

of the screen and the photographic plate, are of distinct value in the diagnosis of pulmonary tuberculosis.

(2) That by virtue of the power given us by the Röntgen rays visually to perceive subtle changes in the thorax, we are often able to recognize the invasion of a pulmonary tuberculous process in an *earlier stage* of progress than it is to-day possible to do by the sense of hearing or touch.

(3) That to depend, however, upon the Röntgen method to the exclusion of others, namely, auscultation and percussion, the tuberculin test, or the staining fluids and the microscope, we do little else than proclaim ourselves bigots.

(4) That, if we recognize this new diagnostic agent, and make wise use of it, together with others already given us, employing *all* energetically for the benefit of the patient, while he is yet in a condition to be cured, we need never reproach ourselves with failure.

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Original Articles.

THE CHANNELS OF INFECTION IN TUBERCULOSIS, TOGETHER WITH SOME REMARKS ON THE OUTLOOK CONCERNING A SPECIFIC THERAPY.*

BY THEOBALD SMITH, M.D., BOSTON.

In choosing this somewhat well-worn subject in answer to an invitation to speak on some aspect of the problem of tuberculosis, I was led by the present rather unusual activity in the study of the digestive tract as a portal of entry. This bustling activity is due in the first place to the somewhat morbid tendency of research to seek out the new, rare and unusual, and magnify and illuminate them so that to our dazzled eyes all the laboriously reared truths of the past become invisible for the time being. It is furthermore due to the dicta of two prominent men, one of whom proclaimed that bovine tuberculosis was of no consequence as a source of the human disease, and

the other that all tuberculosis originates in infancy and that much of it was due to cow's milk.

The widespread movements tending towards the education of the public concerning the nature of tuberculosis and the modes of diffusion and transmission of the bacillus had brought to the foreground the older theories that tuberculosis is largely an inhalation disease and that the chief source of infection is the coughing consumptive. While all agree that the sputum is the vehicle in which bacilli leave the body, that there is, in fact, no other mode of excretion of the bacilli in man, which can be seriously entertained, there has developed a marked disagreement, or at least an attitude of assumed ignorance, as to the chief portal of entry. While inhalation has been and is still looked upon as the most frequently used mode of entry by some, others have gone so far as to deny the aërogenic infection of the lungs completely, and they trace pulmonary disease through the avenues of the intestinal mucosa and the associated lymph nodes, or the tonsils and cervical lymph nodes. In other words, the tendency on the part of a certain group headed by von Behring has been to cut out entirely the direct introduction of tubercle bacilli into the lungs through the respiratory tract and replace it with certain more circuitous routes, dealing with ingestion rather than inhalation.

Associated with and largely responsible for this change of view as to the significance of ingestion tuberculosis is cow's milk. Were it not for cow's milk as an occasional carrier of bovine tubercle bacilli we should probably have heard little of ingestion tuberculosis.

INGESTION AND INHALATION TUBERCULOSIS.

We have thus two main questions before us: 1. Is the path of the tubercle bacillus to the lungs chiefly by way of the digestive tract? 2. To what extent is bovine tuberculosis responsible for the human disease?

The difficulty encountered in taking a definite position on the question of the paths of the tubercle bacillus, both without and within the body, is due to the fact that almost anything we may say concerning the tubercle bacillus has a grain of truth in it, and may be realized at one time or another by observation and experiment. The goal towards which we should strive, however, is to discover the ordinary, common paths, and not the merely possible or extraordinary ones. Even in the experimental disease produced by tubercle bacilli in the lower animals we occasionally encounter peculiar localizations. The cryptogenic tuberculosis of the bones, the kidneys and other organs, wholly outside of the usual paths of the tubercle bacillus in the body, shows well the occasionally irresponsible activities of this organism.

The character of the disease started by the tubercle bacillus, like that of other infectious diseases, is dependent upon a number of variable factors. Among the most important are: the virulence of the infecting organism, the age of the patient, the inherited susceptibility or predis-

* Read before The Massachusetts Medical Society, June 11, 1907.

position, a previous infection, accidents which convert a latent or healing local into a generalized disease, and finally the mode of entry.

As regards the virulence of the infecting organism, I must admit that our methods are not perfect enough to disclose minor differences. Until the facilities of the average laboratory extend to the breeding and rearing of our experimental animals, our tests upon animals can only be relied upon to distinguish such gross differences in virulence as exist between the bovine and the human type. There are, however, differences between cultures of the human type which impress themselves upon the investigator as more or less constant, although it would be difficult to define them readily. We may safely assume that a considerable number of slightly varying races of human tubercle bacilli exists, and it is probably not a matter of indifference to the patient which of them is at work.

