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IMMUNITY AS AGAINST HEREDITY IN TUBERCULOSIS.

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The theory about tuberculosis which has held sway of the human mind for the longest period of time has been that of heredity. From the days of Hippocrates down, this theory has been the refuge of the vast majority of the human race who accept their ideas about things from others rather than upon their own thought or reasoning. In the medical profession it has always been the theory of the rank and file, and especially of those men who are guided entirely by the traditions of the profession. In this regard it stands in strong contrast to the theory of contagion which all through the history of medicine is linked in the views of the greatest leaders and thinkers. The only break from the popular adhesion to the theory of heredity of which we have historical record, is in the eighteenth century, and possibly as early as the seventeenth century, when the Spaniards and the Neapolitans broke loose from it and accepted the theory of contagion. It may be also that the Jewish people, at least during the early part of their existence, held to the contagious theory. Among all the rest of mankind, as far as we know from history, the theory of heredity held sway with the people and with the greater part of the medical profession.

When one takes a cursory view of the phenomena by which tuburculosis manifests itself among a people, one can readily understand why the hereditary theory held sway of the public mind for so many centuries. By its nature, tuberculosis is markedly a family disease. One by one different members of a family succumb to it, frequently at the same period of life ; and occasionally the disease manifests itself in several successive generations in exactly the same way. The most natural conclusion to be drawn from such a series of events was that a disease acting in this way must be hereditary. Then, too, families in which a series of deaths occurred during a generation naturally became associated in the public mind with the disease and such a family very soon got the reputation of being a consumptive family.

Long association of ideas without further inquiry into deeper causes finally established the theory so firmly in the human mind that it became a creed and was handed down from father to son without question, even guarded by a superstitious awe forbidding inquiry. That occasionally a skeptic mind and penetrating intellect broke through this superstitious crust of plausible reasoning and found beneath stronger reasons for rejecting the theory and accepting that of contagion could have but little

effect upon the public mind and it was not possible for the ordinary intellect to explain away phenomena which were so direct in pointing to self-evident conclusions.

The difficulties in the way of understanding the phenomena by which tuberculosis manifests itself lay in the absence of proper knowledge about the incubation period of the disease and about its method of progress from one stage to another. This knowledge could only come with the discovery of the tubercle bacillus and with the information about its life history which has been given us through the laboratory.

When it once became known that the tubercle bacillus has an incubation period of thirty days under the most favorable circumstances, that it may lie dormant in the tissues of the human body which have a meagre blood supply, and that from dormancy it may develop into vigorous activity after years, the singular phenomena by which the disease manifests itself in families, sometimes through several generations, becomes quite intelligible without the assumption of heredity.

In this light, too, those phenomena which never could be rationally explained upon the theory of heredity become reconcilable to reason, such as, for example, the skipping of a generation, or the running backward of the disease from the children to the parents and grandparents. It was chiefly the long time which often elapsed between cases in a family that led to erroneous ideas. In small pox, measles and scarlet fever, and such like diseases, in which the time between exposure and development is short, it was an easy matter to trace the relationship between one case and another, and to understand how the second case must depend upon the first. In tuberculosis, however, in which the exposure is usually of a long period for successful inoculation, and in which the time between exposure and development of symptoms may be years, it is not easy to trace relationship and hence the dependence of the second case upon the first was not apt to suggest itself.

Infection through houses and clothing, in which the germs of the disease might retain vitality for a very long period, also were sources of obscurity. Inasmuch as many cases occurred in the same family it was but natural to deduce that it did so because of heredity. Heredity was the first suggestion that came to the mind and for this reason it was generally accepted as the explanation of the phenomena set up by the disease.

Probably the strongest logical basis for the hereditary theory was the phenomenon which occasionally occurs, that of members of the same family dying at exactly the same age, and of the same thing happening generation after generation.

