Tuberculosis in Various Ages and Different Races: Anachronisms*

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To have the privilege of presenting the 1956 Varrier-Jones Memorial Lecture here, where, within a relatively short radius nearly all of the fundamental inventions and discoveries in tuberculosis were made, is a most significant honor.

With a disease of such antiquity, so widespread and so destructive among people and animals, it was to have been expected that various methods of dealing with the new armamentarium would develop among people in different parts of the world or even in the same nation. Such factors as their improper use, misinterpretations, conclusions drawn from insufficient evidence, formulation of theories, expression of personal opinions, etc., were sure to complicate the problem and mislead workers, thus seriously retarding progress. All of these and more have occurred to such a degree as to cause much confusion. It is particularly fitting that physicians in diseases of the chest from around the world should gather here and evaluate the procedures employed in the past and to recommend abandonment of anachronisms.

Longitudinal Observations

In 1920 vantage ground was provided for observations on tuberculosis in people which has been occupied to this time. From this position, persons of all ages, from birth to death in senility, infected and uninfected with tubercle bacilli, sick and well, engaged in numerous occupations, etc., have been observed. In 1920 and subsequently, views were expressed with reference to varying effects of tuberculous infection acquired at different ages in life of both people and animals.

When it was observed that the adult guinea pig, like the human infant, has a high percentage of lymphocytes, whereas the newborn guinea pig has a low lymphocyte count, similar to that of adult humans, it was thought this might account for the alleged low resistance of young guinea pigs to tubercle bacilli. Various theories and expressions of opinion led Krause⁴ to make the following statement in 1925: "Because paper after paper of those appearing on many subjects in tuberculosis avers that young animals are in general inordinately susceptible to tuberculosis and because many an

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884
TUBERCULOSIS IN VARIOUS AGES AND RACES

385

author easily and lightly solves a knotty problem as it arises with the
statement of the assumption, it is particularly desirable to point out on
how slender a basis of ascertained fact the assumption is based.” This
led him to undertake a study of resistance of young and old guinea pigs.
His experiments revealed that when young and old guinea pigs are infected
intracutaneously with relatively small quantities of virulent tubercle bacilli
that are equal for all the animals, there is an earlier appearance and more
vigorous development of tubercles at the site of inoculation than in the
regional lymph nodes in the old animals. “After infection of this nature
and heavy enough to cause generalized tuberculosis in the old animals,
both young and old guinea pigs developed essentially the same grade of
infection. There was nothing to indicate that the young were more sus-
ceptible than the old.”

When he infected subcutaneously with large quantities of virulent
tubercle bacilli in equal dosage, a more extensive and progressive involve-
ment resulted in the young than in the old animals. Inasmuch as the young
animals received double the quantity of tubercle bacilli per body weight
that was sufficient to cause fatal disease in the old animals, he believed
the more advanced condition found in the young animals was a result of
overdosage.

Veterinarians also found no evidence of low resistance among young
domestic animals.

Infancy and Early Childhood

In 1920 many persons had expressed the opinion that in infancy and
depth childhood the human body has exceedingly low resistance to tubercle
bacilli. However, search of the literature revealed that practically all that
had been said and written was a matter of opinion since no well documented
study had been made to justify a conclusion. Reports in the literature al-
ready available and many subsequently made were based upon mortality
among children with reinfection clinical type of tuberculosis. These in-
cluded such conditions as meningitis, miliary disease and pneumonia, which
were nearly always fatal, as well as clinical lesions in peripheral lymph
nodes, bones, joints, etc., from which children usually do not die. Both of
these acute and chronic forms of tuberculosis are now known to be reinfec-
tion type. They are always preceded by primary disease which rarely
causes significant symptoms but results in endogenous reinfections.

In series of cases reported rarely has there been an attempt to determine
how many infants and young children had been infected with tubercle bacilli
in the areas from which the ill ones originated. Therefore, nothing was
known of what percentage of infected infants developed reinfection type
of tuberculosis.

Krause2 said, “The more I see of tuberculosis in infants and the more I
confirm diagnosis by the aid of new methods, the more tuberculous infants
I find who run along with comparatively little illness and withstand their
infection well.”

Inasmuch as only a few years constitute this period of life and since
many children were being infected, it was possible from our vantage
ground to determine the immediate results of primary infection rather promptly.

Between May, 1921 and November, 1941 we examined 5,537 children from birth to five years of age, of whom 831 reacted to tuberculin (18 could not be completely examined; therefore, only 813 were considered). Among these 813 children, 102 (12.54 per cent) presented primary infiltrates which subsided in the usual manner without causing significant illness. Eleven (1.35 per cent) developed acute fatal reinfection forms of disease, of whom two had tuberculous pneumonia, four meningitis, and five generalized miliary disease. Eleven (1.35 per cent) other children among the 813 developed reinfection chronic type of tuberculosis in bones, joints, lymph nodes, etc.

Among the nonreactors in the group of 5,537 children from birth to five years of age, 198 were subsequently found to be reactors, two of whom died from meningitis and one from tuberculous pneumonia. Two others developed tuberculosis of bones and joints, and three chronic pulmonary lesions. Thus, the toll in illness and death among 1,011 children was 30 (2.96 per cent). The other infected children (97.04 per cent) remained free from clinical tuberculosis during the period of childhood. Had only the children with clinical disease been studied, 14 (46.7 per cent) who died would have given an erroneous impression of the ability of infants and young children to control tubercle bacilli.

