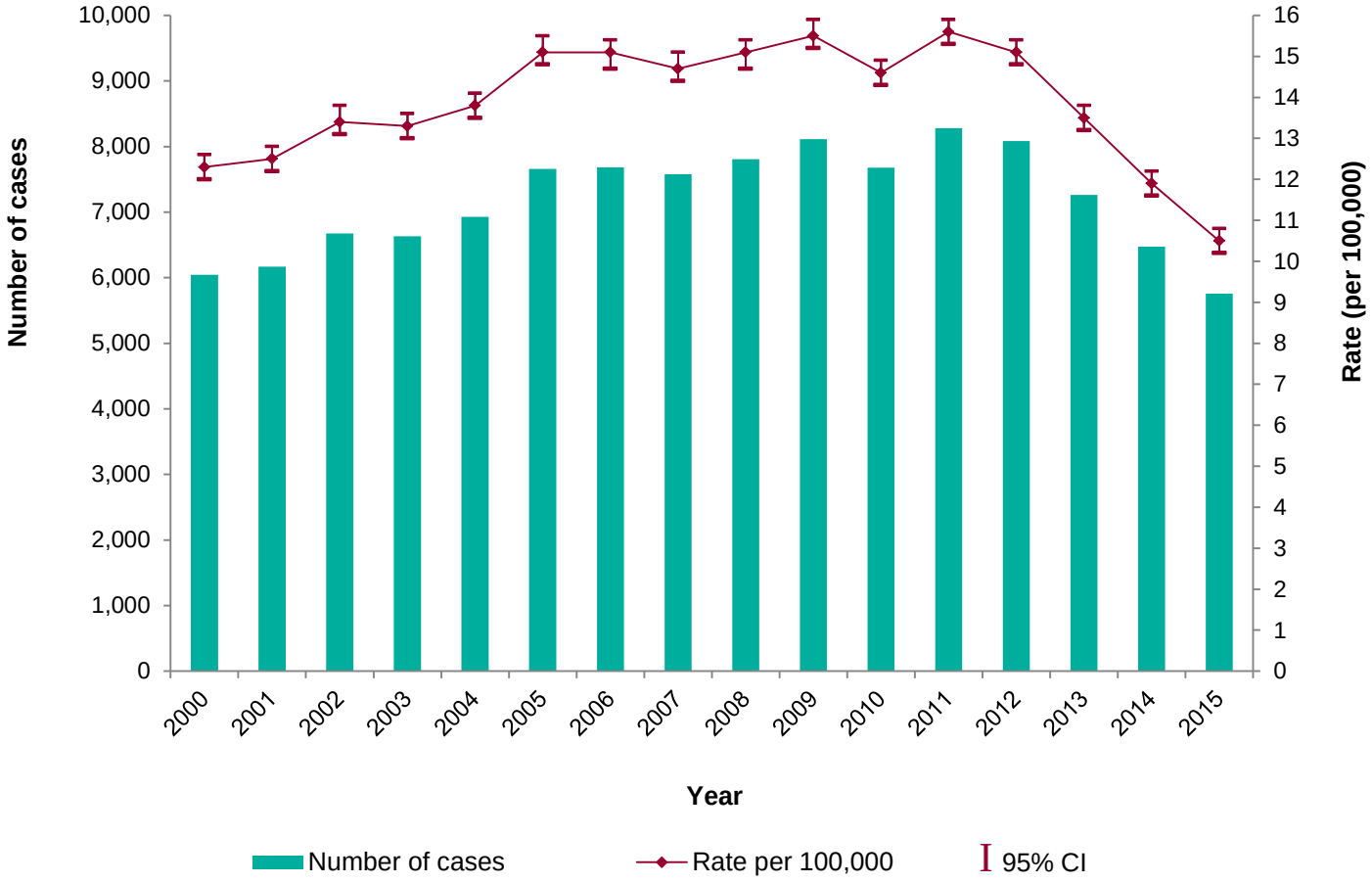
Tuberculosis

## Tuberculosis kills three people a minute as case numbers rise

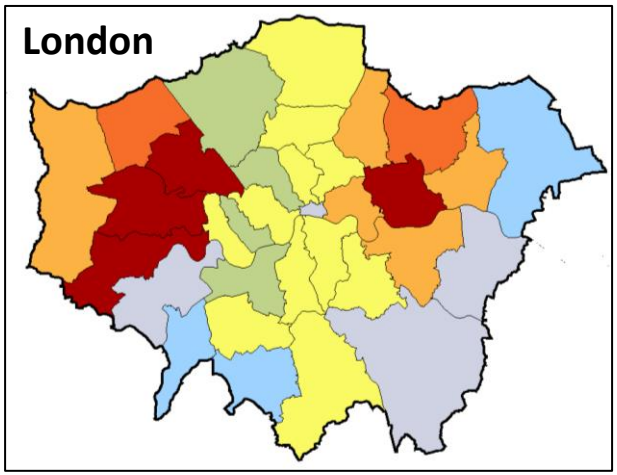
Governments accused of not doing enough after World Health Organisation figures show more TB cases than previously thought

An Indian doctor examines a tuberculosis patient. Cases of multidrug-resistant TB have also risen to 580,000

# TB case notifications and rates, England, 2000-2015



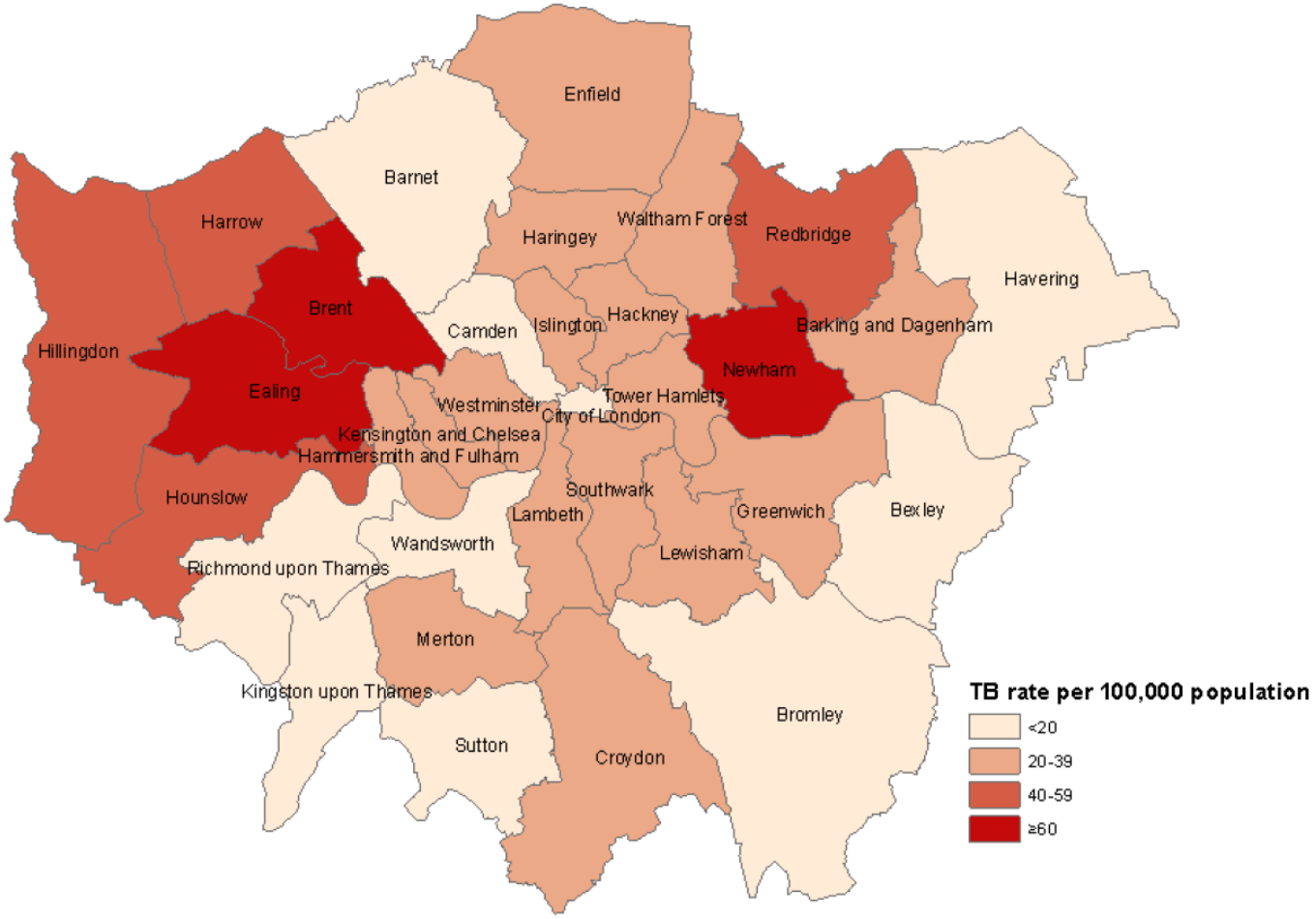
# Three-year average TB rates by local authority district, England, 2013-2015

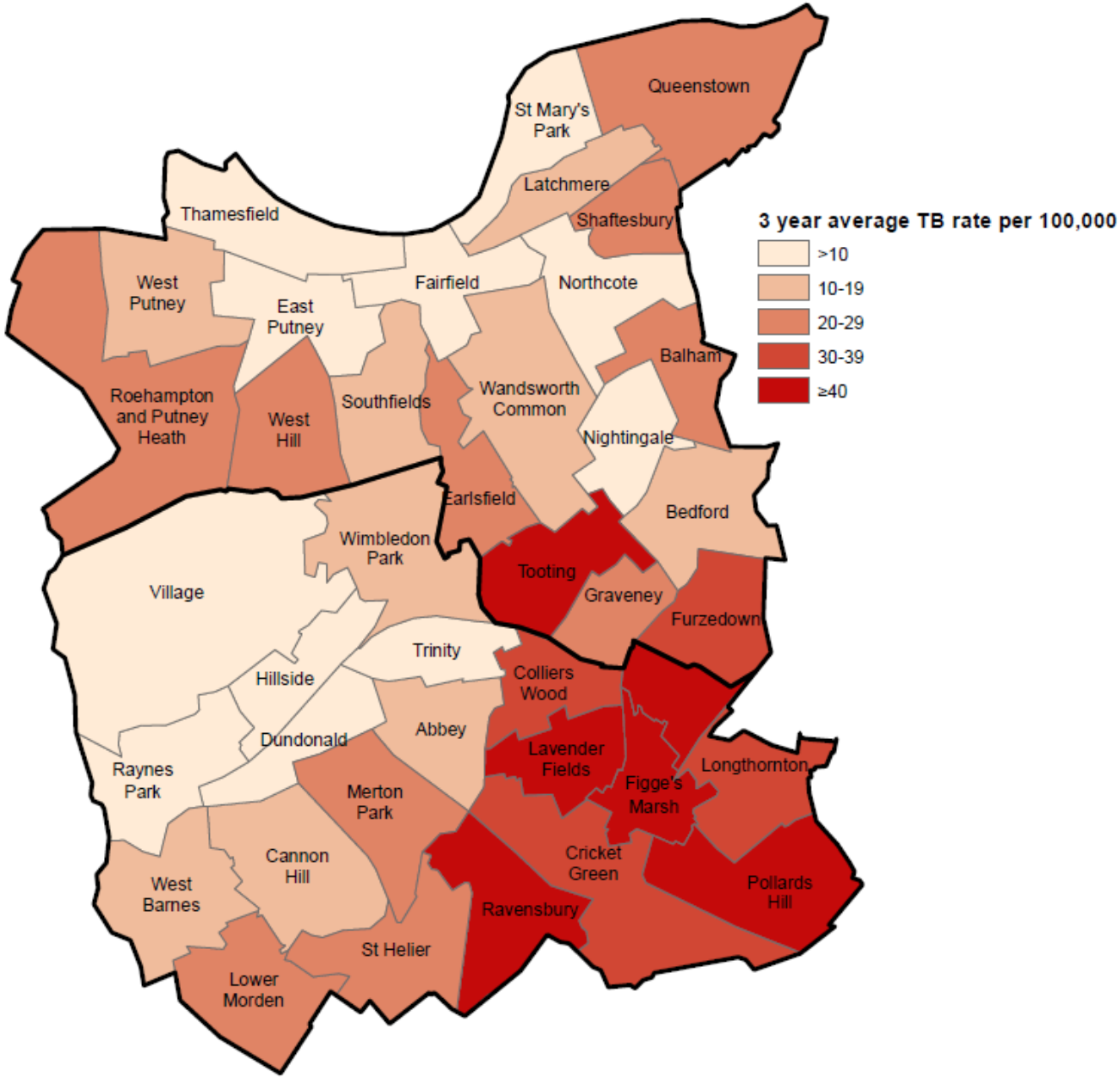



Tuberculosis rate (per 100,000)

