MYENTERIC PLEXUS IN CONGENITAL MEGACOLON

Study of Eleven Cases

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SINCE 1886, when Hirschsprung[1] published a report entitled "Slug-g.shness of the Stool in the Newborn, Resulting from Dilatation and Hypertrophy of the Colon," there have been many reports in the medical literature describing various aspects of megacolon. Generally, the name "Hirschsprung's disease" has been applied to the cases of megacolon reported in the literature but, as Finney[2] has pointed out, there were many reports of cases of megacolon in the literature antedating those of Hirschsprung. For this reason, in our opinion the descriptive term "megacolon" rather than the less precise eponym should be applied to these cases.

Cases of megacolon are rarely encountered.[3] Perhaps as a result of the rarity of the condition, there have been few descriptions of the gross pathologic characteristics of megacolon. There have been a few reports[4] of single cases of megacolon in which the myenteric plexus was studied by microscopic pathologic methods. Except for the studies of Etzel[5] on megaesophagus and megacolon of the acquired type, there has been no series of cases reported in which the micropathologic characteristics of megacolon were studied.

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1. Hirschsprung: Stuhlträgheit Neugeborener in Folge von Dilatation und Hypertrophie des Colons, Jahrb. f. Kinderh. **27**:1-7, 1886.

2. Finney, J. M. T.: Congenital Idiopathic Dilatation of the Colon, Surg., Gynec. & Obst **6**:624-643 (June) 1908.

3. (*a*) Whitehouse, F.; Bargen, J. A., and Dixon, C. F.: Congenital Megacolon: Favorable End Results of Treatment by Resection, Gastroenterology **1**:922-937 (Oct.) 1943. (*b*) de Takáts, G., and Biggs, A. D.: Observations on Congenital Megacolon, J. Pediat. **13**:819-846 (Dec.) 1938. (*c*) Biggs, A D., and de Takáts, G.: Congenital Megacolon, Am. J. Dis. Child. **55**:1348-1351 (June) 1938.

(Footnotes continued on next page)

The facts known in the past concerning the etiologic factors and pathogenesis of congenital megacolon have not been based on studies of the micropathologic characteristics of the colon. In the past forty years there have been several hypotheses concerning the etiologic factors and the pathogenesis of congenital megacolon, all of which were similar in their basic principle. Hawkins[6] in 1907, in a discussion of megacolon, stated that "if by congenital inertness of the colon we mean a neuromuscular defect, through which a section of the colon, though it opposes no obstacle is yet (continuously or from time to time) incapable of forwarding its contents, I believe we have in this the basis of the disease." Alvarez[7] stated that the simplest explanation for the production of megacolon would be a loss of function in certain ganglion cells in the intestinal plexuses. Hurst[8] stated that he thought megacolon was due to a disturbed innervation of the colon which took the form of an underactivity of the parasympathetic autonomic fibers to the anal sphincter.

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4. (*a*) Tittel, K.: Ueber eine angeborene Missbildung des Dickdarmes, Wien. klin. Wchnschr. **14**:903-907, 1901. (*b*) Tiffin, M E.; Chandler, L. R., and Faber, H. K.: Localized Absence of the Ganglion Cells of the Myenteric Plexus in Congenital Megacolon, Am. J. Dis. Child. **59**:1071-1082 (May) 1940. (*c*) Brentano: Ueber einen Fall von Hirschsprung'scher Krankheit, Verhandl. d. deutsch. Gesellsch. f. Chir. **33**:265-268, 1904. (*d*) Dalla Valle, A.: Ricerche istologiche su di un caso di megacolon congenito, Pediatria **28**:740-752, 1920; (*e*) Familial Megacolon, ibid. **32**:569-599 (May 15) 1924. (*f*) Cameron, J. A. M.: On Aetiology of Hirschsprung's Disease, Arch. Dis. Childhood **3**:210-211 (Aug.) 1928. (*g*) Amorim, M., and Correa Netto, A.: Histopathologia e pathogenese do megaesophago e megarecto (Considerações em torno de um caso de "mal de engasgo"), Am. Fac. de med. de São Paulo **8**:101-127, 1932 (*h*) Perrot, A., and Danon, L.: Obstruction intestinale de cause rare, chez un nourrisson, Ann. d'anat. path. **12**:157-165 (Feb.) 1935. (*i*) Robertson, H. E., and Kernohan, J. W.: Myenteric Plexus in Congenital Megacolon, Proc. Staff Meet., Mayo Clin. **13**:123-125 (Feb. 23) 1938.

5. Etzel, E.: (*a*) Megaoesophagus and Its Neuropathology: Clinical and Anatomo-Pathological Research, Guy's Hosp. Rep. **87**:158-174 (April) 1937; (*b*) La dilatación del esófago frente a las lesiones del plexo de Auerbach en el megaesófago, Bol. y trab. de la Soc. de cir. de Buenos Aires **21**:131-148 (May 5) 1937; (*c*) O megacolon e seu conceito moderno, Arch. argent. de enferm. d. ap. digest. y de la nutrición **17**:123-184 (Dec.-Jan.) 1941-1942; (*d*) Distribuição geográfica á do megaesôfago-megacolon: estado atual da teoria etiologica da avitaminose B_1; estudo de 626 casos, Rev. Assoc. paulista de med. **15**:103-158 (Aug.) 1939; (*e*) Neuropatologia do megaesôfago e megacolo: estudo de 5 casos, Ann. Fac. de med. de São Paulo **10**:383-395, 1934; (*f*) O megacolon como symptoma de uma doença systematisada, Brasil-med. **53**:823-827 (Aug. 19) 1939.

6. Hawkins, H. P.: Remarks on Idiopathic Dilatation of the Colon, Brit. M. J. **1**:477-483 (March 2) 1907.

7. Alvarez, W. C.: An Introduction to Gastro-Enterology, ed. 3, New York, Paul B. Hoeber, Inc., 1940, pp. 218 and 283.

8. Hurst, A. F.: Anal Achalasia and Megacolon (Hirschsprung's Disease: Idiopathic Dilatation of the Colon), Guy's Hosp. Rep. **84**:317-350 (July) 1934.

Bockus[9] recently stated that "the literature on megacolon contains no records to support the *frequent* [our italics] occurrence of degenerative or inflammatory changes in the nerve cells of Auerbach's plexus around the anal sphincters. If such changes were found, strong evidence in favor of anal achalasia would be at hand."

Certain experimental observations on the production of megacolon in animals have seemed to support the foregoing hypotheses. Ishikawa[10] stated that in his opinion congenital megacolon is due to a congenital disturbance of the sacral autonomic nerves. He sectioned the sacral autonomic inflow (parasympathetic) to the colon in 12 dogs and found that in 9 constipation developed as the result of this procedure, in 8 dilatation of the colon developed, 7 had hypertrophy of the colon and 4 showed degeneration of the "intramural nerve fibers." He also reported 3 cases of acquired megacolon in which he demonstrated scars of the mesosigmoid involving the sacral autonomic nerves. He considered this to be the cause of the megacolon in the 3 cases. He also sectioned both parasympathetic and sympathetic nerves to the colon in 2 dogs and demonstrated the same results as those obtained by parasympathetic section alone. Adamson and Aird[11] produced megacolon in cats by the section of the sacral autonomic fibers. Kleinschmidt[12] obtained experimental results similar to those of Ishikawa and Adamson and Aird.

On the basis of the foregoing theoretic and experimental observations, it has been our feeling that one approach to the study of the origin and pathogenesis of congenital megacolon would be the study of the myenteric plexus (plexus of Auerbach) of the colon in cases of congenital megacolon in which postmortem examination had been performed. The myenteric plexus apparently has as its main function in the colon the conduction of stimuli and the coordination of movements[13] and, as a result of such function, would be of importance in any consideration of the pathogenesis of congenital megacolon.

PREVIOUS STUDIES OF THE MYENTERIC PLEXUS IN CASES OF MEGACOLON

In 1901 Tittel, [4a] in a report of 1 case, noted that the ganglion cells of the myenteric plexus at various levels of the large intestine were

9. Bockus, H. L.: Gastro-Enterology, Philadelphia, W. B. Saunders Company, 1943, vol. 2, p. 404.

10. Ishikawa, N..: Experimentelle Untersuchungen über die Dickdarminnervation, insbesondere des Colon descendens et sigmoideum, Mitt. a. d. med. Fak. d. k. Univ. Kyushu Fukuoka **7**:295-338, 1923; Experimentelle und klinische Untersuchungen über die Pathogenese und das Wesen des Megakolons, ibid. **7**:339-400, 1923.

11. Adamson, W. A. D., and Aird, I.: Megacolon: Evidence in Favour of a Neurogenic Origin, Brit. J. Surg. **20**:220-233 (Oct.) 1932.

12. Kleinschmidt, cited by Bockus.[9]

13. Alvarez,[7] p. 46.

scanty and showed degenerative changes. He concluded that the normal course of peristalsis might have been influenced unfavorably by the abnormal state of the myenteric plexus.

In 1904 Brentano,[4c] in a report of 1 case, stated that the nerve elements in the large intestine were weakly developed but failed to state from what part the sections were taken.

In 1920 Dalla Valle[4d] reported a case of congenital megacolon, with death of the patient at the age of 10½ months. In 1924 he[4e] reported the occurrence of megacolon in the child's brother. In both cases many sections of various portions of the large intestine were carefully examined, with special reference to the nerve cells of the myenteric plexus. This was the first time that a really comprehensive study of the myenteric plexus had been made. In the first case the ascending, transverse and descending portions of the colon were greatly enlarged but the sigmoid flexure was of normal caliber. In the ascending colon the cells of the myenteric plexus were few and small, in the transverse and descending colon they were normal in appearance while in the sigmoid colon they were absent. In the second case the extent of colonic enlargement was almost exactly the same; the transition from the descending colon to the sigmoid colon was sharply marked, and within a linear distance of 3 cm. the intestinal caliber returned to normal. The cells of the myenteric plexus were normal in number in the appendix, cecum and ascending, transverse and descending colon, but in more than 100 sections from the sigmoid colon no nerve cells could be found.

In 1927 and 1928 Cameron[14] reported studies on 2 cases of megacolon apparently congenital in type. He found no change in the myenteric plexus of the distended and hypertrophied colon except for some fibrous change. The colonic distention stopped at the pelvirectal sphincter, and sections taken in this region showed that "in the intermuscular plexus of nerve cells the changes are of striking character, the ganglia are replaced by inflammatory cells." Cameron felt that these changes were in the nature of a destructive lesion of the nerve ganglions at the pelvirectal sphincter.

In 1932 Amorim and Correa Netto[4g] reported a case of megaesophagus and megacolon (of the acquired type). In this case there were microscopic changes in the plexus of Auerbach of the colon and esophagus.

In 1934 Etzel[5b] reported briefly on studies of the myenteric plexus in 4 cases of megacolon which concomitantly was associated with megaesophagus. He stated that he considered these to be cases of acquired

14. Cameron, J. A. M.: Oesophagectasia in Child, Arch. Dis. Childhood **2**: 358-360 (Dec.) 1927; footnote 4 *f*.

megacolon and megaesophagus and not cases in which the dilatation was congenital in origin. He stated that the myenteric plexus in the lower part of the terminal intestine always presented lesions, which were described as a disappearance of the nerve cells, and cicatrices of the ganglions of the myenteric plexus of the colon.

In 1935 Perrot and Danon[4h] reported a case in which an infant died at the age of 15 days as a result of intestinal obstruction. The small intestine was dilated and thickened above a constriction in the lower part of the ileum. The myenteric plexus became abnormal at the point of the constriction, with nerve cells becoming rare from there to the splenic flexure. The authors felt that the hypoplasia of the plexus had caused a functional obstruction.

In 1938 Robertson and Kernohan[4i] were the first in North America to describe changes in the myenteric plexus in a case of congenital megacolon. They stated that the ganglion cells and fibers of the myenteric plexus were definitely smaller than normal and were vacuolated and that the ganglion cells were either absent or imperfectly formed. They also mentioned that the same appearance was noted in several other cases of megacolon.

In 1937 Etzel[5a] reported further studies on the myenteric plexus in 8 cases of acquired megacolon. The changes noted were similar to those described in the plexus of the esophagus, which were dislocation of the nucleus to the periphery, central chromatolysis, microvacuolation, macrovacuolation and degeneration of the protoplasm. Pyknosis of the nucleus, expulsion of the nucleus, destruction of the neurofibrillar system and neuronophagia were also described. The dendrites were observed to swell, and their extremities became globular. The alterations of the axis-cylinder were classified as cleavage, retraction balls of Cajal, "effilochement" of Cajal, argentophilia and thickening and fragmentation.

