Eighty Years After the First Glimpse of the Tubercle Bacillus*

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Although not an original founder of the American College of Chest Physicians, I was in Albuquerque, New Mexico for another occasion and was invited to attend its first dinner meeting on September 28, 1935. Even after becoming a member in 1936, I was not active until it was evident that the College was filling a niche in diseases of the chest not previously occupied by any other organization. Since that time, it has been most inspiring and educational to work in this international organization with physicians around the world. Inasmuch as Mr. Murray Kornfeld, Founder and Executive Director of the College, gave such an excellent account of the evolution of the organization in the first Founder’s lecture in 1964, my presentation will be confined to the subject assigned by the program committee.

When Robert Koch’s eyes were the first in the history of mankind to catch a sure glimpse of the tubercle bacillus in 1881, there had been and still were millions of people who had observed the destructiveness of this organism in man and animals. Its ravages were recorded among the living many thousands of years ago, and archeologists have traced it much further back into antiquity.4

The experimental work of Villemin5 left no doubt concerning the communicability of tuberculosis. He said, “The phthisical soldier is to his messmates what the glandered horse is to its yoke-fellow.”

In 1874, Hansen6 announced the discovery of the leprosy bacillus. Two years later, Koch published his famous paper on the anthrax bacillus, and in 1878 he reported having identified the bacteria of six different kinds of surgical infections.

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Armed with these experiences and knowing there was something in the discharges from lesions of people and animals suffering from phthisis which caused the disease, he began an intensive search. The first glimpse of the tubercle bacillus only aroused his suspicion, whereupon he diligently proceeded in the most scientific manner with his four postulates and thus reported in 1882 that the bacillus he suspected at the outset is the cause of tuberculosis in people.7 It was assumed that Koch had discovered the only acid-fast bacillus which causes tuberculosis. However, in 1898 Smith8 announced having isolated a different type which commonly causes disease in cattle.

The Most Momentous Disease Problem in the World

Koch9 wrote: “If the number of victims that a disease claims is the measure of its significance, then all diseases, particularly the most dreadful infectious diseases, such as bubonic plague, Asiatic cholera must rank far behind tuberculosis. Statistics teach that one-seventh of all human beings die of tuberculosis, and that if one considers only the productive middle age group, tuberculosis carries away one-third, and often more, of these.”

Discovery of Other Acid-Fast Bacilli

Soon after Koch’s announcement, the avian type of acid-fast bacillus, Johne’s bacillus and acid-fast bacilli of cold blooded animals were isolated. During the same period, several saphrophytic acid-fast bacilli were found including butyricum, phlei, stercoris and smegmatis.9

In 1937, Wells10 isolated an acid-fast bacillus from voles which differs from the other two mammalian types and has been designated the murine type. More recently, numerous acid-fast bacilli have been isolated, the majority of which have not
been found to be pathogenic. However, a few such organisms have been identified in association with lesions which resemble tuberculosis. Wood, et al. made one of the earliest studies of this type of organism originally designated the yellow acid-fast bacillus. This and other recently isolated acid-fast bacilli for awhile were referred to as chromogenic, atypical, or anonymous organisms. They are currently known as unclassified mycobacteria. Runyon arranged them in the following four groups: Group I. Photochromogens. Representatives of this group are most frequently associated with human pulmonary disease including M. kansasii; Group II. Scoliochromogens. The members of this group are rarely pathogenic; Group III. Non-photochromogens. The members of this group may occasionally be pathogenic for man including Battey bacilli; Group IV. Rapid-Growers. They are generally saprophytic except M. fortuitum.

Genus Mycobacterium embodies all acid-fast bacilli. However, only the human and bovine (mamalian) types cause tuberculosis, as we recognize it in humans and cattle.

Sweany, et al. say: "The presence of a variety of Mycobacteria in and around tuberculous lesions has been clearly shown, but the source of these variants is still an open question. No doubt many arise from the vast numbers of Mycobacteria that have evolved over the eons of time since bacteria first appeared, such as those strains that cause leprosy or those that infect the turtle, fish, vole, fowl and other animals, or the saprophytic forms such as Myco. phlei, Myco. butyricum, Myco. leucoflavin, Myco. luteum; or those with variable pathogenicity such as Myco. fortuitum, Myco. johnei, Myco. ulcerans, Myco. balnei and many others that have been described over the last 75 years."

Again Sweany says: "There is still a question as to the possibility of mutation from the regular tubercule bacilli to the recently described unclassified forms."

Feldman wrote: "Of the multitude of classified microorganisms, few are capable of producing such serious, protracted and potentially lethal disease in human beings and animals as certain organisms belonging to the genus Mycobacterium. The two most important and best known species are, of course, M. leprae and M. tuberculosis, both of which are worldwide in their distribution and affect the lives of countless human beings. The numerous recognized mycobacteria include some species that have been identified but not yet classified. In addition, it seems a valid assumption that other species, as yet unrecognized, exist."

Sources of Tubercle Bacilli for Initial Invasion

After Koch identified the tubercle bacillus, it was known that this organism may be eliminated from persons with pulmonary disease by way of sputum and feces, from renal lesions through urine, from otitis media through the external auditory meatus, from bones, joints, peripheral lymph nodes through discharging sinus tracts, mammary glands and from skin lesions.

Portals of Entry to the Human Body

It was observed that after leaving the bodies of their hosts, tubercle bacilli do not multiply in nature and are not able to survive long unless they find refuge in human or animal bodies. Their portals of entry are the digestive tract, the respiratory tract, skin abrasions, conjunctiva and vagina. Investigators including Chauveau, Dobrokiowski, Desoubry, Calmette and Guérin Ravenel and Schroeder observed that swallowed tubercle bacilli pass through the lacticels of the intestines and are present in the chyle within about three hours. Some of these investigators have produced tuberculosis of the lungs by introducing tubercle directly into the intestines. Krause injected tubercle bacilli subcutaneously in the inguinal region of animals and within days they were found in bronchial lymph nodes.

The anatomy and physiology of the respiratory tract from the nares to the bron-
chioles are such that very little inhaled particulate material including bacteria reaches the lungs. The changes in the course air takes before reaching the larynx are such that most particulate material comes in contact with the surface of the passageways and is entrapped in the mucous on the walls of the nasal passages and the pharynx which is blown from the nose, expectorated or swallowed. That which remains in the air and enters the larynx for the most part is entrapped in the mucous on the inner surface of the walls of the trachea, bronchi and their ramifications and promptly swept upward to the pharynx from which it is swallowed or expectorated.