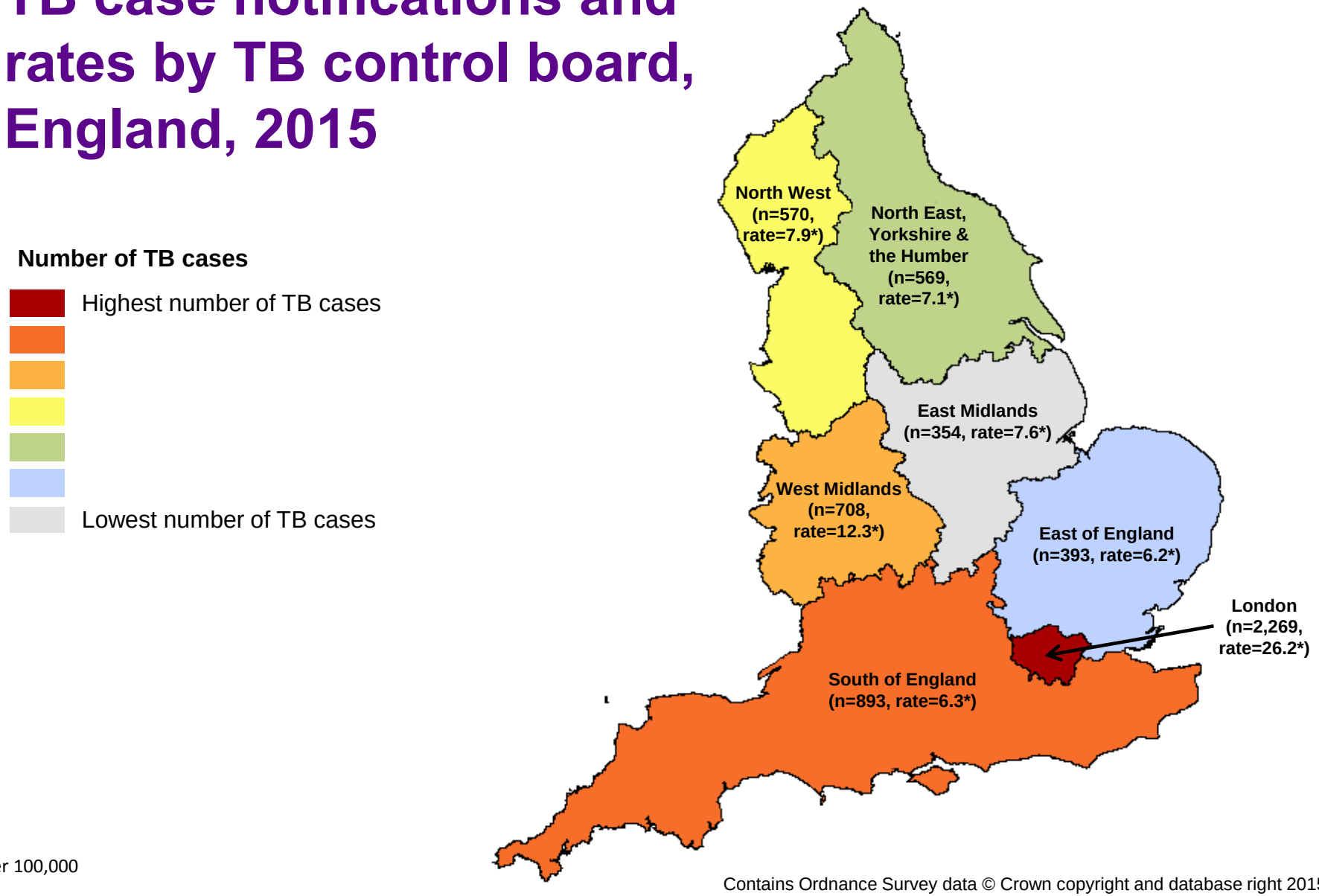
- 0.0-4.9
- 5.0-9.9
- 10.0-14.9
- 15.0-19.9
- 20.0-29.9
- 30.0-39.9
- 40.0-49.9
- >50.0

**Figure 3: TB notification rate by local authority of residence, London, 2014**




3 year average TB rate per 100,000
>10
10-19
20-29
30-39
≥40
Queenstown
St Mary's Park
Latchmere
Shaftesbury
Thamesfield
West Putney
East Putney
Fairfield
Northcote
Balham
Roehampton and Putney Heath
West Hill
Southfields
Wandsworth Common
Nightingale
Earlsfield
Bedford
Wimbledon Park
Tooting
Graveney
Furzedown
Village
Trinity
Hillside
Colliers Wood
Abbey
Dundonald
Lavender Fields
Longthornton
Figge's Marsh
Raynes Park
Merton Park
Cricket Green
Cannon Hill
Pollards Hill
West Barnes
Ravensbury
St Helier
Lower Morden

# TB case notifications and rates by TB control board, England, 2015




* per 100,000

# TB London

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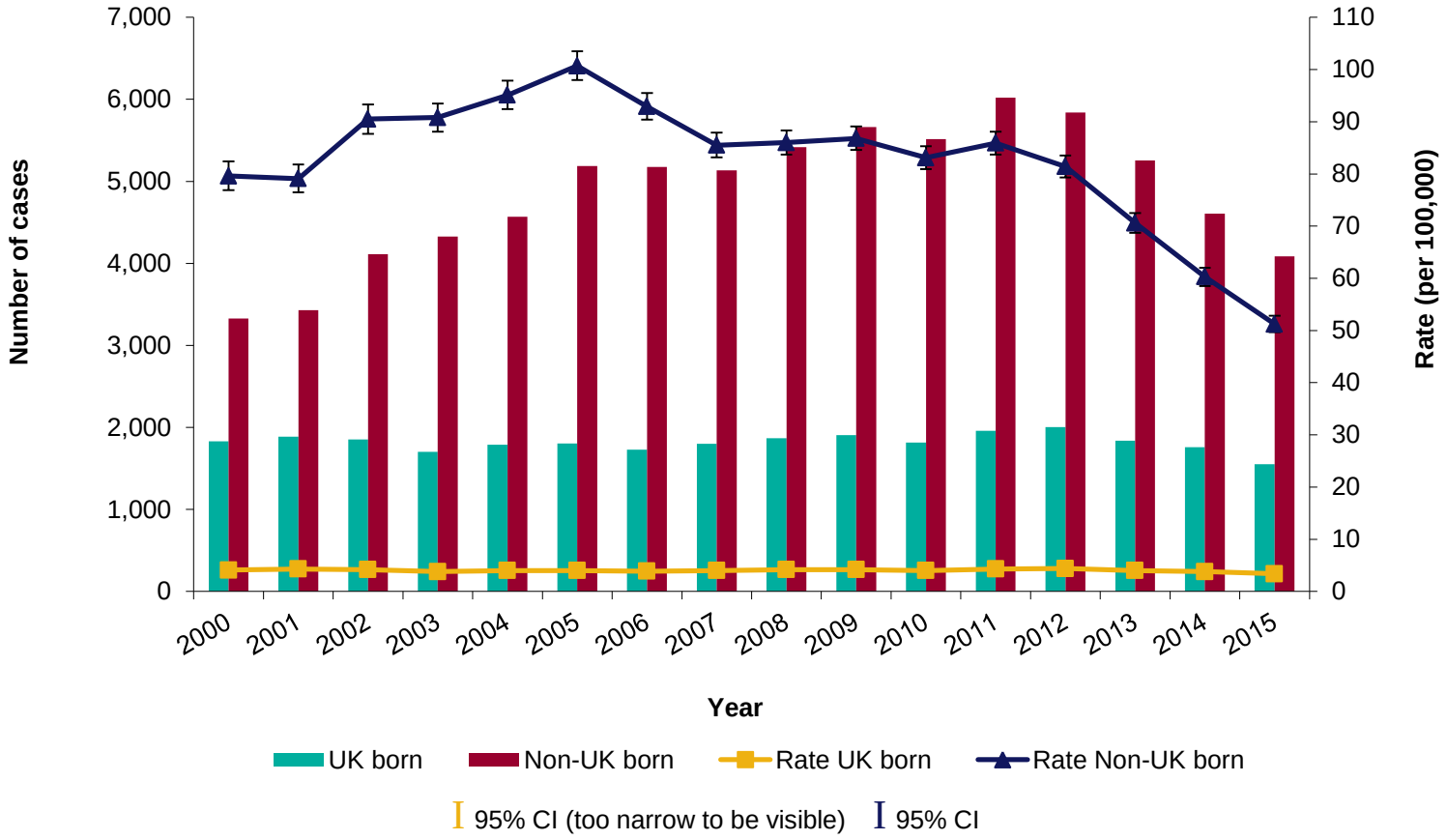
England Regions London

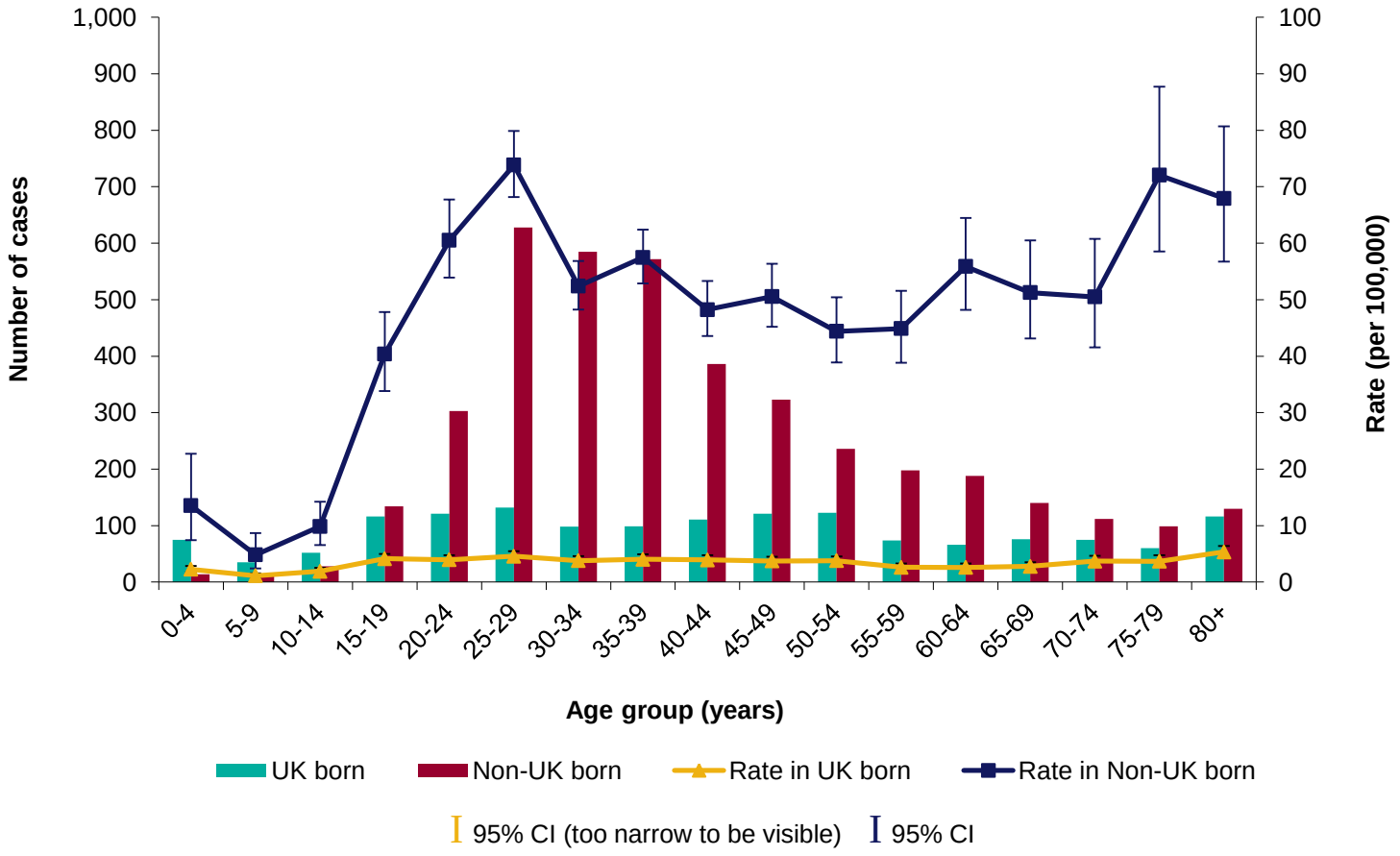
## Parts of London have higher TB rates than Iraq or Rwanda

