P H T H I S I S .

An Infectious Disease.

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Long before the discovery by Koch of the Tubercle Bacillus in 1882, consumption had been recognised by many as a communicable disease. About the fifth century B.C. it was considered "contagious" by Isocrates, though his more famous contemporary Hippocrates was not of the same opinion.[1] Galen believed it to be dangerous to pass a single day in the company of a consumptive. Avicenna (1037) referred to diseases which are "taken from man to man like phthisis."[2] "A contagious principle also propagates this disease," wrote Richard Morton in 1697,[3] and in many writings since then we have the same opinion expressed. Some authorities, as we would expect, have gone further than others; e.g., in Italy for long the disease has been believed to be contagious, and centuries ago when a victim died there, the clothes and bedding were destroyed, and the house thoroughly cleansed and fumigated, and often shut up and never used again. More than 100 years ago, Laennec's marvellous insight foreshadowed much of our present day teaching of the clinical and pathological aspects of phthisis, though he does not appear to have been alive to its infectivity.[4] The fact that it is an inoculable disease was first proved experimentally by Villemin in 1865;[5] but in the year before this, Bowditch of Boston speaks of it as being "infectious under certain circumstances, but not contagious in the

usual sense of the word;[6] and this is the opinion held by the writers of one of the most recent works on Public Health when they state that "it is a true infectious disease, but only a subinfectious one."[7]

To the view that phthisis is an infectious disease there have always been dissentient voices, but as Newsholme points out, this is only a case of history repeating itself. He quotes[8] as examples Cholera and Influenza which even in the face of overwhelming evidence in favour of their infectivity were considered by medical opinion as late as the middle of last century to be non-infectious. Following on Koch's discovery, the question of the infectivity of phthisis roused much attention, and a committee was appointed by the British Medical Association to investigate the subject by finding the collective opinion of the medical men all over the country. Their report is still one of the most valuable contributions to the subject we possess.[9]

The subject may be said to have advanced another step in 1887, when tuberculosis was classified as a filth disease by Sir John Symon.[10] Since that time the opinion of medical men has been coming round gradually to attach more importance to the part played by the infectivity of the disease, and correspondingly less to the theory of an inherited predisposition. But in this as in some other respects, the medical men of our own

country have been more conservative than our brothers on the Continent and in America; so that even yet we find many of our high authorities - shall I say the majority? - ascribing little or no weight to the part played by communicability in the disease, and an undue influence to heredity - a position which is not supported by facts. A few quotations will serve to emphasise this difference of opinion among present day authorities:-

Fansom writes, "Few medical men who have been long in practice will doubt the existence of family predisposition to tubercular disease," and this he argues from the fact that families, when members have separated, have succumbed to it.[11]

F. Burton Fanning lays stress on the same point.[12]

West considers that "Family predisposition is an essential fact," though he grants that almost daily risks are run.[13]

Horton Smith Hartley says, "The hereditary factor cannot be gainsaid."[14]

Walsham, "There can be, I think, no doubt that there is an hereditary transmission of soil."[15]

Notter and Firth say, "As regards direct contagion, it must be confessed that clinical observation is somewhat opposed to the idea that direct infection from another patient is at all common in the etiology of tubercular

disease,"[16] and speaking of infection by inhalation, "We are convinced that this method of contracting the disease is rare."[17]

Sir Hugh R. Beevor states, "That it is not a disease that requires isolation, and that only under certain quite exceptional conditions does it appear to be infectious at all."[18]

R. Douglas Powell, expressing the same opinion says, "My own personal experience and observation convince me that apart from artificial conditions (such as those brought about by experiment) and in the ordinary circumstances of life, phthisis is not an infectious malady."[19]

Professor Pearson says, "Heredity plays a large part in the effective sources of tuberculous disease," and, "A theory of infection does not account for the facts."[20]

On the other hand, Walshe came to the conclusion that "Much phthisis is in each generation non-hereditary."[21]

Dr. J. Edward Squire says, "Susceptibility to suffer from tuberculous affection was a racial characteristic of human beings, and that there was not sufficient evidence to prove that any special predisposition to that disease was transmitted by heredity by some individuals more than by others."[22]

Millier says "The whole tendency of modern research into the nature of tuberculosis is to show that the disease

is communicable, but not except in very rare instances inherited."[23] He thinks it "infectious in the poor, sporadic in the well-to-do."

Heron says, "It cannot be too deeply impressed upon all intelligent people that the spread of consumption means the spread of the Tubercle Bacillus."[24]

Behring - "I must decline to accept another wide-spread view - namely, that hereditary influences are deciding factors."[25]

Latham says, "Modern knowledge has made such a theory (hereditary transmission of predisposition) less and less probable, for it is becoming clearer that the dominating factor in the incidence of tuberculosis is the opportunity for infection," and he concludes that "the theory of an inherited predisposition is based on insufficient evidence."[26]

Newsholme attaches great importance to case/infection, and his book on "The Prevention of Tuberculosis" is devoted in great part to an elaboration of this view.

Niven also, the Medical Officer of Health for Manchester, who strongly supports the infective theory, has given for some years now in his annual reports many examples of infection in phthisis.

At the late Congress of Tuberculosis held in London, there was complete unanimity that tuberculosis sputum is the most potent factor in the spread of infection.[27]

It is useless, however, to multiply such quotations. They simply exemplify the condition of doubtfulness which must be present in many minds when considering this difficult problem. Reasonable criticism, too, should always be welcomed, as against it the advance of truth is more thorough and certain, though it may be somewhat slower.

In recent years the evidence in favour of the communicability of phthisis has brought many more converts to this ~~belief~~ belief; and it may be said that in spite of the contrary opinion of many high authorities, the general view is more in favour now of ascribing to the disease a high degree of infectivity than has ever been the case in the past. In our profession, however, old beliefs die hard; and the remark which the Committee in 1893 applied to a supporter of the hereditary theory might be made with equal truth to-day - "The desire to accept any explanation of the observed facts rather than that of communicability is exemplified in Return 399." [28] Those who will not accept the view that communicability covers all the facts, cling, as we have seen, to the theory of an hereditary predisposition to the disease - a theory which has done much to retard the progress of preventive medicine. This love of the medical profession for a theory of "family predisposition" can be seen in other diseases also, e.g., cancer, where again the facts seem hardly strong enough to warrant it.