In the light of the germ theory this strong argument loses its force and this phenomenon can really be made to tell as strongly in favor of contagion. All living organisms require proper soil for development, and develop better in some soils than in others. The tubercle bacillus finds its most congenial soil in a host that is depressed or whose physical condition is in abnormal state from some cause. We know that there are certain times in life when either from natural or artificial causes the human organism is at a lower ebb of vitality than at others.

In childhood we have the depressing periods of teething and of the development of puberty. In young manhood and womanhood we frequently have the depressing influences of overwork, improper nutrition, and psychological conditions peculiar to that age as well as of dissipation In more mature life we have the disturbing influences of the menopause in women, and of exposure and hardship in men.

These various causes of depression and malnutrition are apt to come on at almost the same period of life in different families according to custom and peculiarities of the family. The resisting power to tuberculosis is therefore at its lowest ebb in each member of the family at pretty much the same period of life and if exposure to the disease takes place at that time a successful inoculation is almost sure to take place. Now in families into which the disease once has been introduced, there is always apt to be a case in some branch of it, and exposure to a greater or lesser degree for all members of the family is liable to occur. If it is not the father or mother or brother or sister, it is an uncle or aunt or cousin or some relative still farther removed and generation after generation brings exposure to the family. Successful inoculation in some members is bound to occur and to the superficial observer conveys the idea of heredity; and yet, with our present knowledge it is easy to forge out of the same chain of events an unanswerable argument in favor of contagion.

Another very strong argument in favor of heredity and a stumbling block to many minds in the way of contagion is the occasional limitation of tuberculosis in certain families to members resembling the one or the other line of ancestry; to the male or the female members of the family; to those following in the complexion of the father or mother; or to those having certain striking peculiarities of bodily formation, of feature or of mental development. The eccentricities and peculiarities being evidently hereditary, it is quite easy to assume that a disease which follows in their train must likewise be hereditary.

According to the old ideas about disease this line of reasoning was logical enough and the conclusions were practically unanswerable. In the light of our present knowledge the fallacy of the argument is very evident. The heredity of complexion, of peculiarities of form, feature, and mental makeup, is in harmony with physiology, because those qualities are intrinsic parts of the parent ; but heredity of disease, which is extrinsic to the parent falls foul of all that we know of the laws of nature. It is but natural that offsprings having the same peculiarities of form, feature and mental make up as the parent, should offer the same soil for disease and should manifest the same weaknesses at about the same time of life ; but it is incomprehensible how a parent could transmit a parasite to its offspring.

The argument in favor of heredity based upon the consecutive order in which tuberculosis sometimes occurs in families, running from grandparents to grandchildren in regular order has been considered a strong one ; but in the new light it becomes as strong an argument for the contagious theory. We now see how the same law which governs scarlet fever, smallpox, measles and such like diseases, applies with equal force to tuberculosis only that all the stages in the progress of the latter disease are usually extended over a much longer period of time.

With our present knowledge of tuberculosis, it is quite amusing to note to what extent the theory of heredity had to rely upon the credulity of mankind for its existence. The fact that the disease frequently did not develop until old age, that it skipped a generation or two or that it began with the grandchild and went back in regular order to the grandparents seemed to offer no serious logical difficulty to the minds of men. How the transmission of the disease could be thus accomplished no one ever attempted to explain. It is true that in those days tuberculosis was looked upon as a disease intrinsic to the organism, that is, a degeneration, but even upon such a supposition it is difficult to understand how the decay could skip one generation and possibly even two and then appear in exactly the same form as it did in the ancestor ; and whilst it is difficult to reconcile such views with reason, it is still more difficult to make them fit to facts.

In those days tuberculosis was more prevalent than it is now and of course a much larger number of families must have been affected by it. Even at the present day very few families escape the visitation of the disease in some branch or other. If we go back three or four generations we will find families so related by marriage that practically no one now living can have escaped contamination somewhere in his ancestry.

