

44th Annual Union World Conference on Lung
Health

An Historical Review of the Quantification of the Burden of Childhood Tuberculosis

Workshop: The inclusion of children in national
TB prevalence surveys: A critical step towards
achieving zero TB deaths

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- Introductory remarks
- Natural history of TB in children
- Attempts at quantification of TB in children; from mortality to morbidity
- Conclusion
- HIV

The more things
change, the more
they remain the
same!

Joint meeting of the British Paediatric Association and the Tuberculosis Association in 1944 reported in: Gaisford WF. Primary tuberculosis in childhood. Br Med J 1946; 1: 84-86

"...in spite of the friendly spirit evident, it was clear that each party viewed the problem in an entirely different light. The Tuberculosis Association members quoted figures from their official returns, both of morbidity and mortality, which were at total variance with the experience of the paediatricians."

Joint meeting of the British Paediatric Association
and the Tuberculosis Association 1944 reported in:
Gaisford WF. Primary tuberculosis in childhood. Br
Med J 1946; 1: 84-86

In the main their conclusion was that
"childhood tuberculosis is not of
great importance to the public health
services," and their plea was for the
paediatricians to preserve **a sense of
proportion!**"

"Get real!"

Joint meeting of the British Paediatric Association and the Tuberculosis Association 1944 reported in: Gaisford WF. Primary tuberculosis in childhood. Br Med J 1946; 1: 84-86

The paediatricians responded:

“ Although the majority (of children) pass through their primary infection and are none the worse for it...” none the less....

“Many cases are seen in children's hospitals of **TBM**, **bone** and **joint TB** and other manifestations.....

Joint meeting of the British Paediatric Association and the Tuberculosis Association 1944 reported in: Gaisford WF. Primary tuberculosis in childhood. Br Med J 1946; 1: 84-86

Many cases are
missed...notification is
either intentionally or
inadvertently overlooked..."

Walls T, Shingadia D. Global epidemiology of paediatric tuberculosis. *J Infect* 2004; 48: 13-22

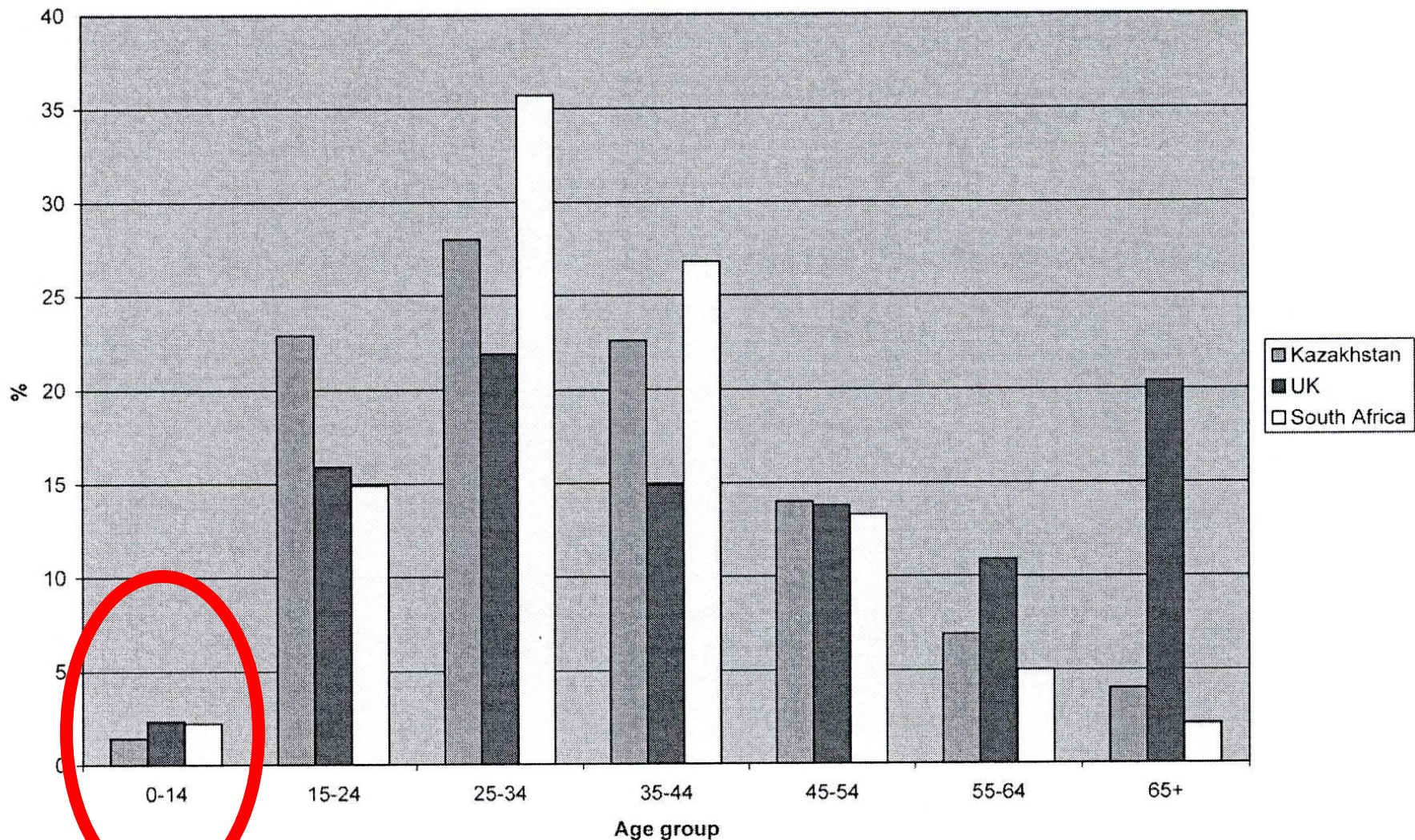
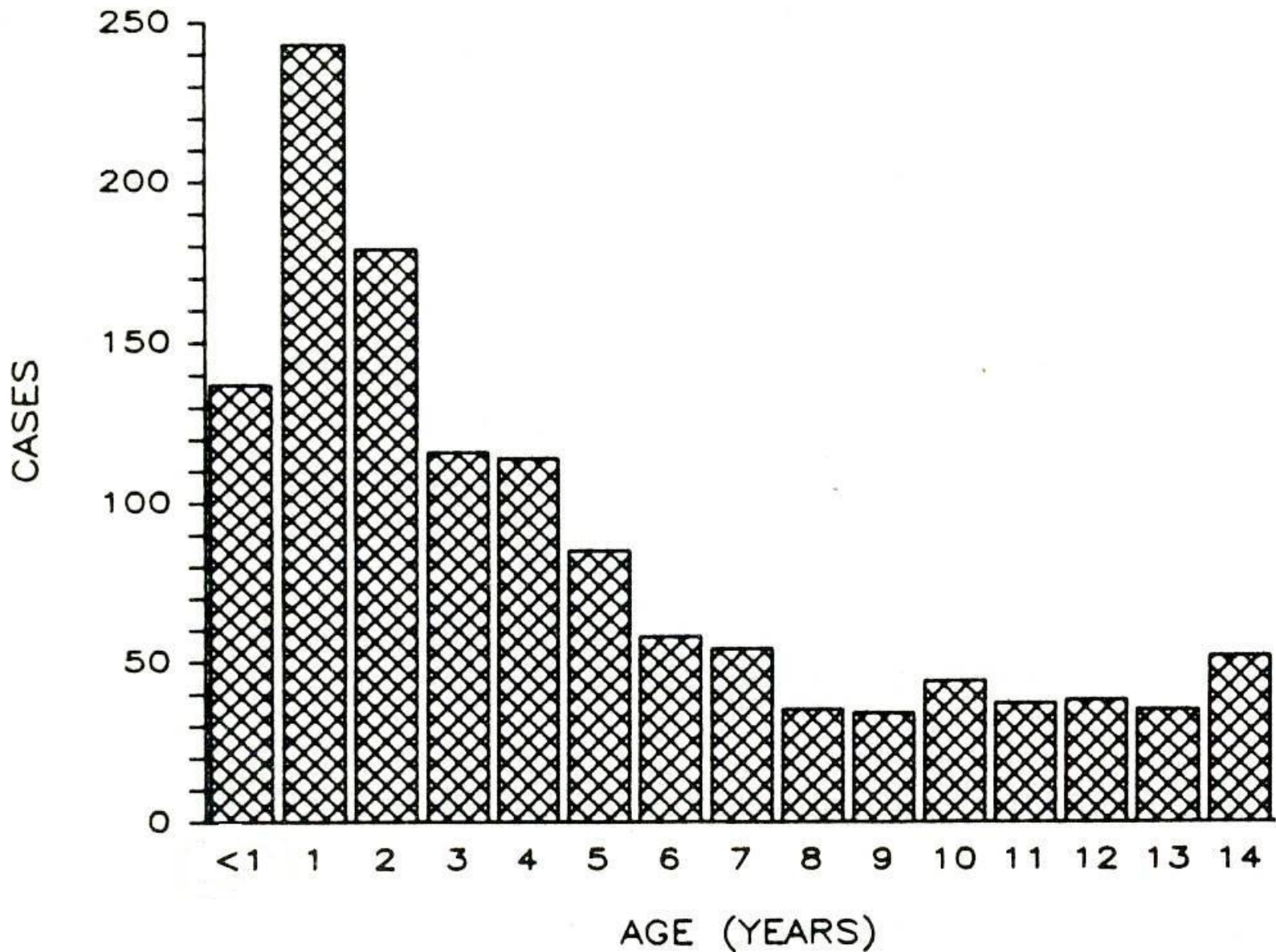
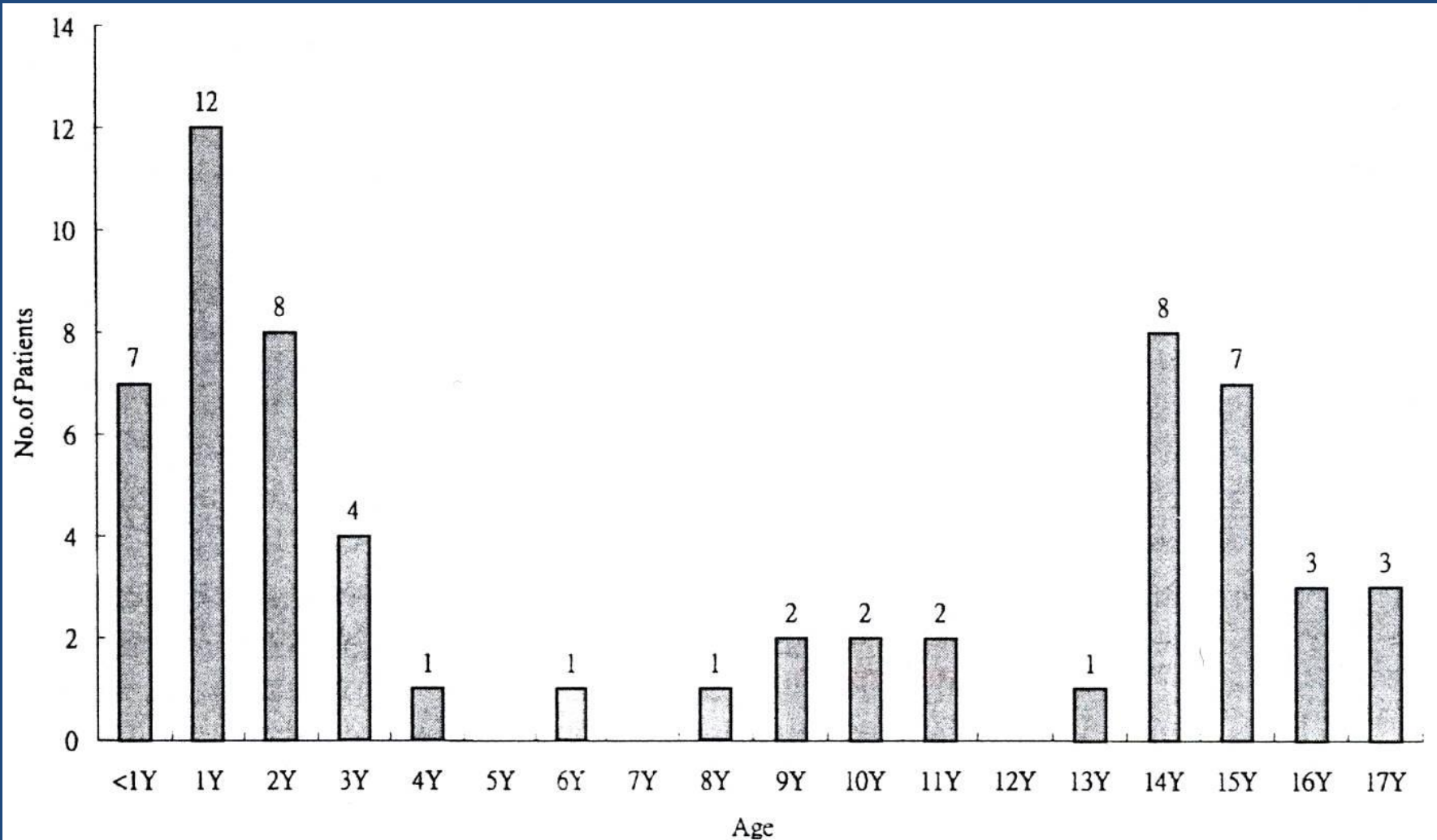


Figure 1 Age distribution of smear-positive TB case notifications to WHO, 2001.

Snider DE, Rieder HL, Combs D, Bloch AB, Hayden CH, Smith MHD.
Tuberculosis in children. *Pediatr Infect Dis J* 1988; 7: 271-278.



Wong KS, Chiu CH, Lin TY. Childhood and adolescent tuberculosis in northern Taiwan: an institutional experience. Acta Paediatr 2001; 90: 943-947.



Murray CJL, Styblo K, Rouillon A. Tuberculosis in developing countries: burden, intervention and cost. Bull Int Union Tuberc Lung Dis 1990; 65; 6-24.

- "To put tuberculosis in the proper perspective we need to know the **number** and the **age distribution** of new cases of tuberculosis which develop in a community each year, as well as the number and **age distribution** of patients who **die** from tuberculosis each year."

What are the alternatives to quantify or document the burden of TB in children?

- Annual Risk of Infection (ARI).
- Inclusion of children in prevalence surveys in addition to determination of ARI.
- “Notification” as at present.

What are the alternatives to quantify or document the burden of TB in children?

- Document all prescriptions of TB chemotherapy for children.
- Notification, documentation of hospitalised children.
- Notification/documentation of TBM and military TB osteo-articular TB.

Key aspects of the epidemiology of TB

- Transmission
- Prevalence
- Incidence
- Mortality
- Annual risk of infection

Purposes of quantification notification/documentation

- Budgeting/planning...staff, drugs, facilities.
- Prevent further spread of infection.
- Ensure adequate treatment.
- Evaluate those in contact with infectious cases.
- Prophylactic treatment.

Gedde-Dahl T. Tuberculous infection in the light of tuberculin matriculation. Am J Hyg 1952; 56: 139-214

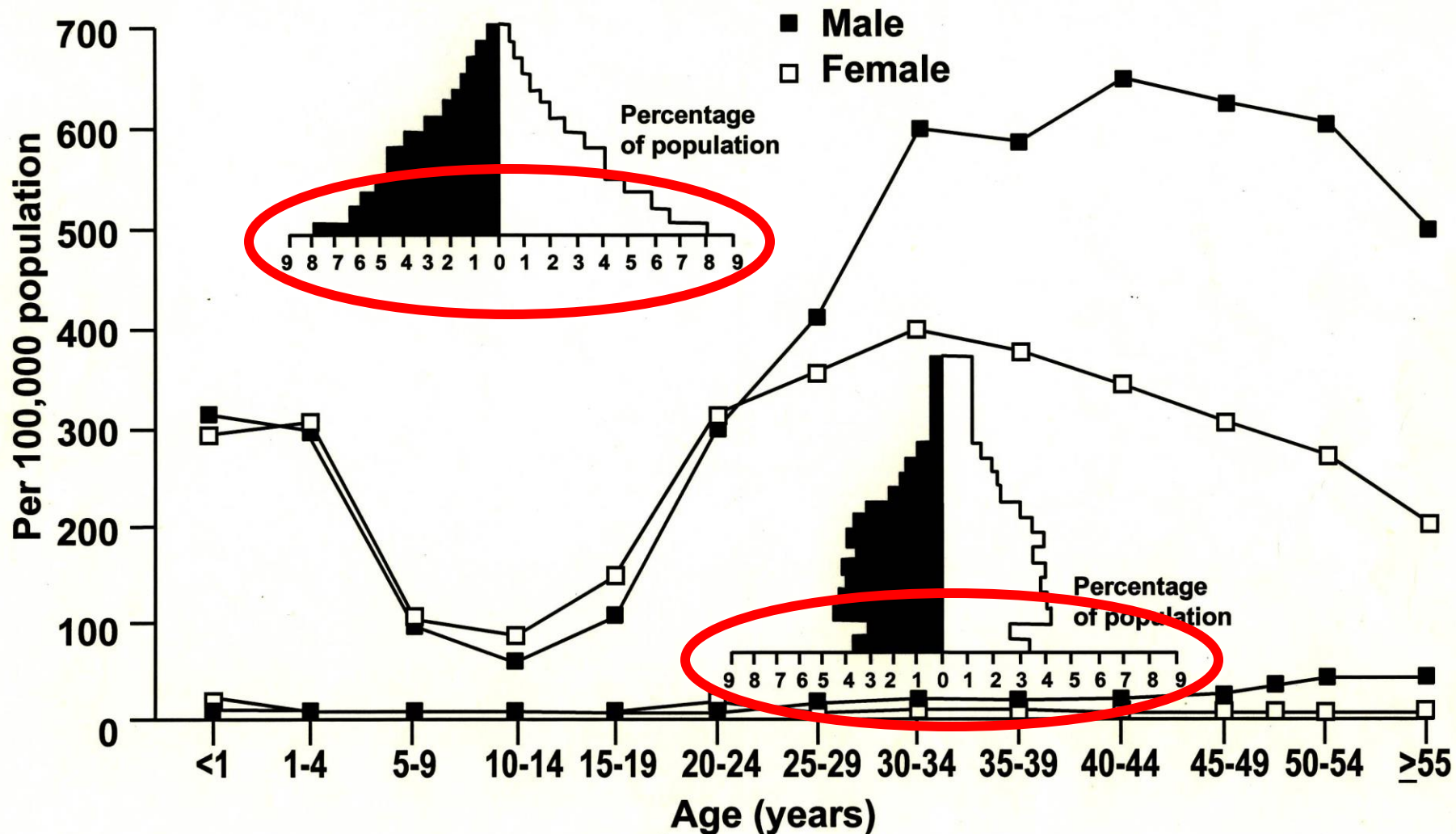
What are we talking about when we speak of childhood tuberculosis?