In 1940 Tiffin, Chandler and Faber[4b] reported a careful study of a case of congenital megacolon in which the patient was a child 20 months of age. There were roentgenographic evidence of progressive dilatation of the entire large intestine above the sigmoid flexure without obstructive stenosis, absence of effect from a parasympathetic depressant (syntropan), production of powerful intestinal contractions without propulsion of contents by parasympathetic augmenter drugs (neostigmine and acetyl-β-methylcholine chloride) and by sympathetic depression (spinal anesthesia) and failure of sympathectomy on the left and right lumbar regions to relieve the condition. Tiffin and his associates stated that "sections, along a taenia coli, of the terminal portion of the dilated colon and the grossly normal portion of the sigmoid colon showed a few scattered ganglion cells of Auerbach's myenteric plexus lying between the circular and the longitudinal muscle only in the undilated sigmoid

colon but none in the 7 cm. above this region." Unusually abundant nerve fibrils were noted in this region. A section taken from the dilated transverse colon showed many ganglion cells. Tiffin and his associates felt that the evidence strongly suggested that at least in some cases of megacolon the primary disturbance is a localized interference with the passage of normal peristaltic waves across a given segment of the alimentary tract due to defective innervation. This interference, they stated, might consist of an inability of the musculature either to relax (achalasia) or to contract, either of which disturbances would prevent the sequence of alternate relaxation and contraction composing the peristaltic wave and thus would render propulsion of intestinal contents across the involved segment noneffective.

TABLE 1.—*Collected Series, Reporting Study of Plexus of Auerbach in Cases of Megacolon*

Author and Date	Cases	Changes Reported
Tittel (1901) [4a]	1	Scanty ganglion cells in whole colon
Brentano (1904) [4c]	1	Nerve elements of the colon weakly developed
Dalla Valle (1920 and 1924) [4d, e]	2	No nerve cells in sigmoid Normal nerve cells in rest of colon
Cameron (1927 and 1928) [4f]	2	Ganglions near pelvirectal sphincter replaced by inflammatory cells
Amorim and Correa Netto (1932) [4g]	1	Degenerative changes in plexus
Etzel (1937) [5b]	8	Absence of plexus in distal end of colon
Perrot and Danon (1935) [4h]	1	Hypoplasia of plexus
Robertson and Kernohan (1938) [4i]	1	Absence of ganglion cells and other changes in nerve cells
Tiffin and associates (1940) [4b]	1	Absence of ganglion cells in sigmoid
Total	18	

Table 1 contains a summary of these studies of megacolon by other authors, including a summarization of the changes noted in the myenteric plexus. It shows that in 14 of the total of 18 cases for which data were collected from the literature there was absence of the ganglions of the myenteric plexus in the distal part of the colon or in a part of the colon not specified. Six of the 18 were apparently definite cases of congenital megacolon, and in these there was absence of the myenteric plexus in the distal part of the bowel. Evidence from the cases reviewed thus supports the previous hypotheses and experimental findings and shows that there is a disturbance of the normal autonomic innervation of the terminal segment of the colon in cases of megacolon and in particular in cases of congenital megacolon. It has been our purpose to carry out a careful study of the myenteric plexus in a series of cases of congenital megacolon observed in one institution.

SELECTION OF CASES

This report has been based on a study of 11 cases of congenital megacolon in the Section on Pathologic Anatomy of the Mayo Clinic. We were able to find 13 cases classified as cases of congenital megacolon. We were unable to study 2 of these accurately because of the fact that surgical removal of part of the colon had been performed and the portion of the colon available for our study was in several pieces, a circumstance which made identification from the anatomic standpoint impossible. These cases were eliminated from the study. All the cases fulfilled the criteria for congenital megacolon which we established for this study. Accurate definition of the type of case which was studied was felt to be essential. The criteria which we established for the diagnosis of congenital megacolon were: (1) symptoms preferably present since birth, though cases were accepted in which the onset of symptoms was in early youth; (2) colonic dilatation and hypertrophy of a high grade; (3) maximal involvement present in the sigmoid colon, and (4) a typical clinical picture, which in essence was that bowel movements almost never occurred normally and the abdomen was huge, with palpable fecal masses, flaring costal margins, roentgenographic evidence of colonic dilatation and redundancy and the absence of a lesion, on rectal, proctoscopic or general examination, that could cause obstruction.

TABLE 2.—*Causes of Death in 10 Cases of Congenital Megacolon*

Cause	Cases
Malnutrition, toxemia, general debility	3
Spontaneous perforation of colonic ulcers	3
Postoperative peritonitis	2
Postoperative shock	1
Intestinal obstruction by huge fecalith	1
Total	10

TABLE 3.—*Age Range of Patients Who Had Congenital Megacolon*

Age, Yr.	No.	%
Less than 5	5	46
5 to 9	2	18
10 to 19	1	9
20 to 29	3	27
Total	11	100

CAUSE OF DEATH

The cause of death was established at the time of postmortem examination in 10 of the 11 cases. In the eleventh case the specimen was obtained after subtotal colectomy, and the patient made an uneventful postoperative recovery.

Table 2 shows the causes of death in the 10 cases in which postmortem examination was performed. It is of importance to note that in 7 of these (70 per cent) the patient died from complications that occurred as a natural result of the disease and not as a result of surgical intervention. Volvulus, which is fairly frequent in cases of megacolon, was not observed in our series.

The age range of the patients who had congenital megacolon is shown in table 3. It can be seen that 64 per cent of the 11 patients were 9 years of age or younger. This is a general characteristic of any series of cases of true congenital megacolon. There were 10 males and 1 female, which is a greater proportion of males than usual. This fact is accounted for by the size of the series.

METHOD OF STUDY

The histologic study of the myenteric plexus in cases in which postmortem examination had been made presented certain problems which were not present in the subject have been performed.[15] This allowed the use of spuravital staining technics and other methods which were not applicable in the study of tissues secured at necropsy and preserved in formaldehyde for periods varying from one to thirty years.

We have been unable to find a study of the myenteric plexus under comparable conditions which could be used to determine the normal findings in a routine necropsy series. As a corollary of the reported study, we have examined material in a series of 78 cases to determine the characteristics of the myenteric plexus of the colon and the normal variations in its distribution and staining. At the same time, we also decided on the staining methods to be used in the main study.

In our study of the series of cases used as controls, we utilized cases of peritonitis, intestinal obstruction and a wide variety of other conditions. To rule out the factor of selection, we incorporated in the control study a series of consecutive cases in which postmortem examination was performed. We have likewise studied for the sake of comparison a group of cases in which megacolon was secondary to obstructing lesions or considered to be acquired rather than congenital. The following are conclusions from the study of our series of control cases which are pertinent in the study of the myenteric plexus of the colon in cases of congenital megacolon:

1. Ganglions are present in practically every section taken from the colon.

2. So-called degenerative changes in the ganglion cells are commonly encountered in sections taken under the conditions of the study of the control cases and the cases of megacolon.

3. Nerve trunks (nonmyelinated) in the location of the myenteric plexus are extremely rare in the rectum and in other parts of the colon.

4. Extreme dilatation of the colon has relatively little effect on the myenteric plexus apart from the fact that the ganglions seem to be somewhat more widely spaced than normal.

5. Inflammatory changes in the colon have little effect on the myenteric plexus in the majority of instances.

6. The rectum contained as many ganglions per unit of area as other parts of the colon or more.

7. No separation of ganglion cells into Dogiel type I and type II could be made (a finding which has been described by Johnson[15e]). This, however, may be due to the method of study that we used.

8. The small cells in relation to nerve fibers and nerve cells we have called "supporting cells." Their exact nature has not been determined by us or others.

The control study aided us in determining the staining methods which we would use in the study of the myenteric plexus of the colon under the conditions of the study as mentioned previously. We found that the Bodian[16] method of silver impregnation showed the nonmyelinated nerve fibers better than any other method and also showed the nerve cells of the ganglions well. The Gros-Bielschowsky method[17] of silver impregnation was used but was found to be satisfactory in a minority of the sections treated by this method. The cresyl violet stain was found to be excellent for the study of the nerve cells. The hematoxylin and eosin staining method was found to be of great general value, but the stains which were more specific in their action were frequently found to be necessary in our study. We have also used connective tissue stains for certain sections, such as the Mallory-Heidenhain, Mallory phosphotungstic acid and Van Gieson stains. These were found to be of limited value.

We took tissue blocks at frequent intervals in the parts of the colon that showed the greatest change in the myenteric plexus. When these original sections were not adequate for a complete study we recut more blocks so that in each case there would be blocks cut from all the necessary locations to prove or disprove that the changes were as stated. Each block was cut into four or more sections, and the silver impregnation methods of Gros-Bielschowsky and Bodian and the cresyl violet and hematoxylin and eosin stains were used on each. The sections were cut

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15. (*a*) Hill, C. J.: VIII. A Contribution to Our Knowledge of the Enteric Plexuses, Phil. Tr. Roy. Soc., London, s.B **215**:355-387 (June 15) 1927. (*b*) Dogiel, A. S.: Zwei Arten sympathischer Nervenzellen, Anat. Anz. **11**:679-687, 1895-1896. (*c*) Lawrentjew, B. I., and Sokolowa, M. L.: Zur Lehre von der Cytoarchitektonik des peripherischen autonomen Nervensystems, Ztschr. f. mikr.-anat. Forsch. **23**:527 (March) 1931. (*d*) Modern, F. S., and Thienes, C. H.: Vagal and Sympathetic Endings in the Rabbit Intestines, Science **83**:522 (May 29) 1936. (*e*) Johnson, S. E.: Experimental Degeneration of the Extrinsic Nerves of the Small Intestine in Relation to the Structure of the Myenteric Plexus, J. Comp. Neurol. **38**:299-314 (April) 1925. (*f*) Irwin, D. A.: The Anatomy of Auerbach's Plexus, Am. J. Anat. **49**:141-166 (Sept.) 1931.

16. Mallory, F. B.: Pathological Technique: A Practical Manual for Workers in Pathological Histology Including Directions for the Performance of Autopsies and for Microphotography, Philadelphia, W. B. Saunders Company, 1938, pp. 228-229.

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1 mm. or more apart, giving a serial section effect. In several of the cases we had a serial section of the entire part of the colon that would show any change in the myenteric plexus. The study of Irwin[15f] showed how unlikely it would be to miss the ganglions of the plexus completely in a section 2 cm. long if the amount of plexus noted in his studies was present in 4 sq. mm. Our series used in the control study adequately confirmed this, as we found no section in the hundreds that we studied in which we could not find nerve cells of the myenteric plexus.

We have not studied in detail the plexus of Meissner (submucous plexus) of the colon because the consensus[18] is that its function depends on that of the myenteric plexus and also because its function is too poorly understood for a study to be of value. The subserous plexus, the deep muscular plexus of Drasch and Cajal and the internal plexus of Henle mentioned by some writers have not been studied for reasons similiar to those stated for the exclusion of the submucous plexus. Also, owing to the location of the submucous plexus in the loose connective tissue of the submucosa, it would be difficult to be sure whether it was present or absent. The myenteric plexus was so confined in its usual location that there was no difficulty in determining accurately when it was present and when it was totally absent in any given section. In general, we can tentatively state that the plexus of Meissner (submucous plexus) seemed to parallel the myenteric plexus in its presence or absence.

Figures 1, 2, 3 and 4 show the gross appearance typical of all the colons used in our study. We have primarily used the various anatomic sections of the colon to delineate the region from which the sections were taken. In 6 cases (54.5 per cent) there was a "normal" terminal segment of bowel, as compared with 57.7 per cent of a series of clinical cases reported by Whitehouse and others.[3a] In some cases this terminal segment which was normal or near normal in diameter was the rectum; in others the terminal segment was as high as the midsigmoid. We have not attempted to delineate accurately the anatomic bounds of this normal terminal segment in our cases. We have coined the term "transitional region" to apply to the part of the colon in which the maximally dilated bowel suddenly narrowed down to a terminal segment of normal size. The photographs of the gross specimens show this region clearly. We feel that the use of the term "transitional region" is worth while in the delineation of a particular part of the colon in which the myenteric plexus demonstrated a change in a good proportion of the cases studied.

