THE EXPERIMENTAL REPRODUCTION OF ENTEROTOXAEMIA IN PIGLETS

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(With Plates 5–6)

INTRODUCTION

Clostridium welchii is subdivided into several types according to the patterns of the major lethal toxins produced. Types B, C and D are of importance in animal pathology: Type B being responsible for lamb dysentery, Type C for 'struck' in sheep and Type D for enterotoxaemia in both adult sheep and lambs. These types have also been found in association with other diseases of livestock. For example, the Type C organism is a cause of enterotoxaemia in the new-born calf (Griner & Bracken, 1953) and lamb (Griner & Johnson, 1954), while a correspondingly acute and fatal disease among very young piglets has been described by Field & Gibson (1955) and Szent-Iványi & Szabó (1955, 1956). The latter condition was characterized by haemorrhagic inflammation of the small intestine, particularly the jejunum, with 'diphtheresis' of the mucosa. Free toxin, which was neutralized by *Cl. welchii* β-antitoxin, was demonstrated in the intestinal contents of the piglets by mouse inoculation tests, and an organism, shown to be *Cl. welchii*, Type C, was recovered in culture from the intestine. Subsequently, the identity of the bacterial strains isolated by Field & Gibson was confirmed by Brooks, Sterne & Warrack (1957).

The first object of the present work was to reproduce enterotoxaemia in piglets experimentally, the work of Szent-Iványi & Szabó (1955) not then being published. This was readily achieved and it was possible thereafter to investigate both the pathogenesis and epidemiology of the condition. In studying the pathogenesis, particular attention was paid to the clinical signs, which in such an acute disease are difficult to follow in the field; the role of hypoglycaemia in the terminal stages was also investigated. The new-born pig is seemingly peculiar, in that it is unable to survive starvation for more than about 2 days (Sampson, Hester & Graham, 1942); the blood-glucose concentration declines rapidly and there is also a concurrent and severe reduction in body metabolism, as evidenced by the heart rate, respiration and body temperature (Goodwin, 1957). It has been postulated, therefore, that any disease process that interferes markedly with nutrition shortly after birth must, unless death follows very rapidly, bring about hypoglycaemia and the consequent collapse of all body functions (Goodwin, 1955). This supposition has

now been satisfied with a number of diseases of the new-born pig, but such observations were of further interest in this instance as Type D toxin, though rarely Type A or Type C toxins, are known to induce marked hyperglycaemia in sheep (Gordon, Stewart, Holman & Taylor, 1940) and this effect can be taken as evidence of successful experimental Type D infection (Bullen & Scarisbrick, 1957).

MATERIALS AND METHODS

The strains of Cl. welchii, *Type C*, used in all the experiments described in this paper had been isolated from natural cases of enterotoxaemia in piglets; they were maintained in the laboratory in egg-yolk media.

Toxin production. The strains of *Cl. welchii* were cultured in Robertson's cooked-meat broth and the presence of β-toxin was checked by mouse inoculation after 6 and 24 hr. incubation at 37° C. Bacteria-free toxin was prepared by taking the supernatant from a meat-broth culture, centrifuging, decanting and passing the fluid through a Seitz filter. The filtrate was tested for sterility by inoculating both liquid and solid media and incubating these cultures under aerobic and anaerobic conditions.

Suspensions of toxin-free bacteria were prepared by centrifuging the supernatants from meat-broth cultures, washing the deposited bacteria twice with normal saline and finally resuspending in normal saline. The density of this suspension was adjusted to that of Brown's Opacity Tube, no. 10, which approximates to 35×10^8 organisms per ml.

Routine tests for toxin production relied on the characteristic effect of the β-toxin when injected intravenously into mice, as compared with α- and ϵ-toxins; the control mice were protected with Type C antiserum only. This procedure reduced the number of tests to manageable proportions for the preliminary part of the experiments, but at the critical stages confirmatory tests, employing in addition antisera for Types A and D, were carried out. The antisera used were the commercial products of Burroughs Wellcome and Co.

A standard bacteriological procedure was followed for the examination of rectal swabs and also for the specimens obtained post mortem from the piglets. Each sample was first inoculated into Robertson's cooked-meat medium and incubated at 37° C. for 6 hr., when a preliminary test on the supernatant was made for β-toxin. At the same time a portion of the broth culture was plated out on 10% horse-blood-agar plates which were incubated anaerobically at 37° C. for 24 hr. Selected colonies were then picked off into Robertson's medium and further incubated. The pure culture was finally identified in accordance with the results of the toxin-neutralization tests in mice.

