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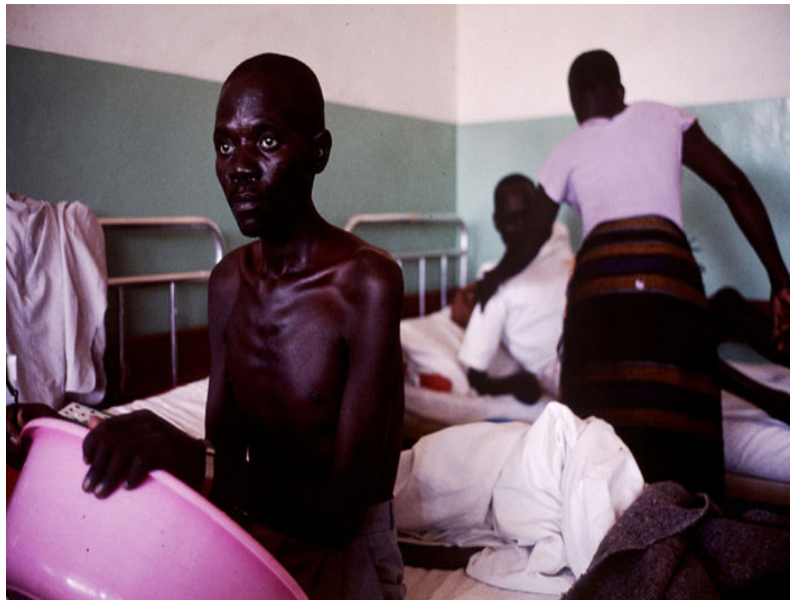
HIV and TB Co-infection

Marsh Gelbart
2010



Learning Outcomes

- To understand that HIV and TB represent the two biggest threats to world public health and in combination are even more deadly
- To appreciate that TB is the most lethal of the opportunistic infections
- To evaluate the future dangers of co-infection locally and internationally
- To apply knowledge to clinical practice

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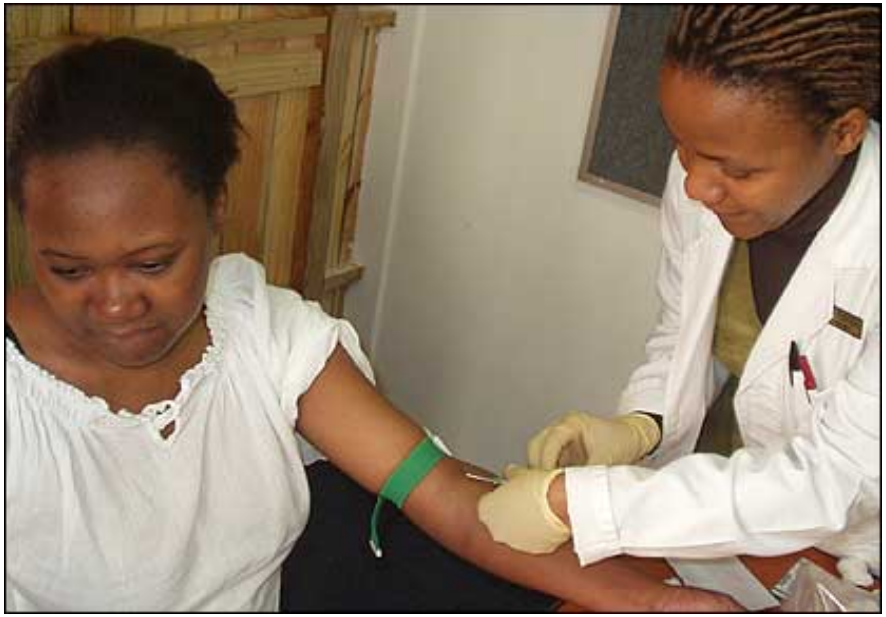
Historical Perspective

- An ancient disease dating back to the time of the Pharaohs
- A new infection dating back mere decades
- In combination - a dual pandemic – TB and HIV joined together in a synergetic “dance of death”

Robert Koch injects one of his patients with tuberculin. He hoped that it would be a cure to tuberculosis.



A deadly combination

- The two epidemics fuel each other, more people will die from HIV and/or TB than any other infectious diseases.
- Tuberculosis-HIV co-infection can be difficult to diagnose and treat
- Those countries most affected, have the weakest healthcare infrastructure, The burden is intolerable
- Tuberculosis is the leading cause of death amongst people living with HIV, about a third of those with AIDS will die of TB.

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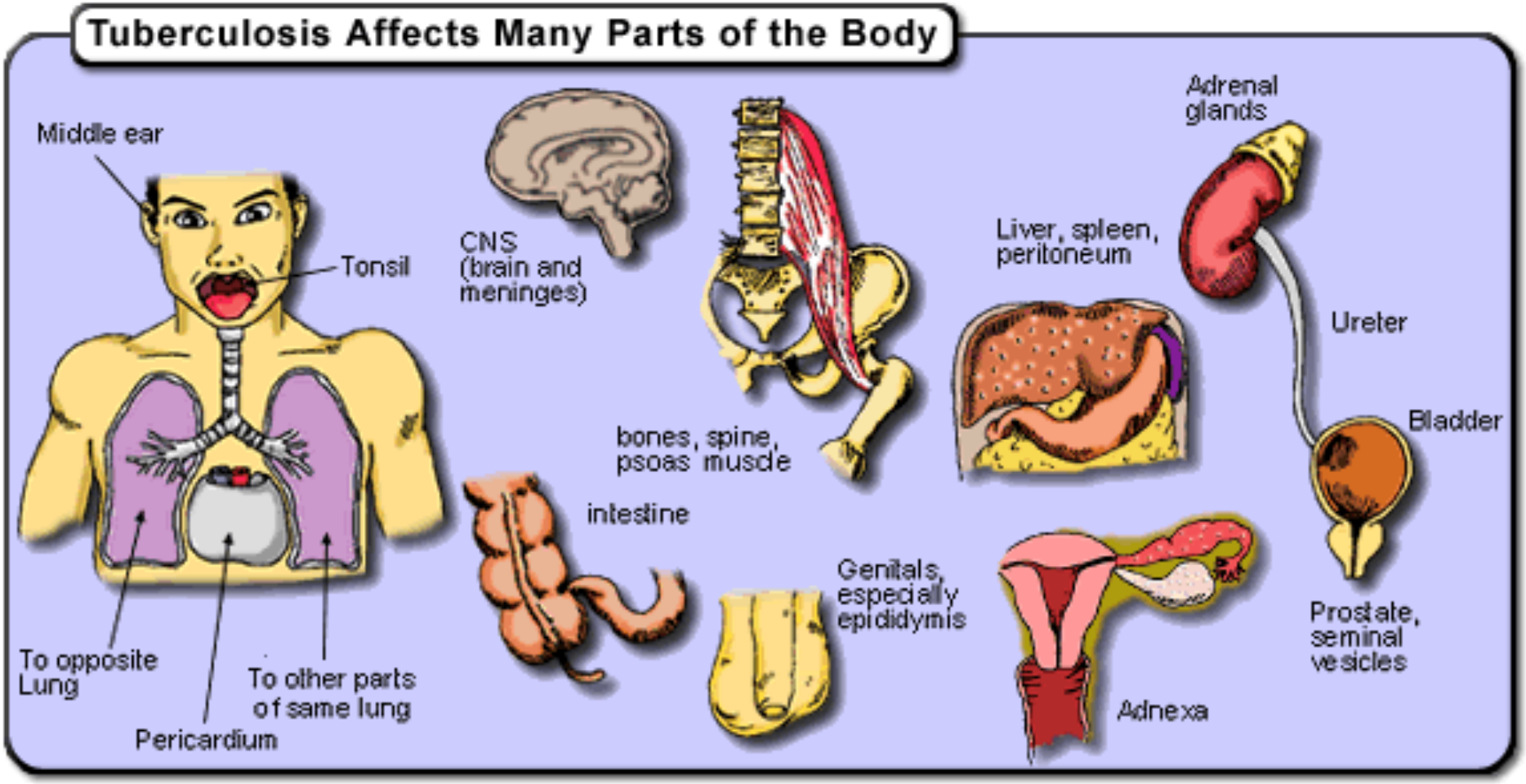
Remember, TB like HIV is a systemic illness