In figures 1, 2 and 3 arrows point to the parts of the colon from which tissue blocks were removed for study. Some of the photomicrographs have the arrow number included in the legends so that reference can be made to the picture of the colon in the case referred to. We have included a few photomicrographs from control cases to demonstrate the usual appearance of the myenteric plexus to be contrasted with the photomicrographs of the sections in which no myenteric plexus is present.

We have reported 5 of the 11 cases in relatively complete fashion and the other 6 briefly. The similarity of the cases was so marked that an accurate description of the customary clinical and pathologic findings seemed to be given adequately in the 5 cases selected for detailed presentation.

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17. (*a*) Mallory,[16] pp. 227-228. (*b*) Kernohan, J. W.: Preparation of Neurological Material for Histologic Study, Am. J. Clin. Path. **4**:410-425 (Sept.) 1934.

18. Babkin, B. P.: Secretory Mechanism of the Digestive Glands, New York, Paul B. Hoeber, Inc., 1944, p. 125. Etzel.[5c]

RESULTS OF STUDY OF THE MYENTERIC PLEXUS IN CASES OF CONGENITAL MEGACOLON

Table 4 demonstrates the most important finding made in the study of the myenteric plexus in 11 cases of congenital megacolon. In 100 per cent of the cases studied there was an absence of the ganglions of the myenteric plexus (fig. 5) in the terminal portion of the colon. In all cases there were ganglions of the myenteric plexus present in the descending colon, transverse colon, ascending colon and cecum. There

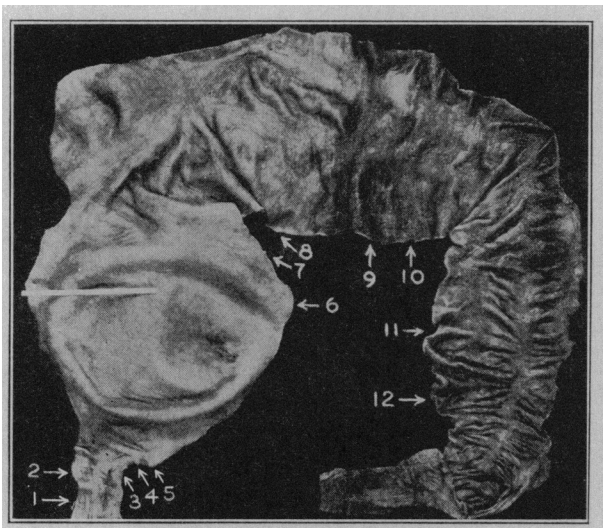

Fig. 1.—Typical maximal involvement of sigmoid, rapid change to normal rectum and gradual diminution of size toward cecum. Locations from which blocks of tissue were taken for histologic examination are marked by arrows. Areas 1 through 6 contained no ganglions, 7 and 8 contained a few and 9 through 12 contained a moderately diminished number as compared with the normal.

was thus a change in the myenteric plexus that occurred distal (toward the cecum being proximal and toward the rectum distal) to the descending colon in every case. In 80 per cent of the cases in which there was a definite transitional region (defined in the section "Method of Study") there was absence of the ganglions of the myenteric plexus from the rectum into the transitional region. In 60 per cent of the cases there was absence of the ganglions of the myenteric plexus down to and including the rectum in the distal segment of the sigmoid, which we considered to begin just proximal to the transitional region. In 20 per cent of the cases studied there was absence of the ganglions of the myenteric plexus in the proximal segment of the sigmoid, in the lower part of the descending colon and in all parts distal to them. By absence of the

ganglions of the myenteric plexus we mean that we were unable to find a single identifiable ganglion cell in any part of any section from the region mentioned.

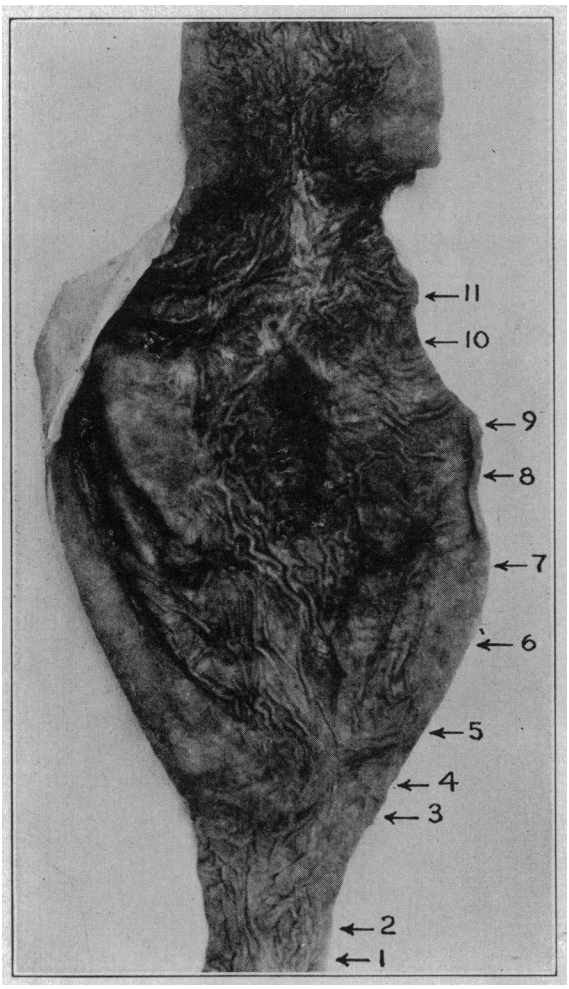

Fig. 2.—Dilated sigmoid and normal rectum. Locations from which blocks of tissue were taken for histologic examination are marked by arrows. Areas 1 through 7 contained no ganglions, 8 contained a few nerve cells and 9 through 11 contained a normal number of ganglions.

Figures 6 and 7 demonstrate graphically the absence of the myenteric plexus and should be contrasted with figure 8, which demonstrates the normal myenteric plexus. Figures 6*a* and 8 *a* should be compared with each other. They are of approximately the same magnification, and the stain in both instances is by the Bodian method. The areas shown are

comparable. The absence of the myenteric plexus is thus seen to be striking. The different thickness of muscle walls can also be seen. One important question cannot be entirely answered, which is, how close to the anal sphincter does the absence of the myenteric plexus extend? In several cases the specimen included perianal skin, and in these cases there was no myenteric plexus in the terminal portion of the rectum. We feel that, with the necropsy technic used, we were able to study all but the terminal few centimeters of the rectum in all our cases, and since there was no evidence of the myenteric plexus being present in

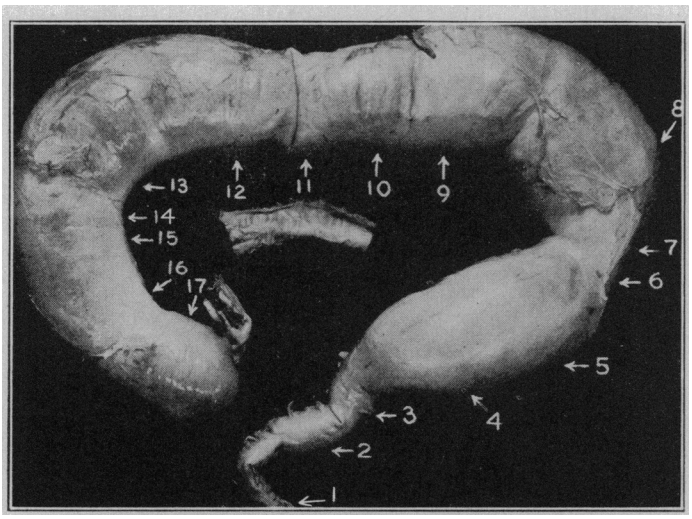

Fig. 3.—Segment of bowel in center is normal colon for comparison. Locations from which blocks of tissue were taken for histologic examination are marked by arrows. Areas 1 through 4 contained no ganglions, 5 through 7 contained a few and 8 through 17 contained a normal number. Note the normal size of the rectum.

the terminal portion of the rectum in the several cases in which we had complete specimens, it is likely that the changes which we have described are present over the entire terminal segment down to the anal sphincter.

A second observation was made in the study of the 11 cases of congenital megacolon, which we can find described only once previously.[4b] In every case studied there was the presence of nonmyelinated nerve trunks between the longitudinal and circular muscle layers in the distal part of the colon. These were not present in the series of cases used as controls, and hence we considered these nerves to be a definite part of the pathologic changes of congenital megacolon. The nonmyelinated nerves were not present to any pronounced degree in the part of the colon which contained ganglions of the myenteric plexus but

were always in the part of the colon in which no ganglions of the myenteric plexus could be demonstrated. These nerves are not to be confused with nerve fibers which are seen in relation to the ganglions in the normal plexus. The nerves which we have described are closely

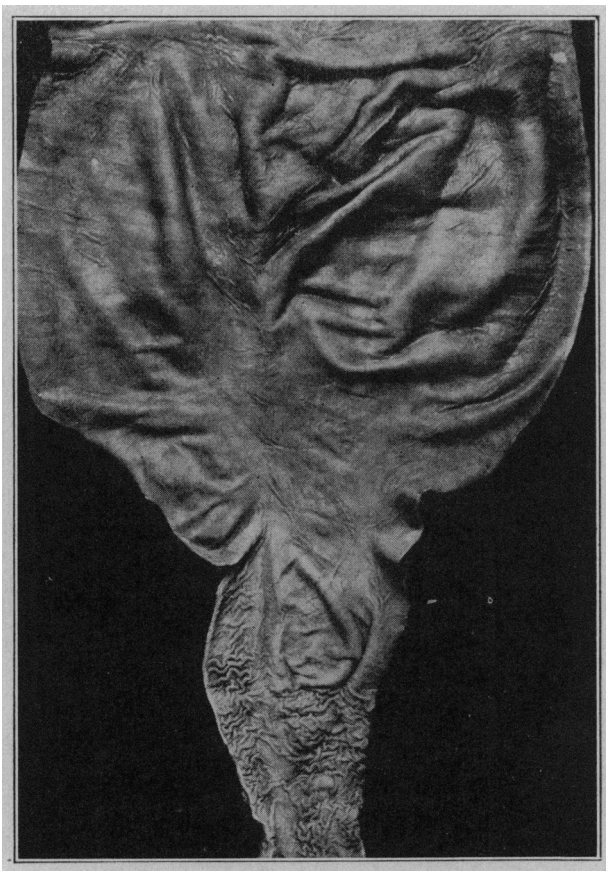

Fig. 4.—Specimen of colon in figure 3 opened in rectosigmoid region. The abrupt transition from the sigmoid to the normal rectum is characteristic. The portion of the colon between the two extremes in size we have called the "transitional region."

packed bundles of nonmyelinated nerve fibers with a definite connective tissue sheath. The size of the nerves varied considerably in individual cases and particularly from case to case. Figures 9 and 10 *a* show the nerves seen in 3 of the cases of megacolon. The variation in size, the connective tissue sheath, the location in the usual site of the myenteric plexus and the entrance into the colon, as noted in figure 10 *a*, in company with the blood vessels can be well observed. Some of the nerves

were smaller and some were larger than the ones demonstrated in the figures. We are unable to state the part (sympathetic or parasympathetic) of the autonomic nervous system represented by these nerves; hence their significance is unknown to us.

Early in our study we were confronted with the question of degenerative changes in the nerve cells. This question can be answered,

TABLE 4.—*Sites in Which Ganglions of Myenteric Plexus Are Absent**

Case	Rectum	Transitional Region	Sigmoid		Descending Colon	Transverse Colon	Ascending Colon	Cecum
			Distal	Proximal				
1	0	0	0	0	+	+	+	+
2	0	0	0	+	+	+	+	+
3	0	x	0	+	+	+	+	+
4	0	x	+	+	+	+	+	+
5	0	0	+	+	+	+	+	+
6	0	x	0	+	+	+	+	+
7	0	+	+	+	+	+	+	+
8	0	x	x	x	+	+	+	+
9	0	x	+	+	+	+	+	+
10	0	x	0	0	+	+	+	+
11	x	0	0	+	+	+	+	+
% with absence	100	80	60	20	0	0	0	0

*0 Signifies absent, + present, and x section not available.

