A SURVEY OF IMPORTANT FACTORS LEADING UP TO OUR PRESENT CON-CEPTION OF TUBERCULOSIS*

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Tuberculosis has been recognized as a clinical disease throughout historical times; and until within the memory of those of the present generation it has been looked upon almost universally with utter despair and hopelessness. During the greatest portion of this time it was known only by its advanced symptomatology.

AUENBRUGGER AND LAENNEC

Not until Auenbrugger (1) described percussion (1760) and Laennec (2) began to make systematic use of auscultation (1815) did any one attempt to critically examine the patient. It seems strange to us to realize that physicians had not previously thought of percussing or listening to the chest of tuberculous patients. It seems equally strange that those who percuss and auscultate today do not seem to realize that they can palpate the chest and differentiate all the things that they now do by percussion, and some with much greater accuracy. It seems doubly strange that when Laennec once listened he heard so accurately and defined his observations so well. He created a new era. He lifted clinical tuberculosis out of chaos and started a process of definition which has required pathology, bacteriology, animal experimentation, serology, rontgenography and the most accurate and painstaking clinical study to complete.

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KLENCKE AND VILLEMIN

In the early centuries certain Greek physicians considered tuberculosis to be infectious. Galen so considered it. Morton in 1689 taught the infectious nature of the disease. In 1782 an edict was issued in Naples based on a belief in the infectious nature of tuberculosis. It required that bedding and furniture in rooms occupied by those dying of consumption should be destroyed by fire. This was a great advance for the time and, while unnecessarily harsh, it shows a conception of the disease which belonged to a much later era.

Klencke (3) in 1843 was probably the first one to transmit successfully tuberculosis to an animal by inoculating it with caseous material from a necrotic tubercle. To him almost belonged the honor of proving the infectious nature of the disease. But he did not carry his work sufficiently far. He left the honor to Villemin (4) to transmit the disease from man to animal and then by taking material from the tuberculous animal again to produce the disease in a second animal. He thus beyond doubt produced the complete experimental evidence which proved the infectious nature of tuberculosis. This he accomplished in 1865—nearly twenty years before the discovery of the nature of the infectious virus with which he was dealing.

BAUMGARTEN AND KOCH

As there were two between whom the credit for establishing the infectious nature of tuberculosis must be divided, so there are two who deserve the credit for discovering the tubercle bacillus. Baumgarten had seen the tubercle bacillus through the microscope previously to the time when Koch made his epochmaking announcement. Baumgarten (5) had seen it unstained; but Koch (6) with his wide knowledge of dyes had heen able to produce a stain which rendered it unquestionably visible. His work was so complete that when be announced the discovery of the bacillus, his experimental proof withstood the scrutiny and

attacks of all experimenters and opponents. While Klencke and Baumgarten are important contributors to the proof of the infectious nature and bacteriological cause of tuberculosis, it is to the greater ones, Villemin and Koch, that our homage is usually paid.

INFECTION AND HEREDITY

After the discovery of the tubercle bacillus had afforded the final argument to Villemin's work we entered on an era of bacterial domination. The tubercle bacillus was considered the essence of tuberculosis, both in the realm of prevention and in the clinic. The idea of the disease being inherited was swept away, and scarcely a trace of the possibility of hereditary factors having any part in the picture was left. Although this was too sweeping, it has taken nearly half a century even to approach an equilibrium and give

heredity its rightful place in etiology.

The interpretation of facts which seem to be indisputable is forcing us now to look upon heredity as offering the only answer to part of the problem of tuberculosis as a clinical disease; not the inheritance of the infection but the inheritance of characteristics or qualities of cell and cell action which permit the almost universal infection to become active in certain instances while it is held within bounds in others. While the dictum of the era of hacterial dominance that "there can be no tuberculosis without the tubercle bacillus" is true, we are gradually recognizing that the bacillus alone may only cause tuberculous infeetion; it does not necessarily cause tuberculous disease. Tuberculous disease implies something different—an inability on the part of the individual to overcome his infection. In present immunological terms this means either a failure to develop or a failure to maintain a sufficient specific defensive mechanism. Ohservation shows that this factor differs with different individuals, depending upon their vigor and their reacting powers, consequently upon both heredity and environment.

No one can observe tuberculosis carefully without

seeing that the ability of different patients to react in the formation of scar and healing differs greatly; likewise the power to prevent the spreading of the process. One person will heal with much scar; another with a small amount. One will make as much progress in recovery in a few months as another in many. This must be accounted for as being due to the total ensemble of the patient's reacting powers; both inherited and acquired, both specific and nonspecific.