27 October 2015 London Share

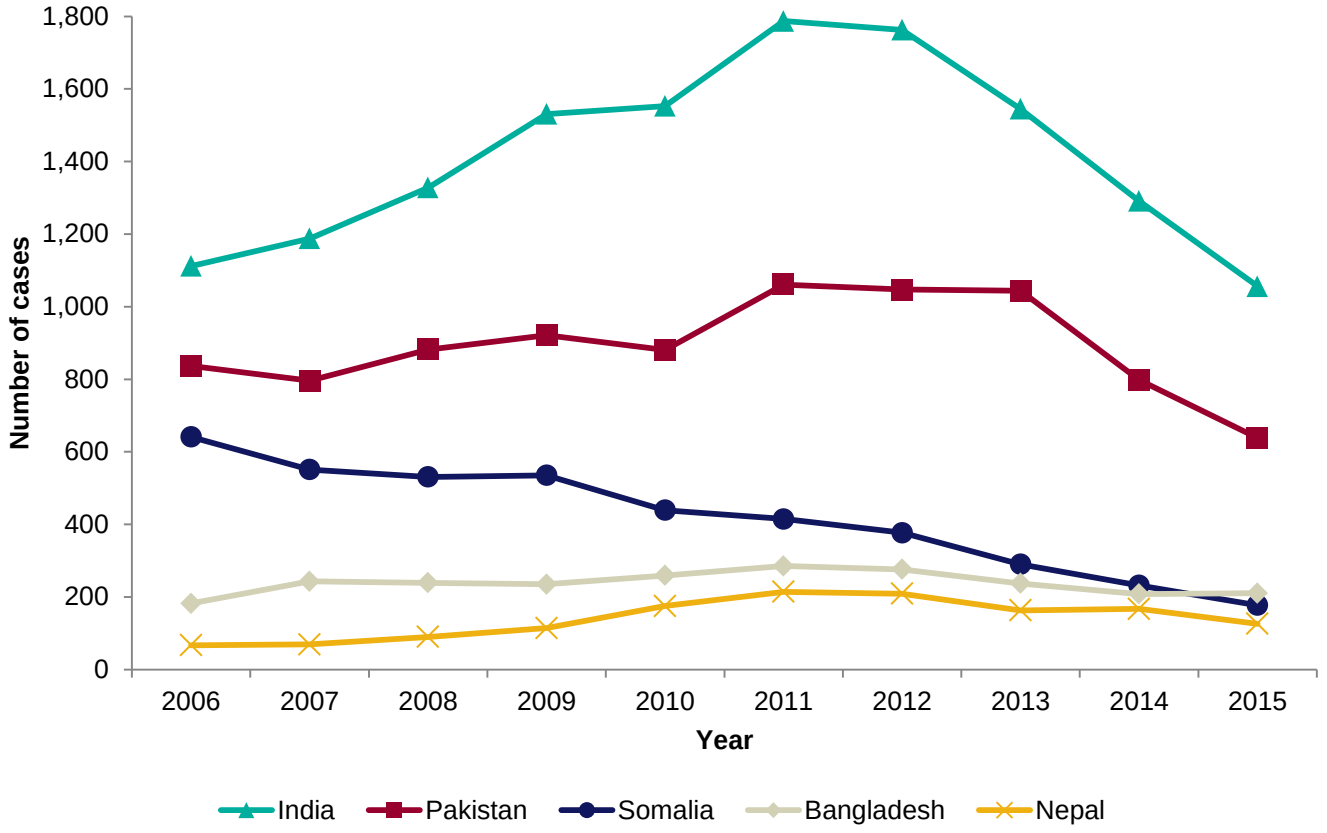
# TB case notifications and rates by place of birth, England, 2000-2015



# TB case notifications and rates by age group and place of birth, England, 2015



# Trend in TB case notifications for the top five countries of birth* of non-UK born cases, England, 2006-2015



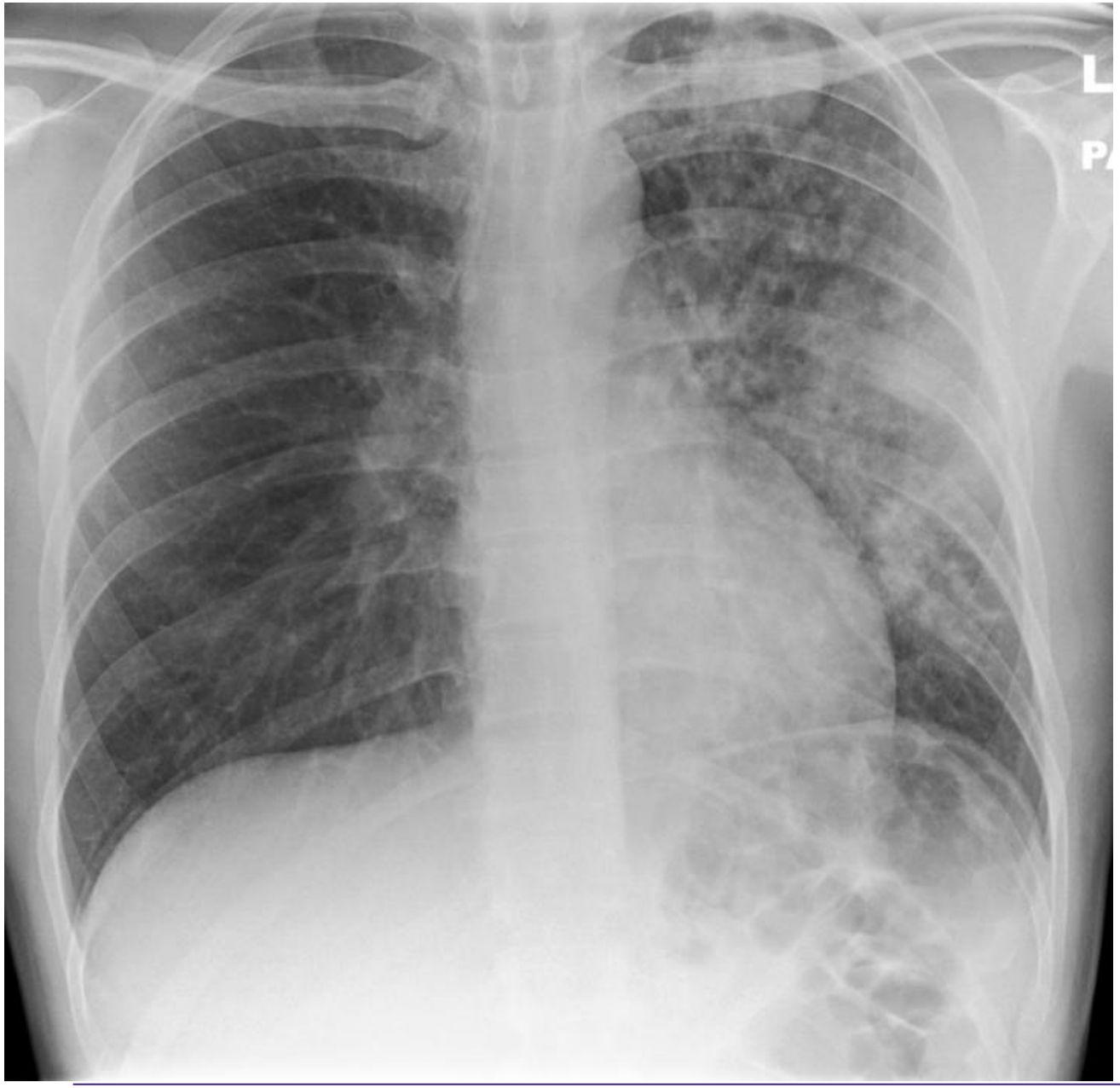

* Five most frequent countries of birth in 2015

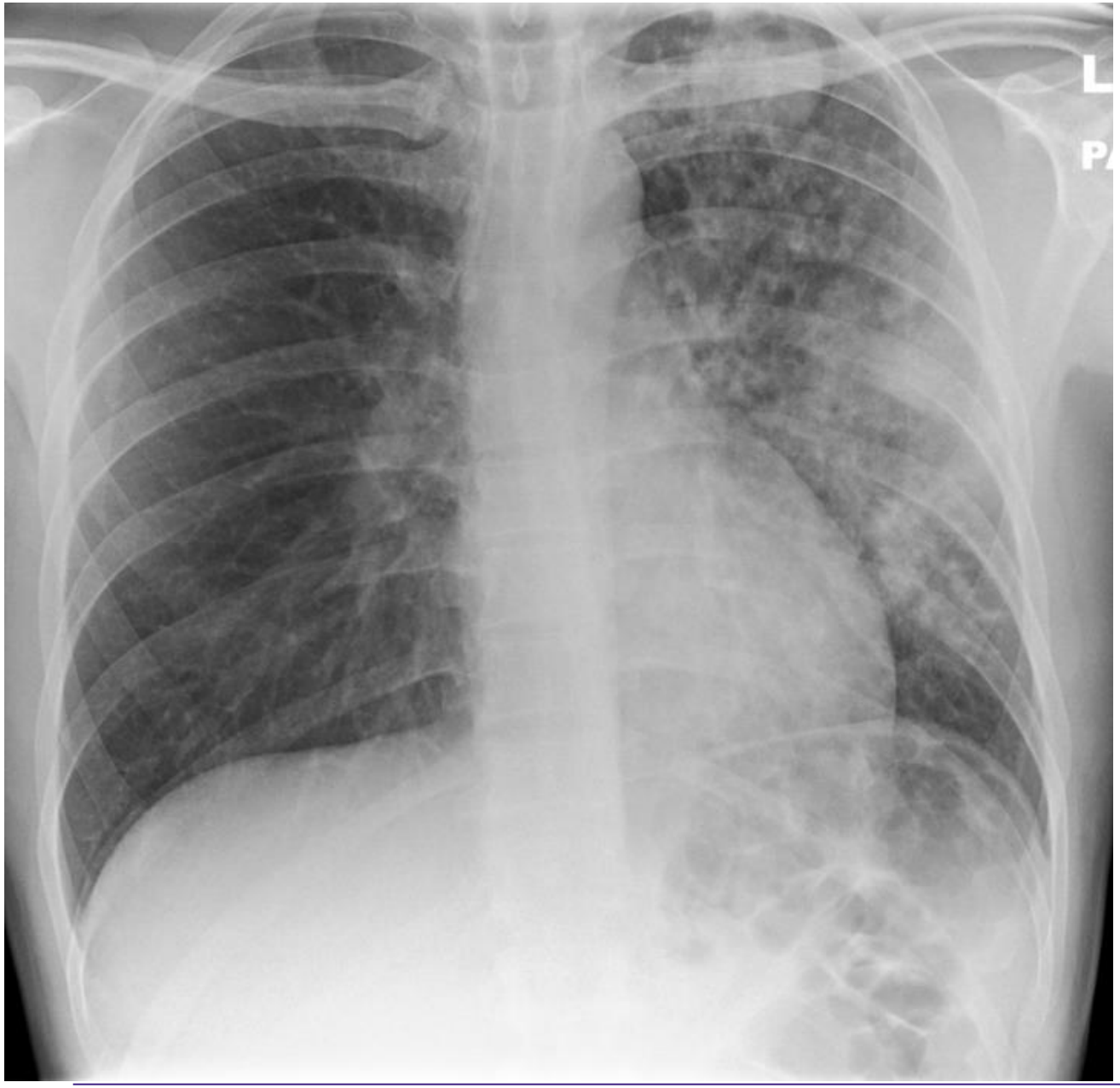
# Case 1

- SM 29 yo Black African male
- From South Africa and in UK for 4 years
- April 2016 presented to GP with a 3 week history of cough
- No response to antibiotics
- 2 weeks later – no response, new haemoptysis
- Further course of antibiotics