For too long we talked about "high susceptibility" and "low resistance" and theorized about methods of increasing resistance to tubercle bacilli when such factors as intimate contact exposure should have claimed our greatest attention. Infants are often subjected to excessive fondling and kissing by members of the immediate families as well as relatives, including grandparents. Elderly neighbors also participate in this activity.

Infants and young children are endowed with an exceedingly efficacious defense mechanism against first invasions with tubercle bacilli as manifested by the relatively few who develop Reinfection type of lesions and succumb soon after becoming infected.

From the age of about five years until adolescence, chronic clinical primary tuberculosis rarely occurs among girls and boys. In the earlier years of this period, of the clinical lesions which do develop, a preponderance are extrathoracically located. Over a 20 year period beginning in 1921, we examined 6,823 children, from six to 14 years of age on the first visit, of whom 2,979 reacted to tuberculin. Of this number, 137 (4.6 per cent) had Reinfection type of tuberculosis when first seen or subsequently developed it. Thus the morbidity rate was higher in this age period than among infants and young children, but their extrathoracic lesions were less fatal. Nevertheless, the low mortality rate in this age period has been attributed theoretically to operation of special resistance. It may be of considerable importance that at this time of life many girls and boys resent fondling. There is a strong tendency for them to engage in separate activities, such as participation in games, parties, etc. Wherever they are assembled, including school, rarely do girls or boys become infected from others of their age.
Teens and Early Twenties

Chronic pulmonary tuberculosis makes its debut as adolescence approaches and has often been reported as prevalent and highly destructive during the teen ages and early 20's. Lowered resistance during this period has been given most attention. Although no indisputable proof has been adduced, numerous factors have been thought to contribute to lowering of resistance, particularly among girls, such as sex hormones, scanty wearing apparel, diet fads, fatigue, etc.

We have previously reported observations on the effects of tuberculous infection acquired among children and adolescents which did not show that the latter are more susceptible to infection than persons in other age periods. The reason for chronic pulmonary tuberculosis making its debut in or immediately preceding adolescence and continuing throughout the decades of life has not been satisfactorily explained.

It would appear that the important factors have been largely overlooked. First, in areas where considerable contagion exists, there has been an accruement of primary tuberculosis from which endogenous reinfections now result in clinical disease. Second, this is the mating period of life. It is when girls and boys assemble in small and large groups with intimate contact. Parents often advise their daughters to have numerous men associates in order to choose the most desirable life mate and vice versa. Thus, a single teen-age girl or boy with contagious tuberculosis may infect many others. Contact exposure occurring outside the home is an extremely important factor. This is the period in life when people are “on the move” more than any other. Downes has shown that approximately 66 per cent of persons who developed tuberculosis in the community under her observation had contracted it from sources outside their families.

Prostitution probably is in vogue to greater extent in this period of life than any other. In one country said to have 1,200 licensed houses of prostitution, a survey of 1,300 inmates revealed that 10 per cent had active pulmonary tuberculosis.

The belief often expressed that clinical pulmonary lesions are more severe and more prevalent in adolescence probably is in part due to failure to differentiate between primary infiltrates (Ghon tubercles) and clinical reinfection type of lesions. Too often, when extensive disease is found in an adolescent on first examination, it has been assumed that the infection was of recent origin. There had been no periodic tuberculin testing, and there was no way of knowing when the infection actually occurred.

In 1916 when 70 per cent of grade-school children in the city of Minneapolis reacted to tuberculin, 268 girls and boys, ages 10 to 19 years, died from tuberculosis in Minnesota, whereas in 1955, when 4 per cent of grade-school children reacted, only one died in the teen-age period (Figure 1).

When in the third decade of this century, special attention was called to the seriousness of tuberculosis among students and recent graduates in nursing in that they developed much more clinical tuberculosis than women or men of the same age in the general population, there were those who stoutly maintained that age of the students was the deciding factor. It
was said that they were in that age period when resistance to tuberculosis is exceedingly low, and the problem could be solved only by admitting older persons to our schools of nursing. Time has proved it was not the age of the students but contagion to which they were subjected that created the problem.5

The prevalence of the disease in clinical form during the teen-age period apparently is dependent upon incidence of infection. We have not seen a relatively higher percentage of infected persons at this age develop clinical lesions than in later life.

The many new infections acquired during the teen ages and early 20's together with those obtained in pre-adolescence are sufficient to account for the surge of clinical cases in adolescence and thereafter.

Later Life

Following marriage, the previous excessive exposure rate tends to subside because of the decrease in the number of intimate contacts. However, in many areas by this time a high percentage and in some places all are harboring tubercle bacilli, and reinfection clinical types of disease
continue to appear among them, increasing through the decades of life.

During the last two or three decades, in parts of the world where good tuberculosis control programs have been in effect, there has been a marked reduction in infections acquired in childhood and early adult life, with correspondingly reduced morbidity and mortality. However, in the upper age brackets, morbidity and mortality have continued high, so much so that tuberculosis has been designated a disease of older people. Here again, it has been contended that this situation is due to lessened resistance among elderly people. In reality, this older age group is composed of individuals, a large percentage of whom acquired tubercle bacilli in early life which they have continued to harbor and which are endogenously causing reinfections.6

Observations on Persons Infected in Adulthood

Since 1920 we have seen 2,315 persons who became infected with tubercle bacilli so as to convert from nonreactors to reactors to tuberculin at the age of 19 years and older. Deducting 34 who were not recently traced, there were 2,281 for consideration. Of this number, 15 had died. They had 199 person years of follow-up with no evidence of clinical tuberculosis having developed.