Age is a most important factor, as all statistics and experimental inquiries show. In this respect tubercle bacilli do not differ materially from other infectious agents which find their easiest prey among the young. Statistics prove that tuberculosis becomes rapidly generalized in infancy and that it is a highly fatal disease. The conception of latency which has been introduced into the subject in recent years by von Behring does not at all tally with such statistical and pathological researches. That a bacillus which is especially virulent for the young should lie fallow in some organ or tissue of the body without multiplying is, to say at least, revolutionary to our current conceptions. Experimenters have been for years familiar with this conception of latency, or persistence, of infectious agents in the body of those who are relatively immune, and of those who have recovered from a disease, but not with the idea that bacilli can be latent in the highly susceptible young. It is possible that such bacilli may be very feebly infectious, and that subsequent disease is not due to them, but to later infection with more virulent types. It is furthermore possible that certain antibodies may be transmitted from mother to child, and that these are slowly excreted and disappear after three or four months unless the mother's milk continues to supply them. Under such conditions it is conceivable that, in the earliest months of life, or even longer, during the period of lactation, bacilli may be restrained and then multiply subsequently.¹ In any case I doubt that such latency could be prolonged over a year at the longest. The subject is a difficult one at best. How we can tell in any case that there has been no fresh infection where we suppose the disease to have been latent, I do not see. The possibility of fresh infection with, perhaps, more virulent material must always be reckoned with.

The influence of inherited predisposition, though an unknown quantity, cannot be given up at present, and I believe it plays an important part in the fight with tuberculosis. The capacity for

producing antibodies, for phagocytosis and the other protective factors probably varies from individual to individual, and has its definite, prescribed limits.

The influence of one attack of tuberculosis, provided structures have not been seriously damaged, must be considered a distinct asset, since we now know that immunization of cattle with human tubercle bacilli is possible.

The influence of accidents, such as trauma, intercurrent diseases, secondary infections in favoring dissemination of the disease, is so well known that I merely mention them.

With all these factors at work and influencing the process, it is obvious that our inferences and conclusions as regards portals of entry, dissemination and the results of different kinds of treatment must be cautiously made, for they cannot safely rest on a few in part faulty experiments, which may strain and largely overpower the physiological protective mechanisms, and which may fail to reproduce the usual conditions present during spontaneous infection, but they must also take into consideration the work of pathological anatomy and histology, and utilize the results of statistics collected at the autopsy table.

Coming to the first controverted question, whether all tuberculosis is chiefly or exclusively alimentary in origin as maintained by some to-day we find that two different lines of research are involved in it:

1. The anatomical and physiological problem of the absorption of tubercle bacilli, soot, etc., by the mucous membrane of the intestines and their conveyance to the lungs and thoracic lymph nodes without being stopped by the mesenteric nodes.

2. The behavior of the organism in the presence of tubercle bacilli in any of its tissues under the influence of different degrees of a specific resistance or immunity.

As regards the passage of bacilli through the mucosa of the intestine it may be said that some twenty years ago the opinion was quite general among pathologists that the tubercle bacillus produces a lesion at the point of entry. With the more exact and detailed study of tuberculosis in infants and children, and the disease in cattle, this position had to be gradually abandoned. To-day most authorities will admit that the tubercle bacillus may pass through mucous membranes without leaving any pathological traces of its passage, to settle down in the nearest lymph nodes.

How the bacilli gain an entrance into the lymph vessels of the mucosa, whether by the aid of normal, physiological processes, or through minute lesions, is not determined. Their next station would be the mesenteric lymph nodes. The original claim held by many to-day is that in the mesenteric lymph nodes the tubercle bacilli come to rest and multiply, producing distinct lesions. If they escape it is only after leaving the well known traces of their passage behind.

Within the past four or five years a further modification of the original position has been

¹ In a former paper I advanced another hypothesis to explain such latency of tubercle bacilli: *The Parasitism of the Tubercle Bacillus, etc.* Jour. Amer. Med. Asso., 1906.

adopted by some, namely, that tubercle bacilli may not only pass through mucous membranes, but also through the related lymph nodes and settle down and produce disease at a point quite distant from the point of entry, without leaving any intermediate traces of their passage. It is obvious that if they escape through the mesenteric lymph nodes their next stopping place would be the capillaries of the lungs and, as a result, we would have a primary tuberculosis of the lungs due to swallowing tubercle bacilli. That this is possible few pathologists will deny; but is it probable and is its occurrence of sufficient frequency and importance to permit the overthrow of the aërogenic infection in phthisis? Two lines of experiments have been made to prove this. Dogs have been fed tubercle bacilli in milk or other fatty foods, and the tubercle bacilli found in the thoracic duct some hours later. Cattle have been fed with tubercle bacilli with stomach tube and slight tuberculosis of the lungs produced. Animals have been fed with various finely divided powders, either with or without stomach tube, and the pigments found in the lungs. These various experiments, though plausible on the surface, do not, in my mind, prove the contention. The large number of bacilli introduced may have overpowered the usual protective agencies, there may have been aspiration into the air tubes following withdrawal of the stomach tube, and finally other investigators claim that if pigments are fed in the usual way and kept wet they are not found in the lungs subsequently.

