

PATOLOGIA SISTEMATICA 1
Lezione 28 Marzo 2012
MICOBATERI: IMMUNITA' E MALATTIA



Cattedra Malattie Respiratorie
U.O.C. Malattie Respiratorie
Policlinico Universitario "Tor Vergata"
Università degli Studi di Roma "Tor Vergata"

Tubercolosi (TB) : Infezione e malattia

- ▶ La TB è una malattia infettiva causata da *M. Tuberculosis* (MTB) ed, occasionalmente, da altri micobatteri del *M. tuberculosis complex* (*M.bovis* e *M.africanum*)
- ▶ L'infezione si sviluppa nel 40–90% dei soggetti esposti, questi sviluppano una reazione tubercolinica positiva (PPD+), che è quindi usata per diagnosticare l'infezione.

Tubercolosi (TB) : Infezione e malattia

- ▶ Entro due anni dal contatto l'infezione può determinare malattia manifesta nel 5–10% degli infetti ma rimane silente nel 90–95%, grazie alla capacità del sistema immune di limitare la crescita dell'MTB.
- ▶ Dopo i primi 2 anni dal contatto, l'infezione latente può andare incontro a riattivazione causando malattia manifesta nello 0.1–0.5% dei soggetti infettati per anno a causa della caduta delle difese immuni dovuta all'invecchiamento o all'insorgenza di immunodeficienza.

Fattori di rischio per la trasmissione della TB

Nell' uomo, una singola esposizione ad una fonte di contagio è sufficiente per contrarre l' infezione e sviluppare la malattia tubercolare.

studi ambientali sulla trasmissione della TB durante voli intercontinentali, così come studi occupazionali sulla trasmissione della TB durante procedure chirurgiche praticate su lesioni tubercolari insospettite, hanno dimostrato che in seguito ad una singola esposizione una frazione consistente di individui esposti può acquisire l' infezione tubercolare.

Fattori di rischio per la trasmissione della TB

- Contagiosità della persona affetta
- Ambiente in cui avviene l'esposizione
- Durata dell'esposizione
- Virulenza dell'organismo

Relazione tra intensità dell' esposizione e sviluppo di infezione da *M. tuberculosis*

<i>Origine e dimensioni della popolazione in studio</i>	<i>Percentuale di convertitori (PPD-positivi) tra:</i>			
	Famiglie di controllo	Contatti familiari con pazienti affetti da TB		
		Coltura negativa¹	Coltura positiva²	BAAR positiva³
Inghilterra (1954, 709 contatti)	22	18	27	65
Canada (1954, 1876 contatti)	2.5	26	26	45
Olanda (1967-69, 148 contatti)	1	8	5	50

¹ Caso indice con TB clinicamente attiva BAAR-, coltura- (< 30-100 CFU/ml)

² Caso indice con TB BAAR-, coltura+ (< 5-10,000 CFU/ml)

³ Caso indice con TB BAAR+ (>5-10,000 CFU/ml)

Classificazione della tubercolosi

Fasi della infezione tubercolare e della TB polmonare (ATS)

- 0. non contatto: tubercolina (PPD) negativa
- 1. Contatto senza infezione: PPD-
- 2. Infezione: PPD+, RX normale, non sintomi
- 3. TB attiva: PPD+, RX anormale, batteriologia positiva
- 4. TB inattiva: PPD+, lesioni RX stabili, batteriologia negativa
- 5. TB sospetta

Classificazione della tubercolosi

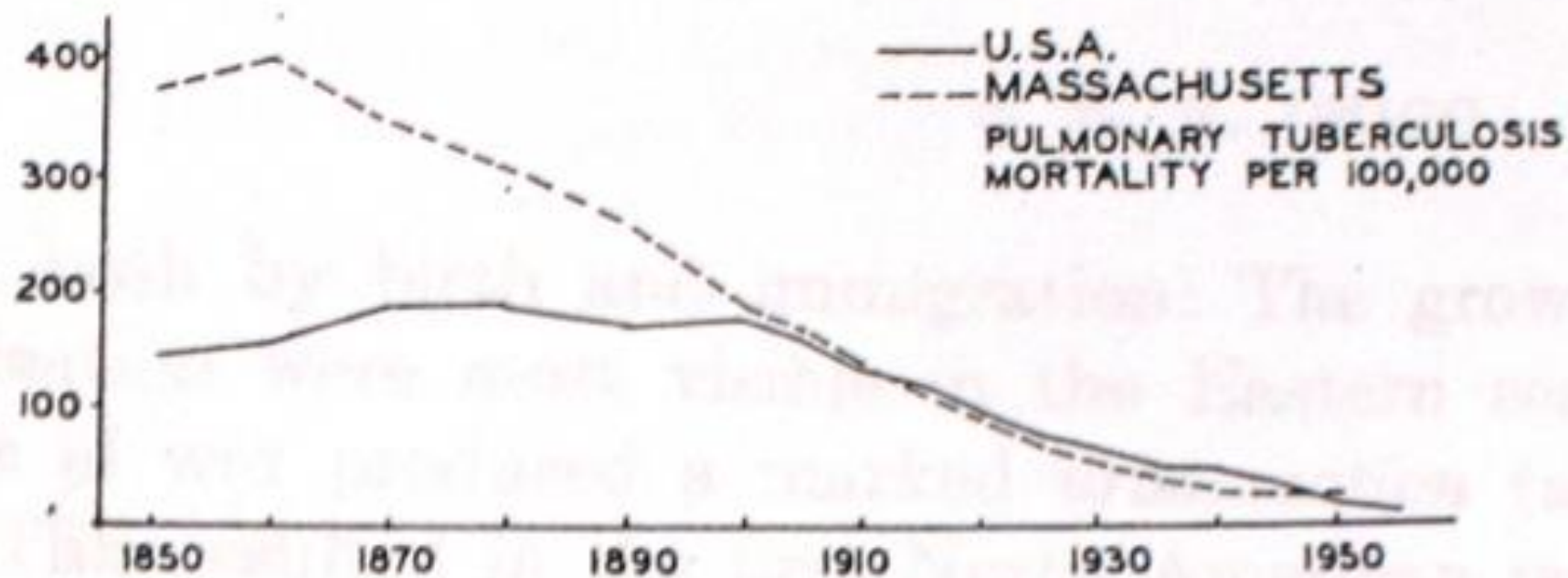
- Infezione tubercolare
- TB primaria:
 - complesso primario con adenopatia, sindrome adeno-bronchiale
 - TB sub primaria: milare, meningite tubercolare, pleurite

Classificazione della tubercolosi- 2

- TB post-primaria
 - areattiva
 - Essudativa: pleurite, infiltrato tisiogeno, lobite, broncopolmonite
 - Produttiva: miliare circoscritta degli apici e miliare cronica
 - Miliare acuta: miliare dell' immunocompromesso
 - Esiti e sequele
 - TB extrapolmonare

Epidemiologia

ARCANA OF TUBERCULOSIS



Storia Naturale ed Epidemiologia
della Tubercolosi

THE AMERICAN REVIEW OF TUBERCULOSIS AND PULMONARY DISEASES

VOLUME 78

August, 1958

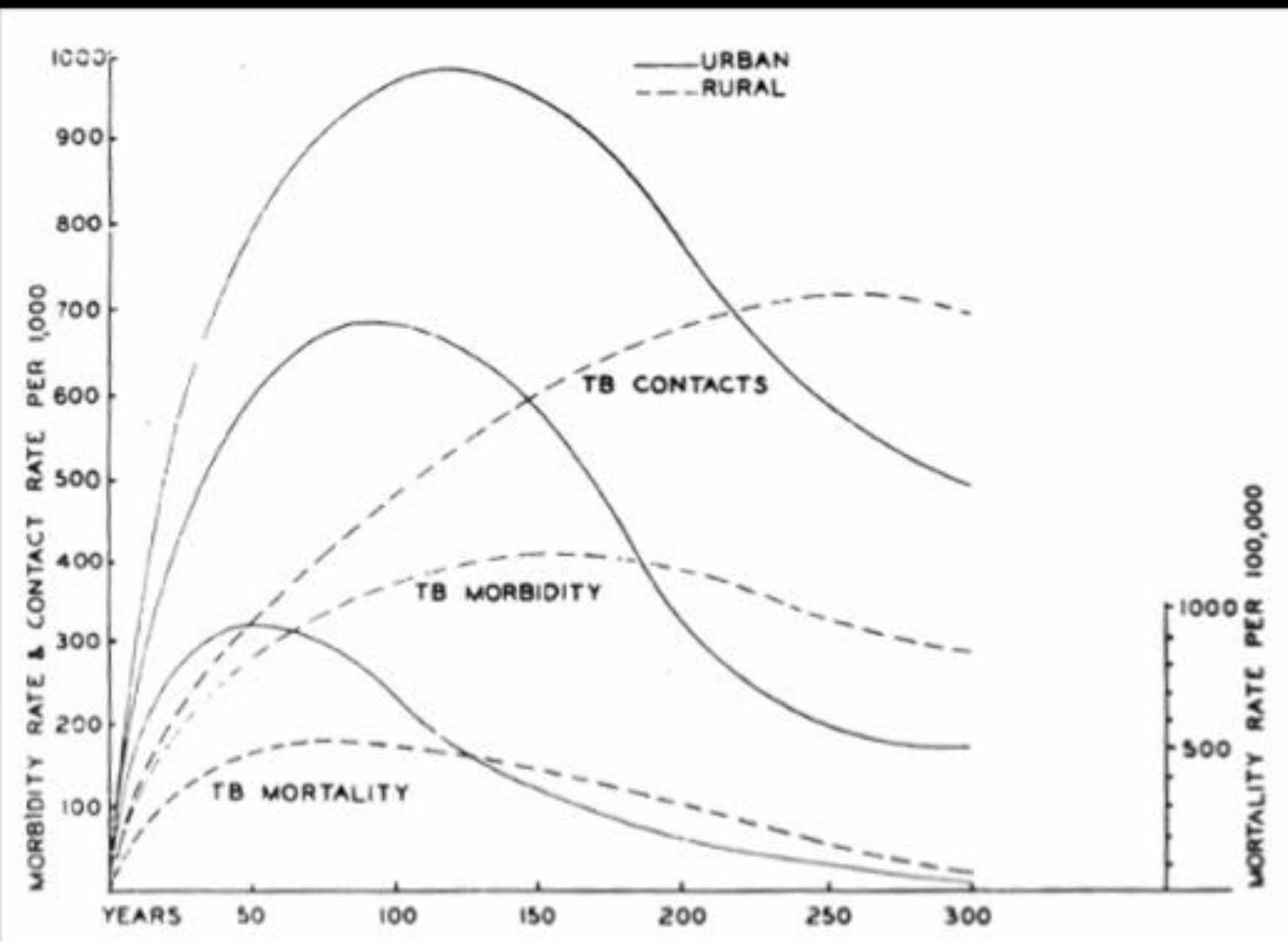
NUMBER 2

THE ARCANA OF TUBERCULOSIS

With a Brief Epidemiologic History of the Disease in the U.S.A.

