

Odds in the Management of Extra-pulmonary TB

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Tuberculosis

A Global Emergency

- TB kills 5,000 people a day – 2-3 million each year**
- One third of the world's population is infected with TB**
- TB kills more young women than any other disease**
- More than 100,000 children will die needlessly from TB this year**
- Hundreds of thousands of children will become TB orphans this year**

WHAT ARE EFFECTIVE TB CONTROL STRATEGIES?

- Risk factors for TB cannot be controlled by a TB program: poverty, overcrowding, HIV
- BCG vaccine has not been shown to be consistently effective (except for childhood TB meningitis)
- Best TB control intervention for both prevention and treatment is early detection and effective therapy: DOTSc

Extra-pulmonary TB

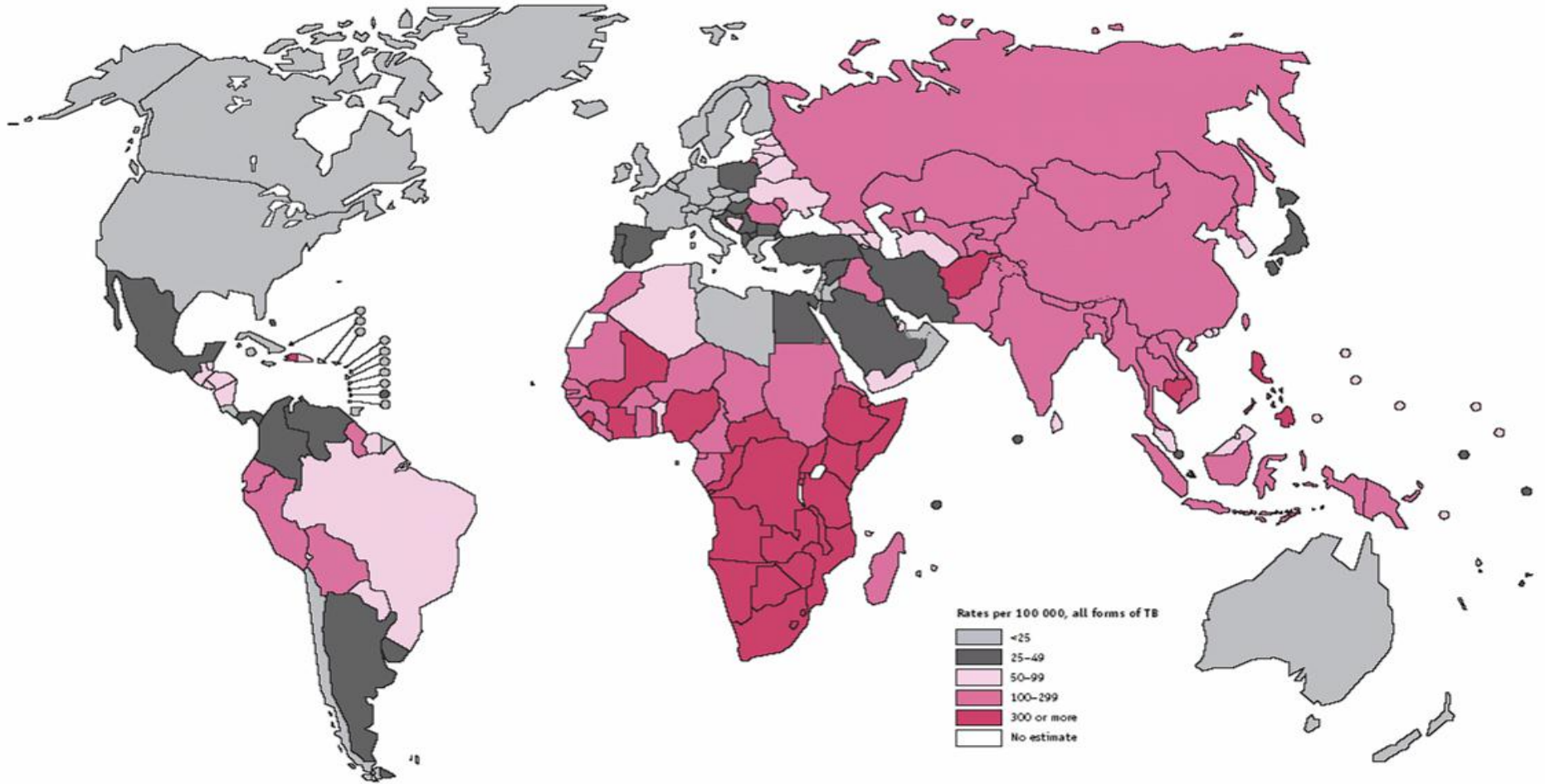
- **TB of organs other than lung parenchyma**
- **Diagnosis based on at least 1 culture +ve specimen from an extra pulmonary site,**
 - **or histological**
 - **or strong clinical evidence consistent with active extra PTB**
- **followed by a decision by a doctor to treat with a full course of ATT.**

WHERE IS TB A PROBLEM?

22 WHO High Burden Countries

<u>COUNTRY</u>	<u>RATE (per 100,000)</u>	<u>COUNTRY</u>	<u>RATE (per 100,000)</u>
India	168	Kenya	540
China	113	Viet Nam	192
Indonesia	256	Tanzania	363
Nigeria	304	Brazil	62
Bangladesh	221	Uganda	377
Pakistan	181	Zimbabwe	683
Ethiopia	370	Mozambique	436
Philippines	320	Thailand	128
South Africa	558	Afghanistan	333
DR Congo	383	Cambodia	549
Russia	126	Myanmar	154

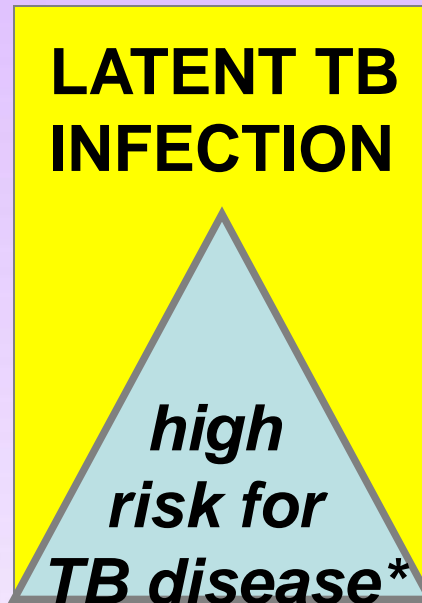
I. Estimated TB incidence rates, 2002



The designations employed and the presentation of material on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dashed lines represent approximate border lines for which there may not yet be full agreement.