Among the remaining 2,266 there are 2,080 with 24,431 person years of follow-up who have developed no demonstrable tuberculous lesion (Table I).

Among the remaining, there were 54 with primary infiltrates (Ghon tubercles in the inflammatory stage) of such size, consistency and location as to cast visible x-ray shadows. They have had 749 person years of follow-up.

Another group of 67 developed pleurisy with effusion, of whom nine had co-existing primary pulmonary infiltrates. They have had 932 person years of follow-up.

<table>
<thead>
<tr>
<th>Age Infected</th>
<th>Number</th>
<th>Normal X-ray Films</th>
<th>Primary Infiltrates</th>
<th>Pleural Effusion</th>
<th>Clinical Pulmonary</th>
<th>Extra-Pul.</th>
<th>Person Years of Follow-up</th>
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<td>85</td>
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<td>969</td>
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<td>1</td>
<td>3810</td>
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<td>278</td>
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<td>0</td>
<td>2688</td>
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<td>9</td>
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<td>2438</td>
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<td>474</td>
<td>428</td>
<td>16</td>
<td>19</td>
<td>10</td>
<td>1</td>
<td>5455</td>
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<td>2</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1345</td>
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<td>2</td>
<td>1</td>
<td>0</td>
<td>499</td>
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<td>41 - 49</td>
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<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>253</td>
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<tr>
<td>TOTAL</td>
<td>2266</td>
<td>2080</td>
<td>54</td>
<td>67</td>
<td>60</td>
<td>5</td>
<td>27,099</td>
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</table>
A third group consists of 65 who presented clinical reinfection type of tuberculosis, of whom five were extrathoracic lesions and 60 were pulmonary. They have had 987 person years of follow-up.

Thus, there have been 27,099 person years of follow-up for the 2,266 converters.

**Primary Infiltrates (Ghon Tubercles)**

In the entire group, (Table II) 54 presented primary infiltrates of sufficient size, density, and so located that their shadows were visualized on x-ray film. No other evidence of disease was seen. These were classified as primary infiltrates because they appeared about the time allergy could first be demonstrated, and because their subsequent course was typical. These persons have been observed from two to 25 years since the primary infiltrates were first seen, a total of 749 person years of follow-up (Table II). Throughout this period, five (9.3 per cent) subsequently developed clinical tuberculosis. One with primary lesion in evidence in 1931 had reinfection type of disease in 1941. One became a tuberculin reactor and primary infiltrate was present in April, 1931. In August of the same year he had tuberculous epididymitis, in February, 1932, tuberculous peritonitis, in April, 1937, involvement of one of the bones of the right foot, and in 1946, tuberculosis of a kidney required nephrectomy. Another who had primary infiltrate in 1932 had reinfection type of disease in 1934. One with primary infiltrate in 1945 had reinfection pulmonary lesion in 1948. One whose primary infiltrate was in evidence in 1948 had reinfection type of tuberculosis requiring treatment in 1949 and again in 1953. The remaining 49 individuals with demonstrable primary infiltrates have shown no evidence of clinical tuberculosis.

**Pleurisy with Effusion**

This is an allergic reaction and most often is caused by sub-pleural pulmonary lesions which extend into the pleura. Many of the cases occur

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**TABLE II—DEMONSTRABLE PRIMARY PULMONARY INFILTRATES AMONG 2,266 PERSONS INFECTED IN ADULTHOOD**

<table>
<thead>
<tr>
<th>Age When Infection Occurred</th>
<th>Number of Adult Converters</th>
<th>Number of Demonstrable Infiltrates</th>
<th>Number with Subsequent Clinical Lesions</th>
<th>Total Years of Follow-up After Infection</th>
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<tr>
<td>20</td>
<td>167</td>
<td>4</td>
<td>2</td>
<td>47</td>
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<tr>
<td>21</td>
<td>272</td>
<td>7</td>
<td>1</td>
<td>72</td>
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<td>167</td>
</tr>
<tr>
<td>23</td>
<td>191</td>
<td>1</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>217</td>
<td>7</td>
<td>1</td>
<td>119</td>
</tr>
<tr>
<td>25</td>
<td>168</td>
<td>5</td>
<td>85</td>
<td></td>
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<tr>
<td>26 - 30</td>
<td>474</td>
<td>16</td>
<td>216</td>
<td></td>
</tr>
<tr>
<td>31 - 35</td>
<td>211</td>
<td>2</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>36 - 40</td>
<td>103</td>
<td>3</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>2081</td>
<td>54</td>
<td>749</td>
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about the time allergy is first detectable by the tuberculin reaction. In fact, pleurisy with effusion, with its usual sudden onset, is often the first manifestation that the individual has been infected. Among the entire group of tuberculin converters traced, 67 developed pleurisy with effusion, of whom 14 had coexisting demonstrable primary pulmonary infiltrates. They have had a follow-up of 932 person years (Table III). In all but four, the effusion appeared within a few months to one year after the tissues were sensitized to tuberculo-protein. One who was infected in 1933 did not have effusion until 1951. Another had effusion two years after infection. In one, infection occurred in 1940 and the effusion in 1948. The fourth was infected in 1933 and effusion developed two years later.