E. R. N. GRIGG¹

(Received for publication January 6, 1958)



Storia Naturale ed Epidemiologia della Tuberculosis

THE AMERICAN REVIEW OF TUBERCULOSIS AND PULMONARY DISEASES

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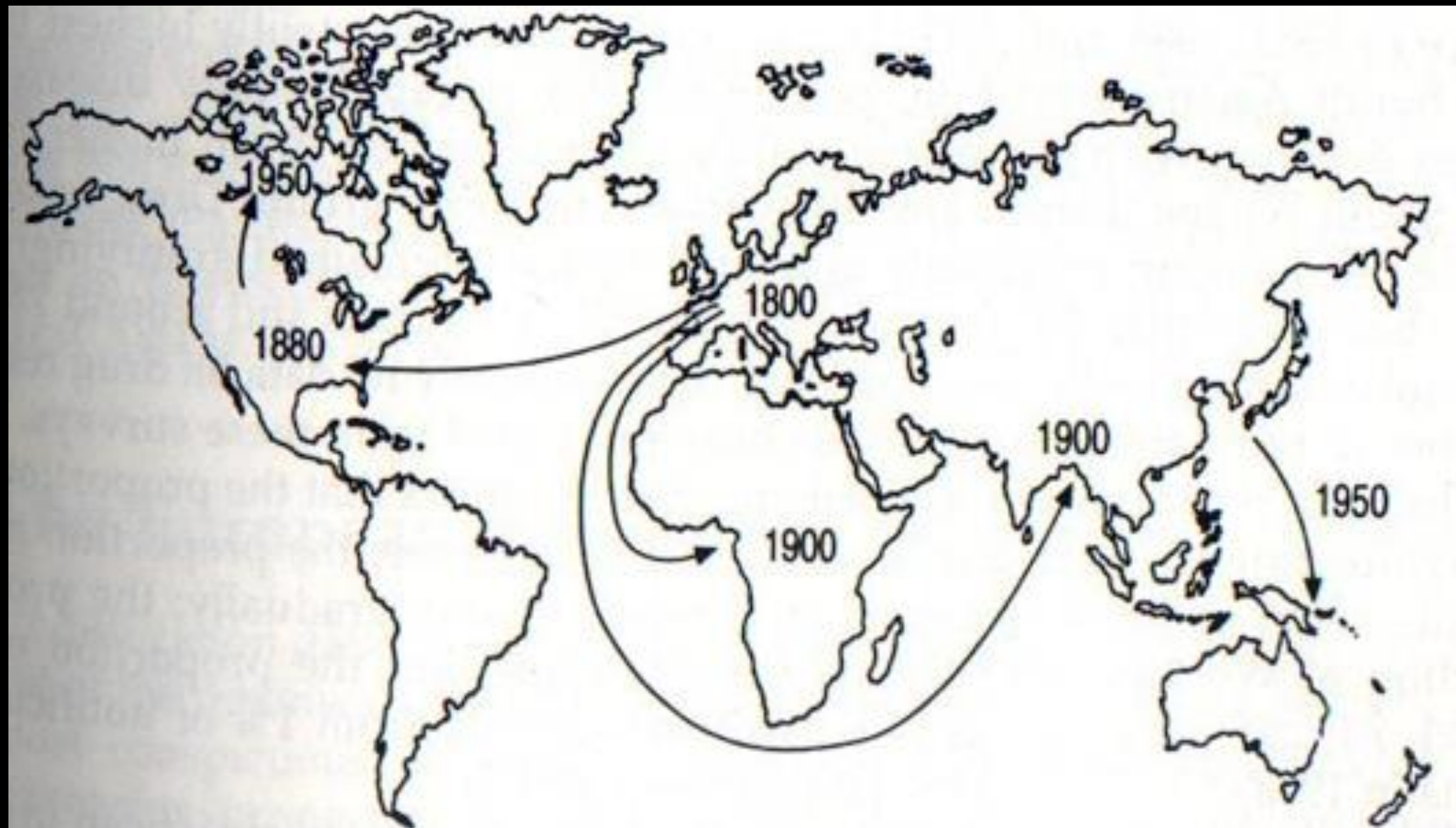
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THE ARCANES OF TUBERCULOSIS

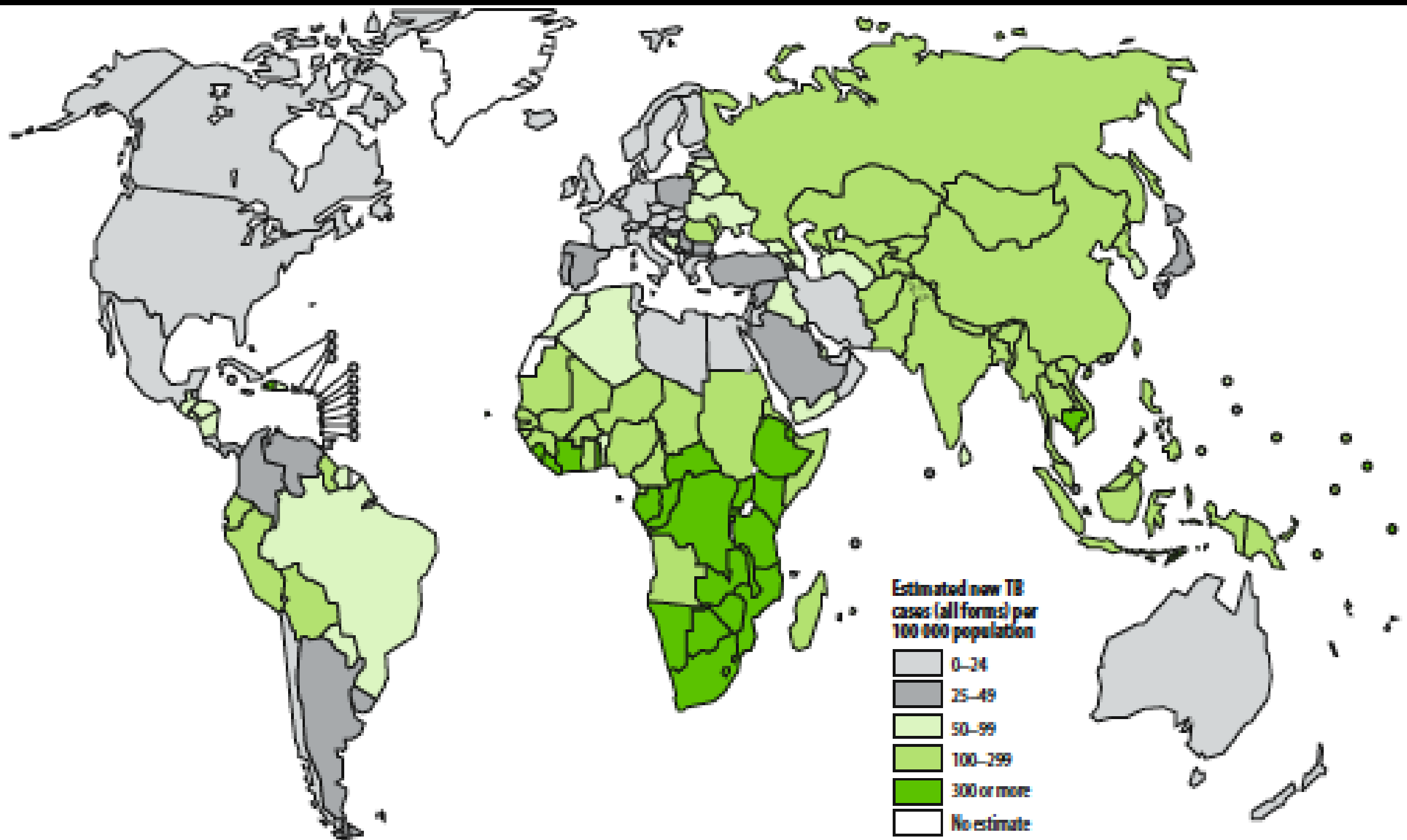
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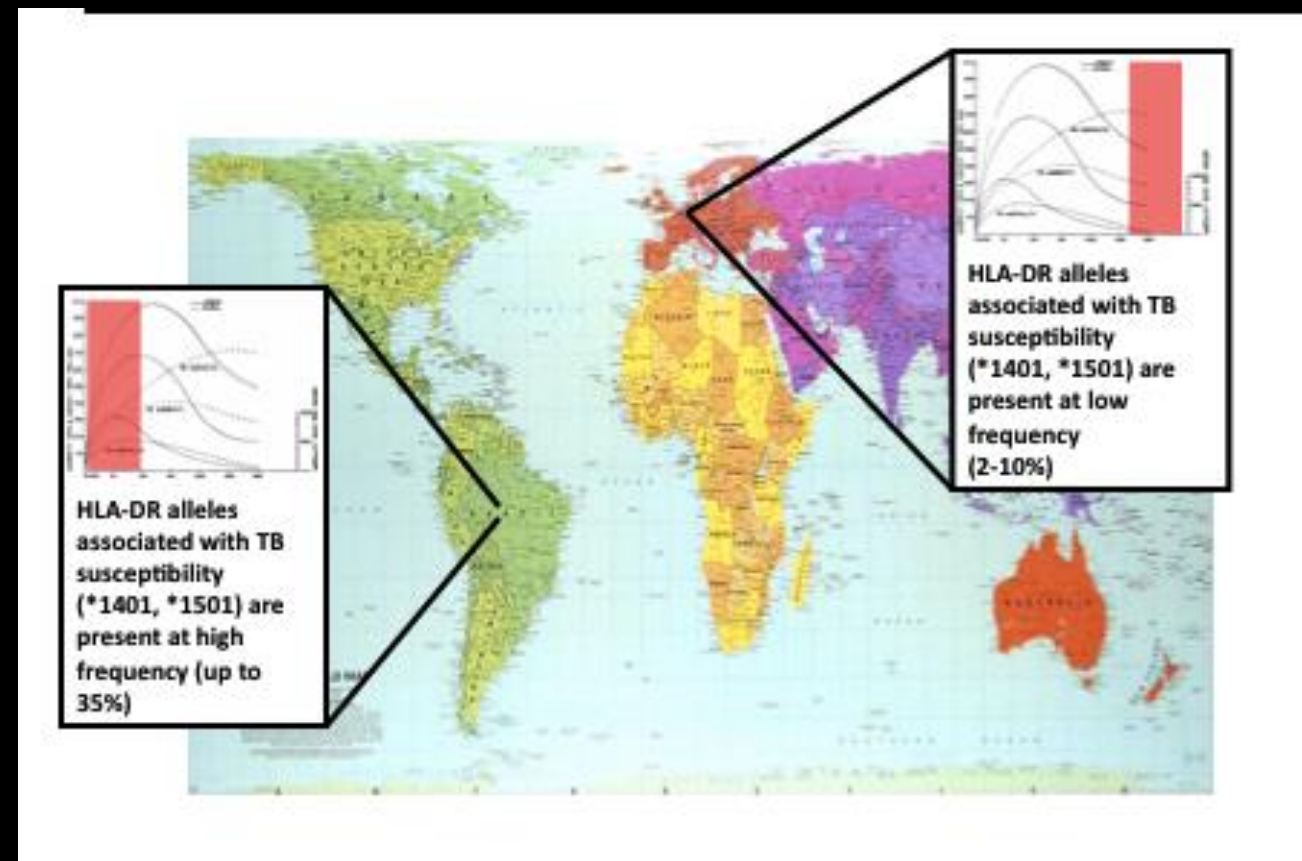


