Advantages of the Test.

1. It may be applied equally readily with bacillary emulsion, with pus or other pathogenic fluid.*
2. The distinctions in the degrees of reaction produced in the joint are absolute.
3. The result of the test is apparent in a comparatively short time; if no acute signs are present three weeks after inoculation the test may be taken as indicating a human infection, and vice versa.
4. The test is specially recommended by its simplicity.

Conclusions.

(a) Just as the general reaction of the rabbit to infection by the human or bovine bacillus varies greatly in degree, so does the local reaction.

(b) The best situation in which to demonstrate such a local reaction is the synovial membrane of the knee-joint.

(c) Infection of the knee-joint of the rabbit with a bovine bacillus produces an intense reaction with acute synovial tuberculosis; infection with the human bacillus results in a chronic synovial thickening.

(d) The test is of value as quickly distinguishing between the human and bovine types of the tubercle bacillus.

I have to acknowledge my indebtedness to Dr. James Ritchie, Director of the College of Physicians' Laboratory, Edinburgh, for his guidance and advice; also to the trustees of the McCunn Research Trust and the Carnegie Trust for defraying the expenses of the research.

THE SOIL AND THE SEED IN TUBERCULOSIS.

BY

HALLIDAY SUTHERLAND, M.D.,

MEDICAL OFFICER, ST. MARILEBONE TUBERCULOSIS DISPENSARY.

THE battle of the soil and the seed—*hérédité du terrain ou hérédité du grain*—has been waged for a century around tuberculosis. If one accepts congenital tuberculosis as a possible but infrequent occurrence, the issue is then centred upon the existence or non-existence of a direct transmitted predisposition to the disease. Those physical signs regarded as evidence of a tuberculous diathesis in childhood are too well known to require recollection, and have generally been ascribed to a transmitted weakness of tissue as the result of tuberculosis in the parents. To D. J. Hamilton² the physical signs of this predisposition were so well marked that he held it to be a true inherited strain of a variation which took place far back in the history of the race. Others have suggested that these physical signs, so far from connoting an inherited predisposition, are the expression of the actual infection of the child after birth. Some years ago, believing in an inherited predisposition, I attempted to controvert this suggestion by a collation of all the myths that had haloed round that blessed word "diathesis."¹

The practice of a tuberculosis dispensary demonstrated to me that which was first proved by R. W. Philip—that childhood is the age at which tuberculous infection is most frequent. If we admit the frequency of tuberculous infection in childhood, it is certain that the actual presence of so profound a neuro-muscular toxin as the tuberculous toxin will exercise a more powerful influence on the metabolism of the child than the influence of a far-off inherited strain. It is not from that standpoint that the question is approached in this paper, but from a consideration of the amount of tuberculous infection among a "contact" population in relation to the absence or presence of the tubercle bacillus in the expectoration of the original patients.

A diagnosis of early pulmonary tuberculosis is made when the following signs are present: Philip's small glands above the clavicle, diminished tidal expansion on the affected side, rapid tailing off of the resonant area above the clavicle, relative dullness, alteration—usually a weakening—of the inspiratory murmur on the affected side, *plus* the presence of a positive tuberculin reaction.

From the dispensary during the year ending December, 31st, 1911, the "contacts" (persons living in the same household) of 204 cases of pulmonary tuberculosis were

The fluid is centrifuged and an emulsion of the deposit injected.

examined. A total of 723 contacts were examined, of whom 420 were found to be healthy, 290 infected with tuberculosis of the lung, and 13 with other forms of the disease. In all 41.9 per cent. of contacts were infected. Of the original patients, some were infectious, having tubercle bacilli in the sputum, while others were non-infectious at the time, since no tubercle bacilli were found. The amount of infection in the contacts showed a marked relationship to exposure to infection. In the families of those in an infectious stage of the disease, the majority (60 per cent.) were infected with tuberculosis. In the families of non-infectious patients, the majority (75.5 per cent.) were healthy. The actual figures are given in the accompanying tables (p. 1435), the original cases being divided into four groups—non-infectious males, non-infectious females, infectious males, and infectious females.

The results are shown graphically in the following diagram:

If we combine certain of these age groups, the amount of infection at different periods of life in relation to exposure or non-exposure to immediate human infection appears as follows:

In Children under the Age of 15 Years.

211 were in relation to non-infectious patients, and 92, or 43.6 per cent., were infected.

161 were in relation to infectious patients, and 120, or 74.5 per cent., were infected.