Blood-sugar estimations. Mixed blood was taken from the tail or, with piglets close to death, from the cut throat vessels. After deproteinization with barium hydroxide and zinc sulphate to give usually a 1/16 dilution of whole blood, the glucose concentration was estimated with the reagent of Somogyi (1945). Included with each batch of test samples was a series of glucose solutions of known strength as controls.

RESULTS

Experimental reproduction of the disease

Feeding whole cultures

In a preliminary experiment four pigs from a litter of seven were dosed with 1 ml. of a 6 hr. meat-broth culture of *Cl. welchii*, Type C (i.e. bacteria plus toxin). The litter was then about 40 hr. old; the three undosed pigs served as controls. After dosing, the whole litter was returned to the sow and about 48 hr. later rectal swabs were taken from all the pigs. Cultures from these swabs, tested for β-toxin, showed that two of the four dosed pigs were positive, the other two and the three controls being negative. There was little evidence of ill health at this time, but about 80 hr. after dosing, one of the infected pigs was found dead. The following day four pigs, including one of the controls, had slightly fluid faeces but their further progress was uneventful. The pig that died showed intestinal changes typical of the natural disease and β-toxin was demonstrated in the intestinal contents.

As the natural disease is usually fatal within 2–3 days of birth, in the second experiment the piglets were infected when only 3 hr. old. Rectal swabs were taken from the sow the day before farrowing and from the whole litter of nine just after dosing: the cultures from all these swabs were negative for β-toxin. Five of the litter were given 2 ml. of a 24 hr. meat-broth culture by mouth and the remaining four were fed 2 ml. of an egg-yolk culture. As in all this work, the litter was then returned to the sow for normal rearing. Three of the piglets fed the broth culture died 15–20 hr. later and two of the other group died after about 40 hr. All five dead piglets showed congestion of the small intestine and in some instances the very fluid intestinal contents were grossly contaminated with blood. In only three of the five dead animals could β-toxin be demonstrated in the intestinal contents, one piglet from each group being negative, but cultures from the intestines of all five dead piglets yielded growths of organisms producing β-toxin. One of the three survivors was shown to be excreting *Cl. welchii*, Type C, 48 hr. after infection, but a further rectal swab taken at 72 hr. was negative.

From the experiments described above it was apparent that the disease could be readily, although not universally, reproduced with whole cultures. The mortality had been higher when the infection was introduced soon after birth and there was an indication that broth cultures were more effective than suspensions of organisms prepared from cultures in egg-yolk media. Nevertheless, a third litter of thirteen piglets dosed with 2 ml. each of an egg-yolk culture resulted in the death of six between 25 and 42 hr. later with the typical signs of enterotoxaemia.

Feeding washed organisms

It was presumed that the natural disease in piglets was associated with the ingestion of *Cl. welchii*, Type C, shortly after birth, a likely route of infection being suggested by Field & Gibson (1955) and Szent-Iványi & Szabó (1955). These authors believed that some sows carried the organisms in their faeces and thereby contaminated their teats and mammary glands when they were housed for farrowing.

The effect was tried of liberally smearing a suspension of washed Type C organisms, mixed with glycerol, over the teats and mammary glands of a sow about to farrow. Eleven piglets were born the same day and, apart from one overlain on the second day, they remained completely unaffected. Although this last experiment was not a very critical test it appeared that while the disease could be produced by feeding whole cultures, suspensions of washed bacteria were not suitable for the initiation of the disease because the washing had deprived the culture of the preformed toxin. It was therefore decided to compare the effects of feeding toxin-free bacteria with those of feeding bacteria-free toxin. These substances, prepared as described above, were fed to a litter of seven pigs about 14 hr. after birth; three pigs received 2 ml. of the bacteria-free toxin and the other four were given 2 ml. of the washed organisms. The results, however, were inconclusive. Although one animal in each group died between 48 and 72 hr. later, in neither case did the post-mortem examination reveal an enterotoxaemia. β-toxin was demonstrated in the intestinal contents of the piglet that had received the toxin but not in the animal dosed with washed bacteria. *Cl. welchii*, Type C, was not isolated from either of the dead pigs.