Nine (13.4 per cent) of the 67 have developed clinical tuberculosis. One infected in 1932 had effusion in 1936 and pulmonary tuberculosis in 1942. One with effusion in 1932 had tuberculous pneumonia in 1933 and died from pulmonary hemorrhage in 1936. One had pleurisy with effusion in 1933 and minimal reinfection pulmonary disease in 1935. One was infected in 1940 and had pleurisy with effusion in 1948, coexistent with disease in the uterus, uterine tubes, and one ovary. One with pleurisy with effusion in 1940 had pulmonary tuberculosis in 1946. One whose effusion appeared in 1941 had pulmonary tuberculosis in 1942. One had effusion in 1945 and bilateral pulmonary tuberculosis moderately advanced a year later. One who had pleurisy with effusion in 1947 had co-existing tuberculous peritonitis. One with effusion in 1949 had tuberculosis of pelvic organs and peritonitis in 1953.

Among these nine persons who had pleurisy with effusion and developed clinical lesions, two had primary pulmonary infiltrates in evidence when effusion was present. These nine persons have had 187 person years of follow-up.

**TABLE III—PLEURISY WITH EFFUSION AMONG 2,266 PERSONS INFECTED IN ADULTHOOD**

<table>
<thead>
<tr>
<th>Age When Infection Occurred</th>
<th>Number of Adult Converters</th>
<th>Number of Cases</th>
<th>Subsequent Lesions</th>
<th>Total Years of Follow-up After Pleurisy</th>
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<tr>
<td>20</td>
<td>167</td>
<td>3</td>
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<td>36 - 40</td>
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<td>TOTAL</td>
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<td>67</td>
<td>9</td>
<td>932</td>
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</table>
Clinical Tuberculous Lesions

In addition to the converters who had primary infiltrates and those with pleural effusion, there were 65 who developed clinical lesions, of which 60 were pulmonary and five extrathoracic. These 65 had 987 person years of follow-up (Table IV).

It is possible that a few primary infiltrates were classified as reinfection type of lesions, because after graduation, in these particular cases, the tuberculin testing intervals were too long for accurate classification. In 34 of the 65, the clinical lesions were in evidence within the first two years after the infection occurred. In the remaining 31, they appeared three or more years after tuberculin conversion. In fact, in seven it was 10 years or more, including three in whom 18 years elapsed.

Death occurred in two cases not included in Table IV because the time of initial infection was not known. One who graduated from a school of nursing as a nonreactor to tuberculin in 1937 died from pulmonary tuberculosis in a sanatorium in 1942 at the age of 27 years. The institution's records were destroyed, and it was not known when she became infected. The other graduated from a school of nursing in 1943 as a nonreactor to tuberculin. In 1947, at the age of 25 years, she died from tuberculous meningitis, but no tuberculin test was administered after graduation.

Another student of nursing (not included in Table IV for the same reason) who graduated as a nonreactor to tuberculin in 1931 was found to have extensive pulmonary tuberculosis in 1948. Although she had worked in a sanatorium, no tuberculin test had been administered in the interim because, "I don't believe in tuberculin tests but have had periodic x-ray films of my chest."

A medical student whose previous tuberculin tests had been negative was found to be a reactor in February, 1935. The next month he had ex-

<table>
<thead>
<tr>
<th>Age When Infection Occurred</th>
<th>Number of Adult Converts</th>
<th>Number of Cases</th>
<th>Total Years of Follow-up Since Infected</th>
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<tr>
<td>31-35</td>
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<td>41-49</td>
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<td>1</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>2266</td>
<td>60</td>
<td>5</td>
</tr>
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themnodosum. Approximately two years later, tuberculosis was found in a costal cartilage. Over the next few years, he had lesions appear in the lumbar spine and one hip joint, from which he made good recoveries.

One nurse 14 years after graduation (1944) developed bilateral pulmonary sarcoidosis. Subsequently she was in a sanatorium for brief periods in 1944 and 1946. In 1948 she was found to be a reactor to tuberculin and a diagnosis of pulmonary tuberculosis was made.

Throughout these observations we have seen no difference in the types of lesions which developed or their subsequent behavior among persons whose initial infections were acquired in adulthood and those whose infections occurred earlier in life. Primary pulmonary infiltrates, which are Ghon tubercles in the inflammatory stage, took the same general course of regression and were just as benign as those we have often seen in children. The rapidly progressive and highly fatal primary disease, sometimes spoken of as the "infantile type," was not seen in any person who became infected in adulthood.

Among these 2,286 persons who first became infected in adulthood we have seen only two cases of tuberculous pneumonia. Each one occurred several years after the initial invasion. There has been but one case of meningitis and no miliary disease.

Those among the adult converters who had pleurisy with effusion were no different in immediate severity or subsequent developments than one sees among those infected earlier in life.

There were 65 persons who became infected as adults who did not have demonstrable primary infiltrates or pleurisy with effusion but developed clinical tuberculous lesions. These lesions were no more extensive or difficult to manage than those which we have seen develop in individuals of the same age but who had carried their infections since childhood. In a study on tuberculosis in physicians, we found that a larger number (3.6 per cent) of clinical lesions appeared among those who had been infected before entering medical school than among those (2.2 per cent) who became infected while in school or later. The logical explanation appears to be that among those who were infected earlier in life, the disease has had more time to mature than among those infected later. We have seen no evidence to indicate that age of the individual when the infection occurred played a significant role.

It is exceedingly encouraging that persons who become infected as adults possess the same effective defense mechanism as children. Therefore, the longer the initial invasion is postponed, the less of life's span remains for clinical lesions to mature.