TABLE 5.—*Plexus of Auerbach in Cases of Secondary Megacolon**

Case	Cause	Rectum	Sigmoid	Descending Colon	Transverse Colon	Ascending Colon and Cecum
12	Carcinoma of rectum	+	+	+	+	+
13	Carcinoma of sigmoid	+	+	+	+	+
14	Carcinoma of rectum	+	+	+	+	+
15	Volvulus	+	+	+	+	+
16	Enterocolitis	+	+	+	+	0

*0 Signifies absent and + present.

as noted previously, from the study made on the cases used as controls. The series of cases used as controls and the series of cases of congenital megacolon demonstrated the same "degenerative" changes to such a degree that we have concluded that none of these should be reported as part of the pathologic changes which occurred in congenital megacolon. Even under the best of conditions it would be difficult to be sure that changes present in the myenteric plexus were not due to age of the specimen, fixation, sectioning or staining.

Cameron[4f] expressed the opinion that inflammatory changes in the myenteric plexus are important in the causation of megacolon. In our study we looked carefully for such changes, but in our cases there was no evidence of recent or old inflammatory change in the myenteric plexus. In fact, we noted that even in the presence of active suppurative colitis, chronic ulcerative colitis and similar conditions there was an "immunity"

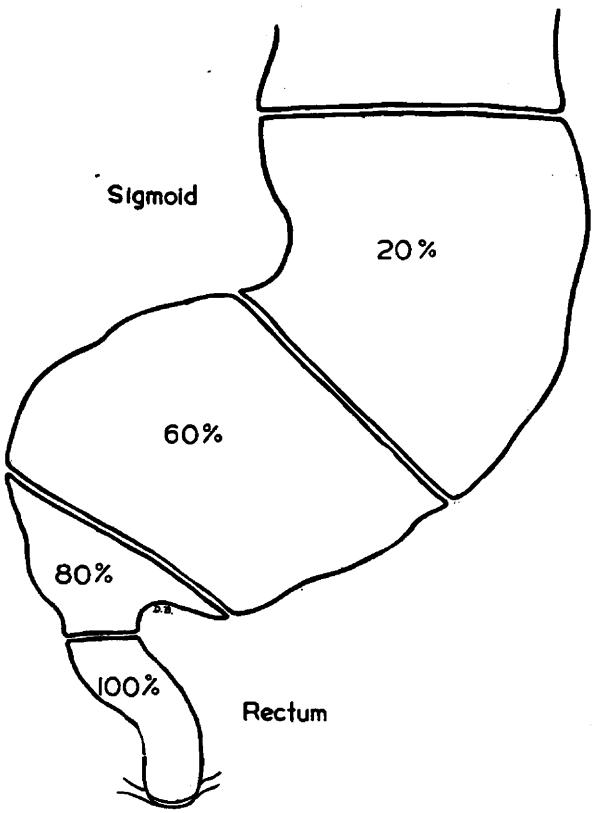

Fig. 5.—Percentage of cases in which the myenteric plexus was absent from the terminal part of the rectum to the indicated level. A rectum of normal size as seen in the majority of cases is shown.

from such involvement of the myenteric plexus. It is our opinion, in view of the study, that we have no evidence which would suggest or support the hypothesis of inflammatory damage to the myenteric plexus.

In view of the fact that we have described a part of the colon in which the ganglions of the myenteric plexus were absent and another part of the colon in which the ganglions were present in more or less

normal numbers, the microscopic changes in the "no man's land" between the regions mentioned would be of interest. The accuracy of any statements made without serial sections would be exposed to criticism, but we felt that our study justified the statement of certain generalities in this regard.

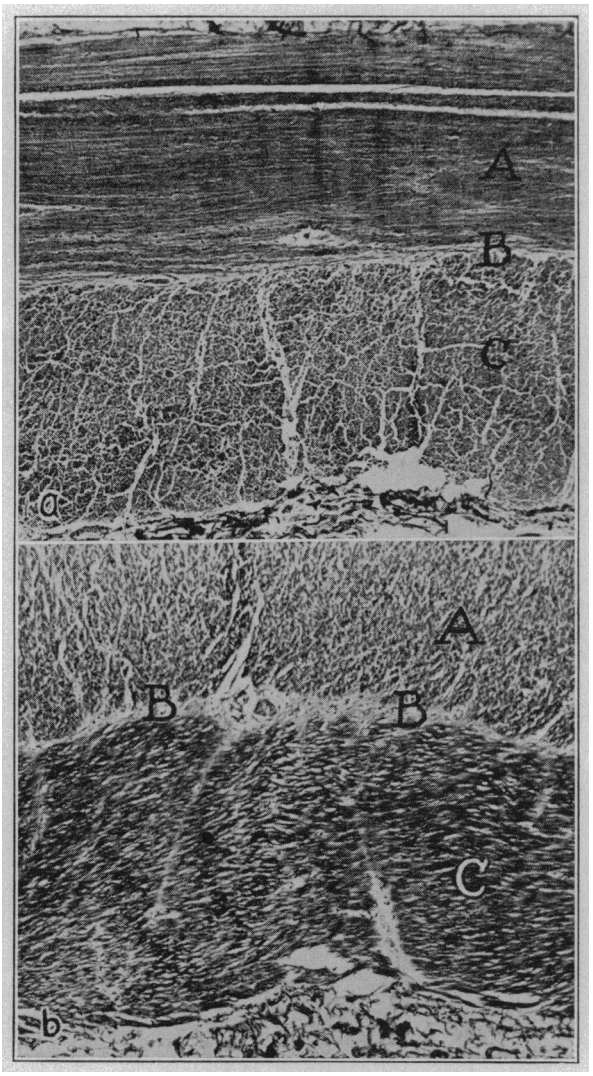

Fig. 6.—*a*, absence of myenteric plexus in transitional region (from areas *3*, *4* and *5* in figure 1). *A*, longitudinal muscle; *B*, usual site of myenteric plexus; C, circular muscle (Bodian stain; ×55); *b*, absence of myenteric plexus in rectum (from areas *1* and *2* in figure 2). *A*, longitudinal muscle; *B*, usual site of myenteric plexus; *C*, circular muscle (Bodian stain; × 60).

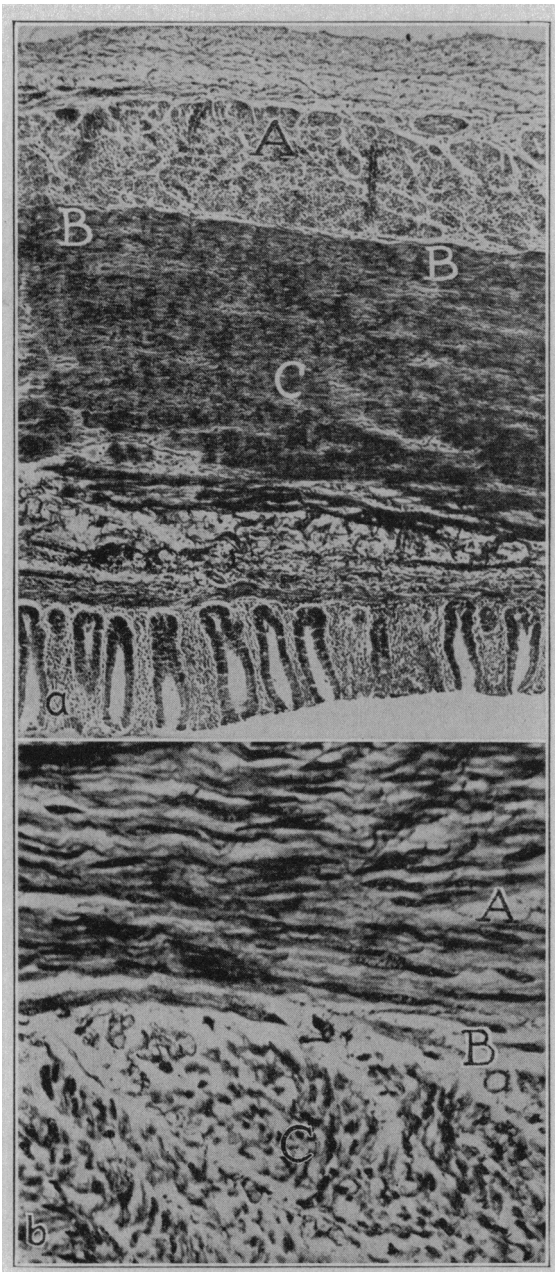

Fig. 7.—*a*, absence of myenteric plexus of sigmoid colon. *A*, longitudinal muscle; *B*, usual site of myenteric plexus; *C*, circular muscle (Bodian stain; × 50); *b*, absence of myenteric plexus of rectum. *A*, longitudinal muscle; *B*, usual site of plexus; *C*, circular muscle (Bodian stain; × 275).

For the sake of simplicity, we have separated the 11 cases of congenital megacolon under three rough categories. The most common finding was a quick change to a relatively normal myenteric plexus in the colon proximal to the region in which the ganglions of the myenteric plexus were absent. It was our impression that in several cases of this

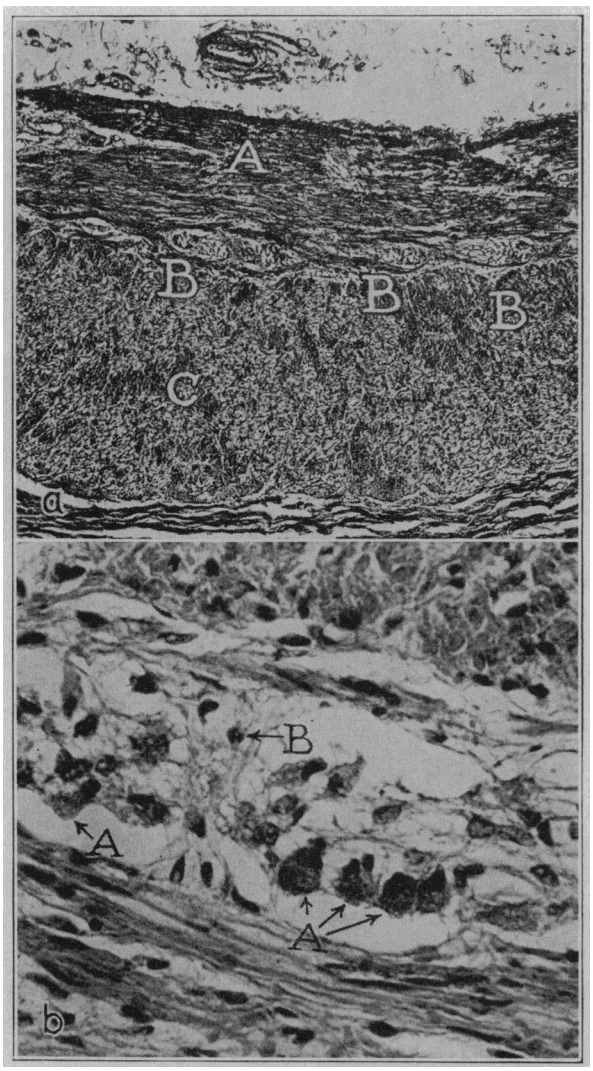

Fig. 8.—*a*, customary distribution of myenteric plexus in rectum from control series. Plexus is well demarcated in zone between longitudinal and circular muscle layers. *A*, longitudinal muscle; *B*, ganglions; *C*, circular muscle (Bodian stain; × 50). *b*, normal ganglion from case in control series. Compare with figure 11*b*. *A*, nerve cell; *B*, supporting cell (hematoxylin and eosin; × 425).

group the change to a relatively normal plexus occurred in the space of a few centimeters. This was considered to be true in 5 of the 11 cases studied. The next most common finding was the presence of a few scattered ganglions in the segment of colon proximal to the part that showed no ganglions of the myenteric plexus. Next to this segment there