TB is a major killer

- TB is one of the world's greatest killer amongst infectious diseases. The latest WHO estimates (2009) indicate that there were 9.3 million tuberculosis cases and 1.3 million deaths caused by tuberculosis in 2007.
- Although readily treatable and preventable, TB is also the most important opportunistic infection associated with HIV.
- It is particularly significant amongst developing countries where there is a considerable overlap in the epidemiological footprint of the two diseases.

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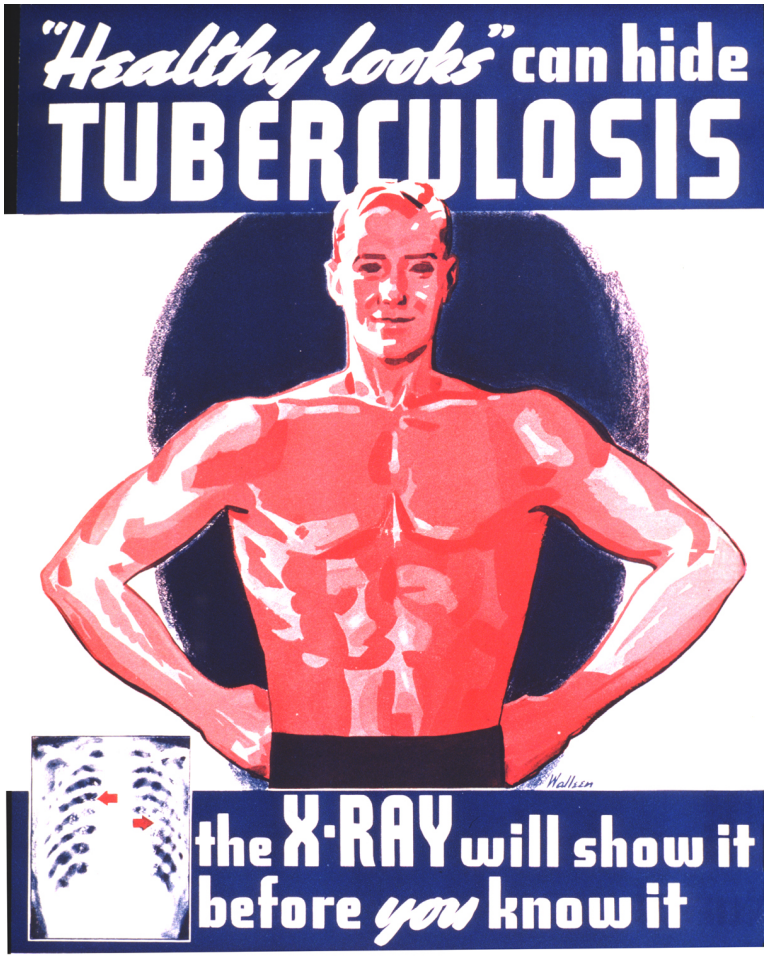
How many people have TB?

- Some two billion people are infected with Mycobacterium tuberculosis, around one third of the world's population.
- In 2008, in the UK, 8,655 cases of tuberculosis were reported, a rate of 14.1 per 100,000 population. This represents an increase of 2.2% in the rate of disease compared with 2007.

- Like HIV, those in the economically most productive age group (15 - 54) are most at risk of developing the disease.



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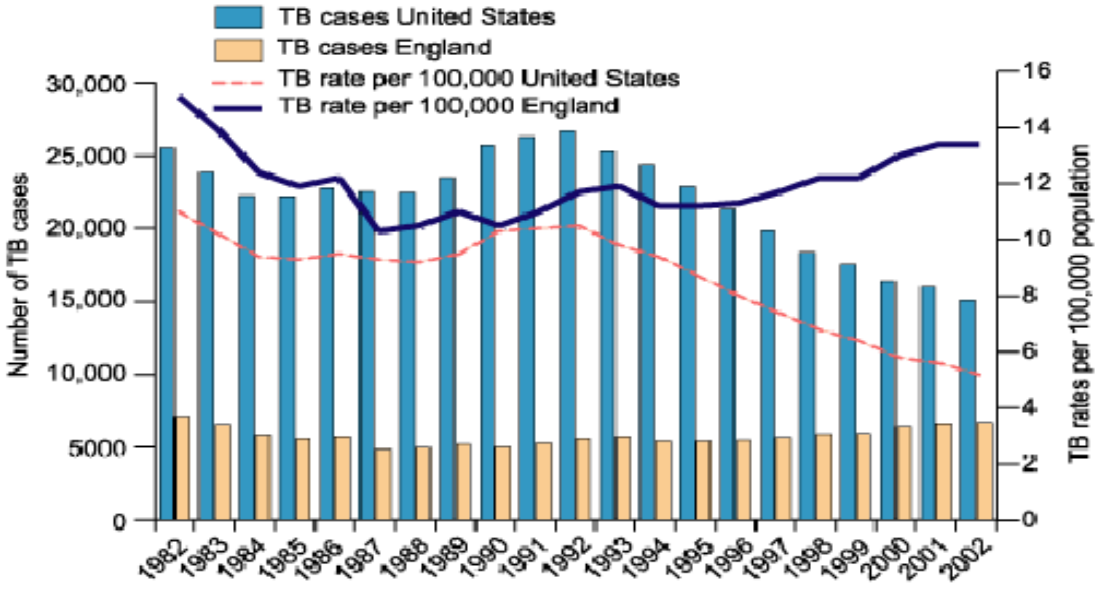
Current TB rates UK and USA

Figure 1 Tuberculosis notification rates and number of cases, United States and England: 1982 to 2002



Data sources: United Sates CDC Division of Tuberculosis Elimination - surveillance reports CDSC NOIDS data – the Office for National Statistics (ONS) population denominators.