Early pathogenesis. By meticulous experimental studies, Vorwald and others observed the pathogenesis of tuberculosis from the first hour after tubercle bacilli invade the body. They found that neutrophils (polymorphonuclear leukocytes) provide the first defense by phagocytosing the organisms. The tubercle bacilli containing neutrophils enter the lymph and blood streams where they are carried and deposited in various places including the lungs, kidneys, bones, joints and brain. More are deposited in the lungs than in any other organ.

The next defense line is composed of monocytes which surround the neutrophils and thus hold the bacilli at their original points of focalization. Later, a wall of lymphocytes appears peripherally. As these walls of white blood cells are holding the tubercle bacilli at their original points of focalization, the connective tissue cells of the area multiply and form a fibrous capsule around the lesion. Later a capsule of lime further surrounds the tubercle bacilli. A last stage occurs in many cases, namely the laying down of bone in the wall of the capsule. In an early stage of tubercle formation some tubercle bacilli travel from the original area of focalization by way of lymph vessels to regional lymph nodes where they are entrapped and set up lesions similar to those of the original focus. These lymph node lesions and the original focus constitute a primary tuberculosis complex.

Of those which are located in the lungs, during their early existence, only approximately 5 per cent attain size and consistency and are so located to cast visible shadows on roentgenograms. However, within two or three years, calcium may be deposited in sufficient amount to cast visible shadows in approximately 25 per cent of the persons in whom they develop.

The lesions of primary tuberculosis result in only slight destruction of tissues and usually cause no significant incapacity of their hosts at any stage of their development. In approximately 95 per cent of the persons in whom they occur, no other tuberculous lesion appears through the remainder of the host's life.

Recognition of Hypersensitivity (Allergy) to Tuberculoprotein. In 1890, Robert Koch made his second great contribution by producing tuberculins. When he administered this substance with the hope that it would serve as a therapeutic and preventive measure, he observed reactions—local, focal and constitutional in those persons who had tuberculosis. Later observers including Pirquet found that the local skin reaction is due to hypersensitivity (allergy) to tuberculoprotein which develops in the tissues during the evolution of primary tuberculous lesions. It was observed that the protein of tubercle bacilli is harmless to animals and people whose tissues are not sensitized. However, in sensitized tissues it can be destructive. This undesirable effect was overcome by Pirquet, Mantoux and others with doses so small as to cause only harmless local reactions.

In experimental animals, Dienes and Mallory produced tuberculous infections and observed that allergy begins to be demonstrable a few days after infection. The degree of hypersensitivity gradually increases until it causes a visible skin reaction to tuberculin. Wallgren's meticulous studies of infants showed that within three to seven weeks after clocked exposure to
tuberculous mothers, allergy was detectable by the tuberculin test.

While Koch’s intended original purposes of tuberculin failed, it became and has continued to be the earliest diagnostic and best epidemiologic agent in the entire antituberculosis armamentarium.

Allergy Responsible for Clinical Forms of Tuberculosis. Although presence of allergy is so valuable in diagnosis and epidemiology, at the same time it makes all clinical forms of tuberculosis possible. Therefore, lesions which develop in allergic tissue represent the second or allergic phase of development of tuberculosis. When tubercle bacilli are brought in contact with allergic tissue, the tuberculoprotein they liberate results in a specific reaction. As protein continues to be liberated, necrosis of the tissue is likely to occur and thus, clinical disease evolves.

Practically all initial clinical tuberculosis, both acute and chronic, results from liberation of tubercle bacilli from primary lesions with implantation on allergic tissue. Thus, clinical lesions are largely due to endogenous reinfections. In reality, this phenomenon is well expressed as recrudescence of the disease. This may occur during the early stages of the evolution of the lesions. For example, if tubercle bacilli are released from a primary lesion in the central nervous system into a ventricle of the brain, or into the subarachnoid space, they are likely to produce acute tuberculosis meningitis. If such a lesion involves the wall of a lymph or blood vessel and liberates tubercle bacilli into the circulation, generalized dissemination results. These acute clinical forms of tuberculosis may occur in the neighborhood of 1 to 2 per cent of infants and young children within a matter of months or a few years after allergy is established.

The chronic forms of clinical tuberculosis usually result from what seems a paradoxic act on the part of nature, namely resorbing parts of walls of capsules of primary lesions and liberating tubercle bacilli. This may involve absorption of bone, lime, fibrous tissue over areas through which the long pent-up tubercle bacilli escape and are implanted on allergic tissue. It has been estimated that acute and chronic endogenous reinfections combined appear in only about 5 per cent of the persons who develop primary tuberculosis. The lesions of chronic clinical pulmonary tuberculosis, for the most part, evolve years or decades after the original invasion of tubercle bacilli.

Inasmuch as only infected persons and hence, tuberculin reactors develop acute and chronic clinical forms of tuberculosis and to date there is no way to determine which tuberculin reactor will develop such lesions, the only satisfactory procedure yet devised consists of periodic examinations of all tuberculin reactors. Since chronic pulmonary tuberculosis is rarely found in tuberculin reactor children under the age of 12 years, it is adequate to begin periodic examinations including roentgenograms of the chests of tuberculin reactors at that age and proceed on through the span of life. In the earlier years of childhood, chronic clinical lesions which evolve are usually extrathoracically located.

The belief occasionally expressed even today to the effect that nearly all infants and young children who become invaded with tubercle bacilli develop acute rapidly progressive forms of tuberculosis is harking back to the 19th and early part of the 20th Century when only children who already had these conditions were thought to be infected with tubercle bacilli. When tuberculin testing of large numbers of infants and children was done, it was learned that of all who had been infected with tubercle bacilli, relatively few develop acute clinical disease.

Thus, tuberculosis develops in two distinct phases. Original invasions of tubercle bacilli in people of any age first cause a benign disease known as primary or preallergic phase of tuberculosis. The body’s defense mechanism proceeds unmolested and the tissue reactions are non-specific. Tubercle formation is well under way and the tubercle bacilli are surrounded by de-
fense elements before allergy attains a high degree. Thus, the lesions are brought under control with very slight destruction of tissues.

It is only when tubercle bacilli are liberated on allergic tissues that a specific reaction occurs. Their protein is so destructive to sensitized cells and tissues as to cause necrosis followed by the various reactions seen in all forms of clinical tuberculosis. This is the second or allergic phase of the development of tuberculosis. Behring's observations reported in 1903 led to his dictum to the effect that death from chronic tuberculosis in an adult is the end of a song begun in the cradle. Thus, he considered the disease causing death as a re-crudescence of the original infection. Concerning chronic pulmonary tuberculosis, Calmette  said: "The condition may disclose itself stealthily and slowly as the remote echo of a benign infection contracted in childhood and remaining latent for years." In some nations, many of the primary infections which occur are acquired in adulthood; hence, the clinical lesions which later appear had their beginning in adult life.

