TUBERCULOSIS*

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For tuberculous disease to develop in a human being two factors are needed, viz. (1) the tubercle bacillus and (2) environmental stress. Infection with the tubercle bacillus alone is not sufficient. An individual who is adapted to his environment develops on infection a primary focus which is non-visible to X-rays, followed by complete resolution and a positive tuberculin reaction. If adaptation to environment is not complete, he gets tuberculous disease. The environmental stresses are all well known; they are as follows:

Food. Inadequate nutrition leads to increased susceptibility.

Housing. Overcrowding leads to increased opportunity for repeated infection.

Sanitation and hygiene. Bad sanitation leads to helminthiasis and other diseases associated with impure water and improper sewage disposal. Bad hygiene leads to increased opportunity for infection.

Prolonged physical effort, leading to fatigue and lessened resistance.

Tuberculin-positive persons can be divided on X-ray into 3 groups, showing respectively (A) nil on X-ray, (B) calcification (Ghon focus), and (C) evidence of tuberculous disease:

(A) *Nil on X-ray* = good resistance: Adaptation to environment.

(B) *Calcification* (*Ghon focus*) ± fair resistance: Moderate adaptation to environment, with breakdown in the disease if stresses are altered from moderate to great.

(C) *Tuberculous disease* = low resistance: Poor adaptation to environment; stresses too great.

PROPHYLAXIS OF TUBERCULOSIS

1. *Mitigation of Environmental Stresses*

This will lead to eventual disappearance of the disease:

Food. In nutrition the ultimate aim is to teach mothers, through education in nutrition, to feed their children adequately by giving them sufficient foods of the right kind. *But* education in nutrition can be effective *only if the necessary foods are available and can be purchased from the earnings of the family at risk.*

The *other environmental stresses* are bound up together in this country and must be removed before we can control tuberculosis properly. There is no doubt that in South Africa we have taken the housing stress seriously. During the last 20 years we have spent £136 million on new housing, particularly for the non-European. During the last decade the tempo of housing has been stepped up until in the last 5 years it has reached an expenditure of £10 million per annum.

It is an axiom that if certain environmental stresses are the cause of a case of tuberculosis disease then, even if you remove the patient to a hospital and treat him to apparent arrest, when he is returned to the environment which caused the disease he will break down in a short time. Hence the high rate of readmissions to hospitals in South Africa.

2. *BCG Vaccination*

Individual biological resistance can be enhanced by BCG. Even if it is increased by 10-20% that is better than nothing. BCG is not of great value in countries where tuberculosis is scarce and in these countries it may interfere with the value of the tuberculin test in diagnosis.

3. *Chemoprophylaxis*

Chemoprophylaxis with INH is very effective if applied to:

(*a*) Babies born in hospital of tuberculous mothers. There have been over 100 babies born in King George V Hospital of tuberculous mothers in the last 3 years, all of whom have been breast fed and cared for by their mothers. None of them developed tuberculosis while under INH prophylaxis. Indeed only 2 have become Mantoux positive, and these only because the parent omitted to give the INH.

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(*b*) Hospital staff in contact with open cases of tuberculosis. Since October 1956 all nursing staff at King George V Hospital have been given INH prophylaxis and from that time to date only one nurse has developed tuberculosis, and she was back on duty after 3 months.

(*c*) Intimate contacts of cases. Contacts of cases treated at home should receive INH prophylaxis, and negative Mantoux reactors should receive INH-resistant BCG while taking INH as a prophylactic agent.

DIAGNOSIS OF TUBERCULOSIS

The best method of diagnosis is a tuberculin test followed, if the reaction is positive, by an X-ray.

Tuberculin tests must be performed with freshly prepared tuberculin given by intradermal injection. A 'Heaf' gun is also effective.

If radiology is not available then there is no need to throw up the sponge. A tuberculin test followed by a combination of clinical acumen and simple bacteriology is a very excellent method of diagnosis. Clinical examination of all symptomatic positive reactors, and sputum examination of all coughers, will turn up most of the cases requiring immediate treatment.

TREATMENT OF TUBERCULOSIS

The keynote of treatment is vigorous, *regular* treatment on first discovery. Irregular initial treatment results in *chronicity* and *inability to cure*. Proper treatment results in resolution of the tuberculous disease and this type of cure should be aimed at in every case.