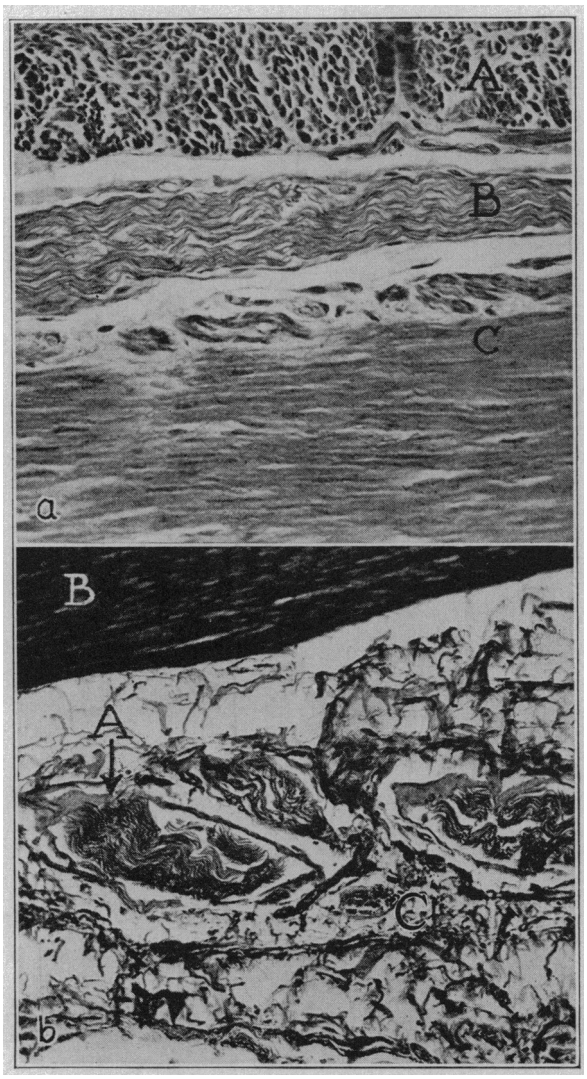

Fig. 9.—*a*, nerve trunk in rectum (nonmyelinated). *A*, circular muscle; *B*, nerve trunk; *C*, longitudinal muscle (Bodian stain; × 200); *b*, nonmyelinated nerve trunk in rectum between longitudinal and circular muscle layers. *A*, nerve trunk; *B*, longitudinal muscle; *C*, circular muscle (Bodian stain; × 120).

was a gradual increase in the number of ganglions and an improvement in their general appearance until a relatively normal myenteric plexus was seen in 4 of the 11 cases studied. The least common finding, noted in 2 of the 11 cases, was the presence of a few ganglions and then a gradual increase in the number in a spotty fashion, with some areas that contained few ganglions. No areas of the colon in these cases were

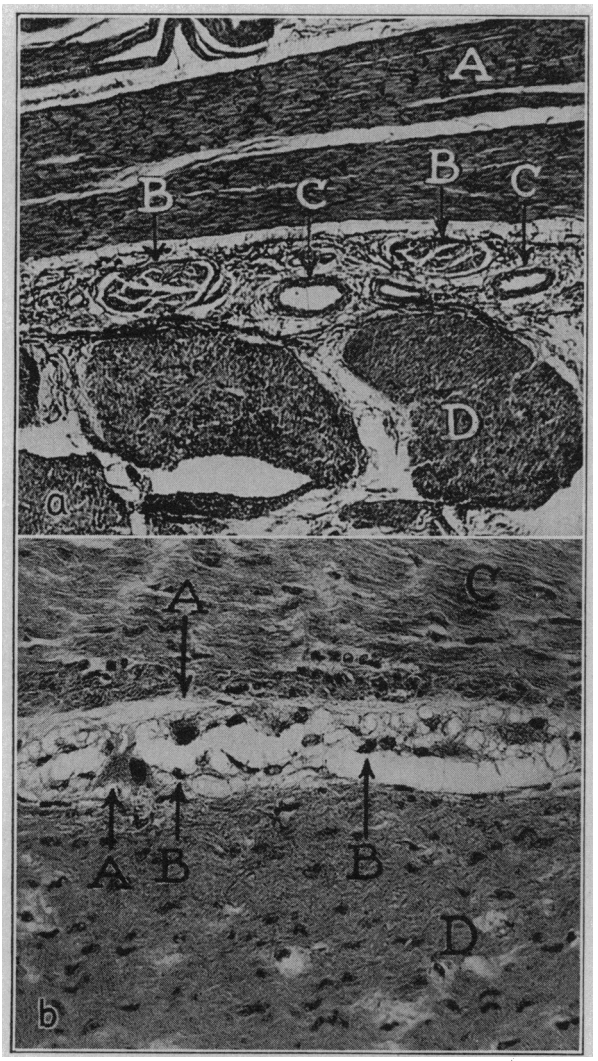

Fig. 10.—*a*, ganglions absent. Nerve trunks in relation to small blood vessels in rectum. *A*, longitudinal muscle; *B*, nerve trunks; *C*, blood vessels; *D*, circular muscle (hematoxylin and eosin; × 90); *b*, ganglion in ascending colon (from area *11* in figure 1). *A*, nerve cell; *B*, supporting cell; *C*, longitudinal muscle; *D*, circular muscle (hematoxylin and eosin; × 200).

seen to contain a normal plexus. Figures 10 *b* and 11 *a* demonstrate normal ganglions (not from the terminal segment of the colon) which are similar to those seen in the series of cases used as controls. Figure 11*b* demonstrates a ganglion, similar to many other ganglions thus

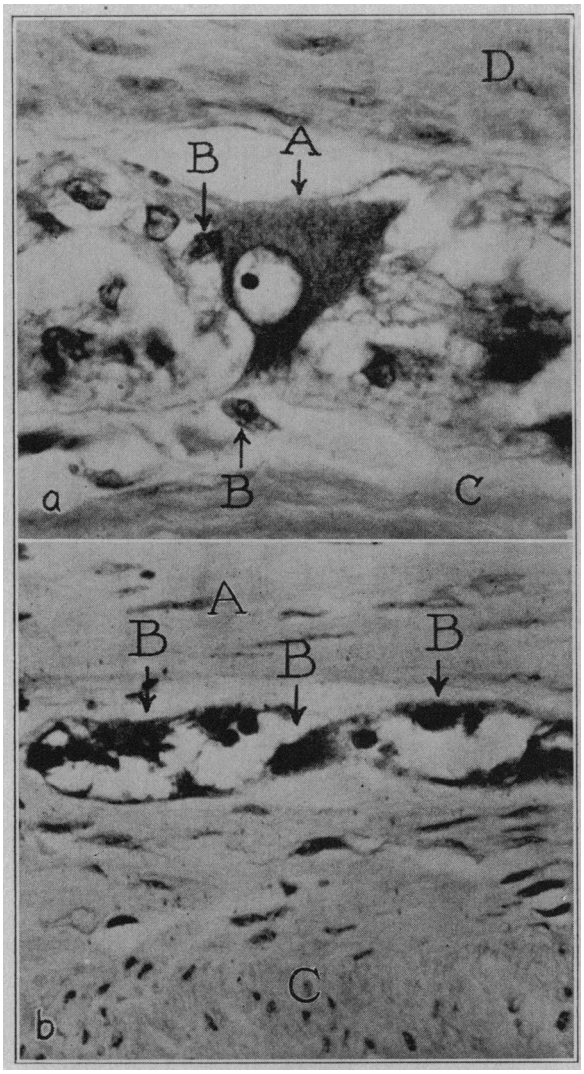

Fig. 11.—*a*, ganglion of transverse colon. Normal nerve cell and a number of supporting cells. Four blurred nerve cells are also present. *A*, nerve cell; *B*, supporting cell; *C*, circular muscle; *D*, longitudinal muscle (cresyl violet; × 880). *b*, ganglion of descending colon. Normal number of nerve cells, few supporting cells and nerve fibers. Compare with figure 8 *b*. *A*, longitudinal muscle; *B*, nerve cells; *C*, circular muscle (Gros-Bielschowsky stain; × 415).

located, from the "no man's land" of change in the myenteric plexus. In comparison with figure 11 from the control series, with which it is comparable in magnification, it can be seen that there are few supporting cells or nerve fibers, definite "atrophy" and a general failure to reach the standard of architecture set by the normal ganglion shown in figure 8 *b*. This is considered to be a characteristic ganglion of the region in which the change from no ganglions to a normal or a diminished number occurred. Many such ganglions showed only one to three nerve cells and hence were much smaller than the average seen in the series of cases used as controls.

REPORT OF CASES

CASE 1.—A 15 year old boy was seen on Oct. 27, 1941, because of constipation and general debility. Since birth there had been considerable difficulty in getting his bowels to move. He had been treated with anal dilation and enemas, with some improvement. Abdominal distention and constipation continued at intervals, and daily enemas were required during certain periods. During the six months prior to his admission to the clinic, increasing difficulty in passing gas, constipation and pronounced abdominal distention had been noted. The patient had also noted fatigability, anorexia, loss of weight and pallor.

Physical examination showed a thin, pale, white boy with an enlarged and tightly distended abdomen. The costal margins showed a pronounced flaring. The height of the patient was 62 inches (157 cm.) and his weight was 99 pounds (44.9 Kg.). The blood pressure was 140 mm. of mercury systolic and 90 diastolic, the pulse rate was 88 beats per minute and the oral temperature was 98.9 F. The abdomen was tense and was doughy to palpation. An easily discernible outline of the bowel was seen under the thin abdominal wall. Rectal examination revealed an empty rectum which was markedly encroached on by an extrarectal mass (feces). Sigmoidoscopic examination revealed a normal mucosa, with the caliber of the bowel seemingly larger than normal. Roentgenographic and roentgenoscopic examination of the colon confirmed the diagnosis of megacolon.

The condition of the patient became worse after his admission. Progressive abdominal distention ensued, and this did not respond to medical treatment. A huge fecalith was present in the sigmoid colon, and it was the clinician's opinion that this was the cause of the partial obstruction of the colon. Emergency colostomy was performed, but this was without beneficial effect. Death occurred on Nov. 2, 1941.

Postmortem examination revealed an emaciated boy with a greatly distended abdomen, the circumference of which was 97 cm. at a level just above the umbilicus. The circumference of the chest was 80 cm. at the level of the nipple line. The apexes of the diaphragm were at the third rib on the right and the fourth rib on the left. The peritoneal cavity revealed no peritonitis and was entirely filled by the tremendously distended and hypertrophied colon, which had pushed the urinary bladder anterior to the symphysis pubis. There was atelectasis of grade 3 (on the basis of 1 to 4, 1 being the least) of the lower lobes of the lungs. The esophagus, stomach, duodenum and jejunum were grossly normal. The ileum revealed a grade 1 (basis of 1 to 4) dilatation of the last 30 cm. of its length. The dilatation of the colon (fig. 1) was maximal in the sigmoid region, with a circumference of 42 cm. in this location. Proximal to the sigmoid there was a gradual diminution of the size of the bowel to the cecum, and then there was slight dilatation of the

terminal 30 cm. of the ileum. The wall of the descending colon and sigmoid was 0.3 cm. thick. The wall of the ascending colon and cecum was thin. The bowel distal to the rectosigmoid junction was normal in diameter and thickness. There was no point of obstruction noted. The mucosa throughout the colon was markedly congested, particularly in the sigmoid. The kidneys revealed a grade 1 (basis of 1 to 4) dilatation of the pelvis, calices and ureter on the left and a dilated pelvis and calices of grade 2 and urethral dilatation of grade 1 on the right.

Microscopic Study.[19]—Tissue blocks were taken from two levels of the nondilated rectum (arrows *1* and *2,* fig. 1). Examination of sections from these blocks showed no nerve cells, supporting cells or architectural remains of the plexus. There were small nerve bundles at intervals, composed of nonmyelinated nerve fibers.

Blocks taken from three levels of the region of transition (arrows *3, 4* and *5,* fig. 1) showed no nerve cells (fig. 6 *a*). In the usual location of the plexus of Auerbach there was a narrow region of collagen interrupted at intervals by nerve trunks. Sections taken from the level of greatest colonic dilatation (arrow *6,* fig. 1) showed no definite nerve cells although there were small, thin groups of supporting cells and nerve fibers at intervals in the usual location of the ganglions. These cells were rather argentophilic. Blocks taken from two levels of the descending colon (arrows *7* and *8,* fig. 1) showed scattered ganglions which contained one to five nerve cells each. There was a normal arrangement of these ganglions, and the nerve pathways between them were present. There were few supporting cells noted in the distal section of the descending colon. The proximal section of the descending colon showed the same diminution of nerve cells, but a normal number of supporting cells was seen. Variation in staining with cresyl violet was observed, with some cells appearing dark and others with apparent lack of Nissl substance. Blocks taken from two levels of the transverse colon (arrows *9* and *10,* fig. 1) showed ganglions and fibers to be moderately diminished quantitatively. All methods of staining showed an irregularity in outline and staining of the nerve cells, with indistinct nuclei and an impairment of the usual regularity of the cytoplasm. This was in spite of the normal appearance of the mucosa and other tissues, which probably demonstrated proper fixation, preservation and staining of the tissues. A block from the ascending colon (arrow *11,* fig. 1) showed a sparsity of the ganglions, which, however, were normal in appearance (fig. 10 *b*). A block from the cecum (arrow 12, fig. 1) showed a similar appearance, after microscopic study, to that of the ascending colon.

