Observations

ON

TUBERCULIN AS A REMEDY IN TUBERCULOSIS OF THE LUNGS.

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TUBERCULOSIS of the lungs is the commonest and deadliest disease that afflicts mankind, especially in civilized communities. It is so common, because for generations the very nature of the disease has deceived and disarmed mankind, and even nowadays, in spite of the certain knowledge of its infectious nature, methods of prevention that are generally adopted in plague and similar diseases are neglected or applied in a perfunctory fashion.

EARLY DIAGNOSIS.

It is so deadly because in the majority of cases the disease is well established before it is recognized. Turban tells us that, of 418 cases, only 11 came for treatment within a month of the appearance of the first symptoms, 103 within six months, and the majority—305—only after six months had elapsed. In the first group (11) permanent results were obtained in 72.7 per cent., in the second group (103) in 67 per cent., and in the majority (305) only in 40.2 per cent. How important early diagnosis is, and how rare. Whatever method of treatment we practise—whether rational, specific, or other—early diagnosis is the key to high success. Twenty years ago the early diagnosis of pulmonary tuberculosis was at most guesswork. Some correct diagnoses were made, but many mistakes. Cases of actual disease were overlooked, and healthy lungs were pronounced to be weak. After Koch's discovery in 1882 the test of tests was the demonstration of tubercle bacilli in the expectoration by certain stains. For many years this test dominated everything. Progress in knowledge has deprived even this test of most of its value. Valuable in certain cases in which the physical signs are absent or misleading, and in mild cases of mixed or concurrent infection, notably in influenza and pneumococcal and streptococcal infections; the discovery of tubercle bacilli in sputum by certain stains too often fails when it is most wanted. It fails as a test in early diagnosis, because the presence of tubercle bacilli in the sputum is itself a sign that disintegration of tissue has occurred. The great lesson of the last decade has been the paramount importance of detecting pulmonary tuberculosis in the first stage before tubercle bacilli escape into the air passages by the disintegration of the superficial tuberculous lesion, while, in fact, the tuberculous formation is still closed, or, in other words, shut off from the external world, represented by the air passages.

MIXED, SECONDARY, AND CONCURRENT INFECTION.

Moreover, Koch and his pupils have taught us that in the great majority of cases the tubercle bacilli play a relatively subordinate part in the severer forms characterized by fever, sweating, and wasting. By the light of Koch's methods as applied by Kitasato and Pfeiffer we have been guided to a clearer and a truer understanding of the variable picture that pulmonary tuberculosis presents to us in its manifold stages and phases. I admit that among English authorities there is still a strong tendency to look askance at, if not to disregard and belittle, the modern view of mixed infection, secondary infection, and concurrent infection. The term "mixed infection"—so full of light and meaning—was first used by Koch's distinguished colleagues, Ehrlich and Brieger, in 1882, in describing a case of typhoid fever complicated with malignant oedema, but Koch himself was the first to recognize the condition in pulmonary tuberculosis. In his own monumental work upon the etiology of tuberculosis one reads thus:

The combination of bacilli and micrococci as they appear in this disease belongs to the mixed infections, the existence of which appears to by no means rare.

In this case the infection was rather a concurrent than a mixed infection. An ulcer in the mouth was the source of a

coccal infection in a case of miliary tuberculosis running a rapidly fatal course.

The part of infection, independent of the tubercle bacillus—sometimes mixed, sometimes secondary, sometimes concurrent—occurring in any stage of tuberculosis of the lungs, may defy exact measurement by clinical methods, but nowadays it is hardly possible to overrate its importance when bacteriological methods are called to our assistance. Diagnosis, prognosis, and even treatment, demand a careful differentiation of the elements constituting these other infections. A careful analysis of these elements by recent methods is an important, perhaps a most instructive, basis of classification. Physical signs may mislead us in diagnosis and prognosis; symptoms may help us to distinguish the acute, the sub-acute, and the chronic—the treatment varying accordingly—but a discrimination of cases by the resources of bacteriological science gives us a basis at once definite and trustworthy. The full meaning and importance of mixed infection did not develop until the genius of Koch, which had guided and inspired the investigations that culminated in the production of the diphtheria antitoxin, proposed a new method of treating tuberculosis on an equally scientific basis.

TREATMENT BY TUBERCULIN.

The treatment of tuberculosis with tuberculin is specific. It is of no avail except for tuberculous diseases, and if other complicating conditions exist—if other micro-organisms are associated with tubercle bacilli in the morbid process—tuberculin may fail absolutely to arrest or modify the morbid process; indeed, tuberculin may then do harm, and perhaps even hasten a fatal issue. I fear that many men have learnt to their cost, and at their patient's expense, that tuberculin may be powerful for harm and powerless for good when the chief cause of the symptoms is not the tuberculous process at all, but the various infectious processes that may be quite beyond the physician's range of vision. Tuberculin treatment aims at a progressive process of active immunization, radically different from the passive process, in which antitoxic serum is supplied ready made. The passive process of immunization may be exploited with impunity and under any conditions. Active immunization, on the other hand, makes a larger demand upon the energy of the tissue cells, and requires that the cells and tissues should be in a relatively healthy state. In the presence of various micro-organisms, such as streptococci, the energy of the cells may be so depressed that active immunization by means of tuberculin cannot be expected. Tuberculin treatment, therefore, has limits unknown in the antitoxin treatment of diphtheria. The failure of tuberculin in 1891 was due to a disregard of the limitations and restrictions laid down by Koch himself, and to a general ignorance of the rôle of mixed infection in pulmonary tuberculosis. It was not that Koch's announcement was premature; it was rather that medical men, by a bitter experience, discovered themselves exploiting a remedy without having had the training essential to success. Failure in their hands was a foregone conclusion, and tuberculin as a remedy for tuberculosis had a mere mockery of a trial. The key to successful treatment with tuberculin is a proper selection of cases by means of bacteriological methods, or, these failing, by a judicious use of tuberculin itself as a diagnostic agent. There is, indeed, no royal road to success in the treatment of pulmonary tuberculosis, either by specific, rational, or other methods. Each case requires skill, judgement, experience, and in no small degree, patience; and, after all, the best and most conscientious efforts may be baffled by the intervention of conditions that can be neither foreseen nor prevented.

