The bacillus tuberculosis and the etiology of tuberculosis : is consumption contagious? : second communication, read, by invitation, before the Philadelphia County Medical Society, November 14, 1883 / by H.F. Formad.

6.

STUDIES

FROM THE

PATHOLOGICAL LABORATORY OF THE UNIVERSITY OF PENNSYLVANIA.

No. XV.

THE BACILLUS TUBERCULOSIS AND THE ETIOLOGY OF TUBERCULOSIS. IS CONSUMPTION CONTAGIOUS?

SECOND COMMUNICATION.

Read, by invitation, before the Philadelphia County Medical Society, November 14, 1883.

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THE BACILLUS TUBERCULOSIS AND THE ETIOLOGY OF TUBERCULOSIS.—IS CONSUMPTION CONTAGIOUS?

SECOND COMMUNICATION.

BY H. F. FORMAD, B.M., M.D.

GENERAL CONSIDERATION.

A LITTLE over a year ago* I had the honor of presenting for your consideration some anatomical points in refutation of the etiological relations of the bacillus tuberculosis.

At that time I announced some original observations regarding the histology of scrofulous tissue, tending to place the question of heredity in tuberculous disease upon an anatomical basis. These peculiarities of scrofulous tissues I submitted as elucidating the etiology of tuberculosis, showing that the peculiar histological condition of the individual, under the influence of simple irritants, and not the character of the irritant, is responsible for tubercular inflammation. It gives me pleasure to state that these observations have since been confirmed by several competent histologists, whose articles on this subject will soon appear in print; besides which a general interest has been manifested by favorable comments both in America and abroad.

Shortly before the publication of these observations, Koch, of Berlin, had brought forward the discovery of the now famous bacillus tuberculosis, affirming it to be the sole cause of pulmonary phthisis and other forms of tubercular disease, and claiming for it, besides exclusive pathogenetic properties, special morphological and chemical characteristics.

In my first paper I denied some of these propositions upon grounds of personal investigation, and subsequently Koch's researches were also severely criticised by a number of other observers.

As interesting and valuable as the discovery of Koch is, from a biological stand-point, its practical value is decidedly overestimated, and has, in my opinion, not nearly the significance for medical science which the enthusiastic followers of Koch ascribe to it. The influence of the discovery was, however, great in strengthening the traditional and unwarranted belief in the contagiousness of phthisis, as held by a small part of the profession and community. On the other hand, this belief led to the popularity of the discovery. In this respect the bacillus theory has perhaps been harmful, and, taking the consequences into consideration, we should not accept such a theory without the closest scrutiny.

Two practical benefits may accrue from this discovery. The first is that the fear of the effects of the bacillus may induce greater cleanliness in hospital management and enforce improvement in hygienic matters in general. It is doubtful whether the removal and prompt destruction of the sputum would have any influence in checking the spread of phthisis, as the disease is found as often, if not oftener, in the clean palaces of the wealthy as in the unclean huts of the poor. The second advantage resulting from the bacillus theory may be that physicians may become induced to make more use of the microscope in diagnosis; yet in this respect the general use of the microscope is hardly practicable, on account of the thorough technique and experience required.

To-day, while the bacillus is acknowledged as a common morphological concomitant of tubercle, the pathogenetic properties are denied it by the best pathologists and clinicians, on account of a want of sufficient confirmation of the evidence thus far offered. The followers of Koch's theory are, however, numerous, but they are recruited largely from the ranks of clinical teachers, book-writers, and others possessing no opportunities for personal investigation.

It may be well to state that, upon my visit to Koch last summer, made with the purpose of doing justice to this important question, I was gratified in many respects. I found Koch an earnest and conscientious worker, and not as dogmatic and extreme

* Studies from the Pathological Laboratory of the University of Pennsylvania, xi.; "The Bacillus Tuberculosis and some Anatomical Points which suggest the Refutation of its Etiological Relation with Tuberculosis, by H. F. Formad." Philadelphia Medical Times, vol. xiii. p. 109, 1882.

in his views as would appear from his writings; nor is he as self-satisfied and as rash to jump at conclusions as are some of his followers. Koch has the co-operation of an excellent staff of assistants, all able mycologists; but it was a matter of surprise to me that there was not a single competent pathologist connected with his laboratory; and such services are evidently much needed to give to the observations made there the proper interpretation from a biological and anatomical stand-point. I was also pleased to learn in Berlin that the discovery of the bacillus was exaggerated not so much by Koch himself as by the Imperial Board of Health, which employs him, and by his over-zealous followers in the profession. There is strong evidence, however, that Koch's investigations are biased by the determination to find for each specific disease a specific fungus.

Following out the various phases in the study of tuberculosis, I am sorry to see that the entire subject is now being considered from a purely etiological basis with reference to bacteria, while the study of the anatomical and biological relations is wholly neglected.

I admire the beautiful bacteridian discoveries of Klebs, and particularly those of Koch in connection with the etiology of tuberculosis. The accomplishment of these results is a triumph for scientific botany and mycology; but these studies are much too one-sided to have an application to scientific medicine. The bacillus is there. It is concomitant with most tubercular lesions. It is diagnostic of tuberculous change. It is, on account of its irritant properties, one of the causes of tuberculosis. But this forms no reason for asserting that tuberculosis should be considered a contagious disease, without further investigation and proofs. A contagious disease can have only one cause. I cannot agree with those who define the predisposition to phthisis as being a condition of the organism which offers merely a favorable soil for the tubercle-bacillus. Nor can I believe that inheritance is explained by subsequent infection from cohabitation, *e.g.*, that children become scrofulous by living with consumptive parents.

The latest fruits of the bacillus studies have even inspired Baumgarten (*Centralblatt f. d. Med. Wis.*, Aug. 4, 1883) and several others to come to the conclusion, in reference to the hereditary nature of tuberculosis, that the bacillus is transmitted in its larval state from mother to fœtus in intra-uterine life! One would think, however, that one of the most wonderful effects of the tubercle-bacillus is manifested by the change it produced in the direction of the reasoning powers of some of our pathological and clinical investigators, both at home and abroad. Some of the younger pathologists are even affected by a regular fanaticism for bacterian studies in tuberculosis. These studies now take the place of their former excellent pathologico-anatomical studies. Consideration is no longer given to the tissue-changes, or the nidus which invites the bacteria and nourishes them. In fact, Koch's followers in their enthusiasm exaggerate matters, and, to Koch's own amusement, go further in their bacillus speculations than he himself thinks justifiable. It is really painful to read how some of the younger German pathologists and a few of the prominent English surgeons, under the influence of the bacillus craze, will make in their publications assertions entirely unwarrantable. They describe, for instance, with the greatest ingenuity and exquisite minuteness, how "one or more bacilli" will produce certain histological changes in the lungs or in the peritoneum, designating the exact route to the same; how the different cells, the lymphatics, and the blood-vessels are affected; how the bacilli convert one variety of cells into another; how they manufacture giant cells and cheesy material; how acute and chronic phthisis is produced by the bacilli, and the quantity necessary for each; how tubercles develop only and exactly in those places where the bacillus becomes lodged; how, if bacilli alone are inhaled, miliary tubercles form; and how, if the bacillus is accompanied by some other irritants, a broncho-pneumonia will ensue.

All of the above statements are made by scientific medical men and pathologists, and offered as broad facts in full earnest! I only have to say that here evidently observation is substituted by imagination and mere speculation; and all this is done for the sake of the convenience in explaining a disease by pretty hypotheses.

The only men who attempted to repeat Koch's experiments, besides the work done in the pathological laboratory of the University of Pennsylvania, were Spina (Studien über Tuberculose, Wien, 1883)

and Watson Cheyne. Of the latter two scientists, Spina came to results entirely different from those of Koch, and they disprove beyond doubt some parts of Koch's hypothesis. From an analytical and critical point of view, Spina's studies of tuberculosis are excellent, but the technical part of his investigation is deficient, and hence not satisfactory. Watson Cheyne, to whom the "British Association for the Advancement of Science by Research" had intrusted the investigation of tuberculosis and the testing of Koch's researches, did not do justice to his mission. From Cheyne's report (*The Practitioner*, April, 1883) it is seen that he made no earnest attempt to study the nature of tuberculosis, because all he did was to study and experiment with bacteria met with in tuberculous lesions. He went to see some of the different mycologists, consulting only believers in the germ theory; obtained some French and German bacteridian material, and, after testing the same, he reports with great emphasis that Koch's bacilli are a more genuine tubercular virus than Klebs's or Toussaint's micrococci. He did not inquire, nor did he care, whether tuberculosis may have any other cause! He simply imitated some of Koch's experiments with the bacillus material in rabbits and guinea-pigs (only), and obtained, of course, the same results. Furthermore, he made some control experiments, which, as I will show, pass for naught, as they are much more deficient than those of Koch.

There are a number of excellent studies in reference to the occurrence of bacilli in the sputum and in tuberculous tissues; but the main part of Koch's hypothesis, *i.e.*, the etiological relation of these bacilli to tubercular disease, remains still unconfirmed.

My own researches on tuberculosis were made from a stand-point different from that of Koch, and they were undertaken five years ago, being carried on continuously since that time by myself and assistants. My object was to investigate the natural history of the disease, without being influenced by any preconceived views. While due attention was paid to external agencies in the production of tuberculosis, the part played by the animal or human organism itself, the behavior of its component cells, and the primary changes in the tissues were not lost sight of.

I may state that I was fortunate enough to be able to utilize the material of over four hundred cases of tubercular disease from the autopsy-table, including a number of cases studied in the pathological institutes in Europe at various times.

My present research on tuberculosis, with special reference to the bacillus question, was carried on during the last year and a half, under the auspices of the provost of the University of Pennsylvania, Dr. William Pepper. This communication should not be considered a report on my investigations, as these are not yet concluded; but a detailed report of these investigations will be made next summer. Some of the positive results achieved will, however, be referred to in the present paper; otherwise it merely embodies a general critical survey of the question of the etiology of tuberculosis, based upon a careful perusal of the literature of the subject and upon personal observation.

I may state, at the outset, that while the results of my observations force me to-day to make some concessions to Koch, namely, that his bacillus, on account of its irritative properties, can produce tuberculosis under certain conditions, I am firmer than ever in my former conclusions, from the results of repeated observations, that tuberculosis may arise from other causes. The bacillus may be one of the causes, conditionally, but it is not THE cause. The question of predisposition stands in the way of the acceptance of the bacillus theory. Furthermore, I will try to show that tuberculosis is not a contagious disease, and it is particularly in reference to this that I am glad to bring the present subject before the Society, desiring to profit by the discussion which is to follow as a result of the experience and the clinical observation of the individual members of the Society.

The question of the contagiousness of phthisis is one of supreme importance, not only from its scientific but also from its social aspects.

For convenience in treating the subject of the etiology of tuberculosis, I shall speak of it under the following headings:

1. The definition, the anatomical character, and the etiology of tubercular lesions, including pulmonary phthisis.

2. The predisposition; the predisposing conditions; scrofulosis.

3. Tuberculosis without predisposition, due to inflammation of serous membranes.

4. Question of contagiousness; clinical aspect.

5. The bacillus tuberculosis.

6. Experiments "pro" and "contra;" traumatic tuberculosis.

Conclusions.

All these considerations will have to be of necessity very brief.

I.—THE DEFINITION, THE ANATOMICAL CHARACTER, AND THE ETIOLOGY OF TUBERCULAR LESIONS, INCLUDING PULMONARY PHTHISIS.

No definite understanding concerning a disease can be arrived at unless some fixed conception of the anatomical characters and various expressions of the lesions of that disease is formed. Thus, as regards the question of tuberculosis and pulmonary phthisis, the matter would be much simpler if a general understanding could be arrived at as to the definition of tuberculosis and phthisis in its different anatomical manifestations. The pivot of the question is what to call a tubercle or a tubercular lesion.

The traditional conception of a tubercle being a miliary node, the belief is that nothing is tuberculosis unless expressed by nodes, and that everything is tuberculosis that appears to the eye as containing nodes. These misconceptions are what bring the confusion and prevent the settlement of the question of tuberculosis, both at the post-mortem table and in the hands of the experimenter.

One of the results of this confusion is that some clinicians divide pulmonary phthisis into catarrhal, cheesy, fibroid, and tubercular proper, because they do not see tubercle-nodules in some of these forms of phthisis. They seem not to be aware of the fact that miliary tubercles do not belong necessarily to the picture of pulmonary phthisis; and, on the other hand, that those nodes which occasionally appear as miliary tubercles are not miliary tubercles at all, but are only miliary foci of broncho-pneumonia, due to aspiration, as will be explained later. Miliary tubercles, if at all present, usually form a part of a general disease, a tuberculosis of the whole body. In rare instances, when the miliary eruption takes its departure from the lung, the miliary nodules may be limited to the lung.

A more serious matter is the mistake that experimenters make of interpreting as tubercles the so-called inhalation tuberculosis, artificially produced in animals by means of a spray with tuberculous and other matter. The nodules produced in the lung under these circumstances are not miliary tubercles,—in fact, no tubercles at all. They are simply miliary broncho-pneumonic foci, limited to those terminal collections of air-vesicles, called acini, in which some of the inhaled irritative material became lodged. The natural round boundaries of these acini correspond exactly to the usual size of miliary tubercles, and appear as such even under the microscope, although filled merely with an unorganized inflammatory exudate. The uniform distribution of these foci is due to the fact that the inhaled irritating particles are distributed only to individual and the most accessible bronchioles and acini, thus simulating a true miliary tuberculosis of the lung. Similar broncho-pneumonic foci occur in the human lung from self-aspiration of tuberculous material from a primary focus to some other portion of the lung or throughout the whole lung. This was proved long ago, but the inhalation experimenters appear not to be aware of that fact. Careful personal observations and experiments, to be recorded in my forthcoming report, have convinced me that such inhalation experiments prove nothing, either for or against the contagiousness of tuberculosis, in connection with which they have been brought forward as the strongest affirmative proofs. Furthermore, it must also be remembered that the so-called experimental inhalation tubercles, as a rule, remain local.

On the other hand, miliary nodes or tubercles are met with, not only in tubercular lesions, but also in a variety of similar and dissimilar lesions, such as pearl-disease or bovine tuberculosis, lupus, leprosy, glanders, actinomycosis, chancre and gummata, cancer, typhoid infiltration, lymphomatous and leukæmic lesions. All these lesions, even cancer ("miliary carcinosis"), are able to give rise to exquisite miliary disseminations, or eruptions, although these are most frequently observed in tuberculosis. We already recognize leprous, lupous, glanderous, syphilitic, and other tubercles, in contradistinction to tuberculous or scrofulous tubercles.

To the above nodular formations may be added a variety of minute inflammatory

foci of granulation tissue, organized around minute foreign bodies introduced experimentally into various tissues; also, "false tubercles," such as mere unorganized collections of lymphoid cells, held together by some fibrin or by some artificial or natural round boundaries, such as is the case with the referred-to "inhalation tubercles;" and further, also, the eruption and follicular enlargements in the skin and mucous membranes.

The question now arises, how to distinguish between these various kinds of nodules, apart from their clinical features. They may all undergo a cheesy or a fibrous change, may calcify, and may contain giant cells. In all, bacilli may be found if a cheesy change occurs, or tends to occur, save in cancer and in leukæmic formation. Without desiring to appear sceptical, I must say, however, that it takes the skill of a Koch to differentiate sometimes the bacilli met with in the various kinds of nodes, even after applying all micro-chemical tests.

The true tuberculous tubercles occasionally do not show any bacilli whatever, as I will prove from personal observation, and from the reliable testimony of others. It will also be shown that the only test now left for determining the pathogenetic peculiarity of tubercle—namely, the asserted exclusive property to produce tuberculosis—is conditional and uncertain, since substances not tuberculous may, under similar conditions, have the same effect.

Therefore, it is impossible to define tuberculosis, either by its anatomical peculiarity or by the pathogenetic property of its nodes.

Another important point in the natural history of tuberculosis is the cheesy degeneration of its products; but here, again, we are surrounded by difficulty if we take only the cheesy product into consideration, because all the lesions mentioned before as being characterized by, and as being capable of, nodular eruptions, have the tendency to undergo cheesy change. Besides this, simple inflammatory products have been observed to undergo a similar change, as is instanced by that form of cheesy hepatization sometimes following croupous pneumonia, and also by certain forms of rapid necrotic changes, such as occur in acute septic inflammations, designated lately by the name of "coagulation necrosis." It must, however, be remembered that the total absence of cheesy masses in the body of tuberculous subjects has been observed.

To tell tuberculosis from allied lesions is only possible after a consideration of the soil in which it develops, and the location of the products, together with the clinical and anatomical manifestations.

What is the origin of tubercle-nodules?

The primary occurrence of miliary tubercle-nodes is, to my mind, very questionable. I have never seen it occur without the coexistence of diffuse granulation tubercle. This granulation tubercle is recognized by all as being a simple inflammatory granulation tissue, characterized by cells somewhat larger than ordinary lymphoid cells, containing usually giant cells, but undergoing very readily cheesy change on account of its deficiency in blood-vessels. This tissue is regarded by most pathologists as secondary to miliary tubercles; but I think, after careful observation, that the reverse is the case; because I have never seen upon the post-mortem table, or in animals, *primary* miliary *tubercle*-nodes without the granulation tissue, while the granulation tubercle-tissue does exist very frequently without the nodes. Moreover, primary *miliary* tuberculosis is unknown.

