CHAPTER IV

THE PROBLEM

In spite of the modern trends in medicine and advances in therapy involving tuberculosis, the emergence of drug resistance among adult Filipino tuberculous patients besets the clinician. Studies on effectiveness and efficacy of the anti-tuberculosis drug regimen had been done in the hope of resolving the problem of drug resistant tuberculosis.

Non-compliance with therapy is invoked as a cause for development of resistant strains to the anti-tuberculosis drugs. Whether this is solely the reason for emergence of resistance or not remains a question. In the Philippines, it was noted that even among compliant patients and those who have not undergone previous treatment for the disease, drug resistance proved to be a problem.

Current investigations showed that initial resistance to anti-TB drugs, particularly with INH, is on the rise. Such finding is observed not only in the Philippines but in other countries of Europe and Africa as well.

With these observations, one wonders if there are other equally important factors responsible for aggravating host susceptibility to develop resistance to the drug or drugs. The persistence of resistant strains of M.

tuberculosis to conventional anti-tuberculosis medications makes tuberculosis a national problem in the Philippines, a country of more than seven thousand islands with sixty two million (62,000,000) people. Three hundred out of a hundred thousand people are infected with the disease.

The government launched education campaigns, built research institutions, encouraged screening initiatives, gave free anti-TB drugs to diagnosed tuberculous patients and supported sanitaria for the seriously ill tuberculous. Despite all these, tuberculosis ranks fourth as a killer disease in the country.[17]

Where do the problems lie?

Drug Resistance in Pulmonary Tuberculosis

For many decades, TB control has progressed. However, the progress is marred with an obstacle which continues to be a stumbling block to the eradication of tuberculosis. This obstacle is treatment failure and is perceived to be due to either drug resistance or noncompliance with the drugs[9]. If compliance on the part of the patient were good, it is assumed that he or she has organisms that are resistant to drugs being used[9].

How then is drug resistance developed in a clinical setting?

It is assumed that a bacillary population not under the influence of any drug, as it multiplies gives rise to mutants that are not susceptible to a particular drug.[9] Applied on such a population within the host's tissue, a drug kills the organisms susceptible to it leaving the non-susceptible ones to continue multiplying and inevitably replacing the originally predominantly susceptible population of microorganisms. This becomes the source of primary resistant infection for other people.[9]

Resistance to a drug is allowing growth at a prescribed concentration of such drug equal to or greater than a certain population of the control, usually 1%, rendering therapeutic success with it not likely to occur.[18,9] The bacteriologic definition is based on the fact that there is certain proportion of mutants above which success of therapy is less likely to occur. This was also discussed on the pharmacologic properties of the drugs.

Toman believed that the tuberculous patient with primary resistance had never taken the anti-tuberculous drug in the past but his source of infection must have done so.[19] In the clinics, it is difficult to differentiate between primary and acquired resistance. The patient may not be aware of or may deny that he had previous chemotherapy intake for tuberculosis. In the Philippines, it was a common notion among subjects that INH is a "vitamin for the lung." To avoid stigma on the part of the patient, the medical practitioner does not directly give the diagnosis of pulmonary tubercu-

losis but rephrases it as "weak lungs." Moreover, in the market, there are cough preparations with isoniazid incorporated to it. Thus, it becomes an ordinary over the counter drug for cough.

In many areas in the Philippines, laboratory tests may not be available therefore clinical assessment of patients has to be thoroughly done and maximized to identify highly probable cases of drug resistance.[9]

A study on the prevalence of drug resistance in the country gave varying figures, depending on which institution carried out the survey and when it was conducted. In all the studies, primary and secondary drug resistances were not identified; neither were specimens from compliant nor non-compliant patients labelled. The summary of the studies done is seen on the succeeding table.

TABLE 2. PREVALENCE OF DRUG RESISTANCE IN THE PHILIPPINES

INSTITUTION (REFERENCE)	YEAR	INH	SM	EM	RIF	PZA
QUEZON INSTITUTE[9]	1979-1980	25%	49%	23%	0	no study
NATIONAL PREVA-LENCE SURVEY[9]	1982-1983	33%	19%			
COMMUNITY-BASED[20] CASE-FINDING:NOVA-LICHES, QC PHILIPPINES/ASTER	1985-1989	60%	47%	42%	8%	5%
LUNG CENTER OF THE PHILIPPINES[9]	1985-1989	42%	29%	28%	27%	
UNITED LAB/QUEZON INSTITUTE[9] SAN ANDRES, MM	1988-1989	46%				
SAN JUAN, MM		89.2%				
STO, TOMAS UNIVERSITY HOSPITAL[21]	1992	35.1%	26.4%	41.9%	27.9%	no study

Studies in Canada, Malawi and USA showed that patients who gave histories of previous chemotherapy had high prevalence of drug resistance. Comparison of results among drug-resistant cultures from sputum of patients who had previous treatment is summarized below.

TABLE 3. PROPORTION OF PREVIOUSLY TREATED PATIENTS WITH DRUG - RESISTANT CULTURE

PLACE	YEAR	SOURCE (REFERENCE)	INH	SM	PAS	EM	RIF
Malawi (AFRICA)	1963	Shennan[18]	16%	9%	11%		
Atlanta (Georgia, USA)	1961-1968	Costello, et al[22]	36.8%	19.2%	17.2%		
Toronto (CANADA)	1961-1968	Cheung[23]	33.3%	18.9%	11.1%	1.3	
New Jersey (USA)	1984	Suwanogool, et al[24]	26%	11.6%	18.9%	6.2%	9.8%

Thirty years ago, studies on isoniazid-resistant cultures among previously untreated African patients were conducted. Results are shown on Table 4.

TABLE 4.[18] **PROPORTION OF PREVIOUSLY UNTREATED PATIENTS WITH ISONIAZID-RESISTANT CULTURES**

COUNTRY (PLACE)	YEAR	SOURCE	PROPORTION OF INH-RESISTANT CULTURES
Uganda, Kenya, Tanganyika	1960	East African/ BMRC Investigation	11%
Uganda	1961	Short	9%
Ghana	1961	Bell and Brown	18%
Zimbabwe (Harare)	1983	Briggs	5%
Malawi	1963	Shennan	8%

Thus, be it in North America, Africa or the Philippines, drug resistance posed and still does pose a threat to tuberculosis control. In America and Canada, drug resistance was particularly high among immigrants particularly Haitians and Southeast Asians.