"Tuberculous disease...a biologically active process which has reached a state demonstrable either clinically or radiologically or by both means"

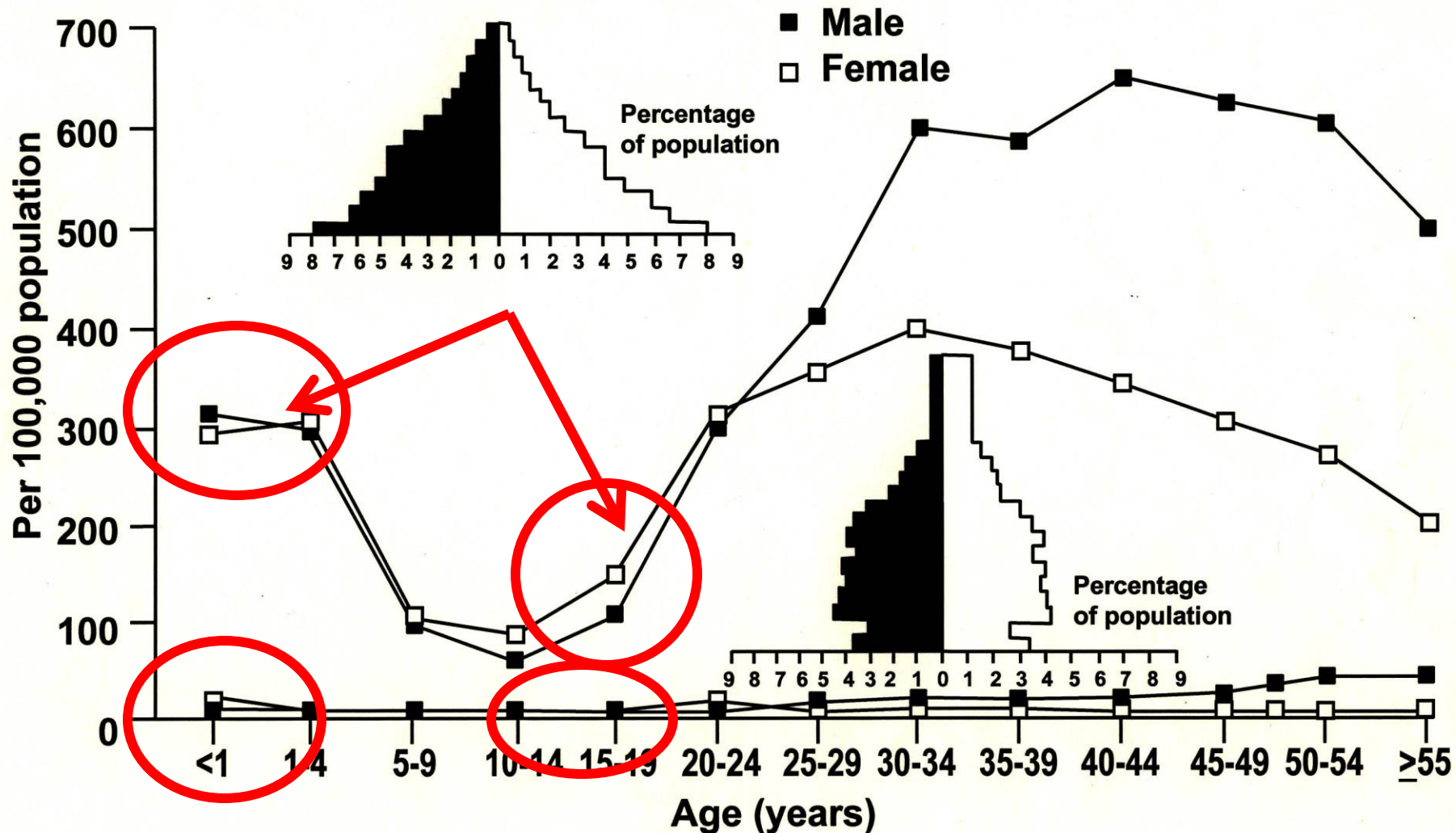
- The **epidemiology** of tuberculosis in different situations will necessarily influence our perspective of childhood tuberculosis.
- The **importance** of childhood tuberculosis will be coloured by our viewpoint.
- **Developed vs Developing communities**
- **TB control vs Clinical health services.**

The TB disease that will be notified and treated in a developing country will differ significantly from that in a developed country.

Donald PR. Childhood tuberculosis: the hidden epidemic. Int J Tuberc Lung Dis 2004; 8: 627-628.



Donald PR. Childhood tuberculosis: the hidden epidemic. Int J Tuberc Lung Dis 2004; 8: 627-628.



- In developed communities there will be **fewer children**.
- Fewer **sources of infection**.
- When infection does occur it will often occur at older ages when the child is more resistant to disease following infection.

The Natural History of Tuberculosis

Summary

- Features of **disease** will be found in the great majority of infected **young** children shortly after infection.
- Certain groups of children are subject to exceptionally high rates of **severe disease**, morbidity and a high mortality.

Summary

- In the youngest children, disease can be destructive and, if untreated, or not prevented, responsible for considerable morbidity and mortality.

The diagnosis of TB and the differentiation of disease and infection

The discovery of *Mycobacterium tuberculosis* by Robert Koch in **1882** made possible the accurate **diagnosis** of TB.

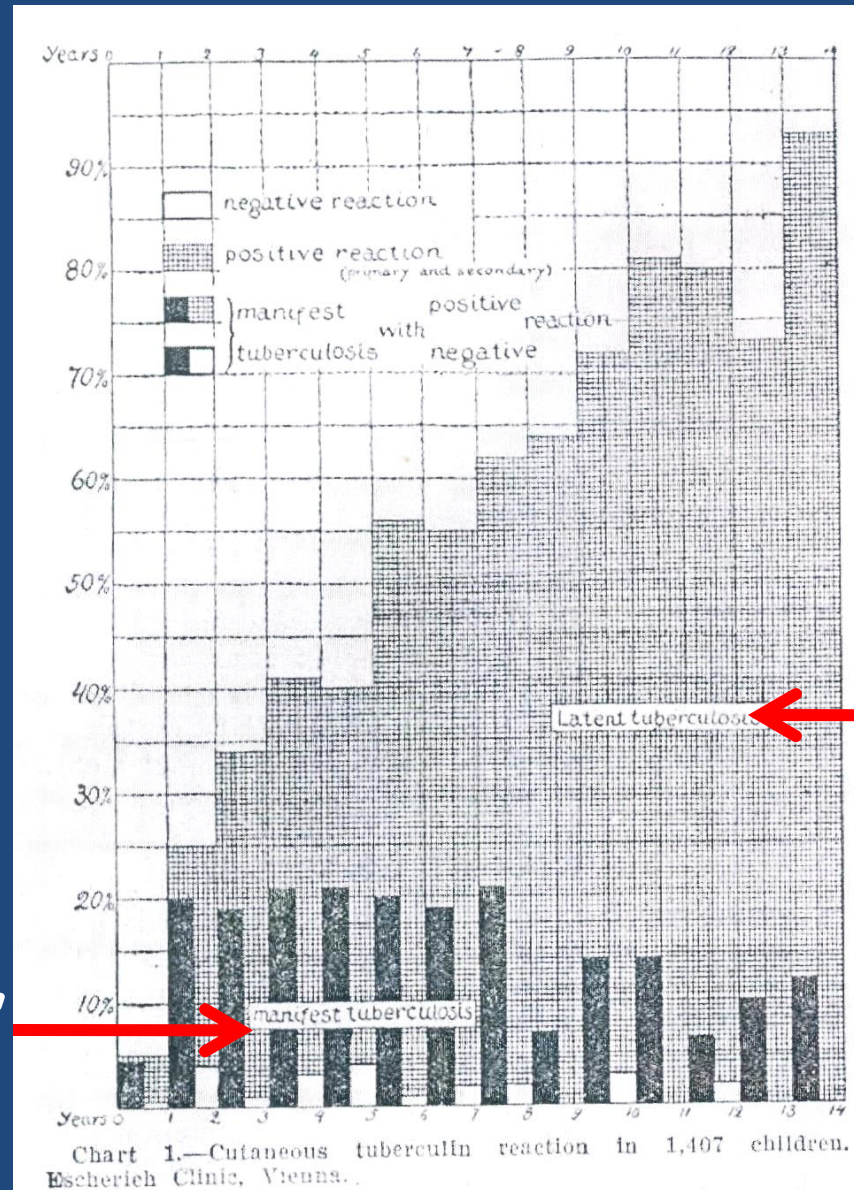
The diagnosis of TB and the differentiation of disease and infection

From approximately 1910 with the aid of

1. sputum culture and microscopy,
2. tuberculin testing,
3. chest radiology,

it became possible to detect TB infection, to differentiate disease from infection and following infection to study the natural history and determine the prognosis after infection.

Pirquet CV. Frequency of tuberculosis in childhood. JAMA 1909; 32: 675-678



"Manifest TB"

"Latent TB"

The diagnosis of TB and the differentiation of disease and infection

- TB infection in childhood was not very often fatal.
- Most children survived infection without any overt signs and only minor symptoms.

HOWEVER

- Certain groups of children were, subject to a considerable morbidity and mortality.

The diagnosis of TB and the identification of high morbidity and mortality groups

From approximately **1920** many studies of children **infected** with *M tuberculosis* or in contact with infectious adults were commenced and elucidated who these groups were and what the risks were.

Arvid Wallgren 1889-1973

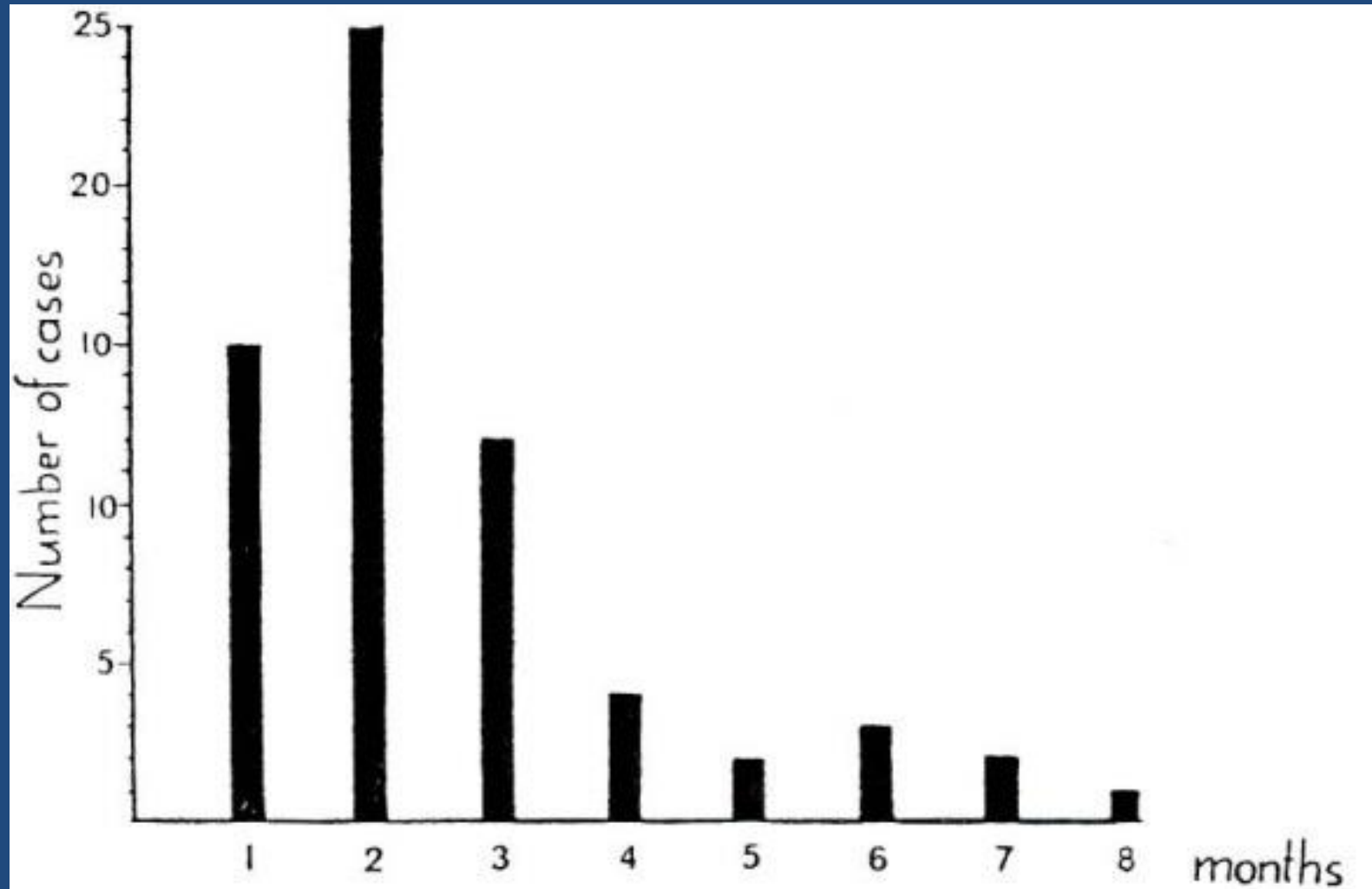


Wallgren A. Primary tuberculous infections in young adult life and in childhood. Am J Dis Child 1941; 61: 577-589

Consequences of manifest primary infection

Age (yrs)	Number infected	Mortality
0-1	39	36.9%
1-3	64	15.6%
3-7	225	4.4%
7-16	125	0.8%

Wallgren A. The time-table of tuberculosis. Tubercle 1948; 29: 245-251.



Manifestation-time of Tuberculous Meningitis
after primary tuberculosis.

Wallgren A. Some aspects of tuberculous meningitis and the possibility of its prevention. J Pediatr 1934; 5: 291-298

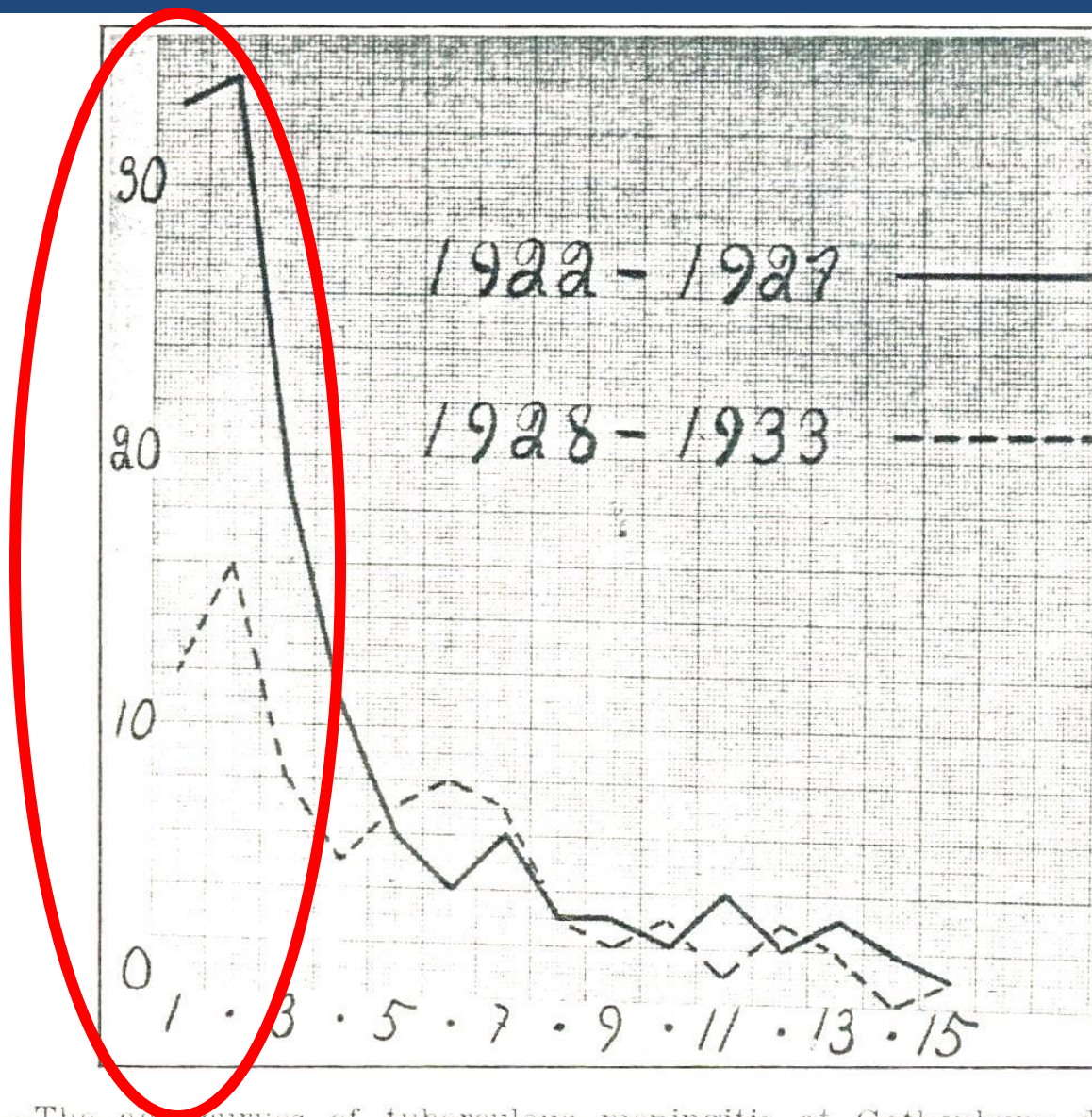


Chart 4.—The age curves of tuberculous meningitis at Gothenburg during the two six-year periods, 1922 to 1927 and 1928 to 1933.

Edith Lincoln 1899-1971

Donald PR. Edith Lincoln, an American pioneer of childhood tuberculosis. *Pediatr Infect Dis J.* 2012; 32: 241-5.



Lincoln EM. Course and prognosis of tuberculosis in children. Am J Med 1950; 9: 623-632.

Children with "manifest primary pulmonary tuberculosis".

Mortality in relation to age

Age of child	Mortality
--------------	-----------

<6-months	55%
-----------	-----

1-2 years	28%
-----------	-----

4-9 years	15%
-----------	-----

Lincoln EM. The effect of antimicrobial therapy on the prognosis of primary tuberculosis in children. *Am Rev Tuberc* 1954; 69: 682-689.

- 1930-1947 **980** children with "**fresh**" **primary PTB** without calcification studied
- Case fatality: **21.5%**
- **90%** deaths within 1 year; highest rates in young children.
- TBM caused **60%** of deaths.
- Miliary TB **10%** deaths.
- Remaining **30%** chronic haematogenous dissemination or progressive primary TB.

Lincoln EM, Harris LC, Bovornkitti S, Carretero R. The course and prognosis of endobronchial tuberculosis in children. *Am Rev Tub* 1956; 74: 246-255

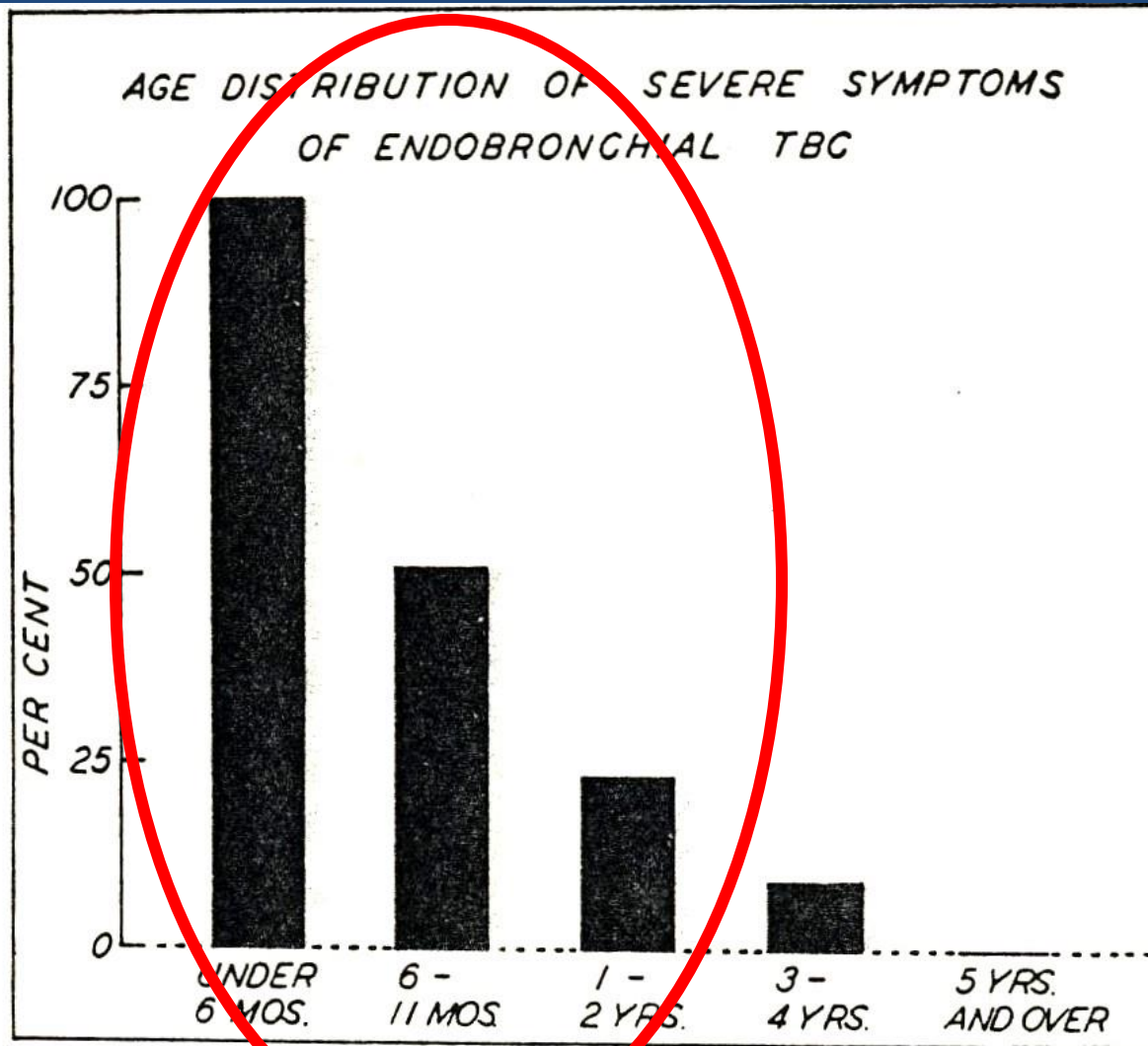


FIG. 1. Symptoms of endobronchial disease in relation to age.