If tuberculosis were hereditary it would be absolutely necessary according to those views that every human being alive would be tainted in his ancestry and would according to the laws of atavism be liable to develop tuberculosis, and yet we know that vastly the majority of mankind escape the disease.

Although under the old way of looking at things there were a good many plausible reasons for believing in heredity, it is singular that many well known facts which strongly militated against such belief were not given more weight in determining conclusions. The strongest of these is the fact that races, peoples and families, who have never suffered from tuberculosis, develop it more readily and in a more malignant form, when brought in contact with it, than those who have been long exposed, or who have had it among their ancestry. In other words, new blood is particularly prone to the disease in its worst form; and in such cases there certainly cannot be heredity, because the disease never existed even in the remote ancestry.

Let us take, for example, the North American Indians, who prior to contact with Europeans were entire strangers to the disease and who, upon contact with consumptives, became infected by the wholesale and died like flies from it; heredity certainly cannot have played any part in the ravages of the disease amongst them. What is true of the North American Indian is also true of the natives of the interior of Africa. The disease does not and has not existed among them in their native country but when they are brought in contact with it they almost invariably die of it. History records the same experience for the natives of Bermuda and the Sandwich Islands; and what is true of these people is true of families.

When tuberculosis attacks families who have remained free from it for several generations, it creates greater ravages and runs a more rapid course than when it attacks families who have suffered from it in their ancestry. The truth of this statement is being forcibly illutrated in some of the southern and western states where the disease has been introduced in recent years by the consumptive invalid. These facts bring us to the parting of the ways between error and truth and we find ourselves with our backs turned for good and for all upon the theory of heredity and are facing the theory of immunity.

There is a law underlying all contagious diseases according to which there is a tendency on the part of the organism producing the disease to exhaust the soil upon which it grows. This tendency is greater or less

with different diseases but exists with all contagious diseases and can, I think, be looked upon as an essential feature of a contagious disease. The law which is thus exemplified seems to govern all organic life and to be a fundamental law of nature. We see it especially well illustrated in the vegetable kingdom, and the practical farmer profits by his knowledge of it in arranging the succession of his crops, being careful not to plant the same seed in the same soil too often in succession, but to rotate his crops so as to make one crop prepare the soil for another. (1)

Some contagious diseases exhaust the soil upon a single implantation and therefore seldom occur a second time in the same individual. Such are, for example, small pox, scarlet fever, measles, syphilis, and typhoid fever; in fact all the exanthematous diseases belong to this group. Other diseases which are due to a living organism, and some of which are likewise contagious in even the narrowest sense of that word, do not exhaust the soil so readily, and in them recurrence may take place after short intervals and complete protection is probably never established. Examples of this latter class are diphtheria, bronchitis, follicular tonsilitis and tuberculosis. But in all temporary immunity takes place and permanent immunity is possible.

In tuberculosis permanent immunity is exceedingly difficult to establish. The reason for this is probably to be found in the nature of the disease; tuberculosis belonging to that class of diseases which may be termed topical in contradistinction to those diseases which are termed constitutional. Although the tubercle bacillus finds its way into the system either through the lymph channels or through the blood vessels, its parasitic life runs its cycle in some restricted portion of the body where it is soon cut off and entombed in such a way, that it cannot have any effect upon the vital fluids until necrosis has taken place and it again finds its way back into the circulation to begin a new cycle of life somewhere else. The operation of the disease is thus usually very limited in area, in the beginning at least, and the exhaustion of soil is trifling because of the limited influence which the disease germ can have upon the entire body. On the other hand the presence of the localized disease in an important organ such as the lungs is very apt to seriously interfere with the normal action of the nutritive system and to contribute to

(1) There is a difference of opinion as to whether the phenomena here referred to are the result of exhaustion of soil or the throwing off into the soil of a new product. The result, however, is the same and for practical purposes we are better understood when we use the expression, "exhaustion of soil."

deterioration and depravity of the entire organism and thus by breaking down normal resisting power aids in preparing the soil for further inroads of the tubercle bacillus.