It will now be my endeavour to show that direct case to case transmission plays a very much greater part in the onset of phthisis than any hereditary transmission. I do not propose to waste time discussing whether phthisis can be communicated or not. The possibility and the probability of this have been absolutely proved by Koch and many other observers[29] of the Tubercle Bacillus, its conditions of growth, resistance, etc. All the links in the chain are complete, and that such <u>can</u> take place would surely not be denied in 1909 by even the strongest supporters of the hereditary theory. Again, it has been shown by Koch and others that in the vast majority of cases in the adult at least, the primary lesion is where we would expect it, viz., in the lungs, if the sputum were the principal means of dissemination; but here we are touching on controversial ground, as some observers still hold that the alimentary tract is the site of the primary lesion in most cases. This, however, does not affect the issue, as a large number of organisms even when inhaled must be entangled in the throat and then swallowed. There are doubtless other agencies concerned in the dissemination of the Bacilli than phthisical sputum, but compared with it in importance they are negligable. Regarding the child, one would not be inclined to dogmatise so much, but even here I think that contact with those

who are suffering from the disease is too often lost sight of, and the importance of milk infection is overrated.

Bacteriology then proves case to case infection to be possible, and all medical men must have been witnesses to cases which could not be explained on any other theory than that of direct transmission. Many such cases have been recorded.[30] It is not a matter of inferring that because tubercle is inoculable, it is therefore contagious - we are long past that stage; as Knopf says, "My own investigations in this respect show that what is proved experimentally and clinically to be possible does occur on a large scale."[31]

The conditions of communicability of an infectious disease show wide variations, and in an inquiry into the natural history of such a disease, it is of the first importance to establish these conditions, as upon them the foundations of our preventive treatment are based. Diverse opinions as to the communicability of phthisis have always been held, and it is confusing to find as one does, that, even at the present time, weighty authorities express diametrically opposite views, and all with apparently good reasons. Each founds his opinion on his own experience; and according as the conditions necessary for communicability are present or absent, so will his opinion be given in favour of its infectivity or against it - this confusion

following from neglecting to attach to these conditions the importance which is their due.

Another fact we must be alive to is that in an infectious malady it is very rare for every case to be definitely traced to its source. In Scarlet Fever, for example, - one of our most infectious diseases, - it is impossible in some epidemics to trace more than half of the cases to a preceding one; and the same holds true to a greater or less extent with Diphtheria, Enteric, and even Measles. One explanation, which has in some cases proved correct, but can scarcely be invariably applied, is that the disease has been spread by infection from mild unrecognised cases going about and mixing in ordinary life; and this argument can surely be applied to tuberculosis of the lungs with greater force than to any of these other diseases. It is so much more common, its incubation period so much longer, its onset so much more insidious, and its diagnosis in the earlier stages more difficult, that even if the patient and his medical adviser realise the danger, it is a matter of difficulty to take the necessary steps soon enough to avoid risk.

To prove therefore that infectivity is the factor of prime importance in the spread of Phthisis, it will not be necessary to demonstrate that the source of every case is an individual already affected with the disease - that

were indeed a Herculean task - it must suffice to show that the bulk of the evidence available is strongly in favour of this contention, and that the theory of communicability covers the facts better than any other.

Let me now briefly consider under what conditions the infectivity of phthisis is most marked - a subject which is best discussed here, as in other infectious diseases, from these two points of view, viz., the "soil" and the "seed." The importance of having the "soil" prepared before the virus can gain effective entrance to the body is greater in this than in most other communicable diseases. If it were not so, if every time a few of these organisms chanced to enter they were able to survive and multiply in the tissues, then, from the very nature of things, not one of us should ever be free from this disease. That a person in rude health is able to deal successfully with the tubercle bacilli which not infrequently he must inhale, is granted by everyone; and in such circumstances only an enormous dose would stand a chance of overcoming his resistance. This resistance, however, may be reduced in many ways - disease, bad or insufficient food, overcrowding, or confinement being some of the more common causes; but this list is not exhaustive. Indeed, the fluctuations in his resistance as gauged by the opsonic index are daily and even hourly. It follows, therefore,

that there is no one so healthy but that at some time or other his resistance must be somewhat lowered, and the tubercle bacilli will then more easily establish themselves, and a dose which ordinarily would prove ineffective will now overcome him. To successfully escape the disease, then, one must firstly avoid those debilating causes which make for it the growth of the bacilli in the tissues, and, secondly, avoid the bacilli themselves.

When a consumptive is breathing quietly, the tubercle bacilli are not actually in his breath: they are ejected only by active movements such as speaking, coughing or spitting, and therefore are present in the air either in a finely divided spray as in the two former, or as dust from the dried sputum in the last. Whether the spray or the dust be the more common method of infection has given rise to some controversy, but does not concern us. The inference of importance is that these conditions will be most commonly met with in careless persons and in dirty houses; and that, especially in the case of persons of more careful habits, the contact will require to be close before the virus can be transmitted: e,g., the spray from coughing does not reach further than three to five feet, and this distance is reduced if a handkerchief be held up in front of the mouth. These particles float in the air for a quarter to one and a half hours. Again, in those

using a linen handkerchief, tubercle bacilli are found on the hands in the majority of cases, while if a sputum 32
mug only be used, the hands are free from infection; and again kissing or sleeping together will increase the risk. This then is what we would expect, and it is exactly what we find. Again and again it has been shown that as the general conditions of life in a community improve, the amount of tubercle steadily diminishes; so that the death rate from tuberculosis has come to be considered as good a gauge of the general sanitation of a district as any other single factor. It is surely a strong argument in favour of the infectivity of phthisis that active preventive measures based on this theory have caused a decline in the tuberculous death rate - a decline which in many cases cannot be ascribed to any other cause. One of the most recent examples of such a fall is in the death rate from phthisis in New York where more active measures against the disease have been adopted than in any other great city in the world, 33
and the fall has been correspondingly rapid.

