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The Horace Dobell Lectures
ON
INSECT PORTERS OF BACTERIAL INFECTIONS.

DELIVERED BEFORE THE ROYAL COLLEGE OF
PHYSICIANS.

By **C. J. MARTIN, M.D., D.Sc., F.R.S.,**
DIRECTOR OF THE LISTER INSTITUTE OF PREVENTIVE MEDICINE.

LECTURE I.

To intervene successfully in bacterial diseases of man and animals it is most important to know accurately the life-history of the parasite outside the host—how it leaves the old host, how it enters a new host, and where and how it passes the intervening period. If we are in possession of these facts, our efforts in the struggle can, at any rate, be intelligently directed and concentrated against the most vulnerable point of the enemy. The exercise of an adverse influence upon bacteria, once they have gained a footing in the body, has hitherto not been generally successful, although recent developments in chemotherapy have shown that there is ground for optimism in this direction.

In the early days of bacteriology, before the large number of pathogenic bacteria had been discovered and their peculiarities had been studied, it was generally assumed that bacteria once let loose from the body survived long periods upon inanimate objects and in water, soil, etc.; and efforts at prevention were directed to an indiscriminate disinfection of the belongings and surroundings of the patient. Some bacteria do, indeed, possess considerable powers of survival under such circumstances, and I would not be understood to deprecate measures of general disinfection. The majority of pathogenic organisms, however, are fortunately delicate creatures, and rapidly succumb to such adverse influences as drying and sunlight.

Another factor which must not be lost sight of is that many organisms which have acquired by selection the property of withstanding the adverse influence obtaining in the animal body fare ill in the competition with hardy saprophytic colleagues outside the body, and, if certain individuals do survive, these, whilst acquiring the capacity to live upon extracorporeal nutriment, diminish at the same time in pathogenicity. In other words, the conditions select a strain tending more and more towards saprophytism and away from parasitism. For these reasons it behoves us to be especially on the look-out for any machinery through the agency of which bacteria may be rapidly conveyed from sick to healthy, and their travels made easier for them.

In not a few diseases the infective agent usually passes almost directly from patient to patient, such as the organisms of syphilis, plague-pneumonia, diphtheria, measles, scarlet fever, small-pox, and numerous parasitic skin diseases. The spread of such highly infectious diseases can be dealt with by isolation and segregation of contacts, for their range is small.

Of recent years much attention has been bestowed upon the study of the rôle of insects in the transmission of

disease. It is not my intention to deal with these discoveries as to the essential part played by insects in the transmission of protozoological parasites made by Smith and Kilbourne, Bruce, Ross; Reed, Carrol, and Agramonte, regarding the transmission of Texas fever, nagana, sleeping sickness, malaria of birds and animals, and yellow fever respectively, further than to point out that it was these researches which focussed attention upon the possibility of bacterial diseases being conveyed by a similar agency. In the latter case the insect plays a less essential part, and no particular phase in the life-history of the parasite takes place within it. I have accordingly, following a suggestion of my friend, Colonel Alcock, employed the term "porters" to describe this passive rôle of insects in the spread of contagion.

HOUSE-FLIES.

A deal of attention has been paid to flies lately in view of their possible influence in the dissemination of infection, more particularly in the case of such diseases as cholera, typhoid, and infantile diarrhoea, in which the infective agent escapes from the intestine and new infections are taken in by the mouth.

The first question is—Can the fly convey infection? Before referring to the numerous experiments which have afforded an answer, I will briefly refer to those points in the life-history, structure and habits of the house-fly which are of assistance in appreciating how it may play such a rôle. These subjects have been submitted to careful

Fig. 1.

inquiry during the last few years, particularly in America and this country, and thanks to the observations of Lowne (1890), Howard (1912), Newstead (1907-9), Griffith (1908), Hewitt (1910), and Graham Smith (1910), we are now well acquainted with this insect, intimate knowledge of which was, until recently, curiously lacking.

The female fly lays about 120 eggs at each laying, and may produce four broods. Under ordinary conditions the eggs are mostly laid on horse, pig, or cow manure, but the excreta of almost any animal, or other fermenting refuse, suffices. The eggs are sausage-shaped with one end sharp, glistening white in colour, and about 1.5 mm. in length and 0.3 mm. in their greatest diameter. The eggs hatch in from three days to eight hours, according as the temperature ranges from 50° F. to 80° F. The larva is a little, active grub 2 mm. long, with a sharp anterior and blunt posterior end (Fig. 1). The larval stage lasts five days to

three weeks, according to temperature. At the time of pupation the grub is 6 to 9 mm. in length. Pupation lasts five days to a month, according to temperature. Thus the whole cycle from laying of egg to emergence of the fly occupies ten days to two months, according as the weather be warm or cold. Shortly after emergence from the chrysalis the young fly spreads its wings, which soon harden, and flies away in search of food. The young female is ready to lay its first batch of eggs in about ten days, or even sooner in warm weather.* During winter a few flies survive in warm and secluded places. In the spring these start the next year's supply. The possible progeny of one female fly from April to September have been estimated at 10^{13} . Howard, of the United States Department of Agriculture, estimates that in forty days the descendants of one fly might number 12 million, or 800 lb. weight.