If possible the first 3 months of treatment should be in an institution. When this is not possible every effort must be made to see that the patient attends regularly for injections and that he actually takes his oral medicines.

One thing must be kept constantly in mind and that is that adequate food of the right kind is as essential a part of domicilary treatment as antibiotics or chemotherapeutic agents.

The suggested regimes are as follows:

Primary Tuberculosis

INH 20 mg. per kg. body weight per day. INH alone is effective in this type of disease and streptomycin and other agents are only required in cases presenting the adult type of disease, or in the presence of INH toxicity.

This regime is also suggested for tuberculous meningitis and for all positive reactors under 5 years of age. INH is the most important drug in tuberculous meningitis and should be given in the above dosage if there is any suspicion of tuberculous meningitis, while laboratory results are awaited. It is best given by injection in these cases to ensure absorption.

Adult Type of Disease

The suggested regime is INH, 10-15 mg. per kg. per day, plus streptomycin, 1 g. daily for 60 days and thence on alternate days.

If after 4 months the sputum is negative and the X-ray satisfactory the treatment can be changed to INH, 10-15 mg. per kg. per day, plus PAS, 12 g. daily for at least a year, but preferably for as long as the patient will take the drugs. If treatment is discontinued after as long as 18 months of continuous therapy, breakdown is frequent.

If the sputum is still positive after 4 months then the regime should be altered to INH 10-15 mg. per kg. per day, plus PAS, 12 g. daily, plus pyrazinamide, 1 gr. *t.d.s.* for 3 months.

If the sputum is still positive after 3 months of this regime then the case should be reviewed for surgery or an institution for chronic cases. In any case treatment with INH and PAS should be continued for as long as the patient will tolerate it in order to maintain high resistance to INH.

Indications for Surgery

These are fairly well defined and are as follows:

1. Large solitary foci, whether tuberculomata or inspissated cavities, provided adequate time has been given for the maximum resolution on chemotherapy.
2. Localized persistent residual cavitation with a positive sputum (where prolonged chemotherapy has failed).
3. Bronchiectatic, fibrotic lobe or lung with persistently positive sputum in spite of prolonged therapy.
4. Repeated attacks or uncontrollable haemorrhage, where the probable source of the bleeding can be localized.
5. A lung which has been destroyed by tuberculous disease and which, apart from the tuberculosis, is a danger to the patient from secondary infection.
6. Chronic tuberculous empyema.

Chronic cases not suitable for surgery are likely to remain positive spitters for the rest of their lives, and the use of one expensive antibiotic or chemotherapeutic agent after another, with resultant resistance to the organisms and no improvement of the patient, is just waste of money. The proper care of these patients is to house them in an institution for such cases, such as a SANTA treatment centre, or allow them to go home if they are fit to do so and to maintain as high a resistance to INH as possible. The patients themselves should be taught how not to infect others, and this drill plus the known biological weakness or lack of aggressiveness of INH-resistant organisms should make them fairly innocuous to their contacts.

Drugs

Drugs of use in tuberculosis are listed below:

DRUGS USED IN THE TREATMENT OF TUBERCULOSIS

INH	Iso-nicotynil acid hydrazide and derivatives	Best so far.
Streptomycin	Antibiotic	Good—but dangerous side-effects on 8th nerve.
PAS	Para-amino-salicylic acid and derivatives	Moderately good. Large dose necessary.
'Viomycin'	Antibiotic	Moderate—nephrotoxic.
Thiosemicarbazone	One of Domag's originals	Poor.
'Pyrazinamide'	Pyrazinoic acid amide	Very good—but said to be hepatoxic.
'Kanamycin'	Antibiotic	New, experimental.
T.40	5-bromsalicylhydroxamic acid	Experimental. Similar effect to PAS but in much smaller doses, viz. 3 g. a day.
Phenazine (Rimino) compound (B663)	2p-chloranilino-5p chlorphenyl-3 : 5-dihydro-3-isopropyl imino phenazine.	Experimental.
'1314'	Alpha-ethyl thio-isonicotinamide	Experimental. Fairly good—side-effects ++ nausea.
'Seromycin'	Antibiotic	Fair—side-effects.