Let us note then that close contact is a necessary condition of transmission; further that the lesion must be an open one, as nearly all clinical cases sooner or later become; and further that this close contact must be continued for such a period as will allow a large dose of the bacilli to be given, or the person to be infected

to get below par. Such conditions are most frequently met with in members of the same family and in the poor. Thus in the light of Bacteriological research, much of the evidence which was formerly considered to be in favour of the hereditary theory really supports the theory of infection; and it must be remembered that the more communicable a common disease like this proves to be, the more certainly will we find it frequently among our ancestors. "There is," says Hillier,[34] "in the majority of carefully recorded cases of tuberculosis a history of continued and generally prolonged exposure to the presence of another consumptive." Newsholme and others agree; and such has certainly been my experience. I think, when we take into account the fact that a healthy person offers so great a resistance to the tubercle bacilli, the percentage of cases in which we find a history of such exposure is very large.

The following examples are by no means rarities:-

A.C.age 35: Electrical Engineer: married, 4 children - all well: no tuberculous family history. He always enjoyed good health till four years ago when he had to work with gas engines. He said "the fumes seemed to irritate his lungs" and he suffered from bronchitis. A fellow workman had phthisis, and used to spit about on the floor so much that the others in the engine house often spoke to him about it. Ever since that

time the patient had a cough, and when I first saw him, he had advanced phthisis.

J.T. age 28:bootmaker: single: no tuberculous family history: ill 7 months: previous health excellent. Five years ago a tuberculous girl had been adopted by his parents. She had lived at home, and had much sputum; and was dying when we admitted him to the sanatorium. He had a well-marked lesion at the right apex.

We must not conclude them that the disease has a low degree of infectivity, or that it is not infectious at all simply because it does not prove itself communicable under different circumstances. At the risk of repeating myself, I would point out that scant attention has been paid to this essential fact by the opponents of the infective theory. They dwell on examples in which infection has not taken place; they quote statistics which serve to show that phthisis under special circumstances is seldom communicated, e.g., in institutions - the very last places, happily, where they would expect such proof did they not ignore the conditions which allow transmission to occur. Thus, against the experience of the world, they ask us to accept as proof the fact that cases have not occurred under such specially selected conditions as among the staff of the Brompton Hospital. The experience of this hospital is quoted in nearly all the books. - In forty years the

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number of cases of phthisis among the staff was "not more common than the average among the civil population of a town." But in contrast with this negative evidence as regards spread in institutions, Bulstrode[36] quotes Corret's figures which show an appalling death rate in the convents of the Catholic nursing orders in Prussia. Even in such selected circumstances as the staff of an hospital, I have myself in a very short experience seen two cases - one a nurse and one a ward-maid - take phthisis in a consumptive ward; and this, be it remembered, is in spite of the fact that the chances are much less in favour of transmission than they are in the ordinary conditions of life.

The contention of those who support the infective theory is that case to case infection is the determining factor in the onset of the disease, and that its action is not governed by any inherited weakness in the tissues of particular individuals to the tubercle bacillus, but is as likely to successfully inoculate the person who comes of a non-tuberculous stock, given an equal chance.

By "Hereditary Influence" is meant a constitutional weakness which is handed on from parent to child in certain families, on account of which the individual is more liable to fall a victim to tuberculosis than a child of non-tuberculous parents - the opportunities of infection

being equal.

The theory of Direct Hereditary transmission of the virus, or "Congenital Tuberculosis" will not be considered, as, even if it does occur in man, which has not yet been proved, it is so rare as to be negligable. This theory must not be confused with the theory of the hereditary transmission of a predisposition to the disease. It has always seemed to me that Bang's classical experiment does not refer to this latter theory, although it is often stated it does; it really disproves the "congenital tuberculosis" theory which already needs no contradiction. (He isolated calves from a tuberculous herd, and in this way produced a herd free from tubercle)

It is difficult to come to an exact understanding of what is meant when speaking of an "hereditary predisposition" in phthisis. Some take it to mean a vague weakness - a "taint" - which is inherited in the tissues generally; while others, in describing it, lay more stress on certain anatomical features - e.g., the apices of the lungs, or a particular conformation of the thorax, depending on say the growth of the first rib, or the position of the sternum, etc. - Altogether it seems rather indefinite.

What then is understood by the terms "tuberculous-diathesis" and "pretuberculous?" It seems to be recognised, since Sir W. Jenner drew attention to it, that

there is a certain type of child who is considered specially prone to fall a victim to phthisis later. Eustace Smith describes the physical conformation of such children as follows:- [38] "They are tall for their age and slightly made; the skin is delicate and transparent-looking, allowing the superficial veins to be distinctly seen; the face is oval and the features generally regular. The complexion is usually clear but not always; the face is sometimes covered with freckles:- and Dr. Cee is of opinion that amongst the poor children of London the existence of freckles is very singular value of a tubercular tendency. These children are often remarkably good-looking with large, bright, intelligent eyes, long lashes and soft silken hair. The limbs are straight; the wrists and ankles small. The nervous system is highly developed, and the general organisation delicate. The teeth are cut betimes; they walk and talk early; and the fontanelle often closes before the end of the second year."

That such children are more liable later to develop symptoms of phthisis has not, so far as I can see, been proved; and even if we take it for granted that they have this special liability, no one asserts that the "habitus phthisicus" is limited to children of tuberculous parents: the statement that we find is that they <u>often</u> have tuberculous parents. What of the others? Again, if such

children often do have tuberculous parents, is that sufficient reason for saying that this condition is an "inheritance" - that it is due to some subtle quality in the tissues of these people which has been handed down from their ancestors, and which condemns them, when they come of age, to receive and harbour the tubercle bacillus, unless perchance they spend a year or so at a sanatorium to remove the curse? Does it not seem preposterous that a few months in the fresh air should make them as other people are? or are we to consider that they are handicapped with a low opsonic index to the tubercle bacillus all through life? I cannot believe that such a condition is to be looked on as a prophesy of ills to come in the future. The following theory is, to say the least of it, a much more reasonable explanation. - The parent who has the disease, in fear that exposure might lay his child open to the "family com_laint," tends in his zeal to make a hot house plant of it. Hence the delicate - almost "refined" look: it is not allowed to play as other children are. This indoor life must in itself have some part in producing the results ascribed above; and if, added to this, we have the effects of small doses of the tubercle poison spread over a long period of time, would not this be sufficient to cause the condition? Is it not possible that the development of this type, instead of indicating that the