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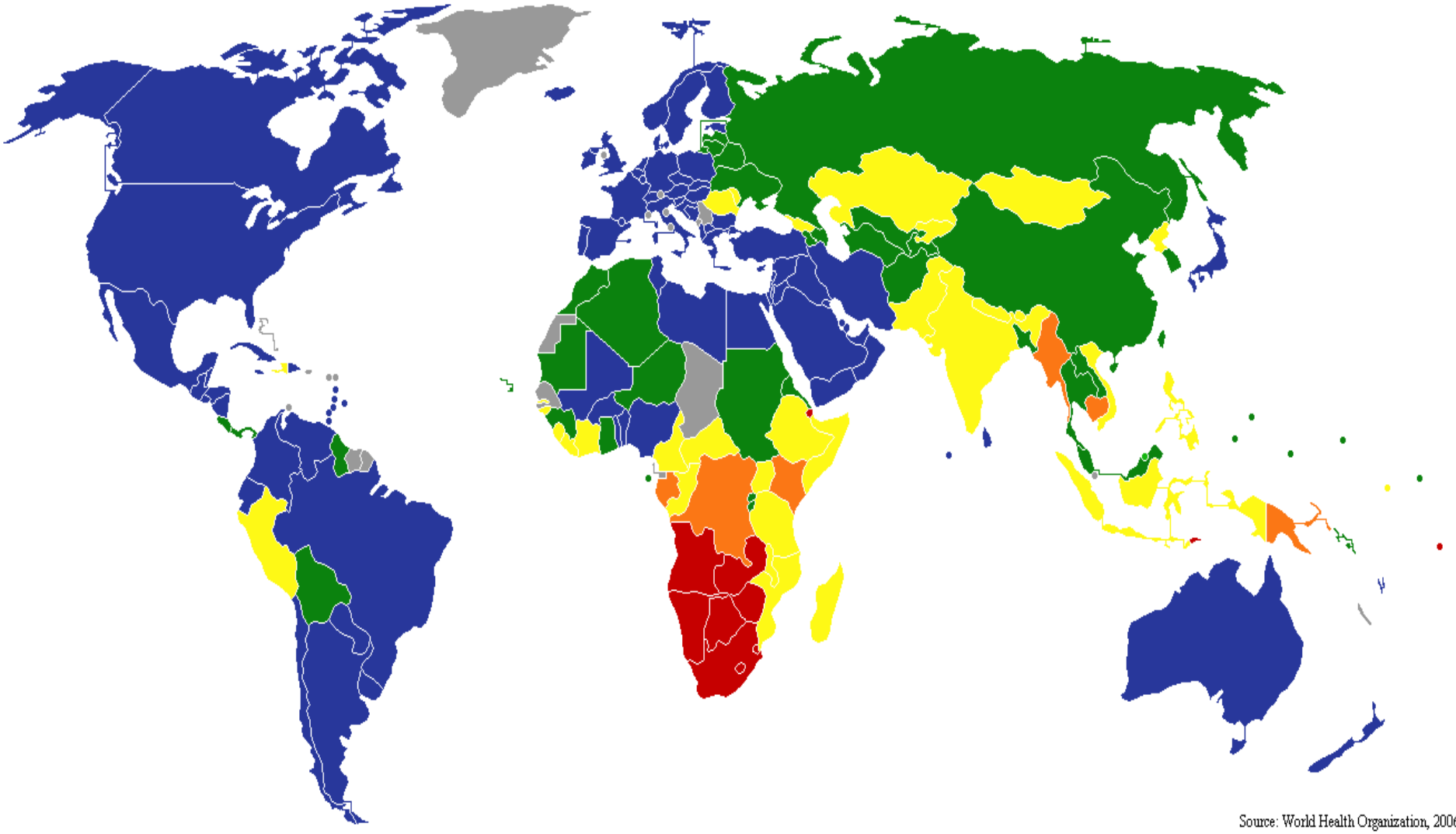

Source: World Health Organization, 2006

How many have active TB?

- For around 90% of people infected with TB, the disease remains inactive.
- There are probably around 200 million people with active TB
- Eight million new cases of active TB occur annually.

(Bloom, B, Small, P (1998) The Evolving Relation between Humans and Mycobacterium Tuberculosis. *The New England Journal of Medicine.* Vol.338. Number 10, March 5th. PP 677-678).

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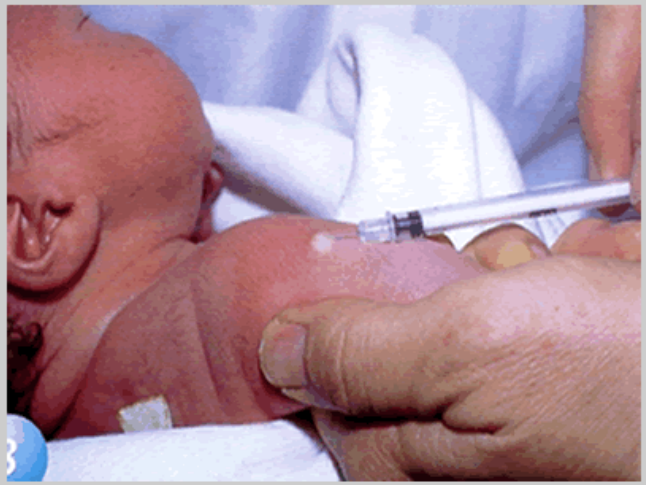
Vaccination against TB Pre –Septembe

- Until recently it was UK policy to vaccinate all children at the age of 13.
- The Bacillus Calmette-Guerin (BCG) vaccine used has an estimated efficacy of 70-80%
- **As a live vaccine BCG is absolutely contraindicated for people diagnosed with HIV**

Nowadays fine focused vaccination programmes

- Routine vaccination for schoolchildren has ended
- Vaccination will be reserved for babies born in areas of high risk and children whose families originate from countries with high rates of tuberculosis
- Unvaccinated recent immigrants from high incidence areas, health care workers and workers in such institutions as prisons or hostels will still be targeted