RESISTANCE TESTS

Regular sputum examination in cases of pulmonary tuberculosis undergoing treatment for the first time reveals the following pattern in the majority of cases:

At first the organisms are numerous; after a few weeks of treatment they are moderate in number; and in a few more weeks they are to be found in scanty numbers only. At the end of a variable period, between 2 and 6 months, the organisms disappear from the sputum, indicating successful treatment.

If the numbers of organisms diminish to 'scanty' or 'nil' and then at subsequent examinations a moderate or large number are found, then it can be assumed that they have become, for practical purposes, resistant to the drugs employed.

Repeated examination of the sputum of cases which have already received treatment before admission to hospital may show the above pattern or may show moderate to large numbers of bacilli in all smears, again indicating resistance to the drugs exhibited.

Resistance to 'viomycin', 'seromycin', 'pyrazinamide', PAS, 'dipasic', '1314', 'kanamycin' etc. develops fairly rapidly, especially if they are not used in combination with other drugs; and if a case is still sputum-positive after 4 months' treatment with these drugs in any sort of combination, then it can be taken that the organisms have developed quite a considerable degree of resistance.

Resistance tests in general should be done for research purposes; for example, to ascertain what percentage of new, untreated cases have organisms resistant to INH and streptomycin, in order to see if resistant strains are becoming disseminated. The clinical and straight bacteriological approach is better for everyday use, and a good rule is that if a patient's sputum is still positive after 6 months of any combination of drugs, resistance to these drugs has developed to a practical degree and therapy ought to be changed. It is advisable, however, to continue to use INH throughout, because it is believed that INH-resistant organisms have a diminished biological virulence.

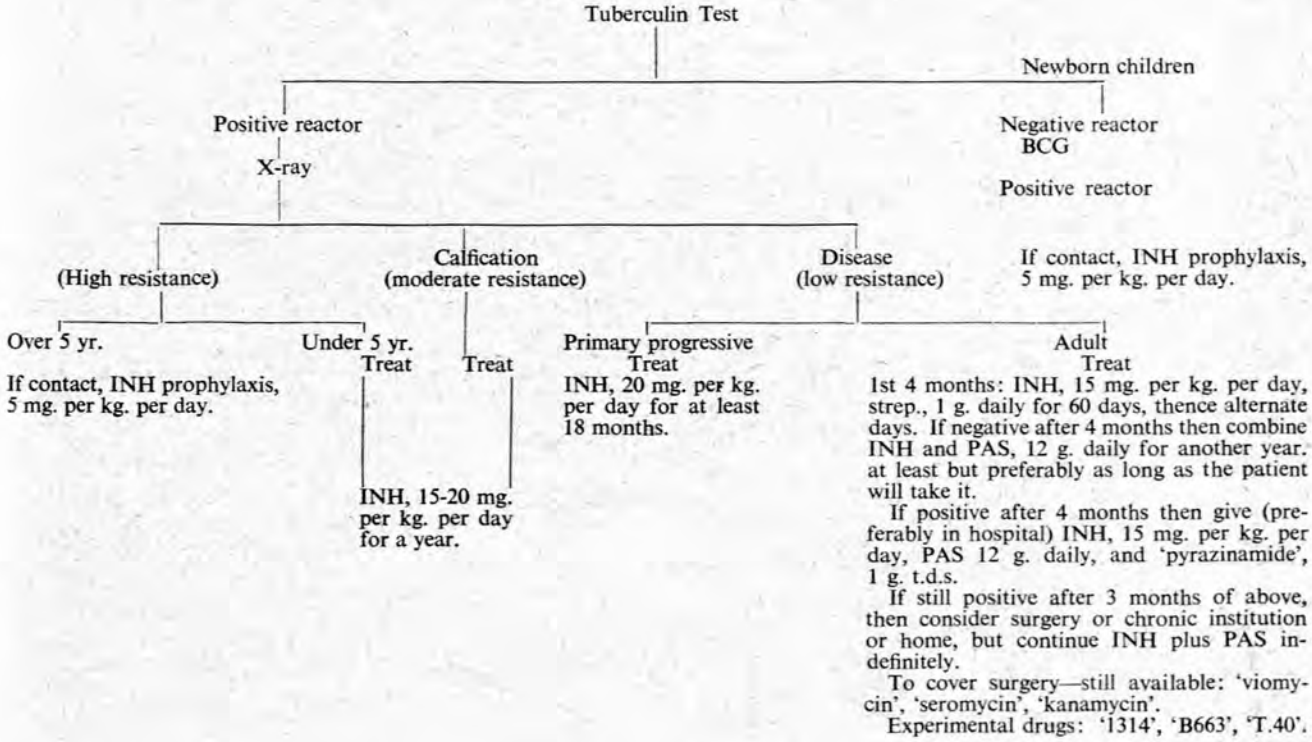
The following chart of a case shows how simply resistance can be detected:

ESTIMATION OF ACID-FAST BACILLI

Date	*Numerous*	*Moderate*	*Scanty*	*Nil*
9.11.58	X			
12.11.58	X			
17.11.58	X			
21.11.58		X		
24.11.58		X		
30.11.58		X		
14.12.58			X	
21.12.58			X	
21. 1.59				X
14. 2.59				X
*21. 2.59		X		
* 1. 3.59	X			

* Indicating resistance. Resistance tests done here would take about 2 months for answer.

CONTROL OF TUBERCULOSIS



APPENDIX: SOUTH AFRICAN TUBERCULOSIS FIGURES OF INTEREST

ESTIMATED POPULATION OF UNION BY RACE AS AT 30 JUNE 1957

Whites	2,957,000	20·8% of total
Coloured	1,319,000	9·3% of total
Asiatics	431,000	3·05% of total
Natives	9,460,000	66·7% of total
All races	14,167,000	

PERCENTAGE LIVING IN URBAN AREAS, 1957; UNION

Whites	81%
Coloured	68%
Asiatics	80%
Natives	30%

ANNUAL NOTIFICATIONS OF TUBERCULOSIS

	Total European	*Total non-European*
1954	1,646	35,996
1955	1,498	38,181
1956	1,530	46,442
1957	1,478	50,818
1958	1,453	56,912

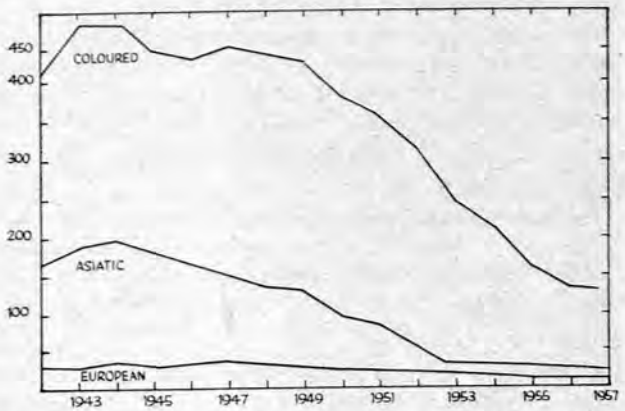
BEDS AVAILABLE FOR TREATMENT OF TUBERCULOSIS (ALL RACES)

	Existing	*Proposed*	*Total*
Central Government ..	4,935	686	5,621
Local authorities ..	2,606	739	3,345
Mission hospitals ..	3,992	294	4,286
Private hospitals ..	2,317	0	2,317
SANTA settlements ..	6,137	1,595	7,732
	19,987	3,314	23,301

ANNUAL EXPENDITURE ON TUBERCULOSIS AND PERCENTAGE OF TOTAL UNION HEALTH VOTE

Year	*Total Health Vote*	*Expenditure on Tuberculosis*	*Percentage of Total Vote*
1947–48	4,108,500	689,332	16·8%
1952–53	7,144,000	1,402,715	19·6%
1955–56	10,000,000	3,000,000	30%
1956–57	10,513,690	3,397,704	32·3%
1957–58	11,276,382	4,254,067	37·7%
1959–60	12,890,000	5,352,765	41·5%

DEATH RATE FROM TUBERCULOSIS PER 100.000 POPULATION OVER A SERIES OF YEARS, UNION OF SOUTH AFRICA



PERCENTAGE OF POSITIVE MANTOUX RESULTS BY RACE AND SEX, UNION OF SOUTH AFRICA 1948-54