A SPONTANEOUS EPIDEMIC IN MICE ASSOCIATED WITH MORGAN'S BACILLUS, AND ITS BEARING ON THE AETIOLOGY OF SUMMER DIARRHOEA.

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(With 4 Charts.)

INTRODUCTORY.

RETTGER and Cheplin (1921) have brought experimental evidence to show that when white rats are fed on lactose the usual putrefactive flora of the intestine is replaced by organisms of the acidophilus type.

It occurred to us that it would be interesting to investigate the effect of alterations in dietary—and presumably of the intestinal flora—on the progress of an experimental epidemic in mice due to a natural parasite such as *Bact. aertrycke*. The results of the few experiments that were carried out with this aim in view yielded very little information; it became clear, however, that before a satisfactory study could be made of the relationship between diet and susceptibility to infection, it would be necessary to standardise more carefully than is at present possible the dose and the virulence of the infecting organism.

During the course of these experiments the interesting observation was made of a spontaneous epidemic in mice associated with Morgan's No. 1 bacillus. Though this organism is not infrequently recovered from sporadic deaths amongst normal and experimental mice, it had never before been the apparent cause of an actual epidemic. Since it occurred in a group of animals fed on an unusual dietary—raw beef—it was suspected that more than a casual relationship might exist between the diet and the infection. The experiments that were subsequently carried out were therefore designed rather to test this possibility than to investigate the wider field first contemplated.

FEEDING EXPERIMENT I, PART 1.

Three cages, *A*, *B* and *C*, were made up, each containing 85 normal mice and 15 mice that had within the past fortnight been fed repeatedly on a broth culture of *Bact. aertrycke* (mutton). Of these 15 mice 9 were excreting, or had on at least one occasion excreted, this organism in their faeces. All mice were given oats in the morning. In the evening Cage *B* mice received bread and water; Cage *A* mice bread and water to which were added 2 grm.

of lactose per mouse; and Cage C mice raw fresh minced beef, 2·5 grm. per mouse. Water was provided in liberal quantity, the vessels being filled twice daily. After the experiment had been running for 6 weeks the drinking vessels in Cage C were discontinued, since the cages were getting damp, and the mice appeared to be deriving a sufficient amount of water from the meat. The cages were changed each day except on Sundays.

A fortnight after the commencement of the experiment the faeces of the mice were examined microscopically. It was expected that there would be a marked difference in the flora of the mice fed on the different dietaries. As a matter of fact there was no discernible difference. In each cage the predominant flora was of Gram-negative coliform bacilli, the next most frequent organisms being Gram-positive cocci. Except in individual mice Gram-positive bacilli were inconspicuous or entirely absent; spore-bearing organisms were very few in number.

All mice that died and that had not been eaten were examined *post-mortem*. The heart and spleen were plated on to MacConkey's medium. Non-lactose fermenters were picked off into broth, and the resulting growths put up against a group and a type serum. If no agglutination occurred, the organisms were tested in the sugars. The spleen, moreover, was seeded into broth, which was then available for plating if the cultures proved sterile or yielded lactose fermenters only.

The experiment was continued for 98 days; the survivors of Cages A and B were killed, and the spleens seeded into broth. Table I and Chart 1 show the results:

Table I. *Mortality in feeding experiment I, Part 1. Duration 98 days.*

	Cage A	Cage B	Cage C
Mice	100	100	100
Died	66	81	53
Examined	61	81	49
Aertrycke mortality	56 %	72 %	24 %
Morgan mortality	1 %	2 %	4 %
Survivors killed	34	19	—
Spleens infected with aertrycke	20	13	—
Spleens infected with Morgan	0	0	—

Note. In all tables the percentages given are calculated on the results of the autopsies, no allowance being made for mice not examined.
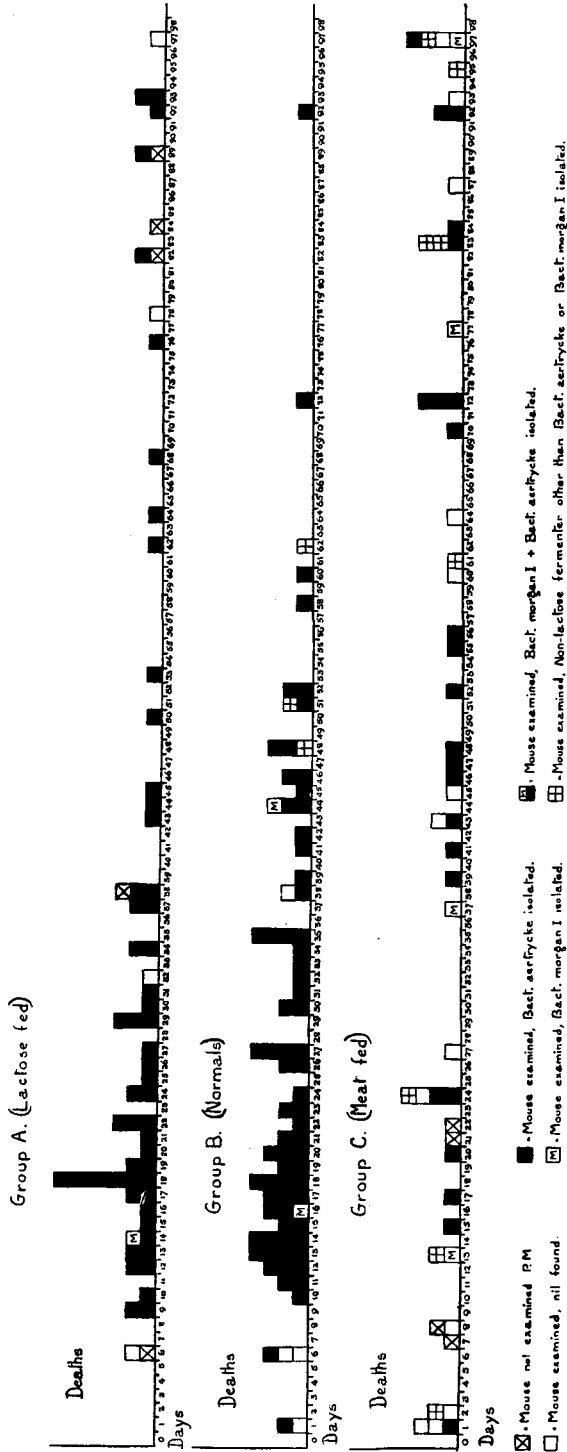
It will be seen that the specific aertrycke mortality was 72 per cent. in the control Cage B, 56 per cent. in Cage A, and only 24 per cent. in Cage C amongst the mice receiving meat.

