Fig. 3, however, showing the phthisis curve (of deaths occurring in each year) from 1860 to 1904, whilst it illustrates indeed the lessening prevalence, equally indicates the influence of wind and rain; and Fig. 4, showing the annual number of fatal cases originating in each year (obtained approximately from the stated durations), makes this influence of rain and wind even more obvious. In order to discover whether a curve in any way comparable to these curves can be obtained from the durations of phthisis cases, Fig. 5 was constructed (of the cases dying

Phthisis—Female Deaths in 23 Parishes of Barnstaple Rural District.

Fig. 3.—All deaths, whether duration is stated or not, referred to the years of their occurrence.

Fig. 4.—All the fatal cases of phthisis whose duration is given referred approximately to their years of origin.

under 50), showing the relative percentage of "short," "medium," and "long" cases in each successive five years between 1860 and 1904. The curve so obtained is, I think, remarkable, indicating most suggestively a relation between (a) rain and wind incidences, (b) phthisis prevalence, and (c) phthisis duration.

Elimination of Error Possibly Caused by Age.

In going through the cases, however, it was impossible to avoid observing how often a "long" duration was associated with an advanced age. Table V was therefore

TABLE V.—Whole 45 Years.

Ages.	Short.	Medium.	Long.
-9	1	1	1
10-19	8	8	6
20-29	17	18	14
30-39	9	8	8
40-49	3	6	5
50-59	4	4	16
60-69	—	4	9
70 and over ...	—	2	3

constructed, to ascertain how far age exercises a disturbing influence.

From this it is obvious that, over 50 years old, age does seem to considerably affect the case-durations. Accord-

TABLE VI.—1860 to 1884, Cases under 50.

	III (50 Cases).	II (11 Cases).	I (14 Cases).
	Per cent.	Per cent.	Per cent.
Long... ..	20	18	56
Medium	46	46	16
Short	34	36	28

TABLE VII.—Group III, Cases under 50.

	1860 to 1884 (50 Cases)	1885 to 1904 (26 Cases).	1890 to 1899 (12 Cases).
	Per cent.	Per cent.	Per cent.
Long... ..	20	29	50
Medium	46	38	25
Short	34	33	25

ingly, it appeared desirable to recalculate Tables III and IV with the exclusion of all cases dying at 50 and over. Tables VI and VII were thus obtained. They tend to show even more strikingly than Tables III and IV the unfavourable influence apparently exerted by exposure to the strong, prevalent, rain-bearing winds. Long cases are much commoner and short cases much fewer under the less exposure to rain and wind.

To conclude, it seems to me that these tables and curves, taken in conjunction with the other evidence to which I have alluded, constitute a considerable prima facie case for the contention that exposure to strong, prevalent, rain-bearing winds tends to exercise an unfavourable influence on the course of phthisis. How far treatment may prove equal to neutralizing this unfavourable effect of these rainy winds remains to be seen. The cases here dealt with were mostly treated before the days of modern sanatorium methods.

I take this opportunity of expressing once more my great indebtedness to my friend, Dr. Harper, for the invaluable help his careful information has afforded me.

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An Address

ON THE

PREVENTION AND TREATMENT OF PULMONARY TUBERCULOSIS.

DELIVERED BEFORE THE MEDICAL AND SCIENTIFIC SOCIETY, UNIVERSITY COLLEGE, DUBLIN.

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MR. PRESIDENT, LADIES, AND GENTLEMEN,—It is my first duty and pleasure to thank you for the honour you have done me in asking me to deliver the address inaugurating the present session of our society. The subject I have chosen is the prevention and treatment of pulmonary tuberculosis—a subject in which I am myself particularly interested, and one in which every medical practitioner in these countries must take the greatest personal interest, since tuberculosis is the captain of the men of death in these lands, and therefore it must form a large proportion of the cases with which the physician has to deal. Moreover, it is a disease which taxes all one's resources and skill to deal with effectually.

I do not, of course, propose to deal exhaustively with the subject in this short paper, but shall only attempt to emphasize certain measures of prevention and treatment which I think will strengthen our hands in dealing with the disease.

It will be well first to know the mortality and incidence of the disease at the present day. In Ireland last year over 10,000 individuals died of tuberculosis, of which 7,527

were affected by the pulmonary form. In 1909 over 38,000 people died of the pulmonary form in England, so that we may take it that about 50,000 people die of the pulmonary form each year in the British Isles.

Now there are two questions to be asked—Is the death-rate from tuberculosis falling? and if it is, is it falling faster than or as fast as the general death-rate?

The death-rate in Ireland from the disease was 2.3 per 1,000 in 1900; in 1910 it was 1.7 per 1,000—a marked diminution. Now as to the second question, I am quoting the deductions of Professor Karl Pearson,¹ which I think are the most accurate attainable.