Indispensable to success is a thorough knowledge of the variable, complex, and treacherous condition—mixed infection. This mixed infection may even parade itself in the garb, and trappings of health. As a rule fever is the danger signal, and strongly suggests a secondary or mixed infection. Yet, in spite of the existence of fever, there may be no mixed infection, as in acute tuberculosis and in those rare forms of acute gelatinous caseous pneumonia which Fraenkel and Troje have have so well described. On the other hand fever may be absent, and yet mixed infection, with all its evils and dangers, may be imminent. Nothing short of a careful and thorough examination of the sputum by the methods of

Pfeiffer and Kitasato gives us unimpeachable evidence of the presence or absence of a mixed infection. Such an examination should and must go hand in hand with specific treatment. Other methods of treatment may be independent of this fundamental knowledge, but in tuberculin treatment an analysis of the infectious processes at work is indispensable. It is impossible to judge fairly the merits of tuberculin treatment, if we disregard the element of mixed infection. Mixed infection made shipwreck of the tuberculin treatment in 1891. By a fatal fortuitous coincidence tuberculin as a remedy for tuberculosis was tried when influenza raged in Europe as a violent epidemic. Altogether, apart from tuberculin treatment, the high rate of mortality from pulmonary tuberculosis in the influenza years proves that influenza was a very dangerous mixed infection in tuberculous disease of the lungs. If perchance tuberculin had been used, the tuberculin was blamed. Tuberculin has been condemned mainly, if not entirely, on the investigations of ten years ago. It was not known then that, although tuberculin might fail and even do harm when influenza or other infection complicated the tuberculous process, tuberculin might do nothing but good when such complications were absent. I was fortunate enough to use tuberculin in some cases before influenza invaded Australia, and my limited experience seemed to prove the undoubted value of tuberculin, if it were used under conditions prescribed by Koch himself. But while tuberculin can and does act favourably upon the uncomplicated tuberculous process, it may do nothing but harm in the presence of a mixed infection. Close upon five years ago I used these words:

Pulmonary tuberculosis, as we see it, is rarely a simple process of uncomplicated tuberculosis. It is a process variable in its nature, in its clinical manifestations, in its morbid anatomy, and in its cause; and these variations depend on the virulence of the tubercle bacilli, the state of the tissue, and especially on the number and character of the organisms that complicate the simple process due to the action of the tubercle bacilli. Now these variations, in their manifold clinical phases, have been analysed by the more exact methods of scientific inquiry, and in consequence method and clearness replace the confusion and vagueness that characterized our hitherto conception of the disease. (*Australian Medical Gazette*, August 20th, 1897, p. 401.)

The phases and stages of pulmonary tuberculosis largely depend upon the manifold combinations embraced in mixed infection. Let me say, too, that certain infections of the lungs that have nothing to do with the tubercle bacillus may simulate tuberculosis of the lungs. This is especially true of influenza and of infections due to streptococci or pneumococci. Such cases cannot be benefited by tuberculin. Two striking cases in my own experience are worth recording. I made a necropsy on a man who died of some obscure septic process. The sole obvious lesion was a small abscess the size of a hazel nut in the apex of the lung. The pus yielded in the smear a streptococcus, and in the growth on agar a pure culture of streptococcus longissimus. From the spleen, which was swollen and engorged, I obtained a pure culture of the same organism. Is there room for doubt that the primary infection attacked the lung?

Even more pertinent is the second case of a brilliant young medical man who fell a victim to his excessive loyalty to duty. He consulted me once and once only for chest trouble with cough and expectoration. For some time he had had irregular fever, sometimes as high as 101° or 102°. Physical signs were practically negative; at most there were some suspicious auscultatory signs at the right apex. The sputum contained no tubercle bacilli, but I obtained therefrom an absolutely pure culture of streptococcus longus. I was inclined to the view that he was suffering from a mixed infection of tubercle bacilli and streptococci.

Cases enough are recorded in which the tubercle bacilli do not get into the expectoration in these mixed infections. As the fever persisted an injection of tuberculin could not be given. If it had been given it might have been held responsible for the sad issue of the case. In spite of my advice this man continued at his post for some weeks during as bad a bout of cold, rainy weather as I have ever known in Sydney. Then he went to the country for some weeks. He returned to town and was carefully tended by his regular physician. I saw him but once, a month before he went to the country. He developed septic endocarditis and died in the course of some months. Surely this was a case of primary infection of the lungs, with streptococci which spread thence