The above experiment was repeated on younger piglets. The suspension of toxin-free bacteria and the bacteria-free toxin were prepared as before and a litter of ten piglets were dosed by mouth 5 hr. after birth, five receiving 2 ml. of washed bacteria and five 2 ml. of the toxin. All the toxin group were showing signs of enterotoxaemia 26 hr. after dosing, when one piglet was dead. Further deaths occurred at 27 and 29 hr. (Pl. 5, fig. 1) and sometime before 36 hr.; only one of the toxin-treated animals survived. Post-mortem examination of each of the four dead piglets showed the typical gross changes of enterotoxaemia and the intestinal contents contained β-toxin. *Cl. welchii*, Type C, was isolated from each animal.

In the group fed with washed bacteria there was one death. The pig was found overlain at 26 hr. It had shown no signs of enterotoxaemia and the post-mortem examination revealed little to favour such a diagnosis; moreover, neither β-toxin nor *Cl. welchii*, Type C, could be demonstrated in the intestinal contents.

This last-described experiment showed clearly that bacteria-free toxin, produced by *Cl. welchii*, Type C, could readily initiate in very young piglets an enterotoxaemia that was indistinguishable, clinically, pathologically and bacteriologically, from the natural disease, but that the condition could not, at least by the methods employed here, be readily reproduced by feeding toxin-free bacteria.

Before investigating further the question of feeding bacteria-free toxin, one more experiment was carried out in which ten out of a litter of thirteen piglets were fed 2 ml. of a suspension of washed organisms about 12 hr. after birth. Only one of the dosed piglets died; this one was found dead 24 hr. later. The post-mortem picture was suggestive of enterotoxaemia but the bacteriological findings were inconclusive.

Feeding bacteria-free toxin

In piglets fed bacteria-free toxin, β-toxin had been demonstrated in the intestine after death. Type C organisms had also been found in these cases and it seemed

likely therefore that some, at any rate, of the toxin recovered had been elaborated in the intestine. On the other hand, although the very fluid intestinal contents would greatly dilute the toxin that had been fed experimentally, it could not be assumed that the toxin recovered was not, in fact, the same as that administered. An experiment was designed, therefore, to study the manner in which toxin given by mouth brought about the death of the animal. The first purpose of the experiment was to determine the origin of both the *Cl. welchii*, Type C, and the β-toxin recovered post mortem.

Preparatory procedures. The concrete box in which the experiment was to be carried out was first washed thoroughly with hot soda and then the floor was covered with strong lysol which was allowed to remain there for 24 hr. After this treatment the floor and walls were flamed. Entry to the box was from an outside concrete yard and the cleaned rubber boots, worn inside the box, were put on in this yard; when not in use the boots were stored in a metal bin in the yard. It was considered that these precautionary measures would reduce the clostridial contamination of the farrowing box to a very low level, but would not prevent recontamination if the sow selected for the experiment was carrying *Cl. welchii*, Type C.

Pre-inoculation tests. Just before farrowing a rectal swab was taken from the sow and further swabs from her rectum and moistened teats were taken shortly after farrowing. Rectal swabs were also taken from her eight piglets before dosing. All these specimens were subjected to the full bacteriological procedures described above under Methods, but *Cl. welchii*, Type C, was not isolated from any of them.

Inoculation of piglets. Three hours after birth six of the piglets were fed 2 ml. each of a toxic filtrate of *Cl. welchii*, Type C, containing 20 mouse-lethal doses per ml., which had been shown to be free from any bacteria. The remaining two animals were not dosed and served as controls.

Within 30 hr. five out of the six dosed piglets were dead and the post-mortem examination in each case showed the typical picture of acute enterotoxaemia. The remaining test animal and the two controls showed no sign of illness, but rectal swabs taken during the course of the experiment showed that one of the control animals was excreting *Cl. welchii*, Type C, 24 hr. after dosing the test piglets. The three surviving animals were sacrificed 42 hr. after the start of the experiment and the post-mortem examinations failed to show any evidence of enterotoxaemia. Cultures taken at various levels of the gut resulted in the isolation of a β-toxin-producing organism from the large bowel of the surviving test piglet, but the cultures from the two control animals showed only *Cl. welchii*, Type A.