Invasions of causative organisms of tuberculosis and syphilis follow somewhat similar courses in the human body. Each promptly produces primary lesions which result in very little tissue destruction and come under control without causing significant incapacity of the hosts. However, the organisms may remain viable and virulent in the host's body over long periods even for the remainder of life. It is from these surviving organisms that clinical lesions may evolve months, years, and decades later. In sharp contrast are such diseases as smallpox and poliomyelitis in which the viruses invade but soon disappear. If clinical disease develops, it does so promptly, but foci of the viruses do not persist to cause subsequent clinical lesions.

People of all Races and Nationalities have Natural Defense Mechanism. It has long been observed that tuberculosis has been more prevalent and destructive among the people of some races and nationalities than among others. From this observation it was deduced that such situations were due to difference in susceptibility and resistance to this disease among the people of the world. This belief was encouraged by the fact that considerable difference in destructiveness of tuberculosis was observed in certain animal species. For example, guinea pigs have little tolerance for mammalian type of tubercle bacilli. Rabbits tolerate the human type fairly well, but show little tolerance for the bovine type of organism. When these observations were applied to people, there was oversight of the fact that humans of all races and nationalities belong to the same species—Homo sapiens—and that they all have the same natural defense mechanism against invading tubercle bacilli. Hematologists have pointed out that it is impossible to differentiate between the races and nationalities of people by the white blood cells. The fact is also overlooked that social and hygienic conditions, density of population, etc., vary a great deal among the races and nationalities, so much so that large numbers of people of one race or nationality become invaded with tubercle bacilli while this occurs to relatively few of those of another race or nationality. The tuberculosis problem in any race or nationality is dependent not on ethnic grouping, but upon the number who become invaded with tubercle bacilli.

In the United States it was long contended that the American Indian and the Negro have high susceptibility and little resistance to tuberculosis because these so-called primitive races' contact with tubercle bacilli was relatively recent. Their situation was contrasted with that of Jews who were said to have the lowest susceptibility and the highest resistance because they had been in contact with tubercle bacilli for many centuries. However, actual observations revealed that the American Indian and the Negro develop the same benign primary tuberculosis as the Jews. Moreover, it has been shown that American In-
dians respond to tuberculosis control measures in the same manner as Caucasians (Fig. 1). This has also been demonstrated among Negroes. The studies of Bogen afforded the explanation concerning the greater mortality among Negroes than among Jews. Tuberculous Negroes were negligent in health matters. They usually did not report until they were seriously ill. They were hesitant about accepting hospitalization. Therefore, a high percentage had advanced disease on entrance to sanatoriums.

On the other hand, among the Jews, diagnosis was made much earlier and treatment was accepted more promptly. Therefore, the percentage of recoveries among them was much higher than among the Negroes. Moreover, more Negroes than Jews developed clinical tuberculosis because of social conditions which permitted many more Negroes to become invaded with tubercle bacilli than Jews.

When Jews have been forced into positions in which it was impossible to carry out the usual hygienic measures, in which there was much exposure and adequate medical care was not available, tuberculosis has been just as destructive among them as among others. Rakower reported observations on tuberculosis mortality among Polish and Jewish populations in Warsaw during World War I. Both suffered in the same manner, and the mortality from tuberculosis rose in the two groups to the same degree. During World War II when the "Jewish suffering in the Warsaw ghetto was indescribable," mortality from tuberculosis of the Polish population increased 2.3 times while that among the Jewish increased 8.5 times and became greater than the Polish mortality.

Lollini called attention to the tuberculosis situation among Arabs and Jews in Tripoli. From 1913 to 1939, the mortality rate with rare exception was lower among Jews than among Arabs. For example, in

Tuberculosis Mortality Rates in Minnesota
1918, the rate was 7.7 per 1,000 among Arabs and 2.80 among Jews. After 1945, with the exception of 1949, the rate was higher among Jews than among Arabs.

These facts are extremely encouraging as they indicate that tuberculosis among all people of the world can be controlled and eradicated by the same method.

A Test for Presence of Tubercle Bacilli in Living Animals and People

W. Gutman,15 Dorpat, Russia, in 1891 apparently was first to administer the tuberculin test to cattle. The same year, Bang16 of Denmark, also conducted a large testing program. During the next two years, veterinarians including Nocard, Pearson, Cotton and Russell also tested large numbers of cattle with tuberculin.

For the first time in history, it was found possible to detect the presence of tubercle bacilli in cattle within weeks after they had been infected and before any other method of examination was of avail.

Although Koch's subcutaneous method of administering tuberculin did not prove satisfactory for people because of the large doses employed, Pirquet17,18 devised a simple, harmless and accurate method of tuberculin administration. This test consisted of applying tuberculin to a superficial scarification of the skin. Pirquet strongly suspected that the reaction he observed indicated the presence of tubercle bacilli in the bodies of reactors. His suspicion was confirmed by Ghon's19,20 meticulous necropsies of bodies of children who died from various causes, but during life had no evidence of tuberculosis except the reaction to tuberculin. Thus, for the first time in history man had a method of detecting the presence of tubercle bacilli in the living human body long before other diagnostic methods were of avail.

A few scientists and physicians whole-heartedly accepted the facts established by Pirquet and Ghon, and proceeded to administer the tuberculin test to persons of all ages at every opportunity. Bushnell21 who made some sound observations on tuberculosis problems among people in various parts of the world during World War I, said: "The role of the von Pirquet test in the epidemiology of tuberculosis is destined, it is believed, to become of increasing importance." He recommended its use on a large scale.

An Exceedingly Practicable Observation

Observations of great practical significance have revealed that in areas where large numbers of children have been tested with tuberculin and both the non-reactors and the reactors have been followed over considerable periods, most of the subsequent clinical disease has developed among the original reactors. In a study dating back to 1921 by Ch'iu, et al22 among 772 non-reactor children at the average age of 6.6 years, and followed for 10.9 years, 12 (1.68 per cent) had developed clinical tuberculosis. Among 446 children who reacted to tuberculin at the age of seven years and were followed for 11.3 years, 67 (15.02 per cent) developed clinical disease. Thus, there was one case of clinical tuberculosis in the original non-reactor group to nine in the original tuberculin reactor group. The ratio between the mortality for the tuberculin reactors and that of the non-reactors was 38 to 1.

When this study began in 1921, it was generally believed that children who reacted to tuberculin were safe from subsequent clinical disease, whereas the non-reactors were an extremely high risk group, all of whom would later be invaded with tubercle bacilli and would provide the illness and death from tuberculosis in the future.