“The World is Divided into 3’s”

Relative Proportions Will Vary

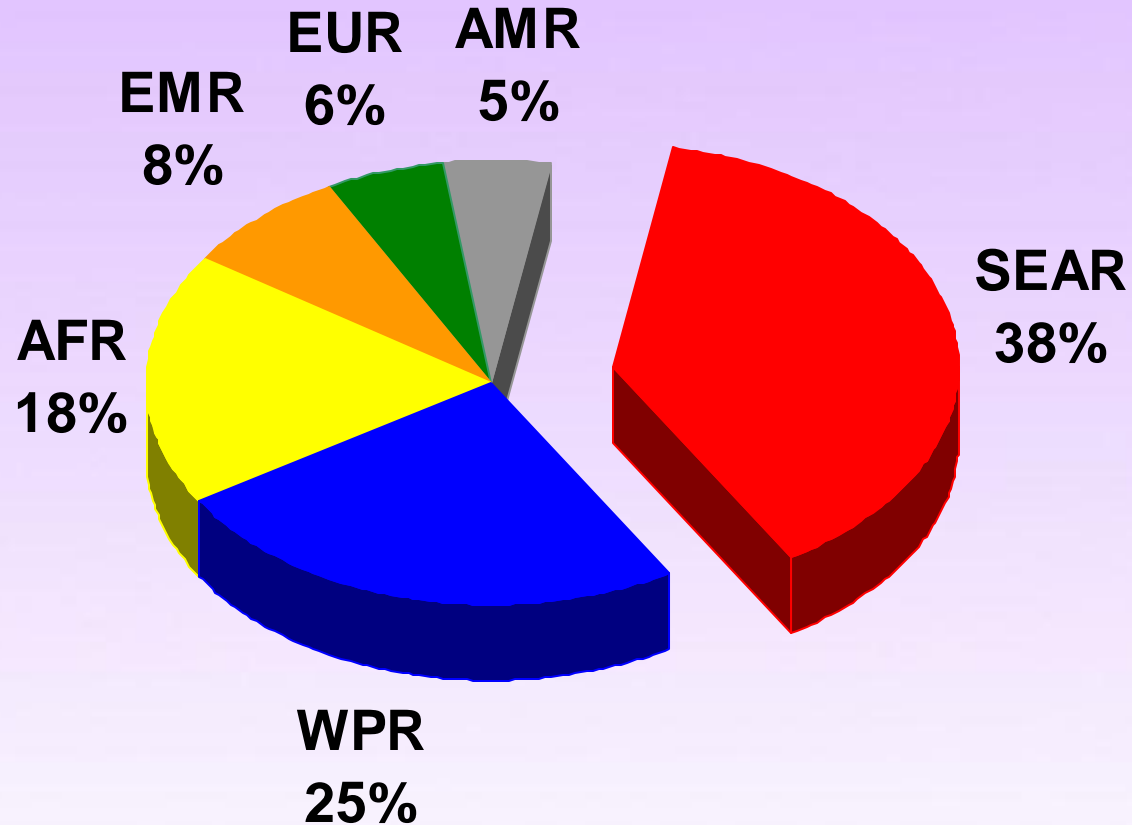


**those recently infected*

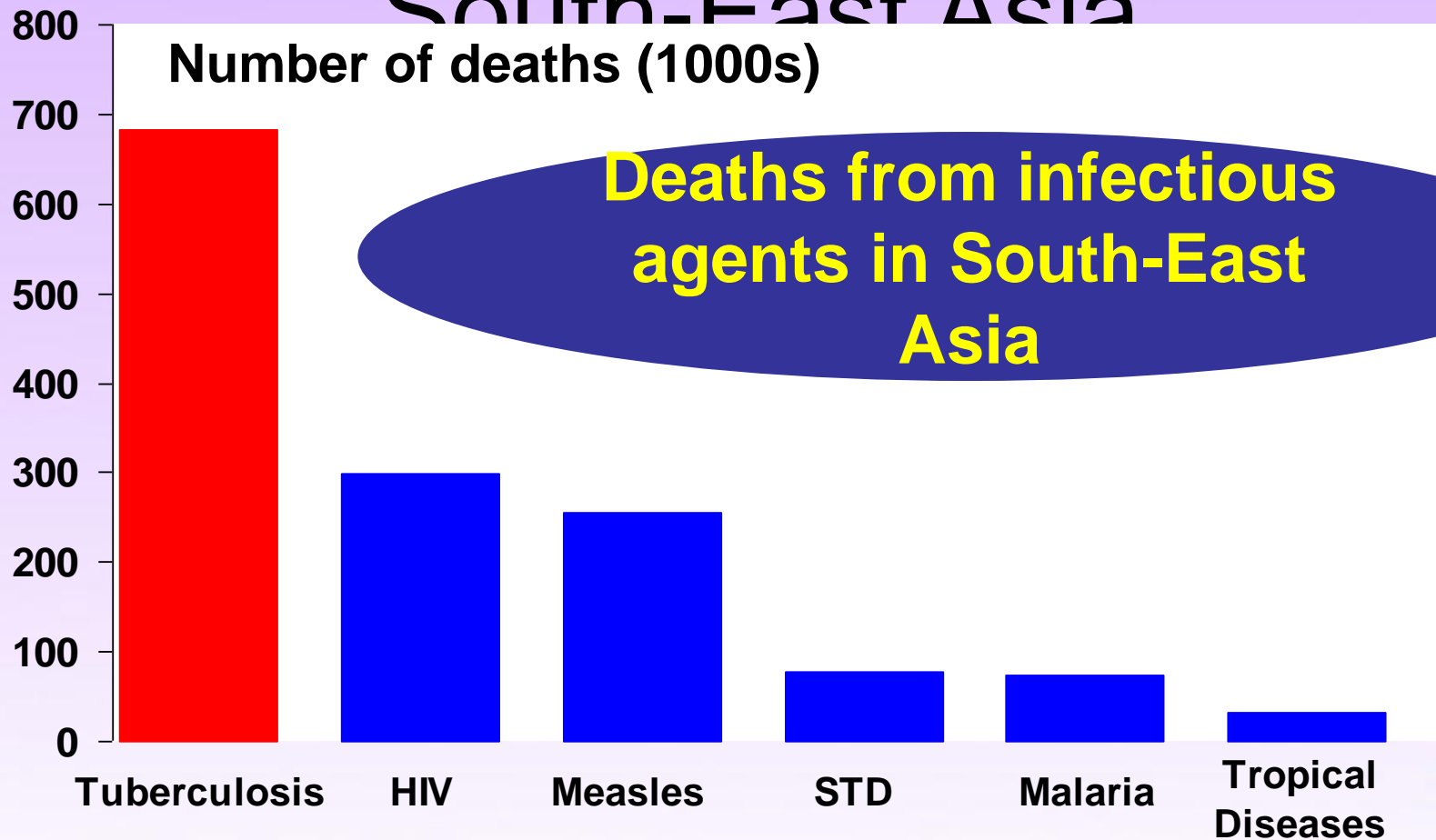
**those infected likely to progress*

**includes social and