BCG Interdemal Vaccination

General principles for the treatment of active TB

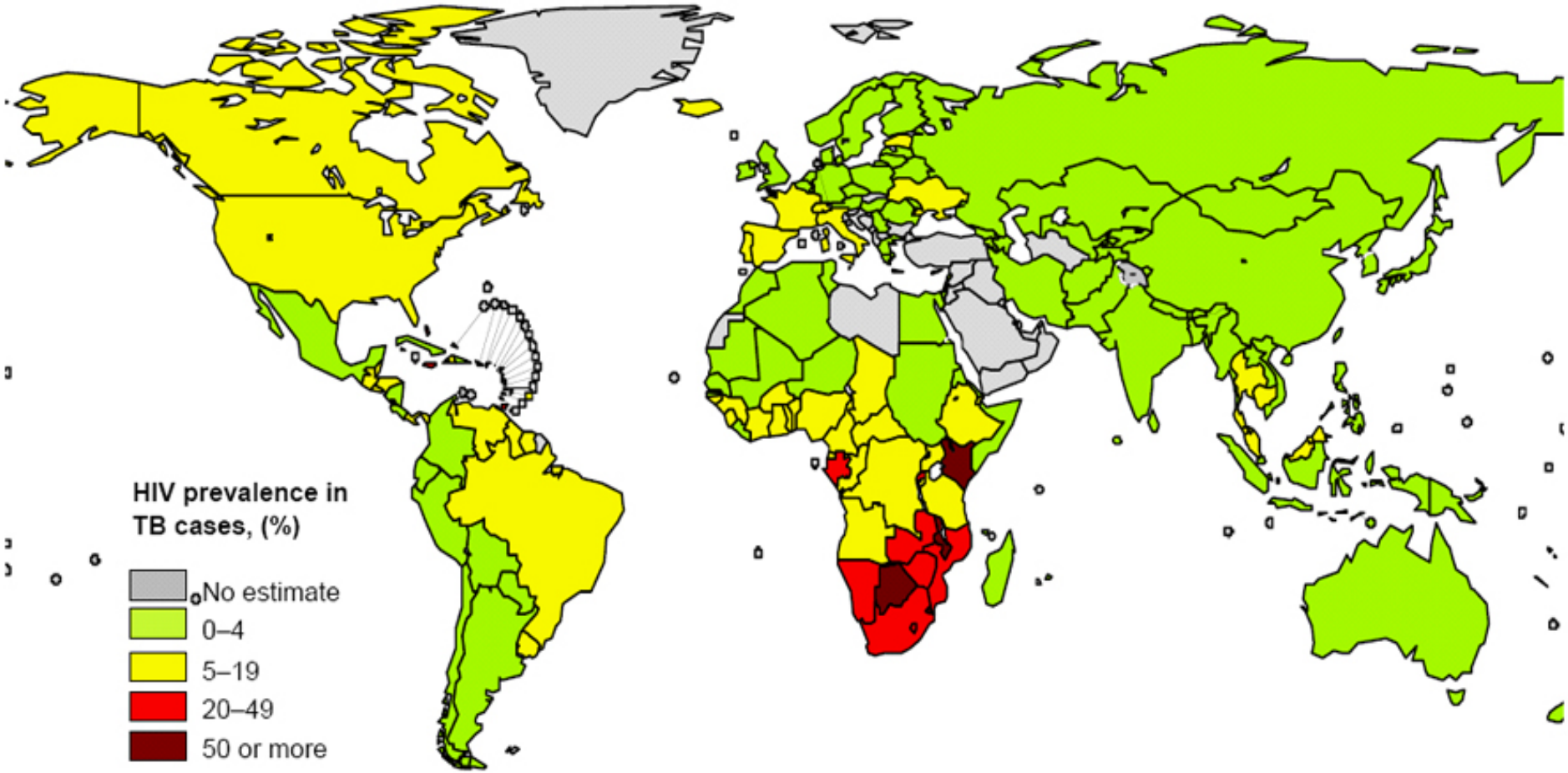
- Treatment should be by a combination of four agents, to which the disease remains susceptible.
- The treatment needs to be of sufficient duration, six months is the accepted norm.
- If necessary, treatment should be directly observed to assure compliance.
- If treatment is failing, then more than one alternative medication should be introduced at the same time.

Treatment regimes

- **Active TB**
  Isoniazid and Rifampicin, for six months along with Pyrazinamide and Ethambutol for the first two months
- **Latent TB**
  Isoniazid given daily over a 6 month period is the favoured option

Estimated HIV prevalence in new TB cases, 2006

WHO THE STOP TB DEPARTMENT



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Scale of co-infection

- In 2003, approximately one third of the 43 million people living with HIV, were co-infected by TB. (Bastian I, Stapledon R, Colebunders R (2003) Current thinking on the management of tuberculosis. *Current opinion in Pulmonary Medicine.* Vol.9 Issue 3, May. Pp 186-192).
- Up to 70% of patients with sputum smear-positive pulmonary tuberculosis are HIV-positive in some countries in sub-Saharan Africa. (Colebunders R, Lambert ML (2002) Management of co-infection with HIV and TB. *British Medical Journal.* Vol.324. Issue 7341 6th April. Pp 802-803).

Susceptibility to TB – if HIV positive

- The incidence of active TB amongst HIV positive people is 100 times that of the general population.
- If a person with HIV has latent TB, there is a 10% chance per annum of it becoming active.
- The spread of the HIV epidemic has significantly impacted the TB epidemic. one-third of the increase in TB cases over the last five years can be attributed to the HIV epidemic
- In 2003, there were an estimated 765 000 new cases of TB in people living with HIV (9% of all new TB cases) and 264 000 deaths from TB in people living with HIV (15% of all TB deaths).