Miriam Esther Brailey

Miriam Brailey received both her MD (1930) and a doctorate in Epidemiology (1931) from Johns Hopkins.

She was one of the first doctoral students in the Dept of Epidemiology, and joined the faculty as its first female member. She taught with Frost. And also served as Director of the TB Bureau of Baltimore City Health Department.



Brailey M. Mortality in tuberculin-positive infants. Bull Johns Hopkins Hosp 1936; 59: 1-10.

- Limited to children <2 years of age.
- Either with a positive tuberculin test.
- Or familial contact with a sputum smear-positive adult.

Brailey M. Mortality in tuberculin-positive infants.
Bull Johns Hopkins Hosp 1936; 59: 1-10.

22 (33%) children in group A were symptomatic; of these 68% died within a year and 82% within 5 years

Findings at 1 st examination	N	Mortality %	
		Within 1 year	Within 5 years
A. Parenchymal lesions	67	31.5	40
B. Tracheobronchial nodes	36	5.6	12.7
C. Normal CR	67	7.5	9.2
B & C.	103	6.8	11.1

Brailey M. Mortality in tuberculin-positive infants.
Bull Johns Hopkins Hosp 1936; 59: 1-10.

- **TBM** 11 (6.5%), generalized TB 6 (3.5%)
- Further 3 (1.8%) **miliary TB** at PM
- If infected age <6 mths mortality **33.3%** in first year and **78%** by end of 5 years

Brailey ME. Prognosis in white and coloured tuberculous children according to initial chest X-ray findings. Am J Publ Hlth 1943; 33: 343-352

1,148 children TB infection diagnosed before age 15 years; 1/5th symptomatic, 4/5th examined because of known TB contact. 97 (8.5%) deaths

<i>Cause of Death</i>	<i>Infected before Age 3 Years</i>	
	<i>No. of deaths</i>	<i>Per cent</i>
Miliary Tuberculosis	32	43.8
Tuberculous Meningitis	26	35.6
Other Extrapulmonary Tuberculosis	2	2.7
Post-Primary Tuberculous Pneumonia	12	16.5
Reinfection Tuberculosis	1	1.4
Total Fatalities	73	100.0

Brailey ME. Prognosis in white and coloured tuberculous children according to initial chest X-ray findings. Am J Publ Hlth 1943; 33: 343-352

<i>Cause of Death</i>	<i>Infection Found Between Ages 3 and 15 Years</i>	
	<i>No. of deaths</i>	<i>Per cent</i>
Miliary Tuberculosis	4	16.7
Tuberculous Meningitis	6	25.0
Other Extrapulmonary Tuberculosis	0
Post-Primary Tuberculous Pneumonia	4	16.7
Reinfection Tuberculosis	10	41.6
	<hr/>	<hr/>
Total Fatalities	24	100.0

Davies PDB. The natural history of tuberculosis in children. *Tubercle* 1961; 42 (Suppl): 3-40.

Child contacts in the Brompton Hospital Child Contact Clinic, London 1930-1952.

Age	N	Deaths
0-1	29	6 (21%)
1-5	369	5 (1.3%)
5-10	634	5 (0.8%)
≥11	535	10 (1.8%)

Davies PDB. The natural history of tuberculosis in children. Tubercle 1961; 42 (Suppl): 3-40

- 29 children infected aged <1 year:
9 (31.0%) developed TBM/miliary TB.
- 369 children aged 1-5 years:
6 (1.6%) TBM/miliary TB
- 535 children aged 6-10 years
2 (0.32%) TBM/miliary TB

JA Myers. The natural history of tuberculosis in the human body. 1. The demonstrable primary pulmonary infiltrate. Am Rev Tuberc 1959; 79: 19-30.

- In 1921 an epidemiological programme instituted by the commissioner of Health in Minneapolis; 20 full time public health nurses appointed and between 1921- 1941 68 nurses took part in this programme.
- Children examined who were contacts of infectious adults or presented with manifestations suspicious of TB.

JA Myers. The natural history of tuberculosis in the human body. 1. The demonstrable primary pulmonary infiltrate. Am Rev Tuberc 1959; 79: 19-30.

- Experience documented in The Minneapolis Division of Public Health from 1921-1941.
- Routine included tuberculin testing, CR, gastric aspirate and sedimentation rate.

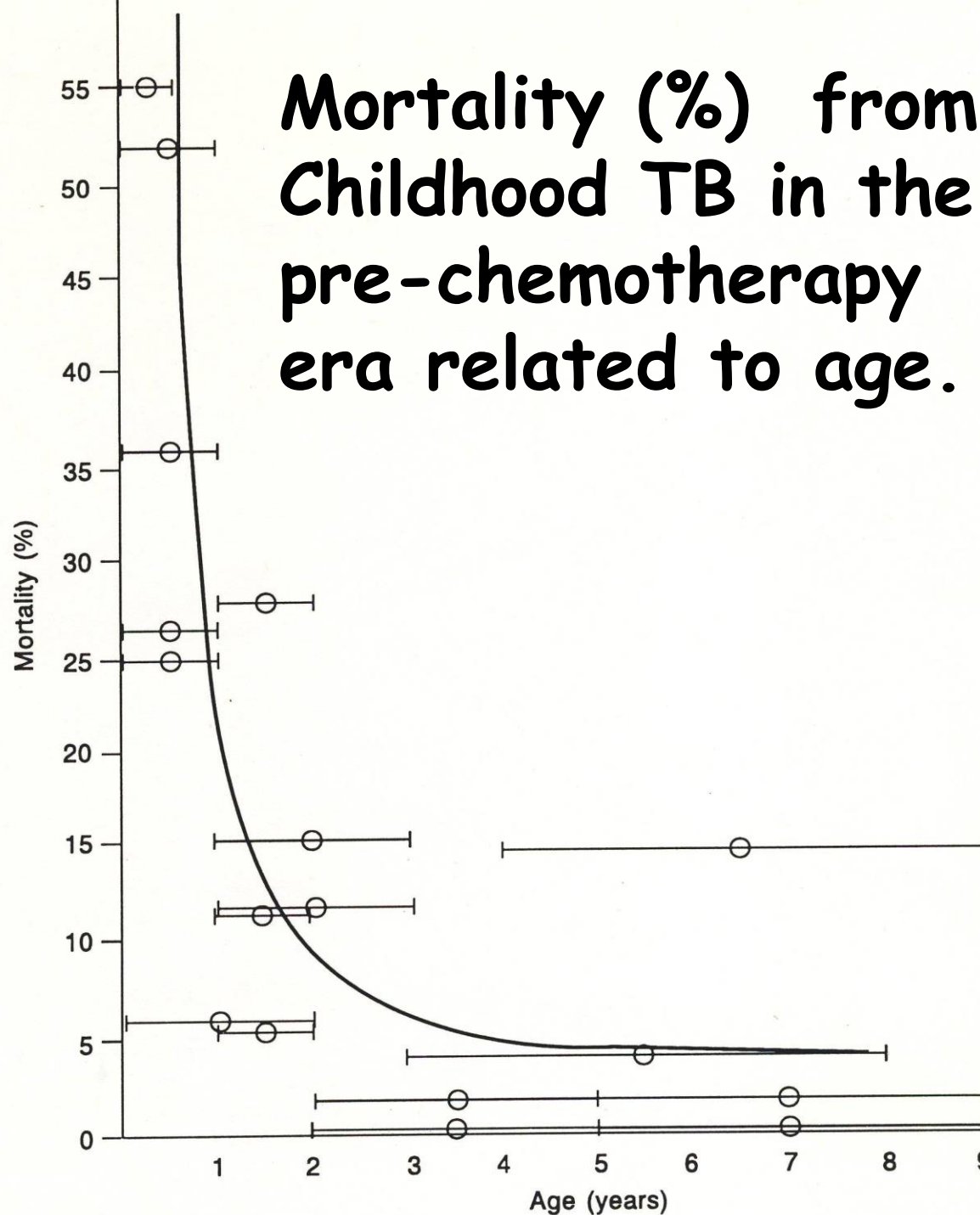
JA Myers. The natural history of tuberculosis in the human body. 1. The demonstrable primary pulmonary infiltrate. Am Rev Tuberc 1959; 79: 19-30.

- 300 children (mean age 6 yrs girls and 5 yrs boys) seen with primary pulmonary infiltrates or subsequent calcification.
- Mild symptoms, when diagnosed.
- 267 (89%) located after 6,305 person years, mean age approximately 31 yrs.
- 9 (3.4%) cases of death as result of TB recorded. (4 TBM, 1 miliary, 2 pneumonia, 2 adult type TB).

JA Myers. The natural history of tuberculosis in the human body. 1. The demonstrable primary pulmonary infiltrate. Am Rev Tuberc 1959; 79: 19-30.

- **Nine survivors** developed **PTB** In only one case was the subsequent lesion in the same lung area as the primary lesion.
- 222 (82%) children developed no evidence of subsequent clinical disease.
- **Had treatment been applied to these children it would have been credited with achieving a "cure" or disease prevention.**

Mortality (%) from Childhood TB in the pre-chemotherapy era related to age.



Küstner HGV. Tuberculosis in children.
Epidemiological Comments 1981; 8: 1-19

Mortality in relation to age
South Africa 1971-1980

<u>Age (yrs)</u>	<u>Mortality (%)</u>
<1	7.1
1-4	2.8
5-9	1.1
10-14	1.5

Features of Childhood Tuberculosis

If evaluated shortly after infection

- Chest radiograph may show adenopathy in as many as 80% of children, or CR may be normal with nodes visible only on CT.

(Delacourt C, et al. Computed tomography with normal chest radiograph in tuberculous infection. Arch Dis Child 1993; 69: 430-432.

- Gedde-Dahl T. Tuberculous infection in the light of tuberculin matriculation. Am J Hyg 1952; 56: 139-214)

Bentley FJ, Grzybowski S, Benjamin B. Tuberculosis in childhood and adolescence. National Association for the Prevention of Tuberculosis; London:1954

AUTHOR	COUNTRY	YEAR	PERCENTAGE WITH RADIOLOGICAL ABNORMALITY	AGE	REMARKS
Myers . . .	U.S.A.	1949	5-10 per cent	Children of all ages	
Brailey . . .	U.S.A.	1936	61 per cent	Infants under 2	
Lincoln . . .	U.S.A.	1950	Over 80 per cent	Infants under 2	
Anderson <i>et al</i> .	U.K.	1951	(a) 23 per cent (b) 16 per cent	Children under 15	(a) Important contacts (b) Other contacts
Daniels <i>et al</i> .	U.K.	1948	8 per cent	Adults	
Nissen Meyer .	Norway	1949	63 per cent 45 " " 27 " " 17 " "	0-3 4-12 13-19 over 20	These figures refer to hilar adenitis only
Gedde-Dahl .	Norway	1948	73 per cent 50 per cent	0-6 7-19	
Hyge . . .	Denmark	1947	58 per cent	12-18	

Natural History of TB

If evaluated shortly after infection

M tuberculosis can be cultured from gastric aspirate (or urine) in a significant proportion of children **even if the CR appears normal (occult TB)**.

Fox TG. Occult tuberculous infection in children. *Tubercle* 1977; 58: 91-96.

Levin N. On the demonstration of tubercle bacilli by means of lavage of the stomach in different forms of tuberculosis in children. *Acta Paediatr* 1935; 17 (suppl): 160-169.

Poulsen V, Andersen AO. Four years' experience with examination of material obtained by gastric lavage. *Am J Dis Child* 1934;47: 307-321.

The Natural History of TB Disease

Lincoln EM. Late discharge of tubercle bacilli in primary tuberculosis. Am Rev Tuberc 1959; 79: 31-40.

“...between 7.7% and 15% of more than 700 children with primary tuberculosis excreted tubercle bacilli six months or more after the original diagnosis, almost always without any clinical or roentgenographic changes.”

Wallgren A. Primary pulmonary tuberculosis in childhood. *Am J Dis Child* 1935; 49: 1105-1136.

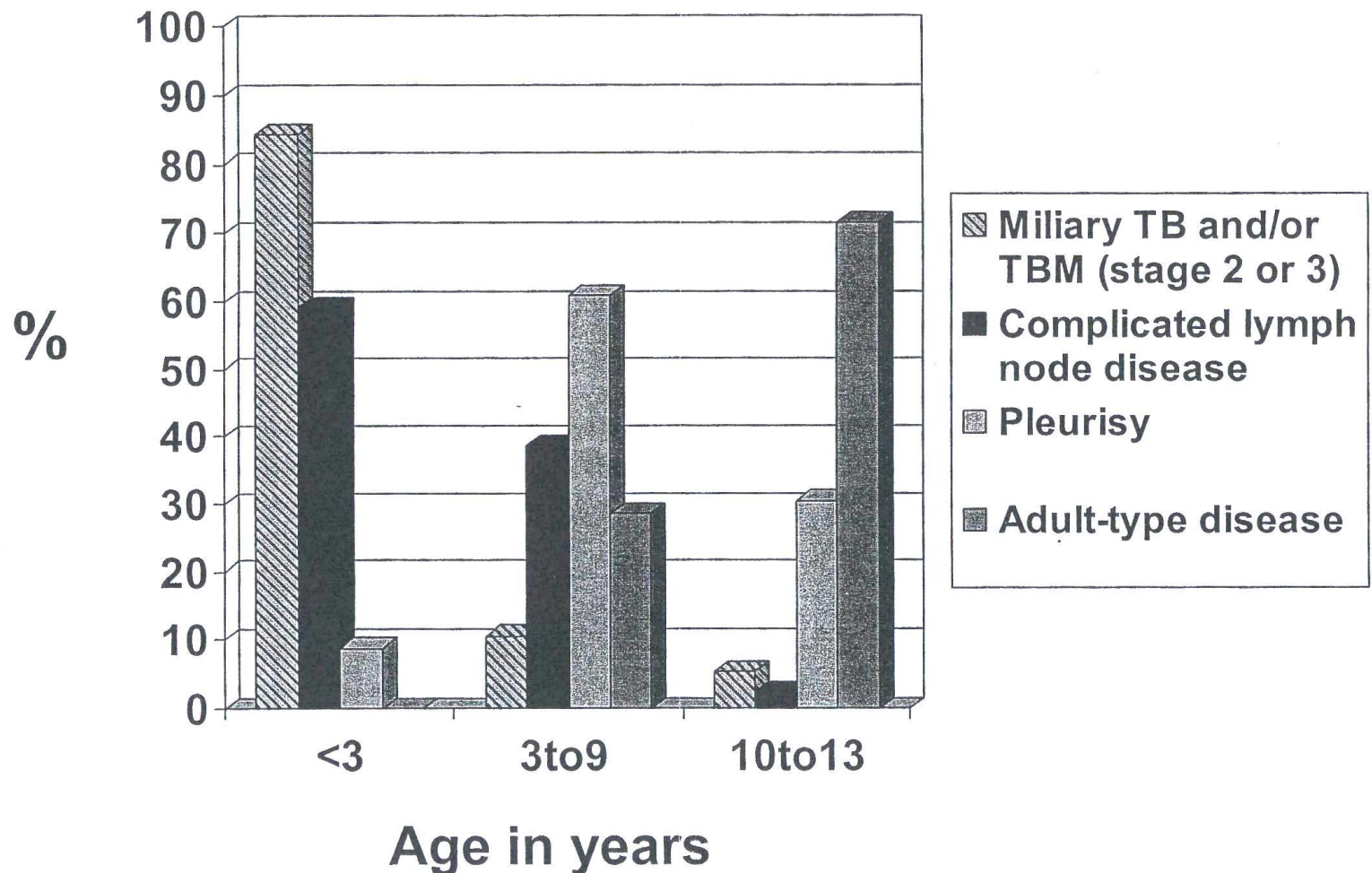
"The presence or absence of bacilli obtained by means of washing out the stomach and the results of testing a guinea-pig with the water from the lavage must not be taken to have prognostic value."

Marais BJ et al. The spectrum of disease in children treated for tuberculosis in a highly endemic area. Int J Tuberc Lung Dis 2006; 10: 732-738.

- A prospective descriptive study of children treated for TB at 5 primary care clinics in Cape Town (2003)
- 439 children treated for TB

Marais BJ, et al. The spectrum of disease in children treated for tuberculosis in a highly endemic area. Int J Tuberc Lung Dis 2006; 10: 732-738.

Age distribution of specific disease entities recorded in HIV-uninfected children treated for tuberculosis



The Natural History of TB

Summary

- During childhood there is a **spectrum of disease** with a gradient of morbidity and mortality decreasing from infancy to 3-5 years of age.
- **Infected infants and toddlers** have a very high incidence of **TBM** and **miliary TB**.
- A very high incidence of **lympho-bronchial TB** and its complications occurs in children <3 years of age.

The Natural History of TB

Summary

- As children enter adolescence there is an ever increasing incidence of **adult-type tuberculosis with cavitation in the apices of the lungs**. Untreated mortality increases.
- These children then start to contribute to the spread of tuberculosis infection and relevance to prevalence studies.