Summary.—There was an absence of the ganglions of the myenteric plexus in the rectum and the sigmoid colon in this case. Beginning at the level of the descending colon there were scattered ganglions which contained a few nerve cells. They became more numerous as sections from more proximal segments of the colon were examined, although atrophy and "thinning out" of the plexus was definite in the remainder of the colon.

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19. Unless otherwise noted, each block was made into four tissue sections cut at a distance of 1 mm. apart, which gave a serial section effect. The cresyl violet, hematoxylin and eosin, Bodian and Gros-Bielschowsky methods of staining were used. Also in the description, unless otherwise stated, all nerve fibers are nonmyelinated, and the word "plexus" means the myenteric plexus. The regions described in each section will be generally understood to be confined to the space between the longitudinal and circular muscle bundles of the colon, where the myenteric plexus is normally located.

CASE 2.—A 6 year old boy was seen on May 5, 1932, because of the diagnosis, made elsewhere, of Hirschprung's disease. At the time of birth the child was noted to have a large abdomen. The birth weight was 8 pounds and 3 ounces (3.7 Kg.), and the subsequent development was considered normal. "Stoppage of the bowels" every few months since birth had been noted by the parents of the patient. At such a time abdominal distention and vomiting were noted. Enemas were given, with eventual improvement of the individual episodes of distention. A particularly severe attack of obstipation at the age of 2½ years had necessitated hospitalization. The patient had had colonic irrigations frequently since then. Cramping abdominal pains were noted during some of the attacks of obstipation. Progressive difficulty in keeping the bowels open had been noted by the parents.

Physical examination revealed a poorly developed and nourished white child, whose height was 43 inches (109 cm.) and whose weight was 45 pounds (20.4 Kg.). The blood pressure was 110 mm. of mercury systolic and 75 diastolic, the pulse rate was 136 beats per minute and the rectal temperature was 99.4 F. The tonsils were enlarged and chronically infected, and there was dental caries. The abdomen was protuberant, and distended loops of bowel packed and distended with feces were palpable. The rectum was not enlarged from the anus to the level of the rectosigmoid juncture. Laboratory studies showed the concentration of hemoglobin to be 16.9 Gm. per hundred cubic centimeters of blood; erythrocytes numbered 5,200,000 and leukocytes 9,800 per cubic millimeter of blood. A roentgenogram showed the chest to be normal. Roentgenographic and roentgenoscopic examination of the colon by means of barium and air showed notable distention of the entire colon above the rectum.

The patient was hospitalized and prepared for sympathectomy by means of daily enemas of diluted hydrogen peroxide, diathermy to the abdomen and oil retention enemas. There was an initial loss of 7 pounds (3.2 Kg.) at the time that the colon was partially cleared of its fecal contents, but the child regained 5 pounds (2.3 Kg.) of his body weight prior to operation. Lumbar ganglionectomy was performed, the second, third and fourth lumbar sympathetic ganglions being removed bilaterally. The presacral nerves were also resected. At this time the large intestine was seen to be 8 inches (20 cm.) in diameter, and the maximal colonic involvement was that of the proximal two thirds of the lower part of the colon and the distal third of the transverse colon. The patient died on the operating table.

Postmortem examination revealed the body of a thin, poorly developed child which measured 115 cm. in length and weighed 46 pounds (20.9 Kg.). The abdomen was greatly distended, and a recent midline incision was noted. The apexes of the diaphragm arched to the third interspaces bilaterally. When the abdomen was opened, the colon was seen to fill the entire abdomen and there was colonic dilatation of grade 4. The colon demonstrated a segmental type of megacolon, being normal from the cecum to the left third of the transverse colon, where thickening and dilatation appeared, and then extended to the upper point of the rectum where the dilatation ended abruptly (fig. 2). The colon at the point of maximal dilatation was 3 to 4 mm. thick. There was a diameter of 20 cm. at the point of maximal dilatation. The rectum was not dilated or thickened. The esophagus, stomach, small bowel, kidneys, pelves, ureters and bladder were grossly normal.

Microscopic Study.—Blocks from two levels of the normal rectum (arrows *1* and *2*, fig. *2*) showed no elements of the plexus (fig. 6 *b*). Nerve trunks were present (fig. 9 *a*). Blocks from three parts of the region of transition (arrows

3, 4 and *5,* fig. 2) from nondilated to dilated bowel showed no plexus. Blocks from two levels of the dilated sigmoid (arrows *6* and *7,* fig. *2*) showed that there was no plexus present in the distal segment of the sigmoid. A block from the sigmoid more proximal to this (arrow *8,* fig. 2) showed a marked sparsity of plexus, with single nerve cells in several places and a few nerve fibers but no other structures of the plexus. Blocks taken from three levels above this (arrows *9, 10* and *11,* fig. 2) showed an apparent sudden change to a normal plexus. Blocks from six levels of the descending colon, transverse colon, ascending colon and cecum showed a plexus that was within normal limits.

Summary.—Seven blocks from the rectum, region of transition and dilated sigmoid showed a complete absence of the myenteric plexus. In the colon proximal to the sigmoid there was a striking paucity of nerve cells and then a rather sudden change to an apparently normal plexus.

CASE 3.—A 5 year old boy was seen on Nov. 3, 1937, because of the complaint of "no bowel movements without help since the age of three days." The child weighed 8¾ pounds (3.9 Kg.) at birth and was a full term baby. Development had been considered normal, the weight at the age of 1 year being 21 pounds (9.5 Kg.). Ever since birth, bowel movements had been "rocklike" and "very few and far between." Enemas were given twice weekly, and spontaneous bowel movements occurred less than once a month. During the year previous to the time the child was brought to the clinic, there had been an increase of abdominal distention. Attacks of distention had been associated with vomiting and low fever.

Physical examination showed a poorly developed and nourished child whose height was 42 inches (107 cm.) and whose weight was 43 pounds (19.5 Kg.). The blood pressure was 118 mm. of mercury systolic and 70 diastolic, the pulse rate was 108 beats per minute and the rectal temperature was 99.4 F. The abdomen was markedly distended, nontender and relaxed, and huge peristaltic waves covering a third of the abdomen were noted. There was no spasm of the rectal sphincter. Laboratory studies showed the concentration of hemoglobin to be 13.1 Gm. per one hundred cubic centimeters of blood; erythrocytes numbered 4,600,000 and leukocytes 10,300 per cubic millimeter of blood. The differential count of the leukocytes was within normal limits. A roentgenogram showed the chest normal, and roentgenographic and roentgenoscopic examination of the colon showed a megacolon with a large opaque residue present in the dilated bowel.

The patient was hospitalized and was given Learmonth's pills (active ingredient, eserine), diathermy to the abdomen, desiccated thyroid, enemas, saline cathartics and a residue-free diet. A large fecalith, which was palpable through the anterior abdominal wall, was present in the colon. The child did not improve during the course of treatment and suddenly became quite toxemic for no apparent reason and died within a few hours after the first signs of toxicity.

Postmortem examination revealed a thin child, 108 cm. long and weighing 40 pounds (18.1 Kg.). There was considerable generalized abdominal distention. When the abdomen was opened, the omentum was seen to be paper thin and stretched over the hugely distended colon. There was no peritoneal fluid present in the abdominal cavity, and the peritoneal surfaces were smooth and glistening. The apexes of the diaphragm arched extremely high bilaterally. The colon was dilated (4 plus) except for the rectum and lower part of the sigmoid, where an abrupt change from dilatation to a normal caliber of the bowel occurred (figs. 3 and 4). The wall of the colon was markedly thickened. The esophagus, stomach, small intestine, kidneys, pelves, ureters and bladder were grossly normal.

Microscopic Study.—Blocks were taken from three levels of the nondilated portion of the rectum (arrows *1, 2* and *3,* fig. 3). The lowest section showed several branches of a myelinated nerve trunk, and there were nonmyelinated nerve fibers running in groups, constituting a nonmyelinated nerve bundle fig. 9 *b*). This was not similar to the usual appearance of nonmyelinated nerve fibers between the ganglions of the normal rectum. These nonmyelinated nerves entered or left the colon in relation to the blood vessels and were present between the longitudinal and circular muscle coats of the colon (fig. 10 *a*). No nerve cells, groups of supporting cells or spaces were seen that would be indicative of the presence of the myenteric plexus. Blocks were taken from two levels of the dilated sigmoid (arrows *4* and *5,* fig. 3). The distal section (arrow *4,* fig. 3) showed no nerve cells, ganglions, supporting cells or spaces (fig. *7a*). The proximal section showed six ganglions, each containing two to five nerve cells, no supporting cells of note and few nerve fibers. The nerve cells were smaller than normal and lacked clarity, and some had an unusual affinity for cresyl violet. There was a definite paucity of ganglions. Blocks were taken from three levels of the descending colon (arrows *6, 7* and *8,* fig. 3). One block showed a moderate diminution of the number of ganglions. There was also decided diminution of the number of interganglionic nerve fibers. The majority of the nerve cells showed a spotty distribution of Nissl substance and a ragged outline. There were few supporting cells. The second block showed only two identifiable nerve cells in one section. The third block (fig. 11 *b*) showed an almost normal number of ganglions but few supporting cells or interganglionic fibers. Blocks were taken from four levels of the transverse colon (arrows *9* through *12,* fig. 3). One block showed a normal number of nerve cells, supporting cells and nerve fibers, but there was an unusual variation in the affinity of the nerve cells for the silver impregnation methods. The other blocks varied somewhat in the number of ganglions yet no definite abnormality was noted. Blocks taken from three levels of the ascending colon (arrows *13, 14* and *15,* fig. 3) showed no essential variation of the ganglions from normal (fig. 11*a*). Blocks taken from two levels of the cecum (arrows *16* and *17,* fig. 3) showed no essential variation from normal.

Summary.—The change from the absence of plexus to a normal plexus occurred in the dilated sigmoid. There was a gradation from an absence of plexus to a normal plexus; this gradation consisted of a paucity of ganglions, nerve cells, supporting cells and nerve fibers and apparent diminution in the size of the nerve cells.

CASE 4.—A 2 year old boy was seen on May 12, 1943, because of the parents' complaint that he "won't eat and has had bloating since birth." When the baby was 3 days old, the parents noted that his bowels had not moved. Castor oil was administered, without a resulting bowel movement. Diarrhea was noted during the second and third weeks of life; at this time as many as six stools were observed in a day. The child had subsequently been in poor health. Nursing was poor, and the feedings were frequently vomited in the early days of life. Some improvement in these symptoms was subsequently noted. The abdomen was distended from time to time. An attack of whooping cough at the age of 4 months was extremely severe, and the parents felt that the bowels had been even more constipated since that time, with an occasional severe attack of abdominal distention being noted. The stools were occasionally foul and foamy but usually were hard and inspissated.

Physical examination showed the baby to have the appearance characteristic of marasmus, with severe abdominal distention, clubbing of the fingers and toes and thrush of the oral mucous membrane. The rectal temperature was 102 F. The abdomen was distended by loops of large bowel, the outlines of which were

visible through the thin abdominal wall. Laboratory studies showed the concentration of hemoglobin to be 6.2 Gm. per hundred cubic centimeters of blood; erythrocytes numbered 3,080,000 and leukocytes 11,900 per cubic millimeter of blood. Differential count of the leukocytes showed 27 per cent lymphocytes, 8 per cent monocytes, 16 per cent stab forms and 49 per cent mature forms of neutrophilic leukocytes. The study of the blood smear showed anisocytosis, hypochromasia, a left shift and toxic changes in the polymorphonuclear leukocytes.

The patient did not respond well to medical treatment and died three days after admission to the hospital. The opinion of the attending physician was that death was attributable to general weakness and debility.

Postmortem examination revealed an infant who was 76 cm. long, weighed 12 pounds (5.4 Kg.) and was emaciated (3 plus). The panniculus adiposus measured 3 mm. in thickness. The chest was barrel shaped, with a wide flare of the lower portion. The abdomen was greatly distended, and when it was opened the colon was noted to be hypertrophied and markedly dilated down to the rectum, which was of normal diameter. The peritoneal cavity contained 50 cc. of clear fluid. The esophagus, stomach, small bowel, kidneys, pelves, ureters and bladder were grossly normal.