In Adults between the Ages of 15 and 25 Years.

41 were in relation to non-infectious patients, and 5, or 12.1 per cent., were infected.

63 were in relation to infectious patients, and 42, or 66.6 per cent., were infected.

TABLE I.

Type of Original Case.	Number of Cases.	Number of Contacts.		Number Healthy.		Number found to have Pulmonary Tuberculosis.		Number found Non-Tuberculous.	
		Males.	Females.	Males.	Females.	Males.	Females.	Males.	Females.
NON-INFECTIOUS MALES (No tubercle bacilli found)...	32	46	69	31 (67.4 %)	50 (72.4 %)	14 (30.4 %)	19 (27.5 %)	1 (2.1 %)	—
Total		115		81		33		1	
NON-INFECTIOUS FEMALES (No tubercle bacilli found)	69	153	122	115 (75.1 %)	91 (74.5 %)	38 (24.8 %)	31 (25.4 %)	—	—
Total		275		206		69			
INFECTIOUS MALES (Tubercle bacilli found) ...	55	76	104	22 (28.9 %)	56 (53.8 %)	52 (68.4 %)	47 (45.2 %)	2 (2.6 %)	1 (0.9 %)
Total		180		78		99		3	
INFECTIOUS FEMALES (Tubercle bacilli found)...	48	99	54	38 (38.3 %)	17 (31.4 %)	58 (58.5 %)	31 (57.4 %)	3 (3.0 %)	6 (11.1 %)
Total		153		55		89		9	
ALL TYPES	204	367	256	106 (28.9 %)	214 (83.6 %)	162 (44.1 %)	128 (50.0 %)	6 (1.6 %)	7 (2.7 %)
Total		723		420		290		13	

In Adults over the Age of 25 Years.

138 were in relation to non-infectious patients, and 6, or 4.3 per cent., were infected.

109 were in relation to infectious patients, and 38, or 34.8 per cent., were infected.

From these figures it would appear that childhood is the age at which tuberculous infection of the lung is most frequent, and that where children are exposed to contagion from their parents the amount of infection is almost double that which exists in children of patients in a non-infectious

stage of the disease. Between the ages of 15 and 25 the amount of infection is five times greater in those exposed to immediate human infection than among those not so exposed. Over the age of 25 there is very little tuberculous infection, except in relation to patients in an infectious stage of the disease. Again, while the child is most vulnerable, the danger of exposure to infection diminishes as life advances.

Why 43.6 per cent. of the children of non-infectious consumptives should show signs of tuberculous infection,

TABLE II.—Showing the Age and Sex Constitution, and Amount of Infection among a Contact Population.

Age Groups.	Contacts of Non-infectious Males.						Contacts of Non-infectious Females.						Contacts of Infectious Males.						Contacts of Infectious Females.					
	Males.			Females.			Males.			Females.			Males.			Females.			Males.			Females.		
	Healthy.	Pulmonary Tuberculosis.	Tuberculosis.	Healthy.	Pulmonary Tuberculosis.	Tuberculosis.	Healthy.	Pulmonary Tuberculosis.	Tuberculosis.	Healthy.	Pulmonary Tuberculosis.	Tuberculosis.	Healthy.	Pulmonary Tuberculosis.	Tuberculosis.	Healthy.	Pulmonary Tuberculosis.	Tuberculosis.	Healthy.	Pulmonary Tuberculosis.	Tuberculosis.	Healthy.	Pulmonary Tuberculosis.	Tuberculosis.
0-5	6	5	1	10	2		17	10		14	4		7	8	1	8	2	1	3	6	3	4	6	4
5-10	4	7		4	9		15	15		14	15		3	14	1	2	12		3	14		1	13	2
10-15	4	1		4	4		9	10		18	9		1	11		3	5		2	10		4	7	
15-20	3	1		1	1		7	1		6	2		4	6		5	8		3	8		1	4	
20-25				3			7			9			2	5		2	6		3	4		1	1	
25-30	1			6			1	1		2			1	3		3	2		2	2		1		
30-35	1			8			18			7	1		1	2		4	5		2	4		3		
35-40	4			6	2		16			6						6	3		5	4				
40-45	3			3			11			7			2	3		9	2		4	4		1		
45-50	1						7	1		5						4			4	1		3		
50-55	2			1	1		3			1						3	1		3	1		1		
55-60				1			2			1						1	1		2					
60-65	1			1			2			1						6			2					
65 +	1			2									1											
Totals	31	14	1	50	19		115	38		91	31		22	52	2	56	47	1	38	58	3	17	31	6
	46			69			153			122			76			104			99			54		

Grand total = 723.

whether this is the result of infection from other sources, and what is its relationship to the amount of infection in the children of healthy parents, will be the subject of further investigation. The fact here demonstrated is that at all age periods of life it is the infectious consumptive who is the immediate source of by far the largest amount of disease among those living in relation to him.