Cultures from the intestines of all five piglets dying from the experimental enterotoxaemia showed β-toxin in the supernatant of the cooked-meat media inoculated with this material and *Cl. welchii*, Type C, was isolated from three of the five sets of these cultures. The identity of the organisms was confirmed by mouse protection tests employing the antitoxic sera prepared from *Cl. welchii*, Types A, C and D; mice injected with the toxin were protected only by Type C, or a mixture of Types C and D antisera and not by Types A or D antisera. The

cultures from the other two piglets were neutralized by Type C and by Type D antisera, but not by that of Type A, so that although it seemed clear that these latter cultures produced β-toxin the results of the critical neutralization tests in mice were inconclusive.

The above experiment was repeated with a sow farrowing a litter of ten piglets, five of which were dosed with 2 ml. of bacteria-free toxin, containing 100 mouse-lethal doses per ml., and five left as controls. The dosing was given 2 hr. after the birth of the piglets and four out of the five animals receiving the toxin died of acute enterotoxaemia within about 40 hr. β-toxin-producing organisms were isolated from the intestines of three out of the four dead animals. Photomicrographs of the intestine from a field case and from a case induced with bacteria-free toxin are compared in Pl. 6, figs. 4–7.

Rectal swabs from the sow and the control animals were taken at various times during the experiment; cultures were also prepared from the intestines of the sacrificed healthy controls. All these cultures were negative for Type C organisms; only Type A strains were isolated from any of the swabs from the sow or piglets. In identifying the cultures, the control mice were protected by Type A and Type C antiserum, respectively.

β-toxin had been demonstrated in the intestinal contents in two of the test piglets in each of the above experiments and in three of these animals the total amount of toxin was estimated. This was done by measuring the volume of the whole intestinal contents, from the duodenum to the rectum, and then finding the concentration of toxin from titrations in mice. In the first experiment, where both piglets were so examined, the total toxin was 600 and 840 mouse-lethal doses, respectively, whereas only 40 mouse-lethal doses had been fed. The corresponding figure for the single piglet examined in the second experiment was 1900 mouse-lethal doses, the amount fed in this instance being 200 mouse-lethal doses. It appears, therefore, that considerable quantities of toxin had been elaborated within the gut of the affected animals.

Clostridium welchii, *Type C, in normal piglets*

Although *Cl. welchii*, Type C, was demonstrated without difficulty in the gut of nearly all the piglets that died after dosing with bacteria-free toxin, it was found only once in several series of rectal swabs collected from the combined total of seven control piglets. In contrast, Type A strains were commonly recovered from control animals.

Further examinations of normal piglets, 1–2 days old, confirmed the above findings. Rectal swabs were taken on four separate occasions from a sow and her ten piglets. After growth in Robertson's medium the cultures were plated out on horse-blood agar and incubated anaerobically. One to four *Cl. welchii*-like colonies were picked off into cooked-meat broth and the supernatant eventually tested for β-toxin and checked with the range of specific antisera. Type C organisms were not found in any of the cultures, but from the swabs of seven of the eleven animals typical *Cl. welchii*, Type A, were isolated.

Natural cases of enterotoxaemia in the experimental herd

In the course of this work, cases of enterotoxaemia occurred naturally among other litters of the herd from which the experimental sows were drawn. The farrowing accommodation consisted of two blocks of eight boxes each, and although there was a tendency to use certain boxes for these experiments, there was no adherence to this. Thus boxes used experimentally were, after cleaning, occasionally used for normal farrowings. The first experiment using whole cultures was in January 1955, and six more experiments had been carried out by July of that year; there was then a gap until December. During the early experiments, two pigs in one litter from the experimental herd died naturally from enterotoxaemia in March; in September 1955 three piglets in a litter of seven died of the disease when 3–5 days old and, within a week, a second sow had lost five out of thirteen piglets at 1–2 days of age from the same cause. *Cl. welchii*, Type C, was recovered from a rectal swab from one of the unaffected pigs in this last litter and also from a swab from the mammary glands of the sow. In November 1955 a third sow lost a single piglet from enterotoxaemia and a fourth lost five out of a litter of eight when they were 1–2 days old. During the period September to November twelve other sows farrowed without trouble, so that the incidence of the disease, on a litter basis, during this time was 25 %. Thereafter, and throughout 1956, all the litters not being used for this study were injected with commercial lamb-dysentery serum (Burroughs Wellcome and Co.) which had been found by Field & Gibson (1955) to be an effective method of protection. Each piglet was given 2 ml. subcutaneously within 24 hr. of birth and no further losses from enterotoxaemia occurred, except in a single litter some months later when the routine injections had been inadvertently omitted. Early in 1957, after the last experiment in the series, the practice of injecting every litter was discontinued, but from then onwards no deaths attributable to enterotoxaemia have been observed.