In practical every day life persons suffering from tuberculosis usually have one exacerbation of the disease after another until they finally go under; and this is so because each attack really prepares the victim for a subsequent attack by leaving him with less power of resistance. From this clinical picture of tuberculosis one would be apt to conclude that there is no immunity created by the disease at all, but it will not do to draw conclusions from the clinical picture alone. Many other factors which enter into the subject must be studied, such as environment and occupation of persons who fall victims to the disease, the number and the virulence of the tubercle bacilli which find their way into the organism upon the first inoculation, the fertility of the soil and the family and individual predisposition of the subject.

Looking at the subject from the broadest point of view possible and gathering in all the facts now available, one is driven to the conclusion that tuberculosis does establish a comparative immunity. First of all this comes out in the history of the disease as it affects peoples and nations. Wherever history records the entrance of tuberculosis into a new territory or among a new people, we find the disease of the most virulent and malignant type ; until after the exhaustion of the richness of the soil, when it becomes less virulent and affects a smaller number of people. Immunity alone can give a rational explanation of such phenomena. While with the introduction of preventive measures the decrease in the death rate can be easily understood we find that even where no preventive measures have been practiced there has been a gradual reduction in all countries where the disease has existed for a long period of time

Let us take the United States for example. When tuberculosis was first introduced into the territory which now constitutes the United States its ravages were so violent that it attracted the attention of writers in both England and America. Dr. Rush wrote, "Its rapid progress among us has been attributed unjustly to the growing resemblance of our climate to that of Great Britain." (1) Mr. de Witt Clinton, of New York, wrote, "If the climate of New York was formerly thus mild and healthy and a constant amelioration in its temperature is consequent upon our numerous settlements and improvements as has been maintained by distinguished writers, to what shall we ascribe the extraordinary mortality occasioned by consumption at the present day?" (2)

(1) Treatise upon the cause and cure of pulmonary consumption.
(2) Gregory's Dissertations, page 153.

About the same time Dr. Lettson wrote from London, "Whilst the phthisis pulmonalis is rapidly increasing in America and on the European continent it is diminishing here." (1)

This was after tuberculosis had obtained a firm foothold in New York and the then American colonies. When the colonies were first settled there was no tuberculosis in them until they became the resorts of the health seeking consumptives of England. Gradually they became infected and it was because they presented a virgin soil to the disease that it became so prevalent and malignant. After a century's ravages the disease began to decline without the institution of preventive measures because immunity began to be established for a larger number of families. In New York City, for example, the deaths from consumption were 1 in 4.2 from 1804 to 1820 ; 1 in 5.4 from 1820 to 1835 ; 1 in 6.5 from 1835 to 1850, and 1 in 8.46 from 1848 to 1859. (2) This gradual reduction continued up until the recent introduction of preventive measures, when it assumed much more rapid strides. It has been said that this gradual reduction in the death rate is due to improved hygiene. But is it really? A century ago there were no large cities in America and no poor people. Whilst there were hardships the hardships were not of a kind which leads to degeneration. There was practically no criminal class. The greater part of the population was made up of farmers and village people, and they had still a healthy water supply. It is true that they had no plumbing, but plumbing was not so necessary then. They were a hardy, vigorous people and remained so up until the time when the consumptive health seeker joined them, and then having been free from the disease for some generations and having lost whatever family immunity they may have possessed when their ancestors lived in Europe they fell easy victims to the disease. Long continued exposure, with the survival of those who could best resist the disease, and the going under of those who were most susceptible, again produced a partially immune race after the passing of many generations.