Influence of Sex in Contacts.

INFECTIOUS PATIENTS.

In Children under the Age of 15.

87 males were exposed to infection, of whom 68, or 80.4 per cent., became infected.

74 females were exposed to infection, of whom 52, or 71.6 per cent., became infected.

In Adults between the Ages of 15 and 25.

45 males were exposed to infection, of whom 35, or 77.7 per cent., became infected.

36 females were exposed to infection, of whom 24, or 66.6 per cent., became infected.

In Adults over the Age of 25.

43 males were exposed to infection, of whom 12, or 27.9 per cent., became infected.

48 females were exposed to infection, of whom 9, or 18.7 per cent., became infected.

According to the English mortality tables from 1881 to 1910, females are less liable than males to succumb to pulmonary tuberculosis under the age of 5, more liable from 5 to 20, and less liable at later ages. In the incidence of infection as determined above, there was no reflection of this, as males appeared to be more liable to infection at all age periods.

NON-INFECTIOUS PATIENTS.

In Children under the Age of 15.

104 males were not exposed to infection, of whom 49, or 47.1 per cent., became infected.

107 females were not exposed to infection, of whom 43, or 40.1 per cent., became infected.

In Adults between the Ages of 15 and 25.

19 males were not exposed to infection, of whom 2, or 10.5 per cent., became infected.

22 females were not exposed to infection, of whom 3, or 13.6 per cent., became infected.

In Adults over the Age of 25.

76 males were not exposed to infection, of whom 2, or 2.6 per cent., became infected.

62 females were not exposed to infection, of whom 4, or 6.4 per cent., became infected.

It is of considerable interest to compare these percentages with certain figures published by J. Edward Squire in 1895 in *The Influence of Heredity in Phthisis*. In the 1,000 families investigated there were 275 in which neither of the parents were phthisical, and in which 24.87 per cent. of the children became phthisical. In my 101 cases of non-infectious tuberculous patients shown above, 26.4 per cent. of the children and contacts developed pulmonary tuberculosis.

Sex of Patients in Relation to Infection of the Contacts.

INFECTIOUS PATIENTS.

Children under the Age of 15 Years.

79 were in relation to infectious males, and 55, or 69.6 per cent., were infected.

82 were in relation to infectious females, and 65, or 79.2 per cent., were infected.

Adults between the Ages of 15 and 25.

38 were in relation to infectious males, and 25, or 65.7 per cent., were infected.

25 were in relation to infectious females, and 17, or 68 per cent., were infected.

Adults over the Age of 25.

63 were in relation to infectious males, and 22, or 34.9 per cent., were infected.

46 were in relation to infectious females, and 16, or 34.7 per cent., were infected.

Under the age of 15 the amount of disease in the contacts is distinctly greater among those in relation to infectious females than among those in relation to infectious males. The difference is still perceptible between the ages of 15 and 25, but over that age it disappears. This points to the quantity of infection as having a direct influence in the causation of the disease among the

contacts, for children are likely to receive a more massive dose of infection from the female parent than from the male.

NON-INFECTIOUS PATIENTS.

Children under the Age of 15 Years.

61 were in relation to non-infectious males, and 29, or 47.5 per cent., were infected.

150 were in relation to non-infectious females, and 63, or 42 per cent., were infected.

Adults between the Ages of 15 and 25.

9 were in relation to non-infectious males, and 2, or 22.2 per cent., were infected.

32 were in relation to non-infectious females, and 3, or 9.3 per cent., were infected.

Adults over the Age of 25.

45 were in relation to non-infectious males, and 3, or 6.6 per cent., were infected.

95 were in relation to non-infectious females, and 3, or 3.2 per cent., were infected.