to the endocardium by the pulmonary veins. Is it not possible that in many cases of cryptogenetic infective endocarditis the infective agents enter the system by the air passages? I know of no record of a similar history and nature. Thus septic infection of the lungs may simulate pulmonary tuberculosis. Far more frequently these infections supervene upon the primary tuberculous process. Streptococci, diplococci, staphylococci, and micrococci tetrageni are ever at hand to complicate the tuberculous process. Influenza bacilli, bacilli pyocyanei, and the bacilli pseudo-diphtheriae may also complicate. In 1899 I isolated pure cultures of the influenza bacilli from 6 cases of pulmonary tuberculosis. This year I have examined no fewer than 9 cases of so-called influenza, and in 8 cases obtained a pure cultivation of a streptococcus, in 1 case of a diplococcus lanceolatus. There has been, according to my investigations, no true influenza in the recent epidemic. One may call it influenza from its clinical characters, but the frequent complication of true croupous pneumonia that was observed is fair clinical proof that influenza bacilli have not complicated the process. Thus acute, and especially chronic, bronchitis may be due to concurrent infection of the bronchial passage causing apical catarrh, and this primary infection of the bronchial mucous membrane may lead to a mixed infection in the localized tuberculous lesion. In mixed infection the streptococci are intimately and inseparably associated with tubercle bacilli in the tuberculous lesion, as Spengler and others have shown both by special examination of the sputum and by examination of the diseased tissues in fatal cases. The tuberculous lesion has of course disintegrated, and tubercle bacilli are also found in the sputum. A mixed infection may cause only mild symptoms, especially if there is much fibrosis of the lungs, or may suddenly cause the signs and symptoms of acute phthisis with broncho-pneumonic exudation. This is important, and teaches a further lesson. Streptococci and pneumococci may attack a tuberculous as well as a healthy lung, but in both the fatal disease is the same. Is it right merely because tubercle bacilli are found in the sputum to make the diagnosis of acute tuberculosis? This is often done, especially during streptococcal and pneumococcal epidemics.

Those who see only tubercle bacilli in the sputum may err egregiously in diagnosis. Haemorrhage may complicate a pure tuberculosis or a mixed infection, and may thus be either the first sign of a simple uncomplicated tuberculosis of the lungs, in which the haemorrhage may be even a favourable sign, or the early symptom of a form of acute phthisis due to mixed infection and running a rapidly fatal course. As a rule the supervention of the mixed infection leads to wasting, loss of appetite, and sweating, accompanied by fever of varying degrees. The clinical picture changes when a mixed infection is superadded to the chronic tuberculous process. Then the tuberculous lesion may extend rapidly and soften; tubercle bacilli may be numerous or scanty in the sputum; the expectoration is greatly increased and swarms with other and various organisms. Kitasato's or Pfeiffer's method readily evolves order out of the chaos of this flora.

In 1891 the effects of the mixed infection of various sorts—influenza, streptococcal, diplococcal—were ascribed to tuberculin. The lesions to which Virchow specially directed attention in fatal cases that had been treated with tuberculin were actually the lesions that commonly occur in severe secondary infections when no tuberculin has been used. The simple oft-recorded fact that death occurred within a few days or weeks of the injection with tuberculin in 1891 proves incontestably that tuberculin was used in hopeless and totally unsuitable cases. Thus the brilliant success of the few were placed in total eclipse by the disasters that followed the rash and indiscriminate use of the remedy by the many. Ten years of patient work and careful observation have hardly succeeded in rehabilitating tuberculin among the useful remedies for tuberculosis. Professor v. Schroeder told the Congress in London in so many words that the work upon tuberculin as a remedy in tuberculosis would have to be done all over again.

Those who use tuberculin must above everything beware of mixed infections. There is no time to discuss the question of mixed infection. Those who use bacteriological methods to their full extent will be convinced in less than a year of

the supreme importance of the condition. Those who disregard the lessons taught plainly by the best bacteriologists will hardly listen to any arguments of mine. "They have Moses and the Prophets; let them hear them." My own experience in 1891 told me that in tuberculin we possessed a specific remedy of great value in suitable cases. My first experiments were made upon patients who were living in a country sanatorium and were free from fever. But the general wave of condemnation overwhelmed me in its flood, and it was practically impossible to persuade any one to undergo specific treatment, at any rate until all other methods and remedies had hopelessly failed. Then unfortunately the stage for tuberculin treatment had long passed. Tuberculin was condemned in the *post-mortem* room, was condemned by many after a hasty and illogical trial, and nowadays is especially condemned by medical men, who have had no experience with it, and the laity, whose ignorance is quite excusable. "Tuberculin treatment has been abandoned in Europe," so said an authority at a recent meeting in Sydney. Gratuitous assertion should have no weight in the balance against extended experience. I do not wish to escape criticism, but I have a right to demand a careful statement of facts and statistics from the experience of those who have used other methods of treatment. I challenge those who believe in the rational system of treatment to compare their results with the results of scientific treatment in competent hands. The immense value of tuberculin as a diagnostic agent has been proved in animals. In animals, also, the curative value of tuberculin in its various forms has been proved by Kitasato, Pfuhl, Spengler, and Beck. These experiments show that even the old tuberculin, which was hastily condemned, not only as useless but harmful, has a decided effect in checking the progress of tuberculous formations, and in causing in them those very changes that are recognized as positive signs of the regression of the morbid process. In guinea-pigs inoculated with virulent tubercle bacilli an ulcer that persists till death forms in the second week at the seat of inoculation, and the animal dies in eight to eleven weeks. In guinea-pigs treated with tuberculin the ulcer healed, and the animals lived five, six, seven, and nine months after infection, though the control animals died in six, seven, eight, and eleven weeks. Kitasato writes:

I was able to convince myself with the greatest certainty that even tuberculosis of the lungs had been influenced in a decidedly favourable way by the tuberculin treatment.

He adds:

In the case of those guinea-pigs, 5 in number, that are still alive seven months after infection, the inoculation ulcer is at length completely healed, the lymphatic glands, previously swollen, are no longer to be felt, the animals have steadily increased in weight, and have in all respects the appearance of healthy animals.