He illustrates the facts by three diagrams. To the graphic records of deaths per 1,000 from all causes are fitted "regression straight lines," which show that they are three distinct periods: from 1835–1866 the average death-rate fell very slowly, from 1866–91 it fell much more rapidly, and from 1891 to 1910 it fell more rapidly still.

Now how does the rate of death from tuberculosis compare with the general death-rate? The records of deaths from phthisis up to 1847 were only partial, but so far as could be made out the fall in the death-rate from it between 1838 and 1847 was immense. The first regression line is fitted only from 1851–66, and shows a marked decrease during the years in which we have seen there was little decrease in the general death-rate. During the next period (1866–94) the fall was accentuated. But during the third period (1894) to the present day the line shows there is a distinct retardation in the rate of the fall. And this has occurred during our period of greatest knowledge and most active campaign against the tubercle bacillus.

The percentage of deaths from phthisis of all deaths from year to year for the last sixty-six years—from 1847 on—shows a fall of from 13 (8 per cent.) in the case of males and of 15 (6 per cent.) in the case of females. But it brings out the grave fact that for the last fifteen years the percentage of deaths from phthisis in the case of males shows a slight rise, while for females the apparent slight decrease is really a rise if we only consider the last ten years.

To sum up, Pearson says: "The relative number of deaths from phthisis has not been diminished by the campaign against the tubercle bacillus, although the absolute number has fallen, but at a sensibly retarded rate."

Now as to the infectivity. The table given by Hamburger and Monti comparing the prevalence of tuberculosis in Vienna determined by autopsy and tuberculin tests will give us some idea of it. So that, taking the lowest figures, we see that the majority of children who reach the age of 14 have been infected. While if we accept Hamburger and Monti's figures we see that 94 per cent. have the bacilli in them. Yet, since the death-rate from tuberculosis in Vienna is only 15 per cent., 80 per cent. have sufficient resistance to prevent the disease killing them. These figures are probably outside ones, but we may take it that the majority of people are infected by the microbe at some time or other.

Man is infected with Koch's bacillus from two sources. First by bacilli that have been living in other human beings, and secondly, from bacilli which have been living in cattle. It is said that bovine bacilli are the chief cause

of surgical tuberculosis, and that human bacilli are the chief cause of pulmonary; but undoubtedly the human type can cause surgical and bovine pulmonary tuberculosis. So that if we want to cut off the sources of infection we have to deal with infected cattle and infected human beings.

The great source of bovine tubercle bacilli is milk, which is partaken of raw as a rule, and to a lesser extent meat. The system of dealing with these sources at present in vogue if conscientiously applied ought eventually to lead to the complete elimination of this source. That it is not conscientiously applied at present in Ireland the evidence given before the recent Viceregal Commission plainly shows.

The other source of infection, namely, the infected human being, and how to prevent him from infecting others is a much more difficult problem.

A person with pulmonary tuberculosis in whose lungs softening of tuberculous areas is going on is excreting tubercle bacilli in his sputum, faeces, and sometimes in his urine. The latter two sources have not possibly received the attention they ought, although perhaps in towns where there is a proper septic tank system they would not be a great source of infection. The contrary, however, may be the case in rural districts and where the sewage is treated by means of sewage farms.

With regard to the sputum a known consumptive can be supplied with a spitting flask containing disinfectant, and so the large masses of purulent expectoration disinfected. But one cannot properly control the fine atomized spray given off when the consumptive coughs, which carries tubercle bacilli in its droplets, and these fall on objects around, dry, and infect the dust; a patient who is warned may control this to a certain extent by a handkerchief, but such control can be only partial and he is bound to infect his bedroom during sleep.

Such a patient, then, is bound to be infectious, and ought to be isolated in a suitable institution. Since this is as a general rule impossible under present conditions, then he ought to sleep in a separate apartment, and those who attend to that room ought to take the same precautions against infection as if it harboured a case of typhoid fever; and, further, when the patient vacates that room it ought to be as thoroughly disinfected as if it had contained a case of small-pox. I can recall an instance where member after member of a family who occupied a certain bedroom became infected, until the room was thoroughly disinfected, when the plague was stayed in that house. Some figures quoted a few years ago by Professor McWeeney bring out the necessity for this measure. Certain Paris lodging houses, numbering 820, and containing in twelve years 106,308 persons, yielded 11,500 deaths in this period. The worst of these houses, known as *hôtels garnis*, actually had a death-rate of 42 per thousand from phthisis in certain wards in Paris.

The habit of promiscuous spitting ought to be put down with a strong hand. Could not suitable spittoons be placed at intervals in our streets to accommodate those members of the community whose handkerchiefs consist of their fingers and thumbs?

The ideal measures for dealing with the disease are those one would use for any infectious disease—namely, notification, isolation, disinfection, and supervision of contacts.

