INCIDENCE OF GASTRIC ULCER IN ALBINO RATS FED DIETS DEFICIENT IN VITAMIN B (B_1)

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PLATES 26 TO 28

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The morbid changes associated with deficiency of the antineuritic factor of the vitamin B complex (hereinafter designated vitamin B) are not well established. This is in large part due to the fact that the vitamin B complex has been only recently separated into its component parts, the earlier anatomical studies having been made of animals which had been given diets deficient in more than one factor. With the perfection of experimental diets the prospects of understanding more satisfactorily the structural derangements occasioned by a deficiency of vitamin B seem brighter. The present report is one result of such a study. It is concerned with the occurrence of ulcerations in the gastric and duodenal mucosa of rats whose diet had been deficient in vitamin B.

Method

64 animals have been studied. All were from the same stock, a strain of rats which has been used in the Department of Physiological Chemistry of Teachers College for many years. Most of the animals had been used by one of us (Kellogg) for various feeding experiments. The animals reported represent consecutive specimens derived from these experiments and no animals have been discarded. Until these experiments were commenced all of the rats had received the identical stock diet. All of them, during their course, were given the same basal ration (Sherman and Spohn's diet No. 107 (1)), which contains:

	per cent
Casein (extracted)	18
Butter fat	8
Cod liver oil	2
Salt mixture	4
Corn starch	68

This ration is deficient in the vitamin B complex and vitamin C. The thermostabile portion of the vitamin B complex (vitamin G) was supplied by adding to the ration large amounts of brewers' yeast which had been autoclaved for 6 hours at 15 pounds pressure. Vitamin C was not supplied because the rat does not require it (2). The animals were handled with great care, in a model animal room, and all of the groups were apparently free of infectious diseases throughout the course of the experiment.

At the termination of the experimental period the animals were killed with gas, the stomach immediately removed, slit open and placed in Zenker's solution. Our original purpose was to observe any evidence of gastric dilatation and intestinal stagnation which have been said to occur in vitamin B-deficient animals (3). Therefore in the first animals examined (Nos. 1, 3 and 11) only two levels of the gastric wall were sectioned. In all the other cases the stomach was cut in five segments and embedded in paraffin. Most of each block was sectioned, every third or fourth section being mounted and stained. More than 2,500 histologic preparations have been examined in the cases reported, each section including the entire circumference of the wall at one level. As routine the preparations were stained in Giemsa solution though other stains have been used for the special investigation of some lesions.

RESULTS

Gross Appearance of Stomach.—Gastric dilatation was observed in only a few animals and it bore no relationship to the degree of deficiency of the diet. Camera lucida drawings of the histologic preparations were used for our comparisons. The results were so inconclusive they need not be given. Many of the completely deficient animals had small stomachs nearly empty of food. In some hair was present, generally in the rumen. Naked eye inspection showed no lesions of the stomach lining; and the ulcers which were found have never been positively identified in the gross specimens.

The Incidence of Ulcers.—Of the 64 animals examined, Nos. 1 to 29 inclusive had had little or no vitamin B in the daily ration, and, of these, twenty-one had one or more gastric ulcerations. Twenty animals (Nos. 45 to 64 inclusive) had larger amounts of vitamin B or were on a complete diet and in none of these were gastric lesions present. Nine animals (Nos. 36 to 44 inclusive) had been used for vitamin B assays. This involved a 40 day period of depletion followed by feeding repeated, increasing amounts of vitamin B sources. They