# Case 1

- 3rd trip to the GP
- Further course of antibiotics
- 4th trip
- CXR – not reported
- June 2016 presented to A&E – large haemoptysis





Cavitation LUL

Consolidation throughout left lung

# What do you do next?

# What do you do next?

- Isolate in a cubicle
- FFP3 masks
- Countries at risk of MDRTB

# What tests?

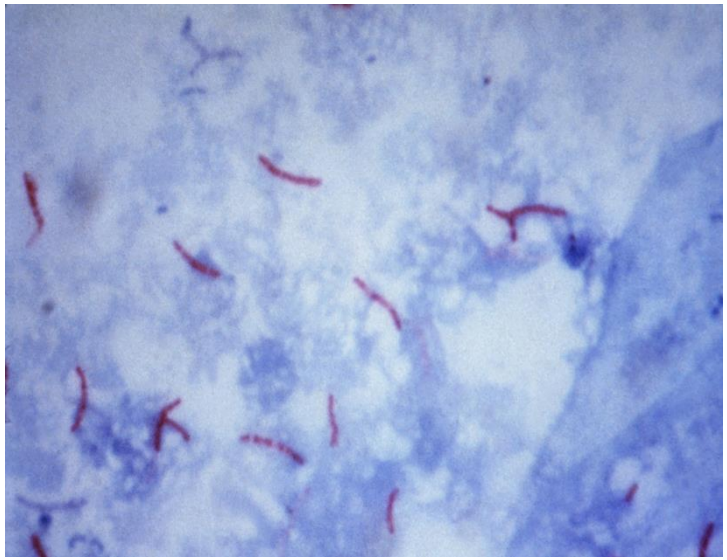
- Interferon Gamma Release Assay (IGRA) eg QUANTIferon GOLD
- Mantoux
- Sputum MC&S
- Sputum AFBs
- TB PCR

# What tests?

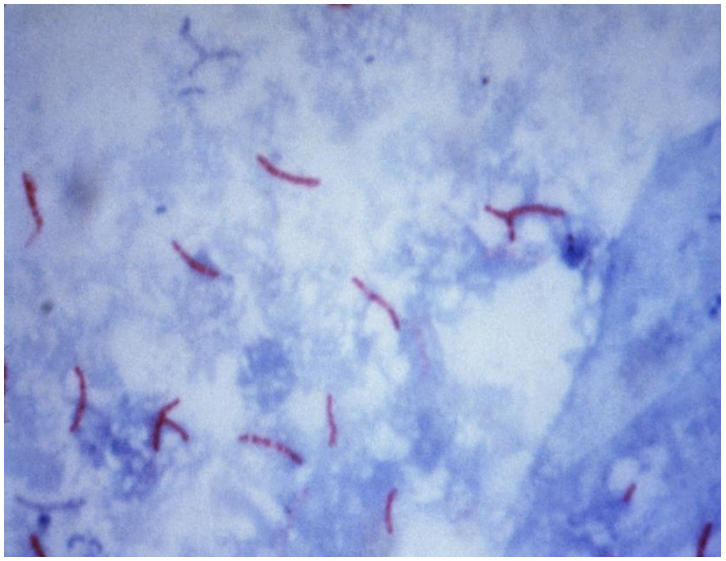
- Interferon Gamma Release Assay (IGRA) eg QUANTIferon GOLD
- Mantoux
- **Sputum MC&S**
- **Sputum AFBs**
- **TB PCR**

## Case 1

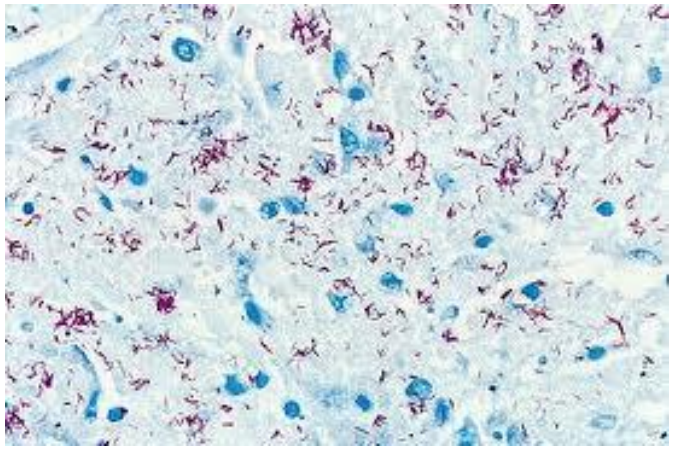
- Sputum AFB smear positive



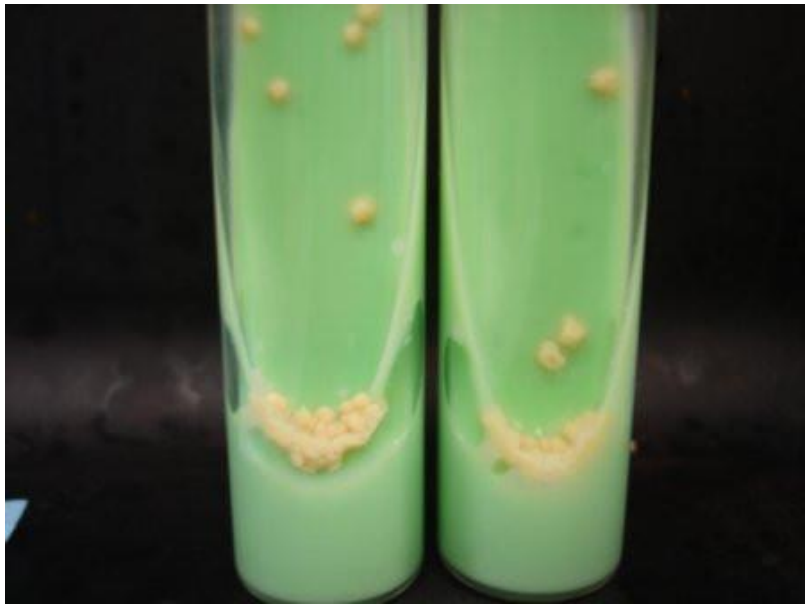
## Case 1



- Sputum AFB smear positive
- Rifampicin resistance PCR negative
- Mycobacterium tuberculosis on PCR



- Acid fast bacilli



- Lowenstein-Jensen culture medium

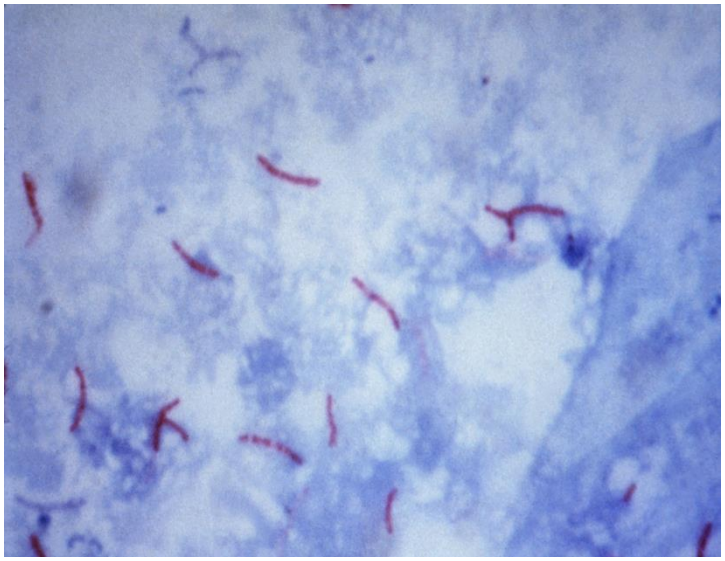
# Rapid diagnostic tests (PCR)

- For MTB complex (M tuberculosis, M bovis, M africanum)
- If:
  - Rapid confirmation would alter care
  - Before large contact-tracing initiative
- Consider TB even if rapid diagnostic tests negative in pleural fluid, CSF, urine
  - Especially in TB meningitis (risk of not treating severe)

# Other tests

- FBC
- LFTs
- U&Es
- Vitamin D
- Hep B/C
- HIV

## Case 1



- Sputum AFB smear positive
- Rifampicin resistance PCR negative
- Commenced on treatment

# Medications

- Rifampicin
  - 6 months
- Isoniazid
  - 6 months
- Pyrazinamide
  - Induction, first 2 months
- Ethambutol
  - Induction, first 2 months