FEEDING EXPERIMENT I, PART 2.

The 47 survivors of Cage C were divided into 4 groups; and to each group were added 68 or 69 mice to bring the total up to 80. These were distributed in 4 cages D, E, F and G. The mice in Cages D and E received the normal diet of oats and bread and water; in Cages F and G the mice were given oats in the morning and fresh raw minced beef in the evening. Water vessels were

CHART I. Feeding Experiment I. Part I.

Group A. (Lactose fed)

Group B. (Normals)

Group C. (Meat fed)

☒ = Mouse not examined P.M.
☐ = Mouse examined, nil found.

■ = Mouse examined, Bact. aertrycke isolated.
Ⓜ = Mouse examined, Bact. morgan I isolated.

▦ = Mouse examined, Bact. morgan I + Bact. aertrycke isolated.
⊞ = Mouse examined, Non-lactose fermenter other than Bact. aertrycke or Bact. morgan I isolated.

provided for Cages *D* and *E*, but not for Cages *F* and *G*. The experiment
was terminated after 49 days, when all the mice in Cage *G* had died (Table II,
Chart 2).

Table II. *Mortality in feeding experiment I, Part 2. Duration 49 days.*

	Cage *D*	Cage *E*	Cage *F*	Cage *G*
Mice	80	80	80	80
Died	4	21	44	80
Examined	2	15	36	74
Aertrycke mortality	2·5 %	12·5 %	35 %	6·3 %
Morgan mortality	0 %	0 %	4 %	32·5 %

CHART 2.   Feeding Experiment 1. Part 2.

Cage D (Normal)

Cage E (Normal)

Cage F (Meat fed)

Cage G. (Meat fed)
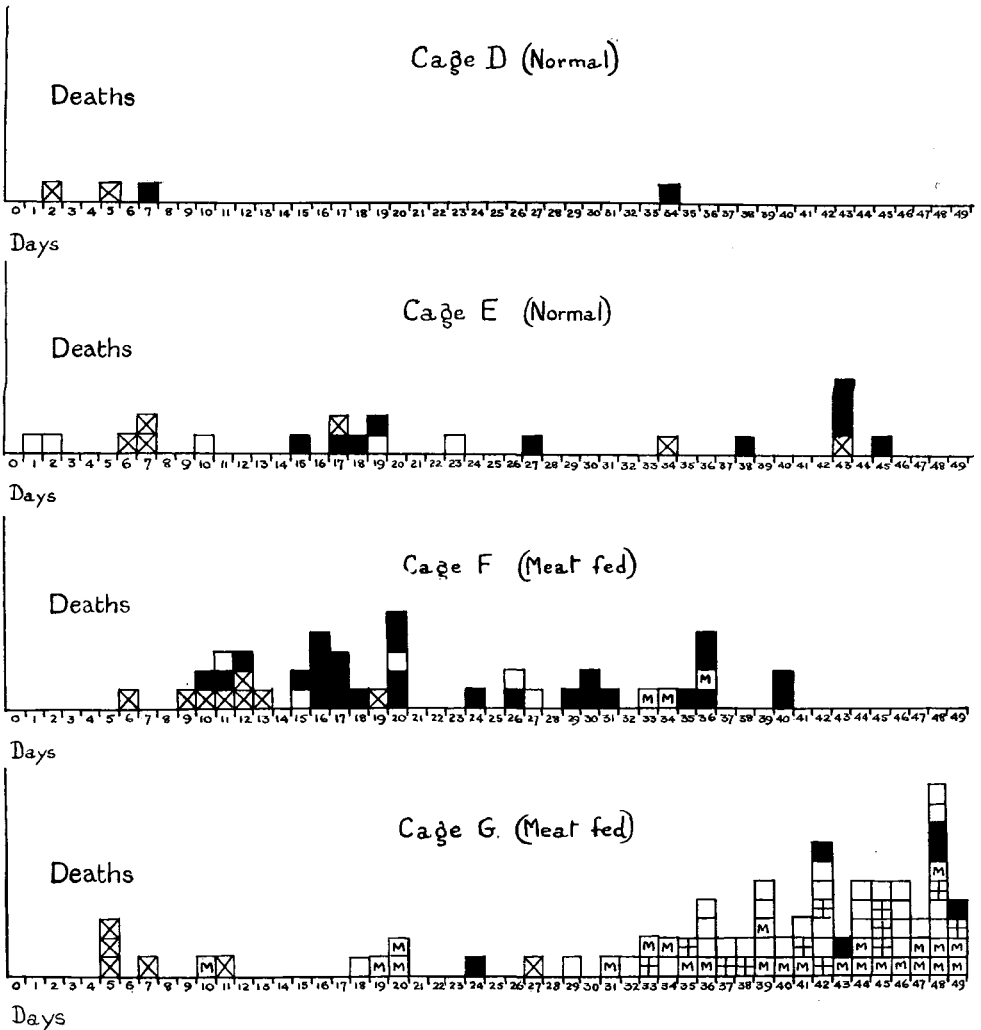
In Cage *D* the epidemic completely failed to spread; in Cage *E* 10 mice died of aertrycke infection, and in Cage *F* 28 mice. Cage *G* resembled Cage *D* in that the aertrycke infection failed to spread; only one of the normal added mice died of infection with this organism. But the total mortality in Cage *G* was 100 per cent., of which 32·5 per cent. was attributable to infection with *Bact. morgani* No. 1. The mice in this cage were unthrifty; they assumed a hunched-up position, and their coats were rough and shaggy. At autopsy they had no resemblance whatever to mice dying of infection with *Bact. aertrycke*. Most of them were emaciated; the abdomen was retracted, and the subcutaneous tissues were very dry. All the internal organs were pale; and the blood, which had a pinkish colour, looked as if the haemoglobin content had been greatly reduced. The kidneys presented a striking appearance; they were large, pale and swollen, bearing a close resemblance macroscopically to the large white kidney found in certain types of nephritis in human beings. The heart was large, pale and flabby. It was clear, in fact, that the animals were in an advanced stage of anaemia. These lesions were present not only in the mice that had died of Morgan infection, but in all the mice, even in the few that were infected with *Bact. aertrycke*. The Morgan and aertrycke deaths accounted for 31 of the mice; what the other 49 had died of was not apparent. Of these 49, 6 were eaten and so were not examined; 12 had non-lactose fermenters other than *Bact. aertrycke* and *Bact. morgani* in the spleen or heart blood; the remainder proved sterile on culture or yielded lactose fermenters.