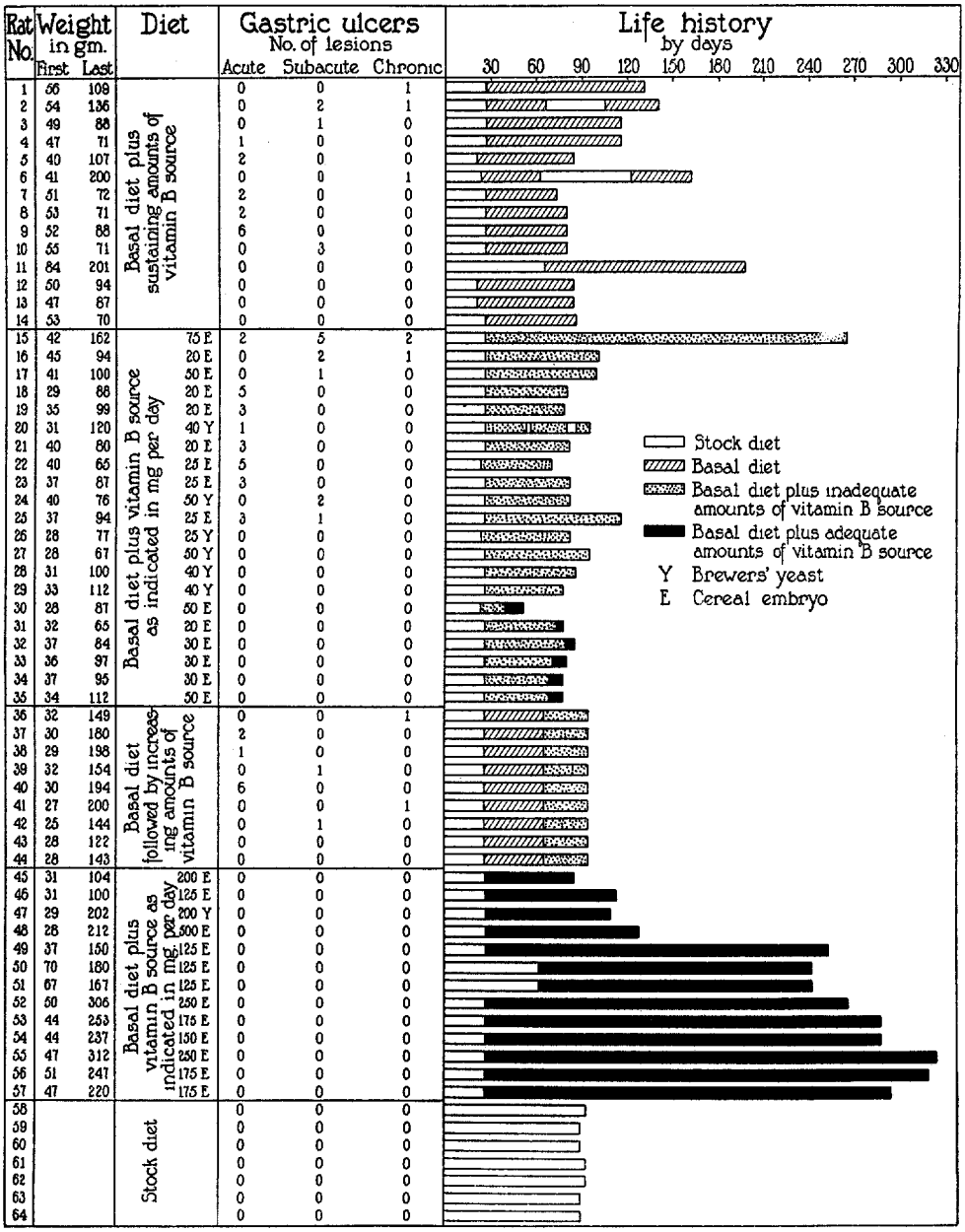

CHART 1

Vitamin B source used was cereal embryo ("Bemax," Schieffelin and Co., New York).

were comparable, in total vitamin B intake, to the first group. Seven of them had gastric lesions. A group of six animals (Nos. 30 to 35 inclusive) received only a small amount of vitamin B for periods of from 15 to 54 days. They were then given sufficient quantities of vitamin B source to relieve them of all clinical evidence of vitamin B deficiency. These animals are therefore not included among the twenty-nine truly deficient animals. In none of them were gastric ulcers found. The incidence of gastric ulcer in the deficient group of rats is 73 per cent, while in those animals protected by larger amounts of the identical vitamin B source no lesions occurred.