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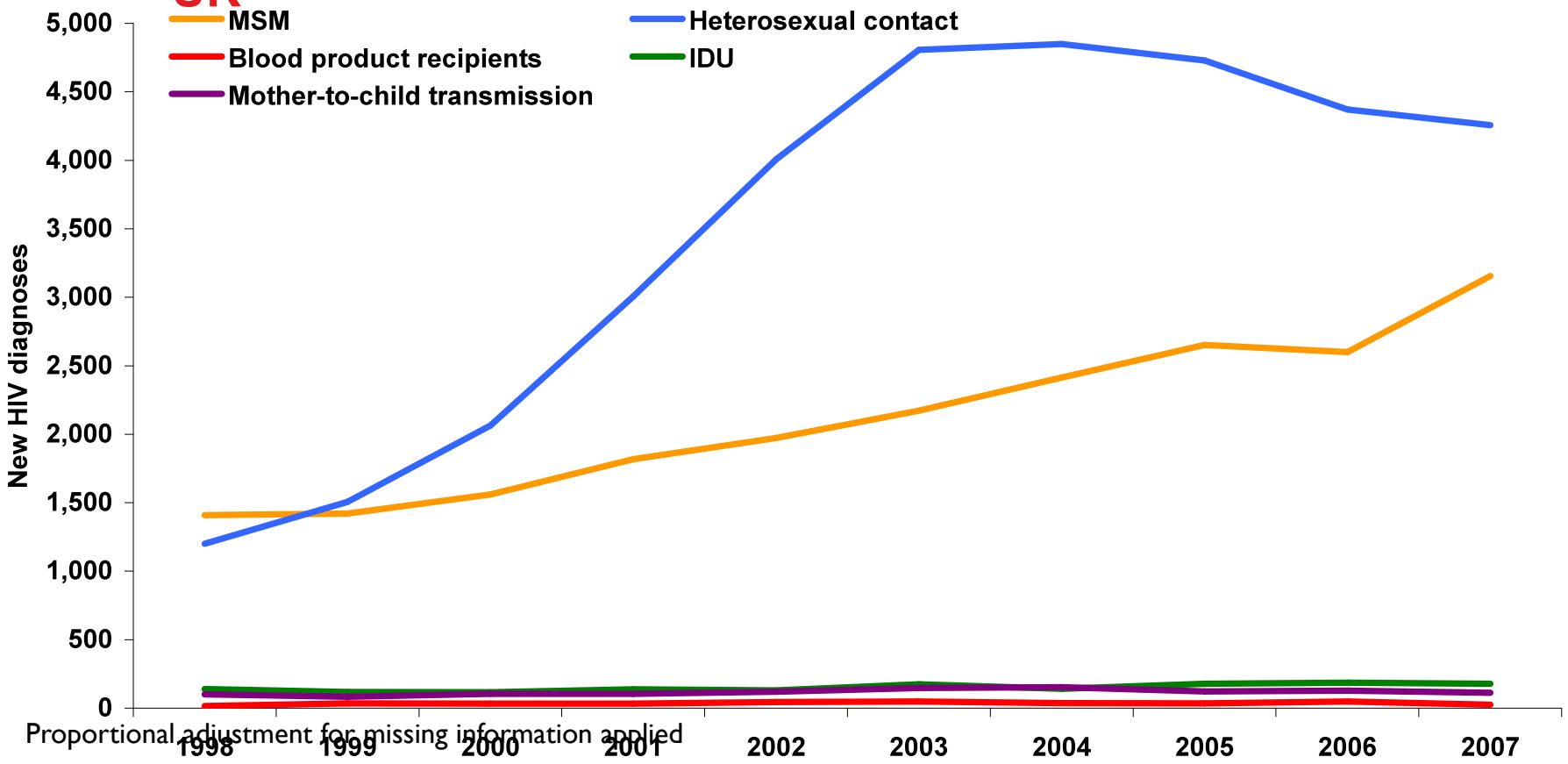
Adjusted number of new HIV diagnoses by prevention group, UK



Proportional adjustment for missing information applied

True extent of the joint epidemic is unknown

- According to the WHO, up to 95% of people in sub-Saharan Africa are unaware of their HIV status.
- As far as TB is concerned, for most of the Developing World the diagnostic test available (sputum microscopy) is insensitive, labour intensive and relatively inaccurate.

The poor bear the heaviest burden

- Ninety five percent of those people with TB live in the developing world.
- Ninety eight percent of fatalities occur in the developing world.
- In South Africa alone there are 2 million co-infected adults