Moreover, these animals were again inoculated by Koch. The second inoculation ran the following course. Some days after inoculation the tissue round the seat of inoculation was swollen and indurated. In a week this infiltrated part was detached by spontaneous necrosis, and exposed a fresh-looking granulated surface. This ulcer was fully healed within twelve days from the date of inoculation, an event that never occurs under ordinary conditions. The second infection had no further effect. These results were repeated by

Spengler. But the use of tuberculin as a remedy has passed the experimental stage, and various observers, notably Rembold, Krause, Petruschsky, Spengler, and Turban speak very favourably of tuberculin, and do not record a single case of generalized tuberculosis after its use. Rembold began as a sceptic but his own results converted him. He waited for six years before he collected his evidence upon the value of the old tuberculin. Out of 70 cases, 27 were cases of mixed infection; of the remaining 43, 16 were in an early stage, 15 of moderate degree, and 12 in an advanced stage; of the 12 advanced cases, 2 were improved at the end of six years; the rest died. Of the 15 cases of moderate intensity, 8 were alive at the end of six years; all of them improved. One case was cured. Of the 16 cases in the early stage one died four years after treatment. The rest were alive; 3 greatly improved, 12 permanently healed, 75 per cent. cured. In these cases judgement was withheld till six years after the treatment.

Krause gives a full account of the treatment of 27 cases treated with old tuberculin; 12 cases were temporarily healed, 13 improved, 1 lately under treatment *in statu quo*, and 1 was made worse by injudicious use of the remedy. Krause says: "We come to the conclusion that tuberculin rightly used would have given exclusively favourable results."

Still more important are the records of Turban, who is one of the first authorities in Europe upon pulmonary tuberculosis and sanatorium treatment. Turban's classification of the stages of pulmonary tuberculosis is now largely followed. He recognises three stages.

It may be useful to give the basis of Turban's classification and the physical signs of the stages as given in Hans Weicker's *Beiträge zur Frage der Volksheilstätten*, p. 22.

(a) Turban treated 21 cases in Stage III with tuberculin: In 8 there was tuberculous laryngitis; 9 cases survived five years, 3 more remained alive for four years; only 5 out of 21 died within two years—25 per cent.; only 1 died of miliary tuberculosis, and that six and a-half years after treatment; none died of hæmorrhage. Hence tuberculin does not increase risk of hæmorrhage nor of generalized tuberculosis. Three were quite well six years after—in all, 5 were well. Tubercle bacilli disappeared from the sputum in 4 cases. Of cases treated in other ways—that is, without tuberculin—61 out of 84 died—5 from hæmoptysis, 3 from tuberculous meningitis; 41 out of 84 died in less than two years—nearly 50 per cent. Compare this with 25 per cent. under tuberculin treatment.

(b) Forty-eight cases in Stage II were treated with tuberculin: 9 died within two years of treatment, 3 in three years and more, 16 were alive six years after treatment, 5 more five years after treatment, 3 more four years after treatment—in all, 36 were alive. Thus, of 48 cases, 36 were alive and 12 dead. Of 152 cases treated in the ordinary way, 45 were dead and 107 alive, but the figures show greatly in favour of tuberculin treatment, because of the 107 a great number (49) had been under treatment not more than one or two years.

(c) 20 cases in Stage I were treated with tuberculin. Tubercle bacilli present in sputum in 17. All were well; 10 of them 6 years after treatment, 2 more 5 years after, 1 more 4 years after, 3 three years after, 2 two years after, and 1 one year after treatment. In all the tubercle bacilli disappeared from the sputum. The 3 cases giving no tubercle bacilli in sputum had to pass through the ordeal of the tuberculin reaction. On the other hand, 57 cases in which tubercle bacilli were not found in sputum were treated in ordinary ways. They were not subjected to tuberculin test. Of the remaining 22 cases there was one death, and in 2 cases tubercle bacilli were still present in expectoration. Turban himself says: "Now, if we compare the results of early cases in which tubercle bacilli were found in the sputum, the result is substantially in favour of tuberculin treatment (wesentlich zu Gunsten der Tuberculin-behandlung). Of the 26 cases with tubercle bacilli in sputum that were treated with tuberculin, 45, that is, 52.0 per cent., yielded a permanent result; of the 24 cases with tubercle bacilli in sputum that received no tuberculin, 95, that is, 39.4 per

Turban's Classification.

	Pathological.	Percussion.	Auscultation.	
			Breath Sounds.	Râles.
Stage I.	Bronchitis, peribronchitis. Scattered foci in one apex. No or little expectoration; generally no tubercle bacilli in sputum.	Normal to slight want of resonance over area of one lobe or over half of both lobes at most.	Over one or both apices harsh or weak vesiculo-bronchial to broncho-vesicular.	None or crackling, fine or medium over area of altered resonance.
Stage II.	Bronchitis, peribronchitis, infiltration of slight degree over both supraclavicular and supraspinous fossae or infiltration of one lobe without other foci.	Decided localized dullness over one lobe, or medium dullness over half of two lobes.	Harsh to broncho-vesicular breathing over the dull areas.	Râles of medium quality.
Stage III.	All cases more advanced than Stage II.	Pronounced dullness. Tympanitic note and variations of pitch. Cracked-pot sound.	Bronchial or amphoric.	Coarse metallic râles.

Cases between I. and II. marked I.—II.
Cases between II. and III. marked II.—III.

cent. gave a permanent result. Still more distinctly does the effect of the tuberculin show itself if we ask how many of these cases are now free from tubercle bacilli in sputum. Of the 86 tuberculin patients 41 are now free from bacilli = 47 per cent. Of the 241 not treated with tuberculin only 66, = 27.4 per cent.