The truth which stands out so strongly in the history of tuberculosis as it affects peoples and nations also is borne testimony to by the clinical history of families in which the disease occurs. According to my own observations, which I have carefully made over a long period of time, the first victims of the disease in a family are usually the most acute sufferers. I have frequently had opportunity of watching the ravages of tuberculosis in families where four and five members of the same family have consecutively come under my observation and invariably there

(1) Ibid, page 150.
(2) The Climate and Stat. of Consumption, by H. B. Millard, page 18.

has been a gradually decreasing malignancy from the first case downwards. These pnenomena are observed in all contagious diseases. What is the explanation if not an acquisition of a partial immunity by those who succumb to the disease last ? It may, of course, be a deterioration or degeneration of the bacillus producing the disease due to exhaustion of soil, but immunity fits in better with our present views about disease. Immunity is also more in consonance with the best of our knowledge about disease and of the laws which govern plant life.

Probably one of the strongest arguments in favor of immunity in tuberculosis is to be found in those few cases of the disease in which either temporary or permanent immunity is established by an outbreak in certain tissues of the body. We have all seen how cases of scrofula and lupus, where the lymphatic glands are involved in the one instance and the skin in the other, will run for years and years and even for a lifetime without involvement of vital organs and without running to a fatal issue. In the same way the old time white swellings, which we now recognize to be tuberculosis, frequently remain stationary for long periods and sometimes end in recovery with subsequent immunity against the disease. Tuberculosis in the cellular tissue, about the anus, commonly known as fistula, also has the reputation of being in a measure a conservator of life in persons suffering from general tuberculosis. In all of these cases there is undoubtedly a partial immunity established by some cause, for whilst the germs of the disease are in the body they fail to secure a foothold in a vital organ and to colonize and propagate as successfully as they usually do when introduced into the soil of the human organism.

From certain cases that I have seen I am led to think that we may even go farther and say that tuberculosis in certain tissues of the body, if recovery takes place, may set up an absolute immunity against future attacks of the disease. I will relate one such case. In a family consisting of seven members one of the children early in life developed caries of the spine with softening and complete collapse, so that he never developed in body and remained in stature and bodily form a helpless child. Although bright and active in mind he was compelled to content himself with the most restricted locomotion unless it could be given to him by others. While in the house he generally sat upon the floor and succeeded fairly well in moving from one part of the house to another with a sliding motion, for which he used his arms as a motive power. Outside of the house he had to depend entirely upon others for locomotion and for this reason most of his life had to be spent indoors and generally in the kitchen in the company of his mother or sister. The

family lived in a small house in a blind alley under the worst possible environment except in so far as these could be improved by cleanliness and a good moral life. First, the youngest daughter, then the mother, then the father, then the youngest son, then the oldest daughter, and then the oldest son all consecutively contracted tuberculosis, and during the course of about ten years passed away. During those ten years there was always some one in that kitchen suffering from tuberculosis, for the kitchen had to serve as a sitting room, dining room, and infirmary as well, and during the greater part of the ten years all the food of that house was prepared by an advanced consumptive. During two or three years the person preparing the food had tuberculosis of the fingers and had almost every organ in the body affected by the disease. The little cripple was housed in that kitchen during all those years and spent the greater part of his time sliding over the floor, but in spite of the intense exposure he remained immune to tuberculosis.

A fair argument in favor of immunity has been worked out in the laboratory. Certain animals are found much less susceptible to tuberculosis than others. In such there is what is called a natural immunity which has probably been acquired through many generations. But even animals which are very susceptible can by the introduction of certain products of the tubercular process into their blood, be made less susceptible. In what manner this artificial immunity is set up we do not understand as yet, but that it can be produced is certain and its production must be in accordance with that fundamental law of nature by which all living organisms show a tendency to exhaust the soil upon which they feed.