The Quantification of Childhood Tuberculosis

(numbers, rates, percentages)

Summary

- By whatever means the burden of childhood tuberculosis is quantified the **very young** have an inordinately high **morbidity** and **mortality**

Walls T, Shingadia D. Global epidemiology of paediatric tuberculosis. *J Infect* 2004; 48: 13-22

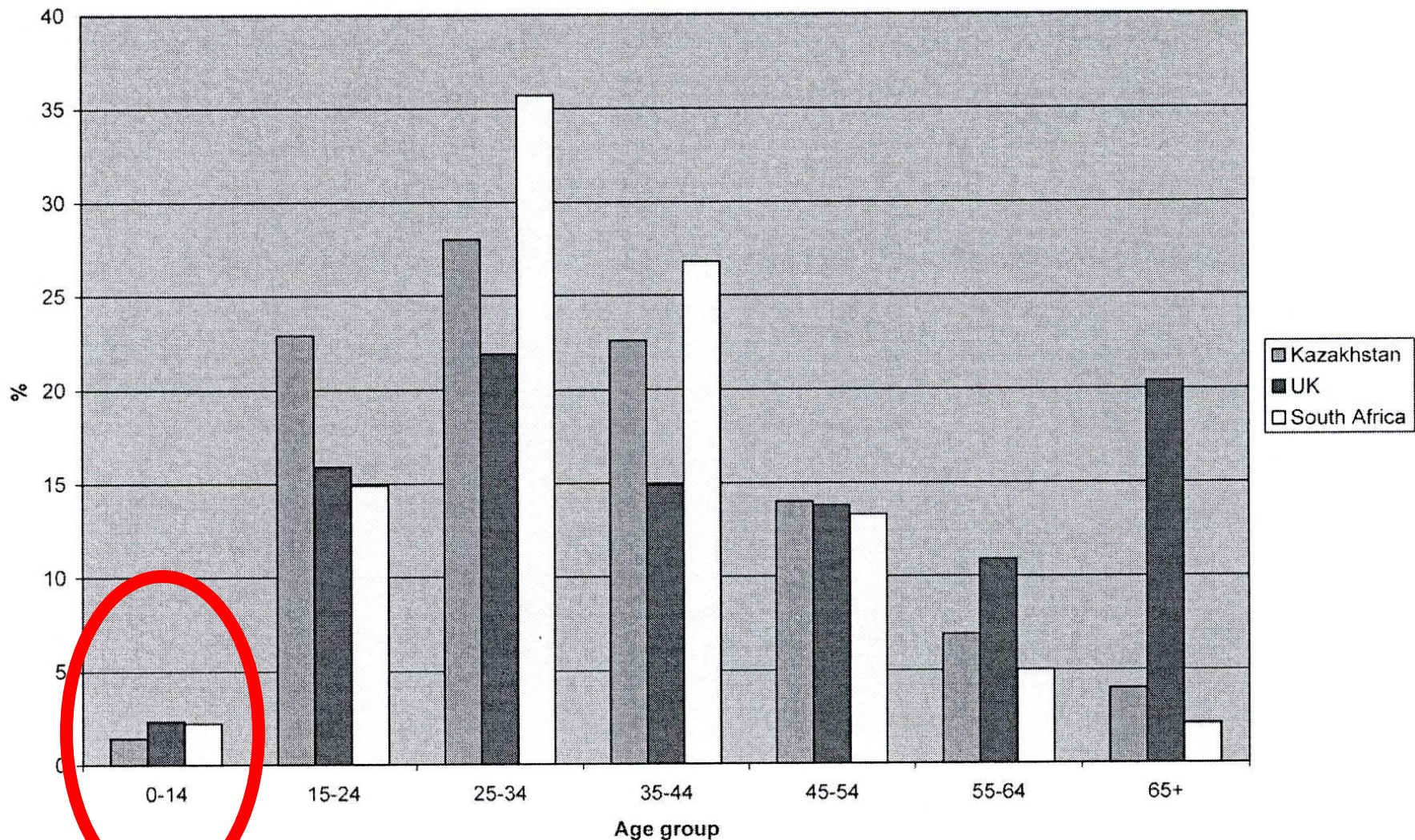
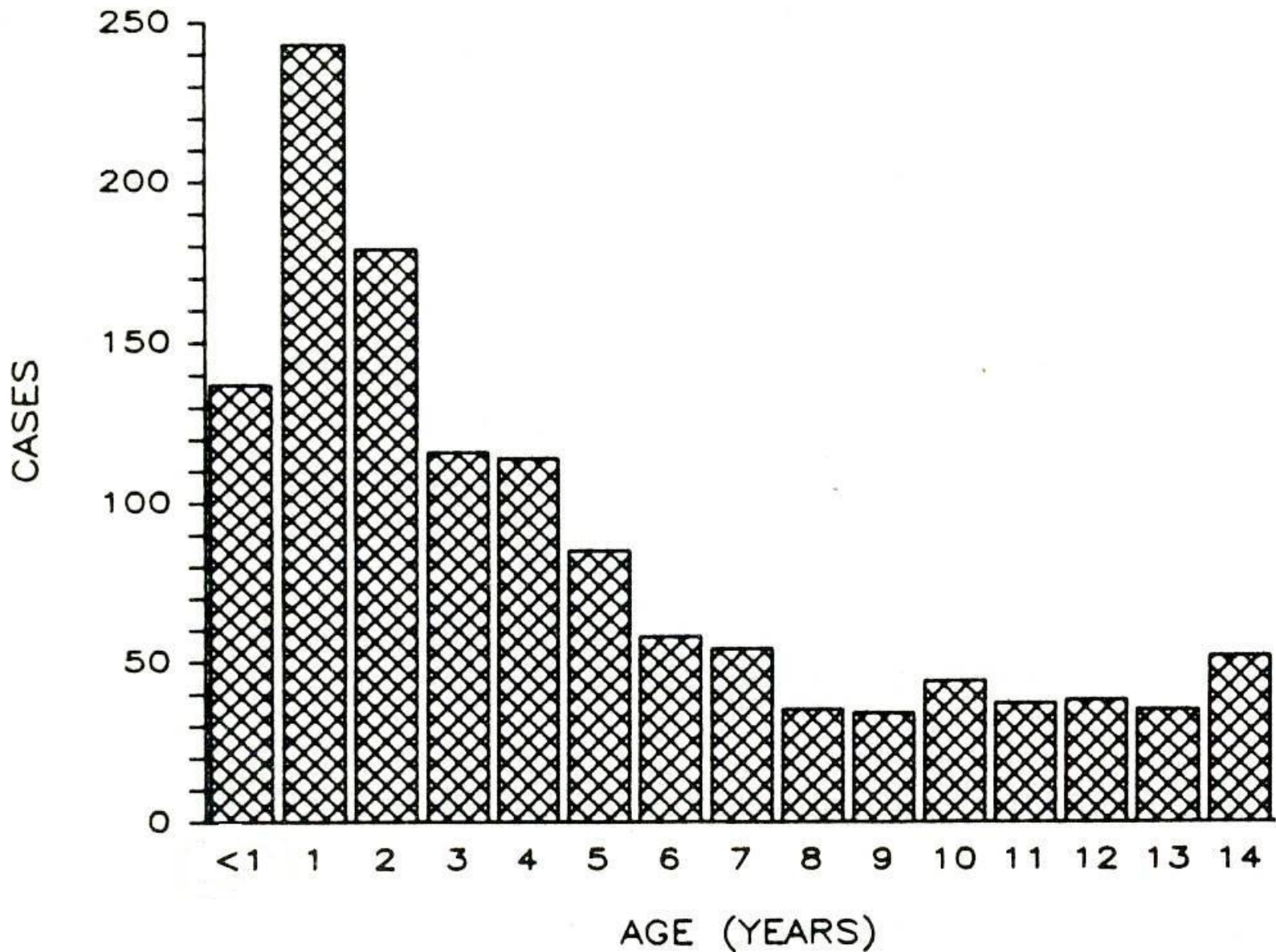
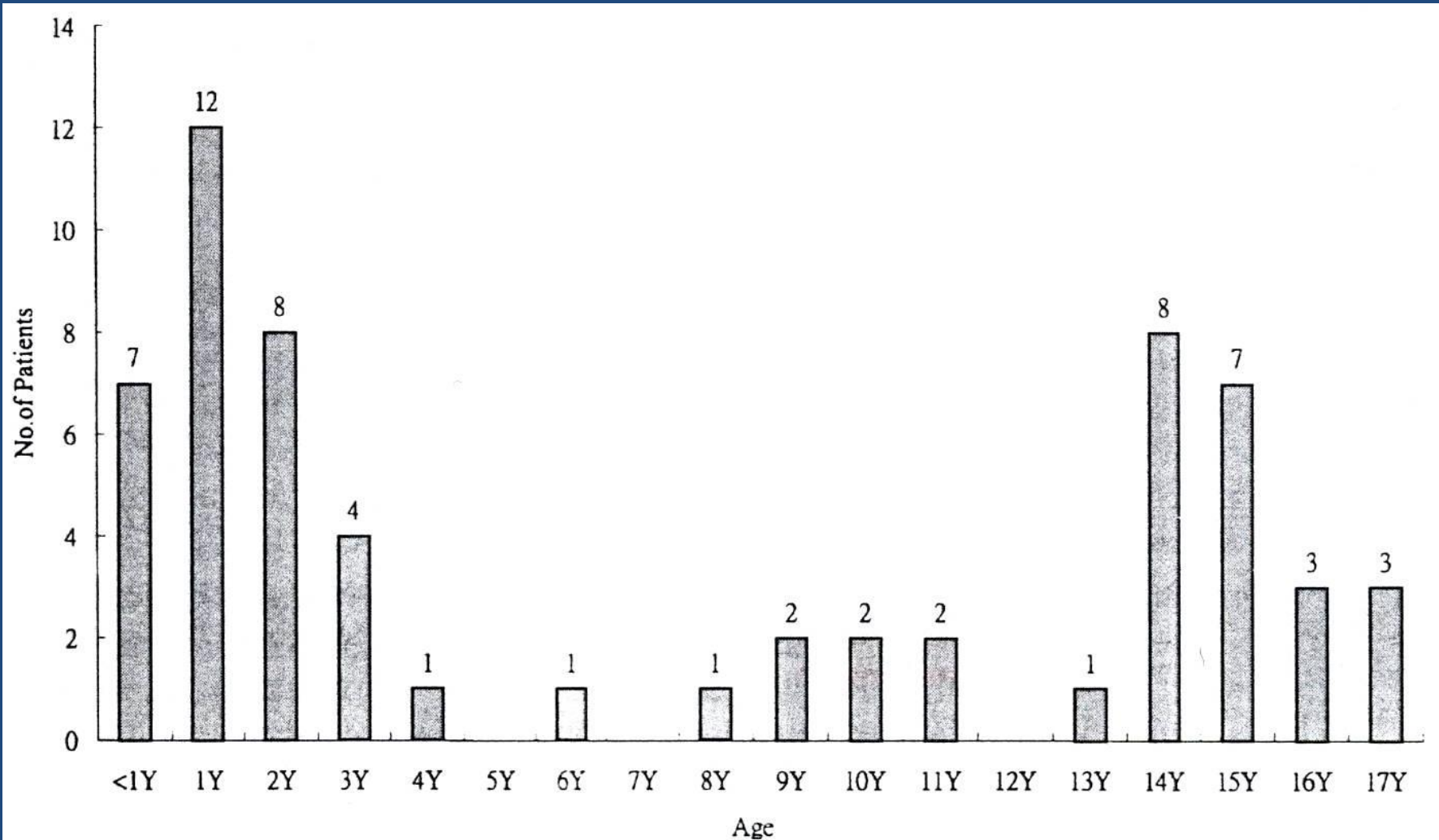


Figure 1 Age distribution of smear-positive TB case notifications to WHO, 2001.

Snider DE, Rieder HL, Combs D, Bloch AB, Hayden CH, Smith MHD.
Tuberculosis in children. *Pediatr Infect Dis J* 1988; 7: 271-278.

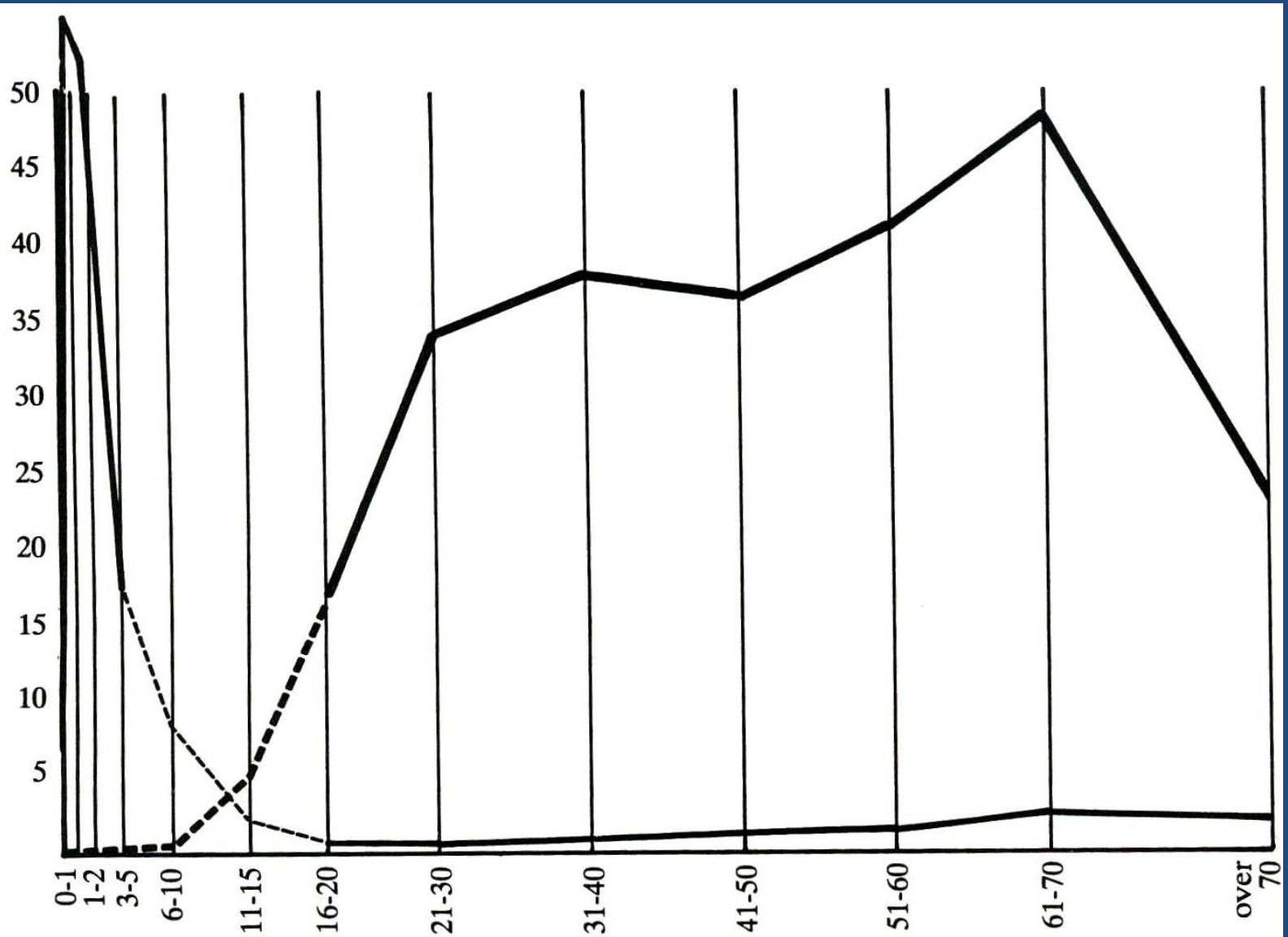


Wong KS, Chiu CH, Lin TY. Childhood and adolescent tuberculosis in northern Taiwan: an institutional experience. Acta Paediatr 2001; 90: 943-947.



Mortality

Krause KE. Diagnose und Epidemiologie der Lungentuberculose des Kindes. Archiv fur Kinderheilkunde 1910; 54: 279-306.



Wade Hampton Frost. 1880-1938

Qualified in Medicine
at the University of
Virginia 1903.

1917 diagnosed with TB;
spent several months in a
sanatorium.

1922. Professor &
Chairman of the
Department of
Epidemiology and Public
Health Administration
at Johns Hopkins
University.

Approximately 1928 he
began to study
tuberculosis.



Frost WH. The age selection of mortality from tuberculosis in successive decades. Am J Hyg 1939; 30: 91-96

Death rates per 100,000 from TB, all forms, Massachusetts, 1880 to 1930, by age and sex, with rates for cohort 1880 indicated.

Age	1880	1890	1900	1910	1920	1930
<i>Males</i>						
0- 4	760	578	309	209	108	41
5- 9	43	49	31	21	24	11
10-19	126	115	90	63	49	21
20-29	444	361	288	207	149	81
30-39	378	368	296	253	164	115
40-49	364	336	253	253	175	118
50-59	366	325	267	252	171	127
60-69	475	346	304	246	172	95
70+	672	396	343	163	127	95
<i>Females</i>						
0- 4	658	595	354	162	101	27
5- 9	71	82	49	45	24	13
10-19	265	213	145	92	78	27
20-29	537	398	290	207	167	92
30-39	422	372	260	189	135	73
40-49	307	307	211	153	108	53
50-59	334	234	173	130	83	47
60-69	434	295	172	118	83	56
70+	584	375	296	126	68	40

AR Rich. The Pathogenesis of Tuberculosis. 1st Ed. Chap V11:180-248. Table X111. Mortality from tuberculosis at different age periods in the general population and in the **estimated infected portion** of the population

TABLE XIII
MORTALITY FROM TUBERCULOSIS AT DIFFERENT AGE PERIODS IN THE GENERAL POPULATION,
AND IN THE ESTIMATED INFECTED PORTION OF THE POPULATION
(U. S. Registration Area, 1940)

Age	Total Deaths from Tuberculosis	Estimated Per Cent Infected*	Deaths from Tuberculosis per 100,000 Persons of Each Age Period			Deaths from Tuberculosis per 100,000 Estimated Infected Persons of Each Age Period
			Male	Female	Both Sexes	Both Sexes
0-1	496	0.5	24.8	24.3	24.6	4,920
1-4	1,047	10	12.6	12.0	12.3	123
5-9	469	25	4.6	4.2	4.4	18
10-14	775	35	5.0	8.2	6.6	19
15-19	3,375	45	19.7	35.1	27.4	61
20-24	5,752	55	41.5	57.5	49.6	90
25-29	6,243	65	52.7	59.7	56.3	87
30-34	5,775	75	60.3	52.6	56.4	75
35-39	5,448	85	67.0	47.3	57.1	67
40-44	5,438	90	83.2	40.4	61.9	69
45-49	5,222	95	90.6	34.8	63.3	66
50-54	5,058	95	101.3	35.8	69.7	73
55-59	4,409	95	109.9	38.9	75.4	79
60-64	3,641	95	110.3	42.8	77.0	81
65-69	2,975	95	105.4	51.1	78.2	82
70-74	2,179	95	107.6	62.5	84.8	89
75 and over	2,057	95	90.3	66.8	77.8	82

* Estimated from recent tuberculin surveys. See Table XII and text discussion for limitations.

TABLE XIII

MORTALITY FROM TUBERCULOSIS AT DIFFERENT AGE PERIODS IN THE GENERAL POPULATION,
AND IN THE ESTIMATED INFECTED PORTION OF THE POPULATION

(U. S. Registration Area, 1940)

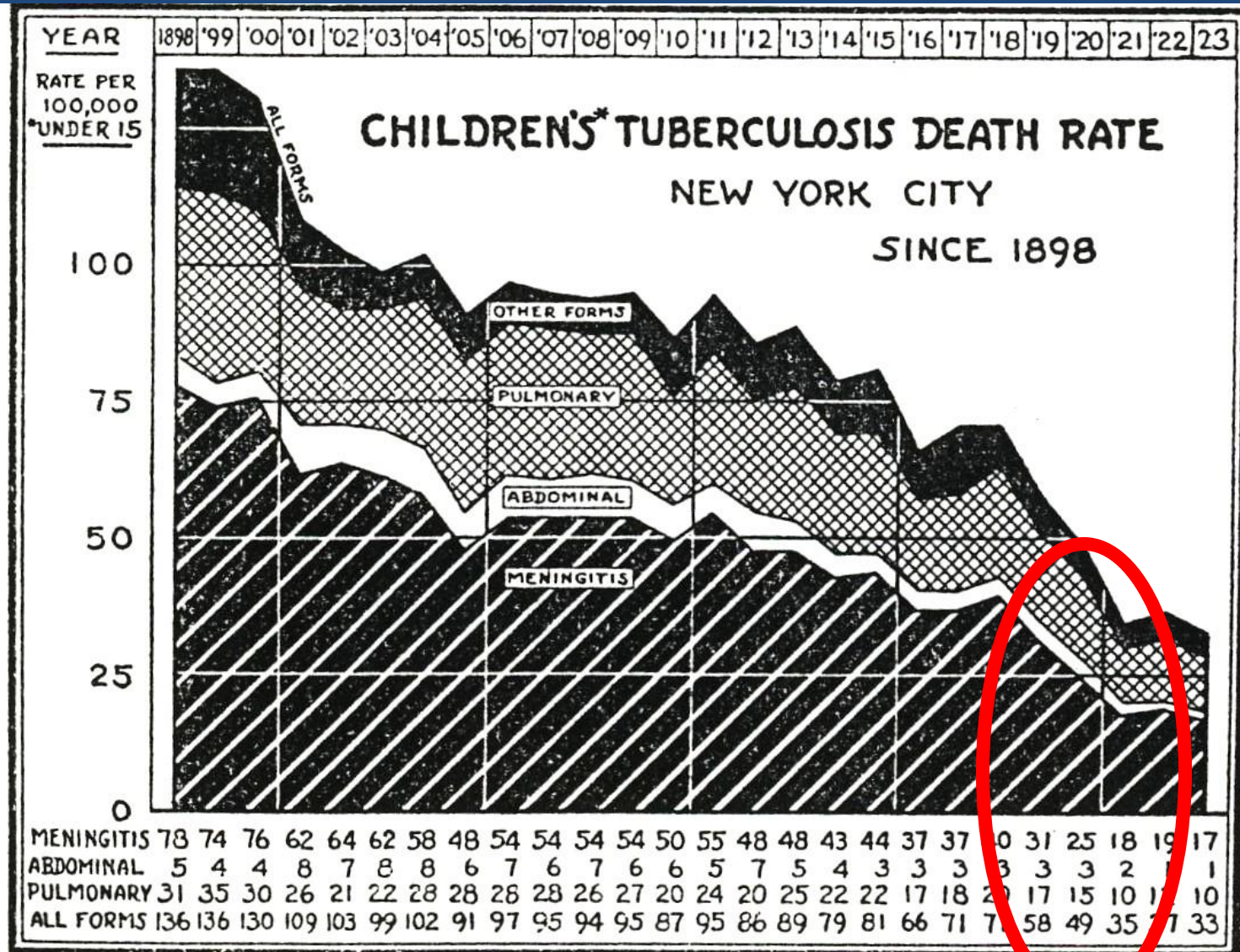
Age	Total Deaths from Tuber- culosis	Estimated Per Cent Infected*	Deaths from Tuberculosis per 100,000 Persons of Each Age Period			Deaths from Tuberculosis per 100,000 Estimated Infected Persons of Each Age Period
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0-1	496	0.5	24.8	24.3	24.6	4,920
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15-19	3,375	45	19.7	35.1	27.4	61
20-24	5,752	55	41.5	57.5	49.6	90
25-29	6,243	65	52.7	59.7	56.3	87