child will harbour tubercle on some future occasion, really shows the effects of tuberculous toxin already absorbed? Here, too, is a significant fact. The description by Eustace Smith reads like that of a case of early tubercle of the abdomen, or, to a less extent, of the lung. If this be the correct theory that there is a chronic or latent tuberculosis of the mesenteric glands in these children, the result we would naturally look for would be that a certain proportion should develop a more acute tuberculosis later - the clinical symptoms then arising either from an exacerbation of the existing lesions, or as the result of repeated infections from the parent in larger doses than can be overcome.

Such a conclusion I find is supported by no less an authority than Behring.[39] He holds the "inheritance" of tuberculosis to be merely a wrong name for infection in early infancy - that the "tuberculous diathesis" simply means the penetration of the tubercle bacilli through the intestinal mucous membrane of the infant after birth.

In discussing such cases - those with weak physique whom we would expect - certeris paribus - to succumb quickly, Dr. F. Burton Fanning[40] draws attention to the fact that "in many of these it runs a chronic course: the resistance is good." He points to this as indicating a variation in virulence of the tubercle bacilli, though he

does not explain why the virulence should be low in "many" of them. It seems to me rather to indicate that a tolerable degree of immunity has already been established by the small continued doses of the toxin, and that therefore the resistance is greater. In this connection it is interesting to note that many high authorities - Turban, Weicker and others have come to the conclusion that treatment in sanatoria gives better results in those who should be "predisposed" to the disease by coming from a tuberculous stock; these patients, they say, resist the disease longer and resent it less.[41]

Again, the rapid course of tuberculosis in some cases - e.g., in growing girls, depends on the presence of other organisms - pneumo~~nia~~cocci, influenza bacilli, streptococci, etc. Are we ready to extend our ideas of predisposition to infections by these other organisms? The factors which produce "galloping consumption" surely depend on circumstances outside the body.

That such an immunity as I have indicated can be acquired by a tuberculous patient is certain; we know from the opsonic index that when the consumptive is recovering, this simply means that his resistance is going up - an immunity is being developed. Lathan says,[42] "A child who has suffered from tuberculous glands and has got well, is less likely in our experience than others to suffer from

pulmonary tuberculosis in adult life." "Man is therefore capable of acquiring a partial immunity to tuberculosis. Can he transmit this?"

This suggestion that a certain degree of immunity is transmitted from parent to child was made by Dr. H. Maxon King at the London Congress on Tuberculosis,[43] and it is certainly more in line with modern bacteriological knowledge than the theory of a family weakness to a particular organism. I cannot think of any analogy to this latter theory in all Biology. Different animals undoubtedly offer varying degrees of resistance to an organism, but these differences depend on the species; e.g., compared with most other animals, guinea-pigs are specially susceptible to the diphtheria bacillus; but would we be inclined to believe that such susceptibility varied in different families of guinea-pigs, and that this special weakness as compared with the resistance offered by other families was handed on from generation to generation? I think not. We would much more readily accept the view that the antitoxin produced in the animal would react on the ovum in such a way that the resistance to that particular organism would be greater in the next generation instead of less. An interesting illustration of this was recently brought to my notice. - A mother was vaccinated shortly before her confinement; and as there was an epidemic of

small-pox in the neighbourhood, it was considered advisable to vaccinate the infant; and this was attempted, but the vaccination was unsuccessful; presumably owing to an immunity conferred in utero. The theory of a transmitted immunity to tubercle is worthy of more attention than it has received; and, as stated above, it is certainly more likely to be correct than the more generally accepted theory- if argument by analogy may be applied. Dr. Latham uses the following argument in favour of the transmission of such an immunity.[44]

If we allow that 50% of phthisical patients have a transmitted family weakness, we should expect a progressive increase in the incidence and mortality of the disease, but the opposite is the case. That our resistance is higher is proved by the great prevalence of mild tubercle as shown in the post-mortem table, taken in conjunction with the fact that the Registrar General's returns show the mortality less; thus the death rate per 1000 fell from 3.89 to 1.15 between the years 1837 and 1896. Again, this higher resistance cannot be due to the early death of susceptibles, and therefore a diminution in tuberculous stocks, because the age of maximum mortality has risen in males from between 20 - 25 to 40 - 45, and in females from between 25 - 35 to 35 - 45; therefore their capacity to produce families has largely increased. The segregation,

improved sanitation and improved medical treatment are not sufficient to account for this great fall in death rate, therefore a certain degree of immunity must have been developed: and Dr. Latham is of opinion that this immunity is transmitted from parent to child, and is greater in those who have recovered from tuberculosis. Hence we are more likely to diminish the amount of tuberculosis by advising such subjects to marry, than by advising them against it.

On the same lines, another suggestion has been made, viz., that there may be an immunising agent in the milk of a tuberculous mother. During the first few months of its life, therefore, the child has an apportunity of gradually undergoing a process of immunisation, so that when it comes to receive doses of the tubercle bacilli themselves, these, unless in excessive quantity, only serve to still further increase the resisting power. Behring has been investigating this subject in cattle; he has studied the immunising effect produced on the calf by the milk of a tuberculous cow, and this effect he holds is considerable; "I have," he says, "to be sure, every reason to hope that we are on the right track when we believe that immune milk constitutes a remedy for tuberculosis with which no other remedy can even remotely compare."

I have endeavoured then to show that the work of comparatively recent years is undermining the strongholds of the hereditary theory, viz., the inference that because the disease tends to run in families, it is therefore inherited; the old view of "tuberculous diathesis;" and the argument that because phthisis is non-communicable in institutions, it is therefore non-infectious; and before going on to a consideration of my own cases, it will be convenient here to discuss the question of marital infection, as it is commonly stated that the relatively infrequent occurrence of this tells heavily against the infective theory.