Microscopic Study.—Blocks from the rectum were stained with hematoxylin and eosin, Bodian, cresyl violet, Mallory-Heidenhain, Mallory phosphotungstic acid, Verhoeff's elastic, Van Gieson and mucous stains. No nerve cells were seen, and no normal nerve fibers were noted. Blocks from six levels of the sigmoid contained nerve cells and nonmyelinated nerve fibers. The more distal sections showed a definite sparsity of the elements of the plexus as contrasted with those sections more proximal. A block from the descending colon showed only a rare ganglion containing an average number of nerve cells, a few supporting cells and almost no nerve fibers. The nerve cells were small and shrunken even for a child. A block from the transverse colon revealed that the ganglions were normal in number and contained the usual number of nerve cells, which stained somewhat poorly with cresyl violet. The interganglionic fibers were decreased in number. A block from the ascending colon showed no abnormality of the plexus.

Summary.—There was an absence of ganglions in the rectum, with an apparent gradual transition toward a normal plexus occurring in the dilated sigmoid. There was a region of "thinning out" and atrophy of the plexus that reoccurred in the descending colon, with small shrunken nerve cells and few ganglions. The nerve cells and ganglions became normal again in the transverse colon.

CASE 5.—A 24 year old man was seen on Jan. 17, 1920, because of abdominal distention and constipation, which had increased in severity during the past year. Five days after birth the patient had had diarrhea, but since that time he had been obstipated. As drugs would not cause the bowel to evacuate its contents, enemas were used frequently. He was unable to pass gas without first inserting a tube into the rectum. As far as was known a normal bowel movement had not occurred since the first days of life. During the past year his condition had been worse, pain had been noted in the right upper quadrant of the abdomen and anorexia was present.

Physical examination revealed a man whose height was 5 feet 11 inches (180 cm.) and whose weight was 190 pounds (86.2 Kg.). The abdomen was markedly distended and tympanitic. The heart was displaced upward to the third interspace as a result of the abdominal distention.

Since the patient failed to respond satisfactorily to medical treatment, a double-barreled ileostomy was performed on January 27. Some soiling of the peritoneum

occurred at the time of operation, and the patient died on the day of operation as a result of peritonitis and bronchopneumonia.

Microscopic Study.—Blocks taken from the rectum and from two levels of the transitional region showed no ganglions to be present. No nerve fibers were seen with the exception of a small nerve trunk in one section. Two blocks taken from the sigmoid showed only a few ganglions. These contained only one to four nerve cells each. The usual supporting cells and nerve fibers were scarce. Two blocks from the descending colon showed that the ganglions were somewhat diminished in number and contained fewer nerve cells than was usual for this part of the colon. There were definitely more ganglions here than in the sigmoid. Two blocks were taken from the transverse colon; one was similar to those from the sigmoid and the other similar to those from the descending colon. A block taken from the ascending colon showed fewer ganglions and fewer nerve cells than the normal amount. The cecum was similar except that there were even fewer ganglions, only five being seen in a strip 3 cm. in length.

Summary.—Ganglions were absent in the rectum and in the transitional segments of the colon. Above this level they were considerably diminished in number as compared to the findings in the cases used as controls.

CASE 6.—A 21 year old woman was seen on Aug. 9, 1917, because of distention of the abdomen and obstipation. She had been constipated since early childhood and would go without bowel movements for two weeks at a time unless enemas or a strong physic was administered. When she was constipated, melena was present.

Physical examination revealed a woman with a hugely distended abdomen. Her height was 5 feet 2 inches (157 cm.), her weight was 97 pounds (44.0 Kg.) and her blood pressure was 130 mm. of mercury systolic and 100 diastolic. The abdomen was distended by a huge colon. Visible peristalsis was present and active. Fecal masses were felt in the abdomen. Roentgenographic examination revealed a megacolon.

The patient did not do well and died the day after examination. At necropsy a perforation of the cecum, with gross contamination of the peritoneum by feces, was found. The diaphragmatic apexes were at the third ribs bilaterally.

Microscopic Study.—Three blocks taken from the rectum and two blocks taken from the lower part of the sigmoid showed no vestige of the plexus of Auerbach. An occasional nerve bundle was seen. A block taken from the upper part of the sigmoid, which was the thickest and most dilated portion, showed a plexus which was normal except for a diminution in the supporting cells and fewer nerve cells per ganglion than were normally encountered. Seven blocks from the descending colon, transverse colon, ascending colon and cecum showed an essentially normal plexus.

Summary.—Absence of plexus was noted in the rectum and in the lower part of the sigmoid. There was some diminution of the number of ganglions proximally, but the descending colon and the remainder of the colon showed a plexus that was within normal limits.

CASE 7.— A 3 year old boy was seen on Feb. 14, 1917, because of constipation. The patient had been constipated since the age of 6 months. At times two weeks would pass without a bowel movement. An infant brother was said to be similarly affected, and a second cousin had died of a similar condition at the age of 31 years.

On physical examination the abdomen was distended (circumference 40 inches [102 cm.]) and tympanitic. The rectum was empty.

The pulse and temperature suddenly rose, and the patient died on February 19. An enormously distended and redundant colon was found at necropsy, with maximal involvement noted in the sigmoid.

Micropscopic Study.—Three blocks from the terminal segment of the colon showed the plexus to be absent. In one block just above this in a transitional region and in seven blocks from the sigmoid, descending colon, transverse colon, ascending colon and cecum the plexus was within normal limits.

Summary.—There was an absence of the plexus in the rectum, and there was an abrupt change to an essentially normal plexus in the transitional region of the lower part of the sigmoid colon.

CASE 8.—A 4 year old boy was seen because of abdominal distention and obstipation since birth. It was stated that he had never had a normal bowel movement. Enemas and suppositories were used, with only a palliative effect. Drugs were of no value.

The blood pressure was 110 mm. of mercury systolic and 80 diastolic. The abdomen was distended. The concentration of hemoglobin was 11.4 Gm. per hundred cubic centimeters of blood. Roentgenographic and roentgenoscopic examination showed a megacolon to be present and to involve the entire colon above the rectum. The patient was hospitalized and prepared for operation over an eighteen day period. Resection of the colon from the ascending colon to the sigmoid and subsequently a double-barreled sigmoidocolostomy were performed. The patient returned two months later for closure of the colonic stoma. Subsequent to the closure of the stoma, peritonitis developed owing to perforation of an ulcer of the cecum. The peritonitis led to the death of the patient on the sixth postoperative day.

Microscopic Study.—Three blocks taken from different levels of the normal rectum showed an abscence of the plexus (fig. 7 *b*). At fairly regular intervals there were nerve fibers somewhat similar to those seen in the normal plexus, but there were no ganglions or nerve cells.

One block from the descending colon showed only a slight reduction of the number of ganglions and nerve cells. The findings in the transverse colon were similar. The ascending colon was within normal limits except for a rather marked reduction of the number of ganglions and nerve cells. The ileum showed a normal plexus.

CASE 9.—A 1 year old infant had had no normal bowel movements since birth. A daily enema had been given for several months with good results until recently, when the infant had been unable to expel all the enema and as a result the abdomen remained distended. Vomiting and blood in the stools had been present during the week prior to the time the patient was seen at the clinic.

On examination the child was fretful and pale, with a distended abdomen. The concentration of hemoglobin was 32 per cent of normal. Roentgenographic and roentgenoscopic examination showed the sigmoid to be enormous. The rest of the colon was atonic but would contract. Resection of the descending and sigmoid colon was performed a month later. General peritonitis and death occurred four days after operation.

Microscopic Study.—Four blocks of the rectum showed no ganglions or nerve cells. Small nerve bundles were frequently seen in the sections. Seven blocks from the sigmoid and the remainder of the colon showed a normal plexus to be present.

Summary.—The plexus was absent in the normal-sized rectum. There was a normal plexus in the remainder of the colon.

CASE 10.—An 8 month old male infant was seen because of obstipation since birth. Up to 3 days of age there were no bowel movements, and the infant vomited all his feedings. He was given posterior pituitary injection at this time, with five bowel movements occurring in the following two hours. The bowels moved freely for the next two and a half weeks but since then had not moved unless a cathartic or enema was administered. Fecal impactions had been removed at times.

On examination the infant was seen to have an enormous abdomen, 51 cm. in circumference. Visible peristalsis was present. There was no beneficial result after medical treatment, and appendicostomy was performed. Death occurred nine days after operation. The clinician in charge felt that toxemia caused the death. No peritonitis was found at the time of the postmortem examination.

Microscopic Study.—Two blocks from the rectum showed that no vestige of the plexus was present. A number of nerve bundles were present in the sections. Two blocks from the sigmoid showed an absence of plexus, and no nerve bundles were noted. The descending colon contained an occasional ganglion with a few nerve fibers and supporting cells. The transverse colon, ascending colon and cecum showed an essentially normal plexus except for the fact that there was a moderate diminution of the number of ganglions and nerve cells.

CASE 11.—A 27 year old white man was seen on Nov. 20, 1946, because of the diagnosis of Hirschsprung's disease made by his home physician. The patient stated that his bowels never moved normally and that his abdomen had always been large. As cathartics were without effect, he was forced to take colonic irrigations at least once weekly to remove the bowel contents. At the time of the colonic irrigations he would occasionally note a retention in the bowel of as much as 1 to 2 gallons (4 to 8 liters) of enema fluid. Crampy abdominal pain had been noted at times. The diagnosis of Hirschsprung's disease was first made when he was 12 years old, and spinal anesthesia was administered on several occasions "to tone up the nerves of the bowel." This was without benefit.

Physical examination disclosed the height to be 68 inches (173 cm.) and the weight 153 pounds (69.4 Kg.); the nutritional state seemed good. The blood pressure was 127 mm. of mercury systolic and 70 diastolic, the pulse rate 88 beats per minute and the oral temperature 98.2 F. The abdomen was greatly enlarged, and flaring of the lower ribs was present. The descending colon was easily palpated and seemed about 10 cm. in diameter. The transverse colon was also palpable. Proctosigmoidoscopic examination revealed the terminal segment of bowel to be normal for a distance of 24 cm. Roentgenoscopic and roentgenographic examination of the colon revealed a normal rectum and lower part of the sigmoid, but the remaining part was notably dilated and elongated proximally from the lower end of the descending colon. Roentgenographic examination of the chest revealed bilateral elevation of the apexes of the diaphragm. The concentration of hemoglobin was 14 Gm. per hundred cubic centimeters of blood; erythrocytes numbered 4,200,000 and leukocytes 7,400 per cubic millimeter of blood. Urinalysis gave results which were within normal limits. The flocculation reaction for syphilis was negative. An operation was performed on December 2, at which time the ileum was divided at a point about 8 to 10 inches (20 to 25 cm.) from the ileocecal valve, the colon was divided in the region of the first portion of the sigmoid and the intervening colon was removed. The ends of the ileum and sigmoid colon were brought out as an exteriorization procedure.

The examination of the removed colon showed maximal dilatation of the descending portion, which was 20 cm. in diameter. There was a normal-sized sigmoid colon, beginning abruptly below the region of maximal dilatation. Proximal to the descending portion there was a gradual diminution of the size until a moderately dilated and hypertrophied cecum was seen. The colon was markedly elongated. The appendix was within normal limits; the ileum was not dilated.

Microscopic Study.—Blocks of tissue were taken from two levels of the nondilated sigmoid. Examination of sections from these blocks showed no ganglions or nerve cells. Nerve trunks were fairly frequent and were large. There was an unusually large amount of connective tissue between the longitudinal and circular muscle coats. This same increase of connective tissue was present in all sections until the distal end of the dilated descending colon was studied microscopically, at which time the connective tissue was found to be not increased. This was the largest and only really significant amount of connective tissue found between the muscle layers of the colon in the 11 cases studied.

Two blocks of tissue were taken from the region of transition of nondilated sigmoid to dilated descending colon. The findings were essentially the same as in the sigmoid except that the nerve trunks were not present in the proximal sections and the connective tissue between the muscle layers was normal in the proximal sections.