The statement so often made that most clinical tuberculosis develops within two years after the initial infection occurs is probably the result of deductions being drawn from far too short periods of observation. While it is true that 34 of the 65 clinical cases observed in this study occurred within two years after the initial invasion, the remaining 31 cases evolved from three to 18 years after the primary infection occurred. All of the cases that could develop within two years after infection are now on record, but
new clinical cases continue to develop in this group of 2,269 who became infected in adulthood. If new lesions evolve at the usual rate, those that appear more than two years following the initial invasion will soon surpass those which appeared during the first two years.

Tuberculosis is a lifetime disease, and it is well known that clinical lesions may appear soon after the invasion occurs or at any subsequent time including senility. In parts of the world where children and young adults have been well protected against tubercle bacilli, most of the morbidity and mortality is now occurring among persons in the upper age brackets. There is good historical and postmortem evidence that many of these older persons have carried their infections since childhood and are developing clinical lesions decades later. There is no reason to suspect that this will not occur among some of those reported here as they reach the upper age brackets.

Race and Nationality

The belief that different races and nationalities of people possess varying degrees of susceptibility and resistance to tubercle bacilli is no longer tenable. The Jewish race was placed at one extreme, with the Negro and the American Indian at the other. The deciding factor was thought to be resistance which was believed to vary enormously in the different groups of people of the world.

To date, no well documented evidence has been found to show that Jews at any time or anywhere have manifested an innate resistance to tuberculosis different from that of other people under the same conditions. There is evidence, however, that in general Jews have not suffered as much from tuberculosis as some people of other races and nationalities. Probably this is because Jews have been protected against tubercle bacilli since the Mosaic laws prohibited the use of flesh as food from animals suffering from consumption. Moore says: “The Mosaic laws (Leviticus xxii, 22) contain rules that the flesh of animals which suffer from “wen or scurvy” should not be used as food. The Talmud, especially the Mishnah, codified at the close of the second century, and the Gemara (fifth century) contain numerous enactments against the eating of such flesh. It is stated on good authority that ‘kandi’ and ‘timari’ refer to tuberculosis.” The well-known, long-standing hygienic practices of Jews, such as washing hands before eating, have been a deterrent against tubercle bacilli. When brought in contact unavoidably with tubercle bacilli, Jews develop benign primary tuberculosis and are as likely later to have reinfection clinical disease as other peoples.

The American Indian and Negro, long pointed to as having such high susceptibility and low resistance, have lived under diametrically opposite conditions. Krause’ says: “Out of a single fact numerous writers have built up a rather stiff doctrine that avers an exceptional lack of innate resistance of primitive peoples to tuberculosis. The basic fact is the common observation that the introduction of tuberculosis among less civilized populations is followed by excessive mortality, the result of comparatively acute illness. The fact is conceded; the conclusion stated is not denied;
yet it is submitted that it need not follow from the premise; and it is maintained that the premise does not prove it."

"And it is suggested that circumstances other than innate lack of resistance, circumstances too that are facts, may contribute toward rendering tuberculosis unusually destructive and fatal for those of low civilizations—at any rate, for those who come in contact with the whites of Europe and America."

"Judged by our standards, the common living habits of savages and semi-savages are inordinately dirty. At any rate, they are supremely adapted to the contracting and spread of bacterial diseases, particularly one like tuberculosis, unique among infections in that it can be contracted in every conceivable way, via every possible portal of entry, directly and through an intermediary carrier. The common bowl without individual utensils at meals; the intimate herding at sleep; the windowless, chimneyless, never cleaned, littered habitations, if dwellings there are; the unwashed, oiled and pomaded bodies or the filthy rags if clothes are worn, must individually and together be regarded as hothouses of infection, if tubercle bacilli are loose. We cannot imagine a more fertile soil in which to spread an infection; as for tuberculosis, all that is needed is the sowing of the bacillus. And if seed-time ever does come, it will be marked by extreme dissemination and quantity of germs."

A quarter of a century ago, mortality and morbidity were so high among American Indians that it was often said tuberculosis would annihilate the race. This fatalistic point of view was based on the supposed inability of the Indian's body to cope with tubercle bacilli. Although much had been done by way of providing sanatoriums and treatment with marked success among Caucasians, nothing whatsoever had been offered the Indians on their reservations. For example, in the state of Minnesota, no provision had been made to protect the Indian population against those who had contagious tuberculosis. Those who died did so among their people, to whom they had disseminated tubercle bacilli. Tuberculin testing in 1931 revealed that 15.3 per cent of the white children reacted while 40 per cent of pre-school-age and over 65 per cent of school-age Indian children in the same county reacted to tuberculin. In 1937, the tuberculosis mortality rate was 529.2 per 100,000 population among Indians but only 33.5 among Caucasians. In 1934, a sanatorium with 117 beds for Indians was opened. Other measures were introduced which had long been in practice for Caucasians. The tuberculosis mortality rate among Indians decreased sharply after 1937, but was interrupted in 1943-44 because of lack of funds to adequately operate the sanatorium. Thereafter, it decreased, and in 1955 no Minnesota Indian died from tuberculosis (Figure 2). This is convincing evidence that it was not a matter of the Indian's susceptibility or resistance to tubercle bacilli but rather one of contagion, which yielded promptly when vigorously attacked. Moreover, the incidence of tuberculin reactors among Indian school children has been reduced to approximately 5 per cent. Those in charge of management, including treatment, of tuberculous Indians
reported that they responded to all forms of treatment in the same manner as Caucasians.

While conducting a tuberculosis survey on the Fort Peck Reservation in Montana in 1931, it was observed that three times as many Indian as white children reacted to tuberculin with a correspondingly high number of clinical cases. However, no difference was observed between the white and Indian response to the infection. Lesions in the two races appeared identical, and the course they took was the same.