Enterotoxaemia, as a disease of new-born pigs, had not long been recognized when these investigations were begun and it is possible, therefore, that isolated deaths from this condition might have previously passed unrecognized in the experimental herd. It is unlikely, however, that losses on the scale just described would have arisen without the post-mortem changes exciting comment and it is more probable that the introduction of Type C organisms to the farrowing boxes had greatly increased the risk of developing the disease. Two further points are worthy of note: first, the sporadic way in which the natural disease may occur, even within a single litter where only one pig may succumb and, secondly, the changing need for protective serum. Once the experimental programme had ended, the repeated cleaning of the boxes probably reduced the number of bacteria to a point where no special risk existed.

Clinical and pathological observations

In enumerating the salient clinical and pathological changes of enterotoxaemia in the new-born piglet, mention can first be made of the very acute nature of the infection. Diarrhoea has been seen 12 hr. after dosing with toxin; two pigs in

another litter were dead in less than 17 hr. after being given broth cultures. The same rapid sequence of events can occur naturally; in one litter the first death from enterotoxaemia occurred within 20 hr. of birth. As the longest time between dosing and death in all the experiments was only 41 hr., it was necessary to keep the affected pigs under almost continuous observation in order to record the entire course of the disease.

The main clinical sign was diarrhoea but this was not always present. The diarrhoea, although not profuse, was very watery and it varied in colour from yellow, which was not uncommon, through all degrees of blood-staining to a chocolate or, most characteristically, a port-wine colour. With the onset of diarrhoea the piglets weakened rapidly, becoming disinterested in suckling and finally prostrate. During this terminal phase of the disease the main signs were those of hypoglycaemia and metabolic collapse. As would be expected the piglets that died in the shortest time had less chance to exhaust their glucose reserves but, even so, some degree of hypoglycaemia was often present by then and this may still have masked other signs. In one piglet, for example, dying as early as 19 hr. after dosing, the blood-glucose concentration was already down to 53 mg./100 ml., and in another group of five piglets, which had yet to develop clinical signs 22 hr. after dosing, there was one animal whose blood-glucose concentration was 70 mg./100 ml., whereas the mean concentration for the other four animals was 89 mg./100 ml. Six hours later these figures had become 63 mg. and 94 mg./100 ml., respectively, and the piglet developing progressive hypoglycaemia was the only one to die later from enterotoxaemia. When piglets took longer to die the hypoglycaemic collapse was commonly complete. In these circumstances, although the heart rate was often faster than the corresponding rate during uncomplicated starvation hypoglycaemia, it is unlikely that the conventional indications of infection, such as pyrexia and tachycardia, could be developed. It may be, however, that these latter signs would not be a feature of enterotoxaemia in any event; enteric infections are often afebrile. Dying piglets were also observed for evidence of the mode of action of the toxin. Neurological signs were conspicuously absent and the only indication of central disturbance, apart from the hypoglycaemic syndrome, lay in the spasmodic, gasping respiration sometimes seen in the prostrate stage.

At autopsy the intestinal changes were dominant and striking: the coils of the small intestine were often a rich reddish-purple and distended with blood-stained fluid contents. In the most acute cases a milder degree of congestion extended over the serous surface of the stomach. 'Diphtheresis' was seen in a minority of the dead piglets but when present it was pathognomonic (Pl. 5, fig. 2). The speckled appearance of this yellow necrotic membrane seen through the red serous surface of the unopened intestine was also characteristic. Almost invariably the greater part of the small intestine was congested, but there was one notable exception. In a non-experimental litter of seven, one pig was found dead at 3 days; the small intestine was inflamed, there was extensive 'diphtheresis' and *Cl. welchii*, Type C, was isolated. The following day two other piglets were affected clinically and one of these, with a watery brown diarrhoea, died at 5 days. The small intestine appeared to be almost normal but on examining it along the whole length a small,

sharply demarcated area of congestion was found which, on incision, exposed a thickly necrotic mucosa (Pl. 5, fig. 3). Neither free toxin nor *Cl. welchii*, Type C, could be demonstrated in the bulked intestinal contents, but the clinical signs, the type of lesion and the circumstantial evidence left no doubt that the animal had died of enterotoxaemia. Histological sections were prepared from both the affected and the apparently unaffected portions of the small intestine: there was very deep necrosis of the obviously affected areas but other portions were also necrotic microscopically, albeit to a lesser degree.

