ON THE PRESENCE OF SUGAR IN THE CEREBRO-SPINAL FLUID FROM CASES OF MENINGITIS.

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WHETHER the reducing substance be dextrose, saccharose, pyrocatechin, or a mucinoid matters not for the purpose of this short paper. There is in normal cerebro-spinal fluid a chemical substance which reduces Fehling's solution, and this is absent in some cases of meningitis and present in others. There appears in the literature of the subject considerable confusion as to the cases in which it is present or absent, and considerable uncertainty as to its value.

My own experience, based, it is true, on only a small number of cases, has led me to a definite conclusion on this subject, and I consider such examination to be of definite value.

The method adopted is to boil together equal portions of cerebro-spinal fluid and Fehling's solution in a narrow test tube and allow it to rest in a sloping position. In the course of an hour there will be a marked yellow deposit forming a band on the lower side of the tube, and with a little practice one can form a fairly accurate opinion as to whether such band is normal in amount or diminished; where sugar is absent no deposit will occur.

My results are as follows:

1. In 9 cases of tuberculous meningitis sugar was present in apparently normal amount in 1 case; was present in diminished amount in 7 cases; was present in markedly diminished amount in 1 case—this was taken only two hours before death.

2. In 7 cases of pneumococcus meningitis sugar was absent in every case.

3. In 3 cases of streptococcus meningitis sugar was absent in every case.

4. In 9 cases of cerebro-spinal meningitis sugar was absent in 2 cases and present in diminished amount in 7 cases.

5. In 7 cases of poliomyelitis sugar was normal in amount in 1 case and slightly diminished in 6 cases.

6. In 3 cases of mixed septic meningitis, secondary to middle-ear disease, sugar was absent in all 3 cases.

Andrew Connell, in a fine paper in the *Quarterly Journal of Medicine*, January, 1910, gives the results of the examination of the cerebro-spinal fluid for sugar in 133 cases of cerebro-spinal meningitis, testing them in every stage of the disease. He comes to these conclusions:

The results prove that sugar is absent from the fluid during the acute stages of cerebro-spinal fever. This finding was invariable, and it depended, as previously shown, on the presence of active acid-forming meningococci. . . . Sugar, however, is not absent at all stages of cerebro-spinal fever, and during the chronic periods of the disease Fehling's solution may be reduced in the presence of living organisms. It may be said, however, with certain reservations, that the reappearance of the sugar is an indication that the disease is in process of cure.

He also examined 122 specimens from 69 cases of tuberculous meningitis. He states his results thus:

In tuberculous meningitis sugar was found to be present in the great majority of the cases, and at all stages of the disease; 122 specimens were examined. An active reduction on boiling of the Fehling's solution occurred in 15, a partial but decided reduction in 102, and no reduction at all in only 4 instances. Complete absence of sugar was observed in only 2 cases. It was noted in the last week of illness, three times in one case and once in the other, and in each case at other times there was a slight reduction of Fehling's solution.

I would state the conclusions thus:

1. In pyogenic meningitis, pneumococcus, streptococcus, and mixed infection sugar is invariably absent.

2. In cerebro-spinal meningitis sugar is absent in the acute stage, but may return in some degree as the infection recedes.

3. In tuberculous meningitis sugar is present, except in very rare cases shortly before death, in which stage difficulty of diagnosis rarely exists.

4. In poliomyelitis sugar is present.

These findings seem sufficiently definite to be of real value.

THE SCIENCE COMMITTEE

OF THE

British Medical Association,

THE ANAEMIA OF ANKYLOSTOMIASIS.

BY

WILLIAM NICOLL, M.D., D.Sc.,

ERNEST HART SCHOLAR.

The Blood Volume in Hookworm Disease (Ankylostomiasis).

IN regard to the first subject of research the conclusions I venture to draw from my experiments are:—

1. Hookworm disease in dogs is not analogous to hookworm disease in man. In the latter the disease is essentially chronic and progressive, gradually leading to a fatal termination. No great degree of resistance appears to be acquired, although some individuals are apparently less susceptible to infection than others. Again, individuals of all ages are equally liable to acquire infection. In the dog, however, the disease is very acute and rapidly fatal. While all dogs appear to be liable to a greater or less degree of infection, only young dogs (under six months) succumb to the disease. In older dogs infection cannot be pushed beyond a certain point, even with long continued administration of infective material. In those a certain degree of anaemia is slowly produced, but it is also gradually recovered from, and the animal may regain its normal state, even although it remains infected with the worm, which infection, it may be added, may last over two years.