From these results the preliminary conclusion was reached that the meat dietary had so altered the conditions in the alimentary tract as to allow the invasion of the tissues by non-lactose-fermenting organisms, chief among which was *Bact. morgani*.

FEEDING EXPERIMENT I, PART 3.

In this experiment an attempt was made to reproduce the conditions prevailing in Cage *G* of the previous experiment. The survivors in Cages *D*, *E* and *F* were thoroughly mixed, and divided into 3 batches, which contained 57, 58 and 55 mice respectively. Cage *F* 1 was fed on oats, and bread and water; Cages *F* 2 and *F* 3 on oats and fresh raw minced beef. Water was

Table III. *Mortality in feeding Experiment I, Part 3. Duration 87 days.*

	Cage *F* 1	Cage *F* 2	Cage *F* 3
Mice	57	58	55
Died	34	58	44
Examined	32	58	43
Aertrycke mortality	42·1 %*	62·1 %†	69·1 %‡
Morgan mortality	3·5 %	20·7 %	7·3 %
Survivors killed	23	0	11
Spleens infected with aertrycke	11	—	5
Spleens infected with Morgan	0	—	1

* 1 mouse had a double infection with *Bact. aertrycke* and *Bact. morgani*.
† 2 mice had a double infection with *Bact. aertrycke* and *Bact. morgani*.
‡ 2 mice had a double infection with *Bact. aertrycke* and *Bact. morgani*.

CHART 3.   Feeding Experiment I. Part 3.

Cage F 1. (Normal)

Cage F 2. (Meat plus Water)

Cage F 3. (Meat plus Water)
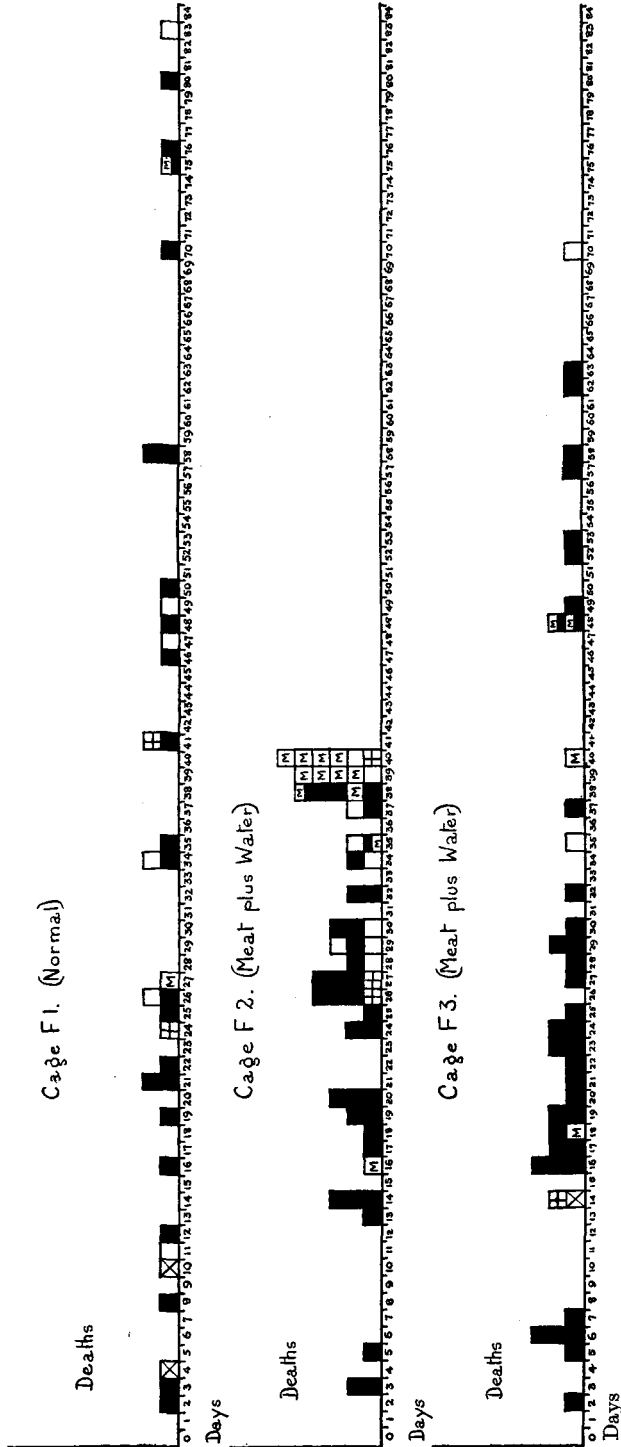
supplied twice daily to all cages. The experiment was continued for 87 days, when the survivors were killed. The results are shown in Table III and Chart 3.