No difference in susceptibility to ulcer formation was noted between male and female animals.

Eight of the lesions were chronic, indurated ulcers or scars of the gastric wall. Forty-seven of the lesions were acute erosions and nineteen transitional forms showing some signs of induration and of reaction on the part of the gastric wall. The average duration of the cases in which chronic lesions were found was 114 days, while the average duration of the feeding period in those animals in which only acute lesions appear was 53 days. Acute ulcers were present with a chronic one in one stomach.

74 lesions were present in all, representing various stages in the development of a chronic ulcer strikingly similar to the chronic peptic ulcer of man, as well as forms that represent stages of healing. Therefore the histologic changes are a matter of considerable interest.

Structure of the Lesions.—The more acute lesions consist of minute punched out areas of necrosis of the gastric mucosa extending into the deeper half of this coat. The necrotic cells are often present in the plugs of debris lying within the crater, the cells and nuclei shrunken and compacted (Fig. 8). Frequently the cells of the necrotic mass and the base of the erosion have a glassy, acidophilic character (Fig. 12). In some of the cases a few polynuclear leucocytes are present. In many more these are absent. As the lesion becomes older it also enlarges considerably, the base becoming broader and slightly indurated. The basement membrane becomes involved, inflammatory cells are generally present and the necrotic mass may be lost. The outline of the lesion is still punched out, however (Figs. 5 and 6).

Later stages resemble chronic peptic ulcer with a dense scarred base overhung by adjoining gastric mucosa, sometimes hyperplastic and redundant (Figs. 1 to 4). The base of the ulcer shows digestion of its surface, contains leucocytes and often

thickened blood vessels and signs of vascular regeneration. Several of these lesions extend well into the muscular coats of the stomach. In such cases there is a pronounced inflammatory reaction in the submucosa about the lesion. Still older lesions have been observed in which the crater has become a dense collagenous scar, and one lesion shows a scar overgrown by a tuft of irregular and hyperplastic mucosa which arises from the margins of the lesion (Fig. 11).

Distribution of the Lesions.—The locations of the lesions are not known in all cases because they could not be seen in the gross specimen and often could not be definitely oriented in the histologic preparations. Most of them occurred along the lesser curvature or near it. This can be determined because the rat's stomach has an area of thickened mucosa along the greater curvature and this portion was affected in only two cases (both of which also had lesions elsewhere). Three of the ulcers occurred in the proximal duodenum.

As is shown in Chart 1 acute lesions were found in all stages and degrees of vitamin B deficiency while the chronic lesions were found only in cases in which the period of deficiency was long.

DISCUSSION

Diet.—The diet used contained neither vitamin B complex nor vitamin C. It is presumably ample in all other known constituents. The vitamin G factor was provided in each case by daily dose of 500 mg. of autoclaved yeast, but vitamin C was deficient in all of the animals. We have found no references pertaining to the gastric mucosa in rats on a scurvy-producing diet. In fact no structural effect from vitamin C deprivation has been demonstrated in the rat. This animal is, indeed, able to live and propagate in apparently normal fashion without antiscorbutic substance and to maintain, under conditions of complete deprivation of vitamin C, large stores of antiscorbutic in its tissues (4). A control group of thirteen animals received the identical basal ration augmented by vitamin B source, but no gastric ulcers were found in this group.

Three studies of rats deprived of vitamin B have been published which are of particular interest in the light of the present work.