The only points in the structure of the fly it is essential to direct your attention to are the legs and feet and the general arrangement of the alimentary apparatus. These will be sufficiently obvious from the diagrams (Figs. 2 and 3). Please note that the feet are covered with minute hairs.

Fig. 2.

The latter are, indeed, more numerous and finer than in the diagram, and extremely fine ones are also placed upon the pads (these are stated to secrete a sticky substance, by means of which the fly grips), the basal part of the claws, and the distal stiff hair which projects from the end of the last joint of the tarsus. Each leg is like a minute paint brush, which is applied to the surface of whatever it rests upon.

Fig. 3.

When this is water the hairs do not appear to be wetted. The essential parts of the alimentary canal are a gullet, stomach, crop, intestine and rectum. (See Fig. 3.) The gullet is prolonged to a minute opening between the flaps of the proboscis, halfway down which it is joined by the salivary duct. At the entrance to the stomach it is bifurcated, and one limb of the bifurcation is extended backwards to the bilobed crop. By a valvular apparatus at the entrance to the stomach, the insect can direct the liquid (driven by the pump in its trunk into either the stomach or crop. The proboscis is a highly elastic muscular organ with universal movement. At the end are two flaps or labella (only one of which is shown), which it can open out like the leaves of a book, and apply the medial surfaces to the material it feeds upon. From the middle line or hinge minute chitinous channels pass outwards to the margin. These are seen in the diagram of the front view of the head of a fly

Fig. 4.

(Fig. 4) in which the labella are shown opened out and facing forwards. These tubular structures are

* No doubt the cycle may be shorter or much longer under a wider range of temperature than that from which these records have been taken.

strengthened at frequent intervals by chitinous rings like a trachea, but are not complete tubes, being open to the surface by a minute linear channel with lateral bays in it. At the base of the trunk a number of muscle fibres are attached to the gullet by the peristaltic contraction of which fluid is pumped up from the mouth and propelled into the stomach or crop. The structural arrangement of the flaps of the trunk acts as a filter. Graham Smith (1911) is of opinion that solid objects larger than 0.006 mm. seldom pass into the gullet. According to Nicoll (1911) the ova of such tapeworms as do not exceed 0.035 mm. in their smallest diameter may be swallowed. These must therefore get into the mouth direct. When feeding on a liquid, the fly applies the labella to the surface, and sucks the liquid through the "strainer" first of all into the crop. When this is full some goes into the stomach. In the case of solid material such as sugar, dried blood or sputum, the insect must first dissolve the material. This is done by pouring saliva upon it or more generally by regurgitating some of the contents of the crop (Graham Smith, 1910).

Graham Smith (1910), by feeding experiments with coloured syrup, found that the meal was first taken into the crop, and subsequently transferred to the stomach at leisure. The fly could, however, first fill its crop and then its stomach. In a quarter of an hour the meal had passed on to the upper third of the intestine, and in a warm incubator at 37° C. reached the rectum within an hour. The fly seems to keep some of the fluid in its crop for days.

A well-fed fly deposits faeces abundantly. Graham Smith (1910) noticed flies to do this ten times in the first hour after feeding. A curious habit of flies, to which, so far as I know, attention was first drawn by Graham Smith, is the regurgitation of the contents of their crops. This has already been referred to as a means by which they are enabled to feed upon dry material soluble in water. They do this very frequently when walking over a clean glass, possibly with the idea of extracting nourishment from it. A fly, after a good meal, may often be seen blowing fluid bubbles from its trunk and sucking them in again, as in the diagram (Fig. 5), perhaps for practice.

Fig. 5.

From the above account it is clear that there are *a priori* reasons for suspecting the fly of carrying bacterial infection. Born in a dunghill, it spends its days flitting between the sugar basin, milk pan, and any faecal matter available. Its hairy, probably sticky, feet and the habit of regurgitating the contents of the crop and defaecating at frequent intervals suggests it to be an excellent inoculating agent for any bacteria it may pick up, in the satisfaction of its unsavoury tastes.

That it does, indeed, operate in this way has been abundantly demonstrated. Flies which have wandered over cultures of organisms and afterwards been allowed to walk upon sterile agar plates leave a rich crop of germs as their footprints, which can be demonstrated by subsequent incubation. Castellani (1907) transferred yaws to monkeys in an analogous way.

The carriage of infection by the alimentary canal and its deposition by regurgitation or faeces has also been shown over and over again—Grassi (1883), Maddox (1885), Alessi (1888), Celli (1888), Sawtchenko (1892), Uffelmann (1892), Yersin (1894), Firth and Horrocks (1902), Manning (1902), Hayward (1904), Lord (1904), Chantemesse (1905), Buchanan (1907).

These modes are probably more important than the carriage of bacteria upon the exterior. Many pathogenic bacteria would soon die from desiccation on the appendages of the insect, and, at any rate, the number so conveyed is small compared to those contained in its crop and intestine.

Carriage within is certainly more lasting, for Graham Smith (1910), to whom we are indebted for the most

thorough investigation of this subject, isolated typhoid and other bacilli from the intestinal contents of flies six days after feeding on material containing the organism under test. The faeces ceased to afford growths after two days when typhoid bacilli were the infecting organism used, but with a more robust organism, such as anthrax, which can protect itself from the effects of drying, the time was much longer.