In each cage there was a spread of aertrycke infection, but only in *F* 2 was the percentage of mice infected with *Bact. morgani* significantly high—20·7 per cent. The mice dying in this cage presented similar lesions to those in Cage *G* of the previous experiment. During life their coats were dry, rough, shaggy and covered with lice; the back was arched; there was a progressive stiffening of the limbs and a disinclination to move; they had little appetite and were generally lethargic; death was frequently preceded by convulsions. At autopsy, the tissues were dry and pale; the kidneys were large, pale and swollen; the heart dilated and flabby; sometimes the liver showed a nutmeg appearance. These lesions were common to all the mice, no matter what organism was recovered from them; but they were more marked in those mice that died towards the close of the experiment. The condition of the mice in Cage *F* 3 was poor for the first 6 or 7 weeks, but afterwards it improved, so that at the end of the experiment there was little to choose in appearance between these mice and those in the control *F* 1 cage.

FEEDING EXPERIMENT 2.

Another attempt was made to reproduce a spontaneous Morgan epidemic. Two cages were made up, *L* and *M*, each of which contained 85 normal mice and 15 mice that had been fed 6 times during the previous week on a culture of *Bact. aertrycke* (mutton). In Cage *L* the mice received oats and bread and water; in Cage *M* oats and fresh raw minced beef. Water was supplied twice daily to both cages. The experiment was continued for 64 days. The results are shown in Table IV and Chart 4.

Table IV. *Mortality in feeding Experiment II. Duration 64 days.*

	Cage L	Cage M
Mice	100	100
Died	32	56
Examined	31	55
Aertrycke mortality	24 %*	45 %†
Morgan mortality	4 %	12 %

* 2 mice had a double infection with *Bact. aertrycke* and *Bact. morgani*.
† 8 mice had a double infection with *Bact. aertrycke* and *Bact. morgani*.

In each cage a definite epidemic due to *Bact. aertrycke* occurred, more marked however in Cage *M*. Morgan's bacillus was recovered from 4 per cent. of the control and from 12 per cent. of the meat-fed mice. In 7 of the aertrycke and 2 of the Morgan mice dying in Cage *M* the kidneys were pale and swollen. Otherwise the mice at autopsy did not resemble those in Cage *G* of Expt. I, Part 2, or Cage *F* 2 of Expt. I, Part 3.

Having failed to reproduce a Morgan epidemic in this way, we endeavoured by various other procedures to infect mice with this bacillus. A number of experiments were performed in which the mice were simply fed on oats and

meat, with or without water. In only one of these was any success obtained. Five mice fed on this dietary without water were kept for 142 days; during this time 4 died, and from the spleens of 3 of them Morgan's bacillus was cultivated.

Five other experiments were performed in which the mice were fed on an 18-hour broth or agar culture of *Bact. morgani*, the usual dietary of meat and bread or oats being supplied. The number of mice in a single cage varied from 5 to 35. The number of feedings varied from 1 to 10, and the dose of living organisms from 0·5 to 186 million. In four of the experiments the culture was delivered directly into the mouth by a calibrated dropping pipette; in the remaining experiment bread soaked in the culture was used to feed the

CHART 4.   Feeding Experiment 2
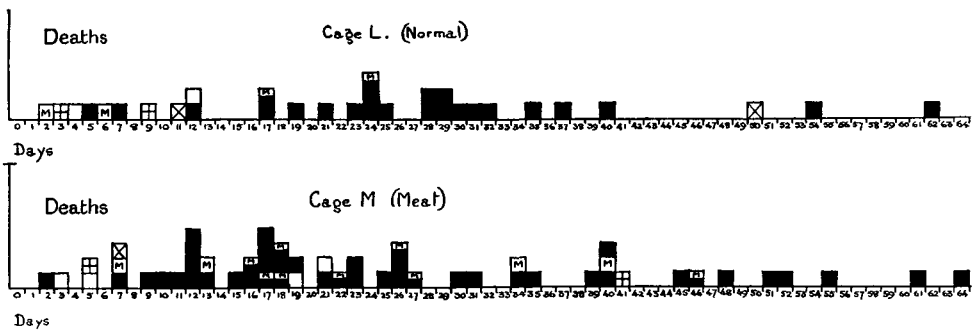
mice. Of 104 mice observed for from 30 to 186 days, 14 died; in only 4 of these was *Bact. morgani* recovered from the spleen. The surviving mice were killed and examined; in not a single one was *Bact. morgani* found in the spleen.