McCarrison (5) found an occasional ulcer in the stomach and intestines of animals deprived of both vitamin B complex and vitamin C, and having a deliberately unbalanced basal ration. He concluded that a faulty diet predisposes

to gastrointestinal infection and therefore to a number of lesions of the tract among which is gastric ulceration. McCarrison did not attempt to associate the lesions found with one food factor alone and was apparently more interested in the other intestinal disorders, which in his series were more frequent. Findlay (6), some years later, studied a group of vitamin B-deficient rats but all of his animals were completely deprived of the vitamin and died after an average period of 32.5 days. He saw no gastric ulcers. A more recent study, by Sure, Thatcher and Walker (7), in which partially deficient as well as completely deficient animals were examined, more nearly resembles our own studies. They found a small gastric ulcer in one animal. They examined many different organs of the body. No importance was attached to the ulcer. None of these authors has described or illustrated gastric ulcers and a structural comparison with those found in our own rats is therefore impossible. It seems likely to us that other lesions might have been found in the animals of Sure, Thatcher and Walker if the search had been more inclusive. Since the lesions are so small that only a thorough histologic examination can be expected to identify them, it is not surprising that they may have been overlooked.

Since the lesions described are structurally similar to those which occur in man it becomes interesting to compare the pathology in the two species. The most widely held view of chronic peptic ulcer seems to be that it depends upon two factors, a preliminary acute lesion the result of a number of possible irritants, thrombosis, infection, etc., and a local or constitutional defect which precludes the healing of the acute lesion when once established. Local neurotrophic or circulatory abnormalities are frequently mentioned as local causes responsible for the non-healing of acute ulcers.

Our own experiments indicate that such is not the case in the rat for the present results can only be explained by the deficiency of one factor in the diet, and yet both acute erosions and chronic lesions appear to have been due to this defect. In other words, the dietary deficiency caused not only a tendency to erosion but likewise a tendency for certain of these acute lesions to become chronic.

The size of the lesions is similar to those which occur in man if adjustment is made for the differences in size of the organs involved. The size of acute lesions, as well as their location, is probably determined by the configuration of the mucosal folds. The exposed tips become eroded while those portions of the gastric mucosa protected by invaginations are spared. From our study of the ulcers in these rats the factor of gastric mucosal configuration as determining the site of the lesions is well substantiated.

SUMMARY

73 per cent of a group of albino rats whose diet was deficient in vitamin B have been found to have ulcerations of the gastric mucosa. A control group was found to be free from gastric lesions.

Of 74 observed lesions eight were chronic, indurated ulcers resembling chronic peptic ulcer in man.

The chronicity of the ulcers seems to be related to the duration rather than the degree of the deficiency.

The lesions were generally located along the lesser curvature of the stomach, as is true in man.

The size of the lesions in rat and man are comparable if adjustment is made for differences in the sizes of the organs.

CONCLUSION

Albino rats deprived of vitamin B commonly develop ulcers of the gastric mucosa.

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EXPLANATION OF PLATES

PLATE 26

FIG. 1. A low power photograph of a chronic gastric ulcer in which the inflammatory reaction extends through the muscularis mucosae. The crater was approximately 2 mm. in diameter.

FIG. 2. Higher magnification of the base of the same lesion.

FIG. 3. A chronic gastric ulcer which has invaginated and is overhung by intact mucosa. This lesion is similar to the chronic peptic ulcer found in man in its minute structure.

FIG. 4. Detail of the base of the same lesion. Note the thickened vessels and scarring.

PLATE 27

FIGS. 5 and 6. Two small gastric ulcers with some induration of their bases but which have not extended through the mucosa.

FIG. 7. Two erosions of the gastric mucosa. The one on the left has scar tissue within it, the other is probably of more recent origin.

FIG. 8. A very small acute erosion with plug of necrotic cells in the crater.