The table below, taken from Dr. Graham Smith's report, summarizes the result of his experiments on the length of time after which various bacilli can be recovered from the outside and inside of flies fed on infected material. As the author is careful to point out, in these experiments gross infection was produced by feeding upon pure cultures, and they do not do more than indicate the duration of life of various pathogenic bacteria under favourable conditions.

Table showing the Longest Period after which Organisms were Recovered from Flies Fed on Cultures (Graham Smith).

Organism.	Legs.	Wings.	Head.	Crop.	Gut.	Faeces.
<i>B. typhosus</i> ...	—	—	—	—	6 days	2 days
<i>B. enteritidis</i> ...	7 days	—	7 days	8 days	7 days	—
<i>B. tuberculosis</i> (culture)	—	—	—	3 days	16 days	13 days
<i>B. tuberculosis</i> (sputum)	—	—	—	—	7 days	5 days
Yeast ...	2½ hrs.	2½ hrs.	2½ hrs.	2 days	3 days	2 days
<i>B. diphtheriae</i> ...	5 hrs.	5 hrs.	5 days	7 days	5 days	2 days
<i>B. anthracis</i> (no spores)	2 days	—	4 days	5 days	3 days	2 days
<i>B. cholerae</i> ...	30 hrs.	5 hrs.	5 hrs.	2 days	2 days	30 hrs.
<i>B. prodigiosus</i> ...	8 days	12 hrs.	11 days	5 days	17 days	6 days
Anthrax spores...	20 days	20 days	20 days	13 days	20 days	13 days

Cao (1906), Bacot (1911), Ledingham (1911), and Graham Smith (1911) have further shown that in the case of larvae fed on material infected with various organisms, *B. pyocyaneus*, *B. typhosus*, and *B. anthracis* respectively, the infection may be carried through the chrysalis stage and recovered from the contents of the intestine of the fly after its emergence. Fortunately, however, according to Ledingham, *B. typhosus* leads a precarious existence in competition with the natural bacterial flora of the larvae and pupae.

There are numerous recorded instances in which the pathogenic organisms of cholera, typhoid, phthisis, anthrax, and plague have been recovered from the interior or dejections of flies which have been captured in the immediate neighbourhood of cases of the disease or, in the last two cases, of carcasses of animals dead of the disease. Cholera vibrios were isolated from wild flies under these circumstances by Tizzoni and Cattani (1886), Simmons (1892), Tsuzuki (1904); typhoid bacilli by Hamilton (1903), Ficker (1903), Faichnie (on seven occasions) (1909), Bertarelli (1910), and Cochrane (1912); tubercle bacilli by Spillmann and Haushalter (1886), Hofmann (1888), Lord (1904), Hayward (1904), Cobb (1905), and Buchanan (1907); anthrax by Cao, and plague bacilli by Yersin (1894) and Hunter (1906).

The spread of ophthalmia in hot countries has, on good grounds, been attributed to the agency of flies in carrying the Koch-Weeks bacillus and the gonococcus from eye to eye—Budd (1862), Laveran (1880), Howe (1888), Axenfeld (1907). The seasonal and local prevalence of ophthalmia corresponds with that of flies, and a visit to Egypt during the fly season is sufficient to convince one that this must happen.

Are Flies the Determining Factor in Epidemics?

Although, however, flies may be discovered with the infection of a number of diseases in or upon them, and by their habits may not unlikely serve as agents in transferring infection, it by no means follows that they are the determining factor of epidemicity in the case of cholera, typhoid, dysentery, etc. In the case of fulminating epidemics of typhoid and cholera associated with an infected water supply this is obviously not so.

Flies in Relation to Typhoid Fever.

The conclusion that fly transmission is the principal means of spread of typhoid in military encampments and

stations has been arrived at by a number of competent observers, amongst them Veeder (1898), Reed, Vaughan, and Shakespeare (1900), in their report on the origin and spread of typhoid fever in the United States military camps during the Spanish war of 1898, and by Tooth and Calverley (1901), Smith (1903), Purdy (1909), and Wanhill (quoted by Purdy).

The sanitary arrangements of a military camp are not exactly those of the Ritz Hotel, and the prevalence of flies in late summer can hardly be appreciated by those who have not had the experience. The conditions are most favourable for transmission by flies. The circumstantial evidence against them is so strong as to have left no doubt in the mind of the American Commission that these insects play a large share in disseminating infection, for page 28 of their general statement and conclusions reads thus: "Flies undoubtedly served as carriers of infection."

An estimate of the fly population and its relation to admissions of enteric was made by Ainsworth (1909) in Poona. The observations showed that enteric had a very definite season, commencing at the end of the hot dry weather with the onset of the rains, and reaching a maximum a few weeks after their cessation. The abundance of flies increased also soon after the beginning of the rains, but earlier than the admissions for enteric, and, speaking generally, the fly curve antedated that for enteric cases by about one month.

Taking into account the incubation period for the disease, this fact is in agreement with the view of a causal relation between cases and flies in Poona. The number of observations is unfortunately small.

In considering the possible influence of flies in the spread of typhoid in a well sewered city, it must be remembered that the opportunities for flies to pick up the infection are vastly less than under the conditions of a military encampment, or even in rural surroundings. In large cities, no doubt, dejecta and urine from patients may be left available to flies, but the bulk goes promptly into the main drain.