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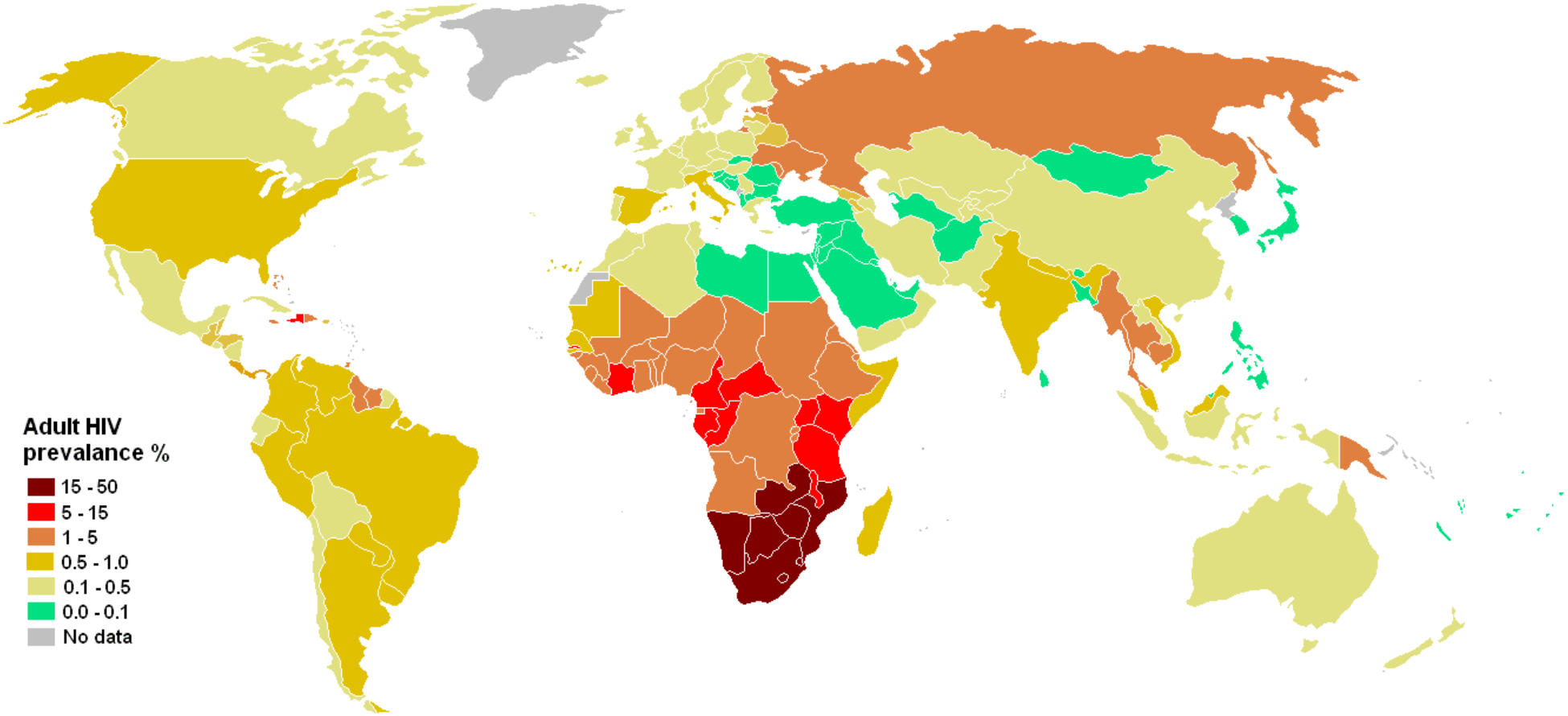
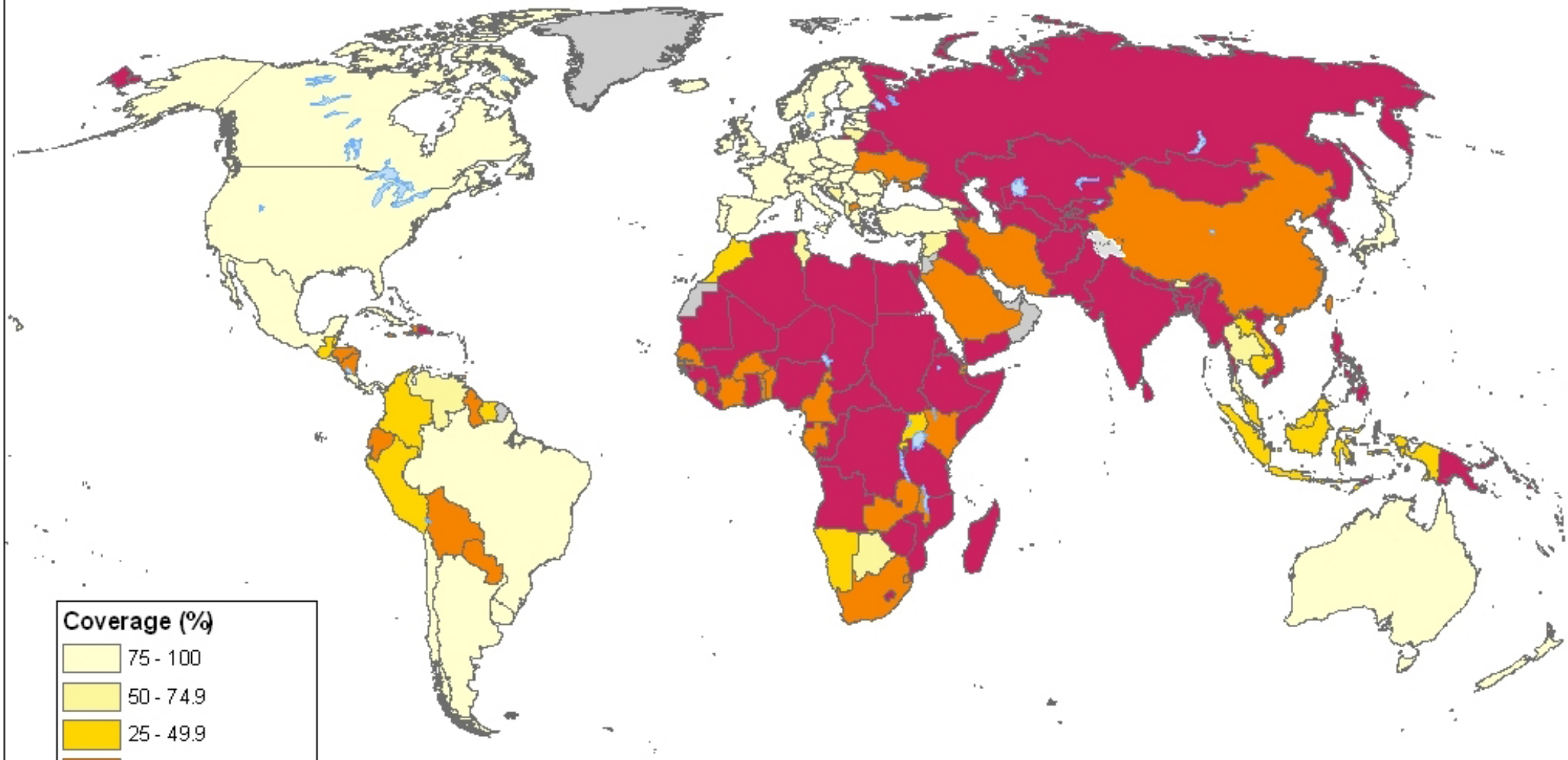


Prognosis for co-infection depends on where you live

- "Today there is a shocking inequality worldwide in the prognosis of HIV and tuberculosis co-infection, and it depends on whether patients or their country have access to highly active antiretroviral therapy." (Lambert M (2002) Management of co-infection with HIV and TB. *British Medical Journal.* Vol.324 Issue 7341, 6th April. Pp 802-803).

Estimated percentage of people on antiretroviral therapy among those in need, situation as of June 2005



Data Source: WHO/UNAI
Map Production:
Public Health Mapping an
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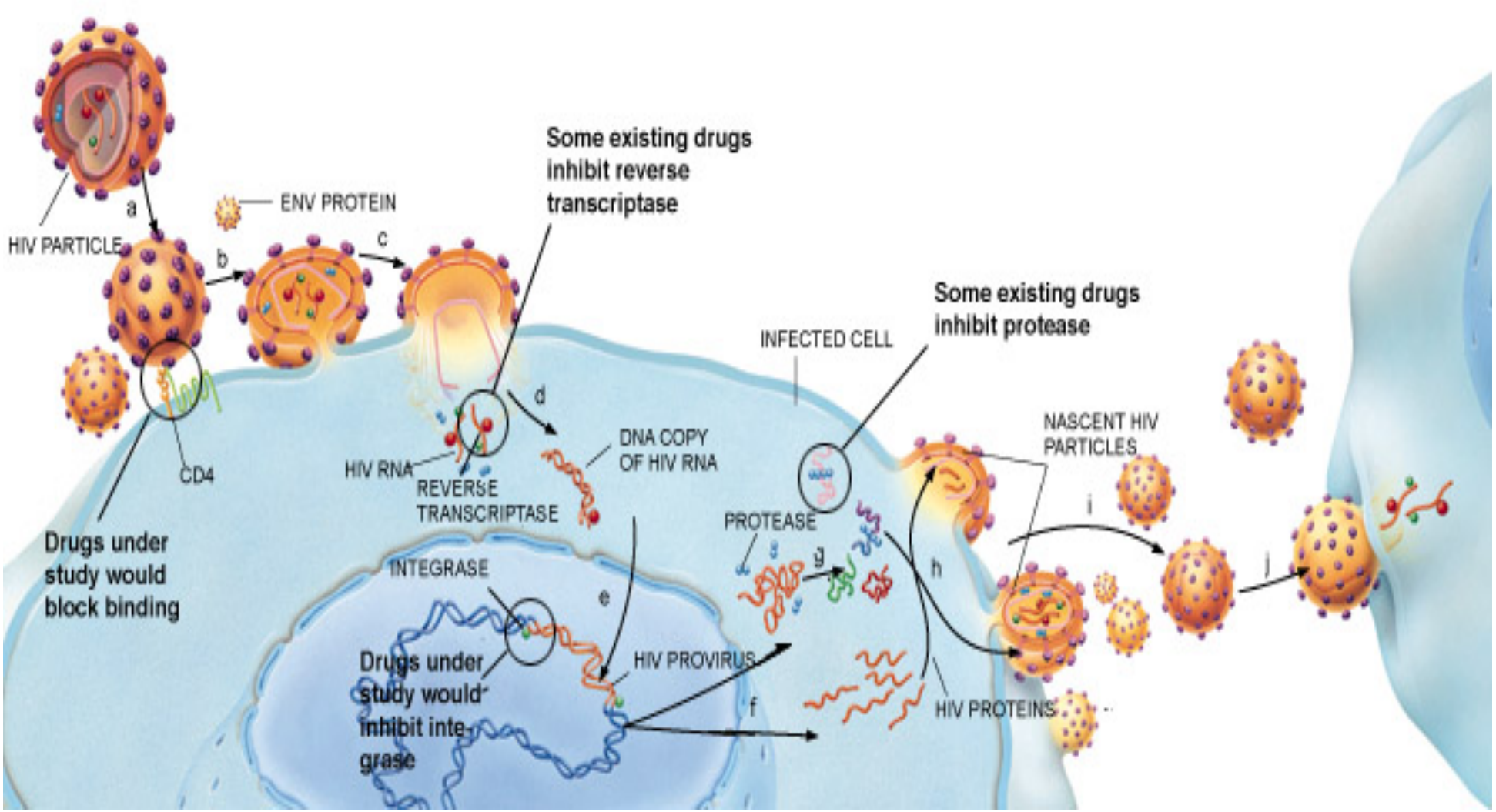