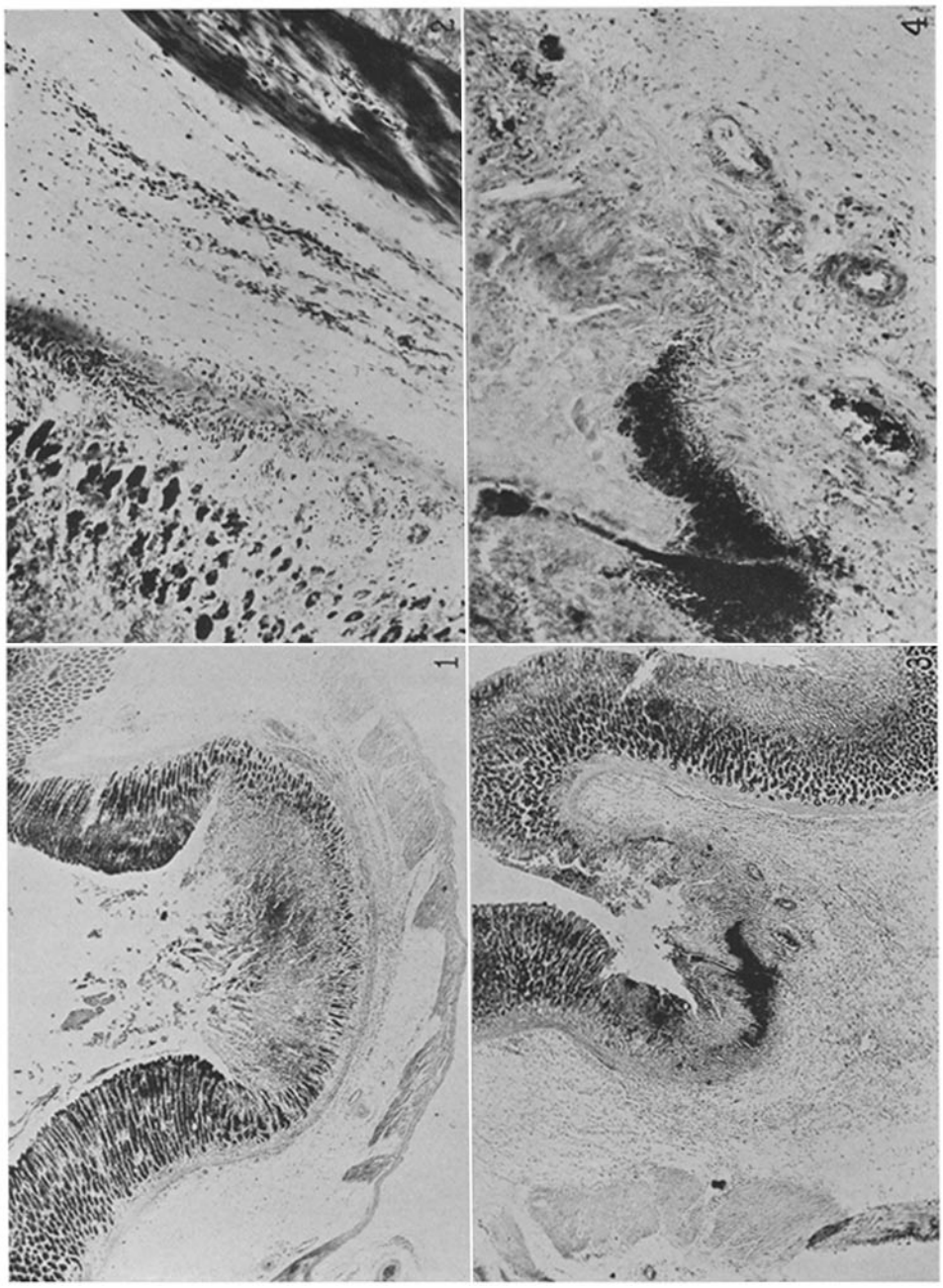
PLATE 28

FIG. 9. A chronic ulcer of the proximal duodenum. The mucosa has closed over the defect. The lumen of the bowel may be seen at 11 o'clock. The ulcer is scarred, shows vascular lesions. Its base contains many polynuclear leucocytes.