Colonizzazione e tubercolosi



Incidenza della Tubercolosi

Tuberculosis estimated rates, 2005, WHO Report 2009

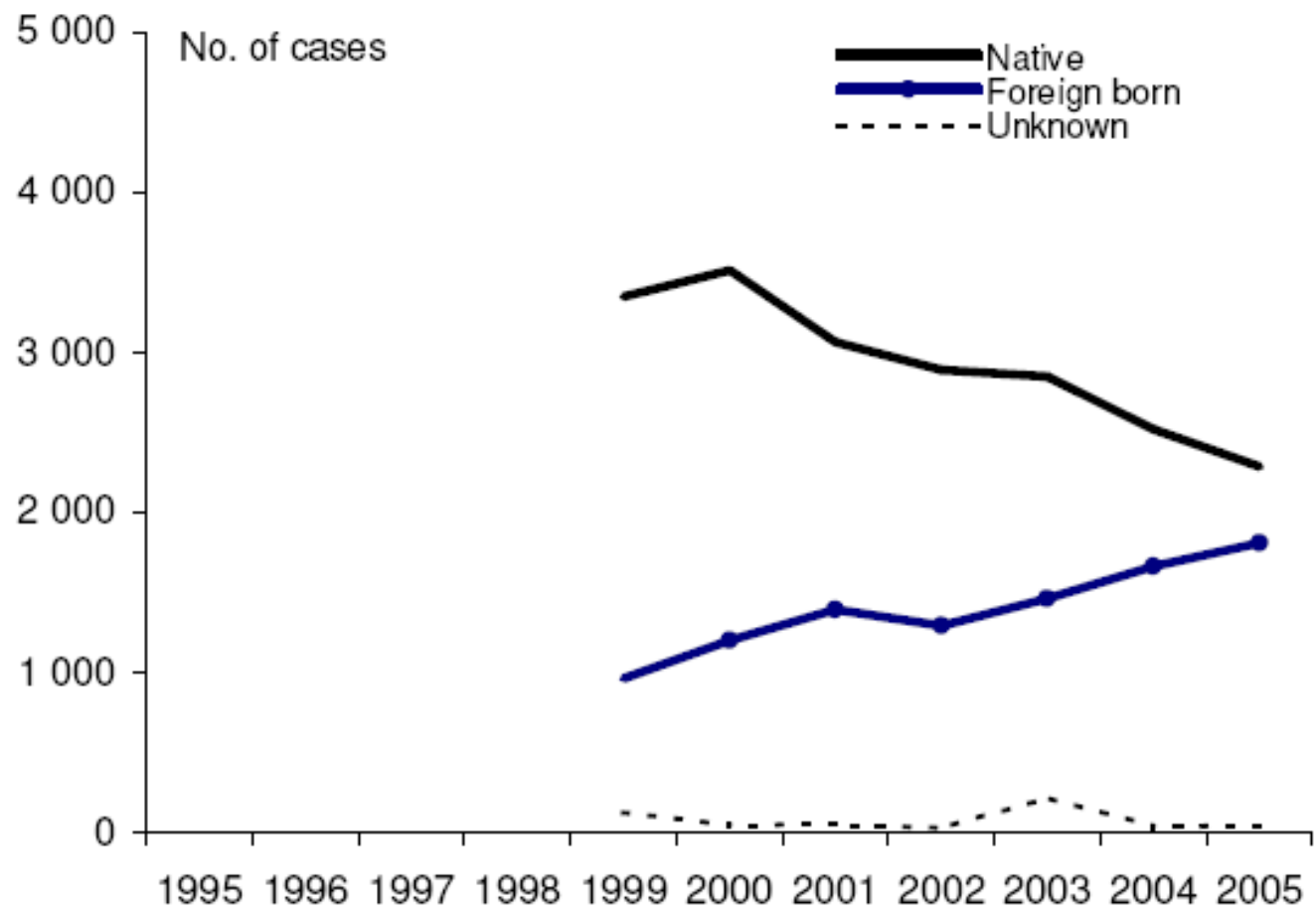


Population studies show that HLA genes play a major role in genetic susceptibility to TB