TABLE 6. *Morbidity and Fatality in Tuberculin Positive Persons**London A.C. 1945-49.***59.6/1,000**

SEX	AGE-YEARS	MEAN POPULATION	TUBERCULIN POSITIVE		TUBERCULOSIS NOTIFICATIONS		DEATHS FROM TUBERCULOSIS	
			Per cent (Estimated)	No.	Mean annual Number 1945-49	Per 1,000 tuberculin positive	Mean annual Number 1945-49	Per 1,000 tuberculin positive
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
Both	0-1	57,100	0.5	285	34	119.3	17	59.6
Male and Female	1-4	187,360	3.4	6,370	275	43.2	49	7.7
	5-9	178,170	16.0	28,510	270	9.5	20	0.7
Female	10-14	172,960	31.0	53,620	221	4.1	19	0.4
	15-24	476,580	62.0	295,480	1,652	5.6	282	1.0
	25-44	1,053,190	88.0	926,810	2,190	2.4	733	0.8
	45 +	1,149,920	94.5	1,086,330	1,290	1.2	996	0.9
TOTAL		3,275,280	—	—	5,932	—	2,116	—

**Bentley FJ,
Grzybowski S,
Benjamin B.
Tuberculosis in
childhood and
adolescence.
National
Association for
the Prevention of
Tuberculosis;
London:1954**

Drolet GJ. Tuberculosis in children. Am Rev Tuberc 1925; 11: 292-303



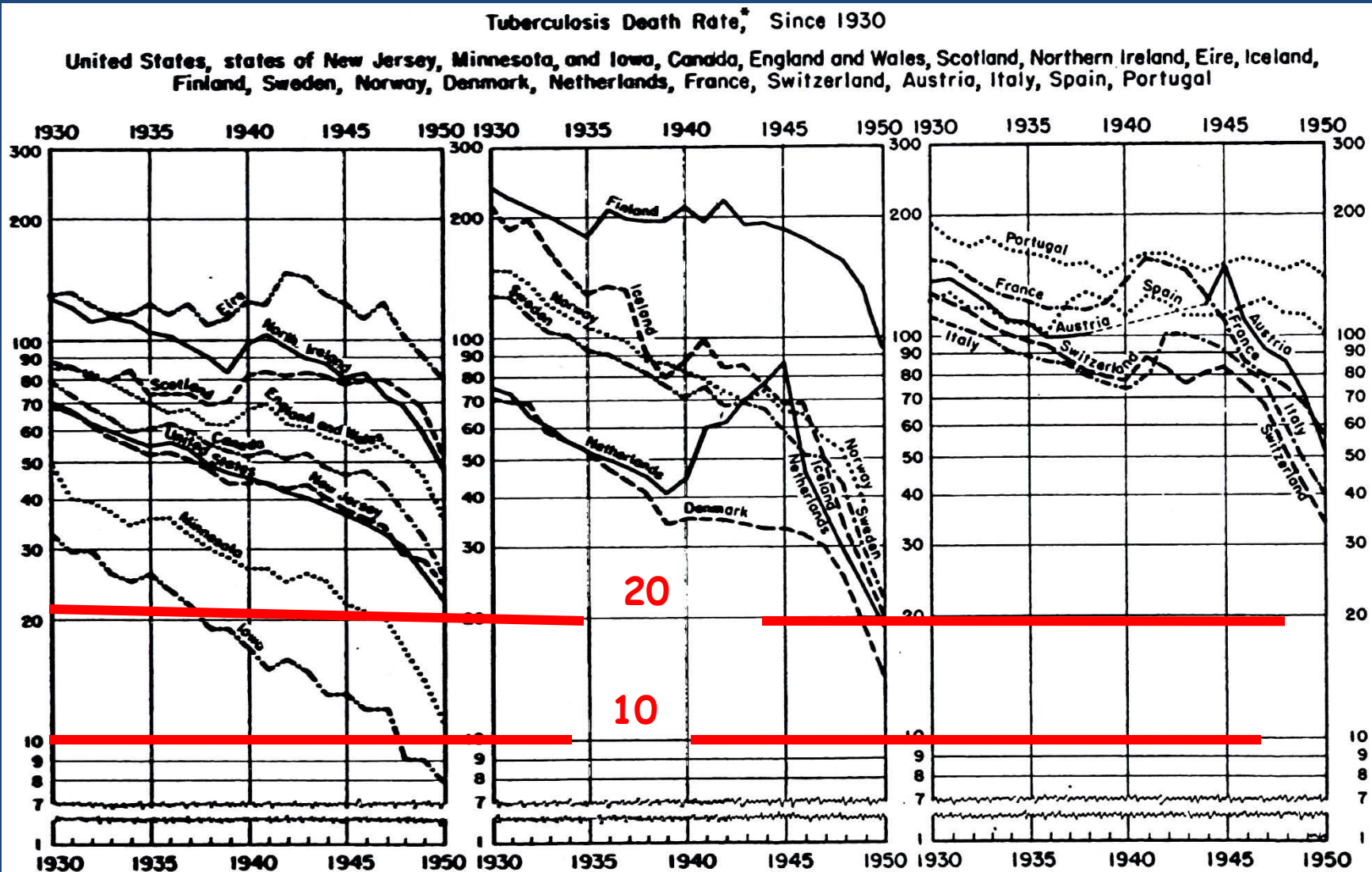
Compiled from Reports, New York City Department of Health by G.J. DROLET, Research Service NEW YORK TUBERCULOSIS ASSOCIATION, INC.

CHART 2.

Drolet GJ, Lowell AM. Whither tuberculosis? A statistical review of reports from selected American and European communities. Dis Chest 1952; 21: 527-561.

- “Just as infant mortality, generally speaking, is a sensitive index of general health conditions, so in tuberculosis the incidence, particularly of active cases, among children is a **prime index of the prevalence of tuberculosis in the community.**”

Drolet GJ, Lowell AM. Whither tuberculosis? A statistical review of reports from selected American and European communities. Dis Chest 1952; 21: 527-561.



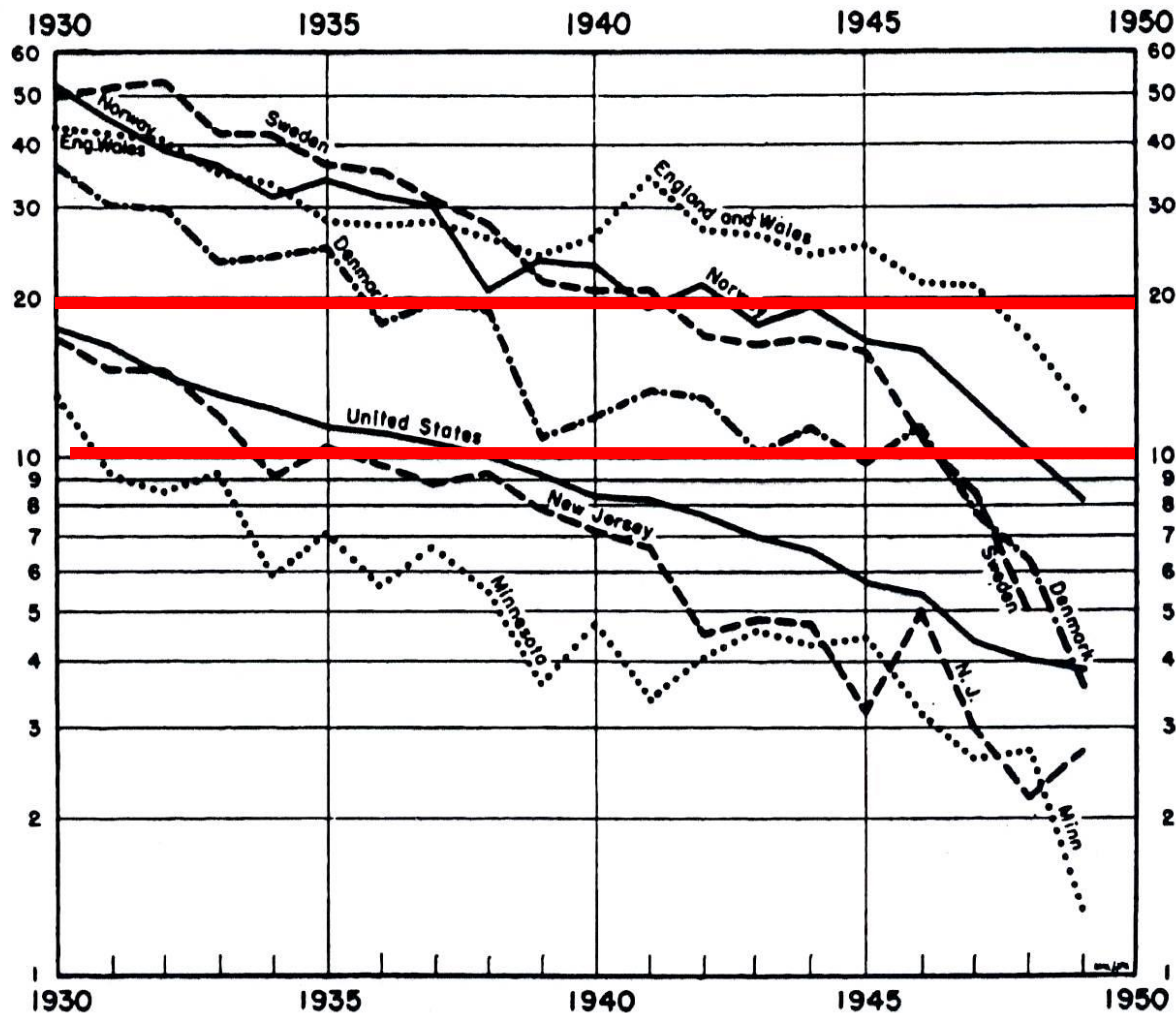
*Per 100,000 population.

Drolet GJ, Lowell AM. Whither tuberculosis? A statistical review of reports from selected American and European communities. Dis Chest 1952; 21: 527-561

FIGURE 4

Tuberculosis Death Rate*, Children under Fifteen, Since 1930

United States, states of New Jersey, Minnesota,
England and Wales, Norway, Sweden, Denmark



*Per 100,000 children under 15 years of age.

Drolet GJ, Lowell AM. Whither tuberculosis? A statistical review of reports from, selected American and European communities. Dis Chest 1952; 21: 527-561

TABLE VI, PART 2: DENMARK, 1931-1949
Tuberculosis Mortality of Children by Age and Sex.

Years*	NUMBER OF DEATHS							DEATH RATE PER 100,000						
	'31-35	'36-40	'41-45	1946	1947	1948	1949	'31-35	'36-40	'41-45	1946	1947	1948	1949
Male:														
0- 4	81	49	36	44	28	24	10	53	31	20	21	13	11	4
5- 9	23	13	12	15	12	8	5	15	9	8	9	7	5	3
10-14	23	16	11	7	8	3	2	13	10	8	5	5	2	1
0-14	127	78	59	66	48	35	17	26	17	12	13	9	6	3
Female:														
0- 4	69	44	27	32	23	21	14	47	29	17	16	11	10	7
5- 9	29	10	10	8	5	5	4	18	7	7	5	3	3	2
10-14	27	14	13	10	8	7	5	16	9	9	5	5	5	3
0-14	125	68	50	50	36	33	23	26	15	11	10	7	6	4
Both Sexes:														
0- 4	150	93	63	76	51	45	24	50	30	18	18	12	10	6
5- 9	52	23	22	23	17	13	9	16	8	7	7	5	4	2
10-14	50	30	24	17	16	10	7	15	10	8	6	5	3	2
0-14	252	146	109	116	84	68	40	26	16	12	11	8	6	4

Denmark child population, 1949: 0-4=434,300; 5-9=362,900; 10-14=308,500.

*Quinquennial figures are averages annually.

**Drolet GJ, Lowell AM. Whither tuberculosis?
A statistical review of reports from selected
American and European communities. Dis
Chest 1952; 21: 527-561**

Country/state	Paediatric portion of mortality (%)	
	1930	1949
Norway	9.9	5.0
Sweden	10.0	2.3
Denmark	14.3	5.1
USA	6.9	4.0

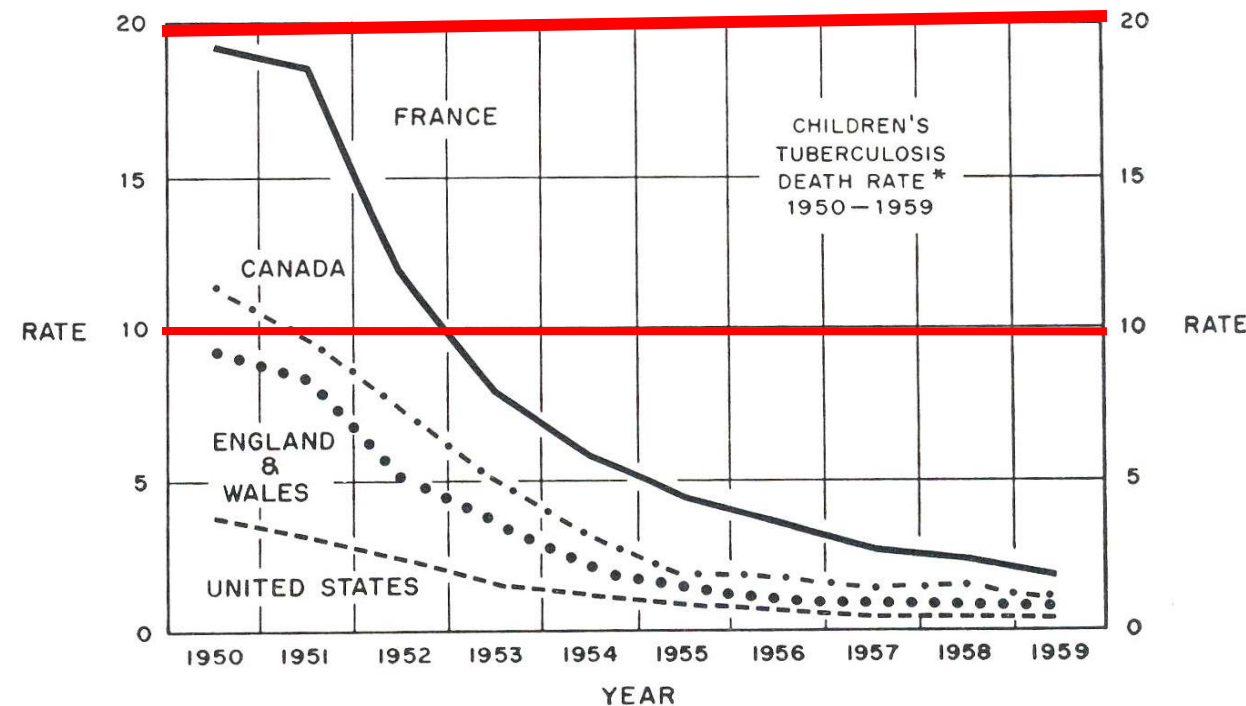
Tuberculosis Mortality Among Children: The Last Stage

A Statistical Review of the 1950-1959 Decade
in Canada, the United States, England and Wales, and France*

GODIAS J. DROLET† AND ANTHONY M. LOWELL†
New York, New York

CHILDREN HAVE BENEFITED MOST FROM the campaign against tuberculosis. A study of mortality records in four different countries reveals a unique record of lifesaving during the last decade—greater than has ever occurred in so limited a period.

CANADA, UNITED STATES, ENGLAND AND WALES
AND FRANCE



* PER 100,000 CHILDREN UNDER 15 YEARS OF AGE.

Dis Chest
1962;
42:364-371

TABLE 5—TUBERCULOSIS MORTALITY*

IN 1950 AND 1959

CHILDREN UNDER 15

Country	Deaths 0-14		Death Rate†		Decline
	1950	1959	1950	1959	
Canada‡	466	51	11.45	0.88	92%
United States¶	1,531	240	3.78	0.44	88%
England, Wales	909	72	9.45	0.69	93%
France	1,771	208	19.40	1.80	91%

*All forms. †Per 100,000 child population. ‡Exclusive of Yukon and Northwest Territories. ¶ Continental United States.

Dis Chest 1962;
42:364-371

TABLE 7—TUBERCULOUS MENINGITIS MORTALITY
IN 1950 AND 1959
CHILDREN UNDER 15

Country	Deaths 0-14		Deaths Rate†		
	1950	1959	1950	1959	Decline
Canada¶	207	30	5.08	0.52	90%
United States‡	671	133	1.65	0.24	85%
England, Wales	594	44	6.17	0.42	93%
France	1,365	141	14.95	1.22	92%

†Per 100,000 child population. ¶Exclusive of Yu-
kon and Northwest Territories. ‡Continental Unit-
ed States.

Dis Chest 1962;42:364-371

3. In 1959, tuberculous meningitis was still responsible for the majority of deaths among children: 55 per cent of those in the United States; 61 per cent in Canada, England and Wales; and 68 per cent in France; but its occurrence has been greatly reduced.

Styblo K, Sutherland I. The epidemiology of tuberculosis in children. Bull Int Union Tuberc 1982; 57: 133-139

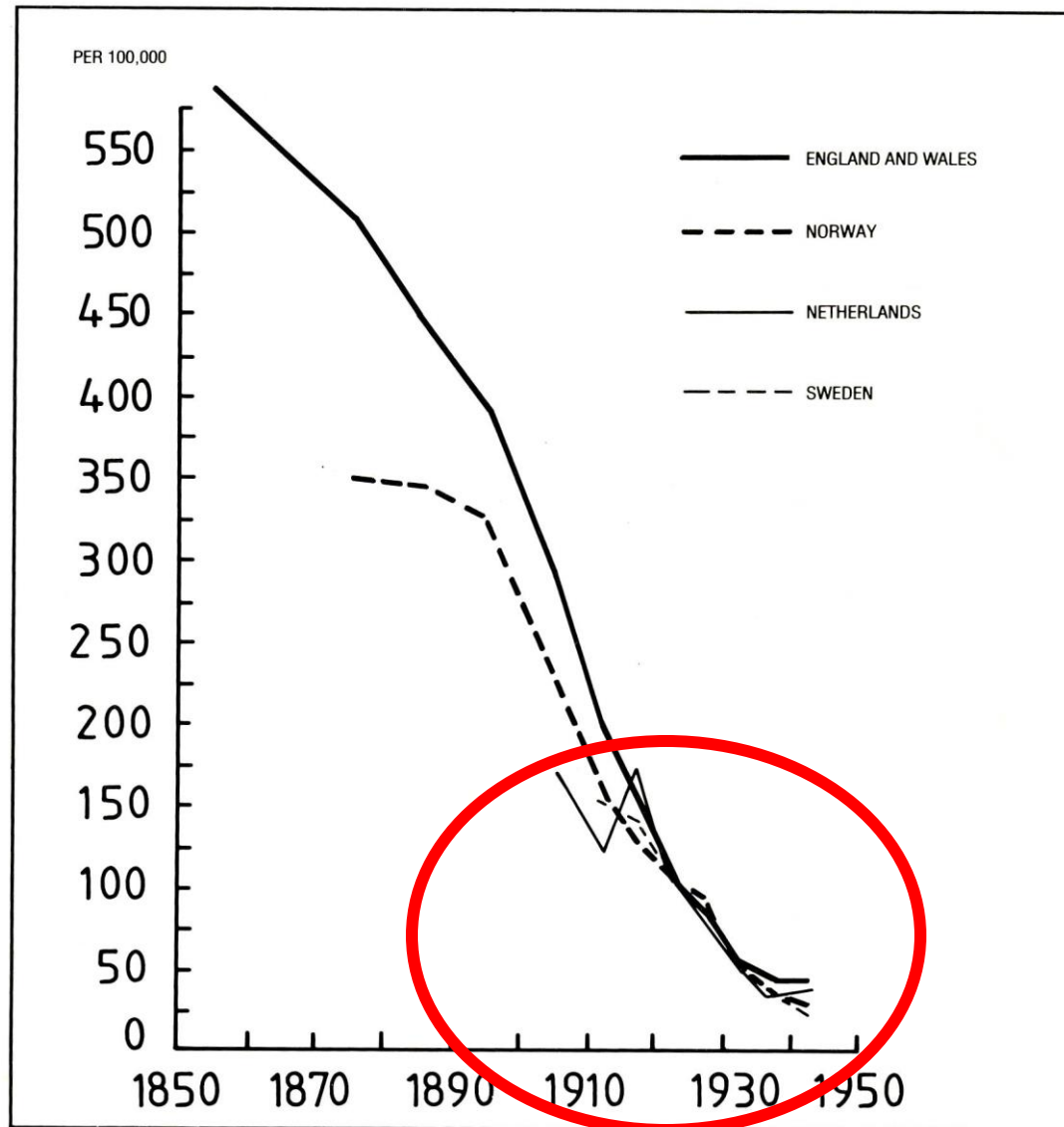


Figure 1. Tuberculosis mortality rates (per 100,000) in children aged 0 to 4 years until 1945 ; England and Wales (from 1851), the Netherlands (from 1901), Norway (from 1871) and Sweden (from 1911).