medical aspects*

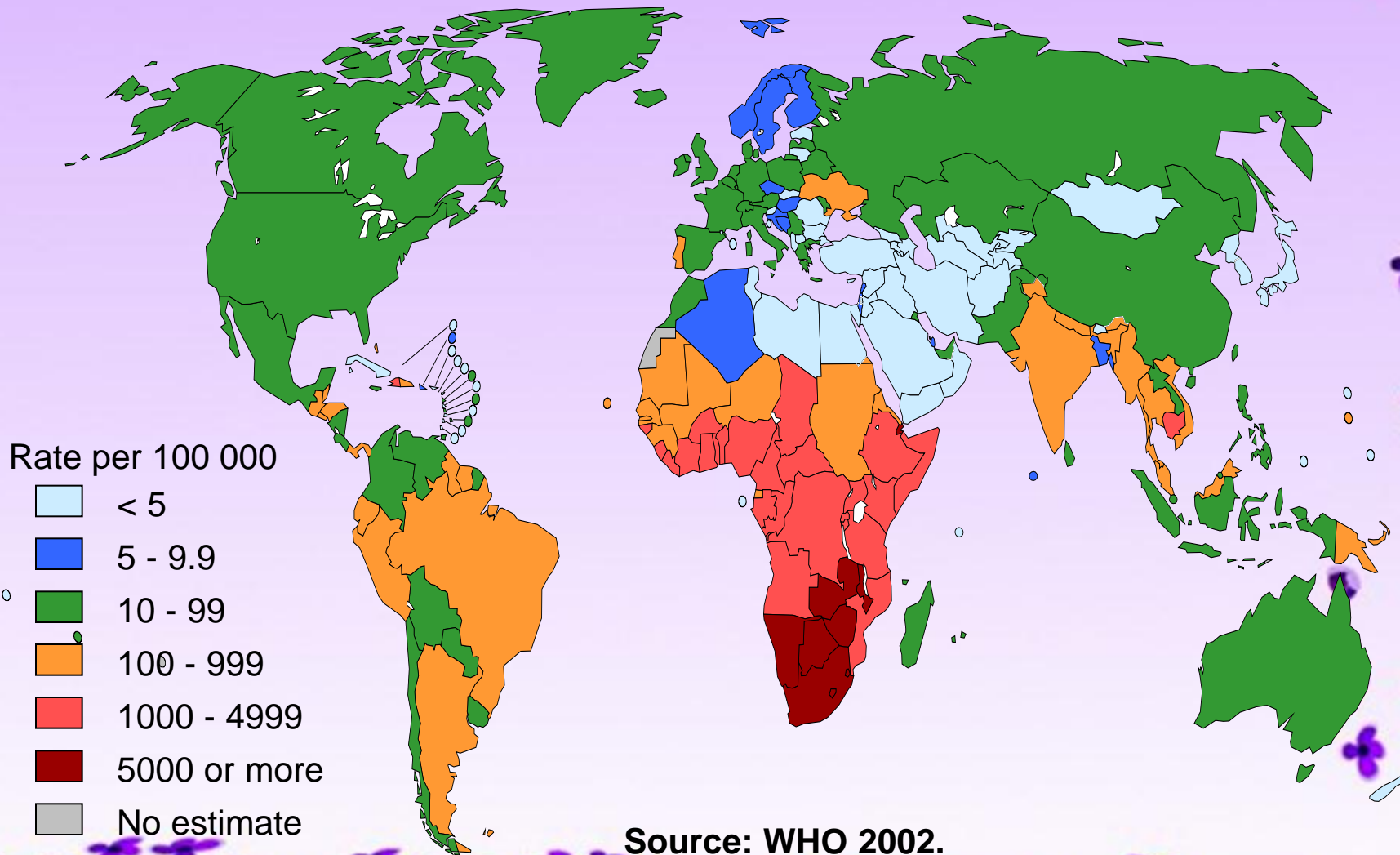
South-East Asia accounts for nearly 40% of all tuberculosis cases



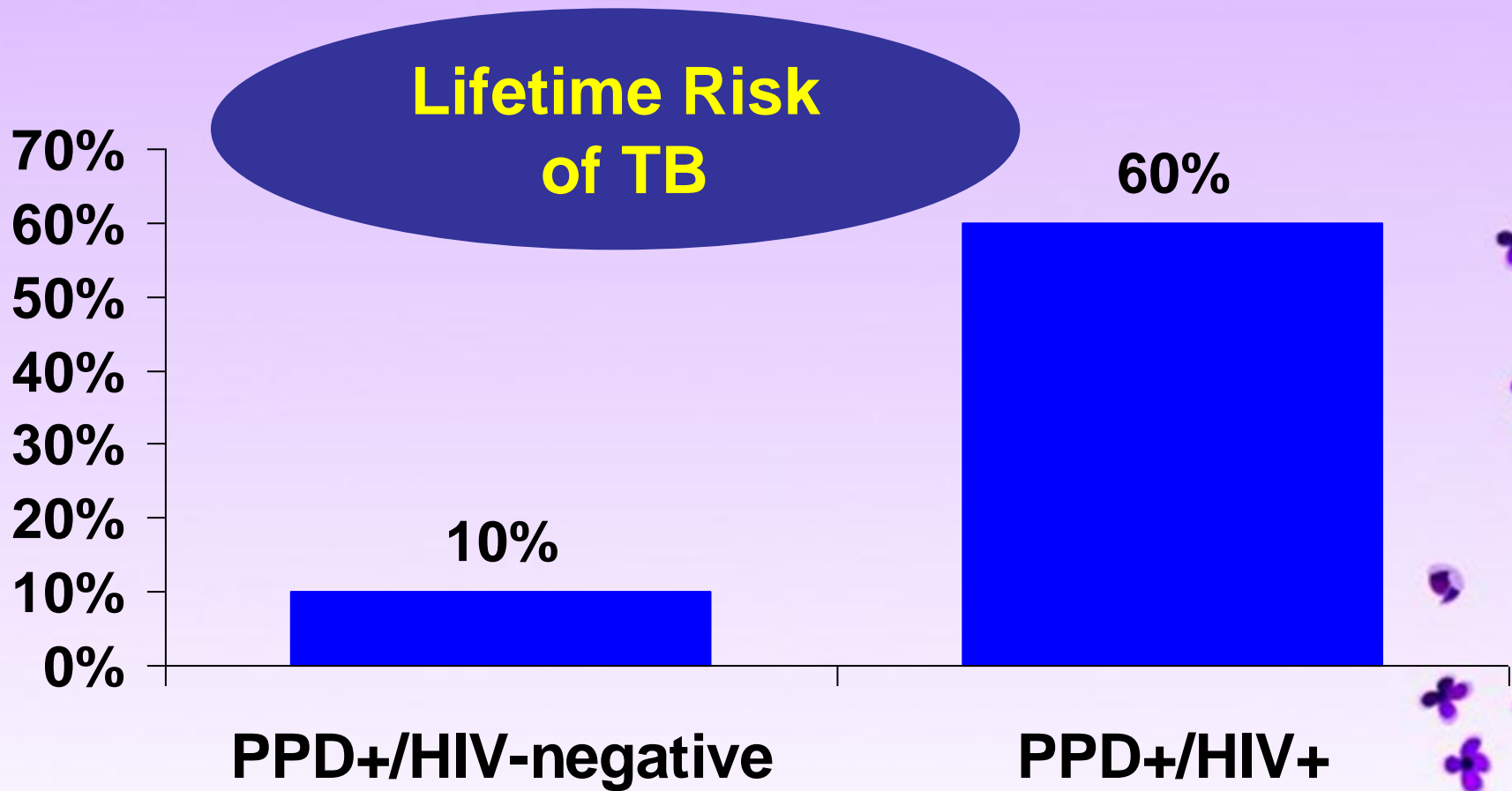
TB is the leading single infectious cause of death in South-East Asia