The discovery, in cities like London and Manchester, of the majority of cases of typhoid, and their removal to hospital before the period when the excreta contain large numbers of bacilli, must also greatly reduce the liability to the dissemination of the disease by flies. The typhoid-carriers, however, remain.

Dr. Niven (1910) has made observations upon the prevalence of flies in Manchester since 1904. Twelve to thirty-four bell traps were served out to the inhabitants of small dwellings in different quarters of the town and the catch collected every few days by his inspector. Data have thus been obtained which are sufficient to afford information as to the general time relationship between fly prevalence and the incidence both of enteric and infantile diarrhoea.

It must be remembered, however, that the number of flies entrapped in twelve or seventeen rooms indicates only in a general way the prevalence of these insects in a large city, so that too much significance must not be attached to other than the main features of the record.

On pages 62 to 69 of Dr. Niven's paper are plotted the numbers of cases of enteric (commencement) and the diarrhoea deaths for each week of the year from 1891 to 1908. Whilst the latter show well-marked rises during some ten to twelve weeks of the summer, the seasonal prevalence of the latter is not striking. Speaking generally, the typhoid season in Manchester is considerably later than the diarrhoea season, and the enteric cases reach a maximum in late autumn, at a time when most of the flies have already disappeared.

The census of flies commenced in 1904, and, for the years 1904-9, coincides fairly well in time with the diarrhoea deaths if these are antedated ten days to allow for the average period ensuing between commencement of the disease and death.

If we assume that the same close time relation existed throughout, the observations taken as a whole seem to me to lend little support to the view that typhoid in Manchester is to any material extent dependent upon transmission by flies.

The time relation of fly prevalence and typhoid cases was also studied in Washington during 1908 by Rosenau, Lumsden and Kartle (1909) in collaboration with Howard, Entomologist to the United States Department of Agriculture.

In Washington in 1908 the flies (*Musca domestica*) appeared in considerable numbers in April, and reached a maximum in July. During August and September they steadily diminished to about one-third, and rose again in October. The relation of the two curves was not such as to suggest that flies play much of a rôle in the transmission of typhoid fever in Washington.

In a subsequent report on typhoid fever in Washington Lennoden and Anderson (1911), from an analysis of the incidence of typhoid upon the population using privies or yard closets, discovered that the greater prevalence of typhoid among these persons during the summer coincided with the fly season.

Fig. 6 shows the time relation of fly prevalence to enteric fever notifications for London during 1908. The

Fig. 6.—Relation in point of time between prevalence of flies, diarrhoea mortality, and cases of enteric fever, London, 1908. The deaths from diarrhoea have been antedated ten days; the cases of enteric notified have been antedated three weeks. A, Enteric cases. B, Flies caught per day ÷ 9,600. C, Diarrhoea deaths per week ÷ 20.

data are taken from Dr. Hamer's (1909) observations giving the mean number of flies caught each day in 141 situations grouped around 9 centres. The observations being upon a larger scale, the sampling was presumably more representative of the fly population than the records in Manchester. I have antedated the records of the number of cases of enteric fever by three weeks—ten days for average lapse of time prior to notification, and eleven days for average incubation period. It will be seen that the number of cases of enteric fever rises steadily during the fly season, but that the rise continues independent of the fact that flies are rapidly diminishing, and reaches a maximum at a time when they have retired for the winter.

As regards seasonal incidence of typhoid fever, 1908 is fairly typical of what has occurred in London during the last twenty years. As the weather became warmer, the number of infections with typhoid increased, and was not cut short by the fall in temperature usually occurring in September, but reached a maximum in October and November—that is, at a time when there are hardly any flies about. Whether, as Dr. Niven believes, increased fly prevalence is a factor in determining the increasing incidence in Manchester and London at the end of the summer, it seems to me impossible to say, but, taking into account the circumstantial evidence against the fly, this may not unlikely be the case. It is clear, however, that other causes are operative, and that epidemics of typhoid occur in these cities in the absence of flies.

This is in striking contrast to the observations in military camps both during the Spanish-American war and the Boer war. In both these instances, with the onset of cooler weather and the first frosty nights, the nuisance from flies was at once relieved, and the cases of enteric diminished shortly afterwards.

Flies in Relation to Infantile Diarrhoea.

As the infective agent of infantile diarrhoea has not been identified, no direct evidence that flies do, on occasion, convey the germs of this disease is available. It is probable that more than one etiological factor for infantile diarrhoea exists. Different organisms have been

found to be particularly prevalent in the stools in different epidemics in various localities. In America some of the epidemics have been associated with the presence of a dysentery bacillus (Flexner's bacillus) in the stools, Wollstein (1903), Park (1903), Duval and Schorer (1903), Cordes (1903), Weaver and Tunncliffe (1905). In other epidemics (in America) no dysentery bacilli were found, and an epidemic in Vienna investigated by Jehle and Charleton (1905) was not found to be associated with dysentery bacilli. Metchnikoff (1909) is of opinion that *B. vulgare* is the causative organism.