Perhaps the most opposition has been aroused by the attempts to trace pulmonary anthracosis to the ingestion, rather than the inhalation of soot, a process firmly established by the exhaustive experiments of J. Arnold over twenty years ago. Without delaying over the experimental data, let me call attention to the fact that large amounts of fine particles are taken into the digestive tract by our domestic animals daily in their food, and if any absorption takes place it would be detected. The mesenteric and meso-colic lymph nodes of the omnivorous dirt-eating pig are free from pigment. In the ox, the mesenteric lymph nodes of the young are quite free from any pigment, but when the milk diet has been replaced by the usual diet of grass, hay and grain, these nodes become heavily pigmented, not with soot, etc., but with pigment particles derived from the blood. When we turn to the thoracic lymph nodes in the same species draining the lungs, another picture presents itself. At first these nodes are unpigmented, but as the animal grows older a faint subcortical line of pigment shows itself which grows heavier and denser with age. This consists of black particles and translucent fragments. In the horse similar conditions prevail. A delicate black tracery of the subpleural lymphatics in old animals indicates a frequent deposit in the lungs as well.

It is of interest, furthermore, to note that in cows the primary foci of tuberculosis are situated in the thoracic lymph nodes among the pigment, suggesting most convincingly the aërogenic source

of both. If this pigment in these nodes comes from the intestines, why does not some of it remain in the mesenteric nodes? Why do these, instead, retain in large numbers, chiefly in phagocytes, the blood pigment, and why is this not passed on? Possibly it may be answered that a special chemotactic affinity exists between the phagocytes on the one hand, and the blood pigment on the other, which does not exist between phagocytes and soot, etc. But if this answer is true, we surely cannot pass over the still more important chemotactic affinity between tubercle bacilli and the cells of the mesenteric lymph nodes.

A careful reading of the recent literature shows that the promoters of the theory that tubercle bacilli may readily pass from the intestines to the lungs without stopping to multiply, and thereby produce disturbances on the way, have not taken sufficiently into account the fact that tubercle bacilli are not like grains of lamp-black, but living organisms which arouse a more or less prompt reaction on the part of the invading tissues, and which cannot travel about the body at will without being recognized and held.

The varying conditions of immunity and predisposition have much to do with the localization of tubercle bacilli and the shaping of the disease process. It is evident that the different stages in life do not react alike towards tuberculosis.

What may be true in earliest infancy is not absolutely so in childhood. Even puberty, middle life and old age have their respective types of tuberculosis from which, it is true, there are deviations, owing to the variable factors already mentioned, but there is as a rule a clearly defined growing immunity with age. There is even a varying immunity of the different organs of the same body towards the tubercle bacillus, and this may not be the same at different ages.

The lungs may be said to be the *locus minoris resistentiæ* for tuberculosis, not only for man, but for the higher mammals as well. Disease starting elsewhere, if not checked by death or recovery, sooner or later leads up to the lungs. In my second paper on bovine and human bacilli, published nine years ago, this behavior of tubercle bacilli was fully appreciated. It is there stated: "The question of phthisis as secondary to infection by way of the digestive organs is, however, one needing more attention. . . . In all mammals the lungs are evidently the most favored place of tubercle bacilli, and wherever the latter may be deposited, they sooner or later, unless the disease is checked, reach those organs, where the process spreads more rapidly than elsewhere."