If we are to believe that in married couples the transference of the virus is as uncommon as the supporters of the predisposition theory asserts it is, then I would be the first to grant that the infective theory seems to break down here; but at the same time, it could not be claimed as a point in favour of the inheritance of the disease, and could not help that theory in other than a negative way. According to the figures usually given, infection of the partner has taken place in a very small percentage of cases (- less than 10%) and when we consider that "in at least 30% of the adult population there is a history of consumption in the antecedents"[46] it is apparent that something is wrong when only 10% of those

most exposed to infection fall victims to the disease. If the figures be correct, both theories must be wrong: if either theory be correct, the figures are wrong.

That such infection does take place is abundantly proved by many recorded cases.[47] I have seen two cases myself where the facts admitted of no other possible explanation - the infected partner in each case having a negative family history, and the patients having an excessive amount of sputum - in one the sputum was teeming with tubercle bacilli and in quantity exceeded any other sputum I can remember. Again, the healthy adult resists the disease much better than the child, so we should be prepared to find a smaller proportion of affected partners than of affected children. In taking a "family history," an enquiry which we very commonly neglect to make, is as regards disease in the husband or wife of the patient, and this for two reasons - firstly, it is not a part of the individual's "family history," and again, although it has a peculiar significance in phthisis, it is of no importance in any other disease, and therefore we are apt to forget it. Is one surprised to learn then, that in only 8 of my cases out of 267 married patients there is a note that the partner is affected? That this figure is considerably below the mark, I am convinced. I know that the partner's health was not enquired into in all these cases, but only in a small

proportion. In our initial investigation, therefore, we are in error. Again, in dealing with a disease which can be latent for so long as tuberculosis, we must pursue such enquiries as these for years. This has not been done.

Another way of arriving at the required percentage - that of marital infection - is to take the total number of affected parents, and find in what percentage of these, both partners proved to be tuberculous, but here we must eliminate those whose non-tuberculous partners died before they themselves developed symptoms, i.e., before the partner had a chance of becoming infected- and this again has not been done in my figures, nor does it appear to have been considered elsewhere.

Unless this part of the enquiry is carried out with much more care than anyone has yet taken with it, the figures as regards marital infection must be so erroneous that they cannot be considered at all.

If such an investigation be undertaken, it should be on these lines suggested above; and the value of the results would be much enhanced by having post mortem records of all the cases, and also records of the opsonic indices of the partners taken for prolonged periods.

TABLES.

The following figures apply to consumptives in Leicester and are culled from the Journals of the Isolation Hospital there. Consumptives are admitted to one of the Wards except when space forbids - Dr. C.H.Millard, the Medical Officer of Health for Leicester being one of the first in this country to put a fever hospital to this use. The Tables therefore apply to working class men and women, whose ages range in the great majority of cases from 18 to 40 years.

TABLE I shows their age distribution.

Age.	-15	15-19	20-24	25-29	30-34	35-39	40-44	45½	Totals
Males.	6	43	87	74	49	41	26	15	341
Females.	12	48	64	52	23	13	12	9	233
Total.	18	91	151	126	72	54	38	24	574

TABLE II.

	Total Cases.	Tuberculous F.H.	Non-tuberculous F.H.
Males.	341	132	209
Females.	233	131	102
Total.	574	263	311
Percentage.		45.8	54.2

In 574 cases the Family History (F.H.) has been enquired into, and of that number it is found that 263 show a tuberculous family history, while 311 do not; or, in other words, 45.8 % of cases have a tuberculous relative. This proportion of positive F.H. cases seems when compared with other statistics to be about the average. Of course wide variations in the number are shown by different investigators, (10% to 80% have been found [48]) depending no doubt on the personal factor, the care taken in obtaining the histories, and on local differences. The following figures correspond fairly closely with our own:-

Dr. Theodore Williams found that 48.4 % afforded evidence of family predisposition; while Pollock estimated the proclivity factor at 30%.[49] West found that about 53% have phthisis in parents or collaterals;[50] Squire, when grandparents and collaterals are included, found 62.3%;[51] and Osler found that 211 cases in 427 had positive family histories - or 49.4% .[52]

I believe that by more careful investigation the figure I have obtained (45.8%) could be raised. At the beginning of the enquiry no special stress was laid on obtaining very full family histories apart from any other item in ordinary case taking; and it is found therefore that the more recent cases show a somewhat higher percentage than the earlier ones. Taking the figure as it is, however, and not considering

the question of infection for the moment, it looks as though the victims of phthisis had an undue proportion of relatives suffering from the disease. As Pyne says, "the broad fact that children of tuberculous parents are on the whole more likely than others to become tuberculous has never been doubted;"[53] and it is not difficult to see how this fact gave rise by induction to the idea that a special weakness may lay in the tissues of these children; but we must remember that a large percentage of people taken at random - especially among the working classes - will have phthisical relatives, so common is the disease.

To differentiate between the results of infection and the results of the supposed predisposition is a task which has long been recognised as one of great difficulty. The 1883 Committee say,[54] "it is almost impossible to decide between phthisis which is communicated and that which is hereditary, as patients are generally nursed by members of the same family." When the supreme importance of infection has been demonstrated to everyone's satisfaction, then follows necessarily as one of its results the fact that people most likely to be attacked are those closely associated with diseased persons - i.e., those in the same family circle. It is this fact which has so complicated the problem, but I think some help is gained by a careful analysis of the figures at our command.

Some criticism has recently been offered by Latham on

the value of figures like these. He points out that family histories on this "hearsay evidence" are incomplete, and says, "Statistics as to the incidence of tuberculosis which are based on the statements of relatives are absolutely unreliable."[55] How otherwise he expects to get the necessary particulars, he does not say. Human testimony we know is always liable to error, but, in a mass of particulars covering a number of cases, we can fairly hope to arrive at an approximation to the truth. Surely he is going too far. It is not often in my experience that an adult does not know or at least have a good idea of the disease from which the members of his own family circle have died. It is different with those not so near to him - the patient who can tell the illnesses of his uncles, aunts, cousins and grandparents is certainly the exception. Therefore it seems reasonable to neglect the "histories" of these more distant relatives, and to direct our attention to the near.