That tubercle is primarily a simple granulation tissue of inflammatory origin has been proved experimentally. E. Ziegler (*Centralbl. f. d. Med. Wis.*, 1874, No. li.) made the following interesting experiment. He inserted below the skin or into the peritoneum of animals, a number of pairs of glass covers, each pair glued together in such a manner that between them there existed an interspace just large enough to allow the entrance of white blood-corpuscles; and these corpuscles, not being severed from the body of the animal, then formed a tissue between these plates of glass, which, upon removal after various periods, could be readily examined under the microscope, and the conditions of tissue-formations traced. Under these circumstances it was observed that whenever blood-vessels had developed in the new-formed tissue between the glass plates, an organization of the cells into a perfect connective tissue took place; but, when the formation of blood-vessels had failed to occur, then a tissue simulating tubercle-

tissue was formed, made up of epithelioid and giant cells, and cheesy changes had occurred. Ziegler very properly declared the latter product to be tubercle-tissue. I have had, and have at present, ample opportunity to corroborate the accuracy of these observations. Ziegler's experiments were repeated in the pathological laboratory of the University of Pennsylvania, by Hammer, and at present are being carried on by Woodnut. By these experiments, made, with slight modification, after the method of Ziegler, under varying conditions and upon various animals, it was shown that the granulation tissue gradually gave origin to tubercle-nodules. Furthermore, these experiments showed that the tubercle-nodes and cheesy changes ensue without the action of bacilli, as the latter were found not to be present when proper care was taken, during the execution of the experiment, to exclude them.

From the examination of tubercular tissue from various sources, I may say that I have seldom succeeded in finding tubercle-bacilli in newly-formed tubercular tissue made up of small lymphoid cells. In older tubercular tissue, made up of opaque epithelioid cells and giant cells with a nodular arrangement, particularly when this tissue is undergoing necrotic change, bacilli are quite common, except in some forms of tubercles of serous membranes, to be referred to later. Tubercle-tissue that has undergone a complete cheesy change contains the greatest number of bacilli. Cheesy matter of any source is a dead substance, and it is usually inhabited by bacilli, if these get access to it; while other bacteria are scarce in this nidus.

Examination of materials from the autopsy-table shows that tubercle expresses itself in various manners. Primarily tubercle occurs as a mere infiltration of lymphoid cells in the adventitia of blood-vessels, or as small nodular masses of lymphoid infiltration around blood-vessels or ducts of any kind; or tubercle-tissue may organize within blood-vessels and various ducts. Sometimes tubercle appears as a diffuse lymphoid infiltration, extending over a larger area, showing a greater or less tendency towards the formation of nodes and cheesy or fibroid change, as in the lungs. Tubercle-tissue may form masses of the size of a hen's egg, particularly in the brain and serous membranes. In the lungs, in racemose glands, and in mucous membranes, catarrhal changes always follow the tubercle-infiltration. On serous surfaces primary tubercles appear often as flat or nodulated patches of various sizes (in peritoneum), or as fungoid vegetations (in synovial cavities), or even as large plastic masses (in omentum). In the skin and mucous membranes, tubercles produce eruptions, ulcers, or nodular indurations; in bones—caries, with abscess formation in surrounding parts (cold abscesses). Fibroid capsules, made up of connective tissue, due to reactive inflammation, enclose often smaller or larger tubercular masses, especially if these have undergone cheesy change.

Primary tubercle manifests itself quite variously in different animals. In guinea-pigs and rabbits, it appears mainly as small cellular infiltrates; in dogs, it often undergoes a fibroid change; in goats, and especially in cattle, tubercle often forms large nodular, sometimes pedunculated masses which often calcify;* in birds it forms, preferably in the liver, large round mulberry masses, which, on section, appear sometimes as horny radiating structures.

Secondary tubercle presents an aspect entirely different from primary tubercle, and it manifests itself in nearly all instances in but one form, namely, as a fine miliary eruption representing those well-known gray, semi-transparent nodules, of the size of a millet-seed, called miliary tubercles. These seem to lie in the perivascular lymph-spaces, and are probably distributed throughout the body mainly by means of these lymph-channels of the blood-vessel walls. Tubercles do not occur in avascular tissues. There is, however, a second form of embolic or metastatic tuberculosis which evidently distributes itself by the blood-current proper, and it appears in the form of conical masses or round nodes which may reach the size of a walnut and are located usually at the bifurcation of arteries. No mention of this form of tubercle is made in text-books, although upon the post-mortem table this variety of tubercle is a very common occurrence. Especially is

* I have met with, on the autopsy-table of the Philadelphia Hospital, two cases of tuberculosis in man that were identical in every respect to bovine tuberculosis. Dr. Creighton, of Cambridge, England, describes a number of cases from his own observation, and collected from literature. Bovine Tuberculosis, London, 1881.

it seen in the lung, and, more rarely, in the spleen and liver.

Taking into consideration the enormous frequency of local tubercular lesions (counting pulmonary phthisis in this category), the occurrence of secondary or true miliary tuberculosis must be considered a rare affection. A tuberculosis affecting the lining of even the whole peritoneal cavity, including its lymphatic glands, or that of the pleural sacs, or that involving one or both lungs, must, when occurring thus in but one locality, be considered a local tuberculosis. In such instances, the tubercle spreads by continuity of structure.

It is a fact, established by Virchow, that tuberculosis is at first a local disease, and only becomes generalized secondarily. This generalization does not affect the blood, as in the infectious diseases, but it takes place simply as an embolic process, as in some tumors. Local tuberculosis in external organs and accessible lymph-glands is often a harmless affection. It is strongly related to primary tumors. Complete early removal of local tubercular lesions is practised successfully in Europe. Volkmann and others have removed, for instance, lymphatic glands, testes, and joints affected with fungoid synovitis, with the object of preventing secondary tuberculosis, and have thus prevented a general miliary tuberculosis.

Nor should a gloomy prognosis be given in early phthisis. It is astonishing what a large number of healed cavities and cicatrices in the apices of lungs are found on the post-mortem table, indicating the healing of phthisis in persons who long subsequently died from some other causes in later life.

We have seen that tuberculosis manifests itself quite differently as to structure, appearance, distribution, and determination, in the various animals, and even differently in the various organs of one individual. Our studies have shown that these variations in the expression of tuberculosis depend upon the structural peculiarities of the various kinds of animals, and sometimes even upon the difference of the structure in animals of the same species.

We have also seen that even in human beings tubercle-tissue may manifest itself in various forms. In some individuals it develops rapidly, and spreads over large areas, becoming generalized and undergoing speedy cheesy change; in other individuals it develops slowly, fibroid change predominating; and in others the tuberculous product may calcify. In most individuals tubercular lesions may remain entirely local.

It is well known from clinical experience that the general condition of the organism has very much to do with the healing of a local tuberculosis. A local tuberculous inflammation may heal or become arrested in its progress, if the patient "gets strong," or it becomes more developed and aggravated if his general health "runs down." Observation has further shown that any simple, non-specific wound in a weak, ill-nourished individual may fail to heal, becoming unamenable to treatment, and probably assuming a tubercular character.

In some animals spontaneous tuberculosis is unknown, and while some animals are easily tuberculizable experimentally, in others tuberculosis cannot be produced.

It is in accordance with experience that in a large number of families the predisposition to tuberculosis is hereditary, and that their members die promptly of phthisis at a certain age from the effects of a simple "cold," while in the history of other families this affection is unknown. Every individual is liable to acquire syphilis, smallpox, and other contagious diseases, but it is proved that not every one can have tuberculosis. A special predisposition and a special individual are required. In such an individual, a simple inflammation resulting from any cause whatever can produce tuberculosis.

Therefore, for the development of tuberculosis two conditions are necessary:

1. A *definite* soil.
2. An *indefinite* irritant.

The reaction of the soil is always the same under the influence of any irritant, whether that irritant be a bacillus or not; since the result (tuberculosis) following a lesion in such a soil depends upon the character of the soil, and not upon the character of the irritant, even though one irritant, say bacilli, may act more readily than other irritants.

In view of the demonstrated fact that simple injuries of any kind can excite a tuberculosis, but only in certain individuals and tissues, it is evident that tubercu-

lization is determined by the kind of soil, and not by a specific irritant. *Tubercle should therefore be defined as being an inflammatory new formation in a specific individual or tissue.*

What is the place for tubercle in pathology? The anatomical criterion for tubercle is a granulation tissue made up of lymphoid or epithelioid cells, which, on account of deficiencies in the soil, does not undergo any higher organization or tend to heal, but tends to form nodes and undergo cheesy change. Under favorable circumstances it may heal through fibroid change. The elements of tubercle-tissue may spread by continuity of structure to surrounding parts, and occasionally tend to the production of metastasis, distributing themselves by means of the lymphatic system principally, and rarely by blood-vessels; and may generalize themselves through the whole body, forming miliary nodes or tubercles.

This miliary eruption of tubercle appears to have the same relation to the primary tubercular growth as the secondary metastatic cancer eruption has to the primary cancerous growth. As in cancer, the elements of tuberculosis may be arrested temporarily by the lymphatic glands governing the affected region.

In tuberculosis lymphoid cells form the nodes; in cancer, epithelial cells. While secondary cancer nodes are, as a rule, much larger than tubercular nodules, on account of the well-known great proliferating power of epithelium, it is also a fact that cancer may appear as a miliary carcinosis, expressed by minute nodules not distinguishable macroscopically from miliary tuberculosis. Cancer is proved to be a local disease. It is not contagious. It is infectious only to the individual who is affected by it; *i.e.*, it is self-infectious. And so is tubercle in every respect, a local, self-infectious disease.*

That local manifestation of tuberculosis in the lung which is designated by the traditional name of pulmonary phthisis forms perhaps nine-tenths of all tubercular lesions, and hence deserves some special consideration.

I class myself with those who regard all forms of pulmonary phthisis as tubercular. There are only three or four lesions of chronic wasting disease of the lung which may be excluded from phthisis. These are atelectasis, or collapse from pressure of effusions; bronchiectasis, in which the enormous dilatation of the bronchi may lead to large cavities and atrophy of lung-structure; primary fibroid changes; and abscess of lung. Yet all these lesions may become tuberculous from secondary inflammatory changes, which usually follow.

The lesions that are known as catarrhal pneumonia, broncho-pneumonia, pneumonic phthisis, cheesy pneumonia, tubercular phthisis, and fibroid phthisis are all manifestations of the one disease. Such a classification may be, however, entirely justifiable and useful for practical clinical and therapeutic purposes. Pathologically considered, phthisis is a local tuberculous inflammation of the lung which may manifest itself in various ways, the appearances depending upon the duration of the disease, the mode of onset, and the constitution and condition of the patient. Lesions representing the different forms of phthisis, and their transition from one form to the other, are often seen in the same lung.

Virchow insists that nothing should be considered tubercular unless it shows true tubercle nodules, and hence he does not recognize cheesy pneumonia—or cheesy hepatization, as he calls it—as tubercular, although he does not object to the term phthisis for this lesion.

I was fortunate enough to attend several times the classical demonstrations on this point of Virchow, the father of the view of the dual origin of cheesy matter and phthisis; yet, from our present knowledge of what constitutes tubercle, I cannot help interpreting all the forms of phthisis as of a unitarian origin. It is, after all, as Virchow himself says, only a matter of nomenclature. If we consider the presence of bacilli of Koch as the differentiating point between what is tubercular and what is not, we find that catarrhal and cheesy pneumonias are the most tubercular of all,

* Cancer and tubercle are considered analogous lesions and classed with tumors by a number of pathologists. This fact would not make it inconsistent to call tubercle an inflammatory product, as the distinction between inflammatory processes and tumor-formation is a purely arbitrary one. Virchow pointed out that the majority of tumors are purely inflammatory products (a statement antedated twenty years by Prof. S. D. Gross). A few years ago I made the question of the etiology of tumors a subject of careful personal study, which I yet continue, and I am forced to the conclusion that *all* true tumors are inflammatory products, and that no line of distinction can be drawn where the process which we call inflammation ends and where tumor-formation begins. (The Etiology of Tumors. Transactions of the Pathol. Soc. of Phila., 1881.)

because they contain, as a rule, more bacilli than any other form of phthisis.

Although cheesy pneumonia, like all forms of phthisis, remains commonly a local affection, it is seen on the autopsy-table to give rise to miliary tuberculosis at least as often as any of the other forms of local tuberculosis.

We are then at present at the same stand-point in regard to the character of tubercle and cheesy matter as Laennec (1819); and it is indeed perfectly reasonable to suppose that any cheesy matter found in a scrofulous person or animal is tubercular. Of course it is evident that tuberculosis of the lung is usually accompanied by simple inflammatory products, such as organized connective tissue (chronic phthisis), or unorganized croupous and catarrhal exudates (predominating in acute phthisis), which may undergo rapid necrotic and purulent changes, resembling cheesy material. For the latter products the name "coagulation necrosis," as applied by the Heidelberg and Leipsic people, may be employed. Tubercle-bacilli are commonly found in this coagulation necrosis. True tubercular cheesy matter should, I think, be considered only that product which is derived from the breaking down of previously well-organized tubercle tissue.

I need not refer to the details of the manifestation of tubercle in the lung, as these are too well known. But I would like to remark here that those small whitish or gray nodules, usually of somewhat irregular shape, which are seen more or less densely scattered throughout the parenchyma of lungs affected by phthisis, are not miliary tubercles, but minute foci of broncho-pneumonia.*

These minute broncho-pneumonic foci take their origin from tuberculous matter disseminated by means of air-passages, as explained before. *Miliary* tuberculosis of the lung distributes itself by means of the perivascular lymphatics, is very rarely accompanied by catarrhal changes or hepatization, and rarely arises from a primary tuberculous focus of the lung itself; it is, as a rule, a part of general tubercular disease.

II.—THE PREDISPOSITION.

Having shown that for the production of tuberculosis we need a special soil, and that the irritant is only of secondary significance, some inquiry into the nature of this soil is necessary.

The question of the predisposition to tuberculosis, as it stands at present, must be considered from three aspects:

1. The clinical aspect.
2. The anatomical aspect.
3. The bacteridian or parasitic aspect.

The consideration of the clinical aspect of the predisposition to tuberculosis is invaluable, as it rests mainly on actual observation, on demonstrated clinical facts, and on conclusions drawn from statistics.

From time immemorial, a clinically well-defined condition of the system, known as the strumous diathesis in its various forms, has been recognized. This condition will be considered later on.

There are a number of ailments which, from the experience of clinicians, are known to have a great, direct or indirect, influence in the development of general tuberculosis and pulmonary phthisis, or are known to create conditions of the system that predispose it to this malady. Such are syphilis, inflammation of serous membranes, bronchitis, croupous pneumonia, diabetes, the exanthemata (especially measles and typhoid fever), deformities of the skeleton, rickets, cerebral and spinal diseases of various kinds, dyspepsia, the puerperal state, uterine diseases, prolonged nursing of children, onanism, change of climate, continuous loss of sleep, distress, etc.

That exhaustion, exposure, deprivation of food, and other hardships of campaign-life, etc., are prominent etiological factors in the production of pulmonary consumption is learned from the accounts of military surgeons, who observe among young, robust soldiers a remarkable increase in the morbility and the mortality of phthisis during and immediately after the close of a war. Such observations have been made in the Franco-Prussian and Turko-Russian campaigns. The fact that consumptive soldiers are not allowed to enter upon a campaign (certainly not in Germany and Russia) excludes here the probability of contagion.

Statistics also show the remarkable prevalence of phthisis in persons of certain occupations, such as stone-cutters, miners, cigar-makers, weavers, telegraph-

* See, in connection with this, the excellent studies of William H. Mercur, from the pathological laboratory of the University of Pennsylvania, published only in abstract form in the *Phila. Med. Times*, July, 1883.

operators, book-keepers, and persons engaged in certain other occupations of a more or less sedentary nature. It is more natural to suppose that the disease, or the predisposition to it, is created by the character and the conditions of the occupation, than that a contagion should affect preferably shoemakers, miners, or soldiers in the battle-field. Again, in most phthisical patients the beginning of the disease can plainly be attributed to an exposure, to "a cold."

On the other hand, there are pathological conditions or diseases which appear to prevent the development of phthisis and tuberculosis in general. It is an established clinical fact that phthisis is extremely rarely, if ever, associated with mitral heart-disease; and, from my own observations, I believe that phthisis is rarely coincident with tumors. For the latter circumstance I can offer no explanation; nor is there any statement to this effect in literature. Rindfleisch has suggested that heart-disease prevents the development of phthisis by inducing repeated slow congestions of the lungs, these congestions producing an overgrowth of the muscular tissue of the bronchioles and air-vesicles, which thus gains strength for repelling the exudates following inflammation.

If tuberculosis were dependent upon a contagium for its development, neither heart-disease nor tumor-growth, nor any condition of the organism, could ever prevent its occurrence.

All the clinical facts above referred to prove definitely the necessity for a predisposition for the development of tubercular disease, and militate against the necessity of a contagium.

The anatomical aspect of the question—the morphology of the soil in which tubercle develops—is the most important aspect.

Beneke* tries to explain the disposition to tuberculosis by a disproportion between the size of the heart and blood-vessels and other organs to the bulk of the body.

Schottelius† made recently some interesting observations concerning the mode of termination of the smallest bronchioles and their relation to the lung-acini in different animals. He found that in the carnivora the entrance of the bronchioles into the acini presented very small apertures, so that the air-vesicles were not easily accessible to irritants; while in the herbivora the terminal bronchial terminations were quite wide, thus permitting the free entrance of irritants. He states that in man the bronchial terminations congenitally approach sometimes those of the carnivora, and sometimes those of the herbivora. In the latter type he believes he has found an anatomical explanation for the predisposition in some individuals to pulmonary tuberculosis.‡ Weigert, of Leipsic (one of the most enthusiastic germ-theorists), properly remarks upon the observation of Schottelius, that it does not explain the predisposition, as the same animals will react upon the introduction of the "poison of tuberculosis" into any other part of the body, where the bronchials do not come into play.