Further observation revealed that the girls and boys who originally reacted to tuberculin were from homes and communities where communicable cases of tuberculosis existed, whereas, those who did not react were from homes and communities where there were few if any communicable cases of tuberculosis. Thus, they had not been infected and their chances of becoming invaded with tubercle bacilli were slight. However, as time passed, the occasional one became infected, but the total
number was relatively small. This observation has since been confirmed many times.

Thus, to control and ultimately eradicate tuberculosis, most attention and work must be focused on the tuberculin reactors. Only periodic tuberculin testing is necessary for non-reactors to identify the occasional one who might become infected. From 1949-1951, Palmer, et al. administered the tuberculin test to children from one to 18 years in Puerto Rico and to children more than five years old in Georgia and Alabama. Among these children there were 112,000 who reacted to tuberculin and 144,000 were non-reactors. When a follow-up study was reported in 1958, it was found that 75 per cent of the clinical cases that had developed were among the original tuberculin reactors. In 1966, Comstock and Palmer made a 14 year follow-up study on the 64,000 former children who were tested in Alabama and Georgia in 1950. Two hundred thirty-four had developed clinical tuberculosis. Of this number, 176 (72.2 per cent) had appeared among the 46 per cent of original tuberculin reactors and 59 (24.8 per cent) among the original non-reactors.

Groth-Petersen et al. observed that 60 per cent of the entire adult Danish population had had a natural tuberculosis infection and that 85-90 per cent of the new cases of pulmonary tuberculosis were being derived from that portion of the population.

Meijer stated that individuals under 20 years of age constitute about one-third of the Netherlands' population; of this group, some 95 per cent have not (yet) been in contact with the tubercle bacillus. Our population also includes about 4 million tuberculin-sensitive individuals (who indeed have been infected) and according to Calmette's dictum, these individuals are "the potential tuberculosis candidates"; it is from this latter group that the sources of infection originate.

Horwitz says: "In many countries, it was until recently a generally accepted theory that the majority of tuberculosis cases were due to recent infection. It was supposed, therefore, that the disease could easily be eradicated, the tools being mass vaccination, case finding and treatment of diseased patients. However, a number of recent studies indicate that the greater part of the cases result from a recrudescence of old infection. As this observation evolves a drastic change in the eradication programs, it is of utmost importance to collect data as reliable and representative as possible on the epidemiology of tuberculosis.

Not all Children are Invaded by Tubercle Bacilli. Although in many places the belief has long prevailed that practically all children become tuberculin reactors by the time adulthood is attained, actual testing has revealed that this has not even been true in those nations with exceedingly high prevalence of tuberculosis. For example, from July, 1948 to June, 1951 through the International Tuberculin Campaign, tuberculin testing was done on 37,694,983 children and young adults in 23 nations in Europe, Asia and South America and 16,650,624 (44.2 per cent) did not react.

In those nations which have provided good sanatorium systems and have controlled tuberculosis among domestic animals and thus protected children against tubercle bacilli, the number of infected children has gradually approached the zero level. Indeed, there are now many grade schools in which no child reacts to tuberculin. In such areas very few become infected with tubercle bacilli as they grow older and the majority escape infection in adulthood. For example, Cowan reported that among more than 11,000 students of 18 to 19 years who were admitted to the University of Minnesota in 1965, 96.8 per cent did not react to tuberculin. In that state, the total tuberculosis mortality rate is now 2 per 100,000 population.

Accurate Diagnosis Imperative

Fortunately, Koch isolated the human type of tubercle bacillus instead of one of the many other acid-fast bacteria. He taught the medical profession how to stain,
culture and inoculate this organism. However, with the later discovery of so many other acid-fast bacilli, it was no longer possible to diagnose tuberculosis by simple staining. Hence, special culture methods, inoculations, etc., have been devised to differentiate mammalian bacilli which cause tuberculosis from numerous other acid-fast bacilli which do not produce this disease. Koch’s work had produced a method for detecting tubercle bacilli in materials exuding from tuberculous lesions, particularly sputum. This was the first time in history that physicians had a specific diagnostic procedure. However, by the time bacilli are being eliminated from lesions, the disease is usually in an advanced stage. In chronic tuberculosis, the tuberculin test detects the disease long before it causes extensive tissue destruction or becomes communicable.

When Roentgen discovered the x-ray (1895), he added a great deal to the ability of physicians to locate areas of disease which previous methods had failed to find. However, time and study revealed that the usual posteroanterior roentgenogram enables one to visualize only approximately 75 per cent of the lungs. This discrepancy has been partially overcome by making exposures of the chest in various diameters and by body section radiography, (planography and tomography). Moreover, in the visualized 75 per cent of the lungs the lesion must be macroscopic and of such consistency as to obstruct x-rays in order to cast visible shadows on roentgenograms.

One of the most important roles of the roentgenogram consists of periodically inspecting the chests of tuberculin reactors of 12 years and older. Among those destined to develop chronic clinical pulmonary disease, lesions attain size and consistency to produce visible shadows on an average of two or three years before symptoms are present or other phases of the examination are of avail.

In diagnosis it is of utmost importance to differentiate between demonstrable primary pulmonary infiltrates which begin to develop in non-allergic tissues and post-primary clinical disease due to endogenous reinfections on allergic tissue. All tuberculin converters have lesions which constitute primary tuberculosis complexes, but primary pulmonary infiltrates qualify in size, consistency and location to cast visible roentgenographic shadows in only about 5 per cent. These are silent benign lesions which resolve in a characteristic manner no matter how much or how little treatment is directed toward them. Without knowledge of this phase of the evolution of tuberculosis, the physician runs the risk of classifying them as clinical lesions and making claims for therapeutic procedures which play no role.

Attempts to Control Tuberculosis in People and in Animals

William Budd, a medical practitioner in England, was so convinced of the communicability of tuberculosis that in 1856 he wrote (published 1867): “By the destruction of this matter as it issues from the body by means of proper chemicals or otherwise—seconded by good sanitary conditions—there is reason to hope that we may eventually and possibly at no very distant time rid ourselves entirely of this fatal scourge.”

In his original manuscript on the etiology of tuberculosis, Koch wrote of measures that might be directed against the disease. He said, “First of all, the sources from which the infectious material flows must be closed as far as this is humanly possible. One of these sources, and certainly the most essential one, is the sputum of consumptives, whose disposal and change into a harmless condition has thus far not been accomplished.”