HAART – types of anti-HIV drug available

- Usually involves the giving of a number of different anti-viral agents in combination
- Typically two Nucleoside Reverse Transcriptase inhibitors (NRTIs) along with either a Protease inhibitor (PI) or a Non-nucleoside Reverse Transcriptase inhibitor (NNRTI)

Kept in reserve are -

- Nucleotide Reverse Transcriptase inhibitors (NtRTIs)
- Fusion inhibitors

Co-infection is aggressive

- TB is likely to be more severe
- There is a greater chance of dissemination, not just pulmonary involvement but miliary TB
- The lymphatic system can be affected, along with the gastrointestinal tract, urological tract and the bone marrow.

Co-infection of HIV with TB has serious clinical consequences

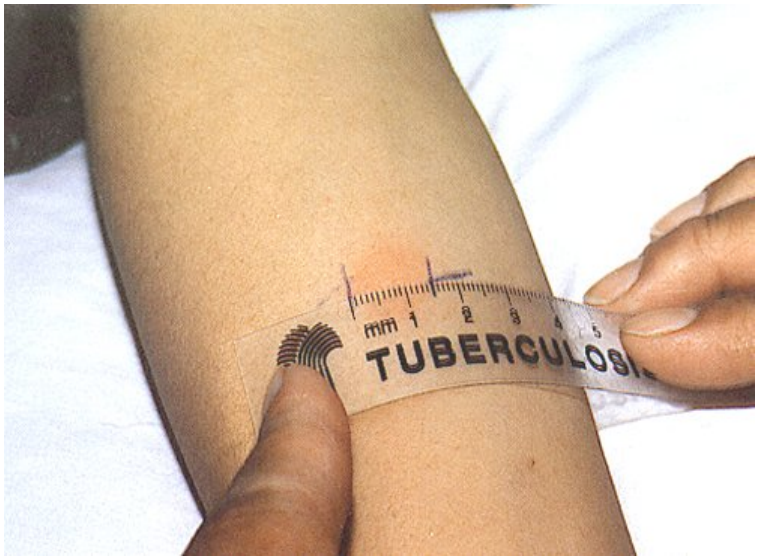
- Cell-mediated immune responses are impaired
- CD4 T lymphocytes are depleted.
- Consequently the normal courses of both infections are accelerated.
- Recurrence of TB in patients co-infected by HIV occurs in individuals with profound immuno-suppression and is associated to high mortality.

Conformation of TB infection in someone with HIV is difficult

- Many of the symptoms of HIV and TB such as fever, wasting and long term malaise, mimic each other.
- In many parts of the world, appropriate diagnostic tools are not available.

Confirming the presence of TB co-infection

- In co-infection, sputum specimens are often negative.
- Tuberculin skin tests may be affected by an impaired immune response and show as negative.
- Chest X rays may be useful along with microscopy and culture of specimens.
- If there is miliary TB, body fluids and/or tissue can be obtained and screened.
- A pleural biopsy may prove necessary.



HAART transforms patient prognosis

- The advent of HAART has seen a dramatic reduction in the number of people living with HIV developing active TB.
- One trial in South Africa showed that the availability of HAART reduced the incidence of HIV associated TB, by 80%. (Bastian I, Stapledon R, Colebunders R (2003) Current thinking on the management of tuberculosis. *Current opinion in Pulmonary Medicine.* Vol.9 Issue 3, May. Pp 186-192).

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Immune reconstitution inflammatory syndrome (IRIS)

- For those people receiving HAART, after starting anti-tuberculosis treatment some patients develop an exacerbation of symptoms, signs or radiological manifestations of TB. The phenomenon is known as immune reconstitution inflammatory syndrome (IRIS),
- Sometimes called immune reconstitution disease (IRD) or paradoxical reaction.
- Involves persistent fevers without an identifiable source or reason and/or worsening or emergence of dyspnoea and swollen lymph glands

Treating cases of co-infection

- The standard six to nine months combination therapy for TB as used in those not co-infected with HIV has proved effective.
- However, *HAART should be deferred until two months after the commencement of TB treatment.*
- Corticosteroids or other anti-inflammatory agents can also be used to reduce the severity of paradoxical reactions.

When to Treat?

- Starting HAART during TB treatment is complicated by overlapping toxicities and drug interactions
- High pill burdens may reduce adherence.
- Delaying HAART may lead to prolonged or worsening immune suppression.
- Physicians have to balance these risks when deciding when to initiate HAART
- Recent data suggest early HAART treatment reduces morbidity and mortality.

If you can't treat HIV, treat TB

- In Africa, where there is only a very restricted access to HAART, preventative therapy for tuberculosis may be the single most affordable intervention for the prolongation of life amongst those people infected HIV.
- If left untreated by appropriate anti-TB medication, 90% of those people with HIV that become co-infected with TB die within six months.

(Stephenson J (2003) Global TB/HIV crisis. *Journal of the American Medical Association.* **Vol.290** Issue 6, August 13th. Pp 740).