TUBERCULIN ERA-INTENSIVE STUDY

Koch (7) noted that, when an animal already tuberculous was inoculated again with bacilli, it reacted differently from what it did when inoculated for the first time. He noted, as a result of the second inoculation, that the animal already infected reacted with an inflammatory process around the previous existing tubercles, and further recognized this inflammation as a part of the mechanism of healing. Shieck saw experimental tuberculosis of one eye protect a rabbit from a later inoculation in the other eye.

Koch grasped more fully than others of that period that healing was an immunity response, and that a primary infection increased the animal's resistance to a later inoculation; and further, that subsequent inoculations had a tendency to produce healing in previously existing foci. He therefore noted two all important effects of tubercle upon the organism: first, that it produced immunity; and second, that secondary inoculation acting through the immunizing mechanism already established produced a specific inflammatory reaction about previously existing tubercle which was often followed by healing. Further observation shows that this healing effect is greater where the secondary infection is not too extensive; and that, where the secondary inoculation results in a too severe process, the primary effect is a severe inflammatory reaction at times followed by softening and sloughing. . Even this destructive process must be considered as conservative for it is Nature's way of eliminating infecting and toxin producing substances even though the process frequently proves too drastic

for the patient.

Koch then set about to find some specific product which would produce the same immunizing and healing response as living bacilli without exposing the patient to the danger of a too severe reaction and a renewed infection. This resulted in the tuberculins prepared by him as well as the many preparations made by others.

In spite of the fact that tuberculin will produce the specific inflammatory reaction which is a necessary part in the healing of tuberculosis the remedy has not come into general use, largely, in my opinion, because of a failure on the part of the profession to understand its action and to master its administration. While tuberculin proved disappointing to those who looked for a specific remedy, easy of administration and perfect in its action, yet directly and indirectly it has been the cause of important contributions to our understanding of tuberculosis. As a result of the discovery of tuberculin and the attempts which were made to employ it clinically, scientific men began laboratory and clinical studies which have been responsible for much of the rapid gain in our knowledge of the disease during the past twenty-five years. Pathologists who had found tuberculosis of little interest before began to study it intently, and clinicians observed their patients more closely and gained a more comprehensive and accurate idea of the clinical manifestations of the disease.

As a result of the diagnostic power of tuberculin, clinicians learned that tuberculosis could be diagnosed before bacilli were found in the sputum; so, the first real early picture of clinical tuberculosis was obtained

as a result of its diagnostic use.

The serological aspects of tuberculosis have also been studied most carefully and we have arrived at a better understanding of immunity, not only in tuberculosis but in infections in general, as a result of studies stimulated by the serological reactions. Nor must we forget the impetus that was given to the

successful treatment of tuberculosis which resulted from the greater interest in the disease and the more careful observations which date from the tuberculin era

While, in the minds of many, tuberculin failed, it was a most successful failure, if we take into consideration the increased knowledge of our understanding of the disease and in the manner of successfully preventing and treating it which resulted directly and indirectly from tuberculin. As to its value as a therapeutic measure, the preponderance of opinion does not recognize its value and is opposed to its use. On the other hand, there are a few men throughout the world who have been so impressed with the therapeutic action of tuberculin, because of its power to produce the specific allergic reaction in tubercle which is essential to healing, that they have diligently striven with what seems to them, at least, a degree of success, to develop a method of successfully employing tuberculin in therapy. It is a significant fact that rarely has one, who has learned to employ tuberculin therapeutically, relinquished its use.

VON PIRQUET'S AND ROMER'S CONTRIBUTIONS

One of the most important and farreaching contributions to the understanding of tuberculosis as a disease was made by von Pirquet (8). When he discovered the fact that the skin of a person once infected by tubercle bacilli is hypersensitive to tuberculin he established a method by which we were able to gain our first real evidence of the extent to which the human race is infected with tubercle. This was followed by the intracutaneous test of Mendel (9), which was perfected by Mantoux (10).

The surprising outcome of the cutaneous and intracutaneous tests applied to large groups of people of all age periods was the knowledge for which we were little prepared, that nearly the whole population is infected with tuberculosis before the attainment of the fifteenth year. The further important fact adduced from these tests, which was likewise revolutionary, was that there is a difference between tuberculous infection and tuberculous disease. While infection is more or less general, disease is restricted to a comparatively small group. Further inquiry reveals that there are two distinct types of clinical tuberculosis; that of childhood, which is of an acute nature, and that of adult life, which is a chronic disease. From this the important facts were established, through the work of Römer (11) and others, that early infection confers an increased resistance or immunity which offers a certain degree of protection against future metastases from foci already present in the body or from bacilli gaining access to the body from without; that adult tuberculosis is directly related to childhood infection, and that the chronic character of adult tuberculosis is due to the increased resistance brought about by the childhood infection.