It was thought that perhaps the culture employed had become avirulent. The strain was therefore passed by intraperitoneal injection through 14 mice in succession; the spleen of each of the mice was then fed to 5 normal mice, which were kept on a dietary of meat and oats. These were observed for 15 to 24 days. Of the total of 70 mice, 6 died; from 2 of these *Bact. morgani* was recovered. The remaining 64 mice were killed, and only 2 of the spleens were found infected. Here again there was an almost complete failure to infect the mice, even though the culture on intraperitoneal injection was extremely virulent, killing the animals in 6 to 12 hours.

Two experiments were carried out in which a culture of *Bact. morgani* or the filtrate of a broth culture was injected per rectum. Only 1 mouse out of 10 treated in this way succumbed to infection with Morgan's bacillus.

Finally, an attempt was made to set up a Morgan infection by conjoint feeding with *Bact. morgani* and *Bact. aertrycke*. Twenty mice kept on a dietary

12–2

of beef and oats were fed 5 times in 7 days on a mixture of these organisms, the dose of each being about 5,000,000 living bacilli. The animals were observed for 206 days. Thirteen died, 6 from aertrycke and 1 from Morgan infection. Of the 7 survivors that were killed, 3 were infected with *Bact. aertrycke* and 1 with *Bact. morgani*.

DISCUSSION.

There are certain points of interest arising out of this work that seem to warrant discussion. Firstly, there is the relation between the diet and the spread of aertrycke infection amongst mice in Expts. I and II. In Expt. I, Cage *C*, the mice fed on meat had a very much lower aertrycke mortality— 24 per cent.—than had the control mice fed on bread and oats—72 per cent. The difference was large enough to appear significant. A repetition of this experiment, however, Expt. II, Cages *L* and *M*, gave precisely the opposite results. Here the aertrycke mortality amongst the meat-fed mice was 45 per cent., whereas amongst the control mice it was only 24 per cent. In Expt. I, Cages *D* and *E*, the aertrycke mortality amongst the control mice was 2·5 per cent. and 12·5 per cent. respectively: in Cages *F* and *G*, amongst the meat-fed mice, it was 35 per cent. and 6·3 per cent. respectively. Calculating the combined aertrycke mortality in Expts. I and II (cf. Table V), we find that there is little difference in the figures for the control and the meat-fed mice; they are 31·7 per cent. and 37·2 per cent. respectively.

Table V. *Showing combined aertrycke mortality and Morgan mortality for mice in Experiments I and II.*

Normal dietary

Mice	B	D	E	F 1	L
Number	100	80	80	57	100
Aertrycke mortality	72 %	2·5 %	12·5 %	42·1 %	24 %
Morgan mortality...	2 %	0 %	0 %	3·5 %	4 %

Total number of mice = 417
Combined aertrycke mortality = 31·7 %
Combined Morgan mortality = 1·9 %

Meat dietary

Mice	C	F	G	F 2	F 3	M
Number	100	80	80	58	55	100
Aertrycke mortality	24 %	35 %	6·3 %	62·1 %	69·1 %	45 %
Morgan mortality...	4 %	4 %	32·5 %	20·7 %	7·3 %	12 %

Total number of mice = 473
Combined aertrycke mortality = 37·2 %
Combined Morgan mortality = 12·9 %

Though the number of animals used was small, we may conclude that there is no evidence relating the spread of aertrycke infection amongst mice to the type of diet on which the animals were fed. The differences noted in the separate experiments must be ascribed to other factors, probably to

the dose, the spreading power, or the virulence of the dominant strain of bacillus.

These results, so far as they go, support the conclusions already drawn by Webster (1923). He found that in mice fed on bread and milk there was a high proportion of *B. acidophilus* and a low proportion of coliform bacilli in the faeces; on the other hand, in mice fed on raw beef the coliform bacilli were predominant, while *B. acidophilus* was almost negligible. To a certain number of each group the mouse typhoid bacillus (*B. pestis caviae*) was administered in a suitable dose by a stomach tube. The mortality within 60 days in the first group was 68 per cent., in the second group 67 per cent. Webster summarises his experiments by saying "that in mice the intestinal flora plays no part in host susceptibility to mouse typhoid infection, and that it does not affect the outcome of this disease."

The second point of interest is the Morgan mortality of the mice in the first two experiments. Not only is this higher amongst the meat-fed—12·9 per cent.—than amongst the control mice—1·9 per cent.—for the whole series of experiments, but it is consistently higher in each individual experiment (Table V). It would appear that though a meat dietary has little or no effect on the spread of *Bact. aertrycke*, it does definitely favour the spread of *Bact. morgani*.

The presence of an epidemic due to Morgan's bacillus—Cage *G*—and of one due to this organism in conjunction with *Bact. aertrycke*—Cage *F* 2—is of considerable interest both from an epidemiological and a bacteriological point of view. It is not unusual to isolate *Bact. morgani* from the tissues of mice dying in the normal or the infected animal houses, but these deaths are merely sporadic. This is the first occasion in our experience on which Morgan's bacillus has assumed the power of spreading epidemically.