TABLE III.

	Total cases.	Positive F.H.	Near Relatives affected	Distant Rel.
Males.	341	132	111	21
Females.	233	131	121	10
Total.	574	263	232	31
Percentage.		45.8	40.4	5.4

From the table, out of 574 cases, 232 (or 40.4%) have a Father, Mother, Sister or Brother affected with tuberculosis of the lungs : more distant relatives only are affected in 5.4%, and these we will neglect.

TABLE IV.

	Total Cases.	Parent + others.	Collateral + others.
Males.	341	53	86
Females.	233	70	80
Total.	574	123	166
Percentage.		22.5	30.4

It is important to distinguish between collateral occurrence of the disease among brothers and sisters, and direct inheritance from a parent. There is some overlapping in Table IV, as in some cases both a parent and a collateral are diseased, and these are included in both columns; this seems the fair way to construct the table, as, if we exclude collaterals when parents are diseased, we are favouring the predisposition theory; while if we omit the parents when collaterals are affected, the "infection" theory gains - "It does not follow that because a parent develops phthisis, his offspring cannot bear witness to the communicability of phthisis."[56]

22.5% of the total cases have affected parents, while in 30.4% a brother or sister is diseased. In 10 of the cases (or 1.8%) both parents are affected. Similar results have been obtained by other observers; thus West finds disease in the parents in 28% of his cases.[57] Williams puts the figure at 24.5%,[58] and Newsholme quotes Walshe and Squire who get 26% and 24.8% respectively, and Wilson Fox whose percentage reached as high as 33%.[59]

If it were the case that "a weakness is transmitted which in the parent has already given rise to the disease," (Niemeyer) would we not expect to find a larger percentage of diseased parents than 22.5? Or we might consider it in this way - 574 patients have 1148 parents, and of these 133 are diseased or 11.5% Does this seem an undue proportion? Dr. J. Edward Squire gives figures of 1000 families he examined, containing 6457 children. In those with phthisical parents, 33.16 % took tuberculosis later, while in those with no phthisical parent, 23.65% took tuberculosis - in the same walk of life. Thus the possible hereditary influence is less than 10%, and when the greater risk from infection is considered, not much is left over for heredity.[60]

Again, why do we find so large a proportion of brothers and sisters diseased? It has been suggested that a common source has "infected" them both; but it seems to me

more probable that the virus is transmitted from the one to the other. It is by no means common for members of a family to die at the same time, or in very rapid succession, though one not infrequently meets cases where they in turn fall victims to the disease with a definite interval between each; the intervals between the cases being usually several years at first, but diminishing as time goes on and the disease assumes a more virulent type. "The very rapid course of so relatively great a number of these cases is noteworthy."[61] This is exactly what one expects to find in an infectious disorder and points to case to case infection. I could give many examples of this, but will limit myself to two:-

SARAH O. age 36, ill 1 year.

Her father died of phthisis 14 years ago, 3 years ill: much sputum. Her mother (who nursed her husband and herself had no tubercular F.H.) died of phthisis 4 years ago: 2 years ill: fair amount of sputum. Her sister (who helped to nurse the mother) died of phthisis 2 years ago: 1½ years ill: much sputum. The patient nursed her mother and sister; when admitted she had been ill one year, and already 3 lobes were involved and her general condition was poor.

Two other sisters are alive and well. They married before the mother took ill, and had not nursed any of

the patients; this was all the family.

It will be noticed in this instance that the periods elapsing between the death of one member and the sickening of the next, are in order 8, ½ and ½ years; and also that the duration of illness steadily diminishes, being 3 years, 2 years and 1½ years, and in the patient it seemed as though it would prove shorter still.

MABEL A. age 16 years: "Hosiery hand:" ill 6 months.

Father died 3½ years ago: ill many years.

Mother " 14 months ago: ill 6 months . (Nursed her husband. Her own father died of phthisis)

Sister died 1 month ago: ill 6 months (nursed the mother)

Patient nursed mother and sister, and slept with sister; she had advanced phthisis on admission.

2 Brothers well: this was all the family.

If,as suggested by some, these patients are infected from the same source, then we must grant a considerable period of latency to the disease, and once latency has been granted, the infectious theory can be argued to any extent. "Latency" is very difficult to establish as opportunities for infection are so frequent, and therefore one cannot exclude the possibility of a recent entrance of the Bacilli when symptoms recur or develop long after a period of

exposure to the disease; on the other hand, the results of post mortem examinations prove that latency must be not infrequent - as we would expect from our ordinary clinical experience. It is for this reason that I have not attempted to sort out the cases into those which developed symptoms when at home, and those taking ill after leaving home. The period of latency which, it is allowed, may be considerable, would make such a table valueless.

By cutting out from Table IV all those cases where both a parent and a collateral are affected, it is found that the parent or parents alone are affected in 66 instances while a collateral alone is diseased in 98 cases. The disease is present therefore in a much larger number of instances in the latter than in the former. Of course those who oppose the infectious theory will contend that an individual has more brothers and sisters than parents, and that therefore the chances of having one of the former diseased are greater than in the latter; but, on the other hand, the collaterals have not all come to the susceptible age, while the parents have passed it. It is instructive to note, however, that the number of cases in which collaterals are affected is actually 50% greater than that in which a parent is diseased.

TABLE V.

Fathers.	Mothers.		Totals.
	Tuberc.	Non-tuberc.	
Tuberculous.	10	69	79
Non-tuberculous	44	451	495
Totals	54	520	574

In this table the diseased parents are divided according to sex. Out of the 123 cases with affected parents, both parents are affected in 10; and of the remaining 113, the father is diseased in 69 instances and the mother in 44: i.e., of the total cases, the father is affected in 12.0% and the mother in 7.7% (i.e., leaving out the ten cases in which both are diseased). These figures are small, but they correspond in results to those of much larger numbers. Thus in the recent report on German Sanatoria,[62] out of 14,069 cases the parent is affected in 3032 instances or 21.5% (compared with 22.5% in our figures).
Of these, leaving out the cases where both parents are affected, the father alone is diseased in 1667 or 11.1% and the mother alone is diseased in 1050 or 7.5%.
We can take it then that our figures are correct.