Notification has at last arrived, complete isolation seems

Prevalency of Tuberculosis as determined by:

Investigator.	Autopsy.		Tuberculin Reactions.			
	Lethal and Non-Lethal.	Only Non-Lethal.	Cutaneous.			Cutaneous and Injectional.
			Ghon.	Ghon.	Hamburger and Monti.	Hamburger and Monti.
Second year of life ...	40	17	2	12	9	9
Third and fourth years ...	60	30	13	27	23	27
Fifth and sixth years ...	56	34	17	47	36	51
Seventh to tenth years...	63	35	35	57	47	71
Eleventh to fourteenth years ...	70	53	55	70	51	94

to be at present impracticable, disinfection can be accomplished and also the treatment of contacts.

Much good work has been done in Ireland by the Women's National Health Association in teaching the people the infectious nature of the disease and making them afraid of it, and in many other ways. I need not go further into the other general measures, such as special dispensaries for advice, diagnosis, etc., special hospitals in the cities, and sanatoriums in the country. No one can deny the value of the latter as educative establishments and places for isolation. Their curative value will be discussed later.

There is just one other point I should like to mention before leaving this part of the subject, and that is that tubercle bacilli received direct from a bad case of the disease are more virulent than if they have been some time isolated from him. So that, just as in the case of small-pox, a susceptible individual, if he gets the disease, will hand on a more virulent strain to those he infects.

Since the Vienna figures quoted above show how ineffectual are our methods of preventing the infection, we have to rely on the natural immunity of the healthy individual to resist the disease, and this seems to be effectual in Vienna in about 80 per cent. of the people who receive the infection, so that if one could make the other 15 per cent. or so like unto the 80 per cent. our object would be accomplished.

In order to keep in good health we must live in decent, well-aired houses, be sufficiently clad, have sufficient and uncontaminated food, sufficient exercise, and must breathe through our noses, so that the air may be warmed and be filtered free from microbes.

Every one, I think, realizes the importance of providing proper housing and sufficient money to supply proper food, and of lessening the opportunities of having that money spent on alcohol.

The system of school inspection is doing away with nasal obstruction in children and attending to other abnormalities.

I believe the proper feeding of the infant has a most important bearing on its health in after-life and his resistance to disease. A sound digestion is the first essential of health, and a child who has been improperly fed during the first nine months of his life starts with an impaired digestion. There is no substitute for its mother's milk. The nearest approach appears to be milk direct from the goat. Even if one can give in a bottle the proper proportion of carbohydrates, fats, and proteins, one cannot give it the natural ferments, including anti-microbial substances and neurones.

I do not believe the majority of women who say they cannot nurse their babies. How often have I seen a few bottles of malt extract produce an abundant supply of milk. A woman who does not nurse her baby when she can, knowing, as she must, that any bottle may contain its death warrant, is, in my opinion, guilty of a very grave social offence. Doctors and nurses, I am afraid, are too prone not to emphasize the importance of this.

Next, why is it that a certain percentage of the community have naturally a low resistance to the disease, and can we correct this? Undoubtedly, the answer to the first question is that the low resistance is most often inherited. Pearson has shown that there is a resemblance between parent and offspring in the matter of tuberculosis of 0.5, and this as between father and child is as close as between mother and child. (The resemblance between husband and wife is from 0.25 to 0.3.) Can this be corrected? I think it can. I consider that every member of a tuberculous family should have his resistance to the disease increased by a series of increasing doses of tuberculin. I have practised and do practise what I preach, and have found that in such individuals the injections act as a splendid tonic, the patient expressing himself as feeling more fit and energetic than before. I believe the mother of a child whose father is tuberculous should be inoculated while she is pregnant, or if not then when she is nursing the child. If she is tuberculous herself the problem is more difficult, as she may not be fit for inoculation. However, she may be rendered fit for it by appropriate treatment, or if not, the baby can be inoculated some months after.

By this means one can bring up the resistance of these susceptible children from subnormal to normal; indeed,

their resistance for a time at least is well above normal. Maragliano states that after using his tuberculous vaccine he found after three years that the patient had three times the agglutinating power of a normal individual. Even if the specific immunizing substances fade away after a time, yet the mechanism for the production of these substances has been produced and can in all probability be aroused to activity with greater ease than in the normal individual. It is, indeed, a question that ought to be considered whether every one ought not to be prophylactically inoculated against the disease. I inoculated my own baby when she was 3 months old.

Turning now to the question of treatment of the individual infected with the disease, it will be useful to give a classification of the forms the disease takes.

The first division is into *acute* and *chronic*. The acute can be further divided into four subdivisions—namely:

1. Acute miliary, generalized.
2. Acute miliary, of the lungs alone.
3. Acute lobar pneumonia due to the tubercle bacillus.
4. Acute bronchopneumonia due to the tubercle bacillus, and generally called "galloping consumption."

The chronic forms are most usefully classified for purposes of prognosis and treatment into four classes, according to the extent of the lung diseased.

In Class I the lungs have so slight an involvement that there are no physical signs. The patient may have a slight cough, a subnormal temperature, and is easily tired.