Estimated HIV-MTB Coinfection Prevalence, 2000



TB and AIDS



The effect of HIV infection on symptoms and signs of TB

Symptom/sign	HIV positive (%)	HIV negative (%)
Dyspnea	97	81
Fever	79	62
Sweats	83	64
Weight loss	89	83
Diarrhea	23	4
Hepatomegaly	41	21
Splenomegaly	40	15
Lymphadenopathy	35	13

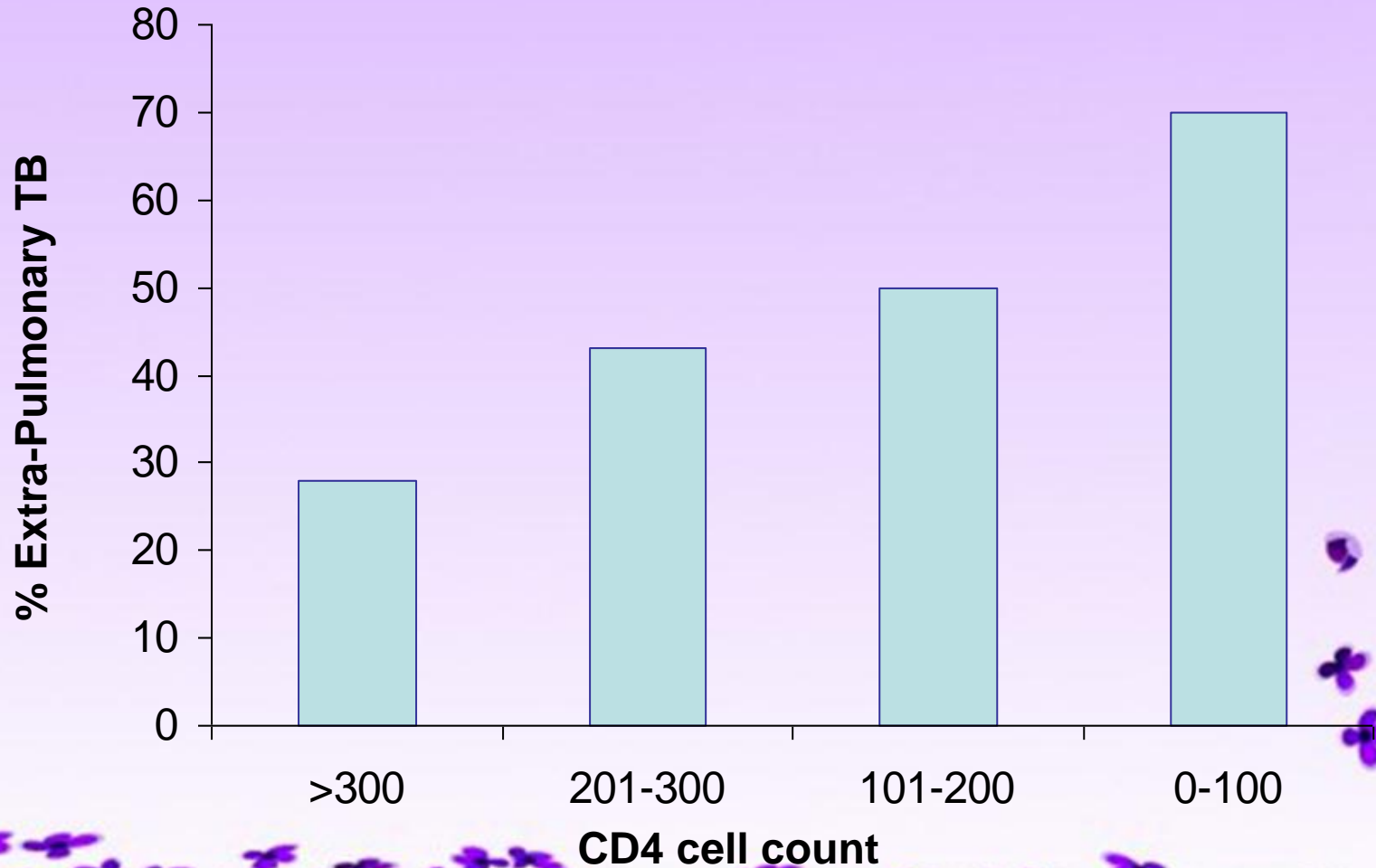
Severe and less severe forms of extra-pulmonary TB

Severe	Less Severe
Meningitis	Lymph nodes
Miliary	Pleural effusion (unilateral)
Pericarditis	Bone (excluding spine)
Bilateral or extensive pleural effusion	Peripheral joint
Spinal	
Intestinal	