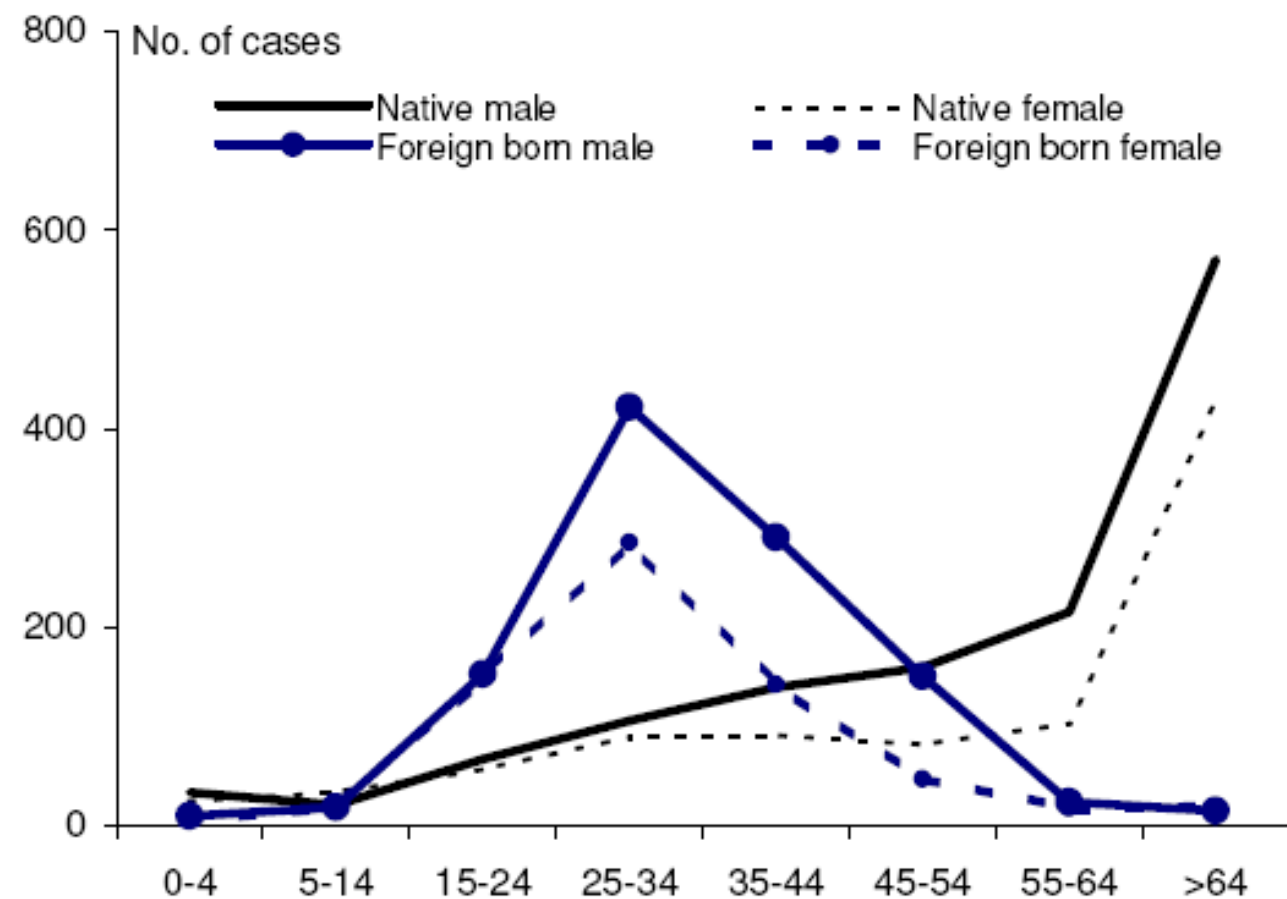
EURO-TB

Epidemiologia 2007: Italia

Tuberculosis cases by geographic origin, 1995-2005

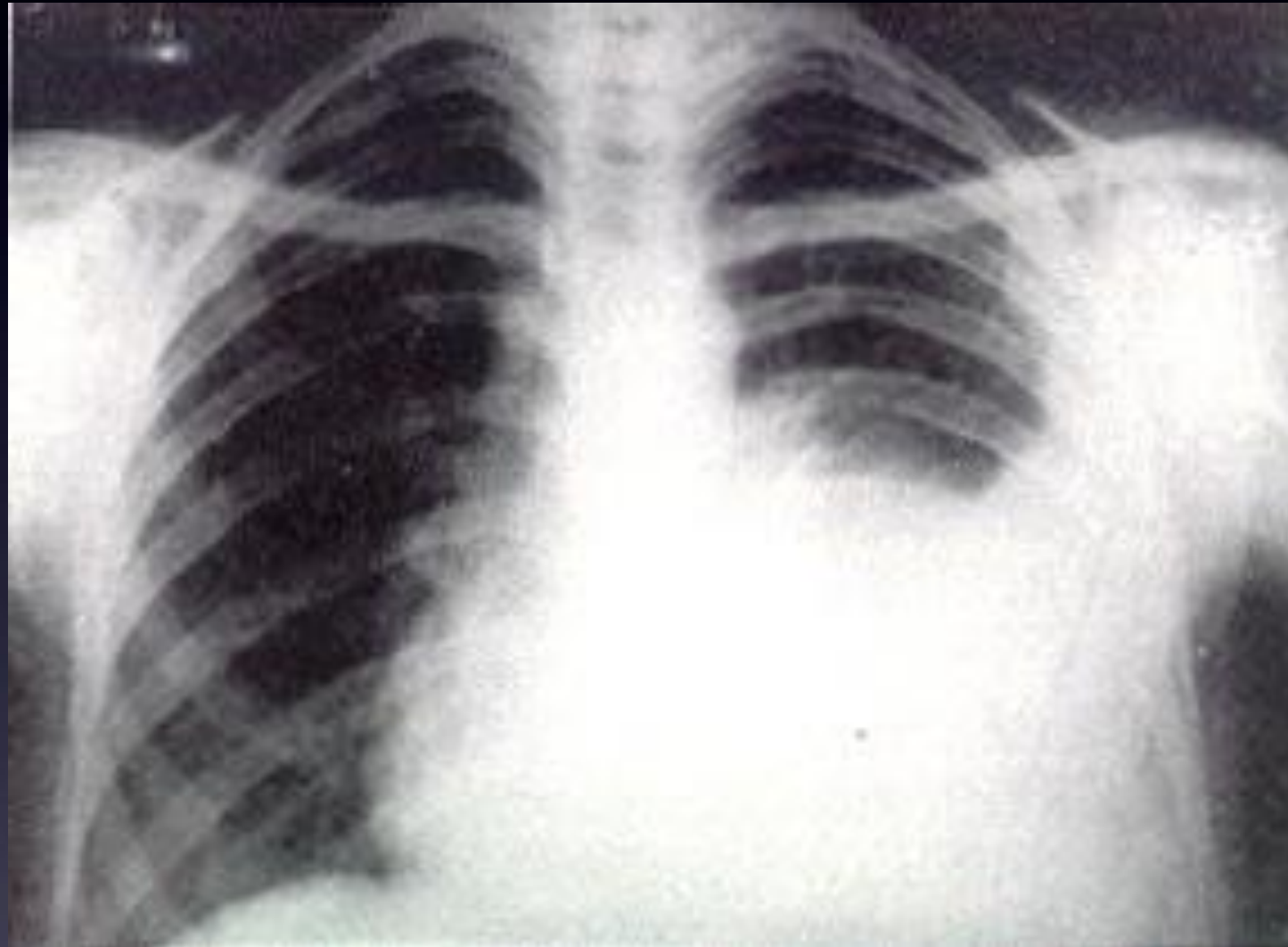


Tuberculosis cases by origin, age group and sex, 2005

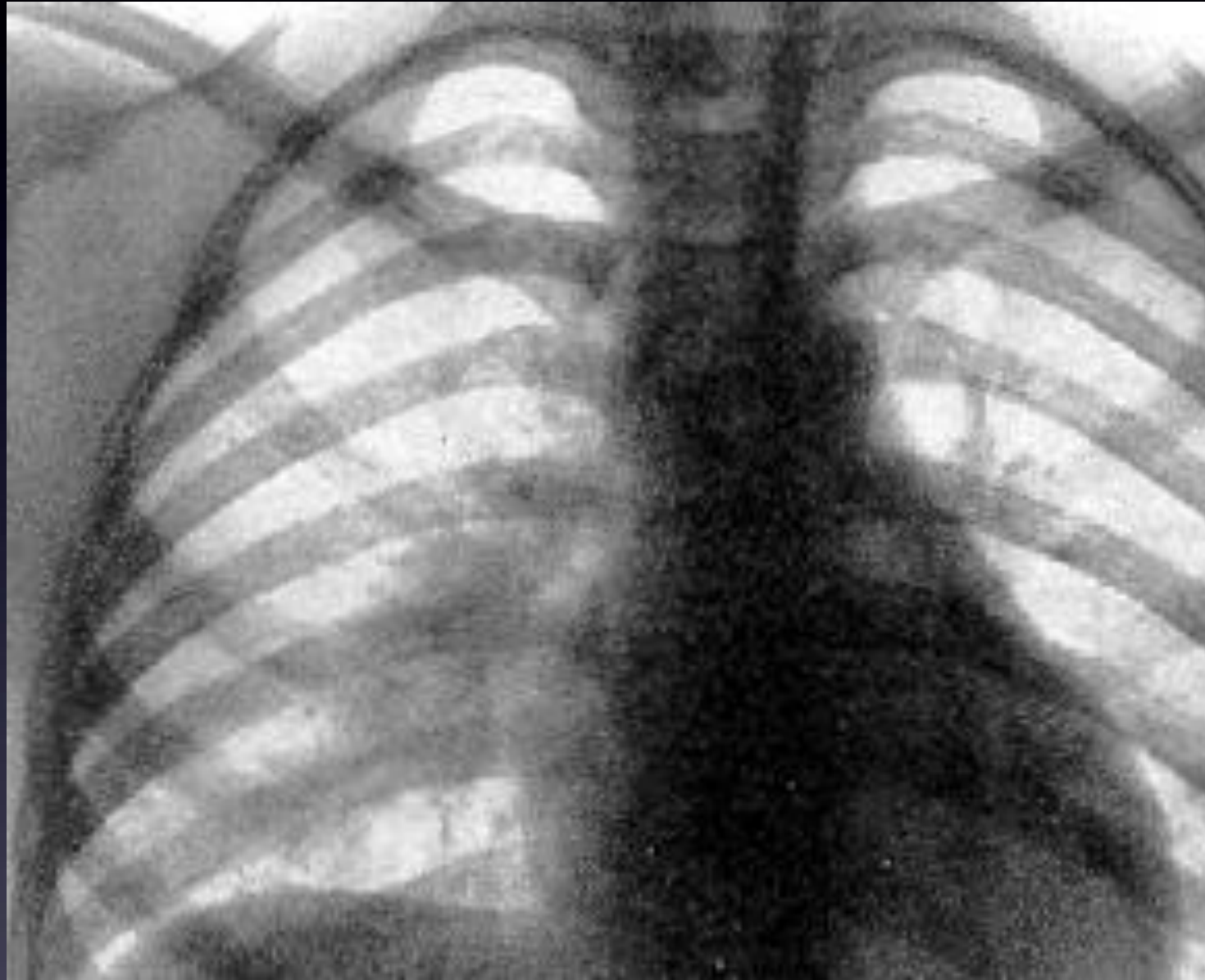


Diagnosi

TUBERCOLOSI POST-PRIMARIA: PLEURITE TUBERCOLARE



TUBERCOLOSI PRIMARIA: ADENOPATIA ILARE DESTRA



TB IN AIDS, CON INFILTRATO
MICRONODULARE DIFUSO, ADENOPATIA
BILATERALE E PLEURITE DESTRA



TUBERCOLOSI POSTPRIMARIA: MILIARE DIFFUSA ED ADENOPATIA ILARE IN HIV



TUBERCOLOSI POST PRIMARIA: INFILTRATO APICALE DESTRO



**TUBERCOLOSI POST PRIMARIA:
MILIARE CRONICA ESCAVATA
DEGLI APICI**



DEFINIZIONE DI CASO DI TB ATTIVA (ATS)

CRITERI DI LABORATORIO	1. ISOLAMENTO DI MTB O, IN PRESENZA DI COLTURA NEGATIVA
	2. DIMOSTRAZIONE DI MTB IN UN CAMPIONE BIOPTICO PER MEZZO DELLA MICROSCOPIA O DI SONDE DNA
CRITERI CLINICI	1. TEST UBERCOLINICO POSITIVO
	2. ALTERAZIONI DELL' RX TORACE E SEGNI CLINICI DI MALATTIA ATTIVA
	3. RISPOSTA AL TRATTAMENTO CON DUE O PIÙ FARMACI ANITUBERCOLARI

CRITERI IDENTIFICATIVI DI CASO TB (WHO)



Fattori di rischio e sintomi sentinella della TB dell'adulto

1. immigrazione recente da aree ad alta endemia tubercolare (Asia, Africa, Est Europeo)
2. povertà e condizioni di vita disagiate
- 3 convivenza e contatto con pazienti con tubercolosi cavitaria
4. tosse
5. febbre che dura da più di due settimane
6. calo ponderale

FATTORI DI RISCHIO E SINTOMI SENTINELLA DELLA TB DEL BAMBINO

- 1. convivenza con uno o più familiari affetti da TB polmonare**
- 2. rallentamento della crescita e calo ponderale**
- 3. tosse persistente**
- 4. mancata guarigione da un episodio respiratorio acuto**
- 5. linfadenopatia periferica**
- 6. febbre o febbre di basso grado**
- 7. positivizzazione della reazione alla tubercolina**

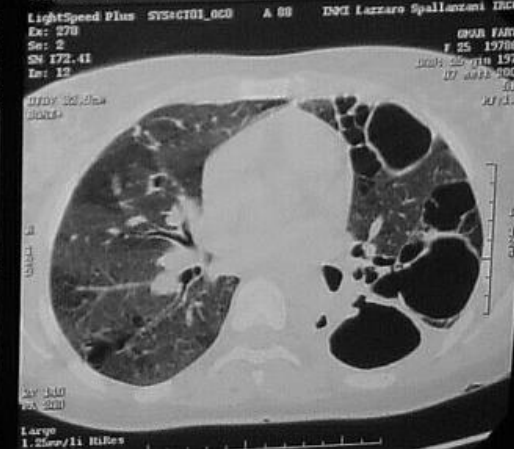
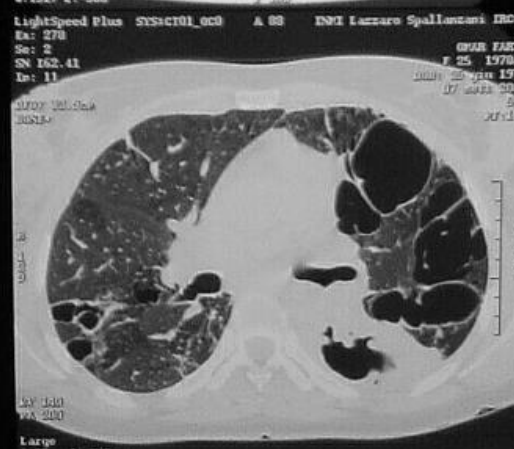
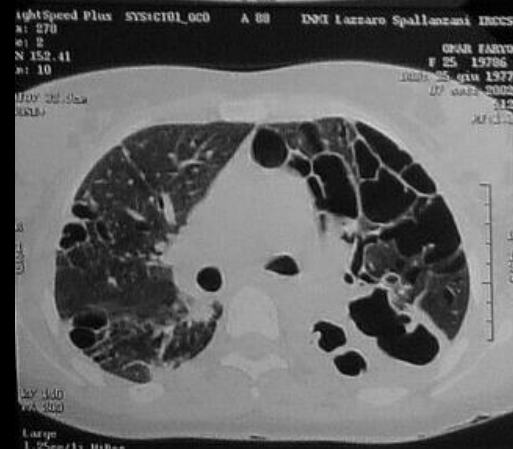
Manifestazioni di
malattia

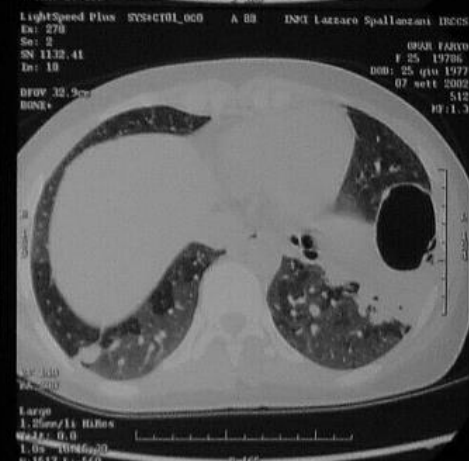
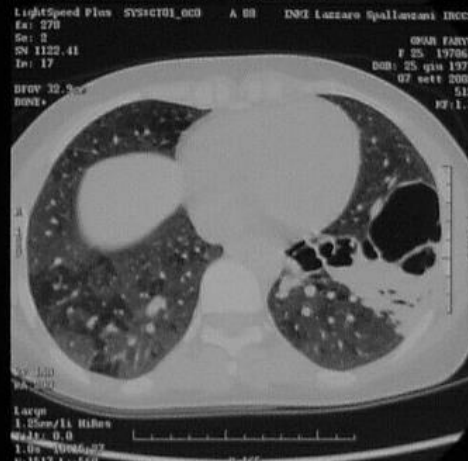
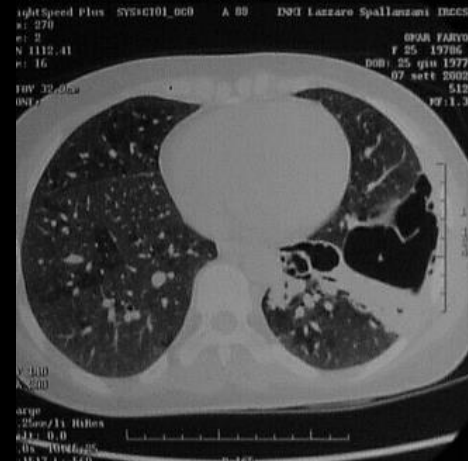
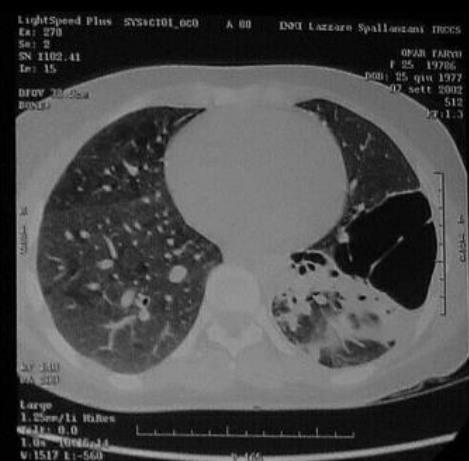
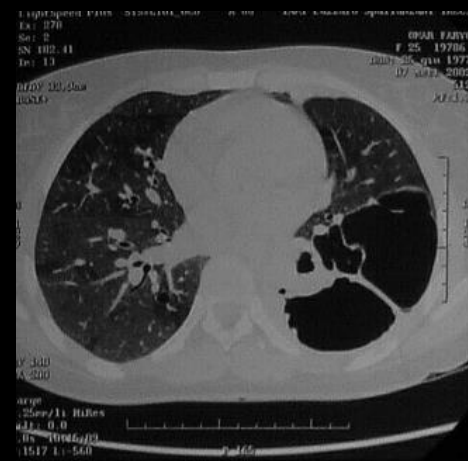
Caso 1

