# Anemia Associated with Blind Intestinal Segments and its Prevention with Aureomycin.* (18335)

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This study was prompted by the observation of ulcerative lesions in blind intestinal segments resected from patients suffering from chronic anemia. Following the construction of a side to side intestinal anastomosis the blind end of the proximal segment is continually subjected to the driving force of intestinal peristalsis. In some instances this blind segment becomes markedly dilated and packed with fecal material. Black and McEachern(3) describe the usual symptoms as abdominal pain, cramps, diarrhea and vomiting. They reported 5 cases, 2 with ulceration and perforation and one with anemia. Pickhardt(11) and Eckel and Holman(6) reported symptoms including anemia occurring as late as 9 and 10 years after construction of a side to side anastomosis. Cameron *et al.*(5) described a case of macrocytic anemia which developed within one year after a side to side anastomosis in the terminal ileum for regional enteritis. Estes and Holm(7) reported 2 cases showing marked ulceration in such redundant blind intestinal segments and were able to reproduce this syndrome in dogs. Pearse(10) however found that ulceration and perforation did not occur in such dogs unless a foreign body was present in the intestinal lumen.

Our purpose was to ascertain whether or not such ulcerative lesions were a constant finding in blind intestinal segments created in the experimental animal.

*Method.* Adult male and female rats of the Sprague-Dawley strain weighing from 300-400 grams were prepared in a manner similar to that described by Watson, Cameron, and Witts(14). Under ether anesthesia the abdomen was opened and the small intestine divided about 5 inches distal to the ligament of Treitz. The cut end of the proximal segment was inverted and at a point 3 inches proximal to this inversion an end to side anastomosis was done with the distal segment using interrupted sutures of very fine silk. In this manner a blind intestinal pouch 3 inches in length was so constructed that intestinal peristalsis would tend to keep the pouch filled. The animals so prepared were divided into 2 groups. Series A consisted of 18 rats which were fasted for 48 hours after surgery and then placed on a standard laboratory diet of Purina foxchow biscuits. Series B of 5 rats was identical except that 50 mg of aureomycin were added to the daily portion of ground biscuit. A control animal of similar size and weight was kept in the same cage and on the same diet as each animal of series A and B. At weekly intervals all animals were weighed, a benzidine test of fresh feces done, and blood was obtained from the cut end of the tail for hematological examination. In addition to routine erythrocyte and leucocyte counts, hemoglobin was determined by the oxyhemoglobin method of Evelyn, and hematocrit by a modification of the technic described by Rosahn(13). When the hemoglobin level had dropped to 10 g or less the animal was sacri-

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3. Black, B. M., and McEachern, S. G. O., 1948, v86, 177.

5. Cameron, D. G., Watson, G. M., and Witts, L. J., *Blood,* 1949, v4, 793.

6. Eckel, J. H., and Holman, C., *Surgery,* 1944, v15, 307.

7. Estes, W. L. and Holm, C. E., *Ann. Surg.,* 1932, v96, 924.

10. Pearse, H. E., *S.G.O.,* 1934, v59, 726.

11. Pickhardt, O. C., *Ann. Surg.,* 1933, v97, 116.

13. Rosahn, P D., PROC SOC. EXP. BIOL. AND MED., 1931, v28, 491.

14. Watson, G. M., Cameron, D. G., and Witts, L. J., *The Lancet,* 1948, v2, 404.

ficed. Post-mortem autolysis of the intestinal mucosa in a rat is very rapid. To circumvent this factor the animal was anesthetized with ether and the entire gastrointestinal tract filled with 4% formalin by means of a syringe and fine gauge needle. The abdominal viscera were then removed en masse and fixed in formalin.

*Results. Anemia.* From 104 examinations on normal control animals the following average values were determined: Hemoglobin, 15.4 g percent: erythrocyte count, 8.6 million: and hematocrit, 46.5%. On the basis of these normal values the color and volume indices were calculated according to Osgood(9).

The hemoglobin level fell to 10 g percent or less in 100% of the untreated rats in series A. The anemia appeared rather abruptly from 22 to 86 days after the formation of the blind segment and was accompanied by a weight loss of from 28 to 103 g. Characteristically, the animals appeared well for one to 2 months then suddenly became anemic and obviously quite ill. If the animal was not sacrificed, the anemia was invariably fatal, usually in 2 to 3 weeks after its first appearance. Color indices indicated a predominantly normochromic type of anemia. In those animals in which the hematocrit was determined, the volume indices showed a fairly even distribution between macrocytic and normocytic types of anemia.

None of the animals receiving aureomycin daily in Series B developed anemia in a period of 127 to 175 days after surgery. All remained well until sacrificed and showed a weight gain varying from 17 to 65 g.

None of the control animals developed anemia.