# Side Effects

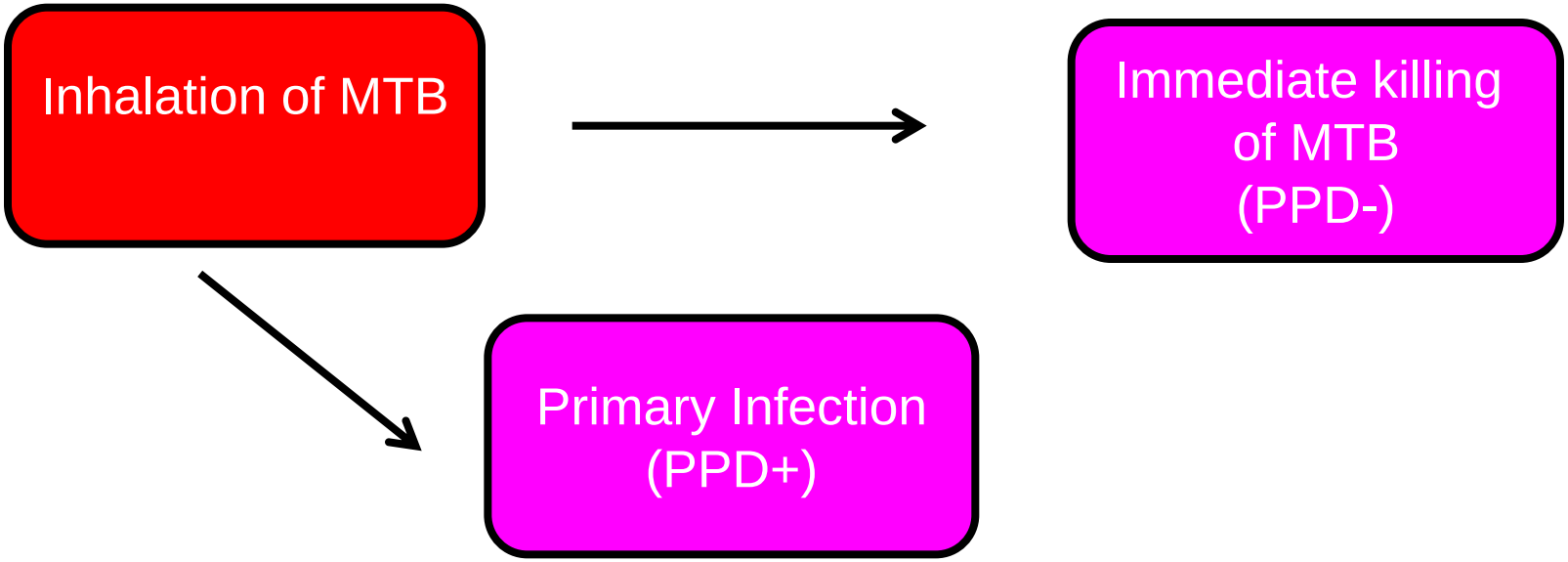
# Side Effects

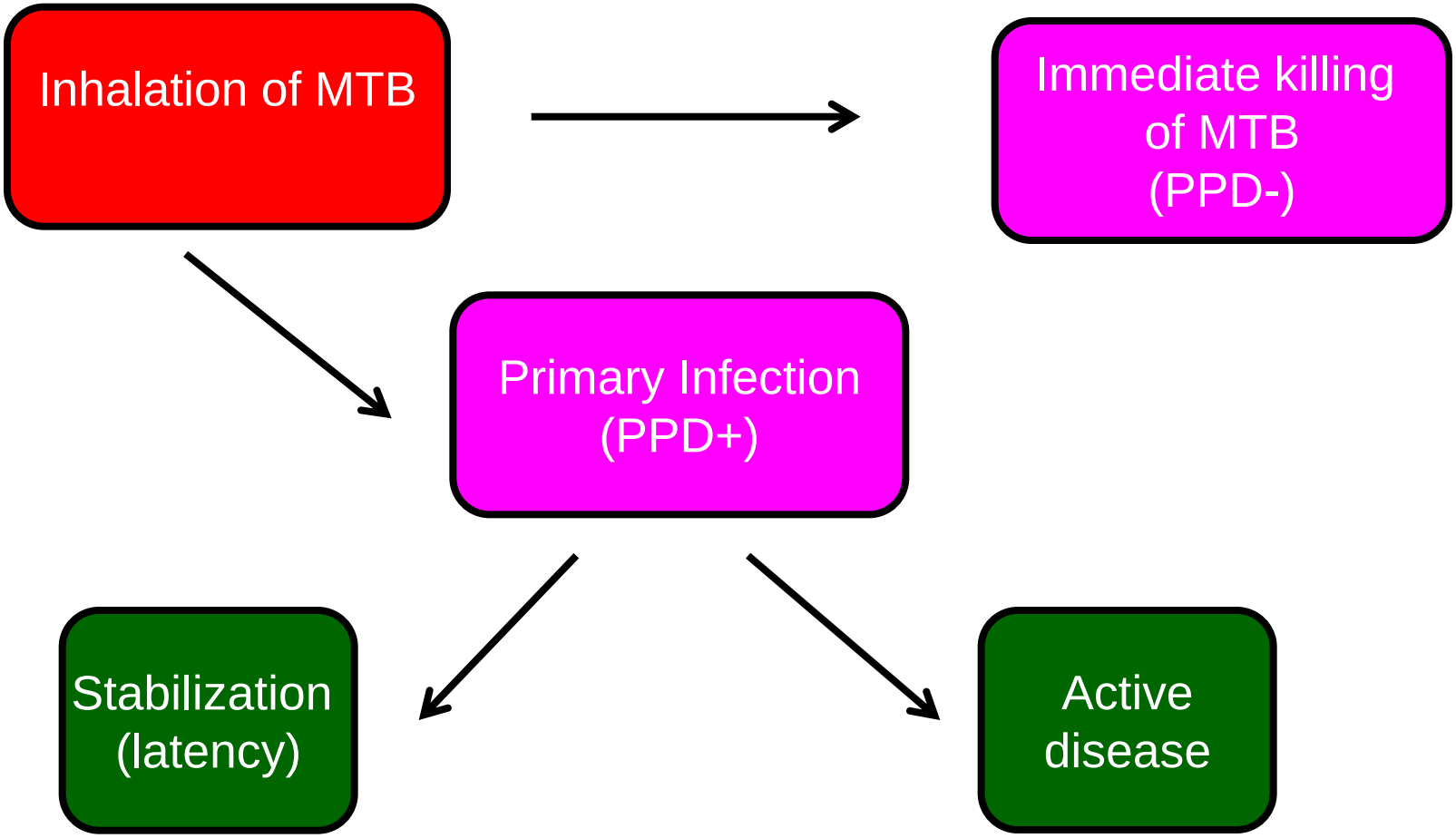
- Abnormal LFTs
- Itchy rashes
- Gastritis
- Urine & tears pinky
- Arthralgias
- SLE
- Gout
- Peripheral Neuropathy
- Optic neuritis
- Flu-like symptoms
- Neutropenia etc

## Case 1

Screening

Wife


Inhalation of MTB
Immediate killing of MTB (PPD-)
Primary Infection (PPD+)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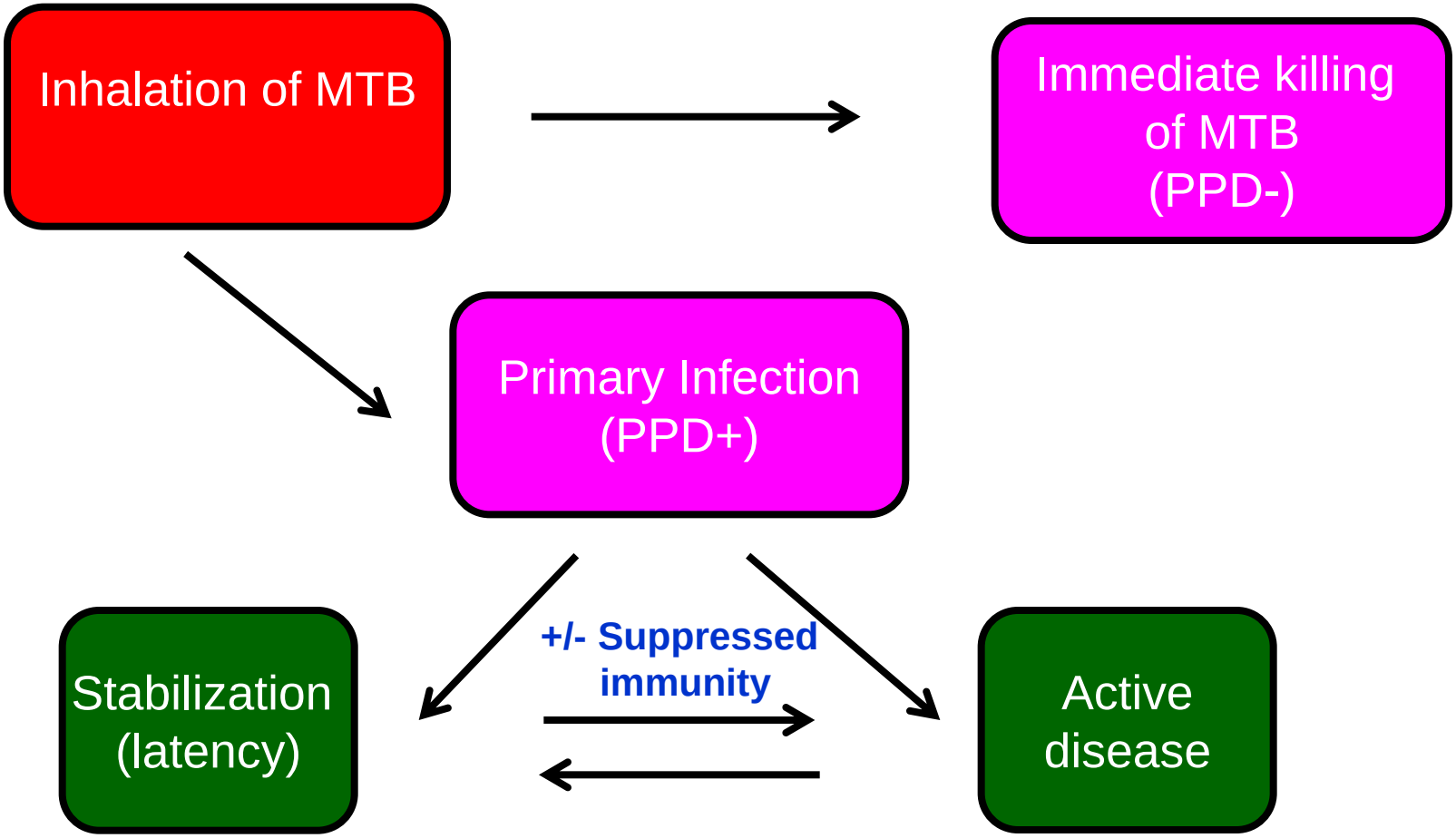
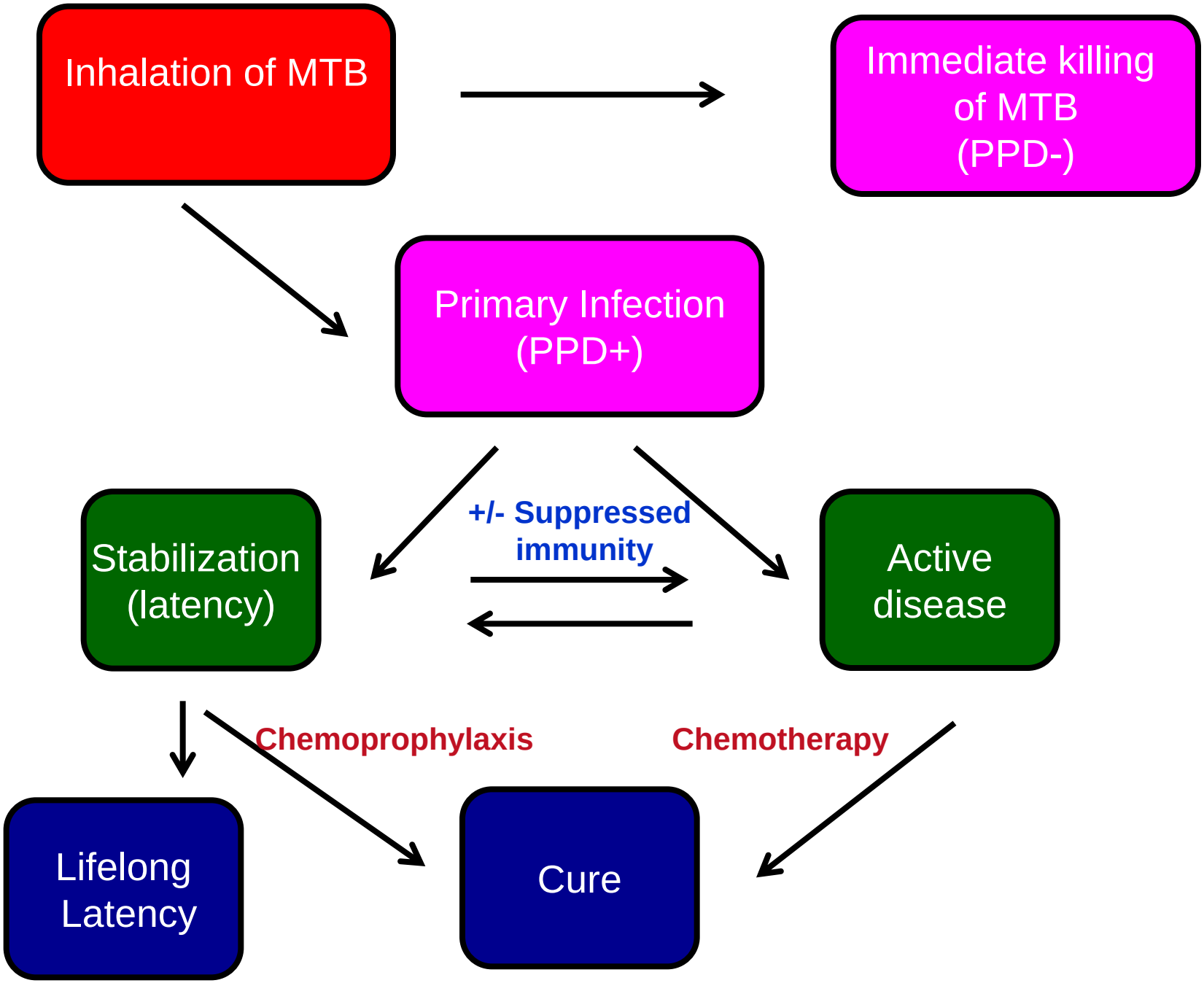
Immediate killing of MTB (PPD-)
Primary Infection (PPD+)
Stabilization (latency)
Active disease