At first glance, it looks as if these facts were more

in favour of an inherited predisposition than of infection. The child comes into contact more with the mother; therefore if the disease be transmitted by personal contact, we would expect more mothers than fathers to be diseased. This may actually be the case in the child. I have no figures myself, nor have I seen any, bearing on this point. But what explanation are we to offer for the fact that the adult tuberculous patient is more likely (in the proportion of 3 to 2) to have a tuberculous father than a tuberculous mother? The theory I have elaborated above (v. pages 18-21) is quite sufficient to account for it:- the tuberculous mother has conferred some immunity on her offspring in utero, or after birth by means of her immune milk, or has infected the child at an early age and it has either died then, or contracted an immunity. In the light of this theory, the relative frequency of paternal tuberculosis as compared with maternal is by no means so much in favour of the theory of an hereditary predisposition as the casual observer might imagine.

On dividing the 574 cases according to sex, several points of interest emerge. The relative proportion of males and females in the Sanatorium was regulated by the number of beds available for each sex - there were 11 beds for males

to 8 for females, and therefore 341 males in the 574 cases to 233 females.

TABLE VI.

	Total Cases.	Near Relative affect.	Percentage.
Males.	341	111	32.5
Females.	233	121	51.5
Total.	574	232	40.4

The percentage of females with tuberculous relatives is higher than the corresponding percentage of males - in the proportion of 5 to 3; i.e., in a family in which a member or members are already affected with tuberculosis, the females are more than half as likely again to become tuberculous as the males. The same difference appears - it is even greater in the next table in which only those with a diseased parent are included.

TABLE VII.	Total Cases.	Parent affected.	Percentage.
Males.	341	53	15.5
Females.	233	70	30.5
Totals.	574	123	22.5

In females, the number of those with parents affected is twice as many as in males.

Again, our result does not appear to be exceptional.

Bulstrode quotes similar figures from a report of the Brompton Hospital for Consumption, showing that the disease was "hereditary" in 18% of the males, and in 36% of the females.[63]

This difference between "hereditary" influence in males and females is all the more striking when we consider that tuberculosis is actually less common in the latter than in the former. "In 1891-1900, the mortality (from tuberculosis) of females did not exceed four-fifths that of the males."[64] The explanation cannot therefore be that females are more liable to tuberculosis; and on the theory of hereditary susceptibility the facts would be very difficult to explain; whereas on the hypothesis that the communicability of phthisis plays an important part in its onset, the reasons are self evident. The male is out at work all day, closely associated there with his fellows: (and in Leicester that association is particularly close, boot-making being the principal industry) he naturally becomes infected "out" of the family more readily than the female, who being indoors and nursing the sick relative not only puts herself in the way of infection, but prepares the "soil" for the "seed." It might be objected that in the working-class to which these figures apply, the women as well as the men go out working: but, while this theory may be true to some extent, they do not expectorate so much as the latter, and

when a relative does fall ill, it is they who nurse him. I have noticed too that it is the particular individual who nurses the sick member who becomes the next victim, (vide examples, page 31) and this not in one or two instances, but in many. The sequence is often very striking.

There is some evidence too in our cases which supports the contention that the male gets the infection outside and so introduces it to the family circle.

TABLE VIII.

	No. with positive F.H.	No. of tuberculous individuals.	Average no. in family.
Males.	111	197	1.8
Females.	121	255	2.2

On the average the male in a tuberculous house has 1.8 tuberculous relatives, while the female has 2.2. This points to the fact that the female was infected at a later date in the history of the family.

From Table III, there are 111 males and 121 females with affected relatives at home. If the communicability of phthisis be a determining factor of importance in its incidence, we would expect that the males should show a preponderance in the number of brothers affected, with whom

they sleep and to whom they would therefore transfer the disease more freely - and that the females should show no such preponderance.

TABLE IX.

	No. of Cases.	Par$ alone	Brother alone or + other	Sister alone or + other	B. +S	Totals
Males	341	25	41	30	15	111
Females	233	41	31	32	17	121
Total	574	66	72	62	32	232

The figure is everywhere higher for females except under "brother's" infection where it is decidedly lower - as 31 to 41; and if this proportion be corrected for the number of cases having tuberculous histories, the difference is even more marked - viz., as 31 to 45, .i.e., as 2 to 3.

This table admits of only one explanation. When we consider how much help it affords us towards the solution of this much-discussed problem, is it not strange that such a significant fact should previously have escaped attention? It is surely a waste of time to contend that any other theory than that of communicability of the disease will suffice to cover these facts.

Professor Pearson thinks[65] that a larger percentage of women claim a tuberculous relative because they know their family history better than men do, and also because they take a sort of pride in belonging to a diseased stock. In this assumption I cannot agree with him. In my experience, when a man takes a "family disease" like phthisis, he will take quite as great an interest in his tuberculous relatives as his sister will. Even if we accept his theory as being the correct one for tables VII and VIII, we will require to modify it when considering Table IX.

TABLE X.

Marital Tables.

	Total No. married.	No. noted with partner affected.
Males.	143	4
Females.	124	4
Total.	267	8

TABLE XI.

Parents.

	Total no. affected.	No. with partner affected.
Fathers.	79	10
Mothers.	54	
Total.	133	10

These tables show 18 cases of marital infection in 574 tuberculous stocks; and this does not appear to be below that of some other observers.[66] Thus Professor Pearson found 6 cases in 384 tuberculous stocks.[67]

For the reasons given above (page 26) I consider the figures valueless.

Turn now to the course of the disease in the individual, and compare the type of tuberculosis we meet with in those

who come of a tuberculous stock, with that in ordinary mortals.

The average duration of life after attack is exceedingly difficult to arrive at for the following reasons:-

(1) Many of the attacks are mild, unrecognised and not fatal.

(2) The onset is so insidious that it is impossible in many cases to fix the date.

(3) It is so variable, depending on the type of disease, social position, treatment or its absence, etc.