*Melena.* The presence of blood in the feces as determined by the benzidine test was never detected in the control animals. In Series A, melena was found very occasionally at weekly intervals in some animals and in others, not at all. When daily examinations were done over a week's time, the results were the same. In Series B, melena appeared only twice, both

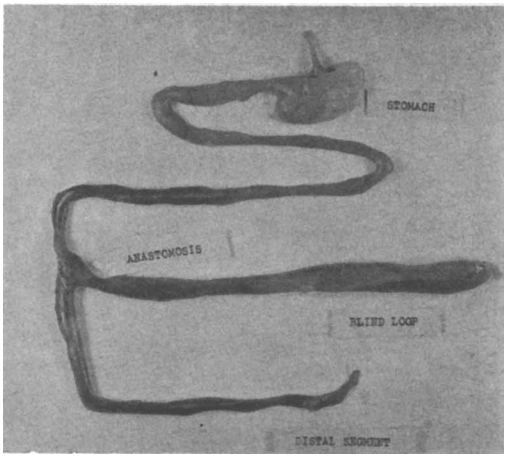


FIG. 1.
The blind intestinal pouch as constructed. Note relative size and position in the intestinal tract.

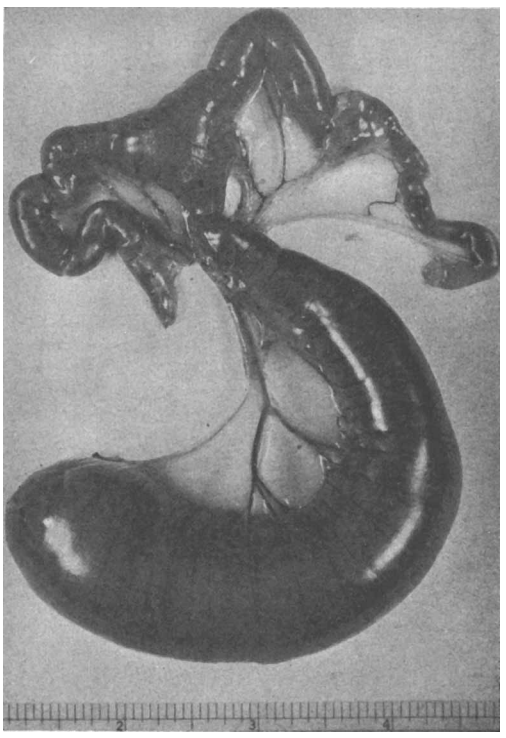

FIG. 2.
A typical example of the blind loop at the time of sacrifice. Note marked enlargement of loop. The efferent channel extends to the right.

times shortly after operation and did not recur.

*Pathology.* With the exception of 2 instances of parasites in the liver, all sections of that organ and of the spleen appeared normal. The

9. Osgood, E. E., *A Testbook of Laboratory Diagnosis,* The Blakiston Co., Philadelphia, 1940.

most striking change that occurred in the blind intestinal segments was a marked increase in all dimensions (Fig. 1 and 2). Some segments were almost double their original length and the increase in diameter was even greater. All specimens appeared more vascular than normal. The majority of the blind segments were filled with very thin intestinal contents indistinguishable grossly from that in the remainder of the small intestine. In one animal gross examination revealed a superficial erosion in the distal part of the blind segment. True ulceration and perforation did not occur. Microscopically there was marked increase in the thickness of the muscularis in all cases, and most instances showed some increase in depth of the mucosal layer when compared to sections from above and below the site of anastomosis (Fig. 3 and 4). Two specimens showed evidence of vascular engorgement and hemorrhage into the mucosa. No ulcerations were found in 20 serially arranged sections from each blind pouch

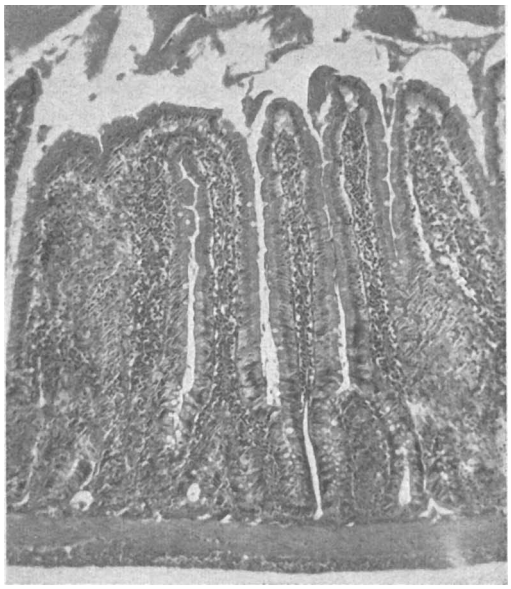

FIG. 3.
Microscopic section of normal rat's intestine. (×100).

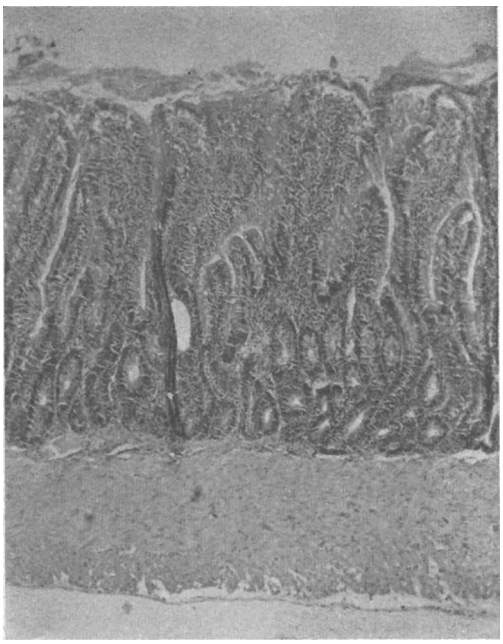

FIG. 4.
Microscopic section of intestinal wall from specimen shown in Fig. 2. Note increased thickness of muscularis.