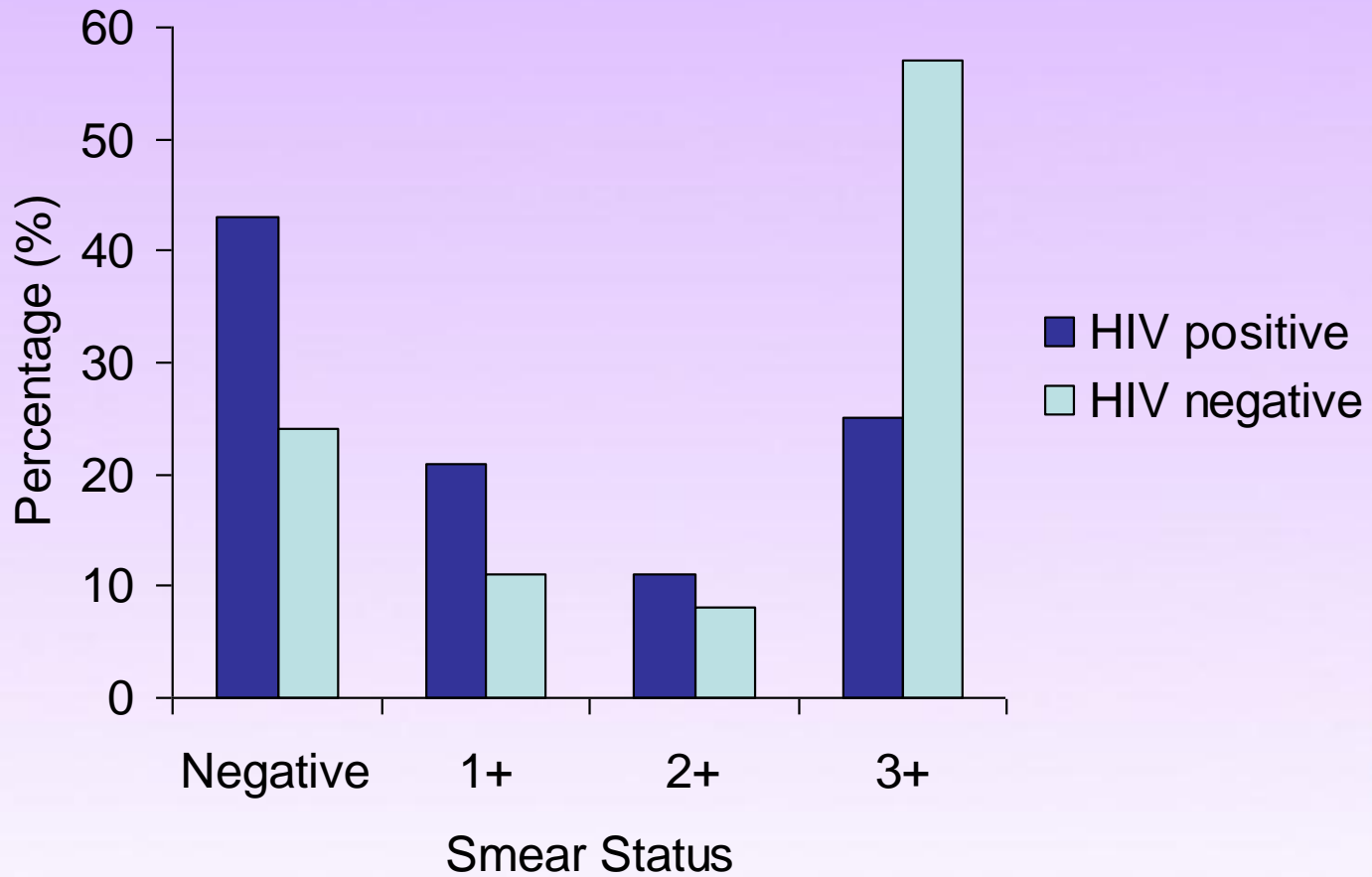
Sites of involvement and HIV status

Site	HIV positive (%)	HIV negative (%)
Pulmonary	40	72
Extrapulmonary	34	16
Both	26	12
Pleural	31	19
Pericardial	15	3
Lymph node	19	3

Extrapulmonary manifestations (%) and the severity of immunosuppression (CD4 cell count)



Sputum smear and HIV status



TB Serous Effusions

- Always examine the aspirated fluid
- A biochemistry lab. Is not essential to diagnose exudate. Simply leave the aspirate standing: if it clots, it is an exudate
- The diagnosis is usually presumptive
- Interpret lab. Result with caution. If there is a delay in lab. Analysis, the result may be falsely low
- IF A PATIENT HAS EXTRA-PULMONARY TB, ALWAYS LOOK FOR PTB

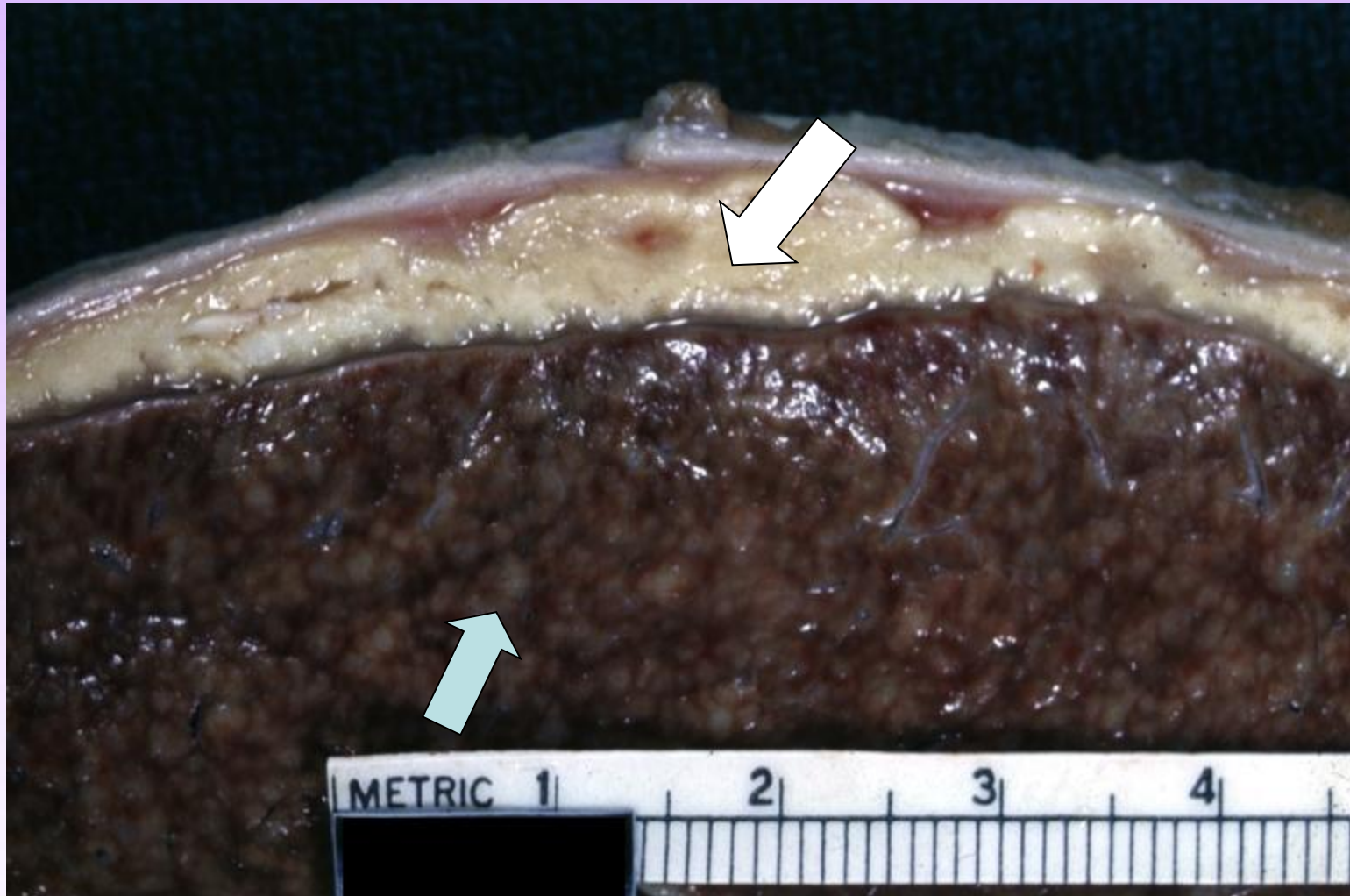
Initial laboratory tests for an undiagnosed serous effusion