A search for evidence of a causal agent was conducted on a large scale by Morgan (1906, 1907, 1909) and his colleagues of the Lister Institute during the epidemic in London in the years 1905, 1906, 1907, and 1908. The search was restricted to aerobic bacilli which neither fermented lactose nor liquefied gelatin—that is, to a group which includes the dysentery, typhoid and paratyphoid, and Gaertner bacilli. Stools and autopsy material were examined from several hundred cases of the disease and from other children. A very large number of organisms were isolated and examined, but the only one whose prevalence was found to be related to infantile diarrhoea was a non-motile bacillus of this group, which was peculiar in that it failed to ferment mannite and is now generally known as Morgan's bacillus No. 1. This organism was not infrequently recovered from the organs in fatal cases and produced diarrhoea when fed to monkeys and young rats. It was rarely encountered in children not suffering from acute diarrhoea.

Morgan's bacillus has been found in flies captured from houses in which cases of diarrhoea occurred, but until its causal relation to the human disease is proven too much significance cannot be attributed to these observations.

We are therefore entirely dependent upon epidemiological facts in testing whether the belief in the dominant influence of the house-fly upon the occurrence of epidemics of infantile diarrhoea, a view which has been warmly exposed by many excellent observers, is valid.

THE RELATIONS IN TIME BETWEEN CASES OF DIARRHOEA AND PREVALENCE OF FLIES.

Unlike the case of typhoid, which has just been discussed, epidemics of infantile diarrhoea in towns exhibit a close time-relation with fly prevalence. Epidemic diarrhoea of children does not occur except during that season of the year when flies are abundant and active, and, as will be seen on studying the charts, the relation between

Fig. 7.—Dr. Hamer's observations on the relation in point of time between prevalence of flies and diarrhoea mortality in London, 1907 (163 fly-collecting centres). The deaths from diarrhoea have been antedated ten days. A, Weekly mean atmospheric temperature. B, Number of flies caught per day ÷ 10,000. C, Diarrhoea deaths per week ÷ 20.

fly population and diarrhoea cases is so striking as to suggest something more than a mere accidental dependence upon the same phenomena.

The charts, Figs. 7, 8, 9, 10, and 11, show the relation of diarrhoea and fly-prevalence in time. The three first are derived from Dr. Hamer's observations in London in 1907, 1908, and 1909. Figs. 10 and 11 are constructed from Dr. Niven's (1910) observations in Manchester in 1904 and

1906. I have selected these particular years from the Manchester data because they represent what happened in a warm summer in which the number of cases was considerable.

The charts have undergone some manipulation at my hands. I have antedated the deaths by ten days, which, according to Dr. Niven's observations, represents the average period intervening between onset and death. They ought no doubt to be antedated further to include the incubation period, but I have no data to determine what this should be. In the case of Dr.

Fig. 8.—Dr. Hamer's observations on the relation in point of time between prevalence of flies and diarrhoea mortality in London, 1908. The deaths from diarrhoea have been antedated ten days. A, Mean atmospheric temperature for the week. B, Number of flies caught per week $\div 9,600$. C, Diarrhoea deaths per week $\div 20$.

Hamer's observations, I have summed his tri-weekly observations and plotted the fly-catch for the whole week. In this way I have eliminated most of the irregularities and obtained smoother curves. I have also added the weekly mean temperature for London for the period comprised by Dr. Hamer's observations, and (in Fig. 8) for about two months previously.

The procedure adopted by Drs. Niven and Hamer to obtain data regarding fly prevalence was common in all cases. The number of flies caught on sticky paper, or entrapped in a series of domestic dwellings, generally in

Fig. 9.—Dr. Hamer's observations on the relation in point of time between prevalence of flies and diarrhoea deaths, London, 1909 (thirty-five fly-collecting stations). The deaths have been antedated ten days. A, Weekly mean temperature of atmosphere. B, Number of flies caught daily $\div 2,500$ (weekly mean) $\times 4$. C, Diarrhoea deaths weekly $\div 20$.

neighbourhoods inhabited by poor people, were recorded every two or three days. This estimate of the prevalence of flies, together with the deaths from diarrhoea, were then plotted as ordinates against weeks as abscissa. Dr. Niven's observations extend over five years, and refer to several districts in Manchester. Dr. Hamer's organization for the capture of flies was on a larger scale, and his observations were made at various parts of London during 1907 and 1908 and 1909, mostly in the neighbourhood of refuse and manure depôts, where flies are bred. Another excellent series of observations was made by Dr. Dudfield (1912) in Paddington during the summer of 1911. It

concerns a smaller number of cases, but this enabled a more intensive study of many factors contributing to the epidemic to be made.

The first point brought out by all these observations is the dependence of both the number of flies and the epidemic upon the cumulative effect of previous warm weather—as, for instance, is indicated by the earth temperature 4 ft. below the surface, a fact to which attention was first drawn by Ballard (1889). The curve for flies rises first, followed soon by that for cases. The latter is longer in getting going; this is particularly marked in the

Fig. 10.—Dr. Niven's observations in Manchester, 1906. The deaths from diarrhoea are antedated ten days. A, Mean weekly temperature. B, Number of flies caught $\div 2,000$. C, Deaths from diarrhoea.

cool summer of 1907. Both flies and cases reach their maxima about the same time. In 1907 the number of cases is diminishing whilst flies are still on the increase. In 1908 and 1909 both curves decline together, but that for flies more gradually.