The history of leprosy control provided encouragement for a somewhat similar attempt with tuberculosis. The communicability of leprosy was so recognized that each patient was required to carry a bell at all times and to ring as “to give timely warning of his approach so that everyone could get out of the way in time.” In the 13th and 14th Centuries, a large number of lep-
rosariums were made available in Western Europe. There were 220 such institutions in England and Scotland, 2,000 in France and an amazing number in the Germanic cities. Isolation for the lifetime of the leper in these institutions was obligatory. This was so effective that at the beginning of the 16th Century, leprosy had become a rare disease in Western Europe and completely eradicated from England. In fact, leprosy had so completely died out by the end of the 16th Century that in 1656 and 1662, Louis XIV was able to abolish the leprosariums and devote their endowments to charity and general hospital construction.

Apparently, the first permanent institution that might be considered a sanatorium for tuberculous patients was established by Bremer in Göteborg, Germany in 1859. In 1887, Sir Robert Philip,55 Scotland, established the first clinic for tuberculous patients. By the second decade of the 20th Century there were literally thousands of sanatoriums and clinics in various parts of the world which were then serving an important role in education of the public with particular reference to communicability of tuberculosis. Moreover, they markedly prevented dissemination of tubercle bacilli from patients to human and animal associates.

When Ravenel56 (1901) demonstrated that the bovine type of tubercle bacillus is transmissible from animals to people and subsequent workers including Griffith,57 Holm58 and Hedvall59 observed the seriousness and extent of this problem, not only with reference to extrathoracic, but also pulmonary tuberculous lesions in people, it was obvious that the flow of tubercle bacilli from the bovine source must be stopped. Pasteurization of dairy products was found to destroy tubercle bacilli. However, Van Es said that pasteurization must be looked upon as a makeshift measure; the final solution of the tuberculosis phase of the milk problem is the eradication of the disease itself. It became obvious that tuberculosis among animals, particularly cattle, must be exterminated, otherwise it would never be possible to eradicate the disease from people. Numerous methods of solving the problem among animals were tried, but the only one that has led to eradication anywhere consists of testing all animals with tuberculin and slaughtering the reactors. This method has now been adopted around the world. Already, there is a considerable number of areas where no bovine tubercle bacillus has been found in animals for a period of twelve or more years.60

When the present antituberculosis drugs became available, they were considered for treatment of animals, but were not found applicable because they only suppress tubercle bacilli. Therefore, after drug treatment, such animals would remain potential shedders of hazardous bacilli not only to other animals, but also to people. Moreover, the bacilli eliminated by these animals may become resistant to drugs as a consequence of prolonged exposure to them in the animals' body. Thus, persons and animals infected with bacteria eliminated by such animals could not be benefitted by drugs. To administer antituberculosis drugs to animals could result in a sense of false security on the part of cattle owners from the assumption that tuberculous animals so treated are no longer a hazard to human or animal health. Tuberculous animals, after prolonged treatment with antituberculosis drugs, may in fact fail to react to the tuberculin test even though living tubercle bacilli may be present in their bodies. Feldman61 is of the opinion that "to combat animal tuberculosis with chemical agents presently available is to perpetuate the disease rather than to eradicate it."

In a few parts of the world advantage has been taken of the large store of information that has been acquired since Koch's first glimpse of the tubercle bacillus. However, it has not been announced anywhere that eradication has been accomplished except in a few places among children up to the age of 15 years. One reason for the delay has been the terrible time lag between establishment of facts and their prac-
tical application with prolonged tangential excursions in the meantime. Another reason is the long period that tubercle bacilli may remain viable and virulent in the human body which may be from infancy through senility. Therefore, wherever infants and children have been invaded with tubercle bacilli, eradication of tuberculosis is probably not possible for the remainder of the span of their lives.

Wherever enough institutions for the tuberculous have been well operated and where pasteurization of dairy products and later elimination of tuberculosis from animals, particularly cattle, have been satisfactorily practiced, there has been a continuous decrease of tuberculous infections in people with corresponding decrease in morbidity and mortality regardless of how many or how few other measures were employed. However, with the extensive use of antituberculosis drugs beginning about 1947, mortality rates declined more precipitously than before. This decline was especially evident in those parts of the world where little had previously been accomplished. In those areas and nations where good isolation of communicable cases and control of bovine tuberculosis had been in operation, the lion's share of tuberculosis control had been accomplished before the advent of drugs (Fig. 2).

A good example of the effectiveness of these procedures is also demonstrated in Fig. 3. Early in this century, the milk supply in New York City was extensively contaminated with bovine type of tubercle bacilli. As this problem was solved, first by pasteurization, and later by milk from tuberculosis free herds, large numbers of children escaped infection. This, combined with epidemiology, isolation in sanatoriums of persons with communicable disease, and intensive education of the citizenry resulted in a continuous decrease in tuberculosis mortality among children under 15 years old from 48 per 100,000 in 1920, to 0.2 per 100,000, 44 years later. The number of deaths in this age period decreased from 1200 in 1915 to four in 1964. There were only 12 children under 15 years reported with tuberculosis meningitis or miliary dissemination in 1964, of whom eight recovered.

Figure 4 is composed of tuberculosis mortality graphs from areas of relatively
TUBERCULOSIS DEATH RATE

CHILDREN UNDER FIFTEEN - NEW YORK CITY

![Graph showing tuberculosis death rate for children under fifteen in New York City over the years 1920 to 1964. The graph includes data for all forms and child population under 15 years, with the number of deaths and population figures provided for each year.]
small populations which for the most part have employed the above fundamental methods and added antituberculosis drugs more recently.

In Puerto Rico, severe hurricanes in the early 1930's destroyed over 200,000 homes and thus unleashed tremendous numbers of tubercle bacilli which resulted in extremely high tuberculosis mortality rates. Promptly thereafter, however, through attempts to close off and protect against sources of tubercle bacilli, the mortality rate rapidly decreased.

Iceland, with a mortality rate of more than 200 in 1930, showed a rather rapid decrease until 1939 with a definite acceleration after 1947 to the lowest mortality rate of any nation in the world in 1964.

Hawaii has had an almost continuous downward course in mortality rates without significant interruption since 1930.

With the ravages of war, the continuously decreasing mortality rate in Holland took a sudden rise reaching a high peak about 1945. However, the postwar offensive attack on tubercle bacilli resulted in phenomenal accomplishment with a mortality rate second only to Iceland in 1964.

In Fig. 5, the tuberculosis mortality graphs of three Scandinavian countries and two states—Wisconsin and Minnesota—are shown. The two states are included because their population is approximately the same size as the Scandinavian countries, because large numbers of their citizens are of Scandinavian extraction and also because all five areas began essentially the same kind of antituberculosis programs at about the same time.