Donna immigrata di 24 anni con febbre

- Donna immigrata di 24 anni, Febbre 40° C, tosse produttiva ed emoftoe
Perdita di peso, circa 12 Kg
- Si ricovera in Malattie Infettive
- Espettorato diretto BAAR+.
- Inizia terapia con INH, RIF, PRZ e ETB, persiste febbre dopo 30 gg
- Inizia metilprednisolone, clari, cipro e strepto, persiste febbre, dopo 50 gg,

- Trasferita in DCMR
- HRCT del torace.
- Espettorato BAAR+
- Modifica terapia:
- Ilevo, etionamide, rifa, clari, INH, EMB e prednisone.
- Persiste febbre dopo 20 gg
- Inizia terapia con pentossifillina (600 mg/die).
- Dopo 30 gg febbre scomparsa, espettorato BAAR-





Diagnosi:

Tubercolosi polmonare

TB essudativa, cavitaria,
resistenza multipla ai farmaci

Caso 2

Donna di 61 anni con anamnesi
familiare per TB

- Donna di 61 anni,
- un caso di TB fatale in famiglia
- pleurite di NDD a 10 anni, cura non precisata
- Bronchite asmatica lieve
- Febbricola astenia e tosse
- Ricovero in Medicina Generale
- Rx torace: lesioni nodulari bilaterali

- Ricovero in DCMR
- Espettorato: BAAR+,
- Inizia terapia anti-TB standard
- Negativizza dopo 25 giorni di cura
- Dimessa in terapia ambulatoriale
- Lenta risoluzione (a 12 mesi) delle lesioni nodulari



Diagnosi:

Tubercolosi polmonare

TB produttiva, miliarica cronica “a grossi nodi”

Caso 3

Donna di 56 anni con artrite
reumatoide e febbre

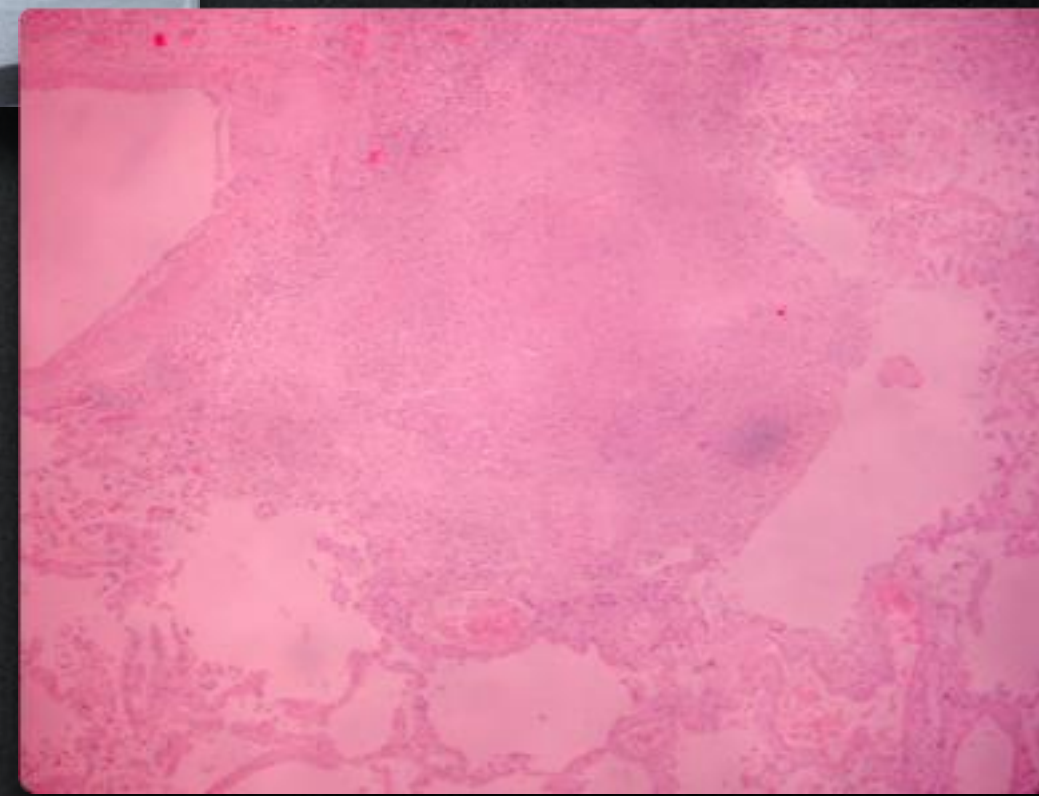
- Donna di 56 anni, pleurite TB ad 11 anni; artrite reumatoide a 42 anni, trattata con FANS e cortisonici per 7 anni e con immunosoppressori per 5 anni.
- **Terapia con anti-TNF- α (infliximab):** 3 mg/kg/mese– 9 infusioni complessive. Dopo 11 mesi la terapia viene sospesa per comparsa di febbre trattata senza successo per sei mesi

- Ricovero in DCMR
- Rx e HRCT torace: lesioni micronodulari di tipo miliarico bilaterali
- Espettorato: BAAR-, coltura- ; Inizia terapi a anti-TB standard
- Emocoltura positiva per MTB a 30 gg.
- Decesso dopo 30 gg di terapia
- Autopsia: infarto miocardio in presenza di grave e diffusa arteriosclerosi polidistrettuale. Parenchima polmonare tempestato da minute formazioni granulomatose di pochi mm di diametro, isolate o confluenti caratterizzate da diffusa necrosi caseosa con bacilli AAR

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ETTI LUCIANA



LUCIANA



Diagnosi:

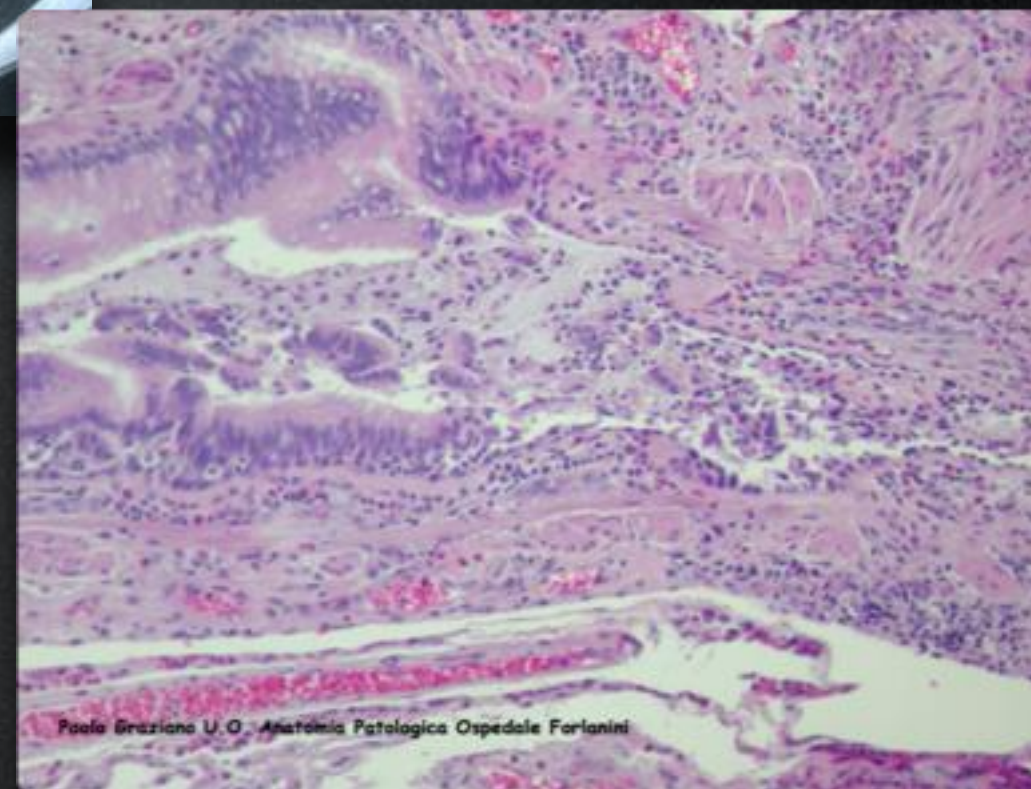
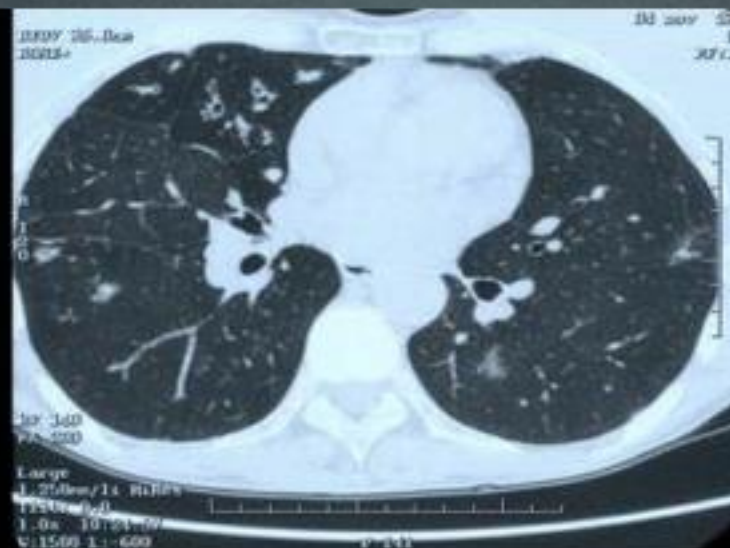
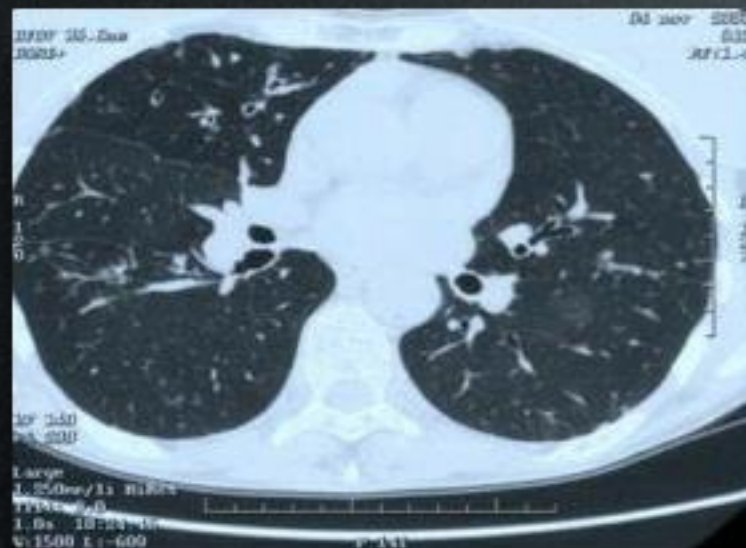
Tubercolosi polmonare