My own studies upon the minute anatomy of the tissues of man and of animals predisposed to tuberculosis extended over a large amount of material, and gave results which, to my mind, satisfactorily explained this condition. These results I announced at a meeting of this Society in October, 1882.

The anatomical peculiarity observed in either man or animals, whether inherited or acquired, I first showed to be, briefly stated, as follows: all the tissues of the body approach somewhat an embryonal type; they are peculiarly rich in nuclei and young cells, and the lymph-spaces of the connective tissues are narrower, fewer in number, and show a great many more cellular elements in the scrofulous than in the non-scrofulous. So far, subsequent observations of others agree with mine. Objections are raised only as to the direct relation between these structural peculiarities and tuberculosis. Here I must state that I only suggested, and never asserted, the necessity of such a relation. It is quite possible that there are some other and more striking peculiarities in the morphology of scrofulous animals yet undiscovered. This much I can, however, reassert to-day: that tuberculosis usually ensues when a simple inflammation is set up by any kind of injury, in animals with the structural peculiarity which I have de-

* Die erste Ueberwinterung in Norderney, Norden, 1882.
† Virchow's Archiv, vol. xci., 1883.

‡ The method of investigating this condition is not without interest. The vesicular structure of the lung was injected, through the bronchi, with a resinous melted mass, which, on cooling, presented moulds of the bronchioles, in connection with their characteristic infundibula and acini.

scribed; but that tuberculosis cannot be produced in animals that do not have this structural peculiarity, so far as my experiments show, unless the injury is inflicted upon serous membranes.

For the details of my researches in this direction I must refer to my first paper upon this subject.*

Koch asserts that the structural peculiarities of the tissues which I described can have no etiological relation to tuberculosis, because an animal not possessed of such tissue-peculiarity—the cat—is easily inoculable by tuberculous material. Here I must differ from Koch, as in my experience with cats this is not the case; and, again, Koch brings no proof for his assertion, and I am unaware that he or anybody else produced tuberculosis in a cat, except by inoculation into some serous cavity. That inoculations into serous membranes prove nothing for tuberculosis, as I have shown conclusively, Koch still seems to fail to see. But here is a way in which cats may become tuberculous with or without the bacillus. In one instance we kept one of the cats in a close box, *deprived* of liberty, with good air, the comforts of life, motion, and sufficient food; she also had been inoculated with diphtheritic material eight months previously, but had recovered. After the lapse of a year the cat was set free, but was accidentally killed, and was found to be affected by general tuberculosis in a high degree.

This, in my opinion, corresponds fully to the conditions in which a healthy young woman is placed, and finally becomes scrofulous, and then tuberculous, from a simple cold, after being the faithful nurse for a couple of years of a consumptive husband.

On the other hand, there is full reason to believe, as it is in accordance with experience, that young scrofulous persons, under proper conditions, may become normal individuals,—*i.e.*, may lose or outgrow the predisposition to tuberculosis. (I have dwelt upon this in my first communication on this subject.)

The scrofulous habit, and consequently also phthisis, may skip a generation, and does not invariably embrace all members of a family. It has been observed that parents may have at first healthy children without any vice, who grow up well, and subsequently the same parents, without being phthisical (but perhaps otherwise becoming deficient in health), may have other children that exhibit a full scrofulous habit. But even the reverse has been observed.

It would be highly desirable if physiologists would furnish some experimental observations on the circulation of the plasma in the lymph-spaces. This is, to my mind, a circulation or movement of vital juices in the tissues, which, for the well-being of the individual, is of importance next to that of the blood. These important channels, the lymph-spaces, are known to regulate the blood-pressure, carry and breed (white blood-corpuscles) food for the tissues, lubricate tissues, and relieve the body if any of its parts are damaged by injury of any character, of inflammatory exudates, dropsy, etc. These channels are nearly blocked up, nearly useless, in the *scrofulous*, and hence cannot perform their functions, thus modifying materially the condition and the fate of the individual in case of disease.

The term "*scrofulous*," which I retain for describing the above-stated anatomical peculiarity of animals and individuals, is as good as any other term; moreover, it is known by all as designating the "predisposition" to tuberculosis. Scrofulosis should be called a *condition*, and not a disease, as it has its hereditary and widely-distributed type (a natural one) in man, and its homologue in some normal animals (rabbit, guinea-pig, etc.). It must be remembered that the scrofulous individual acquires certain lesions, such as enlargements of lymphatic glands, cold abscesses, caries, long-standing catarrhs of various kinds, skin-eruption, and certain deformities of bones, only under the influence of injuries, or of the same agencies which in the non-scrofulous individual lead to transient and curable affections.

Virchow designates simple, permanent enlargement (hyperplasia) of lymphatic glands, with or without cheesy change, as "scrofulous," in contradistinction to "tuberculous" lymphatic glands, which contain miliary tubercle-nodes (heteroplasia), and which also undergo cheesy change.

There is nothing called "scrofulous" or "scrofulosis" by some which by others is not also called "tubercle" or "tuberculosis." There are, strictly speaking, no scrof-

* Phila. Med. Times, vol. xiii. p. 109.

ulous products, but only tuberculous products. The traditional term "scrofulosis" is variously used and interpreted, although it is not evident that any one means by it anything anatomically well defined.

Others take matters easier, calling everything *tuberculous* that contains tubercle-bacilli, and calling scrofulous all cheesy matters in which bacilli are absent.

There is still a third aspect of this question,—viz., the parasitic or bacillary theory of the predisposition to tuberculosis. As I mentioned in the earlier part of this paper, Baumgarten, Marschant, and several others recently brought forward the view that not only tuberculosis but even the predisposition to tuberculosis is to be explained by the susceptibility of an individual to bacilli. Under this hypothesis, the inherited scrofulous tendency in individuals is created through the mediation of the bacilli. It is supposed that the bacilli or their spores may be conveyed to the ovum by the organism of the mother, or in utero by the spermatozoids of the father. Furthermore, they say, inheritance is to be explained in no other way than by a bacillary infection of the infant through the milk of the nursing mother, and by subsequent living together of children and phthisical parents. We may exclude this view altogether from consideration, as it has not been proved. Besides, it is not in accordance with facts from observation. It is as contrary to biological laws to accuse parasites of the transmission of a predisposition to tuberculosis as it would be for that of epilepsy. Hence we may dispose of this view as an unfounded, absurd hypothesis.

I am not opposed to the germ-theory of disease where it has its well-founded and proper application. Bacteridian studies have contributed largely to our knowledge of a certain class of pathological processes and lesions. But misinterpretations of the significance of bacteria, bacillary speculations without occasion for them and without any proper application to the subject, are a check to the progress of medical science. The questions of the predisposition to, and the causation of, tuberculosis demand a great deal more of solid pathologico-anatomical and experimental studies; they can by no means be regarded as settled, and least of all through the discovery of a bacillus inhabiting necrotic tubercular tissues.

III.—TUBERCULOSIS, WITHOUT PREDISPOSITION, DUE TO INFLAMMATION OF SEROUS MEMBRANES.

For some years I have felt much interested in the question whether or not simple inflammation of serous membranes could lead to tuberculosis in the non-scrofulous, that is, in persons who have no family history of tubercular disease; and I would like to ask the opinion of the members of the Society upon this question. It is well known that there may be primary tuberculosis of serous membranes, producing secondary inflammations; and, on the other hand, tuberculosis secondary to adhesive pleurisy or peritonitis is also common in serous membranes. The general belief, however, is that whenever tubercular disease in either case occurs, if not secondary to phthisis or tubercular disease elsewhere, a strumous or scrofulous condition is required.

Traumatic injuries of joints are known to lead often to fungoid (tubercular) synovitis and general tuberculosis, occasionally in individuals with good family history. Simple injuries of the eyeball (the anterior chamber of which, as well as the joints, is lined by serous membranes), under conditions as above stated, have also been known to lead to tuberculosis, as recorded by Wolfe (*Brit. Med. Jour.*, March, 1882) and Gradenigo (*Ann. d' Oculistique*, 1870).*

Dr. M. Litten,† of Berlin, was the first to publish some accounts which demonstrate that miliary tuberculosis may be caused directly and primarily by pleurisy and inflammation of other serous membranes in persons with no phthisical history, and without any cheesy masses being formed in any part of the body. In his (Litten's) experience this was particularly the case when there was a rapid reabsorption of the exudates in case of chronic pleu-

* Primary tuberculosis of the uveal tract was described lately by Eparon (*Arch. d' Ophthalmol.*, November-December, 1883). He obtained his material for investigation from the clinic of Landolt. "His observation was confined to those cases in which the uveal tract was primarily and exclusively the seat of a tuberculous infiltration, usually of slow progress. In one case the tuberculous infiltration was confined to the anterior part of the uveal tract, and at first so deep in the tissues as to be inaccessible to direct examination. It developed rapidly, however, and within a month had caused such grave alterations in the eye as to necessitate its enucleation. There was, however, no tuberculous point of infiltration in any other part of the body, and the patient was cured by the enucleation of the eye."

† M. Litten, Sammlung Klin. Vorträge, No. 119: Ueber acute Miliartuberculose, 1877. For further references, see Wiener Med. Presse, No. 36, 1882; Charité Annalen, vol. vii., Berlin; Krankheiten der Respirations-Organe, in Virchow's Handb. der Spec. Path. und Ther., vol. i.; Virchow, Geschwülste, vol. ii. p. 725, etc.; also, Formad, Transactions of the Philadelphia County Medical Society, and of the Pathological Society, for 1882-83.

risy, or if repeated removal of the fluid of a hydrothorax or ascites by tapping had been performed. He records several well-studied cases of that kind, accompanied by autopsy-records. Litten's observations at no time, however, received the attention which they deserved.

Not only clinically but also pathologically this part of the tuberculosis question is rather neglected. In text-books of pathology the occurrence of primary tubercle in adhesive bands is incidentally mentioned, but no special consideration is devoted to its etiology and manifestations.

Upon the autopsy-table I have repeatedly met with subjects with exquisite primary tubercular peritonitis, pleurisy, or pericarditis, which, upon inquiry into the history of the cases, failed to reveal any phthisical or scrofulous history. The products of these inflammations were often plastic in character, not unlike those of fungoid synovitis. The appearances sometimes present themselves particularly strikingly in the peritoneum; all the viscera may be glued together by plastic material into a solid mass. The omentum is usually retracted and matted together into a solid cord or mass, which, lying parallel with the transverse colon, reaches across the abdominal cavity, and may have a thickness of from two to four inches; the mesenteric and other lymphatic glands are usually normal, but sometimes in advanced cases may be much enlarged and more or less cheesy. The entire absence of any cheesy focus in the body is, however, often a conspicuous feature in these cases.

Some pathologists deny the tubercular nature of these formations and of the flat nodular masses which cover the serous surfaces in these cases. It is true that fibroid changes predominate in these formations; but numerous tubercle-nodules, with all the necessary attributes, epithelioid and giant cells, and necrotic changes, were plainly seen in all cases which I had occasion to examine. Secondary miliary tubercles of quite recent date are also found thickly strewed locally in these parts, and may or may not be seen in the lungs and other organs. As a rule, there is more or less ascites in these cases. My colleague, Dr. E. O. Shakespeare, has recorded similar cases, and Dr. Morris Longstreth tells me also that he has seen and studied such cases. Dr. M. Prudden describes (*N. Y. Medical Record*, June, 1883) an allied case.

In chronic adhesive pleurisy there occur similar primary tubercular formations in the organized plastic exudate, which in some cases give rise to secondary (miliary) tuberculosis of other organs. The lungs may be perfectly normal in all parts, and show only peripherally, just below or bordering the pleura, some indurations of gray color made up of recent tubercle-tissue. These young tubercle-infiltrations may in some cases be seen penetrating into the substance of the lung, as in a pleuro- or dissecting-pneumonia, directly from the old tubercular masses of the adjacent pleural membrane.

I have also examined several cases of plastic adhesive pericarditis, and found the plastic vegetations in this lesion to contain tubercles: two of these had coincident pleuritic lesions.

Cases which came under my observation during the last eighteen months—*i.e.*, since the opening of the bacillary campaign—were, of course, carefully examined for bacilli, and the results may be summarized as follows: bacilli were found in most of the lesions, if the tubercular disease of serous membranes was accompanied by cavities and cheesy masses in the lung, or by tubercular ulceration of the intestines, and if cheesy changes in general were prominent; but no bacilli could be discovered, even after repeated and careful search, in any of the lesions of four cases of primary peritoneal and pleuritic tuberculosis examined. In none of these latter four cases were there any conspicuous cheesy changes in any organ, and no cavities or marked hepatizations in the lung, and no intestinal ulcers, although in two there was slight pulmonary miliary tuberculosis. These cases will be recorded in detail in a future publication.

I have also seen several cases of primary tubercular pleurisy and pericarditis, and a few of primary tubercular peritonitis, in the pathological institutes of Virchow in Berlin and of Von Recklinghausen in Strasburg. I questioned these foremost men of pathology concerning the etiology of these lesions. They, as well as Rindfleisch, of Würzburg, told me personally their opinion, stating their firm belief that these lesions often directly originated from simple chronic inflammatory changes, without the agency of any cheesy focus or any specific agencies whatsoever.

Birch-Hirschfeld also states, in his book

on pathological anatomy (page 183), that "nearly every exudative pericarditis and pleurisy leads to a local tuberculosis, if it takes a chronic course."

How often primary tubercular lesions of serous membranes occur in non-scrofulous persons, and whether this is the only form of tuberculosis in this class of persons, is, of course, a matter of speculation, until thorough statistics and careful studies are made in this direction. Nevertheless, it is a demonstrated fact, as I will show farther on, that primary tuberculosis can be produced in the peritoneum of animals, such as the dog, which are proved not to have any scrofulous tendency. I have seen this myself, and have seen O. C. Robinson in my laboratory succeed in this experiment by the introduction of simple irritants into the peritoneal cavity. Koch also never succeeded, even with the bacillus, in producing tuberculosis in the dog, except when using the peritoneal cavity or the anterior chamber of the eye (which is also a serous sac) as a point for inoculation.

Here is room for hypothesis. I would prefer to believe that tuberculosis could occur only in scrofulous persons, as this would better agree with the *scrofulous anatomy*. It is, however, possible that a scrofulous anatomy of the tissues may be artificially established by the blocking up of the lymph-spaces of the serous membranes by fibrin and molecular *débris* suspended in the serum which is being reabsorbed. This would then be a mechanical process, and not one of infection. If an inflammation occur in serous membranes, resolution becomes difficult through the peculiarity of the exudate. This is fibrinous mainly, and, forming extensive, usually permanent organized deposits, it impairs the function of serous surfaces quite materially: the reabsorption of new exudates is probably sometimes entirely impossible. Thus conditions may possibly be created in serous membranes, not unlike those of scrofulous tissues, and simple irritants, perhaps the fibrin, may induce in them a similar reaction.

IV.—QUESTION OF CONTAGIOUSNESS.—CLINICAL ASPECTS.

The idea of the contagiousness of tuberculosis is not new, and, like other unfounded views in medicine, it has oscillated, as all fashions will, from one extreme to another for many generations. At present it is entertained by a number of scientists and by a part of the profession. This view has called forth, from time to time, a number of researches whose results were either pro or contra. I shall refer to these subsequently.

Of late it appears that the belief in the contagiousness of tuberculosis has won considerable ground, not so much on account of accurate observation as on account of Koch's discovery of the bacillus tuberculosis.

Another element which seems to have had an influence in this direction is the fact that certain experimenters, formerly believing, from their own experiments, that tuberculosis was non-contagious, were led, later on, to change their opinions on account of the results of subsequent experiments. These later experiments will, however, be shown not to be conclusive.

Before discussing the merits of the bacillus question, I should like first to consider the question of contagiousness from clinical grounds; and should it be proved that tuberculosis is not contagious, then the necessity for a contagium surely falls to the ground.

According to the observations of the most prominent clinicians who have paid special attention to this matter, there is not on record a single authenticated case of tuberculosis as a result of contagium. Among scores of experienced men who deny thus the contagiousness of tuberculosis it is sufficient to mention the names of Virchow, Von Recklinghausen, Stricker, in Germany; Gull, William Watson, Paget, Humphrey, Richardson, in England; Bennet, in France; and Hiram Corson and Traill Green in our own midst,—all men of close observation, with ripe experiences extending over from thirty to fifty years.

The statistics of the large Brompton Hospital for consumptives, for thirty-six years, with regard to the resident officials, compiled by Dr. F. Williams (quoted from the *Lancet*, 1883), show that of four resident medical officers, one of whom had served twenty-five years, none had any lung-disease; of six matrons, none were consumptive; of one hundred and fifty resident clinical assistants, eight became consumptive and five died, but in only one was the disease developed during residence at the hospital. Since 1867, of one hundred and one nurses, only one

died from phthisis, and that after leaving the hospital. Before 1867, six died, three of these of phthisis, but only one became so whilst resident, and she had a consumptive sister. She died thirteen years after first joining the hospital, but was not there the whole time. Of thirty-two gallery-maids since 1867, none developed phthisis while at the hospital. Of twenty house-porters, five died, but none of consumption. Non-residents:—Of nine secretaries, three were threatened with lung-disease, but recovered. Of twenty-two dispensers, seven died, three of phthisis, one while at the hospital. Of four chaplains, three died, none of phthisis. Of twenty-nine physicians and assistant physicians, eight died, none of phthisis. At the Chest Hospital, Victoria Park, there have been five resident medical officers during about the last fifteen years; all are alive and well. Two matrons, neither consumptive. There were two clinical assistants appointed every three months; none known to have developed the disease at the hospital. One nurse out of fifty or sixty in the last few years became consumptive while at the hospital, and she died after a year's illness.