In Class II are those in which there are the earliest physical signs, generally in an apex, while the temperature does not go to more than about 99.6°, and the small amount of sputum does not contain tubercle bacilli.

In Class III are those in which there are moist sounds in the lungs, the disease being more extensive and the consolidated lung is breaking down. The temperature is sometimes, and in the worst cases, subnormal, but usually rises to 100° or more. Tubercle bacilli are present in the sputum.

In Class IV are those with extensive disease, large cavities, and septic temperatures. Tubercle bacilli and myriads of other microbes are present in the sputum.

Of course, all cases of phthisis do not fall into these groups, for one finds all sorts of modifications and combinations.

It is obvious that it is of supreme importance to diagnose the disease at the earliest possible moment. I shall not have time to discuss the diagnosis of the acute forms, which are only a small number of cases, but shall confine myself to the diagnosis of the chronic forms.

When there are well-marked physical signs in the lungs and tubercle bacilli in the sputum there is no difficulty about diagnosis, but when there are no physical signs, or when these are present to a slight extent but there are no tubercle bacilli in the sputum, it is another story.

Modern laboratory technique, and our growing but still imperfect knowledge of immunity reactions, have given us several methods of diagnosis. They are:

The tuberculo-ophthalmic reaction of Calmette.

Various skin reactions, such as that of von Pirquet.

Estimation of the opsonic index to the tubercle bacillus.

Local and general reactions produced by inoculation with old tuberculin.

The demonstration of tubercle bacilli in the blood.

Sometimes when tubercle bacilli cannot be found in the sputum they can be found in the faeces, and sometimes when they cannot be found in either by the usual methods they can be found when a large bulk of material is treated by the anti-formin method. It must not be forgotten that some tubercle bacilli are not acid-fast, and that there are other acid-fast bacilli which are not tubercle bacilli.

The ophthalmic reaction has been and is extensively used, but there have been some disasters to eyes although it appears to be safe enough if there is no conjunctivitis. There can be no objection to the skin reactions nor to the use of the opsonic index. Old tuberculin injections can be used with safety in incipient cases.

The demonstration of tubercle bacilli in the blood is difficult and there are many differences of opinion as to its practicability.

My own procedure in a doubtful case is as follows: I first do von Pirquet's skin reaction; if this is negative I do it again; if it is again negative I think the case is not tuberculous; if it is positive in an individual above 5 years

old I think the reaction may be due to an old healed focus or to an active lesion. I then give injections of old tuberculin, beginning with $\frac{1}{10}$ mg.; if there is a rise of temperature of 1° or more I think there is an active form of disease and a local reaction indicates the place where it is. If there is no reaction; I increase the amount through $\frac{1}{5}$ and $\frac{2}{5}$ to 1 to 2 mg. If there is no reaction after any of these, I think there is no active tuberculosis present. In later cases, where the diagnosis has to be made between lung lesions due to the tubercle bacilli and those due to other organisms, it may not be justifiable to use the old tuberculin test, although iodoform injections can control a severe reaction in most cases. I then use the opsonic index; an index below 0.8 or above 1.2, or, better still, a fluctuating index, suggests the presence of active disease.

Unfortunately, in some cases the first indication the patient has is the occurrence of a haemorrhage. This is a common mode of onset in athletes, and is in itself practically diagnostic. If tubercle bacilli cannot be found in the blood-stained sputum the disease can be diagnosed by the procedure just sketched.

In the treatment of tuberculous disease a stitch in time saves so many others that no trouble ought to be too great either for the physician or the patient in order to make a diagnosis.

TREATMENT.

The means we have at our disposal for the treatment of the disease are broadly three in number:

1. The open-air treatment in hospitals and sanatoriums.
2. Therapeutic immunization with one or other of the tuberculins.
3. The exhibition of drugs for bactericidal purposes.

Sanatorium Treatment.

Of these the sanatorium treatment at present holds the field, and enormous sums of money have been spent, and, it seems, are going to be spent, in erecting fresh ones. Leaving out of consideration the value of these establishments as educative and isolating institutions, it is necessary to find out their value as a means of cure. Are the results of treatment in them better than the results of treatment in presanatorium days? I am not myself competent to answer the question, neither do I think that physicians interested in sanatoriums can form an unbiased judgement. A careful actuarial examination has been made by Elderton and Perry, in the department of applied mathematics, University College, London, of the death-rate of patients who have been treated in sanatoriums, and these have been compared with similar statistics of presanatorium days. The results of sanatorium treatment in England, United States, and Germany are included. The conclusions they come to are as follows:

1. The mortality of tuberculous patients who are undergoing or have undergone treatment is much heavier than that of the general population, and even when the disease is taken in the incipient stage the mortality is about four times as heavy.
2. The mortality of the apparently cured cases is about twice as many as that of the general population.
3. The mortality among sanatorium patients does not show any improvement on that of Williams and Pollock's cases (that is, presanatorium cases). The comparison is, however, rendered difficult by the way the older figures were given.