Styblo K, Sutherland I. The epidemiology of tuberculosis in children. Bull Int Union Tuberc 1982; 57: 133-139

Period	Estimated risk of tuberculous infection (%)	Mortality rates from tuberculosis (per 100,000)				Ratio of the mortality rate to risk of infection (per 1,000)			
		0-4		5-14		0-4		5-14	
		◆	◆◆	◆	◆◆	◆	◆◆	◆	◆◆
1911-15	9.68	141.1	69.3	60.7	23.4	14.6	7.2	6.3	2.4
1916-20	7.44	171.0	82.9	83.2	28.9	23.0*	11.1*	11.2*	3.9*
1921-25	5.71	107.0	60.3	44.9	18.3	18.7	10.6	7.9	3.2
1926-30	4.37	77.8	44.3	33.8	14.1	17.8	10.1	7.7	3.2
1931-35	3.34	49.4	30.6	21.9	10.2	14.8	9.2	6.6	3.1
1936-40	2.55	32.1	19.6	14.7	7.2	12.6	7.7	5.8	2.8
1941-45	1.38	34.1	18.0	17.3	7.6	24.7*	13.0*	12.6*	5.5*
Average ratios (1916-20 and 1941-45 excluded)						15.7	9.0	6.9	2.9

◆ : all forms of tuberculosis.

◆◆ : tuberculous meningitis.

* : infection more frequently proceeded to disease and death during war years.

Styblo K, Sutherland I. The epidemiology of tuberculosis in children. Bull Int Union Tuberc 1982; 57: 133-139

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		0-4		5-14		0-4		5-14	
		◆	◆◆	◆	◆◆	◆	◆◆	◆	◆◆
1911-15	9.68	141.1	69.3	60.7	23.4	14.6	7.2	6.3	2.4
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		0-4		5-14		0-4		5-14	
		◆	◆◆	◆	◆◆	◆	◆◆	◆	◆◆
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Styblo K, Sutherland I. The epidemiology of tuberculosis in children. Bull Int Union Tuberc 1982; 57: 133-139

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		0-4		5-14		0-4		5-14	
		◆	◆◆	◆	◆◆	◆	◆◆	◆	◆◆
1911-15	9.68	141.1	69.3	60.7	23.4	14.6	7.2	6.3	2.4
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◆ : all forms of tuberculosis.

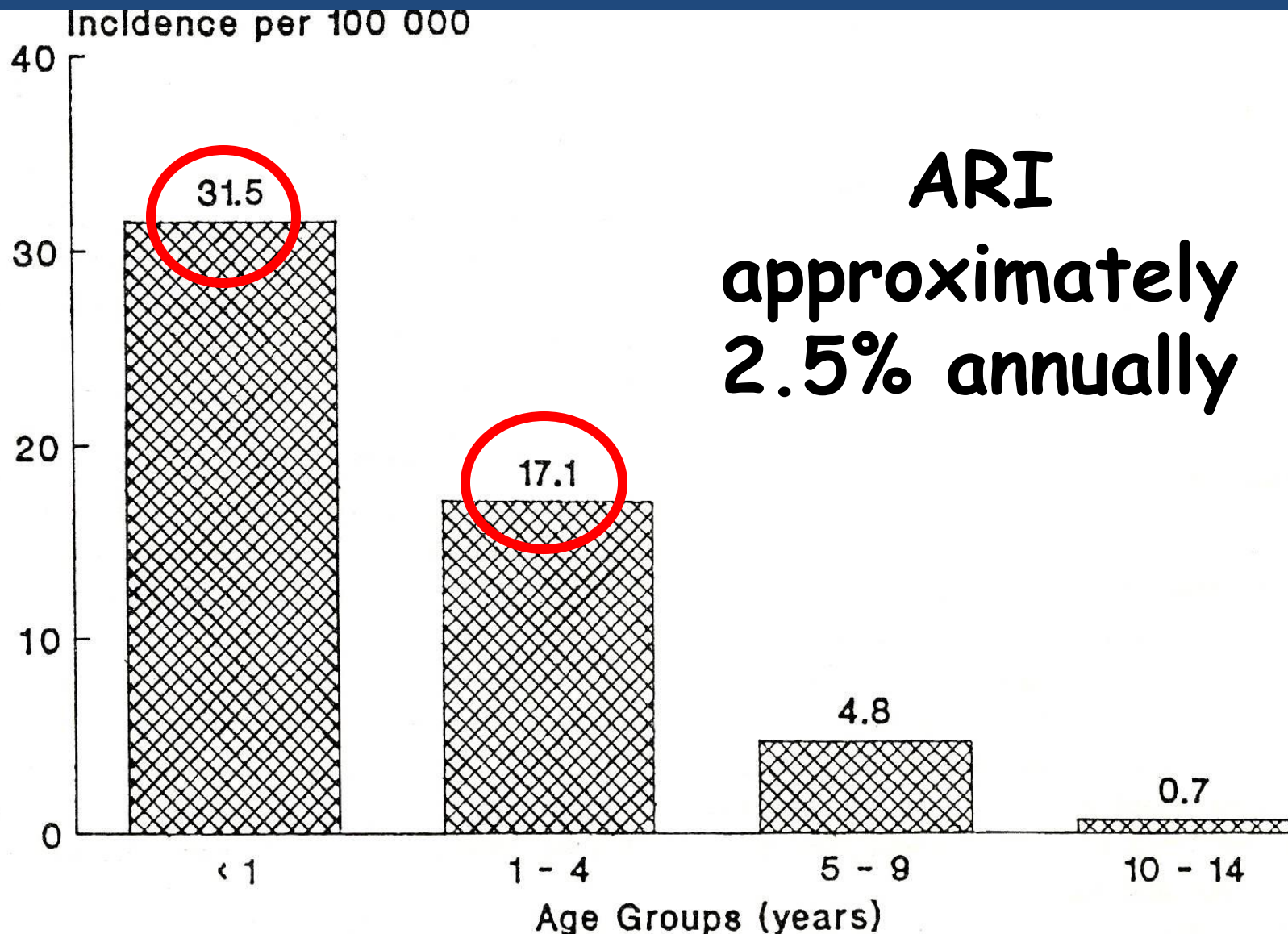
◆◆ : tuberculous meningitis.

* : infection more frequently proceeded to disease and death during war years.

Styblo K, Sutherland I. The epidemiology of tuberculosis in children. Bull Int Union Tuberc 1982; 57: 133-139

Period	Estimated risk of tuberculous infection (%)	Mortality rates from (per 100,000)	
		0-4	5-14
1911-15	9.68	141.1	69.3
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1936-40	2.55	32.1	19.6
1941-45	1.38	34.1	18.0

Berman S, Kibel MA, Fourie PB, Strebel MP. Childhood tuberculosis and tuberculous meningitis in the Western Cape of South Africa. *Tubercle Lung Dis* 1992; 73: 349-355.



Cammock RM, Miller FJ. Tuberculosis in young children. Lancet 1953;1: 158-160.

- Proportion infected children <5years age in Tyneside, UK: **4%=1020** of 25,000
- 258 children with positive tuberculin tests found. 55 (21%) no evidence of disease.
- **42 (4.1%) TBM or miliary TB**
- 16 (1.5%) Osteo-articular TB
- 203 (79%) Primary TB chest, abdomen, cervical nodes, skin.

Cammock RM, Miller FJ. Tuberculosis in young children. Lancet 1953;1: 158-160.

- 36 (14%) deaths; all but 4 due to either TBM or miliary TB.
- 31/42 (74%) cases of TBM or miliary TB occurred in children infected before 2 years of age

Fossemaile JF, et al. The natural trend of tuberculosis. Some of the characteristics of this trend in a developing country: Uruguay. Bull Int Union Tuberc 1981; 56: 38-44

Table 2. Tuberculous meningitis mortality rate per 100,000 population (observed rate and estimated rate) in children from 0 to 4 years of age. Period 1920-1946, Uruguay

Years	Estimated population (Census 1908)	Average number of deaths	Rate	
			a	b
1920-22	201,000	85	42.2	46.6
1923-25	210,000	80	38.1	43.5
1926-28	217,000	92	42.4	40.5
1929-31	217,500	103	47.4	37.8
1932-34	217,500	105	48.3	35.2
1935-37	208,000	70	33.6	32.9
1938-40	216,800	67	30.9	30.6
1941-43	219,000	80	36.5	28.6
1944-46	243,800	51	20.9	26.6

a : rates observed ; **b** : rates estimated (see Appendix).

Source : " Anuario Estadístico del Uruguay ".

Styblo K, Sutherland I. Epidemiology of tuberculosis in children. Bull Int Union Tuberc 1982; 57: 133-139.

“Numbers and rates (per 100,000) for infectious cases.....”

Table 3. Numbers and rates (per 100,000) of « infectious cases » (see text on page) in children aged 0-4, 5-9 and 10-14 years (1936-1940, 1941-1945 and 1946-1950) ; numbers and rates (per 100,000) of all cases of pulmonary tuberculosis (1943-1945, 1946-1950 and 1951-1955), Norway

Period	0-4 years		5-9 years		10-14 years		All ages	
	N	Rate	N	Rate	N	Rate	N	Rate (estimated)
a. « Infectious cases »								
1936-40	42	20.3	74	33.9	154	51.7	270	37
1941-45	28	12.1	35	17.1	76	34.8	139	21
1946-50	20	6.6	18	8.0	39	19.3	77	11
b. All cases of pulmonary tuberculosis								
1943-45	232	92.6	375	180.6	554	262.2	1,161	173
1946-50	252	83.1	356	154.5	377	187.3	985	134
1951-55	148	48.3	227	74.3	187	80.6	562	67

Styblo K, Sutherland I. Epidemiology of tuberculosis in children.
Bull Int Union Tuberc 1982; 57: 133-139.

Norwegian "Infectious cases"

TB bacilli demonstrable in sputum,
and/or "tendency to pthysic progress"

"Cases in which bacilli are
demonstrated only in gastric contents
or laryngeal swabs are grouped as
non-infectious **unless cavity or pthysic
progress is evident.**"

Styblo K, Sutherland I. Epidemiology of tuberculosis in children.
Bull Int Union Tuberc 1982; 57: 133-139

Age group	Total number of PTB	Infectious cases	% infectious
Norway 1946-1950			
0-4	252	20	7.9%
5-9	356	18	5.1%
10-14	377	39	10.3%
Netherlands 1951-1968			0.9%
Denmark 1961-1971			4.9%

Saskatchewan adolescents **32% pos cultures**, but
achieved with intensive culture examination.
Only 2% smear positive

Suryanarayana L, Suryanarayana HV, Jagannatha PS. Prevalence of pulmonary tuberculosis among children in a South Indian community. Ind J Tuberc 1999; 46: 171-178.

- 62 randomly selected villages near Bangalore.
- Children ≤ 14 years 38% of total population.
- ARTI 1-1.25%.
- 17,477 children initially screened.
- Estimate the prevalence of PTB amongst children.

Suryanarayana L, Suryanarayana HV, Jagannatha PS. Prevalence of pulmonary tuberculosis among children in a South Indian community. Ind J Tuberc 1999; 46: 171-178.

Criteria for further investigation:

- Tub test ≥ 10 mm.
- Malnutrition (Quitlet index)
- TB symptoms.
- Past hospitalisation for TB.
- **6075** children eligible for further investigation.

Suryanarayana L, Suryanarayana HV, Jagannatha PS. Prevalence of pulmonary tuberculosis among children in a South Indian community. Ind J Tuberc 1999; 46: 171-178.

- TST \geq 10 mm: **1798** (34.5%)
- Malnutr: **3299** (20.1%)
- Enlarged lymph nodes: **534** (3.2%)
- TB symptoms: **242** (1.5%)
- Household contact: **608** (4%)

Suryanarayana L, et al. Prevalence of pulmonary tuberculosis among children in a South Indian community. Ind J Tuberc 1999; 46: 171-178.

Further investigations 6075/16505 (36.9%)

- Chest radiograph
- **Sputum** all children ≥ 5 years (SM & Cult)

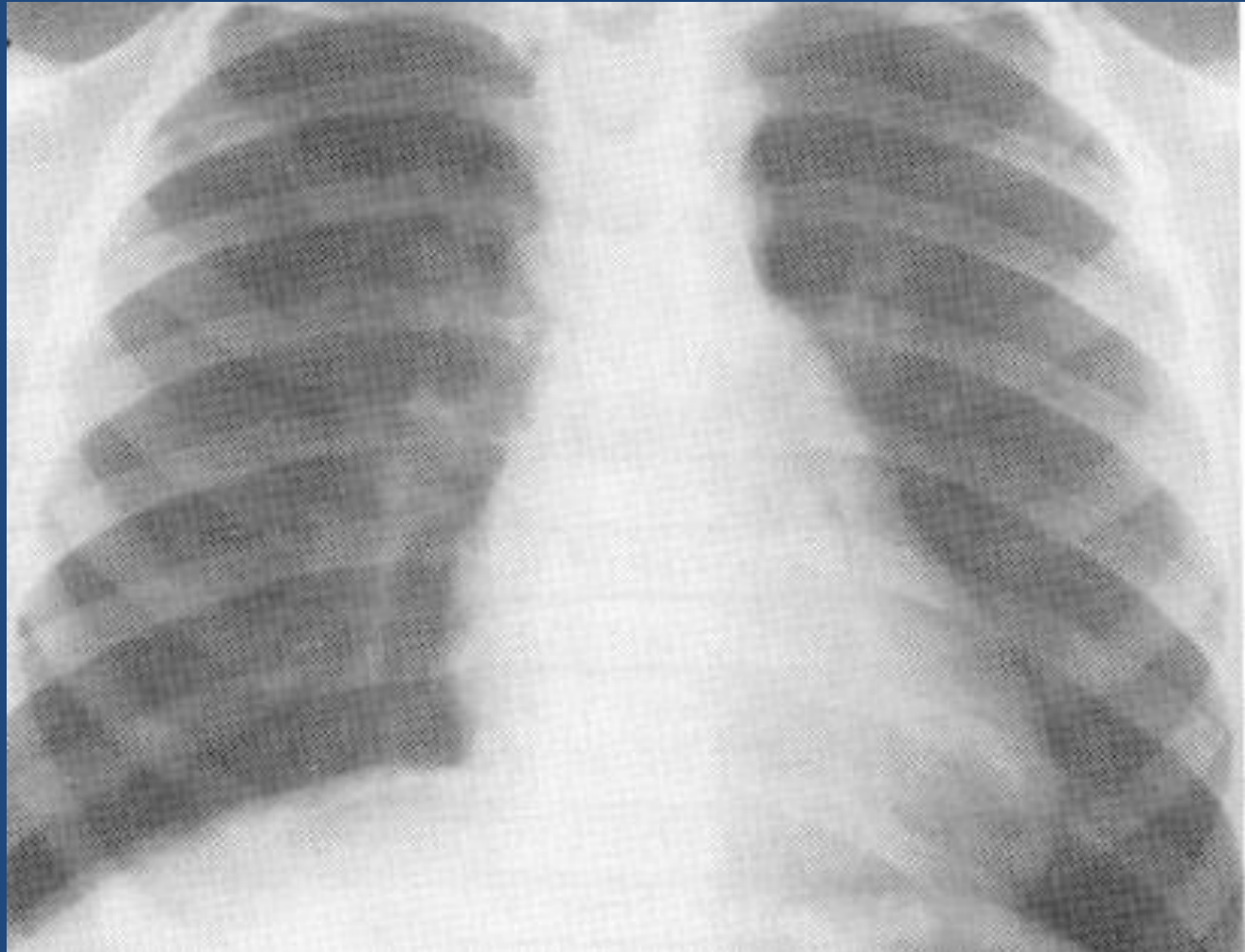
Age (years)	N	Prevalence (%)		
		CR 'Pos'	Culture +	Smear +
≤ 4	1798	11 (0.61)	-	-
5-14	4277	50 (1.17)	14 (0.33)	3 (0.07)

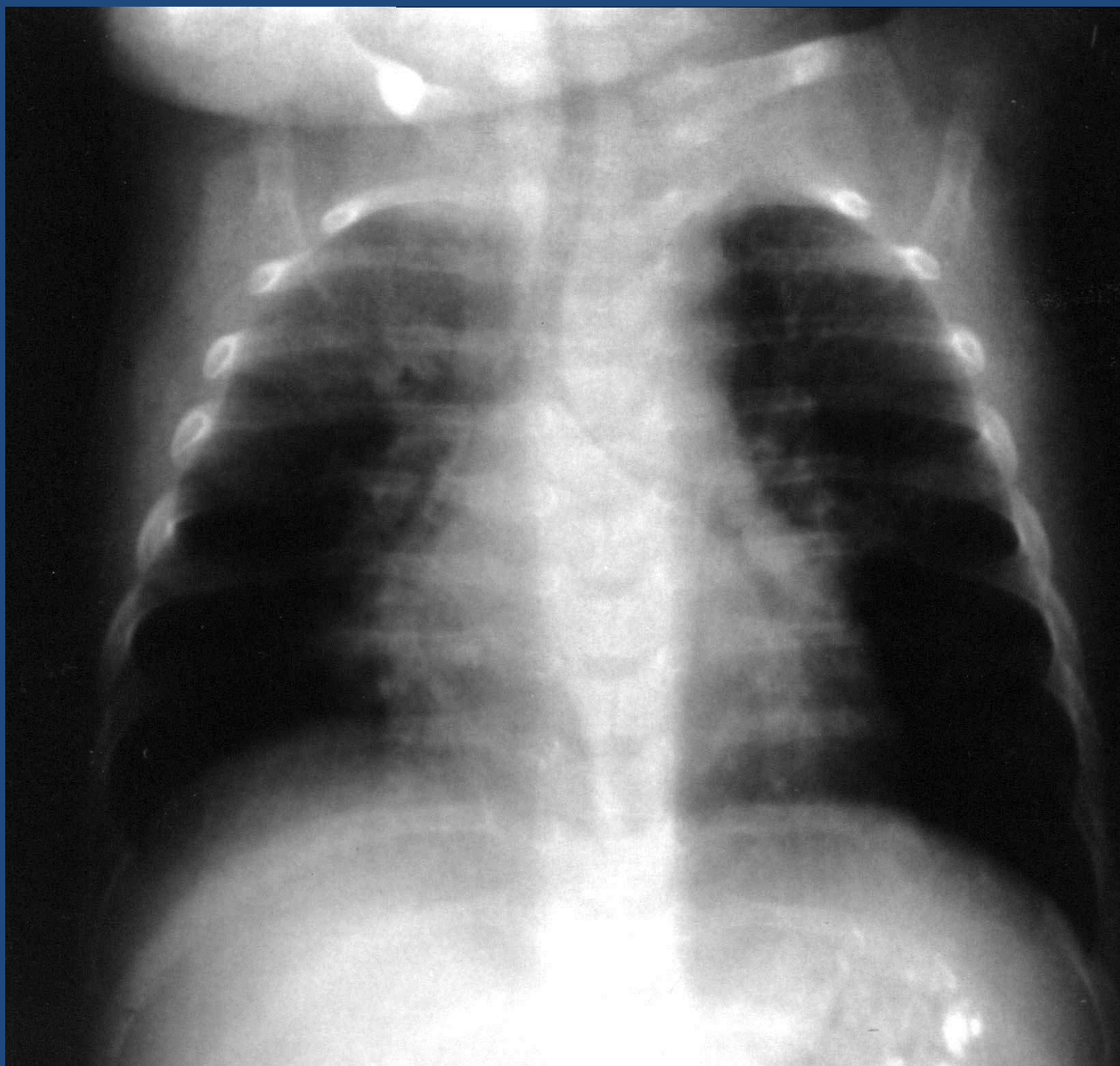
• Only 3 of the 17 microbiological positive cases had radiological evidence of disease.