An ingenious plan to decide the question of the communicability of phthisis was instituted by the British Medical Association by establishing the Collective Investigation Committee. This committee sent out questions relating to this subject to all the members of the Society. Of ten hundred and twenty-eight replies received, six hundred and seventy-three negatived the idea of a contagium, while two hundred and sixty-one replies favored it. According to these statistics, there is a manifest majority in favor of the non-contagiousness of phthisis; yet such a plan is unsatisfactory, as the answers may be of unequal value, since their worth must be estimated in proportion to the experience and authority of the sender.

Not without interest is the observation of Prof. Corradi, of Pavia, who noted that out of one hundred and thirty-three families in which he had cases of consumptives, in only twenty-five of the families were there more than one member of the family ill of that affection.

There is no proof whatever that tuberculosis is conveyed from person to person by contagion. Seeming exceptions to this assertion can almost always be accounted for in some other way.

The assertion that the wife may contract the disease from the husband, I have pointed out, in a former paper, to be untenable; and I have also shown that a predisposition to scrofulosis may be acquired from the unwholesome mode of life led, of necessity, by such individuals.

Besides, it is established statistically that nearly one-third of all deaths occurring in middle life are due to phthisis. In view of the frequency with which this malady occurs, intermarriage between scrofulous individuals may be almost as common as between non-scrofulous ones.

The view taken that children become scrofulous by contagion from phthisical parents may be met by the fact that instances have occurred where a number of young children of phthisical parents were early removed from their homes and distributed among healthy families, and yet all, sooner or later, became phthisical.

Healthy persons have even been fed on bovine tuberculous material (which is considered identical with human tuberculous material) and have thriven on it, as is proved by the interesting feeding-experiments made upon man and recorded by Schottelius (*Virchow's Archiv*, No. 91, 1883). The circumstances which led to this experiment were as follows. In Würzburg the sale of meat affected by pearl-disease, or bovine tuberculosis, is permitted, but, as some opposition to its sale once arose, a community of country-people agreed to use exclusively tuberculous meat, on account of its cheapness and in order to prove that it was harmless. From October, 1867, to November, 1868, forty-nine tuberculous beeves, with well-pronounced lesions, were consumed by these people while they were under the supervision of the district physicians. In many instances the meat was even eaten raw, in consequence of habit. Ever since then, those people have continued the use of tuberculous meat, and thus far no bad results have been noticed: in fact, the record says that the people referred to are unusually healthy.

I wish to quote, however, some of the strongest affirmative evidence that exists in favor of the contagiousness of phthisis, in order to show upon what meagre clinical support this view is based.

The following case is related by Dr. C. Spriggs (one of the replies received by the English Collective Investigation Committee).

Miss R., aged 48, a dress-maker, living in

rather a lonely cottage, had three apprentices, young girls of from 17 to 19 years, not related, from three adjoining villages, who took turns to remain in the house and sleep with her, each one week at a time. During their apprenticeship Miss R. was taken with phthisis, of which she died. In less than *two* years afterwards all these apprentices died of phthisis, although it is said that in the family history of each no trace of phthisis existed; and the parents, brothers, and sisters of two of them are alive and well at the present time.

Another interesting case is related by Mr. G. F. Black (English Collective Investigation Committee), in which a perfectly healthy child, with a family history free from all trace of tubercle, is reported as becoming infected by a phthisical nurse and having died with profuse hæmoptysis, after the disease had run a rapid course.

Lindemann (*Berlin. Klin. Woch.*, July 25, 1883) related two cases of tuberculosis said to have followed the rite of infantile circumcision. The operator was himself subject to tuberculosis, and both children became ill, and one of them died of tuberculosis.

Another instance is thus given (Dreschfeld, *Brit. Med. Jour.*, 1883): In a small town in Germany, where in the course of nine years only five children had died of acute tubercular meningitis, there happened in the course of nine months eleven deaths from that disease in infants all under six months. All these children were assisted into the world by a midwife who subsequently died of phthisis, and who had been in the habit, when attending a confinement, of breathing into the newborn child's lungs with the view of expanding them.

Lindemann (*Verhand. Innere Medizin, Zweiter Congress*, Wiesbaden, 1883) quotes the following:

A soldier at Strasburg was admitted into the hospital for rheumatism, and his bed was between that of two tuberculous patients. A few months after his discharge from the hospital he began to cough. He returned to his family and was pronounced phthisical by the physician. Gradually the mother, brother, and father were affected by the disease. The father was attended by a neighbor, who was attacked and subsequently died, followed also by her husband.

In the *Bayerisches Aerztliches Intelligenz-Blatt*, No. 26, 1883, Dr. Herzerich reports the history of two girls, sisters, aged respectively fifteen months and three months, who, after being nursed by an undoubtedly phthisical mother, the first for five months, the second for three, were reared and fed on soup, milk, and pap. The mother adopted the following disgusting method of feeding: she first chewed the food herself, then spat it out into a spoon and gave it to the children. So long as she had little expectoration, the children bore this feeding well; but as soon as her expectoration became abundant, although the children continued to take their food with appetite, they both rapidly emaciated; ulcers formed in the throat and on the inside of the cheeks, some large and of irregular shape, others small and round, both with infiltrated edges; and extensive swelling of the lymphatic glands occurred. Severe fever, putrid diarrhœa, and progressive atrophy caused the death of both children within a month of each other. The post-mortem appearances were the same in both. All the mediastinal lymphatic glands were swollen and caseated; caseous nodules occurred under the pleuræ and scattered throughout the lungs; also in the liver, spleen, and of smaller size in the kidneys. The mother survived the children for some months, and died after extensive destruction of the lungs had occurred. It is worthy of remark that her children by a former marriage showed no sign of phthisis; also that the two children in question, so long as they were suckled by a comparatively healthy mother, remained healthy.

Dr. Bela Cogshall, of Flint, Michigan, in a paper read before the American Public Health Association, 1882, quotes the following case after Dr. H. Weber:

A young man, with a well-established phthisical history, married four times, and lost all four wives of consumption. His first wife died after her third confinement; the second wife after a year of married life; the third wife after her second pregnancy; and the fourth wife after her first confinement. All four women are said to have come from healthy antecedents, and to have been "apparently" and "exceptionally" healthy prior to the time of marriage. Finally the much-married man died himself.

There is hardly any comment necessary. By the side of the arguments and facts advanced in this paper such and similar evidence is entirely unsatisfactory, on account of the complete absence of direct proof. On account of the isolated character of the cases and the frequency of occurrence of phthisis, there is just as much reason for inferring a coincidence as a contagium. Furthermore, there is no proof that a family history of scrofula or phthisis or some other causes had been fully eliminated in the cases referred to.*

* Since the reading and discussion of this paper, Dr. William H. Webb, of this city, has kindly sent me his monograph entitled "Is Phthisis Pulmonalis Contagious?" Philadelphia, 1878. It presents an admirable and full résumé of that part of the literature in which the so-called communicability of phthisis is favored. Dr. Webb ably advocates the view that phthisis is contagious. The most interesting passage to me in Dr. Webb's paper is a letter of Professor Alfred Stillé, who, from his clinical observation, extending over nearly fifty years, relates the following:

"I have never seen more than *one case* in which it *appeared* to me that the disease was directly communicated. This was a mother, between fifty and sixty, whose husband many

On the other hand, daily observation and statistics show that there are thousands of instances which disprove the hypothesis of the contagiousness of phthisis. In multitudes of married couples where either the wives or the husbands died of phthisis, the surviving parties were known to have remained unaffected by the disease.

V.—THE BACILLUS TUBERCULOSIS—ITS NATURAL HISTORY, MORPHOLOGY, DETECTION, HABITAT, SIGNIFICANCE, AND DIAGNOSTIC VALUE.

I will now speak about the bacillus proper, and will allude here briefly to its natural history, morphology, habitat, significance, detection, and diagnostic value.

The bacillus discovered by Koch, of Berlin, as is well known, is a vegetable organism, and belongs, according to Cohn's classification, to the group of filamentous bacteria (Desmo-bacteria), variety Bacillus.*

The tubercle-bacilli form, according to Koch, a species of bacillus by themselves, and on Koch's authority as a *mycologist* we can accept this statement as correct until proved otherwise.

The tubercle-bacilli present themselves as thin, slender rods, in length varying from one-third to the whole of the diameter of a human red blood-corpuscle; in breadth they do not exceed one-fifth to one-tenth of their length. They vary in size in different locations, and, according to observations made by myself conjointly with George Bodamer, my assistant, they vary also greatly in size in different artificial culture-media. In nearly dry soils they appear, as a rule, much smaller than in moist soils. They are blunt at the ends, and frequently contain unstained spores in varying number which give them a beaded appearance that might be (and has been) mistaken for short torula chains of micrococci. The rods are sometimes slightly curved, and they frequently appear in pairs, forming a V-shaped figure; occasionally the rods are seen crossing one another. Often they appear within animal cells in tissues and other matters which they invade, quite isolated and scanty, so that there may be seen only a few bacilli, or only one bacillus, in a whole microscopic field. Sometimes they occur in large, dense masses, particularly so and most commonly within and around cheesy masses in lymph-glands, and in the cheesy fragments met with in the contents of lung-cavities, as Koch himself first pointed out.

It may be of interest to note that tubercle-bacilli may considerably multiply in sputum when it stands in a bottle for some time, as first observed by Bodamer in my laboratory. Williams, of the Brompton Hospital for Consumptives, records also that he has seen the bacilli multiply in sputum after standing in a warm room for ten days.

For demonstrative purposes it is well to inspissate tuberculous sputum or to dry it (as I have seen in Koch's laboratory); for examination it is then moistened with water, and it will then show more bacilli than when fresh.

The methods of detecting the bacillus are so well known that I will not consider in this communication the merits of the different dyes employed. Moreover, success does not depend upon the method or the dye, but mainly upon the skill and the accuracy of the dyer.†

As is generally known, the principle in staining bacilli rests upon the fact that bacteria absorb and retain aniline dyes more readily than do the surrounding animal organic materials which they inhabit. When sputum dried upon a glass cover, or a section containing them, is well stained, for instance, by aniline violet, and then washed in very dilute nitric acid, only the bacilli will retain the dye, while all the rest of the organic material composing the specimen will be decolorized, and may readily be stained by some other dye without modifying the violet color of the bacilli.‡

years before had died of consumption. She was herself in excellent, *tough* health up to the date of her daughter's last illness, which was with chronic phthisis with cavities. A day before her death the daughter's breath was very offensive, and the mother, who was lifting her to change the pillows, inhaled it. She spoke to me of the foul taste and acrid sensation in her throat produced by the inhalation. Within a few weeks she began to cough, fell rapidly into consumption, and died after several months' illness. This is the only case of my own that appears to bear upon the affirmation of the question. On the other hand, *if pulmonary phthisis were often conveyed by contagion, the cases ought to be of daily occurrence, since the disease is the most frequent of all mortal diseases.*"

*The statements made by Beneke, Klebs, and Schmidt, that the bacilli are crystalline bodies, have been withdrawn; while views to the effect that "bacilli" are to be identified with blood-fibrin, etc., were at no time taken into serious consideration by microscopists.

†To detect bacilli is a very simple matter, although by far not so easy as to prepare a specimen of urine and to find the all-important tube-casts; and yet how many physicians (even those perfectly familiar with microscopic technology) will be sure when they discover tube-casts, if they attempt to examine the urine at all?

‡The staining fluids for bacilli we more commonly use are those after Ehrlich's formula, slightly modified:

First Stain.—Watery saturated solution of aniline oil, *five*

A magnifying power of four hundred diameters is nearly always sufficient to detect stained tubercle-bacilli. In fact, we found that where we failed to find bacilli with a good one-fifth objective, neither our one-twelfth Zeiss oil immersion lens nor the Abbé's condenser would reveal any when used (as we always do) for control. If the bacilli are very numerous (as sometimes in lymphatic glands), a mass of them may be recognized easily by the naked eye in a well-stained section as a small stained speck.

Occasionally bacilli may also be seen when unstained. Baumgarten* discovered the same tubercle-bacillus simultaneously with, and independently of, Koch, in unstained caustic potash preparations of tubercle-tissues. Koch† also states that tubercle-bacilli may be readily seen, especially in artificial tubercles when simply teased in water, or preferably in blood-serum. We have also observed tubercle-bacilli, without resorting to staining, in cultures such as chicken *bouillon*, identifying them subsequently by means of the usual staining process. In stained preparations too much washed in acid, or in specimens ill preserved, a part or all of the tubercle-bacilli may also be seen decolorized, though still quite distinctly visible.

Tubercle-bacilli are, as a rule, motionless as seen in stained preparations made from the substances they inhabit; but the observations of Bodamer and myself appear to show that the bacilli of Koch may also have an actual (not communicated) motion when for some time cultivated in liquid media. But at the same time it was observed that the development of the cultures was not as extensive in liquid media (*bouillon*) as in a solid medium (coagulated blood-serum). Conversing with Koch on this point last summer, he remarked that this was quite possible, and suggested that perhaps the bacilli in their movable state acquire flagelli or cilia at the ends, although he had not yet made such observation. Koch, quite properly, does not seem to consider that motion is an invariably differentiating feature for bacteria.

In cultures (coagulated blood-serum being the preferable nidus) the tubercle-bacilli grow as a dry, scaly, tortuous, whitish-gray mass, spreading themselves exclusively on the surface. The growth is very slow, and is favored by a temperature of 30° to 40° C. (86° to 104° F.).

Dr. Koch kindly demonstrated to me a number of specimens of bacilli, and in particular the appearance of these bacteria exhibiting under low amplification the peculiar S-like figure in the growths in masses. Koch seems now to lay more stress upon this low-power appearance and upon the pathogenetic properties of the bacillus tuberculosis, as a distinguishing feature from other bacilli, than upon the color test. During the conversation he admitted that some other bacilli may also yield the same micro-chemical reaction as the tubercle-bacilli, but insisted that the latter bacilli cannot be stained brown. The failure of the tubercle-bacilli to take the brown stain, he said, was the reason that they cannot be well photographed (blue- and red-stained objects not being suitable for photographing). He obligingly explained to me the details of his methods and the determination of the value of cultures. I learned from him that those cultures in which the bacilli have no spores are not capable of propagation, nor are they fit for inoculation of animals.

Klebs, to whom Koch had given some of his cultures of tubercle-bacilli, declared that they also contained micrococci. Koch presumes that Klebs has misinterpreted the granules of the coagulated blood-serum (in which they grew) as micrococci. I can testify that bacilli alone were present in those cultures of Koch which I had the opportunity of examining. This is also true of a bacillus-culture in a flat salt-dish obtained from Koch's laboratory by Dr. Shakespeare of this city; this culture was still perfectly pure (and free of micrococci) when examined by Dr. Shakespeare and myself, three months after the arrival in America.

Concerning my own bacillus-cultures

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parts; alcoholic saturated solution of aniline violet, *one part;* mix and filter.

Second Stain.—Watery solution either of vesuvin or of Bismarck brown; filtered.

Direction for Preparation and Order of Staining.—Sputum in thin layer smeared upon glass cover and *well* dried; immerse (*a*) into first stain for twenty-four hours (rapid staining being not reliable in doubtful cases); (*b*) into dilute nitric acid (one to five parts of water) for two or three seconds; (*c*) wash in alcohol; (*d*) into second stain for two to five minutes; (*e*) wash in water and then in alcohol; (*f*) dry it and mount in Canada balsam or glycerin. Failures to detect bacilli will occur: first, when specimen consists of salivary mucus instead of expectorated material; second, when sputum too thick or too thin is smeared upon cover; third, when not enough heated in drying, or when burned; fourth, when too long in acid; fifth, when too much washed; sixth, when bacilli are absent; seventh, when not recognizing them.

For preparations to be kept, and for tissues, the fuchsine dye, as first stain, is preferable, and certain modifications of method necessary.

* Med. Centralblatt, 1882, No. 15.

† Berliner Klin. Wochenschr., 1882, No. 15.

which I recommenced last autumn (and which are now more often successful than before I went to Berlin, through the use of the complete outfit of Koch's apparatus, supplied by the University of Pennsylvania) I will report later. But it may be said that, even under the most favorable conditions, to obtain success with the tubercle-bacillus culture is at times a difficult task.

Before leaving this part of the subject I must say that I owe many thanks to the director of the German Imperial Board of Health, Dr. Struck, and to Dr. Koch and his assistants, for the very liberal and kind treatment which they extended to me in their laboratory; also for allowing me to study the whole working of their famous institute, and demonstrating to me their methods of work, including the construction of their ingenious apparatus, and permitting me to exercise all the important manipulations in bacteridian studies after Koch's method; and, furthermore, for allowing me to prove that I had succeeded also in staining and recognizing the tubercle-bacillus before I went to them.