**Tuberculosis Mortality Rates**

![Graph showing tuberculosis mortality rates](image-url)
In Denmark between 1876 and 1900 there was a decrease in mortality from tuberculosis in the towns from all forms of tuberculosis from approximately 325 to 250 per 100,000. The first sanatorium for pulmonary cases was opened in Jutland in 1900. Sanatorium building continued until there were four beds for every death from tuberculosis in Denmark. In 1908, the first chest clinic was established, and by 1945 the country "was covered" with chest clinics.

In that nation Bernard Bang, whose name is enrolled on the wall of the Immortal Hall of Fame, reported his study on tuberculosis of the udder of cows in 1884. Large numbers of tubercle bacilli were found in the milk from such cows. No sooner had Robert Koch announced production of tuberculin in August, 1890, than Bang began to use it as a test for tuberculosis in cattle. He was the first person who fully realized and appraised the problems connected with the employment of tuberculin as a diagnostic agent in combating tuberculosis. He then proceeded to test large numbers of cattle after which he said: "By its help we are able to discover a great number of cases of tuberculosis which were formerly absolutely concealed."

With strenuous effort, 26.5 per cent of cattle herds of Denmark were free from tuberculin reactors in 1937, and this was true of 99.7 per cent in 1949.

Torning5 said that in 1952, one infected herd was found in each 2,000. However,
in 1963 only one such herd was found in 10,000 herds. He recently reported a case of clinical tuberculosis due to bovine type of tubercle bacilli in a 39-year-old nurse. While a child, numerous cows on the family farm were killed because of tuberculosis. Törning was convinced that this nurse was infected with bovine type of tubercle bacilli in childhood, but had remained well until recrudescence occurred at the age of 39 years. He stated that this case “...reminds us that the fight against tuberculosis must be a joint enterprise between physicians and veterinary surgeons. Tuberculous cattle mean a threat to man, and tuberculous man in some cases means a threat to cattle.”

In Sweden prior to the opening of the 20th Century, the tuberculosis mortality rate is said to have been more than 300 per 100,000 inhabitants. Between 1900 and 1911, four large sanatoriums were established, after which at least one sanatorium per county was built. Hedvall pointed out that until 1937 the sanatoriums constituted the most effort against tuberculosis. However, in 1937 the central dispensary came into being in Sweden. This did not replace the former dispensaries, but coordinated and joined them together as a unit in the fight against tuberculosis. Furthermore, in 1940, a new tuberculosis law required compulsory notification by all physicians of newly discovered cases of tuberculosis and compulsory examinations of persons suspected of having infectious tuberculosis with compulsory registration of all known cases of tuberculosis. By means of this, as well as by means of other important resolutions, the center of gravity of the antituberculosis work passed gradually from the sanatoriums to the dispensaries, which now “...are working intensively and very successfully.” The attack on tuberculosis among cattle was initiated in Sweden in 1894 with increased activities in 1937. Hedvall demonstrated a serious problem caused by the bovine type of tubercle bacillus in man which had lurked in the South of Sweden. His report aroused so much activity that in 1965 he wrote: “Sweden is nowadays proclaimed free from bovine tuberculosis.”

In Norway with essentially the same fundamental antituberculosis program as the other areas shown in Fig. 5, the tuberculosis mortality rate decreased with approximately the same rapidity as Sweden. An excellent and practical demonstration was reported in a monograph by Gedde-Dahl in 1948. This work began in 1937 on the west coast of Norway in an area with a population of about 6500. He used the tuberculin test and kept the non-reactors under periodic tuberculin control, while the reactors had roentgenologic chest inspections periodically. From 1937 to 1944 he found that at the age of 15 years about 85 per cent of rural and 80 per cent of the urban population were non-reactors to tuberculin and this was true of 30 per cent of men and 45 per cent of women of 30 years. Thus, he saw the value of extending the test to the upper age groups. The tuberculin test proved much more effective than mass roentgenographic inspection. During this period, a marked decrease of clinical tuberculosis occurred. This fine accomplishment also has had a splendid continuous educational value.

In 1964, Eilertsen published an excellent 27 year follow-up on all individuals born in Bergen in 1935 of parents resident in the city.

In Wisconsin, a state sanatorium was established in 1907. Over the next two decades, 18 county and district institutions were established in addition to a veterans hospital. In that state in 1893, Russell administered some of the first tuberculin tests to cattle in the United States. This work was carried on by Russell, Hastings, and others with removal of tuberculin reactors until now it is necessary to test more than 11,000 animals to find one reactor to M. bovis infection. The tuberculosis mortality rate among people has dropped to 2.5 per 100,000 population.

In Minnesota, a state sanatorium opened in 1907. By 1918, 14 county and regional
sanatoriums were placed in operation. This was the demonstration state for the Certification of Schools project with reference to tuberculosis control work in progress initiated and promoted by the American School Health Association with A. O. DeWeese, Secretary, Kent, Ohio.

Tuberculin testing of cattle was done in 1894 by Cotton in the milk shed of the largest city. This procedure was promoted vigorously and was brought promptly to the milk sheds of the other cities. In 1923, a state-wide program was adopted which provided for testing of all cattle, county by county and certifying counties which reduced the percentage of tuberculin reactors to 0.5 per cent or less. This program has continued and in 1966 only one animal in each 17,900 tested reacted to tuberculin. Among people, the mortality rate has decreased to 2 per 100,000 population.

In Fig. 6, one sees that in Japan the tuberculosis mortality rate had been rising since 1932. By the end of the war in 1945, it was 280 per 100,000. Between 1945 and 1949, 143 sanatoriums were placed in operation as well as a sizeable number of beds for the tuberculous in general hospitals. Diets were improved and streptomycin was administered. The mortality rate rapidly decreased reaching 181.1 in 1948. This decline in tuberculosis mortality was not unique, as this phenomenon was observed in other countries when large numbers of tuberculous persons were isolated in institutions and antituberculosis drugs were administered as has been graphically illustrated by Drolet and Lowell and Lowell. In France, the tuberculosis mortality rate reached a high peak during World War I, a marked decrease followed until a sharp increase occurred during World War II, to be followed by a precipitous decrease. In England and Wales and the

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**Figure 6**

Annual Mortality from Tuberculosis
United States, tuberculosis mortality rates had been decreasing with brief interruptions during World War I and again particularly in England during World War II.

Figures 4, 5 and 6 show that after the first few years of the antituberculosis drug era the precipitous decrease in mortality rate definitely leveled off.

Marked decrease in tuberculosis mortality rates have occurred in some nations reaching the lowest level of 1.1 per 100,000 in Iceland and 1.9 in the Netherlands and a considerable number under 10 in 1964. Areas with the largest populations still have alarming mortality rates. In such areas, there have not been adequate facilities to isolate persons with communicable disease or to eradicate it from domestic animals.