In the attempt to establish the alimentary origin of tuberculosis, some have based their arguments on the fact that inoculation into different parts of the body, even into the tail, may lead to the pulmonary disease. This fact has been known for a long time, and has been mentioned by various observers. The question before us is not whether the lungs can be made diseased secondarily. That this is possible, and occurs frequently, as in miliary tuberculosis, is well known. The real question is whether the usual

types of pulmonary tuberculosis appearing at some one point in the lungs start from the intestines without leaving any signs of their passage or whether they are the result of inhalation. That is to say, Is the pathologist wholly powerless to trace the paths of the tubercle bacillus in the body? I think not. With the aid of our knowledge concerning immunity, the following general laws may be laid down:

In infants, the entry of tubercle bacilli is easier through all portals, and a generalized tuberculosis results from the rapid multiplication of bacilli and their diffusion through the feebly resistant tissues and vessels. With increasing age this indiscriminate passage of bacilli is checked, and the bacilli are held back by the reacting tissues in the nearest lymph nodes, the so called regional nodes. This gives us the common types of tuberculosis of childhood. It is also the type of the disease in young cattle. With increasing resistance, as at puberty and later, we have certain portals of entry, such as throat and intestines completely closed under ordinary conditions, and an inhalation disease appearing almost exclusively because the lungs, the most vulnerable organs, are still accessible through the respiratory passages.

COW'S MILK AND TUBERCULOSIS.

Closely interwoven with this new or revived doctrine of the alimentary origin of pulmonary tuberculosis is the widespread belief or assumption that milk infected with bovine bacilli plays a large part in the etiology of human tuberculosis. The history of this belief is of interest in showing the to-and-fro swing of medical doctrines. Following the epoch-making study of Koch in 1882, the assumed identity of bovine and human tuberculosis, as formulated by him, provided a basis for the world-wide movement against bovine tuberculosis as a source of the human disease. Excessive zeal in this direction was, however, kept in check by the scarcity of alimentary tuberculosis and the universally accepted doctrine that pulmonary phthisis was an inhalation disease.

In 1896 and 1898 I demonstrated the existence of two types of tubercle bacilli, the bovine and the human; emphasized the inadequacy of the evidence on which the transmissibility of bovine tuberculosis to man was founded, and pointed out that with the aid of these two types we could now build up more satisfactory statistics. In 1901 Koch, who had meanwhile studied the same subject, in a now memorable address, claimed that owing to the difference between human and bovine bacilli, bovine tuberculosis was a negligible factor in the human disease. As a result of this address, commissions were appointed in different countries to investigate Koch's claims. The German Commission reaffirmed the existence of the bovine and the human type, as representing distinct races of tubercle bacilli. The same has been done by the English Commission in their recent report. But the latter claim that these two types are simply extremes of an intermediate

series of transition forms and admit, with considerable reserve, however, that there is some evidence of mutation, and that perhaps the bovine type may be converted into the human type by a sufficiently prolonged sojourn in the human body.

Coincident with this study of the relation of bovine and human tubercle bacilli to one another, nearly all observers who have studied series of cases of the human disease have found, in certain cases of tuberculosis, bacilli of the bovine type. The labors of Ravenel, the author, the German and English Commissions, Rabinowitsch, Fibiger and Jensen, and others have collected between 40 and 50 cases of the bovine type in infants and children. Some cases were fatal, others not. In practically all these cases the disease started either in the tonsils and related cervical lymph nodes, or in the mesenteric lymph nodes. So far as I know only one bovine culture has thus far been isolated from sputum, and this by the English Commission. Together with two other types it was isolated from a calf fed with large amounts of mixed sputum.

The cases from which these bovine bacilli were isolated are all selected cases, and we have at present no way of determining what percentage of progressive fatal tuberculosis is due to them. The statistics of alimentary tuberculosis vary from place to place, and even these cases are largely associated with the human bacillus. The only way to gain some adequate insight into the amount of damage done by bovine bacilli would be to take a series of consecutive cases both in sanatoria for adults, and in children's and infants' hospitals, and study the bacilli of every case for a given period. I venture the statement that probably not more than 1% of all cases will show bovine bacilli, and that in individuals over twelve years they will be found only very rarely. However, this is a mere guess and it should not take the place of actual figures.

The methods of isolating and identifying tubercle bacilli of the two types is now so far advanced that the clinical laboratories should take up this study. A series of cases carefully studied clinically as well as bacteriologically may lead to some means of clinical diagnosis between the two types of disease, since the bacteriological diagnosis under ordinary circumstances compels us to wait at least three months before a decision can be made. It is also highly desirable that any aberrant or peculiar type of tuberculosis be studied bacteriologically in order to determine the nature of the invading bacilli.

The issue then would appear to be clear-cut and it would seem as if the whole question might be solved bacteriologically. But those who insist on the old doctrine of indiscriminate transmissibility of the two types of bacilli, and who are fortifying themselves by attempting to establish the doctrine of the general alimentary origin of tuberculosis, go a step farther, and assume that the bovine type may gradually change into the human type in the body, so that the adult phthisical patient would discharge the human type in

his sputum, whereas he may have absorbed the bovine type earlier in life through the digestive tract. This is, perhaps, a plainer and franker statement of the hypothesis than its adherents have been willing to make, but there can be no harm in viewing its bald outlines. The possibility of such a transformation I took into account as far back as 1898, and stated it as one of the theses to be investigated, although I did not then, nor do I now, believe in its realization.