They say in a footnote that the investigation of further material since these results were come to only confirms them. Moreover, these results are chiefly from sanatoriums where people of professional standing are treated, and therefore ought to be able to carry out the hygienic measures they have learnt after they leave the institutions. That the permanent results are not satisfactory is also suggested by the fact already stated that the fall in the number of deaths from phthisis as compared with that of all other causes has ceased; in fact, the percentage is rising.

As to the immediate results of sanatorium treatment, I cull the following figures from 1,200 odd cases treated at German working-class sanatoriums where the minimum stay was ninety days.

Condition on admission very good in 0.0 per cent., good in 30.7 per cent., unsatisfactory in 38.6 per cent., bad in 30.7 per cent.; on discharge was very good in 22 per cent., good in 73 per cent., bad in 5 per cent. Average increase in weight 12½ lb.

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On admission 88.7 per cent. had both cough and expectoration; on discharge 67.4 per cent.; 27.2 per cent. had neither. Out of every 100 who had tubercle bacilli in sputum on admission (51.0 per cent. had), 70.2 still had it on discharge. Of those admitted only 20.8 per cent. were febrile. Out of every 100 that were febrile on admission, 75.5 were so on discharge, and only 24.5 were considered to have a normal temperature; 4.4 out of every 100 patients with a normal temperature developed a febrile temperature at the sanatoriums.

Night sweats: 31.7 per cent. had night sweats on admission. Of every 100 who had, 90.9 had not them on leaving.

These were a favourable lot of cases, only 20.8 per cent. had an evening temperature of 99.2° ; and only 51 per cent. had tubercle bacilli in their sputum, yet the majority of those who had a temperature and bacilli still had them on discharge. However, the general health of 95 per cent. of those admitted had more or less improved. And 22 per cent. of them were in "very good" condition, which, I take it, means apparently cured.

I wish to emphasize the fact that half of these cases belonged to Classes I and II, the fact that they had tuberculosis being diagnosed by tuberculin reactions.

Perry and Elderton estimate the death-rate of those who leave sanatoriums with arrested disease as ten times the normal, while that of those who leave with the disease still active is forty times the normal.

Of course, the results obtained by different sanatoriums vary somewhat according to the class of case admitted, the kind of treatment adopted and the careful adaptation of that treatment to each individual case. I think it would be hard by sanatorium methods to turn out better results than Dr. Paterson at Frimley, where patients are only admitted in the early stages—namely, Classes I and II—and where by carefully-regulated exercises the patient is trained so that at the end of his treatment he has attained such a state of health that he can do hard manual labour for six hours a day without a rise of temperature or undue fatigue.

The conclusions I have come to as to the results of sanatorium treatment are as follows:

It can reasonably be expected to restore a good percentage of Classes I and II to their previous health without conferring on them any guarantee against reinfection.

Many cases of Class III are improved, but in the majority of cases do not lose their tubercle bacilli.

While in Class IV the treatment from a curative point of view is practically useless unless in exceptional cases.

I do not think any one can be satisfied with such results, and it appears to me absolutely essential to adopt some more vigorous methods of treatment during the patient's sojourn at the sanatorium.

Tuberculin Treatment.

I am afraid this treatment is still regarded by many with great suspicion, not having recovered from the terrible fiasco the premature use of Koch's original tuberculin produced. However, our better knowledge of immunity reactions, of proper dosage, and of the kind of cases to employ it on have reduced the risk of disasters to a minimum.

The kinds of tuberculin used are many in number and the methods of administering them vary. The majority begin with a small dose and gradually work the dose up to a large amount, while others give repeated small doses, some regulating them by the opsonic index.

Although most observers who have used the treatment speak well of it, yet it is hard to estimate the ultimate result. Trudeau has used tuberculin in a certain number of cases in the Adirondacks Cottage Sanatorium since 1890. He used chiefly Koch's old tuberculin and bacillary emulsion, his own tuberculin B, Denis's tuberculin, and tuberculo-plasmin. T.R. and tuberculo were given to a few patients.

A study of 185 patients treated with tuberculin and 864 not so treated, all of whom stayed over 90 days, showed for the early stage a slight difference on discharge in favour of treated patients. For the moderately advanced there was a very marked difference in favour of the treated—namely, apparently cured, treated 27 per cent., untreated 6 per cent.; disease arrested, treated 50 per cent., untreated 51 per cent.; active, treated 18 per cent., untreated 43 per cent.

The ultimate results obtained for one to fifteen years after discharge in 135 patients treated and 690 untreated

show that of 100 patients in the early stage treated 79 are alive, of the untreated 63 are alive, while in the advanced stage 61 of the treated are alive and 36 of the untreated.

Those who speak most enthusiastically of the treatment in this country are Nathan Raw and Camac Wilkinson, who used bovine tuberculin, which does not appear to be liable to produce so much reaction as the human type of tuberculins. Undoubtedly the method is worthy of careful trial.