A notable feature of the curve is that the same fly population is accompanied by a rise in the number of cases in early August and with a fall in early September. This fact has been quite properly emphasized by the critics of those advocating the importance of flies.

If we propose to regard the time relations of fly prevalence and diarrhoea cases as more than an interesting

Fig. 11.—Dr. Niven's observations, Manchester, 1904. The deaths from diarrhoea have been antedated ten days. A, Mean weekly temperature. B, Deaths from diarrhoea $\div 10$. C, Number of flies caught $\div 2,000$.

coincidence, we must find a satisfactory explanation for the above facts. Let us consider for a moment how the dependence of diarrhoea epidemics upon the accumulated effect of temperature might be explained.

The reason why the number of flies should be dependent upon this factor is obviously because the generation time (cycle from egg to egg) is dependent on temperature and requires three weeks or upwards in our climate. Months of warm weather are therefore required to produce any multitude of flies from the few surviving the winter.

Why the epidemic should exhibit this dependence is not obvious. Not knowing the etiology of diarrhoea, we must assume some sort of infective agent. From analogy with

typhoid, cholera, acute food poisoning, and dysentery, we will suppose that we have to deal with some form of bacterium with which our aliments might become infected. In this case, would the dose of infection be dependent upon the accumulated effect of temperature during the previous three months? Assuredly not. The generation time of bacteria is so short—in the case of *Bacillus coli* it is one hour at 20° C. and half an hour at 30° C.—that the number present at any moment is to all intents and purposes dependent only upon the mean temperature during the last few days. To take a homely illustration, whether one's milk sours does not depend upon the temperature last month but last night.

Rate of Multiplication (Maximum Observed).

Days.	House-fly, August–September, 1907. Brighton.			<i>B. coli communis</i> , 20° C.
0	1 (Female).			1
	1st Gen.	2nd Gen.	3rd Gen.	
1	—	—	—	10 ⁷ (10,000,000)
2	—	—	—	10 ¹⁴
5	—	—	—	10 ³⁵
10	—	—	—	10 ⁷⁰
20	100	—	—	
30	100	—	—	10 ⁷²⁰
40	100	5,000	—	
50	100	5,000	—	
60	—	5,000	125,000	10 ¹⁴⁴⁰
	Total	...	...	150,000

In the accompanying table I have set out the rate of multiplication of *B. coli* at 20° C. and that of flies inside a house during a summer in England. You will observe that one female fly might under these conditions possess 150,000 progeny in sixty days, but the bacteria derived from one organism become innumerable in two days. Unless, therefore, the effect of two months' summer weather be to change the nature of the organism so as to enhance its virulence, it is quite impossible to account for this striking characteristic of the epidemic by chance contamination of food supply by pathogenic bacteria. In a state of innocence regarding the etiology of the disease, we have no means of knowing whether any such change in virulence occurs under the influence of continued warm weather, but it is just conceivable.

On the other hand, we have excellent *a priori* reasons for supposing that flies could transmit the infective agent of diarrhoea. Any one familiar with the domestic ménage of the average working man on a hot summer day, with the baby sick with diarrhoea and other small children to care for, must realize that the opportunities afforded for fly transmission are adequate enough.

It seems to me, therefore, that before abandoning the view that diarrhoea is a bacterial infection, or making the gratuitous assumption that a long spell of warm weather is necessary to awaken pathogenicity, one must carefully examine the adequacy of the view that the dependence of the epidemic on accumulated temperature is to be accounted for by the operation of this factor upon the means of transmission.

We will now see whether this interpretation fits the rest of the facts.

The greater steepness of the rise of the diarrhoea curve is consistent with this view, for at first the opportunities for a fly to transmit the infection are small, but as the cases increase opportunities increase likewise.

As has been pointed out by Hamer and Peters (loc. cit.), if variation in the number of fly transmitters of an infective agent existing in the stools of patients were the sole factors concerned, the curve for diarrhoea cases should shoot up beyond and come down later and more slowly than that representing the number of flies, because the opportunities afforded to flies to pick up the infective agent are increasing *pari passu* with the development of the epidemic. This is, however, not what happens. On

the contrary, the epidemic is arrested while flies are numerous and declines more quickly than the fly population. We are therefore confronted with the question, What arrests the rise in the epidemic wave?

Exhaustion of susceptible material has been suggested. This obviously plays a part in every epidemic, and the observations of Peters (1910) in Mansfield, where, under similar conditions, in one section of the town the epidemic was nearly finished whilst in another it was beginning, afford a demonstration that it is a factor of importance. As, however, small epidemics in cool summers exhibit the same feature, this cannot be entirely responsible for the arrest.