Inhalation of MTB
Immediate killing of MTB (PPD-)
Primary Infection (PPD+)
Stabilization (latency)
+/- Suppressed immunity
Active disease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Immediate killing of MTB (PPD-)
Primary Infection (PPD+)
Stabilization (latency)
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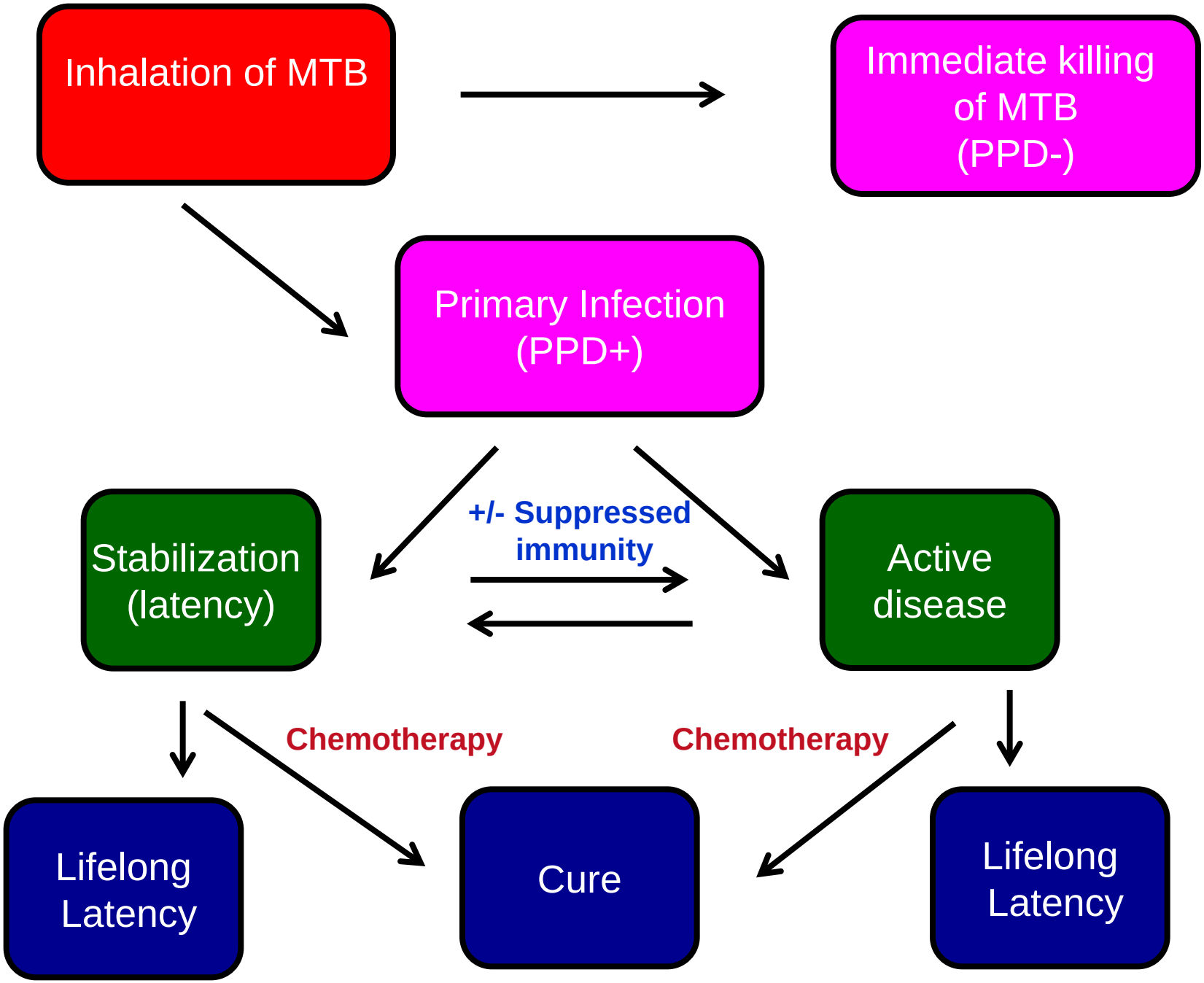
Active disease
Chemoprophylaxis
Chemotherapy
Lifelong Latency
Cure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+/- Suppressed immunity
Active disease
Chemotherapy
Chemotherapy
Lifelong Latency
Cure
Lifelong Latency

# Diagnosis

- **Latent TB**

- Mantoux (skin test)
- Interferon Gamma Release Assays (IGRA)

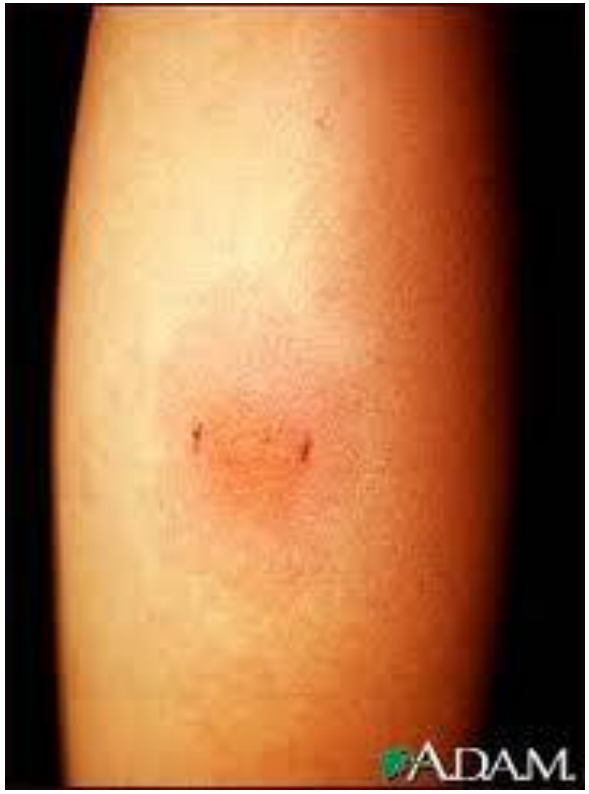
- Latent TB = positive skin test or IGRA + normal CXR + no symptoms

- **Active TB**

- Imaging (CXR, CT, MRI, USG)
- Microscopic staining (AFB)
- TB culture
- Histology – caseating granuloma

# Mantoux test

- Purified protein derivative tuberculin (glycerol extract of tubercle bacillus)
- Standard dose – 5TU (0.1 ml of 1:1000 solution) intradermally
- Read at 48-72 hours



# Interferon Gamma tests

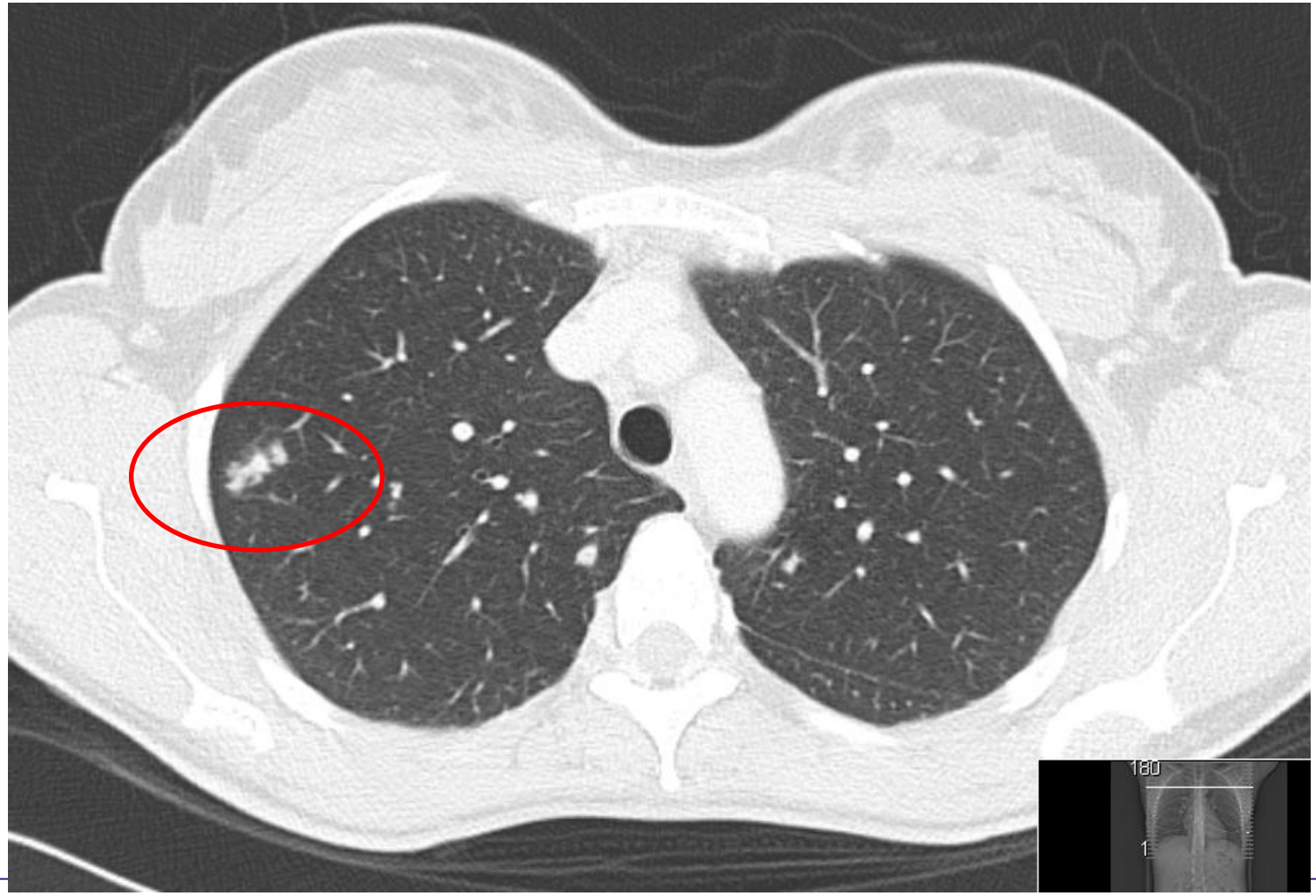
- T-SPOT.TB
- QuantiFERON-TB Gold
  - Detect interferon-gamma released by T cells in response to MTB
  - T-SPOT counts individual T cells (ELISpot)
  - Quantiferon measures total IFNγ (ELISA)
  - ESAT-6 and CFP10 (proteins unique for MTB)
- Advantages:
  - No return visit
  - Result next day
  - No boosting
  - More specific (BCG/ atypicals/
- More sensitive than skin test in children, and HIV positive patients
- Venous, heparinised, room temp, 6-8 hours

| Active TB | Latent TB |
| --- | --- |
| cough, fever, night sweats, fatigue, anorexia, weight loss, haemoptysis | asymptomatic |
| requires urgent treatment with at least 6 months of anti-tuberculous treatment | can be treated with 3 to 6 months of anti-tuberculous treatment to reduce 5-10% lifetime risk of reactivation |
| may be an infection risk dependent on site and progression of disease | never infectious |
| close contacts are screened | contacts do not require screening |
| notifiable disease | not notifiable |

# Wife

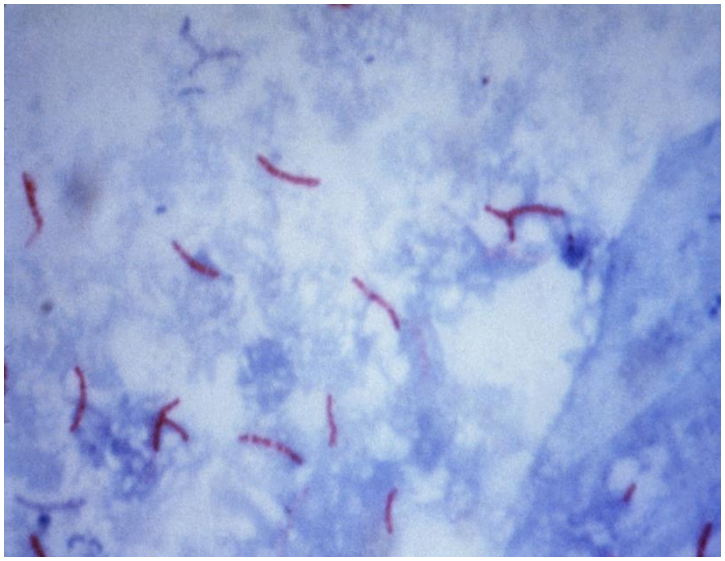
- Positive Mantoux 15mm
- Dry cough for 3 weeks
- No other symptoms