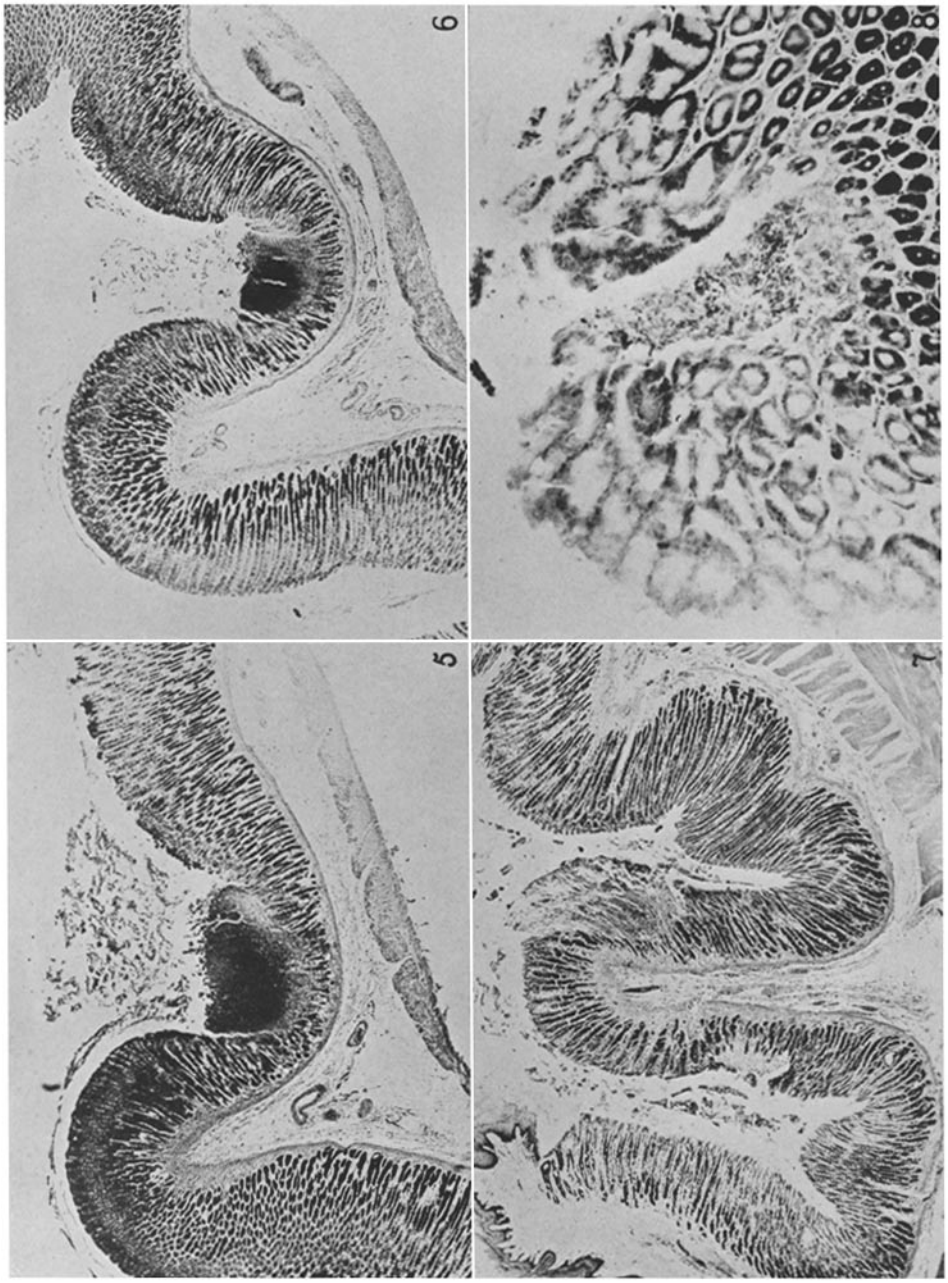
FIG. 10. A large acute erosion in which the cellular necrosis is extending downward and towards the left. Several areas of a glassy, acidophilic appearance are present in the center.

FIG. 11. An area of gastric mucosa interrupted by a scar and overgrown by atypical mucosa which arises from the margins of the scar. This was found in Animal 6 and is assumed to be a healed ulcer. It is not listed in Chart 1.

FIG. 12. An acute erosion of small size but containing leucocytes.