Another factor which must be taken into account is the atmospheric temperature at the time. A glance at the charts (Figs. 7, 8, 9, 10, 11), in which the weekly mean temperature is also shown, suggests that this is playing an important part, for the decline of the epidemic occurs immediately upon a considerable drop in mean temperature, and a diminution of fly prevalence often follows shortly afterwards. The influence of atmospheric temperature appears to be more marked upon the number of infections than upon the number of flies. Whereas in London, 1908 and 1909, following shortly upon the colder weather, both curves drop in a remarkably similar fashion; in the small epidemic of 1907 the number of flies still remains up and even increasing, whilst the epidemic is rapidly disappearing. The same general facts emerge from the Manchester observations. We might invoke the assistance of coincident exhaustion of susceptible material or diminished activity of flies, although still numerically sufficient, in explanation of this. They may indeed be operative, but I think that a completely satisfactory interpretation of the above facts, and also of the fact that, with a given number of flies, the epidemic wave is ascending during the early weeks of an epidemic and subsiding a month or six weeks later, is afforded by taking into account the influence of the variations in atmospheric temperature upon the rate of multiplication of the infective agent. Regard for a moment (Fig. 8) the chart expressing the results of Dr. Hamer's observations in London, 1908. Take the weeks ending August 25th and September 12th, in which approximately the same number of flies were caught. The mean temperature for the former week was 62.6° F.; for the latter it was 54.8° F., and it had been down to 53° F.

The atmospheric temperature is a factor to which insufficient attention has been given, since the origin of the epidemic showed but small relation to it. It is capable, however, of explaining why the epidemic wave rises in August and falls in September, although the number of flies may be the same. Assuming, for the sake of argument, some form of bacterial infection is the etiological factor in infantile diarrhoea, it would be in accordance with general experience to suppose that the chance of infection is determined by the quantity of the infecting agent imbibed.

This will depend upon the multiplication which has taken place in the infected medium prior to ingestion; this, in turn, is a function of the temperature at which the milk or other foodstuff has been kept. The temperature coefficient of bacterial multiplication is not higher than that governing ordinary chemical processes—namely, two to three times for 10° C.—but as bacterial multiplication proceeds logarithmically a comparatively small change in rate is sufficient to produce a large difference in the number of organisms contained in, say, an infected milk, if an interval of some hours elapses between inoculation and drinking. Thus if *N Bacilli coli* be inoculated in milk at 60° F. and 70° F. respectively, the number after twelve hours will be 126 N and 4,000 N respectively.*

We have, then, two factors which may contribute in varying degree to the decline of the epidemic.

1. A fall in temperature diminishing (a) the activity and number of supposed transmitters, and (b) the dose of infection which the child ingests owing to the effect upon the rate of multiplication of the infective agent.

2. The exhaustion of the more susceptible individuals. Sometimes one, sometimes another of the above factors appears to predominate. For instance, we have the fact to

* For the observations on which this calculation is based, see Dr. Janet Lane-Claydon's paper, "Multiplication of Bacteria and the Influence of Temperature thereon," *Journ. of Hygiene*, ix (1909), p. 239.

which attention was drawn by Peters (1909), that in a much hotter climate, such as Australia, the epidemic often declines, notwithstanding the fact that the temperature may continue to rise for several weeks. In Fig. 12 below I have plotted from a paper by Stawell (1899) the monthly mean temperature and monthly diarrhoea mortality in Melbourne for the years 1895-96. In this city, where winter and summer succeed one another without the long intervening periods we have here, the epidemic lasts for six months instead of six weeks. It will be noticed that in 1895 the temperature continued to mount for two months after the summit of the epidemic. In Melbourne the decline cannot be due to diminished dose of the poison owing to slower rate of bacterial growth, but must be attributed to exhaustion of susceptible individuals or to the effect upon the presumed transmitting agents, the flies. In

Fig. 12.—Diarrhoea mortality and mean monthly temperature, Melbourne, Australia. A, Summer, 1895-6. B, Summer, 1896-7.

the absence of definite quantitative observations I cannot speak dogmatically, but, as far as my memory serves me, I think the number of flies diminishes in Melbourne, as in Washington, during the hotter weather. A monthly mean temperature of 70° in Melbourne indicates that there were a good many days with a maximum shade temperature of over 100° F., which in that locality is associated with extremely dry north winds. Such meteorological conditions are very fatal to flies both in larval and imago stage. On hot-wind days flies have to seek shelter out of the sun, or they rapidly become desiccated. For the same reason they succumb on an exposed window pane, and large numbers of dead flies accumulate on the window frame.

The Relation of Fly Prevalence and Diarrhoea on Space.

No quantitative observations upon the relation between number of flies and the distribution of cases of infantile diarrhoea have, as far as I am aware, been made, but I may mention a few impressions by different observers for what they are worth. Nash (1909), who, whilst medical officer of health for Southend, made, during 1904, spot maps of the epidemic there, says: "The great majority of the deaths from diarrhoea were shown to have occurred in streets in proximity to brickfields, in which were deposited daily some thirty tons of fresh house refuse, which bred incalculable numbers of flies" directly the meteorological or seasonable conditions became favourable for their development.

Dr. Niven (1910, p. 45) is of opinion that the close correspondence between flies and cases of fatal diarrhoea receives a general support from the diarrhoea history of sanitary subdivisions of Manchester, and that the few facts available for the study of correspondence of flies and fatal cases in different subdivisions (Manchester) in the course of the same year also lends support. In his view no other explanation even approximately meets the case.

Peters (1910), in his very exhaustive study of the epidemic in Mansfield in 1908, paid especial attention to the possible part played by flies. From an analysis of his observations, he, I think justly, came to the conclusion that the evidence pointed to the fact that whatever part they might play as carriers from an infected household to a neighbour, flies did not bring infection with them from the manure heaps where they had been bred.