These are very weighty words from an independent observer. Thus, with tuberculin in the hands of Turban, permanent results are obtained in a much greater proportion of cases, and tubercle bacilli far more often disappear from the sputum.

CASES TREATED WITH TUBERCULIN.

I may now approach the consideration of the cases which I have myself treated with tuberculin. I have used TR chiefly, but I have also used the old tuberculin (TA) alone or alternately with TR. It is impossible to give an impression of the results of treatment by mere groups and tables. Personal experience has a value of its own that cannot be disregarded, and my personal experience in a large number of cases tells me that tuberculin, properly used, has a very high value in the treatment of pulmonary tuberculosis. I have carefully watched the effects week by week for nearly five years, and I assert that while the degree of improvement varies and the duration of the improvement varies even more, gradual improvement is the almost invariable rule. I have treated nearly 70 cases, and I do not remember a single instance in which there was no improvement, provided, of course, there was no mixed infection. Such uniform improvement under the tuberculin treatment must be due to the tuberculin, for tuberculin was the only uniform remedy. By improvement I mean that the cough grows less and less and ceases; the sputum diminishes in quantity, becomes, if yellow at first, opaque, white, and then clear and frothy, and finally ceases. In all cases in Stage I the tubercle bacilli, if found before treatment began, disappeared from the sputum during treatment, and later there was no sputum.

In many cases in Stage II tubercle bacilli disappeared from the sputum for months or years, or altogether. I never stopped treatment on account of haemoptysis; and, though there were many cases of severe haemorrhage at one time or other, haemoptysis was extremely rare after treatment. The effect of tuberculin treatment in cases of haemoptysis is worthy of close attention, because if tuberculin had the effect, once attributed to it, of causing rapid and extensive softening, it should surely increase the tendency to haemorrhage. My experience is that it does the very reverse, and that in a striking manner. The rapid and extensive softening, if it has been observed, has been due to mixed infection, not to tuberculin. Mixed infection may certainly cause haemorrhage. Tuberculin treatment, then, is specially indicated in cases of haemoptysis, checking the haemorrhage and preventing its recurrence. Like many other observers, I have never seen any evidence in favour of the idea that tuberculin may mobilize a dangerous enemy peacefully sleeping. In no instance did tuberculous meningitis supervene. If, then, tuberculin does not favour haemorrhage, but rather checks it; if tuberculin checks and may completely arrest the cough; if tuberculin does not mobilize tubercle bacilli; if tuberculin diminishes expectoration instead of increasing it, and causes tubercle bacilli to disappear from the sputum, indicating most surely that, so far from favouring disintegration, it favours a healing process; if under or after tuberculin treatment patients invariably gain in weight and strength, beyond a doubt all the dangers that were held to be associated with tuberculin treatment vanish into mist. They were ghosts and shadows, unreal and unsubstantial, which no rational being need fear. I can vouch for improvement in all cases, provided there is no mixed infection. In many cases other physicians have witnessed the effects of the improvement, and admitted the improvement. I have not yet seen a case of pure tuberculosis that did not improve greatly. I do not pay much heed to a country practitioner who saw one of my cases more than two years after treatment. He found that the patient had a chronic abscess, no doubt tuberculous. The abscess was opened. A mixed infection occurred in the wound, and death was the ultimate result. The medical man attributed the abscess and fatal result to the use of tuberculin. Yet this patient under tuberculin treatment lost his cough, the tubercle bacilli disappeared from his sputum, and the sputum practically ceased. If he had had more tuberculin his life might have been saved.

I have never said that one course of treatment for a few months will absolutely and permanently arrest a disease that has been silently destroying the lung for many months, may be even years. In some of my cases I have given seven courses. I often combine the old tuberculin with the new, add I have given as much as seven-tenths of a gram of old tuberculin in a single dose—seven times the dose Koch originally recommended. The patient is alive nevertheless, and the better for the dose. It is by dint of repeated attacks with tuberculin that even in relatively advanced cases we may hope to bring about marked improvement.

If we have learnt anything in the last few years concerning the results of treatment of pulmonary tuberculosis, we have learnt to give up speaking of cure, unless we have at least watched the case for several years after treatment without witnessing any recurrence of the disease. Koch has continually urged that relapses occur often, and that relapses can be treated as the original attack with tuberculin alike with satisfactory results. Even cases in the first stage may require more than one course. Let me give one striking example:

Mr. E., about 47, gave an ominous family history. Four brothers, one after the other, had succumbed to the disease. They had been under various physicians for treatment. They had been sent to the country and treated in the usual way, but it was of no avail. The last survivor, having seen the failure of ordinary methods, came to me when the fatal disease showed itself, in him as in his brothers, by cough and expectoration and general loss of health and weight. I examined him, and found well-marked physical signs of an early stage. There was expectoration; but, although I examined many times in different ways, I did not find a single tubercle bacillus. I therefore advised a test injection of old tuberculin; 0.001 gr. raised the temperature to 103°, and increased the cough and expectoration. All doubt was at an end. He went under a course of treatment with Tuberculin R. up to 20 m. The patient proved to be very sensitive to the action of tuberculin, and the course occupied five or six months. During it the patient had severe attacks of gastritis and enteritis, with diarrhoea. At one time his weight fell considerably, but ultimately the result was satisfactory; the cough hardly troubled him, the expectoration ceased, and he felt greatly improved. The improvement continued for a few months, and then the old symptoms began to reassert themselves. I gave him a second course. The second course he took very well. In two months one was able to give him the full dose. Again the improvement was very marked. Some months afterwards I saw him, and he seemed in perfect health, and has remained so ever since. His weight (originally 11 st. 6 lb.) reached 12 st. 4½ lb. He told me that in the same time from the beginning of their illness his brothers had succumbed to the disease. The treatment was carried out while the patient continued at his business, though he lived out of town. The second course hardly even upset him. Surely some change had been wrought in his system that he bore the second course so easily.