DISCUSSION

One of the main conclusions from this work is the ease with which enterotoxaemia can be produced in very young piglets by feeding with either whole cultures of *Cl. welchii*, Type C, or the bacteria-free β-toxin. The history of *Cl. welchii* infections among animals has, until recently, centred very largely on sheep, in which the enterotoxaemia is mainly due to *Cl. welchii*, Type D. This condition has been reproduced only with difficulty (see Bullen, Scarisbrick & Maddock, 1953; Smith, 1955). It is known, however, that if Type D organisms are fed to sheep, large numbers of the bacteria are destroyed in the rumen (Bullen *et al.* 1953). But this cannot explain the vulnerability of the piglet, because bacteria alone are generally ineffective in the piglet also. Nevertheless, the absence of the large diluting chambers before the true stomach in the piglet might contribute to the reproduction of the disease by allowing toxin to reach the small intestine more rapidly, in greater concentration and in a more active state. The experiments of Griner & Bracken (1953) on the new-born calf, which can be likened in this respect to a monogastric animal, throw no light on this question; although they reproduced enterotoxaemia in one calf out of six by feeding a broth culture of *Cl. welchii*, Type C, in four previous experiments they were unsuccessful. The susceptibility of the new-born piglet could also be a reflexion of the ability with which the small intestine can contain the disease in its early stages. Despite the heavy loss of bacteria in the rumen of experimentally dosed sheep, sufficient bacteria reach the ileum to produce considerable quantities of toxin (Bullen *et al.* 1953); yet the host is able to contain low concentrations of toxin for long periods, or even high concentrations of toxin for short periods, and survive (Bullen & Scarisbrick, 1957). If a high concentration of toxin persists, however, the permeability of the intestine is increased (Bullen & Batty, 1957). The evidence for this was obtained by following the concurrent change in the absorption of diphtheria antitoxin and, as the intestine of the normal new-born piglet is already freely permeable to antibody for the first day or so of life, it is probable that the baby piglet has not the defensive reserve which protects the sheep, and possibly also the older piglet where the natural disease is rare, against all but the greatest concentrations of toxins.

Although our findings offer no direct evidence for the manner in which the disease is initiated some speculation is possible. Natural cases of the disease were much more common in the experimental herd during the period when Type C organisms were being repeatedly introduced to the premises. It can be assumed,

therefore, that the first requirement is for Type C organisms to be present in the intestines. This alone is insufficient, however, because oral dosing with washed organisms has little ill-effect. A comparable situation exists in the sheep, where almost half of the normal animals examined in one survey were found to carry Type D organisms (Bullen, 1952). In piglets from normal litters, however, we have been unable to isolate Type C organisms, the most likely explanation being that the ratio of Type C to Type A strains is normally too small to permit the detection of the former by our cultural techniques. Whatever the answer to this point, it has been shown that bacteria-free toxin readily initiates the disease. A possible explanation for this may be that the toxin given by mouth, aided perhaps by the peculiar free permeability of the gut wall at this time, produces a small area of necrosis in which Type C organisms multiply. The advent of further toxin then cumulatively repeats the process until much of the intestinal lining is destroyed and the ensuing large quantities of toxin overwhelm the piglet. What the initiating factors might be in natural cases of the disease cannot be deduced at this stage.

SUMMARY

1. Whole cultures of *Clostridium welchii*, Type C (organisms plus toxin), produced enterotoxaemia and death when fed to new-born piglets.

2. The disease could rarely be produced by suspensions of washed organisms given in the same way but was readily initiated by feeding bacteria-free toxin from Type C cultures.

3. Piglets dying from enterotoxaemia induced by bacteria-free toxin showed all the extensive pathological changes of the natural disease; their intestines contained Type C organisms and far greater quantities of toxin than had been given by mouth.

4. Type C organisms could not be demonstrated in the intestines of piglets from healthy litters of the same age, although such animals were carriers of the Type A strain.

5. The clinical signs, with particular reference to the development of hypoglycaemia, and the pathology of both natural and experimentally induced cases of enterotoxaemia are described.