I cannot blame Koch for not demonstrating to me how to produce genuine induced tuberculosis with his bacillus within eight days, a favor which he extended only to Watson Cheyne;* not because I have not yet the "faith" in the infallible action of the tubercle-parasite, but because Koch was then working at the subject himself, and does not consider the task as much finished as his over-zealous followers do. I was, moreover, informed, while in his laboratory before leaving Berlin, that no one besides himself and his assistants ever worked in the laboratory on the tubercle-bacillus beyond staining tissues, sputa, etc., containing it. Besides, the cultivation of the tubercle-bacillus takes a longer time than usually is allowed to outsiders who come to be instructed in Koch's laboratory.†

The Habitat of the Tubercle-Bacillus.—After reading most of the numerous compilations in reference to the present standing of the tuberculosis question, it would seem that Koch has established that his tubercle-bacillus is always associated with tuberculosis, and with the diseased products and the various excreta in this disease,—and in this disease alone. Since Koch's publication appeared, a number of observers, authoritatively and otherwise, assert the invariable presence of the bacillus in *all* tubercular products; and, further, it is claimed as a proved matter that the bacillus is found in the beginning of the disease,—viz., in the youngest tubercle-tissues.

This is, however, not in accordance with the facts. Neither in Koch's own publication nor in the records of any microscopist (when the original papers are examined) is the invariable presence of the bacillus in tuberculous lesions or excretions and its absence in non-tuberculous matters either clearly shown or proved. Moreover, the authors of nearly all the literary productions are in favor of the contagiousness of tuberculosis, and they disregard, as a rule, the negative evidence.

The question of the occurrence, and partly that of the significance, of the bacillus called by Koch the *tubercle-bacillus* in tuberculous lesions divides itself into several parts, and hinges upon the results of the following investigations:

1. The examination of tissues affected by tubercular disease for the bacillus; and, if present, the time of its occurrence.

2. The examination, *intra vitam*, of blood of tubercular patients.

3. The examination of the products discharged or eliminated with the excretions by individuals suffering from tubercular disease.

4. The examination of air,—viz., of the breath of phthisical patients, and of the air of sick-rooms and hospitals generally.

5. Comparative studies in animal tuberculosis.

6. The occurrence of bacilli in lesions and substances other than tubercular.

I will state now, briefly, what so far have been the results of the investigations upon these points.

1. Tubercle-bacilli have been detected

* See Practitioner, April, 1883, page 249.

† I found that the "pilgrims from all nations" who (through influence brought to bear upon the authorities) succeed in being admitted for a while to Koch's laboratory, are instructed principally in the most rudimentary manipulations of mycology; and to most of them the assistants have first to point out what a bacterium looks like. Besides these "pilgrims," the German Government sends regularly young sanitary officers to be instructed in mycology. Of course this is a very useful matter to the "pilgrims" and to the young sanitary officers, even if only one out of twenty-five ever devotes himself to mycology; but it is no beneficial matter to Koch and his kind assistants, who, through this constant interruption, are terribly interfered with in their scientific work. In fact, the working of the Imperial Laboratory is sometimes completely delayed in this way, as it was last summer, during the Hygienic Exhibition. Yet the beneficial influence upon sanitary science which this excellent institution exerts is very great.

quite often in the various forms of tubercles of lung, and in scrofulous and tuberculous lymphatic glands; and likewise, although not so frequently, in tubercles of the various serous cavities; and in tubercular ulcerations of the mucous membranes and the skin. But it must be noted that only a few microscopists have recorded examinations of tubercle-tissues for bacilli, and among these there was *not one* who did not meet with a case or a certain number of cases in which tubercle-bacilli were either totally absent in the tissues or only present in some of the tubercles. The great bulk of bacillus work done comprises merely examinations of sputum.

The facts concerning bacilli in tissues are as follows:

Koch* found bacilli in the majority of tuberculous lesions he examined, but still not in all, as he states himself: he only *supposes* that his bacilli, even if they escape observation, are still present in all cases and in all tubercles. His proposition, however, that in some tuberculous lesions only unstained spores of tubercle-bacilli are sometimes present, or that bacilli may be invisible, and not taking the staining when dead, or even may be absent if the tuberculous process comes to a "stand-still," is, of course, purely hypothetical. There is still another good reason for the assumption that the proportion of non-bacillary tubercles may be much larger in Koch's own examinations. As Koch says himself, he pre-eminently recognizes only such structures as tubercular which contain his bacillus, regardless of their morphology otherwise: it is therefore possible that he may have innocently excluded a number of non-bacillary tubercles from the list of his tubercle records. Koch himself, however, says that he failed to detect bacilli in some scrofulous glands and in two cases of tubercular synovitis, and further admits the prevalence of bacilli in degenerated tissues.

As far as examination of tubercle-*tissues* for bacilli is concerned, only the following observations besides those of Koch are recorded (so far as is known to the writer), and with the following results:

Dr. Geo. M. Sternberg, U.S.A.,† who is a man recognized as a competent mycologist, here as well as in Europe, failed to find tubercle-bacilli in the lesions of several cases of tuberculosis.

Heneage Gibbs‡ also failed to discover bacilli in a number of tubercles, particularly in the reticular form: in fact, he had met several times with non-bacillary tuberculosis. Gibbs states§ that "he had examined the lungs of guinea-pigs which had become tuberculous after being kept in the air-shafts of the Brompton Hospital for Consumptives, and had found no bacilli in them; and he knew of an instance in which a guinea-pig, inoculated with sputum from a case of phthisis, presented a glandular abscess in the thigh which abounded in bacilli, whereas the internal organs, although full of tubercles, did not yield a single bacillus."

I do not think it likely that Heneage Gibbs, with his large experience and universally-recognized skill in bacteria-stainings, would fail to discover bacilli if they had been present.

Watson Cheyne,‖ whose anatomical conception of tubercle is inseparable from the bacillus, of course says that non-bacillary tubercles, like the above, are no tubercles at all. Hence his statement, that in all tuberculous structures (that is, in all structures which *he* calls tubercle) the bacilli are invariably present, is, from his standpoint, perfectly warrantable. He also confirms the fact that recently-formed tubercle-nodules made up of young lymphoid cells are, as a rule, without the bacilli, while the older tubercles always containing epithelioid cells (on account of retrograde changes) usually do contain bacilli. Now, Watson Cheyne, in this connection, with great self-confidence propounds, "The bacilli being the cause of this disease [tuberculosis], only the nodules containing epithelioid cells are tubercle."¶ Still, the same writer has expressed surprise** that "very extensive tuberculous processes may be found in animals with only very few bacilli."

T. M. Prudden, of New York,†† who made extensive and excellent morphological studies in reference to the occurrence of the bacillus in tuberculous lesions, *failed to find bacilli in any part of the body in three cases of profuse tuberculosis.* In one case of Prudden's the tubercle-bacilli were

* Berliner Klin. Wochenschr., No. 15, 1882.
† Phila. Med. News, 1882.

‡ London Lancet, February 24, 1883.
§ Lancet, February 12, 1883.
‖ Practitioner, April, 1883.
¶ See p. 309, loc. cit. ** Page 316.
†† Medical Record, April 14, and ibid., June 16, 1883.

abundant in the walls and edges of a lung-cavity and its immediate vicinity, while no bacilli could be found in the diffuse and miliary tubercles of the rest of the body. Prudden further states, "In a large proportion of the cases in which bacilli were present they seemed to have a decided predilection for tubercle-tissue in a degenerated and disintegrating condition, either cavities in the lungs, cheesy and breaking-down areas, or tubercular ulcers; although present with great frequency in small numbers in well-formed, intact tubercle-tissue. . . The bacilli were present in greater abundance in the respiratory organs and intestinal tract than in other parts of the body less directly in communication with the external world. It is further evident that in nearly every case there are many miliary tubercles of all forms, and in many cases much diffuse tubercle-tissue from which the bacilli appear to be entirely absent."

Spina* did not succeed in detecting bacilli in a number of cases. Even if the number of Spina's failures to see the bacillus should be larger than in cases of other observers, Koch's favorite demolishing argument that Spina and all others who failed to detect the bacillus in any case do not know *what* that parasite of his looks like, is entirely unjustifiable. Moreover, Spina's work was controlled by no less an authority than Stricker, of Vienna, and the correctness of the results of the investigation in its essential parts is vouched for by Stricker.

Cornil and Babès† detected the bacillus in the lesions of a number of cases of tuberculosis; but they also showed that bacilli are totally absent in some cases, and not constant in otherwise typical tuberculous lesions.

Malassez and Vingal,‡ from the results of observations of their own, state that there seems to be no doubt that true tuberculous lesions occur which possess very few or even no tubercle-bacilli.

Fräntzel,§ in a discussion before the Berlin Medical Society, stated that he found a number of scrofulous (tuberculous) ulcers and lymph-glands not to be "bacillary."

C. Macnamara‖ reports a case of primary tuberculosis of bone and of the marrow of bone, in which no trace of tubercle-bacilli could be discovered in any of the lesions.

George Bodamer, having succeeded in staining and demonstrating the bacillus in sputum and in tissues in the spring of 1882 (immediately after the announcement of its discovery and the method of its staining by Koch, and probably prior to any one else in America), and having worked together with me nearly incessantly in bacillus stainings and cultures ever since (including also a certain time in the pathological institutes in Germany), also failed to detect the bacillus in a certain number of typical tuberculous lesions.

As will be seen from my report, I found tubercle-bacilli to be absent (or I could not detect them, if this expression should be preferred) in four cases of primary peritoneal tuberculosis, in two cases of primary tubercular pericarditis, in one case of tubercular joint-disease, and in several cases of miliary tuberculosis: this does not include some cases of induced animal tuberculosis which did not show bacilli.¶

Dr. Lawrason, of New Orleans, who worked with me last spring in the pathological laboratory of the University, and who had demonstrated his skill in staining bacilli in tissues before the Pathological Society of Philadelphia and elsewhere, also found tubercle-bacilli wanting in some of the most typical tuberculous lesions.

Weigert, Bollinger, Baumgarten, Ziel, Councilman Schuchart, and Krause, and Koch's own assistants, are yet to be mentioned as having recorded a few examinations of tuberculous tissues for bacilli with negative and varying results; but detailed statements of their investigations in this direction are not known to me.

The direct conclusion to be drawn from the total evidence relating to bacilli in *tissues* just quoted is, that tubercle-bacilli are not invariably present in even typical tuberculous lesions; furthermore, that none of the investigators brought forward any proof or evidence that the bacilli are present or appear in the beginning of the disease. On the contrary, the results of the investigations of all observers, including those of the discoverer of the bacillus

* Studien über Tuberculose, Wien, 1883.
† Le Progrès Médical, 1883.
‡ Le Progrès Médical, No. 20, 1883, and in a second communication quoted by the Lancet, December 15, 1883.
§ Berliner Klin. Wochenschr., December, 1883.
‖ Brit. Med. Journal, December 15, 1883.

¶ At this point I wish to correct an impression which a certain statement in one of my former communications on this subject seemed to convey,—namely, that bacilli are invariably present in tuberculous products.

himself, point plainly towards establishing the fact that tubercle-bacilli inhabit pre-eminently disintegrated tissues.

2. *Examinations of the blood and lymph intra vitam* of patients suffering from tubercular disease, which in my opinion would be quite an important matter in the study of tuberculosis, are not recorded by any observer. All attempts which we made in examining the blood of tuberculous patients during life gave, as will be recorded later, negative results. It is true that we observed in specimens post mortem some blood-vessels filled with thrombi containing a few bacilli. Further, there are records by Cornil, Weigert, Ponfick, and Koch relating to bacilli observed post mortem in the walls of veins, of large lymph-ducts, and of arteries, in tuberculous cases. As to the route and manner by which the bacilli gained entrance to these places inferences might be drawn, but no definite conclusions arrived at until the bacilli have been observed during life in the blood or lymph. I will not touch upon this part of the question at present.

The blood from cases of hæmoptysis as expectorated has been examined by Hiller * and Williams † and bacilli discovered, but no inference from this can be made as to the bacilli in the circulating blood.

3. *Examination of products discharged or eliminated with the excretions* by individuals suffering from tuberculosis has been practised quite extensively and by a number of observers,—especially examination of phthisical sputum. To these sputum-examinations I will return immediately.

There are a few investigations recorded in reference to tubercle-bacilli in the fæces, in discharges from the ears and in those from the nose, and in urine voided by patients affected with local tuberculosis of the pertaining parts. Tubercle-bacilli were often detected, and thus a diagnosis of tubercular enteritis, tubercular otitis, and tubercular meningitis (bacilli in nasal discharge), and tuberculosis of the urinary tract, was made.

The tuberculous nature of ulcers, of synovitis, and of surgical lesions of various locations, is claimed to have been occasionally settled (?) in this way.‡ But, on the other hand, the discharges from some typical tuberculous lesions failed to show bacilli.

Damsch § claims that tuberculosis of the genito-urinary tract can be diagnosticated by inoculating a drop of urine from such a case into the anterior chamber of the eye of a rabbit, which operation will be promptly followed by iris-tuberculosis in the animal. This latter observation, however, I believe, requires confirmation.

The examinations of sputum, practised now probably by all microscopists in the world, has proved to be of much more value. I will quote the observers who made and recorded more or less extensive examinations of sputum, and the results and conclusion they arrived at, to show that there are some points which are misinterpreted by some clinicians and others.

Koch ‖ does not claim that sputum from every phthisical case contains bacilli: he met with cases without bacilli in sputum. He did not find, however, bacilli in cases said not to be tubercular.

Ehrlich ¶ records twenty-six cases of phthisis in which bacilli were invariably present in the sputum; in other lung-affections similar bacilli were not found.

Balmer and Fräntzel ** examined one hundred and twenty cases of phthisis for bacilli with positive results, and came to the conclusion that the quantity of bacilli was in direct proportion to the gravity of the disease, and that the bacilli were larger and often contained spores in acute cases, and were smaller in size and quantity in chronic cases. They never saw bacilli in the sputum of cases other than phthisis. They also quite properly conclude "that the sputum affords to bacilli a more favorable place of growth than does the still living lung-tissue," because they found bacilli to be extremely scanty in the tuberculized lung-tissue surrounding a cavity, while the contents of the latter and cheesy degenerated parts of the lung were crowded by them.

Heron †† records sixty-two cases of examination of phthisical sputum, in which bacilli were constantly present.

D'Espine ‡‡ records examination of sputum from twenty-five cases, but could not confirm the correctness of the assumption

* Deutsche Med. Wochenschr., No. 47, 1882.
† London Lancet, February 24, 1883.
‡ Schuchart and Krause, in Volkmann's Clinic, Chirurg. Centralblatt, 1883.

§ Deutsch. Arch. f. Klin. Med., 1882.
‖ Loc. cit.
¶ Deutsche Med. Wochenschr., No. 19, 1882.
** Berliner Klin. Wochenschr., No. 45, 1882.
†† London Lancet, February 2, 1883.
‡‡ Ibid., January 13, 1883.

that the bacilli stand in any relation of quantity to the gravity of the disease, although he affirms that they are constantly present.

Williams,* having examined the sputum of one hundred and thirty cases for bacilli, with only three negative results, concludes, however, that there was "no definite ratio between the activity of the disease and the number of bacilli, although they were few in cases where the disease was quiescent."

Ziehl† found bacilli nearly invariably present in seventy-three cases of phthisis examined ;‡ Dreschfeld in forty-six cases ; Gradle and Woltmann,§ of Chicago, in thirty-five consecutive cases.

Kowalsky‖ claims to have examined the sputum of six hundred cases of phthisis, with bacilli nearly invariably present.

Chiari,¶ in a number of cases examined, never failed to find bacilli.

Detwiler and Meissen** examined eighty-seven cases of phthisis, finding bacilli in all but two. Although bacilli were more numerous wherever great destruction of lung-tissue existed, they did not observe any definite ratio of bacilli in sputum to the gravity of the disease. The presence of elastic tissue in sputum they consider as significant for diagnosis and as constant as that of bacilli.

S. West†† found bacilli present in every case of phthisis which he examined, though in some cases they were in such small numbers as only to be found after repeated and very careful examination. He further adds, "The more cheesy matter or fluid from a cavity there was in the expectoration, the more bacilli we might expect to find ; consequently, in a case of acute tuberculosis, before breaking down of the lung, we should expect to find none." He also states that there seemed to be but little variation in the size of the individual bacilli in different cases, although bacilli in acute cases appeared to contain spores.

R. S. Smith‡‡ records seventy-seven cases in which he had made the examination of sputum : of these, forty-nine were from "tubercular phthisis," and invariably showed bacilli ; the remaining twenty-eight, comprising various other affections of lungs, some of them closely simulating phthisis, did not show bacilli. The affections examined with negative results were such as "chronic bronchitis, bronchiectasis, chronic syphilitic pneumonia, slight hæmoptysis with no evidence of any disease, chronic pleuro-pneumonia with dulness on percussion and copious purulent expectoration, chronic pleurisy, apex pneumonia with subsequent breaking down from gangrene and with cavity (?), sarcoma of lung, gray hepatization, congestion from mitral disease, diabetes with bronchitis, two cases with strong family history of phthisis, cough with purulent expectoration, but with no evidence of local disease in lungs," etc. Bacilli were also wanting in "slight phthisical cases when the patients were rapidly recovering." I think, however, that errors in physical diagnosis can by no means be fully excluded here.

Heneage Gibbs,§§ from his extensive observations, states that the sputum did not show bacilli in some cases which upon the autopsy-table showed the lungs riddled with tubercular masses : he explains that the patient died before the destructive process had gone far enough to cause the bacilli to be ejected.

Whipham‖‖ records twenty cases which he studied in relation to bacilli in sputum, and made the observation that the bacilli disappear from sputum at times when the condition of the patient improved.