- Protein and LDH in serous fluid and serum for separation of transudates and exudates
- Serous fluid smears and culture
- Cell count and differential
- Serous fluid glucose, amylase, pH
- Serous fluid cytology
- Markers for TB serositis
 - ADA, gamma interferon or PCR

The yield of tests to diagnose pleural TB

Test	HIV pos. (%)	HIV neg. (%)
Pleural fluid - smear	15	8
 culture	91	78
Pleural biopsy - smear	69	21
Sputum culture	53	23

TB Peritonitis + liver Miliary TB



Scrofula

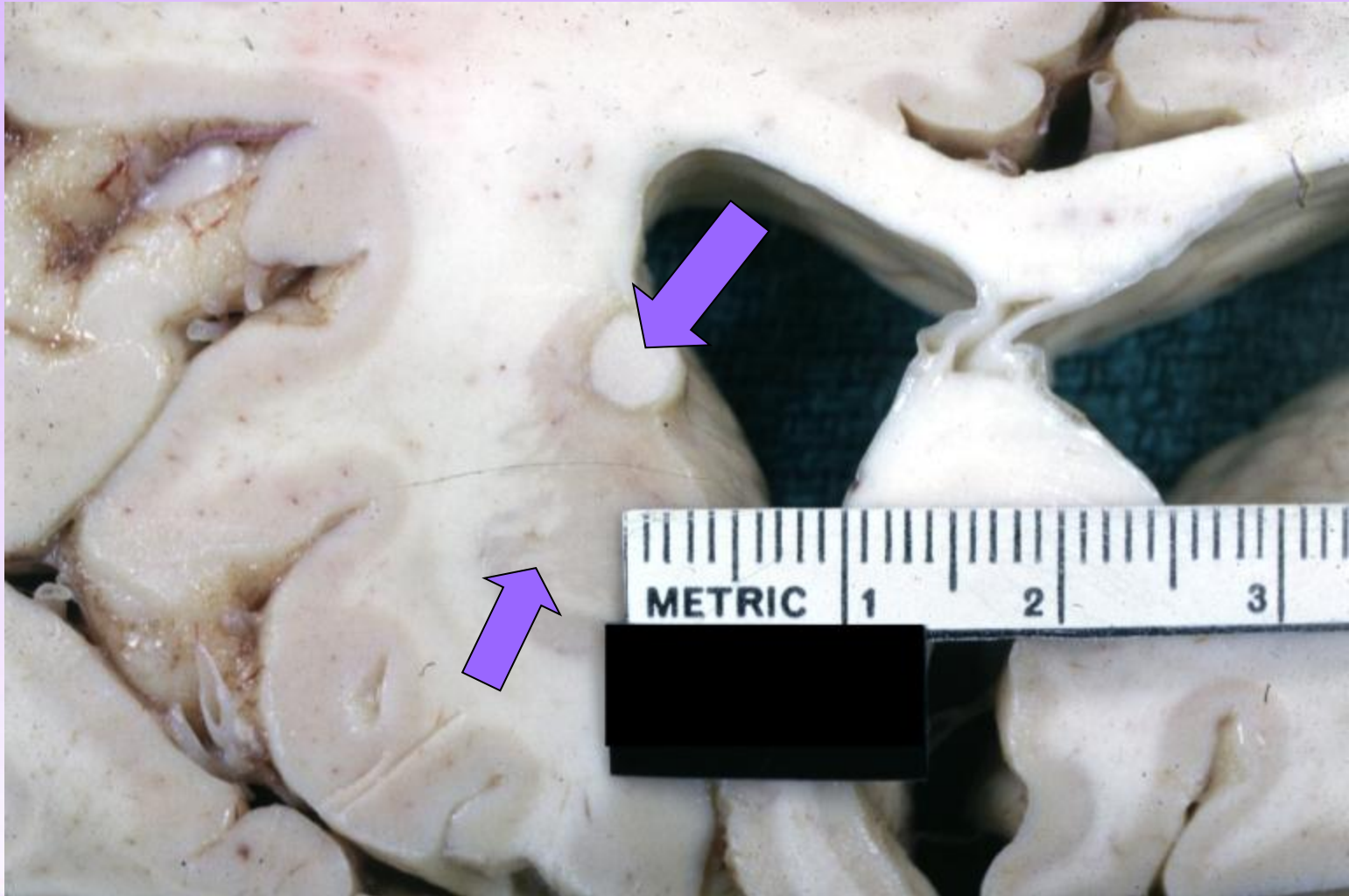
Primary Disease of Cervical Lymph Nodes



© Martin Myers, MD



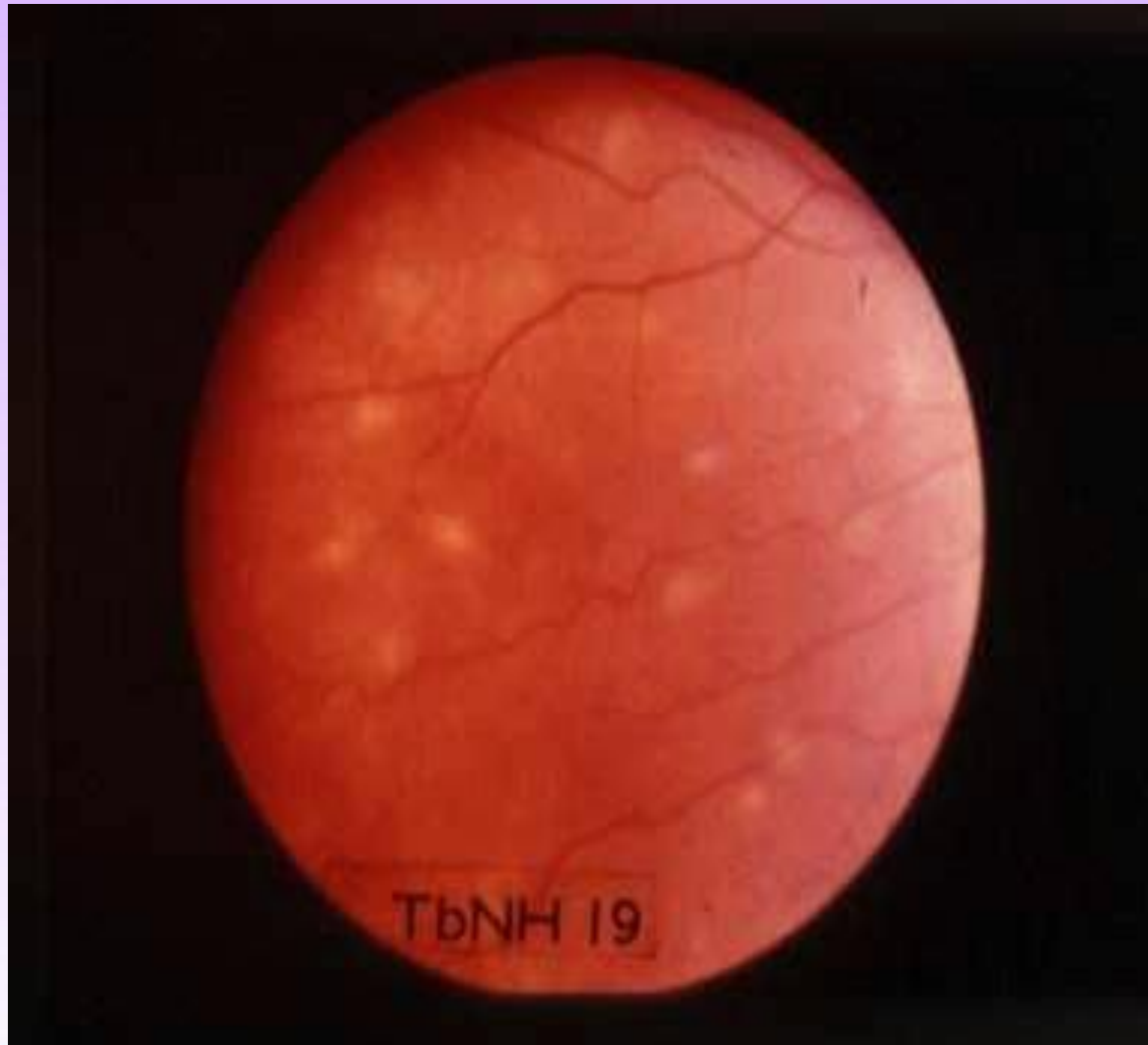
TB Brain – Caudate n.