Dr. Dunn, of the South Dublin Union Infirmary, has used Denis's tuberculin for some years with excellent results in a good percentage of cases.

In pulmonary tuberculosis I have not used tuberculin by itself to any extent; it has generally been used to complement or supplement the last mode of treatment I shall allude to.

Many drugs have been used in the disease, such as creosote, guaiacum, carbolic acid, formalin, etc. The one I wish to refer to is iodine given in chemical combination. The form which I have been using for several years is iodoform, and I have given it intravenously, intramuscularly, and by the mouth. The intravenous method is by far the most potent, and is the method introduced by Dewar of Dunblane, from whom I learnt it. It is given in quantities of $\frac{1}{4}$ to 1 grain dissolved in ether, with a little liquid paraffin added, two to five times a week. The veins usually selected are those of the antecubital fossa. The little operation is quite a simple one. There is no pain or inconvenience to the patient, except a certain amount of coughing, and yet I know of no procedure in medicine which has aroused more *a priori* objections to its use, the bugbears imagined being embolism, thrombosis, gas embolism from ether vapour, in fact, the immediate demise of the patient, and yet no such accident has ever occurred nor have I seen anything approaching to such an occurrence.

But if it does no harm, does it do any good? I will first quote some experimental results, and then relate some cases of my own.

Higgins of the Biological Laboratory, Ottawa, injected rabbits intralaryngeally with virulent bovine bacilli. He then waited until the rabbits, by loss of weight, etc., showed evidence of the disease, and began injecting daily $\frac{1}{16}$ grain iodoform in ether into the auricular vein. For the first week the animals lost weight, but then began to put on as much as 25 to 50 grams a day. When apparently well the lungs were examined, and it was found that the areas where the disease had been were completely replaced by healthy fibrous tissue. I can relate two cases of recovery from acute military tuberculosis of the lungs, both of which I saw in consultation and in both of which the diagnosis was agreed to by eminent clinical authorities. The cases were very similar.

The first was a man, aged about 35, who had been feeling ill for about three weeks. He had a patch of congestion in the lower lobe of his right lung, and fine crepitations over both lungs, with dyspnoea, cyanosis, and a rectal temperature ranging from 102° to 104° F. After the treatment commenced the temperature came down gradually and at the end of three months was normal. He has remained quite well ever since—that is, for three years—and is now in vigorous health.

The second case, a girl aged 20, had been ill somewhat longer, and the temperature sometimes reached 103°. Her symptoms and physical signs were almost identical with those of the first case. It is now just a year since I saw her first, and her temperature is normal and she is rapidly gaining weight and strength.

These cases are, I think, on a par with the experimental results in rabbits given above.

The first case I tried the treatment on was a girl aged 17 whose right lung was involved to 2 in. below the clavicle. She was regularly losing flesh, had temperature rising to over 100° F., and had tubercle bacilli in her sputum. At the end of six months' treatment there were no physical signs to be made out, she had no sputum, she felt well, and her temperature was normal. She used to drive three miles each morning to me for her injections through all sorts of weather.

The two last cases I shall mention are recent.

The first came to me on leaving hospital, where he had been treated for pleurisy, and where tubercle bacilli was found in his sputum; I found them present in large numbers. He had to go to the country for a month, where he took 10 grains of iodoform by the mouth daily. He gained a stone in weight. On returning to town he rapidly got worse, developed physical signs in the right apex, while he had pleuritic thickening over most of the left lower lobe. The temperature rose to 100.6° F. in the

evening. He has now, in four months, lost all cough, has the slightest amount of expectoration with no tubercle bacilli, his temperature is normal, and he is being immunized with tuberculin, while he has never been so heavy in his life.

The second had a large amount of expectoration swarming with tubercle bacilli, and a cavity in the upper lobe of his left lung. In this case the infection was grafted on a chronic bronchitis due to the pneumococcus and *Bacillus septicus*, which also were causing chronic nasal catarrh, middle-ear disease, and perforation of the right drum. After a year's treatment the cough has disappeared almost completely, he has one small piece of sputum in the morning, which contains no tubercle bacilli. He is strong and has a normal temperature. This case has also had vaccines for the original infection.

Both these cases have been living in the city, have been pursuing their ordinary employment, and have come to me each day for their injections.

Even in advanced cases with large involvement I have succeeded in getting the temperature normal, greatly reducing and sometimes abolishing the expectoration and improving the cough. But I think cases who have had large involvement can seldom be anything but delicate in this climate, however much you improve them.

I hope I have said enough to prove that the treatment can do good. The only fact absolutely known as to its action is that it causes a leucocytosis. Dewar suggests several explanations, two of which are that the iodoform may act unchanged, that it may be split up, oxygenation of the CH group producing formaldehyde, the iodine being liberated, and both acting directly as germicides. It is quite likely that the iodoform is split up, for iodoform in solution in ether is very unstable, being rapidly decomposed, for instance, by light, with the liberation of iodine.