In both cages the mice, more especially towards the latter part of the epidemic, displayed an appearance of unthriftiness and lethargy that was unlike that of the mice in the other epidemics. At autopsy the advanced degree of anaemia, the pale and swollen kidneys, and the general pallor and dryness of the tissues was distinctive. This syndrome was manifested by the mice independently of the bacteriological findings; it might therefore be argued that Morgan's bacillus was not responsible for it. But it must be remembered that our bacteriological investigations were confined to the heart blood and spleen; they did not extend to the intestinal tract. There is evidence that this bacillus resembles the dysentery bacillus in being relatively unable to penetrate the intestinal mucosa and invade the body tissues. It is legitimate, therefore to surmise that possibly a greater proportion of the mice were infected with this organism than is apparent from our *post-mortem* records. If this is so, it seems to us that the most probable cause of the peculiar lesions referred to was a chronic intestinal infection with *Bact. morgani*. At first we were inclined to ascribe their production to the meat, but all attempts to reproduce them by feeding on meat alone were a failure. They were certainly

not due to aertrycke infection, because the lesions caused by this infection are well known to us. Since they occurred only in the cages in which there was a Morgan epidemic, we conclude that this organism was directly or indirectly responsible for them.

What the factors were that enabled Morgan's bacillus to spread epidemically, it is impossible to say. Our attempts to infect mice by feeding them on cultures of this organism, either alone or in conjunction with *Bact. aertrycke*, proved almost completely abortive. Though large doses were administered, often repeatedly, and though the animals were kept under observation for 1 to 7 months, the number of fatal infections that occurred was insignificant. It would appear that the bacillus can give rise to infection only in the presence of some predisposing factor, in much the same way as washed tetanus spores are harmless till they are activated by calcium chloride or some similar body. All that we can say is that under certain conditions, which we are unable to define, but which are probably associated with the dietary, it may assume the power of spreading epidemically and of giving rise to fatal infections in mice.

Finally, it is worth while calling attention to the complete extermination of the animals in both Cages *G* and *F* 2. It is usual in epidemics, whether occurring naturally or experimentally, for a certain proportion only of the exposed population to succumb to infection. The remainder either escapes infection completely, or contracts an infection that is not severe enough to prove fatal. In both the Morgan epidemics, however, the mortality was 100 per cent.

THE BACTERIOLOGICAL FINDINGS IN SUMMER DIARRHOEA.

The bacteriological findings in summer diarrhoea are extremely conflicting.

Booker, in America (1896), who was one of the first to investigate the intestinal flora in this disease, reported a general increase in the numbers of certain organisms, particularly *B. proteus* and streptococci. Several years later, between 1909 and 1913, Metchnikoff (1914) in Paris isolated *B. proteus vulgaris* from 204 out of 218 cases of infantile diarrhoea. He produced diarrhoea in chimpanzees by feeding them on the stools of affected infants, and found that *B. proteus* subsequently appeared in their faeces. Though admitting that this organism is often an inhabitant of the normal intestinal tract, he concluded that it was the specific cause of infantile diarrhoea. Bertrand (1914), one of Metchnikoff's pupils, studied 55 cases of the disease in London Hospitals in the summer of 1912, and isolated *B. proteus* from every case; while in the stools of 24 normal children he found it only twice.

Hiss and Russell (1903) in America recovered a bacillus from the colon of a child that had died of acute diarrhoea; this proved to belong to the dysentery group, and was called the Y-bacillus. Duval and Bassett (1904), Duval and Shorer (1904), Wollstein and Dewey (1904), and a number of other workers under the direction of Flexner at the Rockefeller Institute carried out an extensive investigation in 1902 and 1903 into the aetiology of

summer diarrhoea. The results showed the frequent presence of dysentery bacilli in the stools during life and in the intestinal mucosa after death (Table VI).

Table VI. *Dysentery bacilli in stools of infants with summer diarrhoea.*

No. of cases studied	Shiga	Flexner	Shiga and Flexner mixed
412	23	256	6
No of cases with dysentery bacilli			
285	8·1 %	89·8 %	2·1 %

That is, in 69 per cent. of patients the dysentery bacillus was found; this was generally—in 90 per cent.—of the Flexner type.

Examination of the stools of normal infants showed that the dysentery bacillus was quite uncommon.

Similar results were obtained in Boston 11 years later by Tenbroeck and Norbury (1915, 1916). In the summer of 1914 they found Flexner dysentery bacilli in 54 or 68 per cent. of 79 infants with summer diarrhoea, and in 1915 in 51 or 68 per cent. of 75 infants. Again in 1919, 69 per cent. of cases of summer diarrhoea investigated by Davison (1919) in Birmingham, U.S.A., were found to be due to the dysentery bacillus, Flexner's bacillus being twice as common as Shiga's. In Baltimore 82 per cent. of the cases were due to dysentery bacilli; in this series Flexner's was the only type found.

In this country the findings have been entirely different. The dysentery bacillus has but rarely been recovered from cases of summer diarrhoea. On the contrary the organism that has been found most frequently is the Morgan No. 1 bacillus. In the summer of 1905 Morgan (1906), working at the Lister Institute, London, isolated this bacillus from 28 out of 58 cases; in the faeces of 20 normal children it was not found once. He continued his work for the next three years; the results he obtained are summarised in Table VII (Morgan and Ledingham, 1909).