6. In the light of these findings the pathogenesis and epidemiology of enterotoxaemia in the piglet are discussed.

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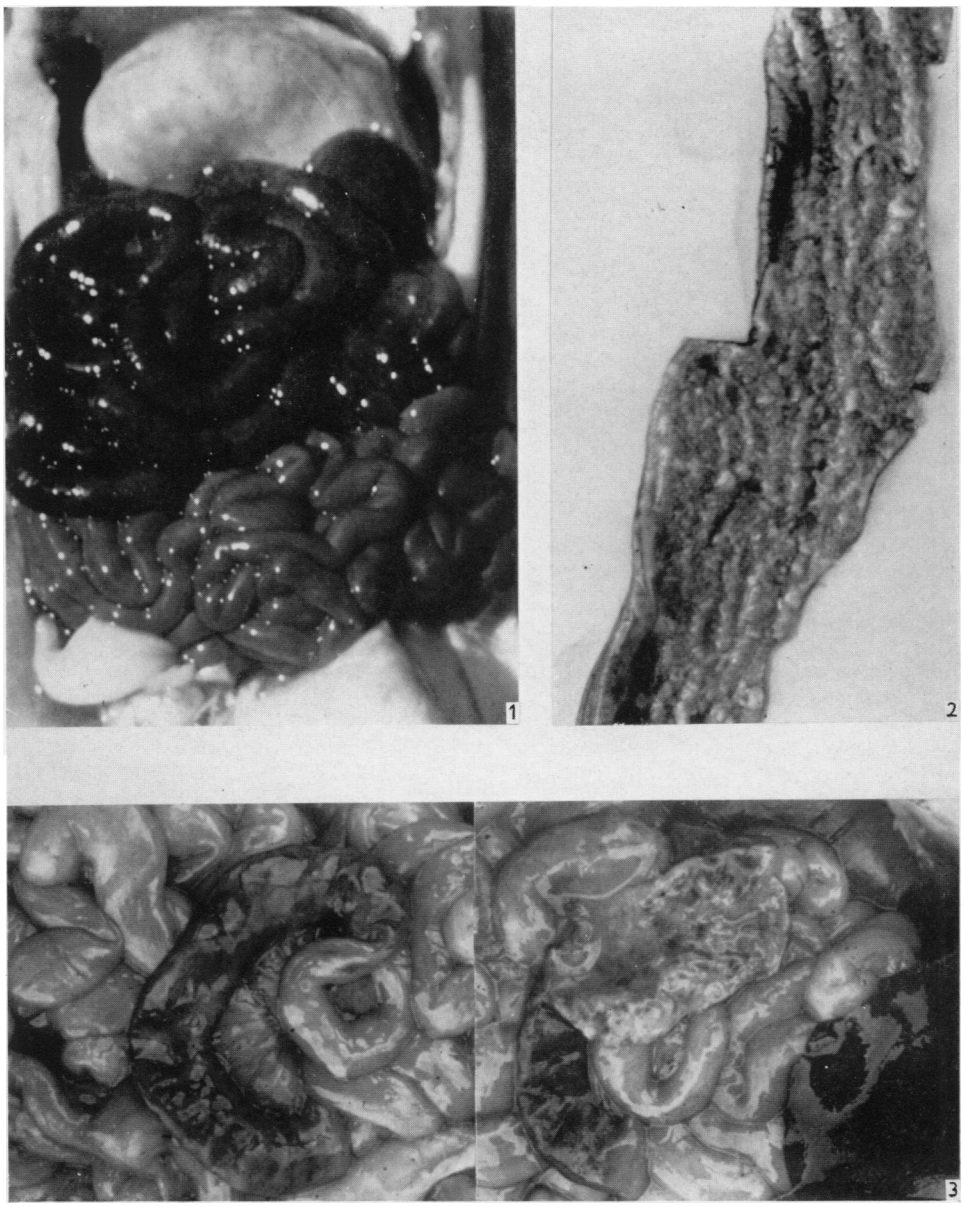