After reviewing statistics of the first seven years of use of antituberculosis drugs, Drolet and Lowell® wrote: "During the seven years from 1947 to 1953, the most rapid decline in tuberculosis mortality the world has ever seen has taken place." Then a survey of 48 countries with 900 million inhabitants revealed a tuberculosis mortality rate of 29.6 per 100,000. Lowell® reported results of a survey in 1962 including 57 countries and 16 small reporting areas with a population of 859 million people with a tuberculosis mortality rate of 18 per 100,000. Thus, in the period of 1953 to 1962, the mortality rate had decreased approximately 40 per cent. "The above figures excluded India, China, Korea, Russia and other large areas for which nationwide-statistics were either not compiled or not published." The inhabitants of these areas compose approximately two billion of the world's citizenry. Candau, Director General of the World Health Organization, estimates that tuberculosis causes deaths of three million lives annually.

Tuberculosis Morbidity Rates

Inasmuch as antituberculosis drugs have postponed death from tuberculosis for many persons, mortality rates do not now provide even as dependable a criterion of the tuberculosis situation as in former years. Tuberculosis morbidity is dependent upon the tuberculosis infection rate; therefore, it is now a better gauge of the tuberculosis problem than the mortality rate. However, morbidity rates do not have the desired dependability because of lack of agreement as to what constitutes a case of tuberculosis. Some physicians do not differentiate between demonstrable primary pulmonary infiltrates and clinical lesions. A few report strong tuberculin reactors as clinical cases. Tuberculosis case reporting may be woefully incomplete. Many persons with tuberculosis are not examined unless severe symptoms appear and large numbers are first reported by death certificates. Nevertheless, the morbidity reports from the various nations provide important but incomplete information. The lowest case rate reported in 1964 was 18.6 in Denmark and the highest was 365.8 in Japan.

In 1957, Lowell® surveyed 47 countries with 700 million inhabitants, and found a case rate of 160 per 100,000 population. In 1962 he made a similar survey in 52 countries and 25 small reporting areas which presented a case rate of 123 per 100,000 population. Thus, the case rate had been reduced by 30 per cent. India, China, Korea, and Russia were not included. Holm states that Candau estimated that between two and three million new cases occur annually and that at least 15 million continue to suffer from infectious tuberculosis.

As late as 1964 Holm® said: "For about half of the world's population no organized efforts are made to control tuberculosis, and this is the half where the problem is most serious. For the other half, efforts to control tuberculosis are conducted in a haphazard manner. Only a small fraction of the world's population is covered by well organized programs in which the most modern means to control tuberculosis are systematically employed." In 1956, Eloesser® wrote: "In Latin America, Asia, and Africa, tuberculosis still ranks foremost among disabling and mortal diseases demanding hospital care. The population of
these parts of the world is estimated at one and two-third billions; their tuberculosis death rates lie between 50 and 100 per hundred thousand; hence, counting from five to ten cases of active tuberculosis for each death, these continents may harbor about 16.6 million sick, who by our standards should be in the hospital. To provide such a number of beds, however, is impossible. That would cost many times the money available for the total national health budget. For the solution of this problem, Eloesser recommends the hospital colony which would provide first class care for patients and rehabilitation at a cost far below that of sanatorium beds.

**Tuberculous Infection Rates**

In those areas of the world where the eradication of tuberculosis is within sight, the only sound and dependable criterion of the tuberculosis problem among people is the tuberculous infection rate. For the determination of this rate, the tuberculin test provides the most accurate and dependable indication of the presence of tubercle bacilli in the animal and human body.

For more than a quarter of a century, all Icelandic school children have been tested with tuberculin and the non-reactors have been retested annually. There the world's lowest tuberculosis mortality rate has recently been recorded. Presently it is planned to administer the tuberculin test to all uninfected school children every six months so that converters be found more promptly and thus sources of infection closed at the earliest possible time. Thus, the attainment of the tuberculosis eradication goal will be markedly hastened.

In the early 1940's, the Committee on Tuberculosis of the American School Health Association established qualifications for official certification of schools. These consisted of tuberculin testing of at least 95 per cent of all children from kindergarten through high school and 100 per cent of personnel members with appropriate procedure of those who reacted to tuberculin. Since certification of the first school system in 1945, thousands of certificates have been issued. To retain certification status, schools are required to repeat the program biennially.

In 1949, a provision of the Danish School Health Act required cooperation between the school health officers and the Chest Clinics that all school children be examined including the tuberculin test and all non-reactors have the tuberculin test repeated annually.

In 1950, a mass campaign was instituted in Denmark covering the entire country except Copenhagen County, the island of Bornholm and a few other small areas previously covered. The campaign was concentrated on selected age groups. Preschool children, ages one to six years, and the adult population 15-34 years were individually invited to come for a tuberculin test and a chest photofluorogram. Persons over 35 years were informed by way of radio and press. Children of school age (7-14 years) were not invited because they were being tuberculin tested in the schools. More than a million persons were examined in this campaign.

Throughout the world practically all infants are born free from tubercle bacilli. In a few places, this status is being maintained among children well into the second decade of life. Only periodic tuberculin testing determines whether this accomplishment is being achieved. It is only when this tubercle bacillus free status is maintained for one generation of children after another throughout their span of life that eradication of tuberculosis will have been realized. This will require identification of all human adults and animals now harboring tubercle bacilli and managing them so as to close present sources of tubercle bacilli and keeping the organisms correled in the bodies which they now inhabit.

The hope of eradicating tuberculosis from any area or nation is nil until all persons and animals in whom tubercle bacilli have taken refuge are identified and managed accordingly. Eradication of tuberculosis is now within the range of possibility...
in several nations. However, total eradication for the whole world is a dream that can only be realized in the far distant future, but like leprosy in Europe, it can be largely eliminated and finally eradicated.

**Summary**

1. After Koch discovered the tubercle bacillus, it was learned that when it first enters the human body, the reaction of the tissues is nonspecific. An encapsulation begins and continues until the bacilli are encased in fibrous, calcific and osseous capsules. This disease, known as primary tuberculosis, causes little destruction of tissue and is exceedingly benign.

2. Within weeks after the first invasion of tubercle bacilli, the body tissues become sensitized to tuberculoprotein so as to be identified by the tuberculin test which is the earliest diagnostic and the best epidemiologic agent available.

3. In an estimated 5 per cent of persons with primary tuberculosis, bacilli may be liberated and lodged on sensitized tissue. The sensitivity causes a specific reaction which may result in acute or chronic clinical tuberculosis.