2. The anaemia in young dogs was characterised by great loss of weight, emaciation, prostration, intestinal hæmorrhage, greatly reduced temperature, and accelerated and irregular cardiac beat. These symptoms were present to a less extent in older dogs suffering from a minor degree of anaemia. In the latter the erythrocytes were rarely reduced in number to any great extent, but the hæmoglobin fell in some cases as low as 50 per cent. of normal. In the acute disease of young dogs, however, the erythrocytes were observed under one million per c.mm., and the hæmoglobin 10 per cent. In both cases the blood picture was characterised by the large number of erythroblasts, not infrequently of large size, and polychromatophilia. Eosinophilia was not a constant sign either of infection or of disease, and, in fact, was observed only on few occasions.

3. Infection is generally accompanied by fairly profuse intestinal hæmorrhage, which is most marked in the early stages, and tends to disappear later.

4. The blood volume of dogs suffering from the minor degree of hookworm anaemia is not materially altered, but, if anything, is somewhat diminished. The oxygen capacity of the blood per unit of body weight is also, on the average, somewhat decreased. In the acute stage of the disease the blood volume appears to be decidedly reduced.

5. In the early stages of infection the worms attach themselves to the lower reaches of the ileum, but in the course of time they are found further forward.

6. Cats are much less easily infected than dogs, while monkeys and man were found to be insusceptible to infection with the dog hookworm.

FLIES AND OTHER INSECTS AS CARRIERS OF INFECTION.

By WILLIAM NICOLL, M.D., D.Sc.,

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The Length of Life of the Rat Flea.

RAT fleas (*Ceratophyllus fasciatus*) were removed from their host and kept under various conditions of light, temperature, moisture, etc., in order to determine their length of life without feeding. Altogether sixty-four experiments were performed, involving a total of 463 fleas. The average length of life at ordinary temperatures was found to be 6·8 days, but the maximum in one experiment was over forty days. Two per cent. of the fleas lived for over three weeks, and 10 per cent. for over a fortnight. They live longer in winter than in summer, the difference being about two and a-half days on an average. At

very low temperatures (0°–8° C.) their life may be prolonged to over two months. Both excessive moisture and excessive dryness are inimical, but a certain amount of moisture is beneficial. Darkness does not prolong their life, for those which were kept in bright daylight lived, on an average, longer than those kept in the shade or in darkness.

It was further found that fleas may remain in the larval and pupal stages for much longer periods than normal under certain circumstances. Several experiments were made to determine this point. In the first, material containing fleas was removed from a rat cage and isolated. It was observed to remain infected with fleas for a period of over five months. A second experiment continued to produce fleas for a period of eleven months. In a third experiment this period was extended to fourteen months. Some fleas in this experiment at the end of a year were placed along with a young rat, and in three months they had multiplied very considerably.

From these experiments it is evident that the larval and pupal stages of the rat flea, which normally last from two to six weeks, may be prolonged to over a year. As seen in the first set of experiments, the length of life of an adult flea under these conditions is generally under a month, and no evidence was obtained that the fleas multiplied during the period, although this may be possible; so that it may be concluded that the appearance of adult fleas after such a long period as a year was due to the larval and pupal stages being prolonged.

The importance of these observations to preventive medicine lies in the fact that as fleas are carriers of disease, it may be—and is—of considerable moment to determine exactly how long they can exist under various conditions. A full account of these observations is being prepared for publication.

THE OPSONIC INDEX IN PLAGUE VACCINATION.

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[ABSTRACT.]

THE production of immunity in rats vaccinated against plague, is correlated with the production of immune opsonin in the serum of such animals.

Various anti-bodies appear in the serum of animals inoculated with plague vaccines, but the development of agglutinins and bactericidal substances, for example, do not lend themselves to satisfactory quantitative study, in the case of pest. The opsonic response has been studied in man by Douglas,* who found a good response after inoculation with Haffkine's Prophylatic. It, therefore, seemed advisable to correlate the development of opsonin with the absolute immunity of some susceptible animal in order to see whether the amount of opsonin produced could be used as evidence of the development of immunity in man.