The only way in which such an hypothesis could be tested would be to find a species of mammal in which the human type is always found, perhaps some race of monkey, and pass the bovine bacillus through a series of individuals. But the possibility of latent foci in such animals might at any moment imperil the accuracy of the experiment, by bringing into our cultures a human type from outside sources.

That the tubercle bacillus possesses a certain plasticity has been brought out by various investigations. Cultures from domestic animals other than bovines, but evidently derived from the latter, I have found slightly different as regards virulence from parallel bovine cultures. But that the bovine type should be converted into the human type has no analogy in the domain of bacteriology, and as long as it is not clearly proved to occur, it cannot be accepted on mere speculation. Again, if the bovine and the human cultures are indiscriminately transmissible to either species, why should two types have arisen? These must have been developed from some parent stock in obedience to the demands of the respective host harboring them.

Bacterial species producing specific invasive diseases in man and animals have their congenies of characters well fixed. Degeneration of such characters may occur, but the transformation of one into another, even closely related, race of variety has not been accomplished. Nocard claimed to have transformed mammalian into avian tubercle bacilli, but this solitary experiment should be repeated and tested with the aid of our present knowledge of the tubercle bacillus before it can be fully accepted.

The transmission of infectious animal plagues to man occurs in the case of glanders, anthrax, rabies and bubonic plague. In these infections which are due to bacteria, only one type of microbe is known, not two. The transmission of glanders to man occurs rarely when we consider the large number of glanders-infected horses in our midst, and the opportunity for infection. Man is predisposed only to a limited degree, and the transmission of infection requires, without doubt, certain specially favoring conditions, as seems to be the case in man when exposed to the bovine tubercle bacillus. If, as is claimed by some, the bovine and human types of tubercle bacilli simply represent a connected series, and if there is no sharp distinction, it is rather strange that adult man should harbor the least virulent type. Usually, the older the attacked individual the more virulent the attacking organism, for it is the old that infect the young.

To look towards another species for the main source of contagion in a human disease which has its own bacillus and machinery of transmission is a bacteriological anomaly, which has no parallel at present, not even in the bubonic plague. The anomaly is in fact so great that no experienced bacteriologist who has studied pathogenic species over any period of time is found to favor it. At the same time, I believe that we should not stop in our investigations, but work out the problem in every direction. If an anomaly is really discovered and proved, we must accept it. But I believe it wholly premature to base upon it far-reaching practical measures, whose cost to the community might destroy the opportunity of saving many times more lives than are injured or destroyed by bovine virus. In short, the entire field of bacteriology may be hunted over without avail to find a precedent for the assumption that two distinct races of bacilli adapted to two widely separated hosts, such as the ox and man, are indiscriminately transmissible. All that we can say is that in certain receptive stages in life, characterized by a low degree of resistance, such transmission may occur, and it does occur under circumstances not yet fully known. I am, therefore, of the opinion that man has only a limited susceptibility to bovine tuberculosis depending on certain still unknown factors. It is from this standpoint that I shall discuss very briefly the practical side of the subject.

The recent attempts to prove all tuberculosis of alimentary origin, if seriously entertained and if finally proved, would lead to a certain readjustment in our sanitary measures. The tuberculous patient would not only be dangerous near us, but at any distance, provided he came into any relations with us. Those who prepare our foods could infect us at any moment. The bread and pastry we buy, the milk we drink if handled by a tuberculous patient, even the clothes we wear would bring an element of danger. Every act of coughing would be dangerous, even if the sputum were carefully destroyed, because the spray might settle down and infect our food.

It seems to me that before placing an additional ban on the tuberculous we should patiently wait for satisfactory proof, and not be stamped from one position into another before we have inquired into the qualifications of the innovators, and the accuracy, if not reasonableness, of their statements. The problem of bovine tuberculosis should be dealt with in a similar temperate manner. We have learned during the past nine years that there is a bovine and a human type of the bacillus which all reliable bacteriologists have recognized. We have furthermore learned that in a selected number of cases of alimentary tuberculosis the bovine bacillus has been found. This is all we know and all the rest is uncertain and speculative.