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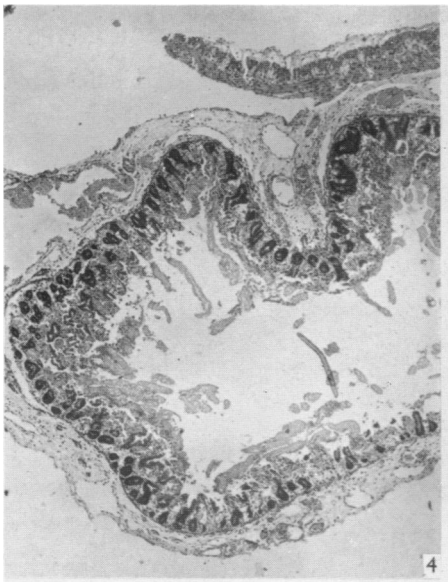
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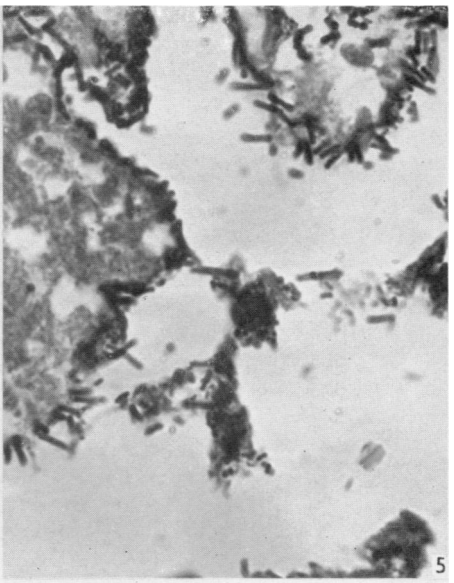
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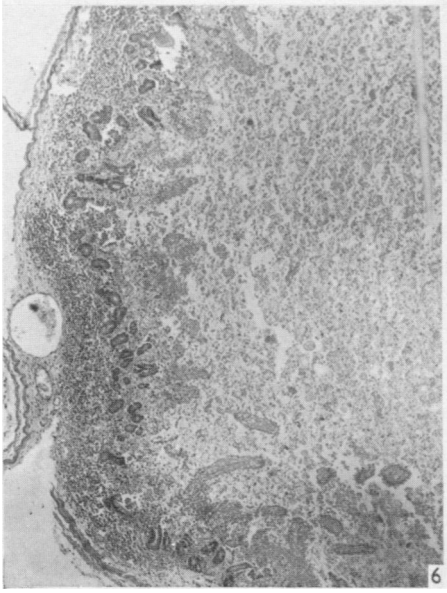
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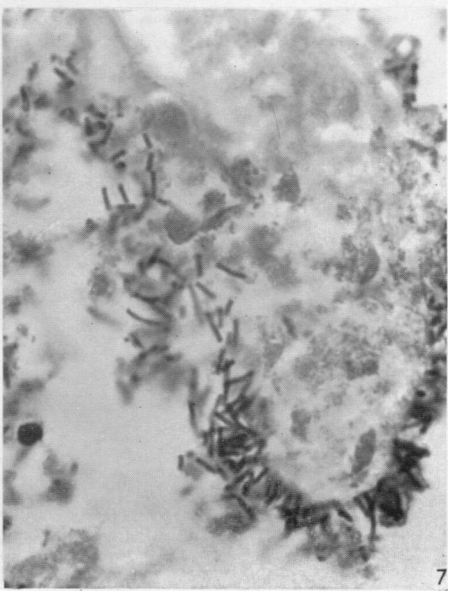
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EXPLANATION OF PLATES

PLATE 5

Fig. 1. Acute enteritis in a piglet that died 29 hr. after being dosed by mouth with bacteria-free, type-C toxin.

Fig. 2. Characteristic necrosis of the small intestine in a piglet dying from enterotoxaemia 48 hr. after birth. This case was from a naturally affected litter in the experimental herd.

Fig. 3. Very localized area of congestion in a piglet dead from enterotoxaemia 5 days after birth. Photographs of the affected loop, before and after incision, are shown side by side.

PLATE 6

Fig. 4. Necrosis of the mucosa in a piglet that died 21 hr. after being dosed with bacteria-free toxin. H. & E. × 40 approx.

Fig. 5. Bacteria and necrotic debris in a parallel section to that shown in Fig. 4. Gram × 1000 approx.

Fig. 6. Necrosis of the mucosa in a field case of enterotoxaemia. H. & E. × 40 approx.

Fig. 7. Bacteria and necrotic debris in a parallel section to that shown in Fig. 6. Gram × 1000 approx.

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