TB miliarica subacuta necrotizzante in
paziente immunodepressa per terapia anti-TNF

Caso 4

Donna di 59 anni con dispnea e
tosse

- Comparsa di sintomatologia con:
- dispnea da sforzo ingravescente anche per sforzi lievi e tosse non produttiva
- Si ricovera per il persistere della sintomatologia



Biopsia: lesioni granulomatose peribronchiali

Microbiologia: M. avium intracellulare

Diagnosi:
micobatteriosi polmonare
“Sindrome di Lady Windermere”

(Oscar Wilde)

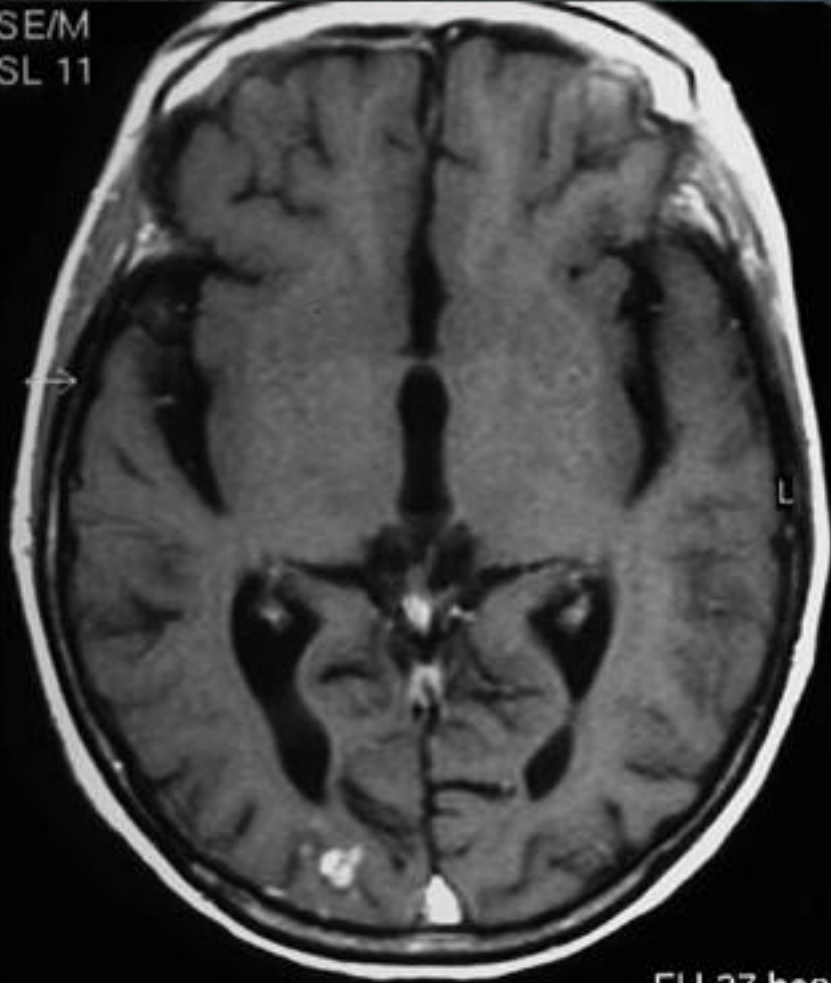
Caso 5

Donna di 47 anni con tosse, febbre e
convulsioni

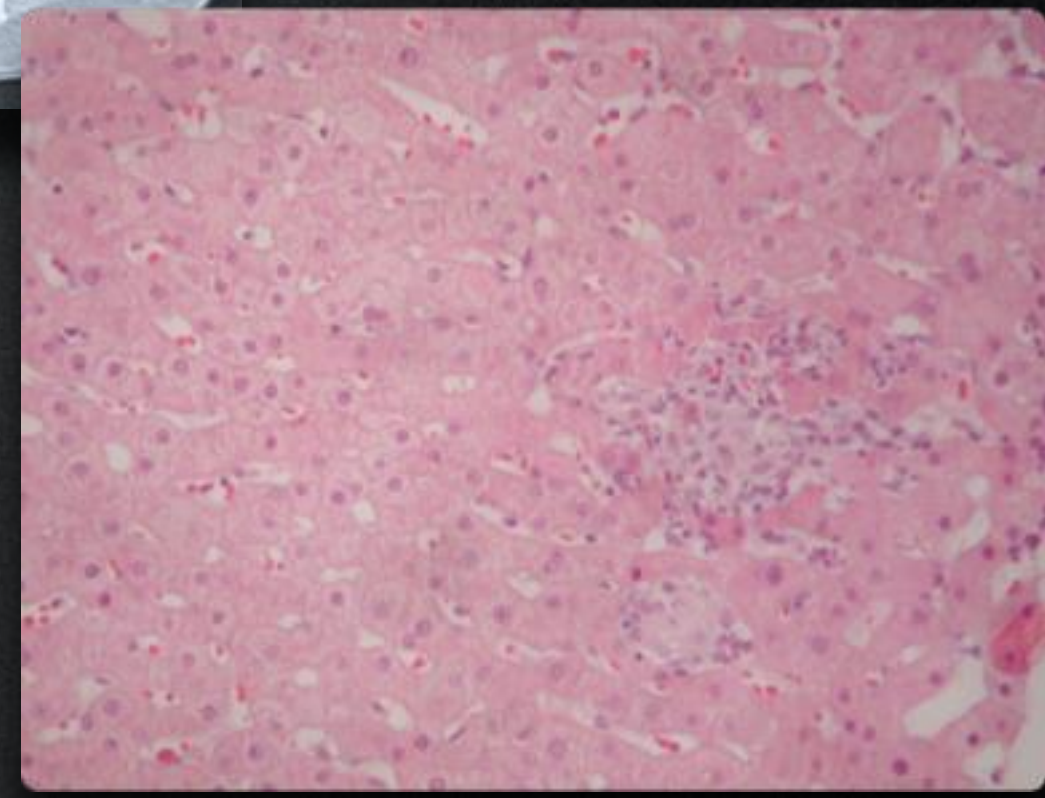
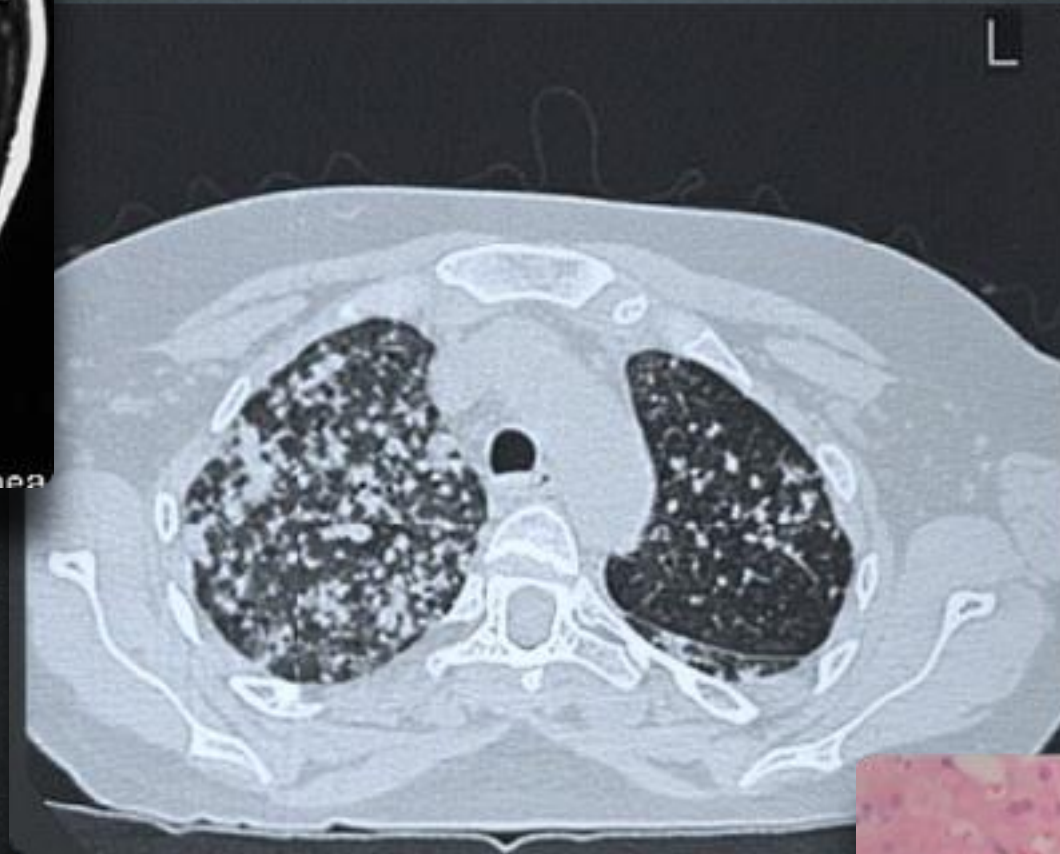
- Donna di 47 anni, condizioni generali scadute, tosse secca, febbre, episodio convulsivo.
- Work-up iniziale:
- RX torace: interstiziopatia miliariforme.
- Espettorato e BAL BAAR-, coltura-, PPD-
- TC cranio: lesioni nodulari “granulomatose”
- Terapia empirica: anti-TB standard per due mesi: progressione

- trasferita per sospetta TB-MDR.
- BAL: CD4/CD8= 6.3
- BAAR e coltura -, rRNA MTB +
- Biopsia TBB: fibrosi micronodulare;
Epatobiopsia: granulomi epitelioidi non
necrotizzanti

SE/M
SL 11



CH 27 hea



- Terapia: inizia prednisone 0.5 mg/kg/die.
- RX torace e RM encefalo a due mesi la risoluzione delle lesioni.