As regards the source of the bacillus, we know that it may come from the udder or from the feces, when sufficient cleanliness is not observed. The udder becomes tuberculous through metastasis in, perhaps, 1% of tuberculous cows, roughly

speaking. The parenchyma or secreting structures become the seat of tubercles, and the milk may contain in certain cases large numbers of bacilli. When children are fed with such milk, they are overpowered by the many bacilli, and where a few might pass through, of the large numbers daily ingested, some invade the body. When udder tuberculosis exists in a herd samples of the mixed milk may prove infectious for guinea pigs, because the large numbers shed by one animal are disseminated through the entire mass, and enough may be present to make all the milk infectious for guinea pigs by inoculation.

There has been a vigorous discussion whether cows which simply react to tuberculin and which show no clinical signs of tuberculosis do or do not shed bacilli in the milk. Some observers contend that they may do so. Others deny the contention. My own experience coincides with the latter. Ostertag, who made a careful study of this subject for the Prussian government and who found no tubercle bacilli in the milk of reacting animals, pointed out that the discrepancies between observers may perhaps be explained by the soiling of the udder with feces. In cows with a discharging focus in the lungs, the swallowed sputum would maintain a slight infection of the feces. He drew the milk himself, and carefully cleansed the udder. In one case in which the feces were infectious, the udder when left uncleaned yielded milk which produced tuberculosis in guinea pigs. After due cleansing it failed to do so.

If Ostertag's interpretation is correct, and I am inclined to believe it is, a careful periodical inspection of dairies by competent and conscientious veterinarians, followed by the removal of clinically tuberculous animals, and all that had any suspicious abnormality of the udder, and the enforcing of cleanliness would eliminate practically all danger. Some chances for slight infection of the milk may still remain, as is equally true of typhoid fever, diphtheria and other infections in the dairy; but the amount of infection would be greatly reduced if not entirely eliminated, and in tuberculosis more than in any other disease, I believe that the number of bacteria plays a very important part in the final infection of the human subject.

THE RESTRICTION OF BOVINE TUBERCULOSIS.

In view of the relatively small percentage of cases of transmitted bovine tuberculosis, and the very slight chances for the infection of the milk of cows in the early stages of the disease, the question, what policy designed for the protection of the public will do the greatest good, is a perplexing one.

It seems to me that competent dairy inspection, the removal of all animals which show evidence of udder disease and which from a clinical examination can be pronounced tuberculous, and the enforcement of strict cleanliness are what should be insisted on.

This supervision, as I pointed out over ten years ago, not only greatly reduces the chances of

tubercle bacilli in the milk, but it also restricts and suppresses two other factors which injure or destroy probably a hundred times more children than the bovine bacillus. These factors are miscellaneous putrefactive and fecal bacteria from filth, and the germs of specific human diseases accidentally introduced by those concerned in the production and distribution of milk.

About ten years ago the hope was entertained in some quarters that bovine tuberculosis might be completely exterminated by some concerted and persistent effort. While the attempt was in itself laudable, it overlooked certain obvious facts, and it was planned on such a scale that it was bound to fail. It was based on the methods of procedure of the National Government in its fight against bovine pleuropneumonia and foot-and-mouth disease. The nature of these two diseases, their relation to other species, the character of the virus and its diffusion over a limited well-defined territory made the task of suppression a reasonably certain one, even though the cost was great. But bovine tuberculosis differs widely from these infectious diseases in almost every one of the details which have made the others manageable. To suppress bovine tuberculosis it will be necessary to have the co-operation, either compulsory or voluntary, of those who produce milk, and to establish, so to speak, islands or centers of tuberculosis-free animals, and slowly increase such territories. To look to our state and national governments for paternalistic aid to control a disease with which the farmers are now well acquainted will not work even if it were just to the rest of the population. The only way to make any progress is for the consumers to insist on milk from inspected herds and pay the price necessary to keep them free from disease.

In our own state, the Board of Health inspects dairy herds and the Cattle Bureau removes, pays for and slaughters clinically diseased animals. It also tests all animals coming in from other states at the public expense. What is the cattle owner doing in response to this paternal assistance to restrict tuberculosis? If we examine the annual reports of the Chief of the Cattle Bureau, Dr. Austin Peters, we find that in 1900 there were condemned, killed and paid for by the state 1,423 head of manifestly tuberculous cattle; in 1901, 1,341 head; in 1902, 1,001 head; in 1903, 1,172 head; in 1904, 1,658 head; in 1905, 1,625 head, and in 1906, 1,202 head.

In other words, the state can buy as many clinically diseased cattle as it cares to appropriate money for. The cattle owner raises his tuberculous crop each year to be shouldered and paid for by public taxation. The only way to make any progress after these many years of patient compensation for diseased animals is for the state to take them without compensation, and for the public to patronize milk from tested herds. It has been amply shown that tuberculosis can be restricted if a little thought be given to the subject. Our national government distributes tuberculin and suitable directions for its administration,

free of charge. Surely the means for individual initiative are not lacking, excepting one, and that is a little judiciously applied coercion. A law to remove the item of compensation after a definite number of years would probably bring about the desired reform.