It is no doubt by the same process that recovery takes place in the tuberculous subject when that happy result is obtained. A person who falls a victim to tuberculosis seldom dies from the first attack because the first deposit of tubercle is usually a small one. From the very nature of the tubercular process, namely necrosis with emptying out through healthy tissues, reinfection is almost certain to occur until the soil will no longer tolerate new colonies. Where recovery takes place, therefore, it is because the soil has been exhausted and new colonies cannot get a foothold in the system. If this immunity is of sufficient permanency to endure until every tubercle bacillus has been ejected from the body the recovery is permanent, but where the immunity is of short duration and the bacilli remain in the diseased tissues for a long time, as they often do, a recrudescence of the disease is bound to be lighted up again sooner or later, and this is why so few cases of tuberculosis get well. If it were not for immunity, however, every case of tuberculosis would

be bound to run a rapid, fatal course, one attack running into another until the fatal termination has been reached.

If immunity is created by tuberculosis, can that immunity be transmitted from parent to offspring ? This question opens up a great field for observation and in the working out of its answer there will be encountered a stifling burden of prejudice. So far as we can see now, either by the aid of philosophy or of accumulated knowledge and observation we must incline to the affirmative. Logically immunity in a disease follows as a corollary upon its contagion. If tuberculosis is contagious it is due to a living organism, and if due to a living organism it must subscribe to the laws governing all living organisms. Our as yet limited knowledge of biology and the history of disease in general and tuberculosis in particular point to this conclusion. There is certainly a fundamental law of nature by which all living organisms gradually become acclimated to the baneful influences of a parasitic foe or, in other words, gradually lose those qualities which make them selective hosts for parasitic life, whether by developing something which resists it or losing something which attracts it. And all along the lines of civilization down through history we find peoples and races gradually acquiring resisting power to certain disease which their ancestors did not possess and which other races and peoples which have not lived under the same environments do not possess. Tuberculosis is a striking example of the acquisition of this power by the white race as compared with the black and red.

What limited observation I have been able to make on individual cases of tuberculosis would lead me to the same conclusion as is indicated by our knowledge of biology and the lessons of history. Whilst as yet I have no statistics to offer on the subject which would be of any value, my case books will, I think, warrant my conclusions. Of the cases in which I have carefully inquired into the family history vastly the majority have had no tuberculosis in their ancestry for at least two generations. In a fair number of cases the parents, one or the other or both, have had tuberculosis, but they contracted it from one of their own children, they themselves not being the first cases in the family. In this connection it may be well to observe that there is a difference between family predisposition to tuberculosis, existing in the parents and children alike and possibly due to the running out of family immunity, and family predisposition existing in the children alone and due to a tuberculous taint existing in the parents and grandparents. The family predisposition in parents and children alike exists very often, but where it does exist it will almost invariably be found that back of the parents the family was free from tuberculosis for some generations. It would look as though

in such cases the family immunity had died out. Instances of family predisposition in children in which the tendency can be traced to the existence of the disease in parent, grandparent or great-grandparent prior to procreation in the immediate descendant are exceedingly rare, and I cannot recall ever having seen a case. Of course this is all negative testimony, and yet it is of some value when taken at its worth and weighed with other testimony.

The proper cases on which to work out the question of parental transmissibility of predisposition or immunity are those in which the parent is tuberculous when the child is procreated. Such cases are, however, unfortunately difficult to get at. So far as my opportunities for observation along this line will permit of conclusions, the preponderance of evidence is very strongly in favor of the transmission of partial immunity. I have repeatedly seen the children of tuberculous father or mother remain healthy and free from tuberculosis in spite of the most intimate exposure to the disease. I have seen but one or two of such cases die of tuberculosis. Of course the answer to this statement is that my observations are incomplete as it would require a lifetime to determine whether or not such children are immune to tuberculosis.. But even the temporary resistance under intense exposure must weigh something in summing up evidence.

There is a vast field for observations along this line and, until such observations have been made, the subject must remain open. So far as a conclusion can be foreshadowed by partial evidence it will, however, be that tuberculosis in the parent established immunity instead of predisposition to the disease, and that the much dreaded heredity of tuberculosis of the past has been a myth.