TB Meningitis



CNS TB – Fundal Photograph



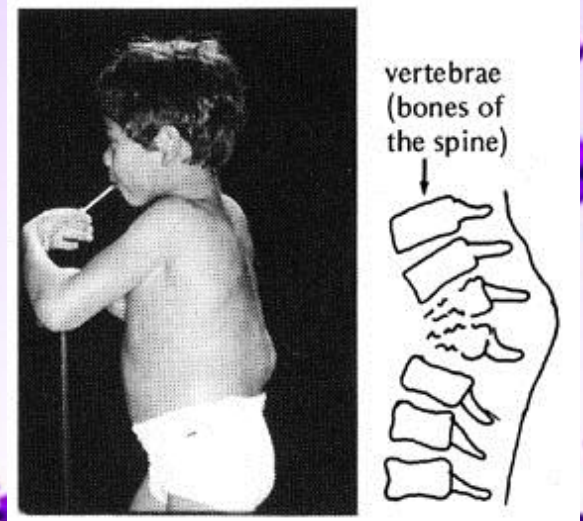
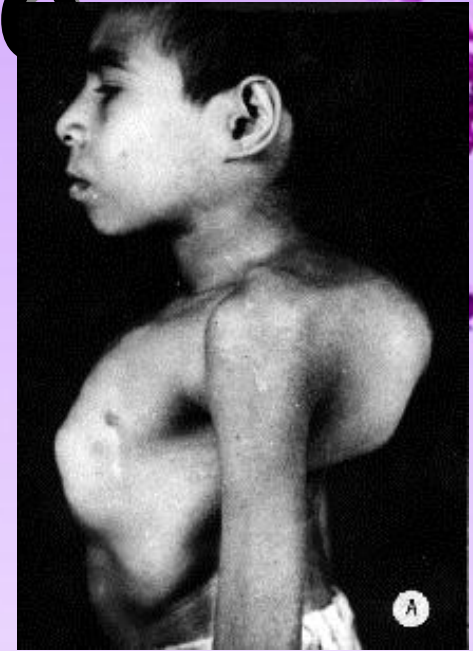
3 or more of the following are required to make a diagnosis of TBM -

- **CSF pleocytosis and protein greater than 0,8g/litre**
- **CSF microscopy positive or ADA greater than 5 units/litre or bromide partition test less than 1,6**
- **Radiographic changes suggestive of TB or sputum or gastric washings positive on direct examination or tuberculin test positive**
- **CT of the brain showing ventricular enlargement, basal enhancement and/or tuberculomata**
- **A clinical course consistent with TBM**