There can be no doubt that the public is in a difficult situation with reference to the milk supply. The congested population of our large cities must draw its stock from a very large territory, and few can trace to the herd the milk that is daily delivered, owing to the multiplication of middle men necessarily engaged in its distribution and the distance from which it is brought. The adjustment of this difficulty is a delicate one and is an interstate question. In the meantime, the helpless and distracted public may protect infants and young children from the occasional chances for infection by pasteurizing the milk. It should be stated in this connection that the lowest temperature which destroys tubercle bacilli is 140° F., and at this temperature the shortest allowable time is twenty minutes. The heating must be done in closed vessels to prevent the formation of a scum or film in which tubercle bacilli may survive the heat.

I wish finally to mention a possible source of infection to which no attention has been given. It is one which I mentioned as worthy of consideration in 1898. If the milk of tuberculous cows may infect children, may not the dust and dirt of cow stables affect adults working in them?

I have already stated that only one not very clear case of bovine bacilli in sputum has been reported. It seems to me that the study of a series of cases of tuberculosis among those working in cow stables is desirable at the present time, and I am prepared to make such a study if the sputum is sent to me fairly fresh and a carefully prepared record of the history and present condition of the patient forwarded with it.

The conclusions which I think are warranted by the investigations upon human and bovine tuberculosis up to the present may be stated as follows:

1. The coughing consumptive is the chief source of infection.

2. The digestive tract is not the exclusive or even predominating portal of entry for pulmonary phthisis. It is highly probable that most cases are due to inhalation or aspiration.

3. In infants the bacilli probably gain entrance through all portals more easily than later in life, and the disease becomes more easily generalized. There are no rational grounds for believing that latency in infancy plays any appreciable rôle in the disease of later decades, but ingestion probably does play a much more important part in infantile tuberculosis, owing to habits and susceptibility of this period of life, than has been granted heretofore.

4. Bovine tubercle bacilli are found associated with a certain, at present not fully calculable, proportion of cases of abdominal and cervical lymph-node tuberculosis in infants and children.

5. There is at present no evidence that bovine bacilli may be transformed and assume the human type in the human body.

6. The discharge of tubercle bacilli into the milk of cows may take place abundantly in udder tuberculosis. In a small proportion of manifestly tuberculous cows without evidence of udder disease, it may take place at times in very small numbers.

7. A reasonable restriction of bovine tuberculosis below the danger limit to man is possible with the aid of tuberculin and segregation, and the removal of clinical cases and of udder disease. An eventually complete elimination can be brought about in this way in any herd, provided other domestic animals, such as pigs, cats and dogs, are kept under control as possible reintroducers of the infection.

8. The complete elimination of bovine tuberculosis may be hoped for in the distant future. An active co-operation of individuals with municipal, state and national forces, by exerting a steady pressure and diffusing more knowledge among farmers as to the nature of tuberculosis and the use of tuberculin, may lead to its final disappearance.

9. The factor of bovine tuberculosis in the human malady is not of such importance that it should be permitted to imperil the proper execution of measures designed to relieve and cure the strictly human disease, or divert attention from it as the chief evil.

THE OUTLOOK CONCERNING A SPECIFIC THERAPY IN TUBERCULOSIS, AS VIEWED FROM THE EXPERIMENTAL AND COMPARATIVE STANDPOINT.

Having been asked to say a few words upon the present status and promise of serum therapy and vaccine in tuberculosis, I do so somewhat reluctantly, and I place myself distinctly upon the experimental standpoint for two reasons. In the first place I have had no personal experience with the use of serums or vaccines as applied to cases of the disease. In the second place I believe that our fundamental data must come from experiments on animals.

Since the various kinds of treatment of tuberculosis may all be classed either as passive or active I shall group my discussion under these heads. It is now pretty generally understood that serum therapy is a method of transmitting one or more antibodies, produced in some animal artificially, to the patient in order temporarily to fill a gap, to provide a substance which is wanting but essential in the struggle against the disease. This want is filled by the serum until the body has sufficiently recovered to manufacture for itself the antibody. The use of serums is most successful in rapid toxic diseases in which there is only toxin to be disposed of, but no bacteria. When we come to the slower invasive diseases, like tuberculosis, the injection of a therapeutic serum would have to be made over long periods of time because its need would be continuous. But even then it is a question whether the serum would be of any permanent benefit, because to

throw off the disease the body must finally make its own antibodies. The serum is like a crutch which must sooner or later be given up when the patient is strong enough to try walking alone.