M. T. Prudden¶¶ found bacilli in sputum in forty-six out of fifty-eight phthisical cases examined ; Guttmann*** and Pfeiffer††† met also with cases of phthis without bacilli in sputum.

The report upon the examinations of sputum for bacilli from the pathological laboratory of the University of Pennsylvania will embrace the results from nearly two hundred cases of pulmonary diseases observed. These show that bacilli in sputum are diagnostic, but not prognostic, in phthisis ; that the old-fashioned test, the presence of pulmonary elastic tissue in sputum, is a very reliable one (gangrene and abscess being so easily ex-

* London Lancet, February 24, 1883.
† Deutsche Med. Wochenschr., No. 5, 1883.
‡ Brit. Med. Journ., Feb. 17, 1883.
§ Phila. Med. News, 1883.
‖ Wien. Med. Presse, February 24, 1883.
¶ Ibid., No 1, 1883.
** Berliner Klin. Wochenschr , Nos. 7 and 8, 1883.
†† London Lancet, February 10, 1883.
‡‡ British Med.-Chirurg. Journal, July, 1883
§§ London Lancet, February 24, 1883.
‖‖ Ibid., February 10, 1883.
¶¶ New York Med. Record, April 14, 1883.
*** Berl. Klin. Wochenschr., No. 52, 1882.
††† Ibid., No. 3, 1883.

cluded); and, further, that the absence of tubercle-bacilli in sputum proves nothing.

Spina and Stricker * met tubercle-bacilli in simple bronchiectasis, bronchitis, croupous pneumonia, etc.

Sattler, in the translation of Spina's book,† page 164, adds the record of an autopsy of a case of similar nature mistaken for phthisis on account of bacilli in sputum.

Kundrat‡ related a case which occurred in the spring in Nothnagel's clinic, where a diagnosis of tuberculosis was based upon the detection of bacilli; but, post mortem, the case proved to be one of chronic catarrh with bronchiectasis. He also mentioned a case, under Prof. Schrötter, where bacilli were repeatedly found by himself and others, and the necropsy showed only bronchitis and emphysema. Hence he was not disposed to admit that the discovery of bacilli in the sputum was absolutely diagnostic of tubercle.

Riegel, of Giessen, and others, failed to find bacilli in the sputum of cases of diabetic phthisis. But I think the diabetes had nothing to do with keeping the bacilli out, as I have detected multitudes of bacilli in the sputum from a case of diabetic phthisis observed and confirmed by autopsy by Dr. Charles H. Reed, of this city.

Levinsky§ and Koryanyi‖ both detected tubercle-bacilli in the sputum of patients with syphilitic lesions of the lung.

It is very probable that many of the cases of pulmonary disease in which bacilli were not discovered might nevertheless have been phthisical: in fact, the character of the control cases, as given by R. S. Smith (quoted above), fully justifies such assumption. From the autopsy-experience of clinicians and pathologists whom I consulted, and from observations of my own, I can testify that the only sure way to decide the nature of doubtful cases, such as, for instance, those recorded by Smith, is the autopsy; otherwise the negative evidence in relation to bacilli goes for naught. This is also substantiated by the observations of Gibbs, Whipham, and West, quoted above, —viz., that bacilli may fail to appear in sputum where there are no cavities and no ulceration in the lung. I have seen autopsies reveal phthisis in cases where no bacilli were found during life, after careful examination over and over again repeated; and I also happened to witness the autopsies of three cases of non-tubercular lung-disease which during life had been diagnosticated phthisis on account of bacilli discovered in the sputum.

The examination of sputum may thus, in doubtful cases, be quite misleading; for, if in any given case bacilli are not found, it should be taken into consideration, *first*, that the bacilli may be enclosed in the tubercle-tissue, as in miliary tubercle, which rarely produces destruction of the lungs, and consequently they may fail to appear in the sputum, and, *second*, that the examiner may fail occasionally in any case to succeed in preparing a successful preparation of stained bacilli. On the other hand, if bacilli are present, they sometimes may not be pertaining to the case, but be accidentally introduced through use of a vessel uncleansed and used by another patient, or otherwise; and, finally, it may be inferred, but it is by no means proved under rules of scientific scrutiny, that similar bacilli do not occur in the sputum of cases other than tubercular.

From our present knowledge of the occurrence of Koch's bacillus in sputum we must therefore conclude:

1st. That the presence of bacilli is a valuable *diagnostic sign* of tubercular disease of the lung.

2d. That the quantity of bacilli found does not, as a rule, indicate the degree of the disease, and hence is *not a prognostic sign*.

3d. That the absence of tubercle-bacilli is *no proof whatsoever of the absence* of tubercular disease.

4th. *The examination of air*—viz., *of the breath of patients* suffering with pulmonary tuberculosis, and of the air of sick-rooms and hospitals generally—has given some positive, although not definite, results.

C. Theodore Williams¶ "recently selected one of the ventilation-shafts at the Brompton Hospital for Consumptives in which the flues of several wards converge, and in which extraction takes place at the rate of three hundred to four hundred feet a minute. In this current he suspended glass plates smeared with glycerin for a

* Loc. cit.
† Cincinnati, 1883.
‡ Discussion before the Vienna Medical Society, Wiener Med. Presse, 1883.
§ Deutsche Med. Wochenschr., No. 11, 1883.
‖ London Medical Record, March 15, 1883.

¶ Quoted from the London Lancet, July 28, 1883.

period of five days. The plates were then washed with distilled water, the fluid mixed with a little mucilage and evaporated down to half, and the residue tested for bacilli, which were found in fair abundance."

R. C. Smith* "succeeded in demonstrating bacilli in the breath of consumptive patients by making them breathe through two thin sheets of gun-cotton placed in the outer compartment of an ordinary respirator. This layer of cotton is then converted into collodion, run in thin films on slides, and stained for bacilli."

A. Ransome,† on examining the breath of several advanced cases of phthisis, found specimens of bacillus in two cases, while in several other cases the organism was not found, and it was not found in the aqueous vapor condensed in the waiting-room of the Manchester Consumption Hospital. The collections had been made by exposing cover-glasses smeared with fresh white of eggs or a little mucus for a certain length of time. Gibbs's method was used in staining.

Celli and Guarneiri‡ made similar examinations with quite different results. They were unable, after the most careful search, to find tubercle-bacilli in the air of an unventilated room in which phthisical patients had been sleeping. The expired breath of those patients was likewise found to be entirely free from bacterial contamination. Nor could the tubercle-bacilli be discovered in air which had been passed through the sputa of tuberculous patients, although in every case the expectorations were found to contain them in large numbers. (They were also unsuccessful in attempts at inoculation with fluids impregnated with this presumably vitiated atmosphere.)

Profs. Sarmoni and Marchiafava§ examined the breath of a number of phthisical patients for bacilli, with absolutely negative results. (They conclude that phthisis is not directly contagious, but might be indirectly so by means of dried, powdered sputum, which floats as dust in the air.)

V. Wehde‖ made, under direction of Bollinger, in Munich, the following experiments in relation to examination of air. Plates smeared with glycerin were exposed for forty-eight hours in closed rooms in which there were a number of advanced acute cases of phthisis. No bacilli could be found after applying the usual tests in the appropriate manner. (He further testifies that after injecting the material collected, as above stated, into the peritoneal cavity of eleven rabbits and guinea-pigs, no tuberculosis was produced.)

5. *Comparative studies of animal tuberculosis.*—Spontaneous animal tuberculosis is unquestionably identical with human tuberculosis. There are a few morphological specializations, which I mentioned in a former chapter,—*e.g.*, in tuberculosis of birds and in bovine tuberculosis or pearl-disease; but the essential, peculiar histological features are the same in all. Tubercle-bacilli appear also to be present in nearly all cases of spontaneous animal tuberculosis. I detected bacilli in a tuberculous bronchial lymph-gland from a phthisical tiger, which I had kept in alcohol for eight years, and in one from a monkey of more recent date; and several times I found bacilli in spontaneous bovine, chicken, rabbit, and guinea-pig tuberculosis. I also studied tuberculosis in the bear, lion, leopard, and in a large variety of apes (dead of typical consumption, from the Zoological Garden), with results identical with those obtained from studies in man. But this was long before the "outbreak" of the "bacillary campaign," and consequently Koch's parasite was not looked for in these latter cases.

Bollinger¶ found bacilli in the udder of a cow affected by pearl-disease (bovine tuberculosis).

There are no observations on record concerning the occurrence of tubercle-bacilli in the excretions and the manure of animals affected by tuberculosis (sputum is not produced by animals),—not even any reliable observation of bacilli in the milk.

Artificial or induced tuberculosis in animals will be considered in connection with the experiments farther on.

6. *The occurrence of bacilli in lesions and substances other than tubercular.*—Bacilli not distinguishable from tubercle-bacilli are met with in lupus and leprosy. The bacillus met with in lupus is unquestionably identical with the tubercle-bacillus, as is evident from the investigations of Max Schül-

* British Medical Journal, January 20, 1883.
† British Medical Journal, December 16, 1882.
‡ Quoted by the New York Record from the Gazzetta degli Ospitali, No. 56, 1883.
§ Annali Universali di Medicina, September, 1883.
‖ Prager Med. Wochenschr., January, 1884.
¶ Centralblatt f. d. Med. Wiss., August 18, 1883.

ler, Pfeiffer,* Dontrelpont,† and Babès and Cornil.‡ Yet the dermatologists are hardly inclined to recognize lupus and tubercle as inseparable, there being already a defined tuberculous lesion (the scrofuloderm) on the dermatological list, and, further, they refuse to identify the two lesions on clinical and anatomical grounds.

The bacillus of leprosy, in specimens which I had the opportunity to examine, appears to me also perfectly identical with the small forms of tubercle-bacilli; although the lepra-bacillus may perhaps look more sharp-pointed to the eyes of others and may fail to take the brown stain. There is nothing surprising in the fact that the same species of bacillus inhabiting soils of different character and different chemical composition, perhaps, may acquire varying micro-chemical properties and slight modification in shape. The experiments and evidence of Damsch,§ Caposi,‖ and Hansen¶ further suggest the identity of leprous- and tubercle-bacilli in their effects. There is no reason to believe that leprosy is a variety of tuberculosis, yet we must either declare lupus, leprosy, and tubercle to be identical lesions, or else declare the tubercle-bacillus not to be peculiar to tuberculosis.

I observed bacilli not distinguishable by the shape and micro-chemical tests from tubercle-bacilli in the false membranes in two cases of diphtheria and in one case of scarlet fever with extensive pseudo-membranous angina. Two of these cases proved fatal; the autopsies did not reveal tuberculosis in any part of the body. The false membrane was prepared by crushing it between two cover-glasses, and was treated like sputum.

George Bodamer** discovered tubercle-bacilli in some of the lesions of actinomycosis bovis.

In syphilis of the lung the cheesy material and the sputum (as above stated) were found to contain tubercle-bacilli by Levinsky,†† and also by Koryanyi.‡‡

Lichtheim§§ and Craemer‖‖ may be mentioned yet in this connection as having each found the tubercle-bacilli, or bacilli like them in every respect, in the fæces of a number of non-tuberculous patients, as well as in the tuberculous. This is, however, energetically contradicted by Gaffky, of Koch's laboratory, on the ground that he (Gaffky) failed to discover in fæces of normal persons in Berlin any bacilli which reacted to micro-chemical tests like tubercle-bacilli.

The discovery of Professor Balogh¶¶ that bacilli similar to tubercle-bacilli are found in the marshes around Pesth, Koch also tries to demolish by the statement that such bacilli were not detected in the mud of a Berlin city canal.

In sections of phthisical lungs I often observed masses of bacilli in those portions which were without tubercles, but which were affected secondarily by simple acute inflammatory changes and the air-vesicles merely stuffed with exudate undergoing rapid disintegration (coagulation necrosis); while the real tubercle-tissue contained no bacilli, or sometimes only a few in the giant cells. I think Prudden*** also noted this.

Surveying now the whole question of the habitat of the bacillus tuberculosis, it becomes evident that Koch's dogma—that only that is tuberculosis, and everything is tuberculosis, where his bacillus is found—is overdrawn and cannot bear criticism. It would be much safer to reverse this proposition, and to *consider that bacillus alone a tubercle-bacillus which inhabits evident tubercular lesions* or their products,—*e.g.*, sputum, and nothing else. For we have no difficulty in diagnosticating under the microscope a tubercle without the bacillus; but *a dilemma arises at once if we see questionable bacilli without the tubercle, or outside of sputum.*

VI.—EXPERIMENTS AND EVIDENCE, "PRO" AND "CONTRA."

It has been shown that the clinical evidence in reference to the contagiousness of phthisis is so meagre that assertions as to its parasitic origin are unwarranted (see chap. iv.). Moreover, statistics negative such theory. This being the case, it would seem as if experimenters are trying to prove that which is not the reality.

The testimony of the defenders of this

* Deutsche Med. Wochenschr., No. 19, 1883.
† Monatsheft f. Praktische Dermatologie, No. 6, 1883.
‡ Loc. cit.
§ Centralblatt f. d. Med. Wiss., July 21, 1883.
‖ Wiener Med. Woch., No. 2, 1883.
¶ Hospitals-Tidndee, No. 32, 1883.
** Inaugural Thesis, Univ. of Penn., 1884.
†† Loc. cit.
‡‡ Loc. cit.
§§ Fortschritte der Med., vol. i., 1883.
‖‖ Sitzungsbericht der Societät in Erlangen, December 11, 1882.
¶¶ Wiener Med. Wochenschr., No. 51, 1882.
*** Loc. cit.

theory, however, appears strengthened since the publication of the discovery of the bacillus and of the experiments of Koch. This is to be in a measure explained by the impression which Koch's well-constructed article made upon the minds of some of our leading clinical teachers, who involuntarily felt themselves induced to teach and to write about the doctrine of the contagiousness of phthisis. The profession at large does not care for Koch's discovery, whatever its value may be; but the opinion of the leading clinicians endorsing such discovery forms a guide, and may prove one of the most efficacious means of influencing the profession in regard to the question of the contagiousness of phthisis.

Having arrived, from my own experiments, at conclusions different from those of Koch, I thought it at present timely to announce at least the results of my observations, as my detailed report cannot appear for some months to come. It is my personal observations, together with my conclusions obtained from a careful perusal of the control experiments and of the records of the observations of others, which have determined my present attitude in the question of the etiology of tuberculosis.

The total evidence *pro* and *contra* gives me the impression that the doctrine of the contagious character and parasitic causation of tuberculosis cannot be sustained.

I will now submit a brief analysis and summary of experiments made and evidence offered in relation to the question of the parasitic origin and specific nature of tuberculosis.

For the establishment of a theory in regard to a parasitic origin of a disease by means of experiments on animals, etc., the following propositions must be affirmatively decided:

1. The disease produced experimentally in animals by means of inoculation with products of the human disease must be proved to be identical with the disease occurring spontaneously in man.

2. There should be some evidence showing that inoculation in man is followed by the same results as follow the inoculation of the same material in animals, and that the disease is really contagious.

3. There must be found a definite parasite at the beginning of the diseased process in all cases and in all tissues involved by the disease, and in sufficient quantity to account for the changes.

4. Given a parasite that is the cause of the disease, its action should be specific, —*i.e.*, it alone should be the causative factor, and should, when isolated and inoculated into an animal liable to the disease, always produce that disease.

5. The lesions of a disease resulting from the inoculation of a specific parasite must also contain that parasite and the specific properties of reproducing the same disease when re-inoculated.

6. Finally, a given parasite and no other substance should, the conditions remaining the same, be capable of producing the disease.

Koch makes an effort to answer all the above propositions in the affirmative in reference to tuberculosis. As a thorough and experienced mycologist, he knew well that this is unavoidably necessary in order to establish the etiological relation of his bacillus to tuberculosis.

Tuberculosis was known before Koch to be inoculable, and was, upon popular notions and traditionally, regarded by some as a contagious disease. Taking such theory for granted, it was necessary to find the parasite. In fact, Klebs, Toussaint, Max Schüller, and Aufrecht made excellent investigations, which even suggested the parasitic nature of tuberculosis, although the proofs offered by these investigators were not sufficient.

Koch's investigations, with his superior advantages, methods, and diligence, have been crowned with better success, and have brought forward facts of standing and permanent value to mycology, botany, and partly to medicine. His evidence in the question of the parasitic nature of tuberculosis is strong, but his conclusions from this evidence were overdrawn and too hasty. They are, thus far, not so much justified as he and his followers think they are. There is great lack of that absolute proof that is necessary for the settlement of a question of such magnitude and social importance.

Koch has, in relation to tuberculosis, brought forward definite affirmative proof for only some of the above-stated propositions, and this, again, *only partial*. Valuable contributions to this end have been also made by others. But we must have *full proof for each and all* of those propositions, and these must be really applicable

to tuberculosis, before we can accept the theory of a parasitic character and of the contagiousness of this disease.

Submitting, now, a brief criticism of the bacillus theory of Koch and his followers, I will take up separately each of the above-stated propositions, all of which it is necessary to prove in the affirmative before there is any reason for the establishment of such a theory in regard to tuberculosis.

1. *The disease produced experimentally in animals by means of inoculation with products of human disease must be proved to be identical with the disease occurring spontaneously in man.*

In favor of the identity of human tuberculosis with that produced experimentally in animals there has been brought forward the fact that the products in both contain identical bacilli. But this surely does not prove the identity, because similar bacilli may be found in the lesions of various kinds of processes, resulting in cheesy products. (See bacillus chapter.) Besides, there are many spontaneous and artificially-induced tubercular lesions in which bacilli could not be demonstrated. Hence we cannot rely upon the bacilli as a proof for the identity of the lesions.