Diagnosi:

Sarcoidosi polmonare e cerebrale

Fasi della infezione tubercolare e della TB polmonare (ATS)

- 0. non contatto: tubercolina (PPD) negativa
- 1. Contatto senza infezione: PPD-
- 2. Infezione: PPD+, RX normale, non sintomi
- 3. TB attiva: PPD+, RX anormale, batteriologia positiva
- 4. TB inattiva: PPD+, lesioni RX stabili, batteriologia negativa
- 5. TB sospetta
- NOTA: il concetto di infezione comporta la presenza, al contrario della malattia, di pochi bacilli nell'organismo

Classificazione della tubercolosi

- Infezione tubercolare
- TB primaria:
 - complesso primario con adenopatia, sindrome adeno-bronchiale
 - TB sub primaria: miliare, meningite tubercolare, pleurite
- TB post-primaria
 - areattiva
 - Essudativa: pleurite, infiltrato tisiogeno, lobite, broncopolmonite
 - Produttiva: miliare circoscritta degli apici e miliare cronica
 - Miliare acuta: miliare dell' immunocompromesso
 - Esiti e sequele
 - TB extrapolmonare



TB miliare cronica

TB miliare acuta HIV+



Diagnosi di TB *post-mortem*

Stati Uniti 1985-1988

	Dead	Alive	Proportions (%)
Total in Model	4,373	81,919	5.1
Age			
0-4	19	2,756	0.7
5-14	12	1,823	0.7
15-24	57	6,517	0.9
25-34	303	14,677	2.0
35-44	388	12,853	2.9
45-54	366	10,809	3.3
55-64	592	11,158	5.0
65-74	858	10,305	7.7
75-84	1,098	8,042	12.0
85 +	680	2,979	18.6

Terapia anti-tubercolare

NUM. 44

31 OTTOBRE 1895

ANNO XLVI

Gazzetta Medica di Torino

COMUNICAZIONI ORIGINALI

CLINICA MEDICA PROPEDEUTICA DI TORINO

PRIMO CASO DI TISI POLMONARE MONOLATERALE AVANZATA
CURATO FELICEMENTE COL PNEUMOTORACE ARTIFICIALE

Nota del Prof. CARLO FORLANINI. (1)

L' inizio

Tubercolosi: la cura

Year	Drug (s)	Cure %	Months
1944	SM		
1944	PAS		
1950	SM, PAS		
1955	INH, SM, PAS	95%	24
1960	INH, SM, EMB	95%	18
1970	INH, SM, EMB, RFM	95%	9
1980	INH, RFM, PZA	95%	6

From the sanatorium to home treatment: the 1959 Madras study

- A 12 month randomized controlled trial of INH plus PAS in the same cachet (200 mg and 10 g, respectively for the average 45 kg person)
- with about 4% INH and 3% PAS resistant subjects at the start of the trial, 90% bacteriological cure rates were obtained at 12 months in both arms.
- less than 1% defaulters from home treatment, with more than 10% quitters of the sanatorium

Principali farmaci antitubercolari

Farmaci	Modalità d' azione	Dose raccomandata (mg/Kg)		
		Giornaliera	Intermittente	
			3x/wk	2x/wk ^a
Isoniazide	Battericida	5 (4–6)	10 (8–12)	15 (13–17)
Rifampicina	Battericida	10 (8–12)	10 (8–12)	10 (8–12)
Pirazinamide	Battericida	25 (20–30)	35 (30–40)	50 (40–60)
Streptomicina	Battericida	15 (12–18)	15 (12–18)	15 (12–18)
Etambutolo	Batteriostatico	15 (15–20)	30 (25–35)	45 (40–50)

Effetti Collaterali dei farmaci antitubercolari di prima linea

Farmaco	Effetto collaterale
Isoniazide (H)	Neuropatie periferiche e centrali, epatite tossica, orticaria e febbre
Rifampicina (R)	Epatite tossica, anemia emolitica, piastrinopenia, insufficienza renale fulminante, altera il metabolismo di farmaci, sindrome pseudoinfluenzale.
Pirazinamide (Z)	Epatite tossica, iperuricemia, disturbi gastrointestinali
Etambutolo (E)	Neurite ottica (dose dipendente, parzialmente reversibile)
Streptomina (S)	Tossicità otovestibolare, eruzione cutanea

Schemi terapeutici per la tubercolosi

ALTERNATIVE TREATMENT REGIMENS FOR EACH PATIENT TREATMENT CATEGORY

TB TREATMENT CATEGORY	TB PATIENTS	ALTERNATIVE TB TREATMENT REGIMENS	
		INITIAL PHASE	CONTINUATION PHASE
1	new smear-positive PTB seriously ill: extrapulmonary or smear-negative pulmonary (severe TB)	2 SHRZ (EHRZ) 2 SHRZ (EHRZ) 2 SHRZ (EHRZ)	6 HE 4 HR 4 H ₃ R ₃
2	sputum smear-positive: relapse treatment failure return after default	2 SHRZE/1 HRZE 2 SHRZE/1 HRZE	5 H ₃ R ₃ E ₃ 5 HRE
3	smear-negative PTB extrapulmonary TB (less severe)	2 HRZ or 2 H ₃ R ₃ Z ₃ 2 HRZ or 2 H ₃ R ₃ Z ₃ 2 HRZ or 2 H ₃ R ₃ Z ₃	6 HE 2 HR/4 H 2 H ₃ R ₃ /4H
4	chronic case (still sputum-positive after supervised re-treatment)	NOT APPLICABLE (Refer to specialist centre if second-line drugs available)	

Tubercolosi farmaco resistente

Definizioni-1

- ***Resistenza primaria:*** resistenza ai farmaci antitubercolari in un paziente mai trattato per tubercolosi
- ***Resistenza acquisita:*** resistenza ai farmaci antitubercolari in un paziente già trattato per tubercolosi

Tubercolosi farmaco resistente

Definizioni - 2

- **Tubercolosi farmaco-resistente** (Drug-resistant TB/ **DR-TB**): causata da una ceppo resistente ad almeno 1 dei farmaci di prima linea (INH,RIF,ETB,SM)
- ***Tubercolosi multi farmaco-resistente*** (MultiDrug-resistant TB/**MDR-TB**): causata da una ceppo resistente contemporaneamente a INH e RIF



Morbidity and Mortality Weekly Report

Weekly

March 24, 2006 / Vol. 55 / No. 11

World TB Day — March 24, 2006

World TB Day is March 24. This annual event commemorates the date in 1882 when Robert Koch announced his discovery of *Mycobacterium tuberculosis*, the bacterium that causes tuberculosis (TB). Worldwide, TB remains one of the leading causes of death from infectious diseases. A major goal of the U.S. Department of Health and Human Services is to reduce the burden of TB by 50% by 2010.

Emergence of *Mycobacterium tuberculosis* with Extensive Resistance to Second-Line Drugs — Worldwide, 2000–2004

During the 1990s, multidrug-resistant (MDR) tuberculosis (TB), defined as resistance to at least isoniazid and rifampin, emerged as a threat to TB control both in the United States

Classification of drugs into 5 groups based on hierarchy of efficacy and safety including 2nd-line drugs (guidelines)

1st-line agents

•INH

Injectable agents

•RIF

•SM

Fluoroquinolones

•PZA

•KM

•Cipro

2nd-line Oral agents

•EMB

•AMK

•Oflox

•ETA/PTA

"3rd-line" agents

•CM

•Levo

•PASA

Not routinely recommended, efficacy unknown, e.g., amoxicillin/clavulanic acid, clarithromycin, clofazamine,

•Moxi

•CYS

•Gati

Tubercolosi farmaco resistente

Definizioni - 3

- ***Tubercolosi largamente farmaco-resistente***
(Extensively Drug-resistant TB/ ***XDR-TB***):
causata da una ceppo resistente a INH e RIF e
anche a un fluorochinolone e ad almeno uno
dei tre farmaci iniettabili di seconda linea
(capreomicina, amikacina, kanamicina)

Prevenzione

Categorie rischio TB

- Persons at increased risk* for *M. tuberculosis* infection
- close contacts of persons known or suspected to have active tuberculosis;
 - foreign-born persons from areas that have a high incidence of active tuberculosis (e.g., Africa, Asia, Eastern Europe, Latin America, and Russia);
 - persons who visit areas with a high prevalence of active tuberculosis, especially if visits are frequent or prolonged;
 - residents and employees of congregate settings whose clients are at increased risk for active tuberculosis (e.g., correctional facilities, long-term care facilities, and homeless shelters);
 - health-care workers who serve clients who are at increased risk for active tuberculosis;
 - populations defined locally as having an increased incidence of latent *M. tuberculosis* infection or active tuberculosis, possibly including medically underserved, low-income populations, or persons who abuse drugs or alcohol; and
 - infants, children, and adolescents exposed to adults who are at increased risk for latent *M. tuberculosis* infection or active tuberculosis.
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Categorie rischio TB

- Persons at increased risk* for *M. tuberculosis* infection
- close contacts of persons known or suspected to have active tuberculosis;
 - foreign-born persons from areas that have a high incidence of active tuberculosis (e.g., Africa, Asia, Eastern Europe, Latin America, and Russia);
 - persons who visit areas with a high prevalence of active tuberculosis, especially if visits are frequent or prolonged;
 - residents and employees of congregate settings whose clients are at increased risk for active tuberculosis (e.g., correctional facilities, long-term care facilities, and homeless shelters);
 - health-care workers who serve clients who are at increased risk for active tuberculosis;
 - populations defined locally as having an increased incidence of latent *M. tuberculosis* infection or active tuberculosis, possibly including medically underserved, low-income populations, or persons who abuse drugs or alcohol; and
 - infants, children, and adolescents exposed to adults who are at increased risk for latent *M. tuberculosis* infection or active tuberculosis.
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Significato Clinico dei Test

FDA has approved both QFT-GIT and T-Spot as in vitro diagnostic aids for detection of *M. tuberculosis* infection (22,23). Both tests are approved as indirect tests for *M. tuberculosis* infection (including infection resulting in active disease) when used in conjunction with risk assessment, radiography, and other medical and diagnostic evaluations. The FDA-approved indications for QFT-GIT and T-Spot are similar to indications for QFT-G and TST using either Tubersol PPD (Sanofi Pasteur Ltd., Toronto, Ontario, Canada) or Aplisol PPD (JHP Pharmaceuticals, LLC, Rochester, Michigan).

Caveats

- Diagnoses of *M. tuberculosis* infection and decisions about medical or public health management should not be based on IGRA or TST results alone, but should include consideration of epidemiologic and medical history as well as other clinical information.

- A diagnosis of LTBI requires that active tuberculosis be excluded by medical evaluation, which should include taking a medical history and a physical examination to check for suggestive symptoms and signs, a chest radiograph, and, when indicated, testing of sputum or other clinical samples for the presence of *M. tuberculosis*. Neither an IGRA nor TST can distinguish LTBI from active tuberculosis.

In persons who have symptoms, signs, or radiographic evidence of active tuberculosis or who are at increased risk for progression to active tuberculosis if infected, a positive result with either an IGRA or TST should be taken as evidence of *M. tuberculosis* infection. However, negative IGRA or TST results are not sufficient to exclude infection in these persons, especially in those at increased risk for a poor outcome if disease develops, and clinical judgment dictates when and if further diagnostic evaluation and treatment are indicated.