Thus our conception of tuberculosis as a disease was greatly modified, and a basis for the better understanding of its problems was established. The true problem as established is not so much to prevent infection, but (1) to prevent massive infection and (2) to prevent infection from becoming clinical disease.

BODINGTON AND BREHMER AND SANATORIUM TREATMENT

Although tuberculosis had caused more deaths than any other disease throughout all the period of recorded history, yet there was no definite concerted attempt to treat it until near the close of the last century. While a few men had appreciated the fact that it was a disease which could best be treated in special institutions, with a special régime, and Bodington of Warwickshire had attempted institutional treatment of the tuberculous before the middle of the last century (1840), yet the first permanent institution for the systematic treatment of tuberculosis was established by Brehmer at Görbersdorf in 1859.

Brehmer developed tuberculosis himself when a medical student in Vienna. He noted something that

seemed to have escaped the eyes of most men. viz., that in the postmortem room there was much evidence of healed tuberculosis. He noticed that the lesions which healed were the small ones. He wrote his graduating thesis on the subject, Early Tuberculosis Always Curable. While looking for hope for himself he found it for others.

He believed that tuberculosis was caused by the heart being relatively small, and adopted exercise, particularly hill climbing, as a part of his therapy, the amount of exercise and climbing being carefully adapted to his clinical conception of the patient's needs

Dettweiler, who was a patient of Brehmer, as well as his assistant for six years, thought he noted that harm was being done to many of the patients by the exercise and climbing; so he advocated rest, and when he left Brehmer he went to the Black Forest and established an institution at Falkenstein (1874), in which one important part of the treatment consisted of long hours of reclining on couches on verandas or in *Liege Hallen*, as they were termed. This was the beginning of the rest cure of tuberculosis, which is emphasized so much in all of our modern sanatoria.

Trudeau established the first sanatorium in America in the Adirondacks in 1884. There, isolated in the wilderness, himself a victim of the disease, he not only made the sacrifice to regain his own health but devised means for aiding others. He there started the first comprehensive investigations on tuberculosis in this country and maintained until his death a keen interest in and an advisory relationship toward everything associated with tuberculosis—its prevention and cure.

Institutions were established here and there at rare intervals until finally the movement was given great impetus by the German Tuberculosis Central Committee, which began its work in 1896. The subject was furthered by the Tuberculosis Congress held in Berlin in 1899. The movement for public sanatoria

made further headway in the early years of this century and the principle that each community should care for its tuberculosis as well as other diseases was emphasized.

The importance of the sanatorium as a factor in solving some of the important therapeutic problems in tuberculosis cannot be overemphasized. The treatment of tuberculosis consists of a definite mode of life under constant control and supervision. This has been worked out by close observation of patients in sanatoria in a manner in which it could not have been done in the home. The measures which are most valuable in the treatment of tuberculosis are so simple that it is difficult for the patient and friends to grasp fully the idea. It is really a life that they must live. In the home with its distractions and interferences it is very difficult for the proper helpful atmosphere and surroundings to be provided.

The greatest number of people who have tuberculosis come from the ranks of the poor, whose homes are ill adapted to giving the tuberculous patient the conditions that he needs and to assist him in carrying out a carefully planned program. The homes of those in better circumstances likewise are rarely much better suited to following out such a program. Many well to do patients, particularly the more wealthy, are in the habit of having what they want, being able to purchase it with money. Now comes something that they cannot purchase. They can only attain it by making the sacrifice. To accomplish this they need as much help as the poor, but of a different kind.

It is equally difficult, if not more so, to adapt the average home of the well to do patient, filled as it is with the joys, gaieties and distractions of everyday life, to the treatment of tuberculosis, than it is that of the poor.

In order to obtain results in a large proportion of patients suffering from tuberculosis, institutions for their proper guidance and control are not only desirable but essential. Getting the patients away from the harmful advice, anxiety and interference of

friends, even though it is for only part of the time, is of tremendous value.

THE PRESENT CONCEPTION OF TUBERCULOSIS

Our present conception of tuberculosis may be stated something as follows: An infectious disease which is mildly transmissible, the first infection usually gaining entrance to the body in childhood. This infection, unless the numbers of bacilli causing it are too large, results in the establishment of tubercle, followed by a stimulation of the immunizing mechanism of the individual. From this early focus of infection, unless it heals completely, likewise from new infections from without, repetitions of implantation with formation of tubercle occur, each of which results in increased immunity. A great proportion of these early infections never result in more than local tubercle and heightened immunity; others result in a more extensive implantation and a failure to heal, terminating in clinical tuberculosis. The time between the first infection and the appearance of clinical tuberculosis varies from a few weeks to many years—usually the latter.

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