To summarize an experience extending over a period of five years, 12 cases in Stage I permanently improved—one after two courses, 23 cases in Stage II, all temporarily improved. One had a relapse and developed a tuberculous abscess about hip, which was opened. Naturally mixed infection might be expected, and death occurred nearly two years after treatment. Another, aged 57, always delicate and poor eater, was extremely cachectic—pulse 124 to 130, vomiting, diarrhoea, and some discoloration of skin; symptoms improving with tabloids of suprarenal; perhaps tuberculous disease of adrenals, had two courses with tuberculin reaction, improved under both, but several months after second course developed coma and died. She never had fever temperature, generally normal or subnormal. A third case had a relapse with mixed infection; could not afford to come to Sydney from Wollongong for treatment. He developed influenza (bacilli isolated), but recovered. Later developed another mixed infection, and died in 1901, four years after treatment; 14 others are in relatively good health, can do ordinary work; 3 have had two courses, 1 has had six courses, and 1 seven courses in various combinations; in all 3 deaths out of 23. In those in first and second stage 3 deaths out of 35 (8.6 per cent.). In third stage

9 deaths out of 16; in all 12 deaths out of 50. Twelve cases were partially treated, but in 9 obstinate mixed infection interfered, and 3 were not able to remain in Sydney. All these cases were in the third stage, and treatment did neither harm nor good.

I regret that owing to prejudice many cases have come under my notice which were far too advanced for specific treatment. For two or three years no one in the first stage would submit to treatment. The tuberculin treatment was thus at the outset placed at a great disadvantage. Yet I can show results that will bear comparison with those obtained by other methods.

SUMMARY OF CONVICTIONS.

Though Koch has not put it in our power to work miracles, he has discovered a method of treating pulmonary tuberculosis in the early stages with eminent success. His method alone rests on a scientific basis. The last word has not been said on any method of treatment, least of all upon the tuberculin treatment. Philip of Edinburgh speaks in high praise of it. Is it the truth to say, then, that the treatment has been abandoned? It is difficult beyond ordinary comprehension to give a right value to the effect of any method of treatment in a disease that runs such a variable course as pulmonary tuberculosis. It is constantly asserted that pulmonary tuberculosis is curable; it is certainly true that we fail more often than we succeed in curing it. A dangerous and most misleading doctrine it is for patients and physicians alike that pulmonary tuberculosis is curable in all its stages. No doubt, in many cases, pulmonary tuberculosis is cured by Nature's own mysterious ways, but man has still to learn how best to imitate and help Nature. Healed tuberculosis is a common *post-mortem* condition, but in most of these cases there has been no history or evidence of tuberculous disease of the lungs. Tubercle bacilli are often missed in the lesions. Even if proved to be present, they may be dead and perhaps were never alive in the tissue. Conditions of cicatrization without caseation do not necessarily depend on tuberculosis. Irritants, especially of dust particles, broncho-pneumonia, and moreover, as Birch-Hirschfeld and others have proved, the arrested developments of terminal bronchioles may lead to the production of dense fibrous areas, quite independent of tuberculous changes. We are deceiving ourselves if we measure the curability of tuberculosis of the lungs by these interesting anatomical curiosities of the mortuary. The practical physician wishes rather to know how often tuberculosis of the lungs that is recognized by signs and symptoms during life is and may be cured by man's various resources. At the very threshold we are met with the difficulty of determining *a priori* the usual or standard course the disease runs. Measles, scarlet fever, diphtheria, typhoid fever, and the like run a fairly typical course and come to an end in a few weeks. We may therefore roughly measure the effect of treatment, notably in diphtheria. Yet even some distinguished authorities still refuse to believe that antitoxin treatment is the ideal treatment. How, then, can we expect unanimity regarding the effects of various methods of treatment in a disease like tuberculosis of the lungs that presents infinite variety, and lasts, not a few weeks, but months and years, and even a lifetime? Some tell us that the primary lesion is in the bronchial glands—some say in the lymphatics, some say in the bronchial mucous membrane (Virchow. Birch-Hirschfeld), some even that the tubercle bacilli enter the lungs by the vessels (Aufrecht). Some believe that the infective agent reaches the lungs by the alimentary tract (tonsils) whence via the lymphatics the apex of the lungs is invaded. The majority hold that infection occurs by the inhalation of tubercle bacilli that may be arrested in the bronchial mucous membrane or may pass through the uninjured mucous membrane into the bronchial glands. Wandering through this maze of discrepant opinions we may realize the intricacy and subtlety of the great problem that is crying out for a speedy solution in the name of suffering humanity. The disease may exist for months and years without arresting the attention of patient or physician—it may become quiescent at any time—it may relapse after months or years—it may reach a serious stage, involving the greater part of a lobe, and then end in perfect restoration of health. In spite of treatment of any and every kind, the disease may never relent. The victim knows no respite till death. With-

out any treatment the disease may come to a standstill, and never again disturb the health. The most affectionate regard for logic may not restrain us from attributing success to our own small efforts and failures to the vagaries of the disease. Our memories seize fast hold of successes; we leave others to record our failures, or leave them unrecorded. Let us adopt what measures we may, more or less failure is the rule, and yet we place a high value on many of our methods. In no other disease is it so difficult to estimate fairly the effect of treatment upon the course of the disease as it is in pulmonary tuberculosis. One sees cases of pulmonary tuberculosis even complicated with tuberculous ulceration of the larynx or epiglottis get well of themselves without any special treatment, without sanatorium treatment, without injections of any sort, without local applications.