# Case 1



# Case 1

- Multiple coworkers exposed
  - **PHE incident**
- Fully sensitive



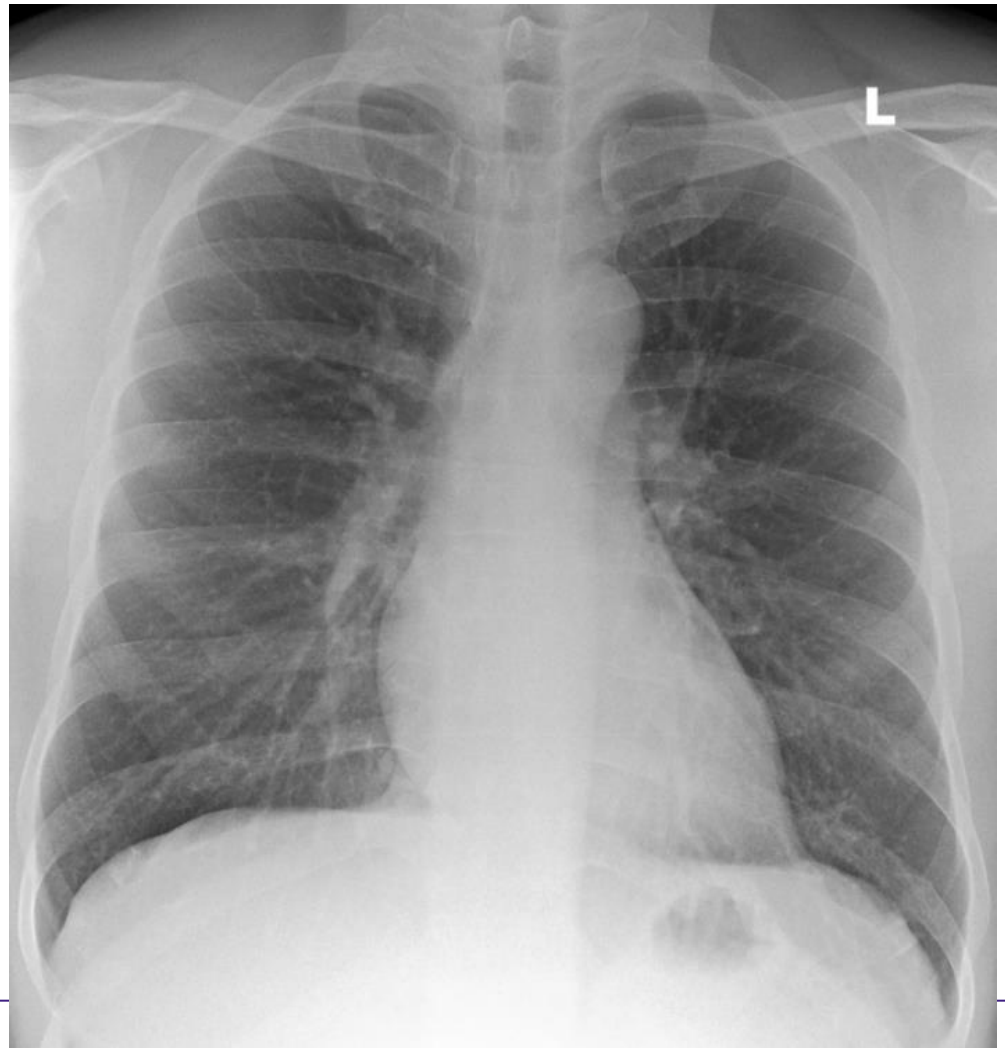
# Delay from symptom onset

- 2015 median time 72 days
- 28% pulmonary delay > 4 months
- 33% UK born cases experience a delay

# Case 2

- A 23 yo Indian man in outpatients
- 3/12 hx of tiredness, weight loss and a dry cough
- BCG in childhood
- TB contact
- 1 year ago had a Mantoux test that was 10mm and a negative interferon gamma release assay (IGRA).
- On this occasion examination and chest x-ray is normal.
- Repeat Mantoux test is 20mm and he has a positive IGRA.
- He is unable to produce sputum spontaneously.

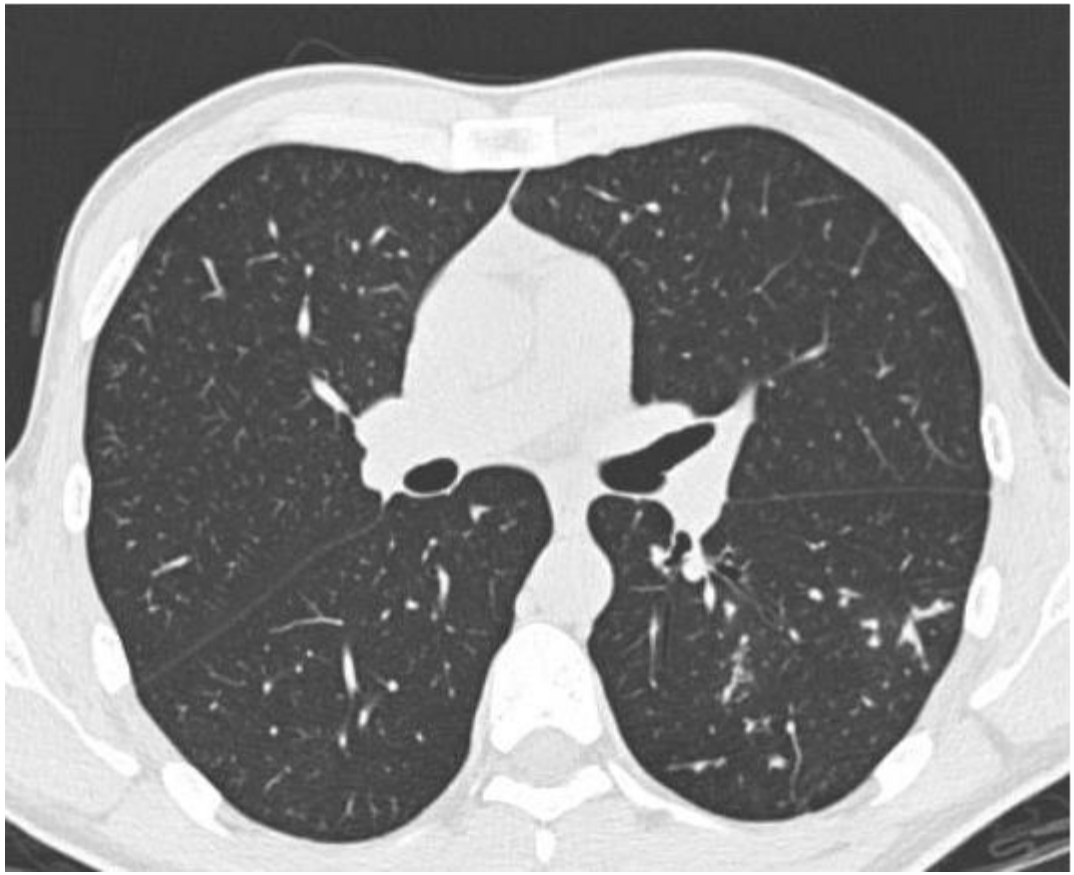
# What do you do next?



# Case 2

- Commence treatment for latent TB infection
- Commence a standard four drug regimen for TB
- Follow-up with a repeat chest x-ray in 6 weeks
- Perform a CT scan and obtain appropriate specimens
- Perform a bronchoscopy or induced sputum

# CT scan



# Next steps

- Directed bronchoscopy and BAL

# Next steps

- Directed bronchoscopy
- What bloods?

# Next steps

- Directed bronchoscopy

- What bloods?
  - FBC, LFTs, U&Es
  - HIV, Hep B&C
  - Vitamin D

# Next steps

- Directed bronchoscopy
- What bloods?
  - FBC, LFTs, U&Es
  - HIV, Hep B&C
  - Vitamin D
- What treatment?

# Medications

- Rifampicin
  - 6 months
- Isoniazid
  - 6 months
- Pyrazinamide
  - Induction, first 2 months
- Ethambutol
  - Induction, first 2 months


# Bronchoalveolar lavage

- Initially AFB smear positive
- 3 weeks later culture positive
- 6 weeks in

MDRTB

# Bronchoalveolar lavage

- Initially AFB smear positive
- 3 weeks later culture positive
- 6 weeks in

# MDRTB

**Aaaaaaaaaaaaaaaaaaagh!**

# What do you do?

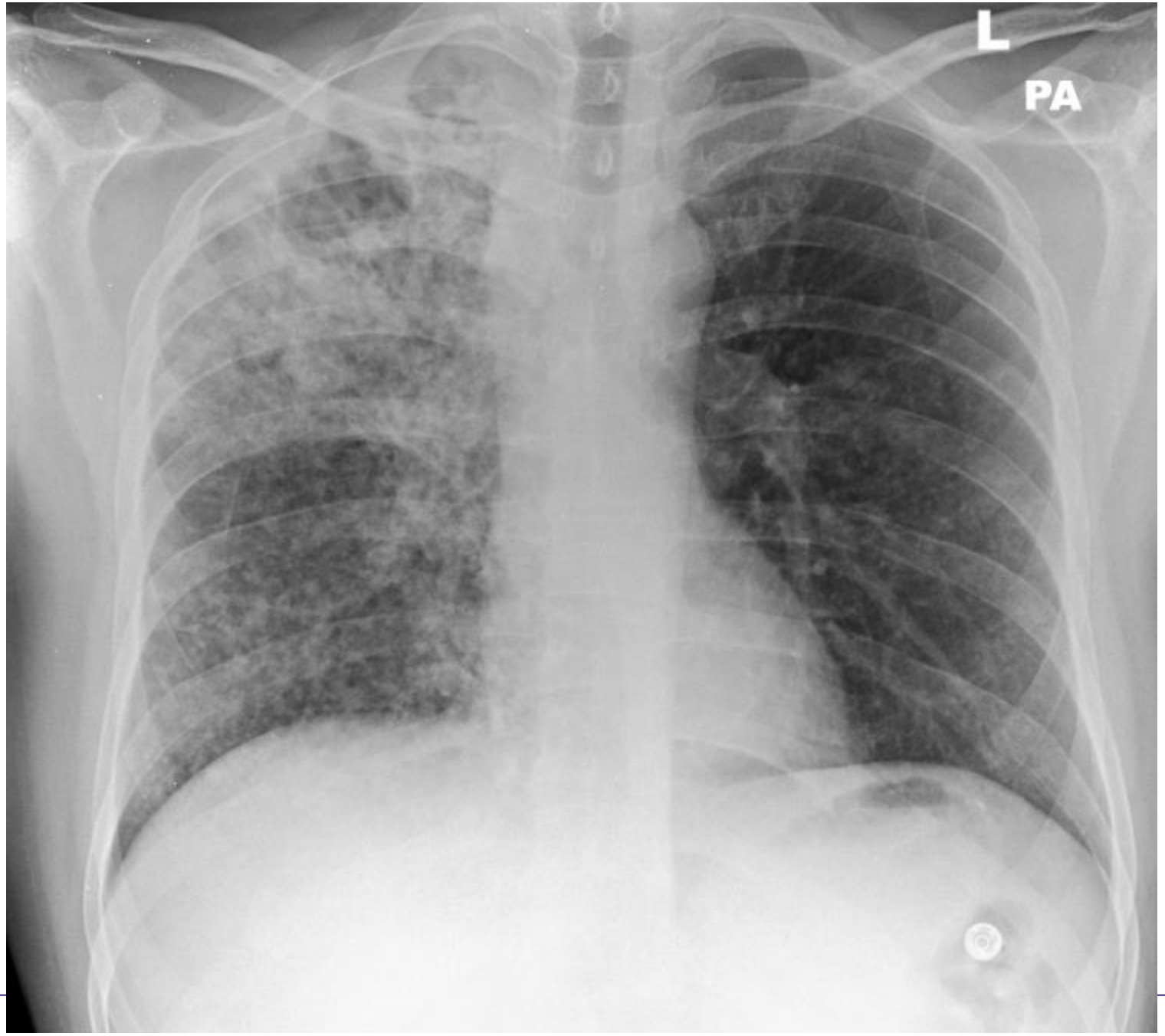
1. Perform a repeat CT to ensure resolution of the initial subtle left changes
2. Stop the isoniazid and rifampicin and continue with ethambutol and pyrazinamide and review with a CT in one month
3. Stop isoniazid and rifampicin and add moxifloxacin and streptomycin
4. Refer him to a specialist
5. Stop isoniazid and rifampicin and add amikacin, moxifloxacin and cyloserine

# Management of MDRTB

- **By clinicians with the expertise to do so!**
- NO NEW DRUGS WITHOUT SENSITIVITIES
- Should be on 3 – 5 drugs to which the bug is sensitive
- At least 18 months and follow-up for 2 years after
- Brilliant case management by nurses and outreach team

# Pulmonary TB again

- 32 yo man
- Presents to A&E
- 2 month history of 2 stone weight loss, cough, sputum, sweats and tiredness
- Homeless
- O/E – spiking temps, thin, crackles
- Chest x-ray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# What are you going to do next?