Pott's disease



Destroyed vertebrae with Cold Abscess





Paravertebral
Abscess



TB Osteomyelitis



TB Arthritis/Dactylitis



TB Arthritis/Osteomyelitis



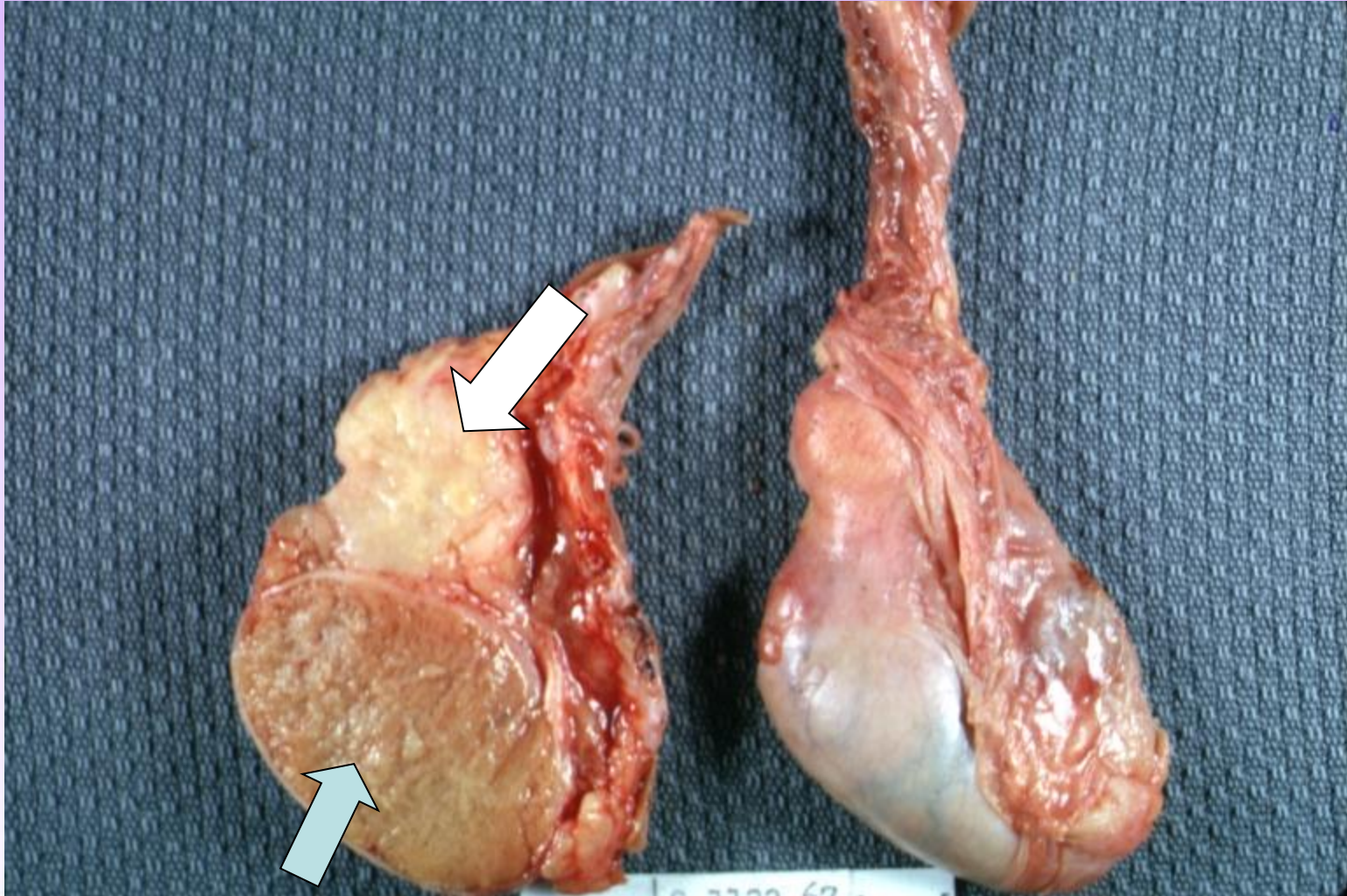
TB Intestine



Adrenal TB - Addison Disease



Testes TB Orchitis.



TB cutis indurativa



TB primary complex





DOIA

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Department of Dermatology



TB cutis scrofulosa

TB cutis verrucosa



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Erythema induratum of Bazin



Erythema Nodosum



Papulo-necrotic Cutaneous TB



Lupus vulgaris



Evaluation for TB

- **Medical history**
- **Physical examination**
- **Mantoux tuberculin skin test**
- **Chest radiograph**
- **Bacteriologic or histologic exam**

“Clinical judgement”

Tuberculosis is one of the great imitator.

Two basic approaches to TB Dx

- **Direct approach**
 - Microscopy
 - Culture
 - Genotypic methods
 - Phenotypic methods
- **Indirect approach**
 - Detection of antibodies for TB Dx
 - Miscellaneous Diagnostic tests

Tissue based diagnosis

- For extrapulmonary TB
- FNAC
- Biopsy – caseous tubercle has high specificity

Other Imaging

- **Still helpful in clinical medicine**
- **Plain Radiographs**
- **Contrast radiology**
- **Computed tomography**
- **Poor sensitivity & specificity**

Clinical diagnosis of TB

- **Chronic febrile wasting syndrome**
- **Characteristic organ specific symptoms & signs**
- **Clinical, laboratory & radiological markers of active disease**
- **Supportive investigations (most of which are not definitive)**
- **Exclusion of other differential diagnosis by investigation combined with observation over a period**

Rx of Extrapulmonary TB

- **Regimen similar to PTB**
- **Duration 6 -12 months or longer depending on clinical response of individual patient**
- **TB meningitis advisable for 12 months**
- **Steroids should be given in TB meningitis, pericarditis, genito-urinary tract TB and may also be considered in miliary TB**
- **If PZA cannot be used in the initial phase, continuation phase must be increased to 7 months**

The Odds

- **Definitive diagnosis of TB depends on isolation of organism from secretions, body fluids & biopsy specimens**
- **In clinical practice, <20% of the cases being treated as TB has the definitive diagnosis, for various reasons**

The Odds

- **NTP- emphasis on diagnosis & treatment of sputum smear positive cases**
- **A substantial percentage of cases are smear negative, delayed diagnosis of such cases has harmful effects on individual patients**
- **RFLP analysis suggested smear negative cases contribute much more to ongoing transmission**

The odds

- **Many of the available know-how & technology for TB diagnosis are at odds for the clinicians & patients**
- **Clinical algorithm (patient characteristics & radiographic findings) are still the basis for diagnosis of TB on a widespread basis**

The odds

- **Despite many diagnostic innovations, there are very few tests of cure and more so for EPTB**
- **Not enough evidence regarding duration of Rx of EPTB**
- **Many clinicians are not satisfied with the duration of Rx for EPTB**

Conclusion (1)

- **In the absence of an effective vaccine, treatment of active cases remain the most important component of NTP**
- **In the absence of a rapid & accurate diagnosis, there are substantial economic costs related to unnecessary empiric treatment & adverse effects**

Conclusion (2)

- **NTP should try improve the diagnostic accuracy over the sputum smear based diagnostic policy**
- **Clinicians should attempt diagnostic accuracy to replace empiric therapy, by using tests of definitive diagnosis more & more**



THANKS