4. People of all races and nationalities have the same natural defense mechanism against tubercle bacilli. The difference in prevalence of tuberculosis among them is dependent upon the number who become invaded with tubercle bacilli.

5. Isolation and treatment of persons with communicable disease and control of tuberculosis among animals continue to be the most effective factors in tuberculosis eradication. Wherever they have been continuously employed mortality, morbidity and infection rates have topped regardless of how many or how few other procedures have been in vogue.

6. Since 1947, antituberculosis drugs have been useful in suppressing clinical tuberculosis. However, in nations where isolation of communicable cases and eradication of bovine bacilli have long been employed the lion’s share of tuberculosis control was accomplished prior to the advent of drugs.

7. Although in a few places tuberculosis has been eradicated from cattle and reduced to phenomenal low levels in people, it is still rampant in parts of the world where approximately two-thirds of the people reside. It will not be eradicated anywhere until one generation of children after another has lived through their span of life without infection.

**Acknowledgement:** My deep indebtedness to Godias Drolet and Anthony Lowell is acknowledged for the large volume of statistical data so kindly provided for this and previous papers over many years.

**Resumen**

1) Después del descubrimiento del bacilo tuberculoso por Koch se comprobó que cuando penetra por vez primera en el organismo humano la reacción tisular no es específica. El proceso de encapsulación comienza pronto y continua hasta que los bacilos quedan incluidos en una cápsula fibrocalcárea de contenido caseoso, —Esta lesión, llamada tuberculosis primaria, es poco destructiva y constituye una enfermedad excesivamente benigna.

2) En las semanas que siguen a la penetración del bacilo los tejidos se sensibilizan a la tuberculoproteína, como lo indica la reacción tuberculínica. Esta es la primera prueba diagnóstica y el mejor agente epidemiológico de que disponemos.

3) En un 5% de los sujetos con tuberculosis de primo-infección puede ocurrir la liberación de bacilos y su alojamiento en tejidos sensibilizados. La sensibilización determina una reacción específica que puede dar lugar a la tuberculosis crónica clínica.

4) Todas las razas y nacionalidades presentan el mismo mecanismo defensivo contra el bacilo tuberculoso, la diferente incidencia de tuberculosis entre ellas depende de la proporción de sujetos invadidos por el bacilo.

5) El aislamiento y tratamiento de los sujetos con infección comunicable y el control de la tuberculosis animal, continúan siendo los factores más efectivos en la erradicación de la tuberculosis. Dondequiera que han sido aplicados en forma continua la mortalidad y morbidad, así como la incidencia de la infección, han descendido con o sin el empleo de otras medidas en boga.

6) A partir de 1947 las drogas antituberculosas han sido efectivas en la supresión de la tuberculosis clínica. Sin embargo, en las naciones en que el aislaramiento de los casos comunicables y la eradicación del bacilo bovino han estado largo tiempo en uso, el control de la tuberculosis había sido obtenido en su mayor parte antes del advenimiento de dichas drogas.
7) Si bien en algunas partes le tuberculosis ha desaparecido, en el ganado y ha sido reducida a niveles fenomenalmente bajos en la población humana, no es menos cierto que dicha infección está todavía rampante en las áreas donde reside las dos terceras partes de la humanidad. De hecho no será erradicada hasta que varias generaciones sucesivas hayan vivido toda su vida libres de esa infección.

ZUSAMMENFASSUNG

2. Innerhalb von Wochen nach der ersten Invasion von Tuberkelbazillen werden die Körperwebe sensibilisiert gegenüber Tuberculoprotein, wie es sich durch den Tuberkulin-Test nachweisen läßt, der das erste diagnostische Mittel und der beste epidemiologische Weg ist, der zur Verfügung steht.

3. Schätzungsweise in 5% von Personen mit Primärtuberkulose können die Bazillen frei werden und sich in sensibilisiertem Gewebe ansiedeln. Die Sensibilität führt zu einer spezifischen Reaktion, die eine chronische klinische Tuberkulose zur Folge haben kann.


5. Eine Isolierung und Behandlung von Personen mit ansteckender Erkrankung und eine Bekämpfung der Tuberkulose unter den Tieren bleiben auch weiterhin die wirksamsten Faktoren bei der Eradikation der Tuberkulose. Wo immer sie fortlaufend zum Einsatz gebracht werden, sind Mortalität, Morbidität und Infektionsraten auf ein Minimum zurückgegangen, unbeschadet, wieviel oder wie wenig andere Maßnahmen in Mode waren.


Bei Nationen jedoch, bei denen die Isolierung von ansteckungsfähigen Fällen und die Eradikation der bovinen Tuberkulose seit langem in Gebrauch sind, wurde der Lüwenanteil der Tuberkulose-Bekämpfung vollendet vor dem Einsatz der Medikamente. Obwohl bei einigen wenigen Gruppen die Tuberkulose zur Eradikation kam brauch sind, wurde der Lüwenanteil der Tuberkulose unter dem Rindviehbestand und zu phänomenal niedrigen Ziffern unter der Bevölkerung führte, ist sie noch immer ein drohendes Verhältnis, in den Teilen der Welt, wo etwa 2/3 der Menschheit zuzahme ist. Sie wird nicht früher ausgemerzt, ehe eine Generation von Kindern nach der anderen ihr Leben lebt ohne Infektion.

Complete reference list will appear in reprints.

For reprints, please write: Dr. Myers, 1316 Mayo Memorial Building, University of Minnesota, Minneapolis 55455.

EFFECTS OF NITROGLYCERIN ON CIRCULATION

Splanchnic, pulmonary and systemic hemodynamics were studied in 18 patients after the sublingual administration of nitroglycerin. The drug produced an over-all vasoconstrictive effect on the splanchnic circulation. There was no evidence of venous pooling in this bed. The data may indicate a splanchnic supportive role in augmenting venous return to the heart with disengorgement of its own volume. In contrast, there was vasodilatation and pooling of blood in the pulmonary vascular bed. The systemic circulation probably sustains several effects by nitroglycerin, including arterial vasodilatation.

A direct change in large artery distensibility probably explains the modest fall in systolic blood pressure seen. Further decline in arterial pressure may depend on venous pooling of a small or large degree. Probably the fall in systemic and specific organ flows is also linked to decreased venous return and the vascular readjustments provoked thereby. FERRER, M. I., BRADLEY, S. E., WHEELER, H. Y., ENSON, Y., PREISSG, R., BRICKNER, P. W., CONROY, R. J. and HARVEY, R. M.; "Some effects of nitroglycerin upon the splanchnic, pulmonary and systemic circulations," Circulation, 33:357, 1966.