Table VII. *Frequency of Morgan No. 1 bacillus in summer diarrhoea.*

Year	Cases examined	Percentage of positive cases
1905	58	48·2
1906	54	55·8
1907	191	16·2
1908	166	53·0

It will be noticed that except in 1907, in which the incidence of summer diarrhoea was low, the bacillus was isolated from about half the cases. During the epidemic of 1908 it was isolated from 12 per cent. of normal children; it was likewise found in flies coming from infected houses. Morgan and Ledingham (1909), in summing up the evidence, regard this bacillus as an important factor in the causation of summer diarrhoea. Attempts to reproduce the disease in animals were not very successful; but the oral administration of large doses to rats, young rabbits, and monkeys sometimes proved fatal.

Investigations made by Ross (1910–11) in Manchester, and O'Brien (1910–11) in London in the summer of 1910, showed that there was an increase in the number of non-lactose-fermenting bacilli in the stools of patients with diarrhoea. Morgan's bacillus was comparatively infrequent—5 per cent. and 14 per cent. respectively. Orr (1910–11) at Shrewsbury did not find it once in an examination of 19 cases. It is to be noted, however, that the incidence of summer diarrhoea in 1910 was very low. In the summer of 1911 Lewis (1911–12) at Birmingham likewise noted an increase in the number of non-lactose-fermenting colonies in diarrhoeal stools. Morgan's bacillus was found in 101 out of 140 cases, or 72·1 per cent., and in 17 of 100 normal children under 5 years of age, or 17 per cent. He found that of 20 strains isolated from diarrhoeal children 14 proved fatal to rats or mice on feeding. Further, he was successful in isolating the organism from 5 out of 18 samples of milk from houses in which there were at the time or had recently been cases of diarrhoea. Graham-Smith (1911–12), examining flies collected in Cambridge and in Birmingham (England) in the summer of 1911, isolated bacilli of the Morgan type (86 per cent. of which were Morgan No. 1) from 5·3 per cent. of flies captured in diarrhoea-infected houses, and from only 0·6 per cent. of flies captured in houses free from diarrhoea. During the third week of August the proportion of flies infected with Morgan reached 15·6 per cent. at Cambridge and 12·0 per cent. at Birmingham.

In the same year, however, Alexander (1911–12) at Liverpool encountered Morgan's No. 1 bacillus in only 23 out of 174 cases, or 13·2 per cent.; moreover he found it in 5 out of 75 normal children, or 6·6 per cent.

In Germany the findings have been diverse. Gildermeister and Baerthlein (1913) examined the stools of 70 infants suffering from diarrhoea in the summer of 1912. Flexner dysentery bacilli were found in 9, *Bact. paratyphosum* B in 4, *Bact. enteritidis* Gaertner in 1, and the Dahlem bacillus (resembling *Bact. suipestifer* Voldagsen) in 22. The following year Baerthlein and Huwald (1914) found *Bact. dysenteriae* Flexner in 21, *Bact. paratyphosum* B in 7, and the Dahlem bacillus in 24 out of 72 cases.

In Australia Patterson and Williams (1922) have found the Sonne dysentery bacillus in 3 cases of acute diarrhoea in babies.

Other organisms, such as *Cl. welchii* and *Bact. pyocyaneum*, have been incriminated by different workers.

There is general agreement that in summer diarrhoea the non-lactose-fermenting organisms in the stools are increased. How far this is justified it is difficult to say, since the presence of non-lactose fermenters in the stools is associated not only with diarrhoea, but with the type of food supplied. The stools of infants fed on cows' milk contain more of these organisms than the stools of breast-fed infants. For example, from 38 specimens of faeces from normal breast-fed infants Lewis recovered non-lactose fermenters only 4 times, but from 27 specimens from normal infants fed on cows' milk he recovered them 22 times. It is therefore not justifiable to compare the

percentage of non-lactose fermenters in diarrhoeal children fed on cows' milk with that of normal breast-fed infants.

The exact species of non-lactose fermenter that is preponderant varies in different countries. In America it is chiefly the Flexner dysentery bacillus, in this country Morgan's No. 1 bacillus. Metchnikoff found *B. proteus* to be predominant; others have been struck with the increased frequency of *Bact. pyocyaneum*, the Dahlem bacillus, or *Cl. welchii.*

How are we to reconcile such diverse findings? Before forming any opinion on the aetiological significance of these organisms it is well to remember that epidemiologically summer diarrhoea is a disease that is widespread in every part of Europe and America. It may be difficult to believe that a disease which reaches its maximum about the 32nd to the 36th week in London, Paris, Berlin, Moscow, Chicago and New York, which produces a clinical syndrome of diarrhoea, vomiting and collapse, with the passage of stools containing frequently mucus and sometimes blood, and which is specially fatal to infants under two years of age, can be determined by more than one main cause. It may be difficult to believe that one and the same disease is due to *Bact. dysenteriae* in America, to *B. proteus* in France, to the Dahlem bacillus in Germany, and to Morgan's bacillus in this country. Yet we are faced with the alternatives either that the disease is due to a different agent in each of these countries, or that it is uniform and is due to a primary agent with which we are at present unacquainted.