Koch and those who imitated his experiments diagnosticate and declare all those artificially-induced lesions as tubercular which occur in nodes and in which they found the tubercle-bacillus, without taking (so far as I know) into consideration any structural peculiarities or other conditions. Now, tubercle-bacilli will surely be found in the lesions, whatever these may be, as they were introduced into the animal in those experiments. Further, in the opinion of these gentlemen nothing is tubercle where there are no tubercle-bacilli. Therefore, how can we rely upon their statements as to what the lesions they induced in animals really were?

It is hardly within the province of the mycologist to teach us what is tubercle and what is not tubercle.

Tuberculous lesions with extensive cheesy changes and tissue-destruction, cavities, etc., such as occur spontaneously and often quite speedily in man or animals, cannot be induced experimentally by means of inoculation, unless very large quantities of some purulent tuberculous materials are used, and abscesses result. When an animal dies several or many months after the operation of natural tuberculosis, extensive caseation of the organs may occur.* The only kind of induced or artificial tuberculosis in animals which may be ascribed to the effects of inoculation is one that corresponds in naked-eye appearance to secondary miliary eruption of tubercle as occurring in man, —the acute miliary tuberculosis. This acute miliary tuberculosis in man, which I observed also in animals as a spontaneous disease, occurs only in wasting diseases accompanied by various grave symptoms, anæmia, and great emaciation; while the induced disease in animals occurs suddenly, and induces no symptoms, no blood-changes, no emaciation, etc.

In many instances where the experimenters have produced, by means of tuberculous materials, within two to eight days after the operation, a miliary eruption, it is not probable that those miliary nodes were tubercles, and were due to the effects of bacilli, which are known to grow extremely slowly, and it is not certain that the experimenters took pains to distinguish them from true tubercle, or were competent in all instances to do so. This is eminently true of the inhalation tuberculosis.

Tappeiner's induced inhalation tuberculosis of dogs,† so much relied upon by Koch and others for the establishment of the mode of the spreading of phthisis, and partly of the bacillus doctrine itself, has been proved to be a fiction. Tappeiner, as so often quoted, subjected dogs to an atmosphere heavily charged with phthisical sputum, so that the dogs were nearly bathed in the latter (known to contain bacilli) for weeks. But, in spite of this, the animals grew fat, if anything, and, after the lapse of a certain time, acquired local pulmonary affections in the form of nodules, not likely to have been tubercular in nature, of which only in one case were some observed in the liver and kidneys.

The experiments of Schottelius,‡ Wargunin and Rajewsky,§ Weichselbaum,‖ and of others,¶ and my own experi-

* I was much surprised last summer to see in Berlin, at the Hygienic Exhibition, in Koch's pavilion, specimens of the character just stated exhibited as inoculation-tuberculosis, and still more to hear the demonstrator explain (surely without being authorized by Koch) that these specimens were to demonstrate the rapid effects of the bacillus.

† Virchow's Arch., lxxiv., 1878, and ibid., lxxxii., 1880.

‡ Virchow's Arch., lxxii., 1878, and ibid., xci., 1883.

§ Vratsch, No. 6, 1882.

‖ Centralblatt, No. 19, 1882.

¶ To the same conclusion, I hope, will also come my esteemed friend Prof. Brose, if he repeats his experiments published in the Medical Record, January, 1884.

ments also (to be reported subsequently), make Tappeiner's assertions perfectly untenable. Tappeiner's own account of his experiments and the microscopical description of the structure of Tappeiner's "tubercles" by Grawitz and Friedlander in Virchow's institute clearly indicate that he had nodular broncho-pneumonic foci, and not tubercles. (See explanation of these formations in the first chapter of this paper.)

I will, however, show later that pulmonary tuberculosis may occasionally be produced in rabbits by these means.

Furthermore, the bacillus theorists assert that inoculation-experiments, and these alone, can prove the tubercular nature of the nodular eruptions obtained artificially in animals. The identity with human tubercle is considered established, because inoculation nodes from the animal and tubercles of man act alike. They claim that whatever can produce tubercle on inoculation contains the tubercular virus, and is tubercle. Under such conception, finely-powdered sterilized glass should be classed with tubercle, because it, as I can reaffirm now, is capable of inducing tuberculosis when introduced into the tissues of healthy animals.

The following deserves a passing mention. According to Orth* and Bollinger,† there is some doubt as to the identity of human and animal tuberculosis. The results of the experiments of both these observers show that tuberculosis could only be induced by feeding animals with materials from animal tuberculosis; while tuberculous materials taken from man had no effect upon animals when given as food. On the other hand, the Würzburg feeding-experiments upon man‡ prove that animal tuberculous materials have no effect on man.

Although, judging from my own experiments, there is to my mind no doubt that some forms of artificially-induced tuberculosis in animals acquire gradually characters which make them identical with the spontaneous tuberculosis in man or beast, yet I do not think it is at all proved that the lesions so rapidly arising from the effects of the inoculation with the bacillus of Koch are identical with tuberculosis in man. The proof, then, upon this point, the supreme one for the settlement of the question of the nature of tuberculosis, is yet to be furnished.

2. *There should be some evidence showing that inoculation in men is followed by the same result as follows the inoculation of the same material in animals, and that the disease is really contagious.*

In favor of the direct inoculability of tuberculosis in man the following is presented: At a recent meeting of the Académie de Médecine, M. Verneuil related the following history. In July, 1877, a house surgeon (*interne*) at the Ste. Eugénie Hospital, who performed all the post-mortem examinations, one day noticed a papule at the base of the nail of his third finger. The apex presented a white spot, and a few drops of pus escaped from it. It was frequently cauterized, but the phalanges became attacked, and a cold abscess spread over the back of the hand. After three years' treatment, having failed to produce any improvement, M. Verneuil amputated the finger. The house surgeon was believed to be cured, and practised in the provinces. Quite recently he has been again attacked by cold abscesses in the lumbar region, causing intense pain; during violent attacks of pain the arms exhibit clonic convulsive movements. M. Verneuil has operated a second time. He is convinced that his patient became inoculated with tuberculosis when performing a necropsy. A similar misfortune happened to Laennec. One day, when operating on a tuberculous patient, he slightly cut himself with a saw. A swelling appeared on the wounded part. Laennec cauterized it with antimony chloride. The swelling disappeared, but twenty years subsequently he died from tuberculosis.§ Is there any sense in these stories.

We have seen that clinical evidence and statistics do not elucidate a contagion for tuberculosis, and that the few isolated instances of apparent contagion offered cannot stand the test of scientific scrutiny. An infectious or contagious disease can have only one cause, and cannot be at one time due to a contagion and at other times arise from a variety of causes: hence the latter part of the proposition must be answered in the negative.

This being the case, the *parasitic* origin

* Virchow's Archives, vol. lxxvi.
† Arch. f. Exper. Path., vol. i.
‡ Schottelius, loc. cit.

§ Paris Correspondence of the British Medical Journal, quoted by Boston Med. and Surg. Journal, No. 10.

must also be denied it, as a necessary consequence.

As to the first part of the proposition, too little is known of scientific observation upon this point in regard to tuberculosis. According to the exhaustive investigation of Dr. Law,* there is no evidence that tuberculosis has ever been conveyed through vaccination.

I must mention, though, an actual inoculation-experiment upon man, not so much on account of its inherent value, as because it has been quoted with great reliance in support of the infectiousness of tuberculosis. Demet, Paraskeve, and Zallonis, in Syra, Greece,† "inoculated a man of 55 with tubercle. He was suffering from gangrene of the left great toe, due to the obliteration of the femoral artery, and his death was inevitable, as he had refused to submit to amputation. His lungs were carefully examined and found to be sound. They inoculated the upper portion of the right leg with sputa from a man who had abscesses in his lung. Three weeks later there were signs of commencing induration at the summit of the right lung. The patient died on the thirty-eighth day after the inoculation, from gangrene. At the necropsy there were found at the apex of the right lung seventeen small tubercles, varying in size from that of a mustard-seed to that of a lentil. Two similar tubercles were found in the left apex, and two others in the liver. The experimenters concluded that the embryonic state of the tubercles and their limited number were due to the short time since the inoculation."

This isolated experiment, as well as any of the experiments on animals, is valid only when we take it for granted that the experimenters are able to differentiate spontaneous from artificially-induced tuberculosis. This is not probable in the case just quoted. We are told that the man experimented upon was suffering from an exhausting disease, and it is well known that at least one-third of the autopsies in such cases reveal tubercular disease.

Directly bearing upon the proposition under consideration are again those Würzburg feeding-experiments, in which material known to be infested by tubercle-bacilli was used, often raw, for years as food, under strictly scientific supervision, with absolutely negative results, and which tended to show that man does not react at all upon the tubercle-bacillus.

3. *There should be found a definite parasite at the beginning of the diseased process, and in sufficient quantity to account for the changes in all cases and in all tissues involved by the disease.*

In relation to tuberculosis this proposition cannot be answered in the affirmative; and it is by no means as definitely settled as some high clinical authorities hold with Koch, that there is but one "specific parasite" in tuberculosis.

Klebs,‡ Toussaint, and Schüller§ have observed *micrococci* to be constantly present in tuberculous lesions and products (and have induced artificially the disease with the isolated micrococci), and no one has *proved* anything to the contrary; while Koch and Baumgarten‖ discovered *bacilli* in the same lesions. Koch claims for his bacillus more than is consistent with the laws of physiological and pathological life and sound argumentation, and more than is in correspondence with the actual proofs offered in relation to the pathogenetic properties of this bacillus.

The reports of some competent microscopists and pathologists (when the originals are examined) show that the tubercle-bacillus is not invariably present in all cases and all products of tuberculosis; and, if present, it is often not seen in sufficient quantity to ascribe to it the claimed significance; and, furthermore, it is, as a rule, not present in the beginning of the disease. On grounds of personal investigation I can offer similar testimony.

The bacilli should be present in every lesion and in all cases and in the beginning of tubercular disease, and not chiefly in its degenerated products, if tuberculosis is to be called a parasitic disease, in accordance with the laws of pathology. In all well-established parasitic diseases the parasite is a necessary factor and is invariably present,—unless there should be established for the "tubercle parasite" an exceptional, new, and mysterious mode of action.

The truth of the matter appears to be, and, indeed, from my daily observations

* National Board of Health Bulletin, No. 40, 1882.

† Quoted by Med.-Chir. Review, October, 1874, from Gazette Médicale, 1872, page 192.

‡ Klebs now admits the bacilli, but denies that they are invariably present, and denies on grounds of experiments their exclusive pathogenetic properties, although he admits that they are a not unimportant admixture to his micrococci.

§ Loc. cit.

‖ Loc. cit.

in the laboratory upon a large quantity of material, I regard it as a fact, that the tubercle-bacillus of Koch is a mere concomitant of cheesy disintegrated materials, even if it be pre-eminently of tuberculous cheesy materials.

4. *Given a parasite that is the cause of a disease, it should, when isolated and inoculated into an animal liable to that disease, always reproduce that disease; but its action should be specific,—i.e., it (the parasite) alone should be the causative factor.*

There is no doubt that Koch's tubercle-bacillus when isolated and cultivated for many generations and then inoculated into certain animals is capable of inducing tuberculosis, or a nodular eruption not distinguishable from it, more readily than other irritants, so far as tried. Success in inoculating is particularly frequent in rabbits and guinea-pigs (although not so common as Koch claims), but only conditional and rare in other animals.

Thus it appears that the above proposition could be answered for tuberculosis and the bacillus in the affirmative if only the following points were proved:

1st. That the nodular lesion thus induced is really tuberculosis, identical with the human disease.

2d. That this bacillus is the only bacterium or the only irritant capable of inducing tuberculosis; and,

3d. That its action is specific,—*i.e.*, that the bacillus is the only agency or factor at work, the sole cause of the disease.

The first point is not proved, as probable as it may appear. The other points are open to the following considerations and objections:

It has been proved that in tuberculosis micrococci, as well as bacilli, are causal, the evidence being "strong" for either "parasite;" whereas the bacillus alone should be the causal factor. As long as not *disproved*, Klebs's, Toussaint's, and Schüller's investigations (in relation to the micrococci as causal factors) have as much claim as Koch's. The method of cultivating those tubercle-micrococci, as practised by those investigators, was one not favorable for the development of the tubercle-bacilli. Further, Watson Cheyne's assertion that bacilli *must have been* present in the cultured materials with which those investigators inoculated successfully, is altogether a gratuitous assumption, and his few and imperfect control experiments with Toussaint's micrococci were not satisfactory, and, in fact, neither prove nor disprove anything.* Koch did not try the effects of any other fungus than that of his bacillus in relation to tuberculosis.

Koch further claims that the specific character of his bacillus is supported by the rapidity of its effects, and brings forward the inhalation experiments of Tappeiner and the experiments upon the eye. The former I have shown to be valueless, as those nodules produced in the lung, especially if rapidly formed, are not tubercles. I have also reason to believe that the same is the case with many of the experiments on the eye, especially in those cases in which an apparently acute miliary tuberculosis of the lung rapidly followed the inoculation: in fact, in some instances this eruption occurred in a much shorter time than is at all possible for tubercles to develop.

Koch has not proved that his bacillus is the only agency at work in the production of tuberculosis. Although he undoubtedly inoculated the pure bacillus, he ignored the specific reaction of the soil; and it is the latter which I hold plays the most important *rôle* in determining the formation of tubercle. In introducing the bacillus into the animal organism, another factor —the injury inflicted, and its effects upon the living cells of the body—must be taken into consideration.

In some animals all the tissues of the body react equally upon the introduction of irritants; in others only some one of the tissues responds, such as the serous membranes. This surely demonstrates the specific action of the soil.

I must again call attention to the fact that in making his experiments Koch injected the bacilli into any part indiscriminately in scrofulous animals, while in non-scrofulous animals (dogs, rats, cats) he injected them only into the peritoneum or the anterior chamber of the eye, where, we know from experience and from repeated experiments, any irritant of sufficient intensity may create tuberculosis.

This cannot be explained by the assumption of Koch that the bacillus must merely be enclosed in something so as not to be eliminated before it can exert its effect.

To me it appears that the reason why we must inoculate in serous cavities to pro-

* See Watson Cheyne's report, Practitioner, April, 1883, pp. 272–276.

duce tuberculosis in the dog or cat, is, because we want not so much the specific action of the irritant (say of the bacilli) as the properties of the serous membranes. It is now well known that any chronic inflammation of serous membranes may lead to primary tuberculosis. It is proved that we do have a primary tubercular synovitis or a primary tuberculous pericarditis; and that bacilli could be instrumental in its production is highly improbable.

In surface tuberculosis like that of the lung the bacilli, in my opinion, also play only a secondary *rôle*.

Koch himself admits that it is not likely that the bacillus when inhaled by man could get a foothold in a normal lung. He says distinctly in his original articles that the lung must be predisposed for the reception and the action of the bacilli. Under such predisposition he understands and enumerates the following lesions: "*desquamation of the epithelial lining of the respiratory tract, stagnating exudates and secretions in the lung, adhesions, anomalies of respiration,*" etc. Now, here is a matter of mere interpretation of these lesions. Koch innocently calls them "predispositions," while every pathologist will designate some of these lesions as suggesting already-existing pulmonary phthisis. In fact, at the present standing of our knowledge of pulmonary phthisis we can have no desquamation of the vesicular epithelium without preceding tubercular infiltration.

Watson Cheyne is also considerate enough to say,* " . . . it seems to me that the lung must in addition be prepared for the reception of the bacillus, as may be the case if congestion or slight inflammation be present at the time of the inhalation of the organism."

That in inoculations into serous cavities the latter do not act merely in preventing the bacillus from escaping or being eliminated, and that the stagnating secretions in the lung do not act merely as a glue to retain the bacillus in order to allow the accomplishment of its effects, is, to my mind, proved by the following experiments of Bollinger. Bollinger,† in order to show that tuberculosis could not be transplanted by vaccination, made superficial *cutaneous* inoculation in rabbits with tuberculous materials with negative, and deep *subcutaneous* inoculations with the same material, followed by intense inflammation, with positive results. In both cases the wounds were covered by a layer of collodion to prevent the "elimination" of the bacillus.

Thus it appears that the bacilli by themselves have no effect upon the healthy organism or the normal tissues. A predisposed soil is the chief factor and is preeminently necessary for the production of tuberculosis; while, on the other hand, it is not proved at all that the bacillus is invariably necessary for the production of tuberculous lesions. Although the tubercle-bacillus is more liable to excite tuberculosis in an already inflamed and ill-nourished soil than all other simple irritants so far tested, it (the bacillus) might be readily substituted by other irritants.

The matter must unquestionably be tested further, but from the above evidence it is clear that a general fear of the bacillus tuberculosis as a contagion is unjustifiable, and that the ordinary dust suspended in the air is to certain persons as dangerous as the bacillus.

5. *The specific lesions of a disease resulting from the inoculation of a specific parasite must also contain that parasite, and have the specific properties of reproducing the same disease when re-inoculated in other animals.*

Koch claims that the products obtained in animals by inoculation with bacilli are capable of producing tuberculosis when inoculated into a second animal, while the products obtained by inoculation with innocuous substances do not have this effect. The former proposition is true, but the latter, I hold, is not in accordance with facts. In my own experiments, to be detailed in my forthcoming report, tubercles produced by inoculation with innocuous material under antiseptic precautions were likewise capable of producing tubercles when inoculated into other animals, having thus the same action as the innocuous material primarily used.