I think myself that one of its chief actions is the well-known action of iodine in converting toxin into toxoid, which is not poisonous, but acts as an excellent stimulant and for the formation of antitoxin. The power that an injection of iodoform has in abolishing a reaction after an injection of tuberculin would tend to confirm this hypothesis.

Since there seemed to be so much prejudice against the intravenous use of the drug, and since its intramuscular injection did not seem to be as efficient, I have tried to intensify its action when given intramuscularly by adding to it other drugs. The first I used was a 2 per cent. solution of benzoyl chloride in liquid paraffin. This drug also produces a leucocytosis, and *in vitro* dissolves the tubercle bacillus. I obtained some encouraging improvements in a few cases and a complete apparent cure in the only early case I have used it on, and I think the combination worthy of further trial.

Lately I have been using Szende's combination of iodoform or iodized peptone with menthol and radium, and, although I have completely failed with it in three very advanced cases which were probably beyond all treatment, the majority of cases have very much improved. I cannot say more yet, as the cases are too recent. Unfortunately this last combination is being exploited commercially at a ridiculous price; I can make the preparation for about one-sixth what is usually charged for it. It is a pity, because the preparation is undoubtedly useful.

I think it is essential, before ending the treatment of a case, to give a series of injections of tuberculin, in order to increase the patient's immunity, and if possible to leave him with at any rate the mechanism for producing specific antibodies with ease. Otherwise the patient has no guarantee that he will be able to resist the reinfection that he is almost certain to get. The form of tuberculin used will depend on the physician's own particular fancy in this direction. I do not think T.R. a good form. A.T., I think, is; also A.F., P.T.O., P.B.E., and B.E. I have used with success in several cases a preparation of my own made by dissolving tubercle bacilli in benzoyl chloride and diluting with liquid paraffin. I usually give it combined with iodoform, the latter being given with the idea of reducing the reaction. It is a very powerful preparation, the initial dose being a millionth of a milligram and the largest dose I have used is a thousandth of a milligram. That the iodoform does reduce reaction I have proved by giving a case several doses of the combination without a reaction and then giving it without the iodoform, when a reaction occurred.

Let me end by stating that I think that the adoption of treatment with combined iodine *plus* immunization will enormously increase the output of apparently cured cases.

Time and carefully kept records alone will enable a judgement to be formed of the permanency of such results.

I look forward to the time when the resistance of the units of the nations has been so raised that it will be only exceptionally that the tubercle bacillus will be able to live in human tissues.

REFERENCE.

¹ *The Fight against Tuberculosis and the Death-rate from Phthisis.* By Karl Pearson. London: Dulau and Co.

NOTES ON CLINICAL TRIALS WITH MARMOREK'S ANTITUBERCULOUS SERUM.

BY

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RECENT discussions on the value of tuberculin have shown that much diversity of opinion exists as to its efficacy. My experience with tuberculin has been unsatisfactory, but I have obtained rather more success with another agent—namely, Marmorek's antituberculous serum. This serum has been before the profession for a number of years, but no definite opinion of its utility has been formed in this country though many foreign observers have spoken very highly of it.

I here record the treatment and results of 10 cases which were treated by me in the Royal Waterloo Hospital, London, S.E. For allowing me facilities for this purpose I have to thank Dr. Guthrie Rankin.

Two methods of injection are used—hypodermic and rectal. The former is supposed to be beneficial in acute and rapidly advancing cases, while the latter is more efficacious in chronic and apyretic cases. The great drawback to the subcutaneous injection is supersensitiveness, which is common to the injection of all serums.

The dose used was 2½ c.cm., given hypodermically, until anaphylaxis was seen, when 5 c.cm. was given rectally daily for fourteen to twenty-one days. This was followed by an interval of seven to ten days without serum, which was again followed by daily injections for fourteen to twenty-one days. This routine was carried on as long as the case demanded it. Marmorek recommends that even after recovery seems complete weekly doses of 5 c.cm. should be given for several months.

CASE I.—W. S., aged 3, admitted January 9th with great dyspnoea, a harsh, dry cough, almost incessant sunken features, wasted and in an advanced stage of disease, seemed in some measure improved after four injections. By February 8th there were signs of cavitation at the right apex, and death took place on February 24th. Serum had been given daily.

Post mortem: The right pleura was greatly thickened and covered with tuberculous deposit. At the right apex a large cavity with extensive infiltration throughout the lobe was found. The left lower lobe was consolidated, and the bronchial and mesenteric glands were tuberculous.

It was notable that, in spite of the steady progress of the disease, the temperature and pulse were steadied, the symptoms were less severe, and the patient was more comfortable.