There are two or three reasons that seem to us to point in favour of the former of these alternatives. First of all it is not justifiable to assume that because summer diarrhoea is an epidemiological entity it is necessarily a bacteriological entity. It may be caused by a number of different organisms, in much the same way as enteric fever is caused by a number of different organisms. Presumably the conditions that favour the growth and trans-ference of one of these organisms likewise favour the growth and transference of the others. The finding of a number of different organisms in a disease that appears to be epidemiologically uniform is not therefore incompatible with our present knowledge of bacteriology.

Secondly, we know that at least one of the organisms found in summer diarrhoea—*Bact. dysenteriae*—is able to spread epidemically in adults and give rise to serious and often fatal disease. The presence of this organism is an all-sufficient cause for the explanation of the disease. By analogy, we may therefore suppose that the other organisms found in summer diarrhoea are likewise able to spread epidemically and give rise to disease. If we do not make this assumption, we must conclude that summer diarrhoea, which in America is due to *Bact. dysenteriae,* in other countries is due to an agent of whose nature we are at present ignorant.

Thirdly, it is certain that during the past 20 or 30 years diarrhoea in this country has gradually assumed smaller and smaller proportions. The better disposal of garbage, the diminution of dust, the replacement of horse by

motor traffic, and the decrease in the number of flies have probably all aided in lessening the chances of bacterial contamination of food. That these two processes should have gone on simultaneously suggests that there may have been a causal relationship between them.

Lastly Brownlee and Young (1922) have brought forward evidence that summer diarrhoea is a mixed disease consisting mainly of two separate components. On analysing the data for London during the last 60 years they found not only that the mortality from diarrhoea had diminished considerably from 1890 onwards, but that the maximum of the annual epidemic had gradually become later and later. Previous to 1899 the maximum fell about the 30th to the 33rd week of the year; in 1899 there was a change, the epidemic reaching its acme later. From 1907 onwards the maximum did not occur till the 35th to the 40th week, and with the single exception of 1911 the number of deaths was comparatively small. Further analysis showed that the curve of the annual mortality from diarrhoea could be split up into an early and a late epidemic; the early one, which reached its maximum about the 31st week, had a steep ascent and a rapid decline, and levied a heavy toll on life; the second one, which reached its maximum about the 36th week, had a more gradual slope throughout, and was less fatal. During the present century the early epidemic has become less and less evident, having been replaced largely by the late epidemic. The composite nature of the diarrhoeal mortality curve was substantiated by examination of the records for other English cities, and also Paris, Berlin, Moscow, Chicago and New York. Each of the annual curves could be analysed into two symmetrical curves, whose means were separated by an interval of about 5 weeks.

These findings are of peculiar interest, indicating, as they do, that a disease which has hitherto been regarded as an epidemiological entity is not so in reality.

Summing up then, we may conclude that during the warm weather certain factors, of which the chief appears to be the accumulated heat registered by the 4-foot earth thermometer (Ballard, 1889), favours the growth and transference of a number of organisms belonging to the non-lactose-fermenting group. Gaining access to the peculiarly susceptible intestinal tract of the infant, they multiply and set up diarrhoea. The available evidence suggests that no one organism can be regarded as the specific cause of summer diarrhoea, but that any one of a number of potentially pathogenic bacteria, either alone or in conjunction, may be capable of giving rise to the disease.

It is evident that the analogy between summer diarrhoea and the epidemics in Cages *G* and *F* 2 is very close. In summer diarrhoea there is a general increase in the number of non-lactose-fermenting organisms in the faeces, chiefly consisting of *Bact. dysenteriae*, *Bact. morgani* and *B. proteus*. In our *G* epidemic, though no examination was made of the faecal flora, a large number of the mice that died were infected with *Bact. morgani*, *B. proteus*, and other members of the non-lactose-fermenting group. In summer diarrhoea

examination of the faeces and of the tissues often proves entirely negative; likewise in our *G* epidemic from 31 out of 74 mice that were examined we failed to recover any organism of the non-lactose-fermenting group.

The fact that under experimental conditions in mice Morgan's bacillus was able to give rise to a definite and fatal epidemic seems to have a bearing on the bacteriological findings in summer diarrhoea in this country. Though naturally cautious of comparing conditions in such small animals with those in human infants, we cannot but think that the demonstration of the power of this organism to assume epidemic spread in mice adds a little to the evidence incriminating Morgan's bacillus as one of the causes of summer diarrhoea in this country. It is interesting in this connection to note that both the epidemics in Cages *G* and *F* 2 occurred during the late summer or autumn months.

SUMMARY.

Two epidemics among mice are described that were closely associated with Morgan's No. 1 bacillus. In both of these epidemics the mice, which were fed on oats and raw beef, were found at autopsy to be suffering from peculiar lesions—an advanced degree of anaemia, pale and swollen kidneys, and general pallor and dryness of the tissues—not hitherto encountered in any other epidemic. Evidence is advanced to show that *Bact. morgani* was the specific cause of these epidemics; and it is suggested that the peculiar lesions described were the result of a chronic intestinal infection with this organism.

The close analogy existing between the bacteriological findings in summer diarrhoea and in our experiments is discussed. The tentative conclusion is advanced that summer diarrhoea is not a bacteriological entity, but is a disease that can be caused by a number of different members of the non-lactose-fermenting group.

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NOTE:—We regret having overlooked the excellent discussion on Summer Diarrhoea by Dr David Nabarro (*Brit. Med. J.*, 1923, **2**, 857). During 1921 he recovered the *B. coli anaerogenes* from 21 out of 68 children with summer diarrhoea. It is probable that this organism was identical with Sonne's dysentery bacillus.