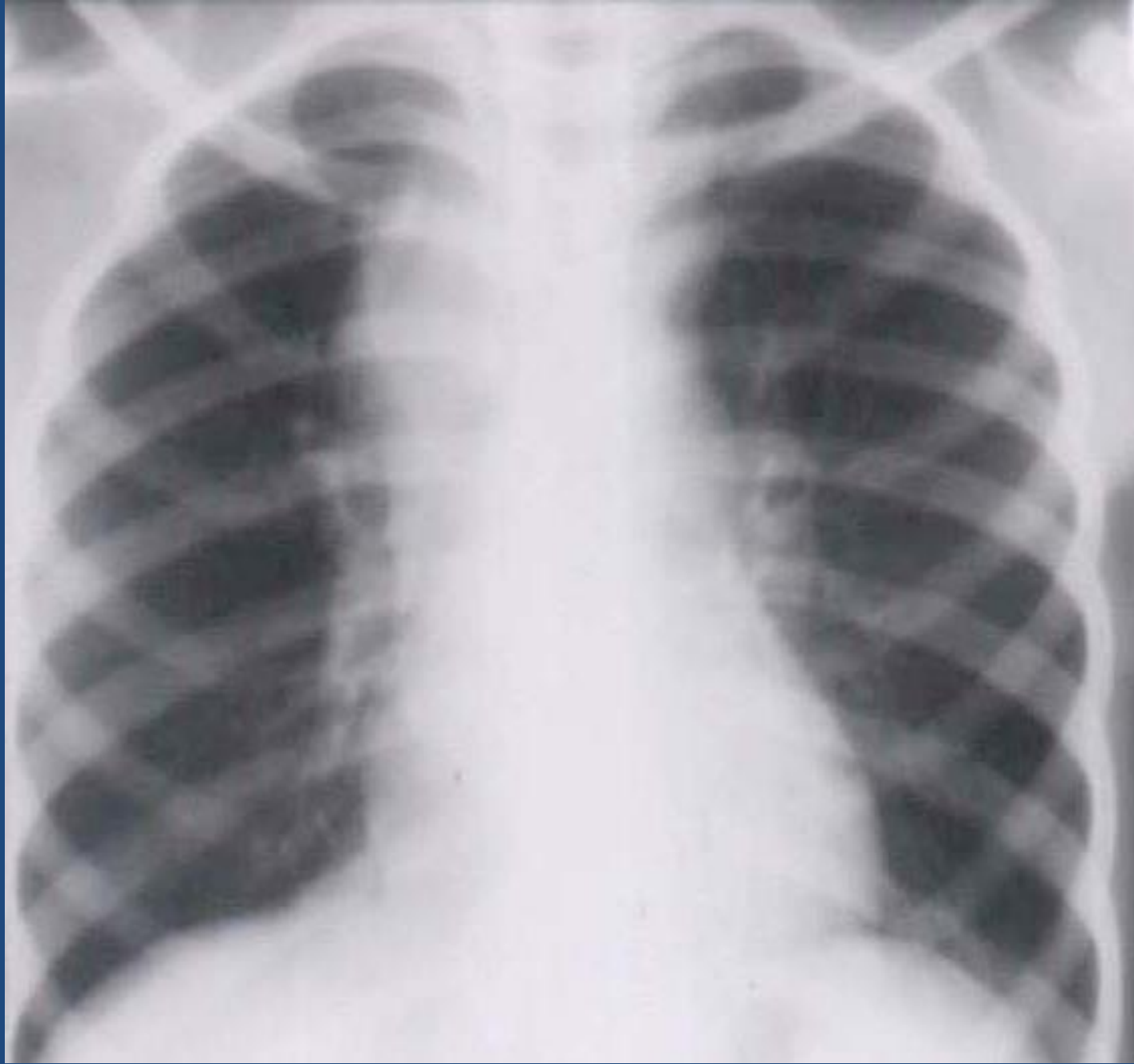
Suryanarayana L, Suryanarayana HV, Jagannatha PS.
Prevalence of pulmonary tuberculosis among children in a South
Indian community. Ind J Tuberc 1999; 46: 171-178.

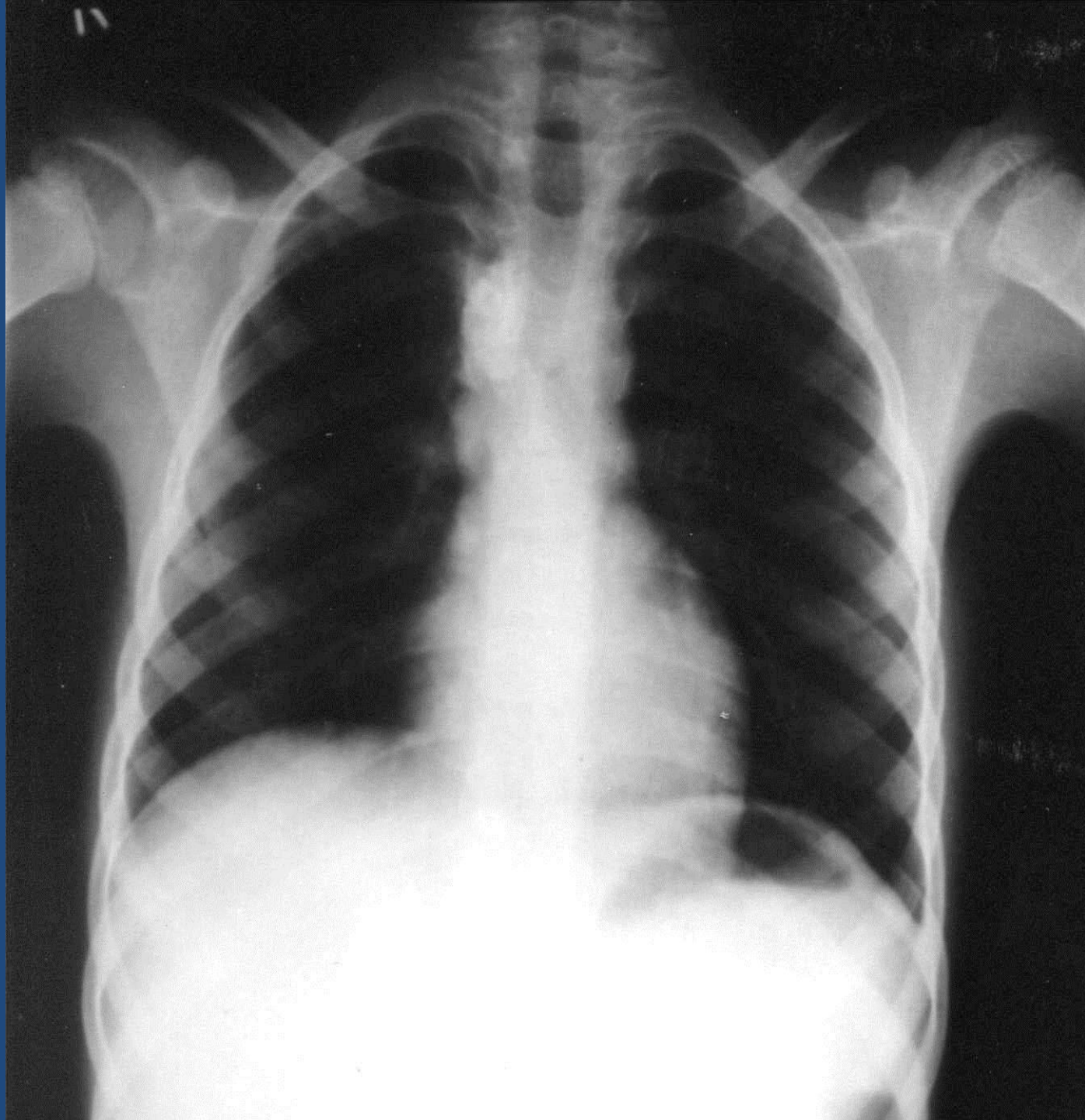
“...it would be better to resort
to the inexpensive method of
estimating ARTI and indirectly
compute serious forms of
tuberculosis like tuberculous
meningitis”

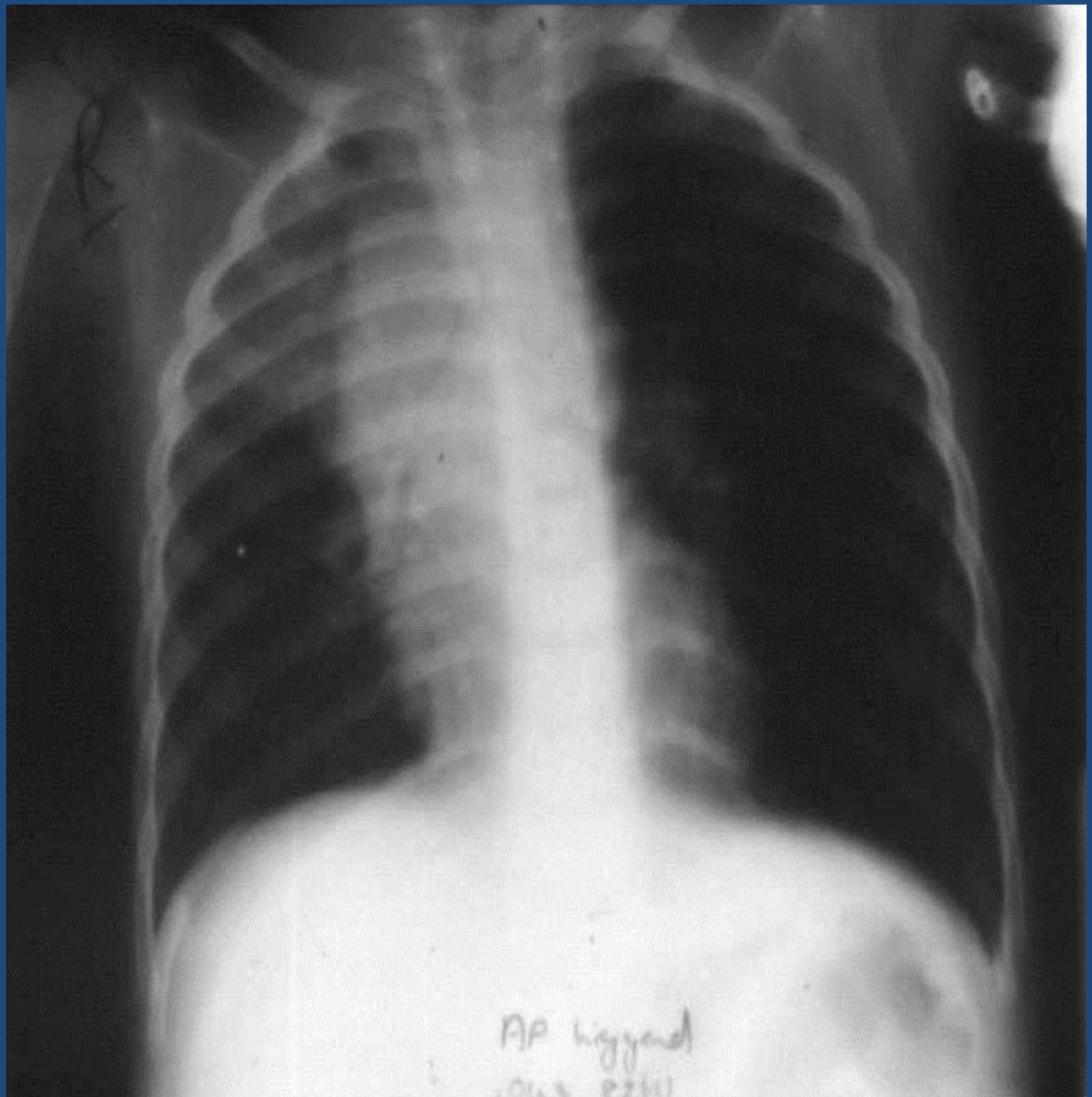
The appropriate notification or documentation of the more serious cases of TB in hospitalised children, especially TBM and miliary TB, would greatly assist in correcting the view of the place of childhood TB in a community.

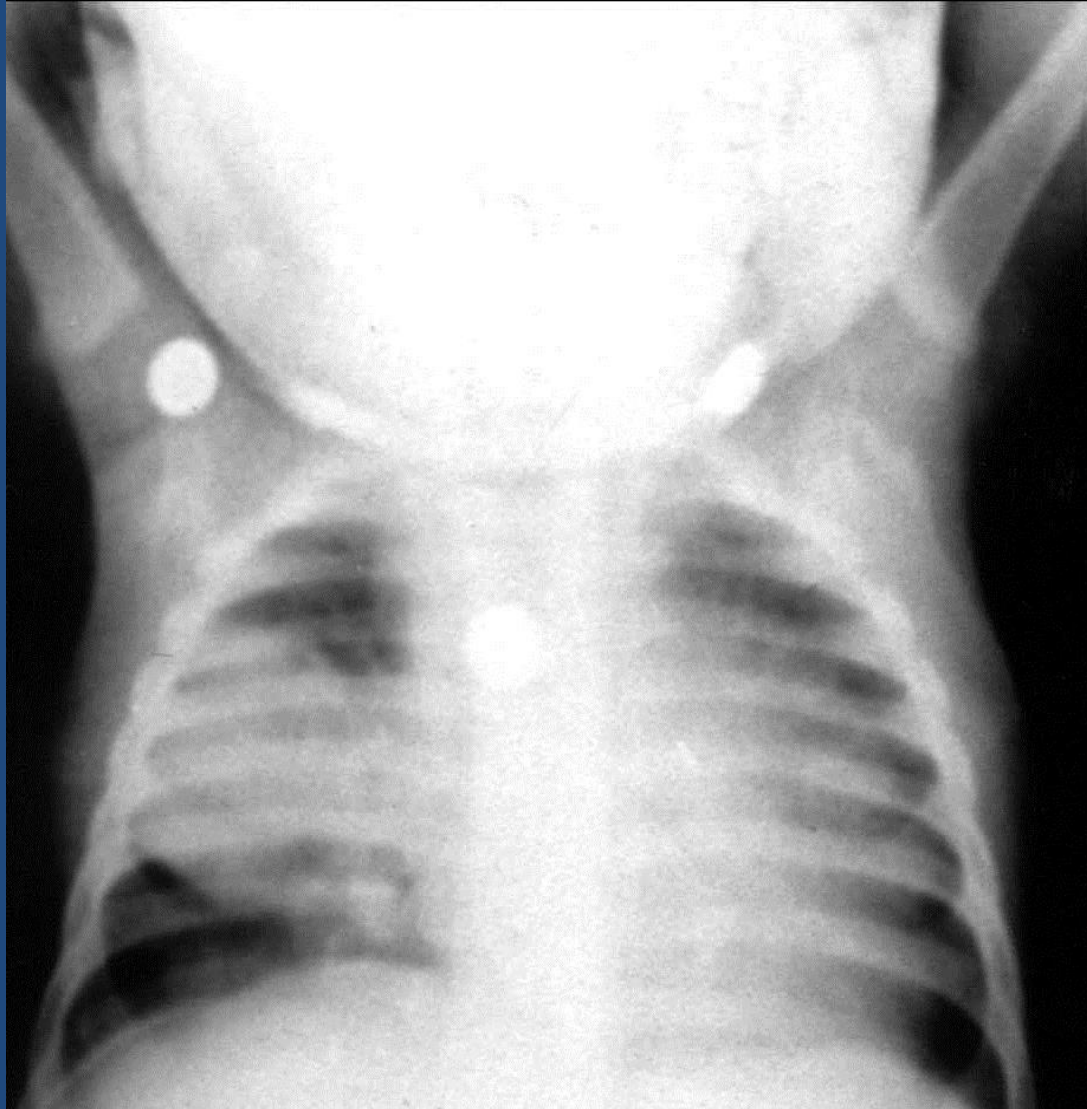


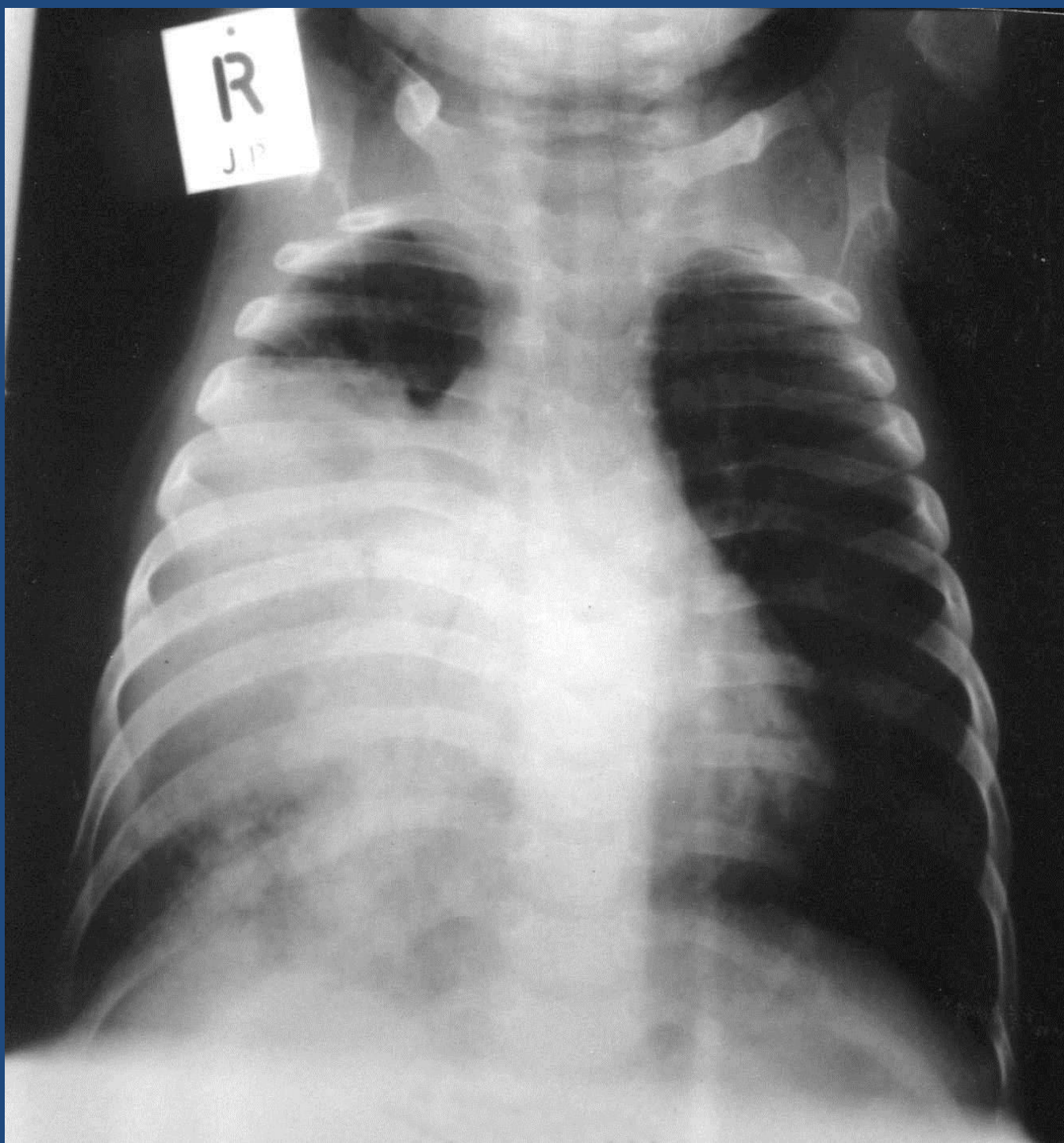






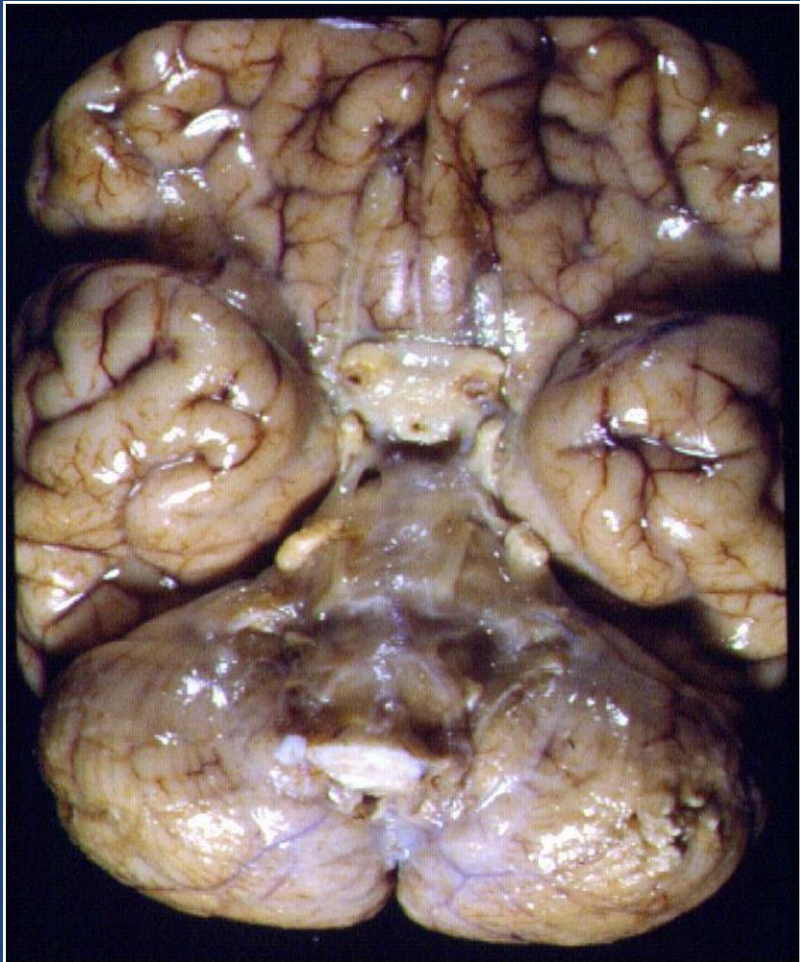








Macro-pathology in TBM



Tuberculous hydrocephalus:

clinical outcome in 143 children.