Approaching the subject from the practical side we know that no serums have proved to be of any generally recognized value in the treatment of invasive diseases. The immunization of large animals is slow and difficult, and it can be carried only to a certain point. Such sera would in any event be very expensive and hardly within the reach of the average patient. Then, again, the repeated injection of foreign serum over a long period is not to be looked upon lightly.

From both the experimental and the practical standpoint the outlook for serum therapy is not encouraging, though I should not wish to say that it is hopeless. In some one form or another, unknown to us at present, there may be built up from the fragments of the present passive and active forms of treatment a successful method accessible to all patients.

Owing to the difficulties, both theoretical and practical, surrounding the use of a curative serum, investigators have again turned to the method of inducing active immunity. This consists in stimulating and rousing the latent activities of the diseased body to produce its own antibodies. Begun with the introduction of the old tuberculin by Koch in 1891 it has had various fortunes, but it seems again fairly well established to-day. All the methods are based upon the introduction into the body of the products of tubercle bacilli. The fundamental underlying principle appears to be a reliance upon the diseased body itself with the understanding that it possesses sufficient forces to establish its own cure if these forces are properly husbanded and properly called forth. These forces are limited in amount at any given moment, and perhaps in time exhaustible. They should not be wasted because we know that the organism reacts with a very lavish production of antibodies. In the treated horse, for example, diphtheria antitoxin present in the blood can neutralize thousands of times the amount of toxin which is injected at any given time.

The presence of tuberculosis indicates that these antibodies are below normal, or have been so at some time in the past. These considerations suggest the use of very small doses of the stimuli and only at the proper time. Sir A. E. Wright maintains that in the antibodies known as the opsonins we have such a guide, and the index of this guide is phagocytosis. Some are inclined to neglect this guide, and utilize clinical symptoms in the treatment.

It follows from the theory of action of these stimulating substances that they are not called for in active, febrile stages, when the body is apparently fully roused and needs no stimulus from without. Under such conditions an antitoxic serum might be helpful to neutralize the over-abundance of toxins until the system had recovered itself.

It is furthermore evident that the application of these substances may bring into action various

tissues of the body beside the immediate focus of disease. The whole body may thus be laid under contribution artificially to relieve a limited area, which is unable to protect itself.

In the practical development of this mode of treatment by gradual cautious stimulation, many substances have been used, all of them derived from the tubercle bacillus. The old tuberculin comes first in the order of time; next the new tuberculin, representing ground-up bacilli; then there are the watery extracts of tubercle bacilli used by Maragliano, the filtrates of the culture fluids as used by Denys, and lastly the mystical tulas of Behring. Whatever may be the perfection to which these methods of active immunization may be carried in the future, there still remains the unknown quantity of the capacity of the individual patient to produce the necessary antibodies and bactericidal forces. If these are lacking therapy is powerless to check the disease.

This discussion, brief though it be, has led up to three propositions:

1. Serum therapy is at best a temporary palliative method in infectious diseases which are long drawn out, and which must finally be met by the specific resources of the body itself.

2. The need of discriminating power on the part of the practising physician between individual and individual in the application of remedies which stimulate the production of antibodies. He is evidently not going to be eliminated by an advance in medical science. In fact, he must be better trained than ever, especially in the fundamental principles of immunity — a subject quite new but already rich in acquisitions, which may be called the physiology of the infectious diseases.

3. To each human being are given certain talents to husband and develop and not to squander, for therapy cannot add to them. It falls to the lot of the physician to discover during disease the size of those hidden talents, if he can, and to utilize and manipulate them in the best interests of his patient.

SEPARATE NURSING AND ISOLATION IN TYPHOID FEVER.

BY ELLIOTT P. JOSLIN, M.D.,
AND
CHARLES L. OVERLANDER, M.D.,
BOSTON.

IN 1888 Dr. R. H. Fitz¹ demonstrated that typhoid fever was occasionally contracted in this vicinity by patients during their stay in a large hospital, as well as by nurses and other attendants, and he appended a list of directions for the prevention of future contagion, which received universal adoption. Yet cases of typhoid fever thus acquired continue to occur, and it is pertinent to inquire if there are not other practical, preventive measures which might advantageously be employed.

Exposure of patients. — Most private hospitals in this vicinity refuse to accept typhoid patients at all, while others do so only on the condition that the typhoid patient shall have one or more

¹ Fitz: BOST. MED. AND SURG. JOUR., 1888 vol. lxxviii, p. 513.