TB treatment cheap and effective… but woefully underfunded

- *When taken correctly,* medication for TB has a 95% success rate in curing the infection, and cost as little as $10 per patient for a six months course of treatment.
- Yet in July 2003, the WHO released a report stating that its $9.1 billion plan to halt the spread of TB had been under funded by $3.8 billion.

A new danger……

- MDR-TB (Multidrug Resistant TB) is resistant to at least the two main first-line TB drugs - isoniazid and rifampicin.
- XDR-TB, or Extensively Drug Resistant TB (also referred to as Extremely Drug Resistant) is also resistant to three or more of the six classes of second-line drugs.
- XDRTB in an HIV-positive population in Kwazulu-Natal in South Africa was characterized by alarmingly high mortality rates.
- Of the 544 patients studied, 221 had MDR-TB. Of the 221 MDR-TB cases, 53 were defined as XDR-TB. Of the 53 patients, 44 had been tested for HIV and all were HIV-positive.
- 52 of 53 patients died, on average, within 25 days, including those benefiting from antiretroviral drugs

HIV/MDR outbreak

- An outbreak of MDR in Buenos Aires early 1990s
- Affected 162 patients in an HIV unit - the MDR outbreak lasted over 2-3 years
- Patients were on an open ward (Nightingale ward) and were infected, ironically, by a non-adherence nurse with TB
- 87 patients died without knowing they had TB
- 49 died on standard TB drugs
- 10 died on tailored TB drugs
- only remained16 alive on tailored TB drugs

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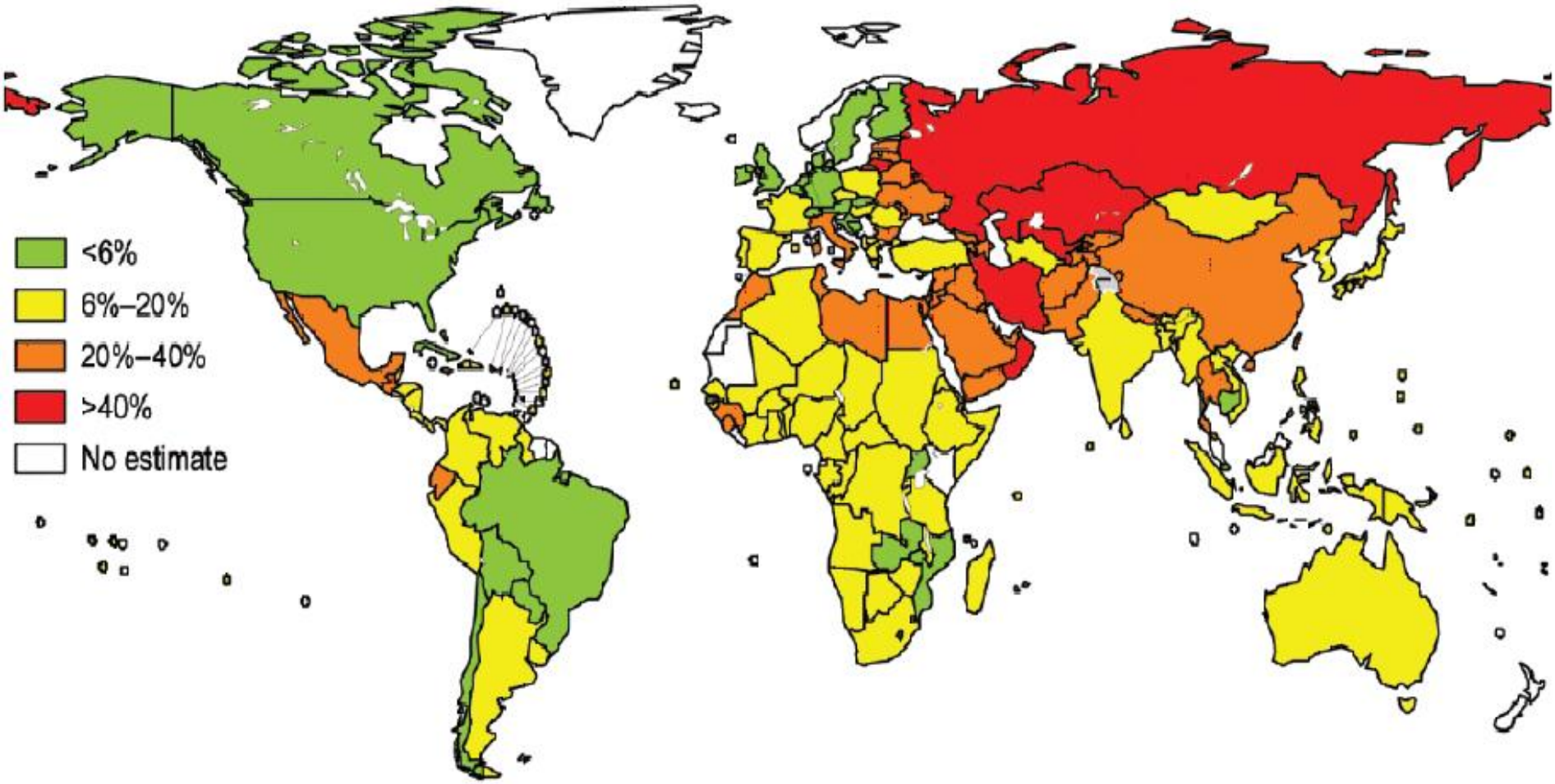

The Developing World faces multiple burdens.

- Poverty, malnutrition, rapid population growth, social deprivation, rapid urbanization. Together they provide a fertile seed bed for epidemics.
- A lack of resources, infrastructure, war and social strife prevent an adequate response to the high incidence of both TB and HIV.

Care in the community

- Provide information and education on TB and HIV to increase community awareness of both infections and their inter-relationship.
- Include TB case detection and care in training of HIV/AIDS caregivers (family members, volunteers, and health care workers).
- Prevent new cases of TB among HIV positive people and their families by offering Isoniazid preventive treatment when appropriate.
- Intensify tuberculosis screening in areas of high HIV prevalence,

Care in a clinical setting

- Those people with diagnosed TB should be encouraged to screen for HIV, along with appropriate counselling and support.
- Those people with a diagnosis for HIV to be routinely screened for latent TB and if found, it should be treated.
- Staff in specialist settings can provide comprehensive care. TB nurses to become conversant with HIV issues and HIV nurses to be aware of the impact of TB.

A grim future?

- Two preventable and treatable illnesses are growing in parallel.
- *TB feeds on the ravages caused by HIV, whilst HIV confounds efforts to control TB.*
- The danger is that the rich West will abandon the developing world. For the West – outside of the occasional hotspot – TB and HIV will become “tropical diseases” – of little concern.

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Reading

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