*Comment.* It is apparent that some relationship exists in the rat between anemia and blind intestinal segments. In 100% of the animals in which such a segment was made and no therapy given, anemia eventually developed. It did not occur in any of the controls. The exact mechanism, however, by which such anemia is produced is not so definite. Alt(1) has shown that 40% of the rat's small intestine may be resected with no chronic ill effects. It is unlikely therefore that the loss of such a short segment as 3 inches would seriously interfere with the absorptive mechanism. Liquid stools were never observed in any of the animals. Although both operated and control animals in Series A were fed the same diet, some element of deficiency may be a factor in the later stages when the animals begin to lose weight.

It is difficult to indict chronic blood loss as a major etiological factor in the anemia on several scores. Ulcerative or erosive lesions were not demonstrable in the blind pouches of rats. This is in contrast to the clinical cases where erosions or ulcerations were consistently found in the distended terminal end of the proximal segment of a side to side anastomosis. The detection of blood in the stools was a very inconstant finding

1. Alt, H. L., *Am. J. Dig. Dis. and Nutrition,* 1936-37, v3, 167.

TABLE I. Terminal Values.

| Series | A | | | B | | |
|---|---|---|---|---|---|---|
| No. of animals | 18 | | | 5 | | |
| | Min. | Max. | Avg | Min. | Max. | Avg |
| Survival time, days | 22 | 86 | 46.5 | 125 | 175 | 165 |
| Weight change, g | —28 | —113 | —83 | +17 | +65 | +45 |
| Hemoglobin, g % | 2.6 | 10.0 | 7.4 | 15.0 | 18.1 | 16.6 |
| Erythrocytes, millions/cu mm | 1.6 | 6.3 | 4.5 | 8.0 | 10.5 | 9.0 |
| Leucocytes, thousands/cu mm | 8.5 | 40.0 | 21.2 | 11.0 | 26.3 | 19.7 |
| Hematocrit, % | 12 | 36 | 26 | 47 | 57 | 51 |
| Color index | 0.73 | 1.02 | 0.92 | 0.86 | 1.15 | 1.04 |
| Volume index | 0.89 | 1.62 | 1.20 | 0.9 | 1.19 | 1.05 |

and the hypochromic type of anemia usually associated with chronic blood loss never occurred.

Intestinal stasis has been postulated by many authors as a prime factor in the etiology of this type of anemia. Butt and Watkins(4) reported 20 cases of anemia associated with such lesions of the bowel as terminal ileitis, ileal ulcer, tuberculosis with stricture, fecal fistula, etc. Of these anemias 11 were macrocytic, 5 microcytic, and 4 normocytic. They noted that the only cases of small intestinal ulceration that showed a macrocytic type of anemia also had obstruction. They suggested that any lesion of the bowel that produces obstruction may so interfere with the absorption or utilization of the hematopoietic principle that an anemia, usually macrocytic, will develop. Barker and Hummel(2) have reviewed 51 cases of macrocytic anemia associated with intestinal strictures and anastomoses. They subscribed to the hypothesis that the primary cause of the anemia was the absorption from the stagnant obstructed gut of a toxic material that interfered with blood formation. Little *et al.*(8), and Richardson(12) have reported on the occurrence of anemia, usually macrocytic in type, following short circuiting operations for small intestinal obstruction secondary to inflammatory adhesions. In these cases the by-passed intestine constituted a blind segment and an element of intestinal stasis. Cameron, *et al.*(5) described a similar situation in a case of regional enteritis and suggested toxic absorption as the most likely etiology.

Although by no means conclusive, the evidence in these animals would favor the thesis of intestinal stasis and unusual bacterial activity as a significant factor in the etiology of the anemia. In all animals a marked enlargement and hypertrophy of the blind segment characteristic of intestinal obstruction was observed and the majority showed filling of these segments with fecal material to the point of distention. In addition none of the operated animals that were fed aureomycin—a known antibiotic—developed anemia during a similar time interval.

*Conclusions.* 1. Anemia, either macrocytic or normocytic in type, can be consistently produced in the rat by the formation of blind intestinal segments. 2. Aureomycin appears to be a potent agent in the prevention of this anemia. 3. Ulceration of the blind intestinal segment does not appear to be the major etiological factor in the causation of this anemia.

2. Barker, W. H. and Hummel, L. E., *Johns Hopkins Hosp. Bull.*, 1939, v64, 215.

4. Butt, H. R., and Watkins, C. H., *Ann. Int. Med.*, 1936, v10, 222.

8. Little, W. O., Zerfas, L. G., and Trusler, H. M., *J.A.M.A.*, 1929, v93, 1290

12. Richardson, W., *N. Eng. J. Med.*, 1938, v218, 374.

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