There are three factors, on one, two, or all of which successful inoculation with tuberculosis may depend. From experiments on animals we have a right to assume that the amount of infection has a definite bearing on the fact as to whether or not the infected organism develops tuberculosis. In susceptible animals of the same species a massive dose will be followed by development of the disease, where a smaller dose has been successfully resisted. Secondly, it will be generally admitted that, given the same amount of infection, a person in a low state of general health is more likely to develop the disease than a person in good health. The third possible factor is heredity, it having been held that there is a transmitted predisposition to tuberculosis, whereby under equal conditions of infection the children of tuberculous parents are more liable to develop tuberculosis than the children of healthy parents.

It is known that, while some 60 per cent. of the total population has been infected with tuberculosis, a less proportion actually develops the disease. That in itself proves nothing. The fact that the disease does not advance in all who are infected may have a relationship to one or more of the three factors—to the amount of infection, to the resistance as represented by the general health of the infected person at the time, or to some hereditary qualities in his make-up.

There is a greater incidence of tuberculosis among children exposed to infection from their parents than among children not so exposed—the children of healthy parents. That in itself does not prove that exposure to infection is the determining cause, for it does not eliminate the factors of general health and heredity. It is a fair query to ask, "Would the amount of infection required to infect the children of tuberculous parents be sufficient to infect the children of healthy parents?" To answer this question it would be necessary to have the children of both classes of parents exposed to the same conditions of infection. This does not occur under actual conditions of life, but let us grant it. Suppose that the same amount of infection was sufficient to infect the children of tuberculous and of healthy parents. In that case heredity would be eliminated, and infection alone would remain as the determining element. Suppose that the dose of infection sufficient to successfully inoculate the children of tuberculous parents were not sufficient to inoculate the children of healthy parents. That is no proof that the immunity of the latter is due to the absence of a transmitted predisposition present in the former, for there is still the factor of a possible difference in the state of their general health.

It is a complex equation, but is yet capable of solution, provided we are able to prove that susceptibility or immunity to an equal amount of infection is associated with the presence or absence of some factor which is not hereditary.

When we apply the above test as between the children of infectious tuberculous parents and the children of non-infectious tuberculous parents, the issue rapidly clears. Both these groups are the children of tuberculous parents. The question of whose infectiousness is simply an incident in the disease, and the heredity of their children in regard to tuberculosis is the same. Let us put the question, "Would the same amount of infection required to infect the children of infectious patients be sufficient to infect the children of non-infectious patients?" Granted it were

possible, which it is not, that each group receive an equal amount of infection. Then if the same amount of infection were to equally infect the children in both groups, it would follow that infection must be the principal determining cause of the disease. Again, if the same amount of infection which infected the children of infectious cases did not infect the children of non-infectious cases, it is clear that this difference in susceptibility would be due to some factor other than transmitted qualities common to both, and other than the amount of infection which we postulated as common to both. There is no alternative but that the greater susceptibility in the children of infectious tuberculous patients would be due to a variation in their general health, as representing a lowered resistance to infection. It is also obvious that this variation in general health in the children is in relationship to the presence or absence of infectious qualities in the parents. That is to say, susceptibility to tuberculous infection is dependent in an equal degree upon the amount of infection and the general health of the infected person, and that in the case of children the general health is lowered as a direct result of the presence of infectiousness, as distinct from the amount of infection, in the parents. Heredity has no place in this equation.

Is this theorem compatible with clinical facts and experience? It has been shown that in two groups of children, whose heredity is the same, there is a larger proportion of tuberculosis among the children of infectious parents than among the children of non-infectious parents. At first sight this might appear to indicate that exposure to infection in this case was the sole determining factor. That is not so, for before we could prove it the factor of general health would require to be common to both groups. It would be essential that the children of both classes of parents should be of the same physique, the same development, should have the same amount of nourishment, and should be in similar circumstances of home life. Such conditions, however, immediately render any comparison impossible. The infectious parent is generally in a more advanced stage of the disease, which has begun to affect the smallest circumstances of his life. He is less fit for work, his employment is intermittent, and his wages are less. The female with advanced disease is less able to look after her house and children. She is often laid up, meals are less regular, and the selection and preparation of food is indifferent. All these immediate factors tell on the children. They are poorly nourished and ill covered, so that windows are kept closed for warmth. This alone will lower their resistance to tuberculosis and to any other infectious disease, and render them more susceptible than the children of parents in a non-infectious stage of the disease—the heredity of both groups of children being equal, and the amount of infection being equal.

CONCLUSIONS.