There is no well documented evidence to support the idea that the American Negro has suffered such devastation from tuberculosis because of high susceptibility or lack of resistance. Just as with the American Indian, tubercle bacilli were allowed to prey upon him for some time after good control measures had been instituted and practiced among Caucasians. Thus, tuberculous Negroes remained in their homes and communities to disseminate tubercle bacilli to others, many of whom in due time followed the same contagious course.

Wherever Negroes have lived under social conditions comparable to those of Caucasians, the tuberculosis problem has been essentially the same in the two races.

It has been pointed out that among Negroes there is a tendency to tolerate the disease without examination or treatment much longer than is true of Caucasians. Therefore, when they do report, Negroes are more likely to have advanced and fatal tuberculosis. Negro children respond to primary tuberculosis invasions in the same manner as white children.

In 1931, Bogen reported on 4,730 patients admitted to the Olive View Sanatorium in Los Angeles. During the previous decade, more than one-half of the Negroes admitted had already died from tuberculosis, while only one-fourth of the Jews had died. On analysis of data, however, the reason was clear. The stage of disease at the time of admission to the sanatorium varied just as widely as did the mortality figures and generally in the same direction. More than three-fourths of the Negro patients were in the far-advanced stage on admission as compared to less than one-third of the Jews. More than half of all the patients in the sanatorium with far-advanced disease died during this period, less than one-fourth of those with moderately advanced, and only 3 per cent of those with minimal disease had succumbed. “This fact alone accounts for the wide apparent disparity in the death rates of the different nationalities.”

There is no evidence to support the idea that special racial or national resistance is acquired by reason of tuberculosis having existed among the people for many decades or even centuries. If this were a reality, one would not expect that today the highest morbidity and mortality rates obtain in those nations where tuberculosis has been known to be rife for so many centuries. Or is there good evidence that tuberculosis in a family for several generations enables the present generation to fight off the disease better than in those families where there has been no tuberculosis for many generations.

It is well known that animal species vary in susceptibility and resistance.
For example, human type of tubercle bacilli multiply and produce disease rapidly in the bodies of guinea pigs, whereas they cause relatively little disturbance in rabbits and, especially, rats. Apparently, this observed difference in species of lower animals is partially responsible for the belief that people of various races and nationalities differed in a similar manner. The fact was overlooked that human races belong to a single species.

Resistance Among the Mentally Ill

When so much tuberculosis was seen among persons in institutions for the mentally ill, the concept was advanced that mental illness lowers resistance. Apparently, this was generally accepted, and it was thought futile to attempt to solve the problem because so much mental illness was permanent. Late in the 19th century, Bracken pointed out that the prevalence of tuberculosis among institutionalized patients was solely a matter of contagion. Persons with mental aberrations were being sent to these institutions with total disregard for possible co-existing contagious tuberculosis. So many were admitted with this disease and so many acquired a from them that such hospitals became infested with tubercle bacilli.

In Great Britain during World War I, there was increase in tuberculosis mortality among patients in hospitals for the mentally ill. In fact, between 1910 and 1914, it varied between 15 and 17 per 1,000 resident patients. During the war, however, it rose to 37 per 1,000 in 1917 and to 52 in 1918. By 1923 the rate had fallen to 10 per 1,000. Early in World War II, there was also an increase in the tuberculosis mortality in such institutions. In fact, in the institutions for the mentally deficient of England and Wales the tuberculosis death rate in 1941 exceeded that of 1937-39 by 80 per cent for men and 73 per cent for women.

Tuberculosis Mortality Rates in Minnesota and in State Institutions

![Figure 3](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21291/)
The increase in tuberculosis mortality in the institutions for the mentally ill in World War I was ascribed mainly to insufficient diet. However, the Committee on Tuberculosis in Wartime of the Medical Research Council of Great Britain reported in 1942 that it was not so much of that opinion. This committee pointed out that a great deal of attention had been paid to both the quality and quantity of food provided these patients in World War II. Apparently, the increase was due to dissemination of tubercle bacilli resulting from overcrowding in these institutions. Blackouts reduced ventilation and many of the patients were unable to control cough and expectoration.

Thus, the low resistance concept prevailed until recently when the lack of resistance factor was discarded and the attack was made on the tubercle bacillus. Wherever this has been well done, tuberculosis among inmates of institutions for the mentally ill has declined precipitously (Figure 3). However, because the attack was started so late in such institutions, the disease has not yet been reduced to the same low level as in the general populations of the same areas. Moreover, there remains a large residual of infected older permanent residents among whom clinical disease will continue to evolve.