(Dalldorf and Kellogg: Gastric ulcer in rats lacking vitamin B)



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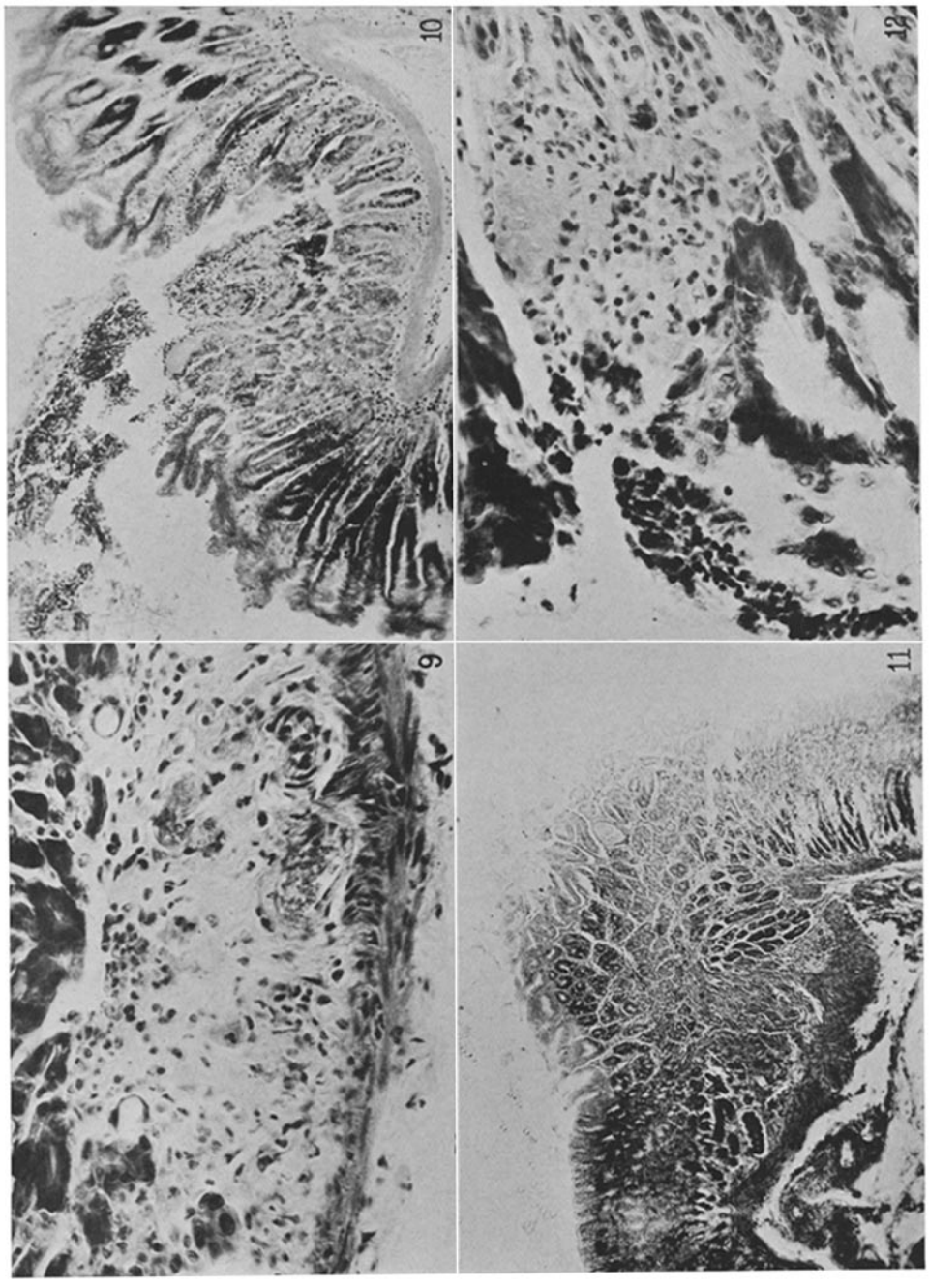

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