CASE II.—I. H., aged 3, was admitted December 21st with history of having recently had pneumonia, while phthisis was rampant in his family. The entire right lung was affected. The usual treatment was adopted, but the disease made rapid progress, and when serum treatment was begun on January 19th the child was almost moribund, with a temperature swinging between 101° to 104° F. By February 12th the child was eating and sleeping well, cough and dyspnoea had disappeared, and physical signs were clearing up, and on March 4th she was sent home much improved, with normal temperature and pulse. Seen a month later, improvement was well maintained, and there had been great increase in weight.

CASE III.—L. D., aged 10, admitted February 25th with tuberculous history and well-defined physical signs throughout the right lung. Serum was commenced on March 1st and continued up to April 4th, when her condition was so much bettered that she was sent to a convalescent home. The physical signs had not altered, but the temperature was normal and the weight steadily increasing. Reported on two months later the child was at school and thriving well.

CASE IV.—S. B., aged 7, admitted February 3rd, complained of rapid wasting, night sweats, cough, and dyspnoea, and was found to have definite signs in the right lower lobe, while bacilli were found in great numbers in sputum. Serum was given from February 8th to March 5th, and he was discharged on March 26th with practically no physical signs in the chest, greatly increased in weight, no cough, and no night sweats. A report on this child could not be obtained two months later.

CASE V.—G. G., aged 3, admitted February 23rd, in a very much emaciated condition, with extensive physical signs all over the left chest. Serum commenced on admission and continued up to March 26th without effect. Death took place on April 3rd, and *post-mortem* examination showed typical miliary tuberculosis.

CASE VI.—A girl, aged 6, admitted January 6th with a large indurated mass of submaxillary and cervical glands, which, in spite of antituberculous treatment for over eighteen months, had persisted. The general condition was good and the lungs were healthy. Serum was commenced on February 2nd and continued up to March 26th, when she was discharged. During this time the glands, which were about as large as walnuts, hard and adherent, diminished to the size of small almonds, and became simultaneously soft and discrete.

CASE VII.—S. E., a boy, aged 7, was admitted on January 7th with swelling around the ankle and a sinus on the external aspect of the os calcis, which had been discharging for about a month. The sinus was opened up and cleaned on admission, but when serum was commenced on January 28th had not ceased to discharge. Injections were continued up to April 2nd, when, after much coaxing, the sinus cleaned up and healed, and good movement in the joint was obtained. One cannot think that in this case the serum had much curative effect, as with the usual surgical treatment a good result would have been anticipated as soon.

CASE VIII.—S. W., aged 2½ years. Admitted February 27th with swelling in right knee. Skiagram showed definite rarefied patch in the diaphysis of the lower end of the femur, with what appeared to be a sequestrum in it, while the joint capsule was much thickened. Serum injection was commenced on admission, and continued up to April 3rd, when the patient contracted measles and had to be discharged from hospital. Before discharge a skiagram of the bone showed very slight improvement, but clinically there was no change.

CASES IX AND X.—Two girls suffering from tuberculous hip disease, with considerable deformity, and, as shown by skiagrams, considerable destruction of the heads of the femora and acetabular cavities. Serum in each case was given for about two months and a half, but recovery was not more rapid than would have been expected with strict surgical treatment alone.

At the Seamen's Hospital, Greenwich, I continued the treatment of phthisis with Marmorek's serum. Eight cases were treated, all in an advanced stage of disease, and, with the exception of one case, no improvement was noted. In this case the patient was a lad of strong physique, in whom weight and chest measurements rapidly increased, and in whom the fever and average weekly weight of sputum diminished correspondingly.

At the time of discharge, however, the sputum was still muco-purulent, and contained bacilli, and the physical signs had not much altered.

It is claimed for this serum that under its influence tuberculous sinuses of old standing rapidly cease to discharge and heal. But in those cases selected for trial this was not found to be so. It is, however, but fair to state that, besides having these discharging wounds, the three cases were in an advanced stage of pulmonary phthisis, and, although treatment extended over three months, no change took place in the amount of discharge from, in the first case, an ischio-rectal sinus; in the second, an old tuberculous empyema wound; in the third, a submental sinus.

Anaphylaxis was a troublesome feature in the administration of the serum by the hypodermic method, and the rectal method was chiefly employed.

The dose for adults was 5 c.cm. for hypodermic and 10 c.cm. in saline solution to 3ij for rectal injection. The frequent rectal injection was much resented by the patients, and this was a decided objection to the treatment.

I cannot claim on these results the success which some Continental writers have claimed. But, in my opinion, the following conclusions are warranted:

1. There is no danger in administration apart from anaphylaxis, which can be overcome by adopting the rectal method.

2. In certain cases the general improvement is most striking, although physical signs are not altered to a similar extent.

3. The undoubted success obtained in some of the cases justifies further clinical trials.

THE next examination of candidates for the Royal Naval Medical Service will be held in London on April 1st and following days. Fifteen appointments will be offered for competition. Application forms, which must be returned by March 21st, and the regulations for entry can be obtained from the Medical Director-General, Admiralty, S.W.