Happily such a figure - it is variously placed at from 2¾ years to over 8 years - is not required for our purpose. The following table is an analysis of the returns obtained in Leicester at the end of 1907. I have included only those who had been discharged for at least one year.

TABLE XII.

		Parent affected	Brother or + Sister.	Distant Rel.	Total + F.HS	Neg. F.HS
After 4 years	Living	10	4		14	17
	Dead	15	3	1	19	13
" 3 "	Living	15	7		22	40
	Dead	7	13	1	21	38
" 2 "	Living	20	14	4	38	58
	Dead	11	13	3	27	34
" 1 "	Living	3	12	6	21	21
	Dead	2	6		8	19
Totals	Living	48	37	10	95	136
	Dead	35	35	5	75	104
	Total	83	72	15	170	240

The point to which I wish to direct attention is that of

240 with no tuberculous F.H. 104 had died = 43.3%

170 " a " " 75 " " = 44.1%

83 " " " parent 35 " " = 42.2%

i.e., the death rate from each of these classes is practically identical, and considering that the opportunities for repeated infections and large doses of the virus must be greater in those living in a tuberculous house, the fact that their death rate is not higher than the death rate of those more fortunately placed seems creditable to their degree of resistance. It points to some process of immunisation instead of to any inherited weakness. (cf. page 20.)

A method of checking this result is to ascertain what percentage of the fatal cases had a tuberculous family history: again, find what percentage of all the cases have a positive family history; and compare these figures. From the above table -

TABLE XIII

	Total	No. with positive F.H.	Percentage
Total Cases	410	170	41.5
Fatal Cases	179	75	42

According to these tables the mortality is not greater among those from a tuberculous stock.

To find if there was any difference with regard to rapidity of course between those cases with a tuberculous family history and those without, the following table has been constructed.

TABLE XIV.

Stage	Tuberculous		Non Tuberculous	
	No. of cases	Av. duration	No. of cases	Av. dur.
1.	22	8.6	15	7
2.	18	8.2	11	6.8
3.	27	7.3	18	10.1
Total	67	8	44	8.4

The number of available cases is 120. Of these 9 had suffered from the disease for more than 3 years before admission, and they were therefore omitted as being somewhat exceptional - being either very chronic, or, as was more usual, recrudescences. Of these 9, 5 had a tuberculous family history, and 4 had not. Nearly all were in Stage II.

The classification which has been adopted is that 68
recommended by Dr. K. Turban -

Stage I. Disease of slight severity affecting at most one lobe or two half lobes.

Stage II. Disease of slight severity more extensive than Stage I, but affecting at most two lobes; or

severe and affecting at most one lobe.

Stage III. All cases of greater extent and severity than Stage II.

The figures in the right hand column represent the average duration of symptoms before admission - in months. It will be noticed that the number of months is slightly less in those cases with a tuberculous family history. This may be because the disease is slightly more rapid in them, or, on the other hand, it may simply mean that they were more on the look-out for symptoms, and presented themselves sooner; and the same may be the explanation of the fact that of the 19 cases with "bad" family histories, the average duration of illness before admission was 7.5 months.

The method of selecting cases for admission would of course have a marked effect on this table - no advanced cases being taken; so that the figures for Stage III must be small out of all proportion.

These numbers are too small to generalise upon, but are included for what they are worth. As they stand, they tend to show that the resistance offered to tubercle by those with a diseased relative is on the whole no less than that offered by other patients. They corroborate the finding of Tables XII and XIII.

From the foregoing analysis of my cases, I think these conclusions might reasonably be drawn:-

(1) The only argument in support of the theory of an

inherited predisposition to phthisis which the figures do not contradict, is that the disease tends to be more common in certain families; and this otherwise unsupported assumption falls to the ground when we attempt to apply it to a further analysis of the cases. Our evidence does not suggest that there is an inherent susceptibility to phthisis, that the rapidity of advance is increased, or that the chances of recovery are on the whole lessened in those who, we are told, have inherited "a special idiosyncrasy of the tissues whereby they become more than merely favourable to the development of the tubercle bacillus."[69]

(2) Our facts support the contention that is based on the work of many observers of the pathological, bacteriological and clinical aspects of the disease: viz., that the onset is determined by opportunity for infection. The theory of transmissability covers all the facts.

When my work first brought me into contact with consumptives and their treatment, I believe that I was prejudiced in favour of the hereditary theory. There my scepticism was roused by finding strong men with unblemished family histories succumbing to the malady with a rapidity which the offspring of a tuberculous stock could hardly equal. It is no exaggeration to say that instances

of infection were to be seen every day: I have refrained - but with difficulty - from quoting more than one or two examples; but what is to be gained by such a course when they are occurring in the practice of every professional man?

Far be it from me to imagine that I am writing the last word in this most complicated problem. The supporters of the theory of an inherited predisposition are surely demanding strong evidence before they will be convinced - evidence quite as extraordinary as they must adduce in favour of ~~the~~ their theory before they could convert us. Such evidence as they seek I do not pretend to have; but I am of opinion that in the near future it will be available by means of the opsonic index. We possess in it a method of testing the individual's resistance to tubercle, much more accurately than was possible only a few years ago; and a careful series of records of opsonic indices, contrasting the tuberculous stock with the non-tuberculous, should go far towards a final settlement of the question. As yet such work has not been done, though, with so many enthusiasts in this branch, we should not have long to wait. We might be pardoned, however, for considering that its results up to the present do not add weight to the theory that one class of person is permanently handicapped through life with a lower opsonic index than another.

This conclusion - that dissemination of the seed alone keeps the malady in our midst - gives us much more reason to expect a rapid diminution in the amount of tuberculosis in the world than we would have dared to hope for had hereditary influences been the deciding factor. Against these we are powerless. Now we can have little doubt that working on those preventive lines which have already borne fruit, the result in the near future will be an enormous saving of life.

So clear is the evidence in favour of our theory, so potent is this factor of infection, and so appalling are its results, that no responsible man, however high be his position, who is not using his utmost power to further the application of those practical measures which are its logical outcome, can be considered guiltless.

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