The best results of sanatorium treatment do not present such a satisfactory picture of success that we should rest satisfied. Analyse the statistics of Weicker's sanatorium or Engelmann's more extensive analysis of the results in German sanatoria. We shall have to travel far before we can be satisfied. To paraphrase Lord Rosebery's epigram: The physician who is satisfied with sanatorium treatment is lost. The rational method of Brehmer was sound as far as it went, though often laborious and tedious in practice, but no other method was possible in his day. Sanatorium treatment holds out much hope of success, especially in the early stages of the disease; but surely any method that fails in at least 50 per cent. of the cases does not satisfy the conditions of an ideal method. The plague, dreadful as it is, is more merciful; it kills quickly, but it hardly kills 50 per cent. of its victims. The results of sanatorium treatment disclosed in Weicker's careful table show that there is plenty of room for improvement. Of 881 cases, 209 had no sputum. Of the remaining 672, only 243 had tubercle bacilli in the sputum; that is to say, 72 per cent. had no tubercle bacilli in the discharges from the lung; 72 per cent. were cases of closed tuberculosis. If no tubercle bacilli were found in the sputum tuberculin was used as a routine method of diagnosis. Thus early cases were selected.

	Results.	Per cent.	Per cent.
1900 ...	Cured ...	0	
	Improved ...	740 ... 84.0	Able to work ... 645 ... 72.9
	Unimproved..	110 ... 12.5	Partially... 82 ... 9.3
	Worse ...	27 ... 3.1	Not able to work 154 ... 17.4
	Dead ...	4 ... 0.4	
1899 ...	Able to work ...	523 = 63.0 per cent.	comprd. with 72.9 per cent.
	Partially... ..	42 = 5.1	" " " 9.3 "
	Not able to work	181 = 21.8	" " " 17.4 "
	Dead ...	84 = 10.1	" " " 0.4 "
1898 ...	Able to work ...	268 = 45.6 per cent.	
	Dead ...	104 = 33.0	"
1897 ...	Able to work ...	167 = 41.6	"
	Dead ...	170 = 41.3	"
1896 ...	Able to work ...	43 = 24.2	"
	Dead ...	111 = 63.3	"

Of cases treated in his sanatorium—carefully selected cases—the mortality had risen from 0.4 per cent. to 63.3 per cent. in the four years from 1896 to 1900. In the course of four years over 60 per cent. are dead; in the course of three years 43 per cent.; in the course of two years 33 per cent. Sanatorium treatment at its best falls far short of the ideal. May not tuberculin be the means of greatly increasing the value of sanatoria by establishing permanent arrest of the disease? But sanatorium treatment, whatever its success in selected cases may be, is an absolute impossibility in the vast majority of cases. It is a utopian idea that we can deal with pulmonary tuberculosis by means of sanatoria. Pulmonary tuberculosis is essentially the poor man's disease, and sanatorium treatment can hardly be brought to bear upon the very fringe of the disease. The system cannot be applied when and where it is most needed. To the well-to-do it offers fair prospects and sometimes even splendid results, if tuberculin is recognized as an indispensable weapon in arresting tuberculosis of the lungs in an early stage. To the poor and needy sanatorium treatment is not only costly but entails such sacrifices that those who enjoy the relatively good health that is not uncommon in the early stages of the disease will hardly be persuaded to seek the sanatorium. Sanatorium treatment, therefore, is no ideal plan for the majority. Further, in treating other infectious diseases—small-pox, plague, even leprosy, we do not lose sight of measures of prophylaxis. In treating pulmonary tuberculosis prophylaxis

hardly appeals to us. Yet it is more important in tuberculosis than in leprosy. From a hygienic standpoint we cannot be satisfied with any method of treatment that ignores the purpose of prevention. Can we say too often that the best treatment of pulmonary tuberculosis is its prevention? Now, all the results of sanatorium treatment show that as a measure of prophylaxis sanatorium treatment largely fails. It is stated that sanatorium treatment does not cause tubercle bacilli to disappear from the sputum in more than 20 per cent. of the cases; 80 per cent. of the infectious cases leave the sanatoria as foci of infection. The best training and the best regulations cannot remove the danger, though they minimize it. Such persons are all the more dangerous if they expel tubercle bacilli from their lungs when they think themselves cured. No doubt on an ideal plan those who leave sanatoria, as those who enter, should not discharge infectious sputum, but, as matters are, many enter and leave sanatoria with tubercle bacilli in their sputum, especially in the case of the sanatoria for the better classes. In this respect, then, sanatoria are not of the same public service as hospitals for consumption. On the other hand, evidence shows that tuberculin treatment has this great advantage, that in a far greater number of cases tubercle bacilli disappear from the sputum. Of cases treated by Turban with tuberculin, only 1 out of 20 had tubercle bacilli in sputum at end of treatment. Of similar cases treated in other ways, 7 out of 21 had tubercle bacilli at end of treatment. Accordingly, as a measure of prophylaxis tuberculin should be used in all sanatoria.

Tuberculin treatment can be carried on without loss of employment. For the poor, therefore, who have to earn their daily bread the treatment may well be recommended. The majority of my early cases have suited themselves, and many of them have hardly lost a day's work. Although the treatment has involved many thousands of injections, there has never been even a small accident, not even a small abscess. This is surely the best testimony of the care with which the preparations are made and dispatched.