**Natural Defense Mechanism**

The human body, regardless of age or race, possesses an exceedingly effective defense mechanism against its first invasion with tubercle bacilli. Neutrophils and monocytes constitute the first two lines of defense. Lymphocytes enter the picture a little later. Lymphocytes normally predominate in the blood up to the age of four or five years. Thereafter, their percentage and absolute number gradually drops until the age of nine to 12 years, when the adult blood picture is established, which apparently persists for the remainder of life. For the ages of two to five years, the polymorphonuclear leukocytes constitute about 45 per cent and the lymphocytes 50 per cent. Between the ages of nine and 12 years, the polymorphonuclear leukocytes are 68 and the lymphocytes 29 per cent, which are the figures of adult life. Monocytes range from 3 to 6 per cent. No reference has been found to show that the ability of these cells to phagocytose organisms varies at different ages of life or in races of people. Irrespective of their portal of entry they are promptly phagocytosed by neutrophils, many of which enter blood and lymph streams. This is fortunate, for if all bacilli of the initial invasion remained at the site of entry, an exceedingly serious situation could obtain within a few months. Not all of the originally invading tubercle bacilli are ingested by a single neutrophil or are the numerous participating neutrophils focalized at the same point. If they were, a serious situation could soon obtain. Fortunately, the numerous tubercle bacillus-bearing neutrophils circulating in the blood and lymph streams quickly lodge in various locations, so that relatively few organisms are deposited in one place. This is of tremendous advantage to the defense elements, including monocytes, lymphocytes, and fibroblasts in that they can cope more successfully with relatively few in each of many places than a large number in one location. Apparently, this accounts in part for the
almost uniform benignity of primary tuberculosis \textit{per se}. The defense mechanism encountering relatively small numbers in any given place is able to surround them effectively before sensitivity to tuberculoprotein is well established and the subsequent more permanent encapsulation proceeds without interruption.

Obviously, if an overwhelming number of tubercle bacilli participate in the initial invasion, the defense elements may not be able to cope adequately at all of the points of focalization. Thus, when allergy appears, tuberculoprotein liberated from foci not well encapsulated may immediately produce reinfection type of tuberculosis. This was observed by Lemon and Montgomery\textsuperscript{12} who introduced bovine type of tubercle bacilli into pleural spaces of healthy rabbits. Some of the bacilli remained in pleural spaces but others were phagocytosed and deposited in regional lymph nodes, and in remote organs. The immediate reaction was non-specific. The number of tubercle bacilli originally introduced was so large that many of the intracellular organisms could not be removed but remained within the lymph spaces or were included in cellular masses attached to the pleural surfaces. Up to this point, the reaction remained entirely non-specific. When the rabbit's tissues were demonstrably sensitized, the allergic tissues responded to reinfection as vast numbers of virulent bacilli were released. "The acute reactions and the lesions which bring about illness and death are final evidences of a specific reaction."

While with rare exception among people tubercle bacilli of first invasion are so well controlled by the defense mechanism as to cause only minute areas of destruction, the encased tubercle bacilli remain alive for indefinite periods of time. Sweany has shown that after foci of tubercle bacilli are well encased, even with calcium and bone, this material may be resorbed, thus liberating the organisms, resulting in endogenous reinfection. Implantations on allergic tissues are responsible for practically all of the acute and chronic destructive clinical tuberculosis. While the defense mechanism succeeds at least temporarily with many reinfections, it fails often enough to account for all the illness and death from tuberculosis among the people of the world.

Obviously, people possess a defense mechanism that protects far more effectively against the first invasion of tubercle bacilli than against subsequent attacks. The failures to protect against reinfections are the result of allergy to tuberculoprotein. This protein, released from tubercle bacilli of first invasion organisms, (before allergy appears) is innocuous. It offers no handicap to the defense mechanism. However, after allergy is established, tuberculoprotein becomes a violent poison to cells and tissues. Therefore, tubercle bacilli of reinfection require much more effort on the part of the defending elements and the response of these white blood cells is much greater in point of numbers than is true of primary infections. In fact, the response is so great that tubercle bacilli are temporarily held at their sites of invasion. This often results in serious destructive situations in that so many bacilli are present and so much tuberculoprotein is liberated in one place as to destroy the adjacent defending cells, as well as the
fixed tissues in the area. Thus, areas of necrosis of varying size are produced.

This temporary fixation of tubercle bacilli of reinfection at their sites of invasion was long misinterpreted as representing resistance thought to have been built up by the presence of tubercle bacilli in lesions of primary tuberculosis complexes. This erroneous concept resulted from conclusions drawn without sufficiently long periods of observation.11

The reaction is so intense and tuberculoprotein so poisonous that it is impossible for individual neutrophils to ingest and distribute bacilli to other places where, in small numbers, the defense mechanism would be more likely to succeed. Thus when large numbers of tubercle bacilli are suddenly discharged on allergic lung tissue, acute tuberculous pneumonia results and often so much necrotic material is expectorated that large pulmonary cavities are in evidence in a matter of weeks. When smaller numbers of tubercle bacilli invade allergic lung tissue, the defense mechanism may operate more successfully so as to reduce and hold the lesions in smouldering, chronic stages.

Anachronisms

Nearly a decade ago Wilson12 employed the phrase "public health anachronisms" indicating "practices that are carried on now because they have been in use for the past thirty years or so even though it has been shown that they are of little or no value for the purpose for which they were originally intended." The field of tuberculosis now abounds with such anachronisms, including teachings and practices. The beliefs and teachings that people in certain ages of life, those of some races, and the mentally ill are more susceptible and have lower resistance to tubercle bacilli than others belong in this category as well as the belief that first infection type of tuberculosis protects against clinical disease.

SUMMARY AND CONCLUSIONS

Since 1920, longitudinal observations made on persons in various ages of life have revealed that: (a) Among 1,011 infants and young children infected, 30 (2.96 per cent) developed clinical tuberculosis. The others remained free from clinical disease during the period of childhood. (b) Among 2,979 children who reacted to tuberculin between the ages of 6 and 14 years, 187 (6.6 per cent) developed clinical lesions. (c) Chronic pulmonary tuberculosis usually made its debut during adolescence and throughout the remainder of life.