In most of the following experiments the results obtained with a single dose of vaccine are recorded in relation to the opsonic index; in others the results of repeated dosage are shown.

* Private communication.

The scope of the enquiry resolved itself into the following points:—

1. Is there any correlation between immunity and opsonic production in plague infection?
2. What is the influence of previous vaccination in the experimental animal?
3. What is the source of opsonin in immune plague serum?

METHODS OF EXPERIMENT.

In all cases the dilution method of Klien (1) was employed. A strain of avirulent plague bacillus killed in 50 % formalin solution was employed in the opsonic technique.

The nucleo-protein used as a vaccine was prepared in the manner described by Rowland in the *Journal of Hygiene* (2).

The bacterial emulsions were prepared from 24 hour agar slopes.

The pooled serum of ten rats were used in each experiment.

EXPERIMENTS ON RATS.

The following is a summary of the results obtained on estimating the opsonic indices of the various pooled sera from day to day (see table at foot of page).

By plotting out curves based on these figures, it will be seen that those obtained with 1/10 mg. whole bacillus vaccine, and 1/100 mg. nucleo-protein are very similar, though in the former case the maximum is displaced somewhat to the right. The doses correspond, as it has been shown that the nucleo-protein contained in the bacillus is about 1/10 the weight of the whole organism. The smallest response is elicited with the smallest dose (1/12000 mg. nucleo-protein) and the largest response with the greatest dose (1 mg.). No response is elicited with the bodies of the bacilli washed free from nucleo-protein, and used as a vaccine, or with nucleo-protein solution which had been hydrolysing for several months, though the hydrolysing process has no effect on the immunising property of the nucleo-protein.† The general conclusions from these experiments would seem to show, as found by S. Rowland, by directly determining the protection aroused in rats to a subsequent fatal dose of living pest, that the soluble nucleo-protein contained in the plague bacillus is the responsible agent in the production of opsonin. The production of opsonin as first rises with the immunity. In the first two series on the table the maximum response is reached by the first day, by which time full immunity is established with this dose of vaccine.

HUMAN EXPERIMENTS.

The dose used in each case was 1/10 mg. of hydrolysed nucleo-protein, which is about the quantity of nucleo-protein contained in 1 cc. of Haffkine's Prophylatic. The first experiment was conducted on myself (R. St. J. B.), the second on five persons who had been inoculated, like myself, some time previously with Haffkine's Prophylatic (P. I.), and the third on

† In the latter experiment the absence of opsonin is somewhat remarkable and may possibly be due to hydrolysis having gone too far, or to the carbolic added as a preservative interfering in some way with the opsonic response. It was subsequently shown that rats, inoculated with this particular vaccine, did not acquire immunity.

DOSE AND NATURE OF VACCINE.	HIGHEST DILUTION OF SERUM WHICH SHOWS A GREATER PHAGOCYTIC INDEX THAN SALINE CONTROL.											
	Before in- oculation.	10 hours.	22 hours.	2 days.	3 days.	4 days.	5 days.	6 days.	7 days.	8 days.	9 days.	10 days.
1/100 mg. nucleo-protein ..	1/16	1/2048	1/4096	1/2048	—	1/1024	1/1024	—	1/256	on 18th	day.	
1/10 mg. whole bacillus ..	1/16	1/1024	1/4096	1/4096	1/2048	1/1024	—	1/1024	1/64	on 21st	day.	
1/12,000 mg. nucleo-protein	—	—	1/512	1/1024	1/2048	1/2048	1/1024	1/828	—	1/512	—	—
1 mg. nucleo-protein ..	—	1/4096	1/6044	1/4096	1/6044	1/2048	1/2048	—	—	1/1536	—	—
1/10 mg. whole bacillus (re- peated dose after 35 days)	—	1/4096	1/16384	1/24476	1/24476	1/16384	—	—	1/4096	—	—	—
1/10 mg. nucleo-protein (hy- drolysing for 8 months)			No	response.								
9/10 mg. of washed bodies of bacilli			No	response.								