ESTIMATION OF THE EFFECT OF TUBERCULIN.

Space will not allow me to do more than mention the latest development in the matter of specific treatment. Koch has at length devised a means of estimating the effect of tuberculin treatment. The object of treatment is to immunize the tissues against the tubercle bacilli and its toxins. In most other diseases immunity is brought about by the formation of certain specific protective substances that reach the blood and lead to the phenomenon of agglutination. The agglutination phenomenon is probably a more or less accurate measure of the degree of acquired immunity. In tuberculosis, as a rule, such agglutinative properties generally fail to develop, and accordingly the disease does not naturally produce its own proper remedy. But in animals by various methods immunizing substances can be artificially elaborately, so that the agglutinating power may be raised from 1 in 10 to 1 in 1,500 in goats and 1 in 3,500 in donkeys. Similarly Koch has found that by the use of various forms of tuberculin in human beings the agglutinative substances can be increased so that the power of agglutination is raised from 1 in 10 to 1 in 50, 1 in 100, even 1 in 175, 1 in 200, 1 in 250, even 1 in 300. Agglutination, valueless as an aid in diagnosis, is likely to be very valuable as a gauge of success in tuberculin treatment.

Thus there is absolute scientific proof that tuberculin of various forms used in various ways—by subcutaneous and even intravenous injection—does lead to the production of protective or immunizing substances in the blood. To quote Koch's own words:

That in phthisical persons the appearance of the power of agglutination is bound up with the formation of protective substances we think may be deduced from the fact that the state of health visibly improves from the moment the serum has acquired agglutinating properties. The appetite returns, and correspondingly the weight increases, often to a considerable degree; night sweats cease; rales greatly diminish, and also the amount of sputum. In many patients the sputum ceases altogether, and therewith, of course, tubercle bacilli disappear. The most striking phenomenon in this regard was the state of the temperature. In such patients, who had no high temperature, we have never seen, after the reaction had passed away, any rise of temperature that could have been regarded as the result of these reactions. On the contrary, we have regularly observed that in phthisical patients with fever, moderate and medium degrees of fever have been favourably influenced by the reactions. At first a fall of temperature, only transient, occurred on the third or fourth day after the reaction, at the very time when the process of immunization sets in. The temperature then remains low for

several days but again gradually rises. If again a powerful reaction is produced the temperature again falls, and the fall is more persistent than after the previous reaction. By repeated reactions such rises of temperature can be permanently arrested. In individual cases we have succeeded even in causing high fever of a pronounced hectic type to disappear; therefore, the condition of fever is now no longer a contraindication as was the case in the use of the old tuberculin. We have only excluded from treatment such cases as are in too weak a state, or those in whom the destruction of lung is so extensive that improvement is out of the question.

All these results were shown in cases of phthisis in the second and third stages.

The time will come when it will be generally admitted that Koch has not only taught us all we know of the etiology of pulmonary and other forms of tuberculosis, but has found also a remedy which in skilled hands will prove an inestimable boon to the large section of humanity afflicted with pulmonary tuberculosis.

THE ADMINISTRATIVE CONTROL OF THE TUBERCULOUS DISEASES.

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THE British Congress on Tuberculosis, which was held last year in London, will be memorable for more than the dicta of Professors Koch and Brouardel. It will be memorable as the first organized effort made in these islands to bring clearly into focus the magnitude of the task which lies before the community in the campaign it is urged to wage against the tuberculous diseases. Professors Koch and Brouardel committed themselves to statements each of which requires for its confirmation fuller and clearer evidence than the Professors themselves furnished. Koch says that bovine and human tuberculosis are not transmissible reciprocally, and Brouardel that alcoholism is the most potent factor in the propagation of tuberculosis. Neither of these gentlemen provides us with adequate proof of the truth of his proposition. On the other hand, the facts brought to the knowledge of the Congress in its various sections provide us with only too much evidence of the need of a national and systemic campaign against the tuberculosis; and even there we did not get all the facts.

The Congress, with a judgement with which I do not quarrel, in so far as it prevented attention being diverted from the most common and dangerous of the tuberculosis, practically confined itself to debating and resolving how best to deal with the tuberculosis which affects the lungs, and is commonly called phthisis. Of this form of tuberculosis over 40,000 persons are certified to die every year. It is reasonable to assume that for every person dying from this disease there will be at any given time ten times as many living with the disease in a slighter or severer form. Nearly half a million persons are, upon this computation, actually suffering from tuberculosis of the lungs in some stage. But this figure does not represent the total number of those who are the victims of the tubercle bacillus.

The Primary Site of Infection.

In the district with which I am associated officially nearly two out of every five deaths certified to be due to the tuberculosis are caused by forms of the disease other than phthisis. It is my belief that closer investigation into the true antecedents to death would heighten the proportion of the deaths due to non-pulmonary forms of tuberculosis. In my opinion, too, pulmonary tuberculosis is the primary lesion much more rarely than commonly is assumed to be the case. I believe this to be true of those who die of phthisis. My experience in dispensary and general practice before taking up municipal work led me to form this opinion. In fact, I came to the conclusion that phthisis is rather evidence of the development of the disease than of its invasion. It can be affirmed safely that if a victim of any other type of tuberculous disease live long enough the lungs are certain to become implicated, which implication, in many instances, masks the original seat of infection. My personal experience being limited to a little over 1,000 cases, inclusive of all kinds of tuberculosis, I am not entitled to dogmatize upon the matter, and can only express the hope that my confrères who are in practice, and in particular those