Peters constantly noted that the individual seemed to

be a source of infection to the neighbours adjacent to the house within the precincts of which his excreta, if infectious, would most likely be deposited. This, he points out, could be most readily explained by the supposition that flies were the agents of dissemination of the infection, but from the frequent want of correspondence in different localities between numbers of flies and amount of diarrhoea, although not negating it, gave no support to this view.

I doubt very much whether any evidence of great value could be obtained upon this point. Even supposing it to be true that fly-carriage is of first importance, I should expect that, if all the facts were known, a much higher correlation would be discovered between diarrhoea and carelessness with regard to disposal of excreta and protection of food from the visitation of flies, than between diarrhoea and fly prevalence.

Many of the facts which I have brought forward merely indicate some form of infective agent and do not necessitate recourse to the hypothesis that carriage by flies dominates the situation. I would point out, however, that—

1. The fly-carrier hypothesis is the only one which offers a satisfactory interpretation of the extraordinary dependence of the epidemic upon the accumulated effect of temperature.

2. That it offers a ready explanation of the spread of infection to neighbouring children who have no direct personal contact with the patient.

3. That the peculiarities of the relation in time between fly prevalence and the epidemic in different localities are not inconsistent with the view that fly-carriage is essential to epidemicity. No other interpretation which is at present forthcoming is nearly so satisfactory, and it is at least worthy to guide in the meantime our efforts at prevention.

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THE Swiss Society for the Scientific Study of Tuberculosis will hold its first meeting at Lausanne on January 18th and 19th. The society has eighty-eight members.

By way of promoting *esprit de corps* among those who are still nominally serving, or have served, in the civil medical departments of the West African Colonies, two dinners are annually held, one in the summer, one in the winter. The next winter gathering is to take place at the Grand Hotel, Charing Cross, on January 15th, its official title being the dinner of the West African Medical Staff. The honorary secretary is Dr. J. P. Fagan, 27, Scarsdale Villas, Kensington, to whom early application for tickets should be made.

An Address

ON

GALL STONES.*

BY

SIR BERKELEY MOYNIHAN, M.S., F.R.C.S.,

PROFESSOR OF CLINICAL SURGERY, UNIVERSITY OF LEEDS.

ONE of the most interesting advances made in recent years by the intrepid surgeon into the dim territory of abdominal afflictions was that which disclosed to us the frequency, the symptoms, and the appropriate modes of treatment of cholelithiasis. In this direction, as in so many others, the new vision which has come from a study of the pathology of the living has compelled us to rearrange our ideas and to adjust them in accordance with the different modes of examination which can now be conducted in all the various stages of this disease.

It is now a matter of general acceptance that gall stones are caused by an infection which, having its origin, or at least its refuge, in some part of the alimentary canal, reaches the liver either by way of the blood stream or ascends to it through the common bile duct. Lartigau has shown that the organisms carried to the liver by the portal vein are generally destroyed by the liver's action; but that when from any cause the number or the virulence of the micro-organisms is increased, some may well escape in the bile and find a lodgement within the gall bladder. As soon as any bacteria which have escaped with their lives from the liver reach the gall bladder they begin to act as a menace to the welfare of the patient. The economy, therefore, exerts the protective influence which it seems here also to possess. When a needle intrudes into the knee-joint it is covered over by a plastic exudation and converted into a "loose body." When a bullet is embedded in the soft parts, or in the chest or abdomen, it is wrapped up securely in a coating of fibrous tissue. When a hairpin or a catheter lies in the bladder it is surrounded by salts normally present in the urine, which crystallize out probably in an effort to render the intruder harmless. So in the gall bladder, when germs which have perhaps undergone the process of "clumping" find lodgement there, they are safely immured in a covering of salts, cholesterin in whole or in part, or bilirubin calcium, with the purpose, no doubt, of rendering them inert and of destroying them. Indeed, every gall stone is a tombstone erected to the evil memory of the germ that lies dead within it. Among the organisms which perish in this manner, the bacillus of typhoid, the colon bacillus, and the pneumococcus, which I have on several occasions recovered from the bile, appear to be the most frequent.

It is true that stones, as in cases of cirrhosis of the liver, may be formed within the intrahepatic or hepatic ducts. But such cases are of merely pathological importance. In all cases of cholelithiasis which come for surgical treatment it would appear to be quite certain that the stones have formed within the gall bladder. When calculi are found in the hepatic duct, the common bile duct or the ampulla of Vater, the gall bladder itself may be void of stones. Yet the stones which are removed bear clearly the traces of having been formed within the gall bladder, from which long ago or recently they have migrated. As soon as stones are once formed within the gall bladder symptoms begin to assert themselves. In medicine fallacies die hard, but rarely is one so tenacious of life as that ancient one which expresses the view that in a great majority of cases gall stones do not give rise to symptoms. In all my experience I have only twice met with a case in which an attack of "hepatic colic" was the first indication of the presence of a stone. Indeed, in those rare cases in which the diagnosis admits of doubt, the presence or absence of what I have described as the "inaugural symptoms" of gall-stone disease may nearly decide the question. The description of these symptoms, which I gave some years ago, has been corroborated by other writers—Sherren, Mayo, and more recently by Grube and Graft in their little work on gall-stone disease (see also Rolleston, our first authority, *Diseases of Liver*, etc., second edition).

* Abstract of a paper read before the Halifax Medical Society.