Among 2,266 persons who became infected at the age of 19 years or older and were recently traced, 2,080 with 24,431 person years of follow-up had developed no demonstrable tuberculous lesion. There were 54 in whom primary pulmonary infiltrates (Ghon tubercles in the inflammatory stage) cast visible x-ray shadows about the time allergy could be elicited. Pleurisy with effusion appeared in 67, mostly about the time allergy was detectable. Clinical reinfection type of tuberculosis subsequently developed in 65, of whom 60 had pulmonary and five extrathoracic lesions.
All demonstrable lesions behaved in the same manner as those previously observed in children and among adults who had been infected in childhood.

The natural defense mechanism of the human body apparently does not differ with age of life or races of people. Mental illness per se does not influence resistance.

The defense mechanism of the human body is handicapped when reinfections occur because of allergy which has been introduced following the primary invasion. Although the defense mechanism copes at least temporarily with many reinfections, it fails often enough to account for all the illness and death from tuberculosis.

RESUMEN Y CONCLUSIONES

Desde 1920 se ha hecho una observación a lo largo del tiempo en personas de edades diversas habiendo revelado tal estudio: (a) que entre 1,011 infantes y niños de corta edad infectados, 30 (2.96 por ciento) desarrollaron tuberculosis clínica. Los demás permanecieron libres de enfermedad clínica durante la infancia; (b) Entre 2,979 niños que reaccionaron a la tuberculina entre los 6 y 14 años de edad, 137 (4.6 por ciento) desarrollaron lesiones clínicamente comprobadas; (c) la tuberculosis pulmonar crónica generalmente hizo su principio durante la adolescencia y a través de todo el resto de la vida.

Entre 2,266 personas que se infectaron a la edad de 19 años o más y que fueron recientemente localizadas, 2,080 con 24,431 personas años de seguimiento, no han desarrollado lesión tuberculosa demostrable. En 54 personas de éstas, se observaron sombras correspondientes a infiltrados primarios (nodos de Ghon en estado inflamatorio) visibles a los rayos X cuando la alergia se descubrió. La pleuresia conderrame apareció en 67, la mayoría alrededor de la aparición de la alergia.

La tuberculosis de tipo reinfección se desarrolló subsecuentemente en 65, de los que 60 tenían lesiones pulmonares y 5 extrapulmonares.

Todas las lesiones demostrables evolucionaron del mismo modo que las antes observadas en niños y en adultos infectados durante la infancia.

Aparentemente el mecanismo natural de defensa en el cuerpo humano no difiere con la edad, las razas o las diferencias en los pueblos. Las enfermedades mentales por sí solas no influyen en la resistencia.

El mecanismo de defensa del cuerpo humano es desventajoso cuando ocurren reinfecciones con motivo de la alergia que se ha provocado des pués de la primoinfección. Aunque el mecanismo de defensa es eficaz por lo menos temporalmente ante muchas reinfecciones, bastante a menudo falla como para que permita la ocurrencia de todas las enfermedades y muertes por tuberculosis.

ZUSAMMENFASSUNG UND SCHLUSSFOLGERUNGEN

Seit 1920 an Personen verschiedener Lebensalter durchgeführte längsschnittmässige Beobachtungen haben ergeben, dass: (a) sich unter loll infizierten Kindern und jugendlichen Erwachsenen bei 30 (2.96%) eine klinische Tuberkulose entwickelte. Die anderen blieben frei von klinischer Erkrankung während der Periode der Kindheit; (b) unter 2979 Kindern,
die auf Tuberkulin reagierten im Alter zwischen 6 und 14 Jahren, entwickelte sich bei 137 (4,6%) klinisch manifeste Herde; (c) die chronische Lungentuberkulose nahm gewöhnlich ihren Anfang während der Jugendzeit und im Verlauf des späteren Lebens.

Aus einem Kreis von 2266 Personen, die sich mit 19 Jahren oder später infizierten und die jüngst nachkontrolliert wurden, hatten sich bei 2080 mit 24431 Personen-Jahren der Nachkontrolle keine nachweisbaren tuberkulösen Herde entwickelt. Es waren 54 Personen, bei denen primäre Lungeninfiltrate (Ghon'sche Tuberkel im entzündlichen Stadium) zu röntgenologisch sichtbaren Schatten führten ungefähr zu der Zeit, in der eine Allergie zustande gekommen sein konnte. Eine Pleuritis mit Erguss entwickelte sich anschliessend bei 67 Personen, meistenteils ungefähr zu dem Zeitpunkt, an dem eine Allergier feststellbar war. Formen mit klinischer Reinfektions-Tuberkulose entwickelten sich darauf folgend bei 65 Personen, von denen 60 pulmonale und 5 extrathorakale Herde hatten.

Alle nachweisbaren Herde verhielten sich in der gleichen Art und Weise wie diejenigen, die zuvor bei Kindern beobachtet worden waren und bei Erwachsenen, die in der indheit infiziert worden waren. Augenscheinlich ist der natürliche Abwehrmechanismus des menschlichen Körpers nicht verschieden in verschiedenen Lebensaltern oder Rassen oder Völkern. Geisteskrankheit als solche beeinflusst die Resistenz nicht.

Der Abwehrmechanismus des menschlichen Körpers ist gehandicapt, wenn Reinfektionen eintreten, infolge der Allergie, die sich im Anschluss an die erste Invasion entwickelt hat. Obwohl der Abwehrmechanismus mindestens temporär beeinflusst wird durch häufige Reinfektionen, sind ihm oft genug nicht alle Krankheits- und Todesfälle an Tuberkulose zur Last zu legen.

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