Schoeman JF et al. J Child Neurol 1995; 10:
320-29

<u>Normal</u>	<u>Mildly</u>	<u>Severely</u>	<u>Died(%)</u>
<u>(%)</u>	<u>disabled (%)</u>	<u>disabled (%)</u>	

Medical

(n = 112)	15	45	28	12
------------------	-----------	-----------	-----------	-----------

Surgical

(n = 31)	26	35	29	10
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Donald PR, et al. *S Afr Med J* 1995; 85: 167-170.

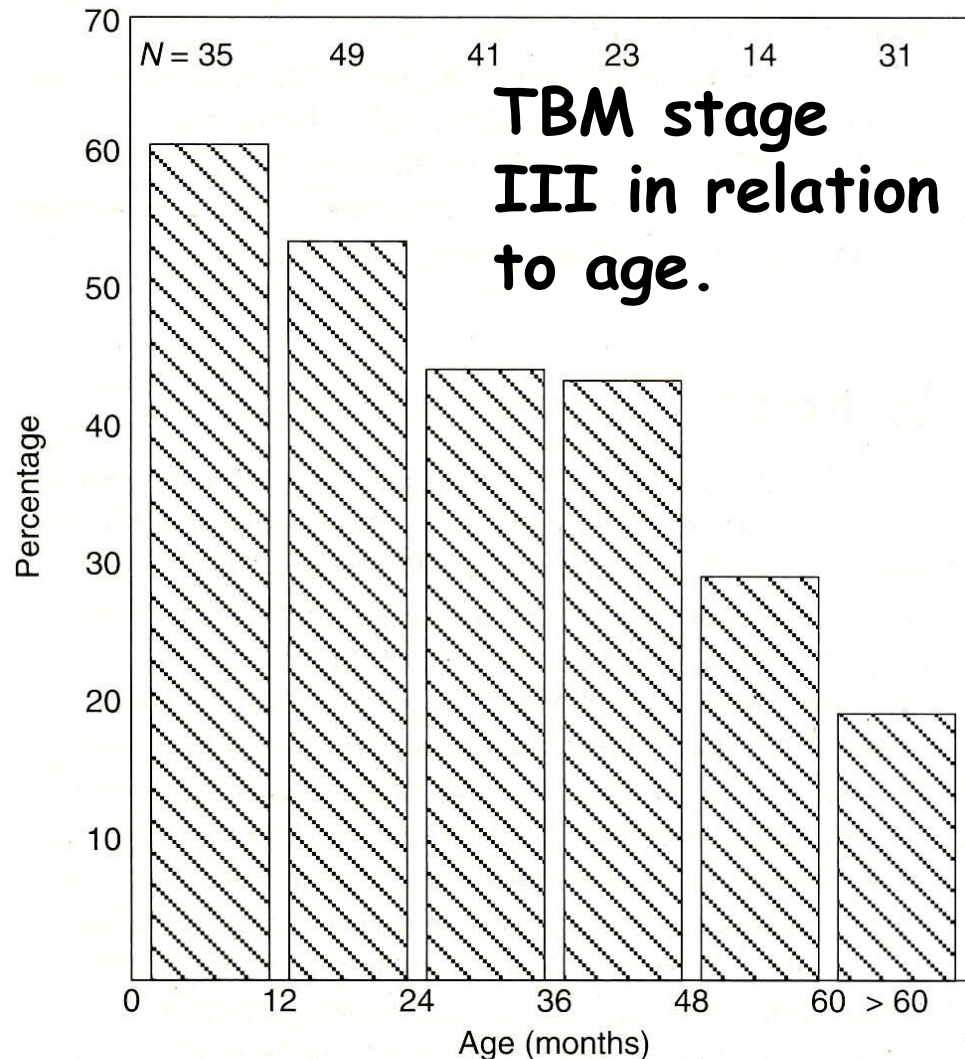


Fig. 1. Percentage of children at stage III of tuberculous meningitis relative to age at presentation.

- 193 Children TBM, median age **26 mths.**

- **77** Close household TB contact.

- **17** prescribed INH

- **7** completed 3 months.

Shimao T. Surveillance of tuberculosis. Bull Int Union Tuberc 1983; 58: 47-50.

- Derived from tuberculin surveys on appropriate samples of population either at a certain time interval or of different age-groups
 - **Good correlation with other epidemiological indices:**
 - Incidence of TB meningitis in children 0-4 years of age per 100,000
= ARI (%) X 5
 - Incidence of smear positive TB in whole population per 100,000
= ARI (%) X 60
 - **Limitation of its use:**
 - High coverage of BCG vaccination in children
 - High prevalence of low grade sensitivity to tuberculin

Figure II. Annual risk of infection.

“Good correlation with other epidemiological indices:

Incidence of TB meningitis in children 0-4 years of age per 100,000 = ARI(%)X5”

Conclusion

- We must be able to quantify the burden of childhood TB
- One effective way of drawing attention to childhood TB and quantifying the most serious forms of disease would be the use of TBM, miliary TB and osteo-articular TB as sentinel manifestations.

Conclusion

- Combine ARI studies with the accurate quantification of TBM, miliary TB, osteo-articular TB.
- Emphasize repeatedly the family nature of TB in young children.
- Promote chemoprophylaxis especially in infants and children under 3 years of age.

Conclusion

- TB is a family disease.
- Are you in contact with any young children?
- Are there any young children in the household?

Conclusion

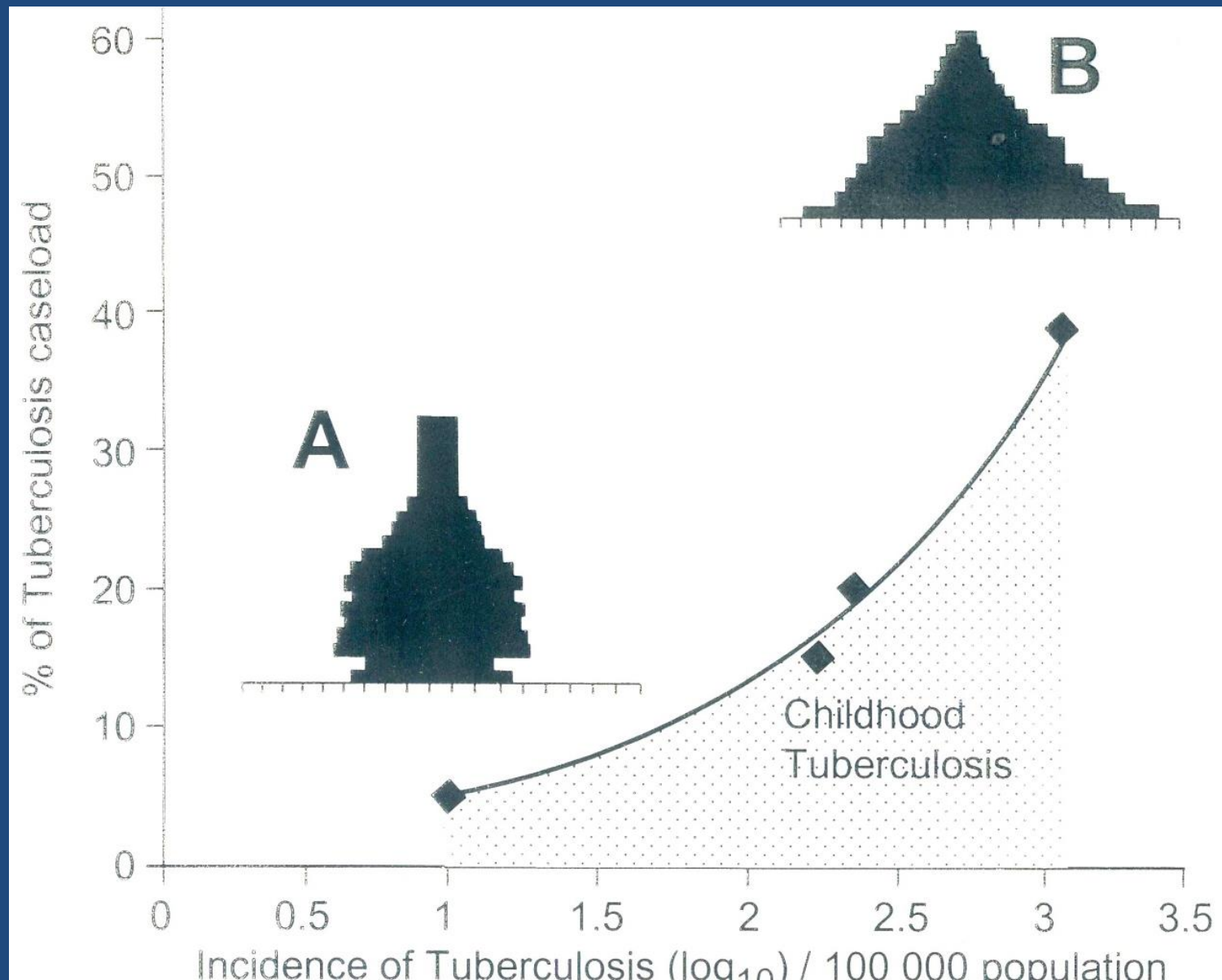
- Include adolescents down to age 10 years in prevalence studies?



Paediatric Burden of Disease

- In developed countries childhood TB is responsible for **5% or less** of an already low case load.
- In developing countries childhood TB is responsible for **approximately 20%** of the case load, rising to **40%** in some selected communities.

Burden of tuberculosis disease



Styblo K. Epidemiology of tuberculosis. KNCV
selected papers 1991; Vol 24: 15-16

Three distinct events are relevant:

1. The **transmission** of tubercle bacilli.
2. The development of bacillary pulmonary tuberculosis capable of **transmitting** bacilli.
3. The progress of bacillary tuberculosis to recovery or **death**.

Styblo K. Epidemiology of tuberculosis. KNCV
selected papers 1991; Vol 24: 15-16

Prevalence: TB prevalence
gives the number of
registered cases of
tuberculosis **at a particular
date** per 100,000 of the
general population ("point
prevalence")

Styblo K. Epidemiology of tuberculosis. KNCV
selected papers 1991; Vol 24: 15-16

Incidence: TB incidence
indicates the number of
new cases of TB during a
year, ie the number of
cases that occurred in this
period

Styblo K. Epidemiology of tuberculosis. KNCV
selected papers 1991; Vol 24: 15-16

Mortality: TB mortality indicates the number of **deaths** from TB in a given population and is computed per year per 100,000 population.

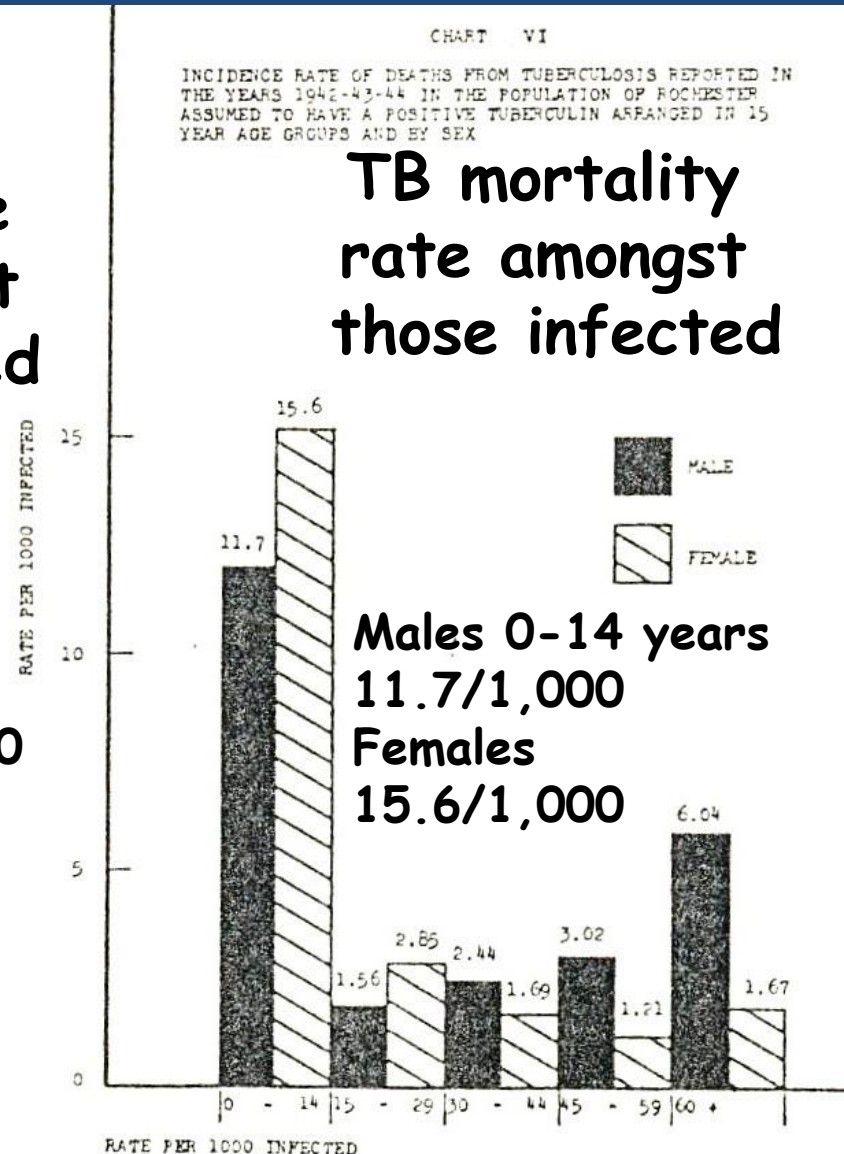
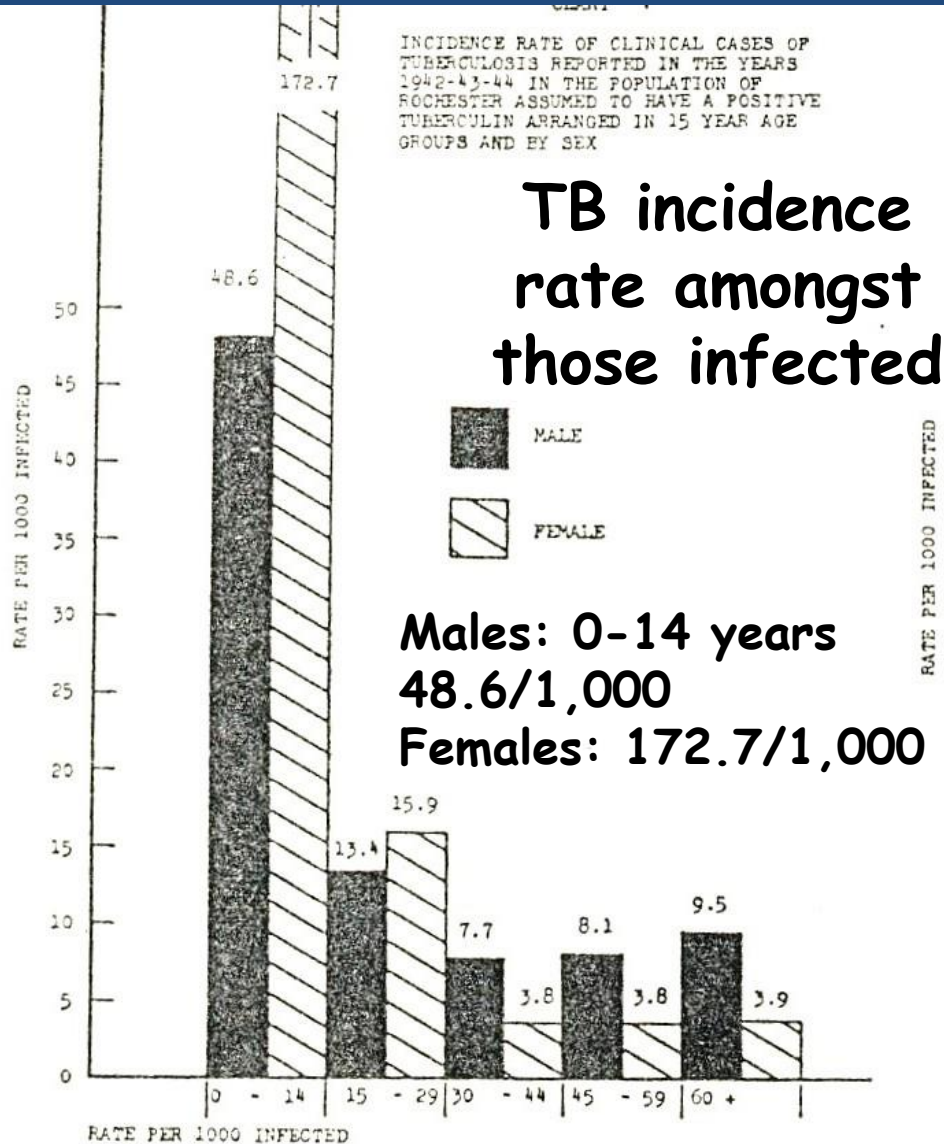
Styblo K. Epidemiology of tuberculosis. KNCV
selected papers 1991; Vol 24: 15-16

Prevalence of TB infection: The proportion of infected individuals in a given population on a particular date. It is based on tuberculin sensitivity and is usually expressed as the percentage of reactors at a given age.

Beaven PW. Analysis of tuberculosis infection from birth to old age: its relationship to clinical tuberculosis and deaths from tuberculosis. Dis Chest 1950; 17: 280-292

- The author sets TB morbidity and mortality in relation to the risk of infection.
- TB incidence rates determined with the calculated number of infected individuals as denominator.
- 1942-1944 extensive tuberculin testing in Rochester, New York by the TB and Health Association of Rochester: 9252 adult factory workers and 3,000 children to age 14 years. From these figures the number of infected individuals in the general population is calculated and used to determine TB morbidity and mortality.

Beaven PW. Analysis of tuberculosis infection from birth to old age: its relationship to clinical tuberculosis and deaths from tuberculosis. Dis Chest 1950; 17: 280-292



Arnold Rice Rich

(1893-1968)

MD from Johns Hopkins 1919. He remained associated with Hopkins the rest of his career. He was appointed Chairman of the Department of Pathology and pathologist-in-chief of the Johns Hopkins Hospital in 1944, until he retired in 1958.