Blocks of tissue were taken from four levels of the dilated descending colon. The most distal of these showed several ganglions to be present. These contained two to twelve nerve cells each. This was an abrupt change, as the previous block, 2 cm. distant, showed no ganglions. The other blocks from the descending colon showed a few more ganglions than the first, the maximal number being eight in a section 4 cm. long (the next most proximal). These were all larger than are seen as a general rule in normal cases and contained a greater than average number of nerve cells. They were present in the longitudinal muscle coat rather than between the longitudinal and circular muscle coats. This was the first time that this location had been occupied consistently by the myenteric plexus. It had been noted at times and in the case of single ganglions had been seen frequently, but at no time had the myenteric plexus been in the longitudinal muscle coat for almost its entire extent. The muscle walls were the thickest that we have examined.

Three blocks were taken from the descending colon. These showed many ganglions, with numerous nerve cells, present in the usual location of the myenteric plexus.

Two blocks were taken from the transverse colon. These showed the ganglions of the distal section to be few and small. Those in the proximal sections were essentially normal.

Blocks taken from the ascending colon and the cecum showed a normal number of ganglions and nerve cells.

STUDY OF THE MYENTERIC PLEXUS IN FIVE CASES OF SECONDARY MEGACOLON

In addition to the series of cases used as controls, we have studied 5 cases of secondary megacolon (table 5). The gross pathologic changes of the colon in the first 3 cases were identical with those seen in cases of congenital megacolon, and the gross changes in the last 2 were likewise similar except for the absence of great hypertrophy. It is not

intended to report these cases in detail but rather to bring out the features which distinguish secondary megacolon from congenital megacolon.

CASE 12.—A 54 year old man had for two years noted constipation and the frequent urge to defecate. For four months blood had been observed in the stools, which were smaller and more frequent than usual. For two months he had noted distention of the abdomen, which was partly relieved by enemas. Appendicostomy was performed without benefit, and death occurred seven days after operation. Postmortem examination revealed an annular, hard, fixed rectal tumor 2 inches (5 cm.) above the prostate. There was grade 3 to 4 dilatation of the colon (on the basis of 1 to 4, in which 1 designates the least and 4 the greatest dilatation) and the walls were 5 to 7 mm. thick. Microscopic sections taken from the rectum, rectosigmoidal region, sigmoid colon, transverse colon and cecum showed ganglions of the myenteric plexus in every section. These were considered to be normal.

CASE 13.—A 36 year old man had noted cramps, constipation and abdominal distention for the past five years. At the time of postmortem examination a grade 4 dilatation and thickening of the colon was seen to be present proximal to a carcinoma of the upper part of the sigmoid. Microscopic sections taken from regions below and above the tumor showed normal ganglions of the myenteric plexus in every section.

CASE 14.—A 25 year old man had noted persistent constipation for three months, and for three weeks there had been involuntary defecation and bleeding from the rectum. He died suddenly the day after registration at the clinic. The entire colon was dilated (grade 3 to 4), with thickening of the wall. There was an annular adenocarcinoma 3 cm. proximal to the anus. Microscopic sections taken from the rectum, rectosigmoidal region and the remainder of the colon showed the ganglions of the myenteric plexus to be present in every section.

CASE 15.—A 62 year old woman had noted an intermittent watery diarrhea for two years. Ten months before her admission to the hospital she had had an episode of abdominal distention, which had been relieved by enemas. Four days before admission, mild abdominal distention had been noted, and two days afterward a rapid increase of abdominal distention occurred, with persistent obstipation. Transverse colostomy was performed, but death occurred six hours after operation. Postmortem examination showed the colon to be distended (grade 4), with a greatly redundant and elongated sigmoid colon and mesentery which had permitted a volvulus of the sigmoid. The wall of the bowel was thickened. Microscopic sections taken from many regions of the rectum, sigmoid and the remainder of the colon showed ganglions of the myenteric plexus to be present in every section.

CASE 16.—A 33 year old woman had been well until sixteen hours before her admission to the hospital, when she noted abdominal pain and distention and vomited several times. The colon was hugely dilated, as shown by roentgenographic examination. On the day of admission cecostomy was performed, but death occurred shortly thereafter. The colon was hugely distended and thin. The diameter of the colon was 14 cm., and the length was 170 cm. Severe acute colitis was present, with a pseudomembrane over the mucosal surface. The submucosa, muscle layers and peritoneum revealed microscopic evidence of severe inflammatory changes. Microscopic study of the myenteric plexus showed only a fourth of the usual number of ganglions to be present in the rectum, sigmoid and the descending and transverse colon. The ascending colon contained only a few nerve cells, and

there were no visible nerve cells in the cecum. There was considerable diminution of the number of ganglions in the ileum, but the jejunum showed a normal plexus. The changes in the myenteric plexus differed from those seen in cases of congenital megacolon by the fact that the plexus was absent proximally rather than distally and there was generalized damage to the plexus.

Gross examination in the 3 cases in which the megacolon was secondary to obstructing carcinoma showed great dilatation and hypertrophy of the colon above the obstructing lesion. The myenteric plexus was entirely normal in all 3. In the cases of congenital megacolon there were the same dilatation and hypertrophy of the colon above a bowel of normal diameter, with no obstructing lesion in the lumen, but there was an absence of the myenteric plexus in the wall of the distal portion of the bowel. The changes in the myenteric plexus in case 16 were probably related to the severe and fulminating pseudomembranous colitis, although there was no apparent universal involvement of the myenteric plexus by the inflammatory process.

TABLE 6.—*Summation of Authors' and Collected Series*

Series	Cases	Plexus Absent in Distal Portion of Colon	
		No.	%
Our series	11	11	100
Collected series*	18	14	78
Total	29	25	86

*The 4 cases in the collected series in which changes in the distal part of the colon were not reported may not have been completely studied.

COMMENT

Table 6 shows a compilation of the collected series and our series which represent the cases of megacolon in which studies of the myenteric plexus have been carried out. There was a total of 29 such cases, in 25 of which the myenteric plexus was observed to be absent in the distal portion of the colon. In 4 cases there were changes in the plexus other than absence of the ganglions. Since this group of 29 cases consisted of cases of megacolon without reference to the type, we have separated the cases of congenital megacolon. There were 6 cases of definitely congenital megacolon among the 18 collected cases, but since the case reported by Robertson and Kernohan has been used in our series it will be included only in the group that we studied. We have thus collected from the world literature 5 cases of congenital megacolon in which the myenteric plexus had been studied. We have added 11 cases of our own, making a total of 16 cases. In 100 per cent of these cases there was absence of the ganglions of the myenteric plexus in the distal segment of the colon (fig. 5). It is our impression that similar changes can be observed in all cases of congenital megacolon in which the criteria that

we have used are fulfilled. As can be seen from the reported cases, there is absence of the ganglions of the plexus in some cases of acquired megacolon. We consider this as a separate but related problem, and a brief mention of another opinion should be made here in this respect. Etzel[20] stated that in all cases of nonobstructive acquired megacolon which he studied there were lesions of the myenteric plexus in the neighborhood of the pelvirectal sphincter.

We have described a pathologic lesion present in 11 of our own cases and in 5 collected from the literature that represent congenital megacolon of a type defined by us. Hawkins, Alvarez, Hurst and Bockus all have stated that a disturbance of the innervation of the colon is the most likely cause for megacolon. Our findings are indicative not only of a pathologic change in the myenteric plexus and in the colonic innervation but of changes which are present in the distal segment of the colon where an obstructing lesion, either neurogenic or gross, would most likely be of significance. The experimental production of megacolon by Ishikawa, Adamson and Aird and by Kleinschmidt is based on an interference with the innervation of the colon.

It is impossible to deny the presence of the changes in the myenteric plexus in cases of congenital megacolon. Likewise, from the theoretic and experimental standpoint the significance of the changes in the myenteric plexus seems to be all that could be desired to explain the pathogenesis of congenital megacolon. When we reviewed the physiologic studies on the innervation and functional activity of the colon, results of various forms of treatment and effects of denervation on the myenteric plexus, we found a wide and chaotic field of contradictions which we have not attempted to untangle. The field is a difficult one to investigate, and the conclusions that are incontrovertible are few.

The following is a brief review of certain aspects of the subject which summarizes the function of the myenteric plexus, although not from an unassailable viewpoint, as related to the consideration of the pathogenesis of megacolon. The sympathetic nervous system is generally conceded to have an inhibitory action on the colon and thus causes retention of the fecal contents and retards the emptying of the colon. The parasympathetic nervous system has an augmentative action on the colon that causes evacuation of the fecal contents and accelerates the emptying of the colon. The internal anal sphincter will relax after parsympathetic stimuli and undergo an increase in tone after sympathetic stimuli.[21] With such a physiologic basis, it has been postulated that the cause of

20. Etzel, E.: Personal communication to the authors.

21. Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice: A University of Toronto Text in Applied Physiology, ed. 4, Baltimore, Williams & Wilkins Company, 1945, p. 501. Hurst.[8]

the fecal retention in cases of megacolon is an overactivity of the sympathetic nervous system in the presence of a normally active parasympathetic nervous system. The tendency generally, however, has been acceptance of the hypothesis that there is a diminished activity of the parasympathetic nervous system, which has a causative effect in the production of megacolon, aided also by the postulated presence of a relative increase in the action of the sympathetic nervous system. A lesion of the autonomic nerves to the colon or of the myenteric plexus or both would be expected to be present if a pathologic lesion were the cause of the autonomic unbalance.

We have found no studies of the nerves leading to the colon in cases of congenital megacolon and have been unable to carry out such a study with the specimens available. Etzel[5e] studied the vagus nerves in cases of megaesophagus and found them to be normal although he demonstrated changes in the myenteric plexus of the esophagus similar to those that he found in cases of acquired megacolon. Hence we have only minor inferential evidence in regard to the absence of a lesion of the autonomic nerves leading to the colon.

The myenteric plexus and other nervous plexuses of the gastrointestinal tract have been studied in laboratory animals,[22] and most of the reported studies have been made on the esophagus, stomach and small bowel rather than on the colon. Therefore there have been relatively few reports in the literature that have a direct bearing on the problem of the myenteric plexus in the colon of man. According to the studies on animals, the plexus in the colon basically consists of nerve cells collected in groups or ganglions which are connected by nonmyelinated nerve fibers of extrinsic and intrinsic derivation. A large percentage of the nerve fibers in the wall of the colon come from the extrinsic nerves and disappear after degenerative section of these nerves.[23] Hill's[15a] impression was that nearly all the sympathetic fibers in the colon are postganglionic and end on the muscles of the colon. She also described most of the parasympathetic fibers as preganglionic and ending in relation to the nerve cells of the myenteric plexus. There would thus be an absence of parasympathetic impulses to a segment of colon that exhibited an absence of the myenteric plexus. A possible physiologic correlation has thus been added to the theoretic, experimental and pathologic aspects of the pathogenesis of congenital megacolon.

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22. Footnote 15. Babkin.[18]

23. Alvarez,[7] p. 192. Modern and Thienes.[15d] Johnson.[15e]

SUMMARY

1. The myenteric plexus has been studied in 11 cases of congenital megacolon, a series of cases used as controls and 5 cases of secondary megacolon.

2. The myenteric plexus was found to be absent in the most distal part of the colon in all cases of congenital megacolon. In 80 per cent of the cases it was absent also in the "transitional region." In 60 per cent of the cases it was in addition absent in the lower part of the sigmoid. In 20 per cent of the cases the absence of the myenteric plexus extended from the rectum into the upper part of the sigmoid and the descending colon.

3. In all cases of congenital megacolon there were nerves present in the location of the myenteric plexus which were not seen in the control cases.

4. The strategic location of the changes and a review of previous theoretic concepts, experimental studies and certain physiologic and anatomic studies point toward the significance of processes in the myenteric plexus in the pathogenesis of congenital megacolon.

News And Comment

GENERAL NEWS

Urology Award.— The American Urological Association offers an annual award of $1,000 (first prize $500, second prize $300 and third prize $200) for essays on the result of some clinical or laboratory research in urology. Competition shall be limited to urologists who have been in specific practice for not more than five years and to residents in urology in recognized hospitals.

The first prize essay will appear on the program of the forthcoming meeting of the American Urological Association, to be held at the Biltmore Hotel in Los Angeles, May 16 to 19, 1949.

For full particulars write to the secretary, Dr. Thomas D. Moore, 899 Madison Avenue, Memphis 3, Tenn. Essays must be in his hands before Feb. 15, 1949.