I have also shown above (see bacillus chapter) that in secondary tuberculous products bacilli may be absent.

The experiments of Martin,‡ which tend to show even the progressive virulence of products obtained from re-inoculation with tuberculous material in a series of animals, have been substantiated by no one.

* Loc. cit., p. 314.

† Zur Aetiologie der Tuberculose, Prager Med. Wochenchrift, Nos. 4 and 5, 1884.

‡ Journal d'Anatomie et de Physiologie, April, 1881.

Martin's assertion also, that inoculations with products obtained by the introduction of innocuous substances never produce true tuberculosis, and that after a series of re-inoculations these products lose their power of acting even as local irritants, is, according to control experiments, positively wrong. On the other hand, views have been expressed, based upon experiments (I think also by Martin), that products obtained by inoculation with non-tuberculous substances when re-inoculated may gradually become specific, and increase in virulence in producing tuberculosis.

6. *Finally, a given parasite and no other substance should, the conditions remaining the same, be capable of producing a parasitic disease.*

In my previous studies, judging from the literature alone, I was fully impressed with the idea that tuberculosis had a specific exciting cause, and that it could be induced by inoculation with tuberculous materials. Moreover, having made numerous inoculations with tuberculous matters, I convinced myself of this fact. Hence I accepted the view that tuberculosis is inoculable in certain animals.

But, at the same time, after repeating, under various modifications, the well-known control experiments, I found that, beyond doubt, even true tuberculosis could be induced by substances other than tubercular, and that failures to induce tuberculosis with tuberculous materials were in certain animals nearly as common as successful inoculations with innocuous substances.

To these experiments I will return in my forthcoming report.

It will be also necessary to first consider the evidence of those observers who, from the results of their own exhaustive experiments, negatived the exclusive or specific infectious properties of tuberculous materials. This negative evidence is by far more voluminous and strong than the admirers of the hypothesis of the contagiousness of tuberculosis suppose; excited admirers having especially arisen since the ingenious article of Koch appeared.

It is, however, remarkable that some of the writers on tuberculosis fail to understand that the pivot of the question of the etiology of tuberculosis does not rest upon the fact alone whether or not the bacillus induces lesions analogous to tuberculosis, but pre-eminently upon the fact whether innocuous substances have or have not the same effects.

Thus, above all, the negative evidence must be carefully inquired into, not by relying upon the crippled and sometimes misrepresenting and meagre quotations of some of the compiling writers, but by submitting the original communications of the authors and experimenters to a careful perusal.

Together with the accounts of the much-quoted experiments of investigators who succeeded in inducing tuberculosis in animals with tuberculous substances only, the reading and thorough examination of the records and results of experiments of the observers to be mentioned below are unavoidably necessary.

The following observers all refer to many or few experiments of their own in which tuberculosis resulted from the inoculation with either innocuous substances or with specific matters other than tuberculous:

Lebert, *Allgem. Med. Central-Zeitung*, 1866.
Lebert and Wyss, *Virchow's Archiv*, vol. xl., 1867.
Empis, *Report of the Paris Internat. Med. Congress*, 1867.
Burdon Sanderson, *British Med. Journal*, 1868.
Wilson Fox, *British Med. Journal*, 1868.
Langhans, *Habilitationschrift*, Marburg, 1867.
Clark, *The Medical Times*, 1867.
Waldenburg, *Die Tuberculose*, etc., Berlin, 1869.
Papillon, Nicol, and Laveran, *Gaz. des Hôp.*, 1871.
Bernhardt, *Deutsch. Arch. f. Klin. Med.*, 1869.
Gerlach, *Virchow's Archiv*, vol. li., 1870.
Foulis, *Glasgow Med. Journal*, 1875.
Perls, *Allgemeine Pathologie*, 1877.
Grohe, *Berliner Klin. Wochenschr.*, No. 1, 1870.
Cohnheim and Fränkel, *Virchow's Archiv*, vol. xlv., 1869.
Knauff, *41te Versamml. Deutsch. Naturforscher*, Frankfort.
Ins, *Arch. f. Experim. Pathologie*, vol. v., 1876.
Wolff, *Virchow's Archiv*, vol. lxvii., 1867.
Ruppert, *Virchow's Archiv*, vol. lxxii., 1878.
Schottelius, *Virchow's Archiv*, vol. lxxiii., 1878; *ibid.*, xci., 1883.
Virchow, *Virchow's Archiv*, vol. lxxxii., 1880.
Stricker, *Vorlesungen über Exp. Pathologie*, Wien, 1879.
Martin, *Med. Centralblatt*, 1880, No. 42.
Wood and Formad, *National Board of Health Bulletin*, Supplement No. 7, 1880.
Robinson, *Philadelphia Med. Times*, 1881.
Weichselbaum, *Med. Centralblatt*, No. 19, 1882, and *Med. Jahrbücher*, 1883.
Balough, *Wiener Mediz. Blätter*, No. 49, 1882.
Wargunin, *Allg. Med. Centralblatt*, April 8, 1882.
Hänsell,* *Arch. f. Ophthalmologie*, vol. xxv.

* Hänsell, who inoculated animals with gummous growths and syphilitic pus, obtained an exquisite miliary tuberculosis from the effect of these substances. In this connection may also be mentioned the following:

Damsch (*Centralbl. f. Med. Wissen.*, July 21, 1883), who obtained tubercular eruptions and nodes in the brain in rabbits through inoculation into the eye with the cultivated bacilli of leprosy. Similar inoculation with leprous material led to a perfect miliary tuberculosis in rabbits in the hands of Kaposi, of Vienna (*Wiener Med. Presse*, January 21, 1883).

Pfeiffer, Dontrelpont, Cornil and Babès (loc. cit.) had the same experience with lupous material.

Bodamer (Inaugural Thesis, Univ. of Penn., 1884) had, as the result of inoculating with the pure cultivated actinomyces fungus, a striking general miliary tuberculosis in rabbits.

Inoculation with materials from glanders gives also rise to tubercles in the lungs, etc., not distinguishable under the microscope from true miliary uberculosis. But Löffler, who kindly

Some of the observers enumerated did not consider the miliary eruptions obtained experimentally as true tubercles, but the majority did so, and, as I will show later, presented excellent and reliable experiments and sound reasoning in support of their views.

Shall all the above evidence go for naught merely because Koch has discovered a bacillus which is capable of inducing in animals lesions resembling tuberculosis?

I trust it will not. Koch has, so far, no authority to claim *exclusive* pathogenetic properties for his bacillus, as he made himself no satisfactory control experiments with substances other than tuberculous. The few control experiments he offers, viz., that *sterilized* blood-serum (!), tuberculous material soaked in alcohol, and fresh scrofulous glands, or pus from tuberculous lesions, did not induce tuberculosis, prove little or nothing in favor of his bacillus.

Watson Cheyne, in his excellent report,* displayed great care, diligence, and skill in his experiments and observations intended to corroborate Koch, but in making his control experiments he likewise was not very particular. So in relation to inoculations with non-tuberculous substances he came to the conclusion that "not one of the twenty animals (inoculated with innocuous substances) became tuberculous"! But when the detailed account of Watson Cheyne's experiments is read over, it is amusing to learn that only nine out of the twenty-five supposed negative experiments were really known to be negative, because eleven of the rabbits experimented upon had been stolen before Cheyne had a chance to examine them, two rabbits died within a few days, or long before tubercle could develop, and in three rabbits the experimenter really records lesions that might have been tuberculous, in spite of the absence of bacilli in them, which latter circumstance, however, induced him to call the result a negative one.

These are instances of the way in which experimenters with preconceived and peculiar ideas upon a subject may unconsciously be misled in forming conclusions from their own experiments.

Further, it is interesting to note that in the "classical" experiments of Solomonson,† Baumgarten,‡ Tappeiner,§ etc., among other substances, the following materials were used extensively for control: "caseous glands from scrofulous child," "caseous material from various sources," "muscle, testicle, and kidney from tuberculous guinea-pig," "cheesy pus from man and animals, cheesy infarcts, caseous tumors," etc. All these substances, which are known usually to contain the bacillus, were inoculated while fresh into animals, and are recorded by the experimenters above stated as having failed to produce tuberculosis. This is surely not consistent with the doctrine of Koch.

Wherever inoculation with innocuous substances was followed by positive results, the over-zealous germ-theorists call it "*accidental tuberculosis.*" They say that at the time of former experiments the communicability of tubercle by a mediate contagion was not recognized, and as the precautions necessary for thorough disinfection of instruments, surroundings, etc., were probably not observed, the channels for the introduction of the *bacillus* were in all previous experiments left unguarded: hence, they argue, *it must have been* this ubiquitous bacillus which induced the tubercle. ‖

Further admitting, however, that innocuous substances may induce tubercle-like bodies, they claim that these bodies are not infectious, *i.e.*, they are *false* tubercles.

demonstrated to me this fact in Koch's laboratory, and who also gave me a specimen demonstrating it, explained that the nodules in the lungs were not tubercle, because the bacilli found therein behave differently in staining.

* Loc. cit.

† Aftryk fra Nord. Med. Arkiv, vol. xi., 1879.

‡ Loc. cit. § Loc. cit.

‖ In this connection the following incident is interesting, particularly on account of the high authority of the observer:

Some experiments were made under the supervision of Virchow (*Berlin. Klin. Woch.*, 1880), principally with the view of testing whether the milk of animals affected with "pearl-disease" or bovine tuberculosis could reproduce the disease when fed to other animals. Virchow's own objection to experiments of this kind is that the various chronic inflammatory processes which occur spontaneously in animals are not sufficiently well known even to veterinary specialists. Further, in pigs, which he used in considerable numbers, scrofulous glands occur so frequently, from their alliance to man through their omnivorous habits, and their detection during life is a matter of such great difficulty, that results founded upon their presence must be accepted with great caution. The possibility of coincidence was also well illustrated by two cases in which several animals were found to be tuberculous after having taken the milk for some time from a cow which was diagnosticated during life as affected with bovine tuberculosis, but whose lungs were found at the autopsy filled with echinococcus cysts, and with no trace of tuberculosis.

The milk of another animal which subsequently was found to be profusely affected by bovine tuberculosis had, on the other hand, no effect when given as food to a number of healthy animals.

The only result that Virchow thinks is perhaps justified from these experiments, is that more animals were found to be tuberculous among a certain number which had been fed upon the "pearly" milk than among the same number which had been fed upon healthy milk.

(The above statements, first quoted by Dr. Whitney, of Boston, Professor Virchow corroborated in a conversation with me upon this subject last summer. H. F.)

All these objections would be very plausible if they were based upon actual observations and facts; but, unfortunately for the bacillus theory, they are not: they are *mere unfounded assumptions.*

The fact established by experiments, that a true tuberculosis can be induced in animals by inoculation with innocuous and various other substances, and the significance of this fact, can surely not be overthrown by the imperfect evidence that the bacillus is more liable to do so, and still less by the mere unauthorized opinions of some of the writers.

Erroneous conclusions and views may easily be formed through the misconception of the significance of experiments.

At the meeting of the Pathological Society of London (December 4, 1883, quoted from the *Lancet*, December 8, 1883), Dr. Wilson Fox announced the following: "He was unwilling that his former observations* should still be quoted as opposed to the doctrines of Koch and those who had been more recently working at the subject; and therefore he had felt bound to come forward and make known the modification which his views had undergone. At the same time," Dr. Fox, however, added, "there was perhaps some danger of phthisiophobia or phthisiomania. During the past thirty years there had been many changes in the doctrine of phthisis, and hardly any doctrine has lasted more than five years."

But what had happened to induce Dr. Fox to lose faith in his own honest and excellent former work? So far as I could learn, it was the following. Dr. Fox had requested a Dr. Dawson Williams to repeat his former experiments. This bacillus-excited gentleman introduced *carefully* some "*putrid fluids*" and some *setons* into a few guinea-pigs and—did not obtain tuberculosis! Now, they think, it was at once evident that in all the former successful inoculations with non-tuberculous materials the mischievous bacillus of Koch must have gained entrance.

The reasoning of the London gentlemen appears to have been here as follows: *Putrid matter and setons do not induce tuberculosis; but the bacillus does. Hence the bacillus is the sole specific cause!*

But what is gained or proved for the bacillus theory if any one given substance, when inoculated into an animal, does not induce tuberculosis? Does, through this, the necessity of contagion at once arise? Surely not. If, for instance, as I will prove, finely-powdered, sterilized glass is capable of inducing a true tuberculosis, then it does not matter if putrid matter or setons failed to do it.

Cohnheim's acceptance of a theory of a specific poison for tuberculosis, which formed, as its direct outgrowth, the basis of the bacillus theory, was also not justified from Cohnheim's own experiments. If he once succeeded† with innocuous substances in producing *peritoneal* tuberculosis, it is of no consequence that he subsequently‡ failed to induce an *iris-tuberculosis.*

Negative results prove nothing under the above circumstances and in the presence of positive results. Most of the observations made in bacillus studies prove really nothing for the etiology of tuberculosis, and some interpretations of the results of experiments in this direction are quite deficient and not consistent with the principles of experimental pathology. Furthermore, some of the positive evidence must be excluded on account of the evident deficient knowledge of pathological anatomy on the part of some of the experimenters.

I am glad to be in the position to offer in my next communication a new series of observations and experiments on tuberculosis. These experiments, instituted under the auspices of Dr. Pepper, provost of the University of Pennsylvania, and executed by myself and assistants under all rules of scientific precautions and with full facilities for such work, plainly demonstrate that *the etiology of tuberculosis does not rest with Koch's "parasitic" bacillus or any other "contagion."*

The experiments referred to will be given in full details in a special report now in progress and soon to be published with appropriate illustrations, etc.

I desire, however, to announce here that *my experiments prove that finely-powdered, sterilized glass, ultramarine blue, and other substances are by themselves capable of producing tuberculosis in animals or tissues liable to this affection.*

Further, I will offer proof that this effect (tuberculosis) ensues without the intercurrent

* Loc. cit.

† Loc. cit.

‡ Sitzungsberichte d. Schlesischen Gesell., 1878.

action of any bacterium. And, finally, that in those instances where miliary, nodular eruptions have been induced by the tubercle-bacillus (or substances containing it), the action of the latter is a purely mechanical one, like that of simple irritants.

Further, these experiments show that the only advantage which the bacilli have over other finely-divided matter and simple irritants is that the former multiply and thus intensify their action, while mechanical irritants have not this property, and hence must be introduced in larger quantities. The more finely divided the matter, the more prompt seems to be its effect, and I believe it is impossible to render any matter more finely divided than the bacilli.

Like others, I also often succeeded in tracing the formation of the tubercle-nodules to the effects of the irritating particulate matter, if the latter were or could be made distinct enough to be seen within the nodes. When ultramarine blue was used for inoculation, granules of the latter substance were seen within the nodes; when bacilli were used to that end, then bacilli could be detected within the nodes. But in either case these primary nodular eruptions, *if rapidly formed*, do not yet represent tuberculosis, as I will show.

It is generally conceived that a specific infectious disease, such as instanced by variola, syphilis, anthrax, etc., can have only one cause or one poison, which will produce that disease and nothing else, and cannot be substituted by anything else.

For tuberculosis this is not true, for we have bacillary and non-bacillary forms of tuberculosis.

It is now no more a question of observation and experimentation, but rather one of interpretation and understanding of the results; for we have seen that the evidence from experiments and microscopical studies is nearly sufficient.

But there are misconceptions. If that only is tuberculosis where the bacillus of Koch is found, or that only which arises from the effects of this bacillus, then Koch's theory of the exclusive pathogenetic properties of the bacillus is correct, and under such a definition tuberculosis has only one cause. But if true tubercles exist and can be produced without the bacillus, which has been shown to be the fact, then Koch's theory cannot be accepted from a pathologico-anatomical stand-point; or else we are obliged to admit two or more kinds of tuberculosis,—one due to Koch's parasite, and others to a variety of causes.*

So far, however, we have no reason, from a pathologico-anatomical stand-point, to subdivide tuberculosis, and therefore I am of the opinion that Koch's view of the exclusive pathogenetic property of his tubercle-bacillus is decidedly overdrawn and even not warranted by facts. Neither the specific action of Koch's bacillus, nor the specific character of tubercle, nor the contagiousness of phthisis or of any form of tuberculosis, is proved.

Only after a complete harmony of the facts derived from pathologico-anatomical, experimental, and clinical studies in tuberculosis with those revealed by mycology, and not from either of these alone, can we arrive at a settlement of the question of the etiology of tuberculosis.

Further details concerning this question will be incorporated in my report. This will embrace also studies into the onset and the distribution of tuberculous affections.

From the above analysis of the bacillus question and of the etiology of tuberculosis the conclusions follow—

1. That the bacillus of Koch is a valuable diagnostic sign of tubercular disease.
2. That nothing is proved by its discovery for the etiology of tuberculosis.
3. That the too ready acceptance of the bacillus doctrine is not justifiable, and is likely to do more harm than good.
4. That neither phthisis nor any form of tuberculosis is contagious.

* A suggestion to separate an "infective" form of phthisis from ordinary phthisis has been made by Dr. Reginald Thompson (*London Lancet*, No. 6, 1880, quoted by R. S. Smith, Bristol, *Medico-Chir. Journal*, No. 1, 1883). "In a series of fifteen thousand cases observed, fifteen cases (only one per one thousand) proved to be of an infective kind,—viz., with history of contagion and absence of phthisical family history."

PATHOLOGICAL LABORATORY, UNIVERSITY OF PENNSYLVANIA, February, 1884.