Indicazioni per la chemiopprofilassi dell' infezione TB latente

- bambini <2 anni PPD+ o PPD-, esposti a pazienti TB, da vaccinare se ancora PPD- dopo 45 giorni
- bambini <16 anni PPD+, esposti a pazienti TB o immigrati da aree ad alta endemia
- Adulti esposti a pazienti TB, con conversione documentata del test tuberculinico a PPD+
- Adulti, di età da 16 a 34 anni, immigrati da aree ad alta endemia, se fortemente PPD+
- Adulti HIV positivi, se PPD+

Protocolli di Chemiopprofilassi dell' infezione TB latente

- Isoniazide 12 mesi (A)
- Isoniazide 6 mesi (B)
- Rifampicina ed isoniazide 3 mesi (B)
- Rifampicina 6 mesi (INH resistenti) (C)

Dimensioni del
problema sanitario
della TB in Europa

TB ogg i

- In 2011, 29 EEA countries, 27 of them EU countries, reported 72 334 tuberculosis (TB) cases with an overall rate of 14.2 cases per 100 000 population; 44 361 (61.3%) of these cases were laboratory-confirmed.
- Of 72 334 cases reported, 55 939 (77.3%) suffered from pulmonary TB, 16 116 (22.3%) from extrapulmonary TB, and for 279 (0.4%) of all cases, no site was reported.
- Between 2006 and 2011, the reported TB rate decreased by an annual average of 4.0%, with a net decrease in 22 countries.
- The highest rates in 2011 were reported by Romania (89.7 per 100 000 population), Lithuania (58.7), Latvia (39.7), Bulgaria (32.1), Estonia (25.4), Portugal (23.9) and Poland (22.2).
- In 2011, 18 646 (25.8% of all notified TB cases) were reported as being of foreign origin.
- Multidrug-resistance (MDR) remained most prevalent in the Baltic States (14.8%–29.8%) and Romania (8.8%). Generally, MDR was more common in cases of native origin.
- In 21 countries reporting drug susceptibility testing results for second-line anti-TB drugs, 13.4% of MDR TB cases were also extensively drug-resistant (XDR).
- Among previously untreated, culture-confirmed pulmonary TB cases, 76.8% had a successful treatment outcome at 12 months, as opposed to 53.7% of previously treated pulmonary TB cases and 31.6% of all culture-confirmed MDR TB cases at 24 months.

Country	National coverage	Report type	2011					2010		2009		2008		2007	
			Total cases and rate		Confirmed cases and rates			Total cases and rate		Total cases and rate		Total cases and rate		Total cases and rate	
			Cases	Rate	Cases	Rate	Age-standardised rate	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate
Austria	Y	C	687	8.2	466	5.5	5.5	691	8.3	696	8.3	817	9.8	874	10.6
Belgium	Y	C	1 044	9.5	797	7.4	7.3	1 086	10.0	994	9.2	990	9.3	1 020	9.6
Bulgaria	Y	C	2 407	32.1	1 071	14.3	13.9	2 649	35.0	2 910	38.3	3 150	41.2	3 038	39.6
Cyprus	Y	C	54	6.7	44	5.2	5.2	61	7.6	55	6.9	50	6.3	42	5.4
Czech Republic	Y	C	600	5.7	426	4.0	4.0	669	6.4	694	6.6	864	8.3	846	8.2
Denmark	Y	C	381	6.9	272	4.9	5.0	366	6.6	334	6.1	380	6.9	391	7.2
Estonia	Y	C	341	25.4	264	19.7	19.7	333	24.8	411	30.7	444	33.1	491	36.6
Finland	Y	C	325	6.0	252	4.7	4.6	325	6.1	417	7.8	344	6.5	348	6.6
France	Y	C	4 942	7.6	2 309	3.6	3.7	5 116	7.9	5 276	8.2	5 758	9.0	5 574	8.8
Germany	Y	C	4 316	5.3	3 071	3.8	3.6	4 388	5.4	4 427	5.4	4 523	5.5	5 000	6.1
Greece	Y	C	489	4.3	278	2.5	2.4	487	4.3	589	5.2	664	5.9	639	5.7
Hungary	Y	C	1 445	14.5	597	6.0	5.8	1 741	17.4	1 407	14.0	1 619	16.1	1 685	16.7
Ireland	Y	C	425	9.5	288	6.4	6.8	420	9.4	479	10.8	468	10.6	480	11.1
Italy*	N	C	3 521	5.8	982	1.6	1.6	4 692	7.8	4 244	7.1	4 418	7.4	4 525	7.7
Latvia	Y	C	885	39.7	671	30.1	29.7	935	41.6	977	43.2	1 070	47.1	1 255	55.0
Lithuania	Y	C	1 904	58.7	1 403	43.8	43.2	1 938	58.2	2 081	62.1	2 250	66.8	2 408	71.1
Luxembourg	Y	C	26	5.1	19	3.7	3.7	29	5.8	27	5.5	28	5.8	39	8.2
Malta	Y	C	33	7.9	24	5.7	5.8	32	7.7	44	10.6	53	12.9	38	9.3
Netherlands	Y	C	1 007	6.0	732	4.4	4.5	1 065	6.4	1 158	7.0	1 015	6.2	998	6.1
Poland	Y	C	8 478	22.2	5 581	14.6	14.7	7 509	19.7	8 236	21.6	8 080	21.2	8 614	22.6
Portugal	Y	C	2 540	23.9	1 588	14.9	14.7	2 626	24.7	2 871	27.0	3 002	28.3	3 139	29.6
Romania	Y	C	19 212	89.7	12 446	58.1	57.3	21 059	98.1	23 164	107.7	24 680	114.6	24 837	115.2
Slovakia	Y	C	399	7.3	188	3.5	3.6	439	8.1	506	9.3	633	11.7	682	12.6
Slovenia	Y	C	192	9.4	182	8.9	8.6	172	8.4	188	9.3	213	10.6	218	10.8
Spain	Y	C	6 762	14.7	4 383	9.5	9.3	7 239	15.7	7 592	16.6	8 216	18.1	7 768	17.5
Sweden	Y	C	586	6.2	476	5.1	5.3	668	7.2	617	6.7	546	5.9	482	5.3
United Kingdom	Y	C	8 963	14.3	5 285	8.5	8.7	8 483	13.7	8 917	14.5	8 606	14.1	8 329	13.7
EU total	-	-	71 964	14.3	44 095	8.8	8.5	75 218	15.0	79 311	15.9	82 881	16.7	83 760	16.9
Iceland	Y	C	9	0.2	4	1.3	1.3	22	6.9	9	2.8	6	1.9	14	4.6
Liechtenstein	-	-	-	-	-	-	-	-	-	-	-	-	-	5	14.2
Norway	Y	C	361	6.9	262	5.3	5.4	336	6.9	358	7.5	313	6.6	302	6.5
Total	-	-	72 334	14.2	44 361	8.7	8.5	75 576	14.9	79 678	15.8	83 200	16.5	84 081	16.8

Source: Country reports. Y: Yes; N: No; A: Aggregated data report; C: Case-based report; —: No report; U: Unspecified.

TB e HIV

Tuberculosis and HIV infection

HIV status was reported for 21530 (53.6%) of 40188 TB cases from 16 countries. Five countries only reported HIV-positive cases and so were excluded from the analysis. Of the 21530 cases with known HIV status, 1003 (4.7%) were reported as HIV positive. Among Member States with at least five HIV-co-infected TB cases, the proportion of co-infected cases among TB cases with known HIV status was highest in Ireland, Malta and Estonia at 20.2%, 16.7% and 15.0%, respectively.

TB e Immigrazione

Origin of TB cases

In 2011, 51 191 (72.2%) of 72 334 reported TB cases were born in an EU/EEA Member State or had citizenship in an EU/EEA Member State, 18 646 (25.8%) were of foreign origin¹, and 1 497 (1.8%) of unknown origin. Of all foreign TB cases, 6 226 (33.4%) were from Asia (outside the WHO European Region), 5 767 (30.9%) from Africa, 1 880 (10.1%) from other EU/EEA countries, 1 596 (8.4%)

from non-EU/EEA European countries, 1 021 (5.5%) from the Americas and 2 183 (11.7%) from other or unknown countries. In 10 Member States, cases of foreign origin accounted for the majority of cases, reaching 89.4% and 87.8% in Sweden and Norway, respectively. Overall, the proportion of foreign cases has been on the rise since 2001 which in some countries was due to a real increase, whereas in others, it was attributable to the sizeable drop in native cases.

TB: Trattamento

Treatment outcome

Of 62 655 TB cases notified in 2010 with known treatment outcome, 46 545 (74.3%) had been treated successfully, 4 560 (7.3%) had died, 1 122 (1.8%) had failed their treatment, 3 877 (6.2%) had defaulted, 1 835 (2.9%) were still on treatment and 4 716 (7.5%) had been transferred or had an unknown outcome. France, Greece, Italy and Portugal did not report treatment outcome.

Treatment success had been achieved in 76.8% of new laboratory-confirmed pulmonary TB cases, 53.7% of previously treated cases, and 31.6% of MDR TB cases.

Of extrapulmonary TB cases with treatment outcome information, 82.2% were treated successfully as compared to 72.4% of pulmonary TB cases. Among cases with extrapulmonary TB, the lowest treatment success ratios were found in those with disseminated TB (52.3%),

Table 2.1.5. Numbers and percentage of multidrug-resistant and extensively drug-resistant tuberculosis cases, EU/EEA, 2011

Country	Laboratory-confirmed TB cases with DST for first-line drugs	Total multidrug-resistant TB		Total MDR with DST for second-line drugs (N)	Extensively drug-resistant TB*	
		N	%		N	%
Austria	450	19	(4.2)	19	6	(31.6)
Belgium	754	15	(2.0)	15	3	(20.0)
Bulgaria	733	55	(7.5)	46	0	(0.0)
Cyprus	40	1	(2.5)	1	0	(0.0)
Czech Republic	408	7	(1.7)	5	2	(40.0)
Denmark	271	3	(1.1)	2	0	(0.0)
Estonia	262	78	(29.8)	75	14	(18.7)
Finland	245	5	(2.0)	-	-	-
France	1568	40	(2.6)	-	-	-
Germany	2 821	56	(2.0)	2	0	(0.0)
Greece	159	5	(3.1)	5	2	(40.0)
Hungary	479	7	(1.5)	5	0	(0.0)
Ireland	239	3	(1.3)	1	0	(0.0)
Italy	2 542	81	(3.2)	50	6	(12.0)
Latvia	644	95	(14.8)	95	12	(12.6)
Lithuania	1 403	296	(21.1)	295	53	(18.0)
Luxembourg	19	2	(10.5)	-	-	-
Malta	22	0	(0.0)	0	-	-
Netherlands	726	15	(2.1)	-	-	-
Poland	4 993	41	(0.8)	9	1	(11.1)
Portugal	1 252	22	(1.8)	-	-	-
Romania	6 026	530	(8.8)	248	30	(12.1)
Slovakia	185	3	(1.6)	3	0	(0.0)
Slovenia	182	0	(0.0)	0	-	-
Spain	1 273	41	(3.2)	41	1	(2.4)
Sweden	475	17	(3.6)	17	0	(0.0)
United Kingdom	5 127	81	(1.6)	79	6	(7.6)
Total EU	33 298	1 518	(4.6)	1 013	136	(13.4)
Iceland	4	0	(0.0)	0	-	-
Liechtenstein	-	-	-	-	-	-
Norway	257	4	(1.6)	4	0	(0.0)
Total	33 559	1 522	(4.5)	1 017	136	(13.4)

* Percentages calculated from cases with second-line drug susceptibility testing