1. There is more tuberculosis among the children of consumptives than among the children of healthy parents.
2. This may be due to their exposure to infection, to their lowered general health, or to their heredity.
3. There is more tuberculosis among the children of infectious consumptives than among the children of non-infectious consumptives.
4. This must be due to exposure to infection plus lowered general health, inseparable from it as the result of the stage of the disease in the parents.
5. Therefore it is not heredity which determines whether the children of consumptives will develop the disease, but the existence of certain immediate factors which are under our control.

It is not necessary to argue the case further, but it is possible to imagine a last stand being made for the influence of heredity on the following lines: "Granted an equal exposure to infection and an equal lowering of general health, would the children of healthy parents develop the same amount of tuberculosis as the children of consumptives?" If they did, it would prove that heredity had no influence whatsoever. If they did not, it would indicate that the absence of a tuberculous heredity protected them from infection (incidentally simplifying the tuberculosis problem to an extent no one has dreamt of), and that the presence of a tuberculous heredity was the determining cause in the development of tuberculosis among the children of consumptives, which has been proved to be impossible.

Owing to the rapidly increasing number of tuberculosis dispensaries in this country, the data on which these deductions are based may be tested on an unprecedented scale. If they be corroborated, it means that the influence of heredity is disproved once and for all. Of greater import, it will imply that if our present activity against tuberculosis be augmented we may look with confidence to the total eradication of this disease. On the other hand, should it be proved, as has too long been taken for granted, that soil and seed are independent factors, then, even by a direct attack on the seed (by diminishing the sources of the tubercle bacillus), it would be more difficult to completely exterminate the malady so long as the soil remained (as represented by inherited qualities). This is not so. The children of infectious tuberculous patients and of non-infectious tuberculous patients are all the children of consumptives. The difference in their susceptibility to infection is the direct result of the stage of the disease in their parents. What has been termed for a century "soil" is really the result of the pathogenic action of the "seed." Soil and seed are not independent factors, for they are one and the same. If, then, by the co-ordinated Edinburgh system, the disease is controlled at every point, the resistance of the population exposed to infection will also be raised. The truth is this—that the seed creates the soil.

REFERENCES.

- ¹ Halliday Sutherland, *Edin. Med. Journ.*, 1908. ² D. J. Hamilton, quoted in *ibid.*

A NOTE ON RAT-BITE FEVER, WITH REPORT AND TEMPERATURE CHART OF A RECENT CASE.

By ROBERT W. CRUICKSHANK, M.B., C.M.,
LYNSHAM, OXON.

THIS disease seems so rare in this country, so far as reported cases go, that I think the case described hereafter may be of some interest.

Rat-bite fever, or sokòdu or sokòshio, is a disease, according to Castellani and Chalmers (*Tropical Medicine*), which has been known in Japan, and also in China, for a considerable time and many cases are cited by them, but, so far as I have been able to find, the only cases in this country were three reported by Dr. T. J. Horder¹ (1909-10) and a case in a girl of 3 (1895) by Dr. George S. Middleton (Glasgow).² In America several cases have been noted.³

In the *Epitome of Current Medical Literature* (BRITISH MEDICAL JOURNAL, August 24th, 1912), a case is quoted by Cesare Frugoni, published originally in the *Berl. klin. Woch.*, February 5th, 1912, which he claims to be the first case occurring in Europe diagnosed clinically and carefully observed. There appear, however, to have been at least two others, one in France and one in Spain.³

Diagnosis.

Castellani and Chalmers give the following points:

1. Occurrence of a rat bite.
2. Incubation period of from one to twenty-one days.
3. Periodic form of fever.
4. Negative results of bacteriological culture. (Since then a special parasite, protozoon associated with the neosporidia, has been alleged as the cause. Certain blood changes also noted.)⁴
5. Spontaneous recovery after prolonged duration of disease.

Symptoms.

Three types are described (Miyake):

- (a) Febrile with a marked eruption.
- (b) Afebrile with nervous symptoms.
- (c) Abortive.

The feverish state is accompanied by an eruption of purplish spots. The wound heals during incubation—fever begins abruptly. The site of the bite becomes red and swollen, dropsy may appear, local gangrene is found in some cases. Onset with chilliness, headache, marked weakness, fever, and eruption of dusky-coloured purple spots. Pain may be felt in the abdomen, and diarrhoea may occur. The pulse is rapid and weak, and a feeling of precordial pain and palpitation is complained of. Breathing short; delirium may be present. The disease runs a prolonged course, and recurrences are common at varying intervals.