- Admit to side room
- Masks?
- 3 x sputa
- Bloods
- CSF
- Discharge?

# Sputum smear positive

- Extra test?

- Other considerations?

# Sputum smear positive

- Extra test?
  - PCR
  - Rif probe

- Other considerations?
  - Infectivity
  - 6 months treatment to complete
  - DOT
  - Homelessness

# DOT?

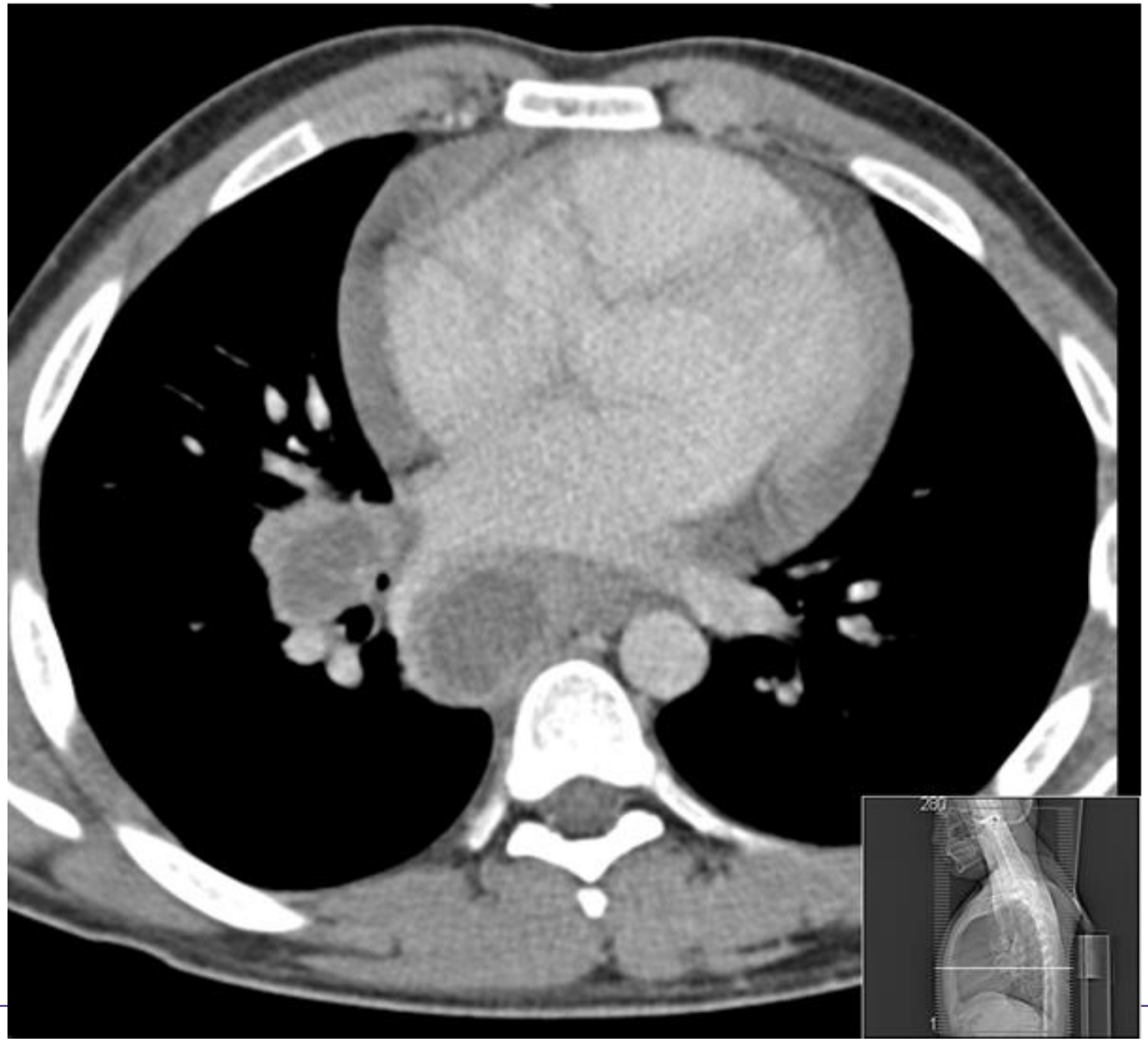
# Directly Observed Therapy (DOT)

- All patients should be risk assessed
- Previous history of treatment
- Current poor adherence
- Homelessness
- Drug or alcohol misuse
- Cognitive or psychiatric disorders
- Denial
- History of imprisonment

# Barriers to treatment

- Social risk factors
- Minimum 6 months treatment
- Side effects

- Brilliant case management key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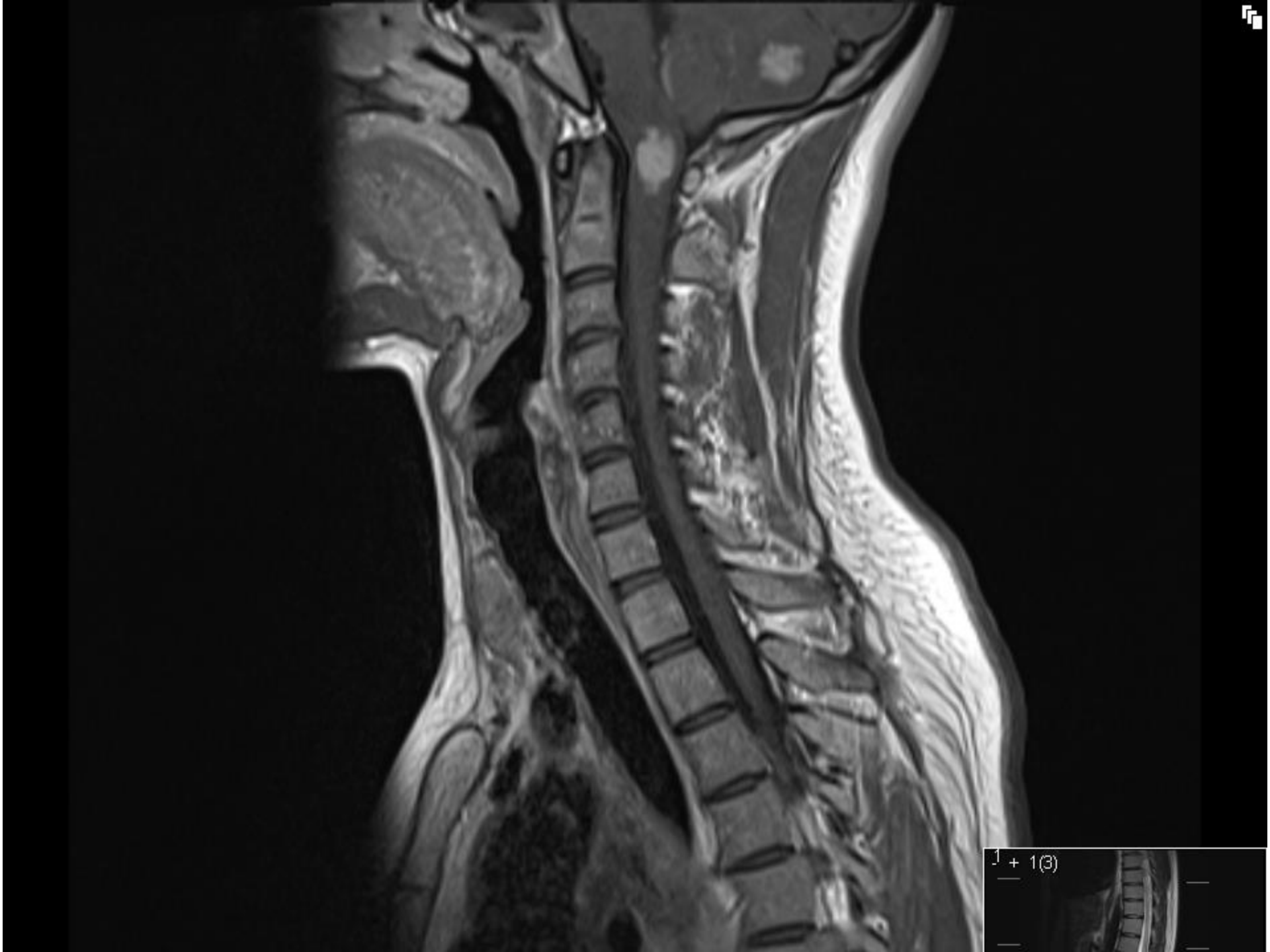
# Pericardial Disease

- Lymphocytosis
- Prednisolone 60mg
- At risk of restrictive pericarditis
- Consider operative treatment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# TB meningitis

- High protein and low glucose
- Polymorphonuclear cells do not exclude
- Not usually AFB smear positive
- **Repeat samples**
- MRI with contrast best
- Always perform a CXR

# TB Meningitis

- High mortality
- 1 year treatment
  - 2 month induction phase
  - Prolonged induction phase
- Prednisolone 40mg
- Monitor carefully

## Common symptoms

- Cough
- Fever
- Sweats
- Weightt loss
- Fatigue
- Lymphadenopathy
- Haemoptysis

## Uncommon symptoms

- **Headaches**
- **Abdominal pain**
- **Back pain**
- Depression
- Thirst
- Clear sputum
- Pallor
- Cold extremities

## Uncommon symptoms

- **Headaches**
- **Abdominal pain**
- **Back pain**
- Depression
- Thirst
- Clear sputum
- Pallor
- Cold extremities

**ANY OTHER SYMPTOM!**

# Remember

- Only 50% of cases are pulmonary
- You need prolonged contact to catch it
- It is treatable
- The more you think TB the more you'll diagnose it early
- BCG does not prevent TB

- **Beth Villanueva** – TB Nurse Lead
- **Dr Anne Dunleavy** – TB Resp Cons
- **Dr Catherine Cosgrove** – TB ID Cons
- **Dr Angela Houston** – TB ID Consultant
- **Prof. Tom Harrison** – TB ID Consultant
- **Dr Derek Macallan**– TB ID Consultant lead
- **Dr Amber Arnold** - Locum ID Consultant
- **Gale** – TB service administrator
- **Veera Pavlova** – Senior TB nurse specialist
- **Innocent Dunstan** – TB nurse specialist
- **Csaba Koczkas** – TB nurse specialist
- **Marcos** – TB nurse specialist
- **Michael Nayagam** – TB outreach worker

# How to Refer


- **stgh-tr.stgeorgestbhnurses@nhs.net**
- **TB Nurses Tel: 0208 725 1466, bleep: 8481**
- **MON – FRI 09:00 – 17:00 excl. public holidays**
- **For out-of-hours urgent queries please contact:**
- **on-call ID registrar on bleep: 7568**

excellent
kind
responsible
respectful

St George's University Hospitals NHS
NHS Foundation Trust

# Thank you

Any questions?

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