

Myenteric plexus in Hirschsprung's disease

BARBARA SMITH

From the Department of Pathology, St. Bartholomew's Hospital, London

EDITORIAL COMMENT By cutting sections parallel to the gut wall a much better picture of the disordered myenteric plexus may be obtained. These studies demonstrate considerable nerve abnormalities in the distended section of the bowel above the aganglionic zone.

The absence of ganglion cells and the presence of abnormal bundles of unmyelinated fibres in the affected segment in Hirschsprung's disease was first well described by Whitehouse and Kernohan (1948). However, previous authors who have studied this problem have used standard transverse sections of the gut to demonstrate the abnormalities but these give a very inadequate view of the plexus which is a complicated network lying parallel to the gut wall. If the intestine is cut in this plane the plexus can be viewed *en face* which gives a much better picture of the anatomy and pathology.

MATERIAL AND METHODS

Two specimens of colon were examined, both of which had been removed surgically.

CASE 1 was a woman of 26 who had been constipated from birth having her bowels open about once weekly. During a pregnancy at the age of 24 she became much better but relapsed after the baby was born, having her bowels open only once a month.

CASE 2 was a man aged 28 who had been constipated all his life, sometimes going for as long as two months without a bowel movement.

The specimen from case 1 consisted of the sigmoid and upper rectum and was 40 cm. long with a bowel circumference of 15 cm. The specimen from case 2 was similar also measuring 40 cm. long with a circumference of 25 cm. There was some reduction in calibre at the lower end but not as marked as is usually seen in Hirschsprung's disease.

Blocks were taken from each specimen at the lower end; at 5 cm. and 20 cm. from the lower end and from the upper cut end. At each of these four levels a paraffin section was cut and four other blocks were impregnated with silver Schofield (1960). A piece of gut was placed mucosal surface down on the flat tissue-holder of a freezing microtome and sections cut at 100 μ . The junction between the circular and longitudinal muscle could be seen macroscopically and was shown in two or three sections from each block.

RESULTS

The paraffin sections showed no ganglion cells in the lower two blocks but they were present higher up in both specimens. At the lower end bundles of unmyelinated fibres could be seen.

One of the features of the normal myenteric plexus is that in spite of its complexity it shows considerable anatomical regularity. A cholinesterase preparation of rabbit colon is seen in Fig. 1 to demonstrate the layout at low magnification. A whole mount of gut muscle from a human neonate is shown in Fig. 2, which in spite of the poor impregnation at that age, shows that the anatomy is the same as in the animal. In the human adult it is impossible to show more than a small area as the sections are very thick and the axons do not remain in the same plane of focus for more than a short distance (Fig. 3). The basic pattern is, however, the same. There are small groups of neurones with interconnecting axons running in bundles containing relatively thick, straight, widely spaced axons. Single axons are seen entering both muscle coats. Deviations from this pattern can be recognized.

In these two cases sections taken from the caudal ends of the specimens showed an occasional ganglion cell. In place of the normal plexus was a network of bundles of unmyelinated fibres. These bundles were wavy in contrast to the straight fibres seen in the normal and contained a large number of fine, closely packed axons (Figs. 4 and 5). There were no muscular branches visible. Nerves with this histological appearance were present throughout the lower quarter of the specimens; more proximally they were broken up and occurred only as short segments. In addition in more proximal areas, the individual axons could be seen fragmented (Fig. 6). The number of ganglion cells increased proximally but many were abnormal in shape and showed either dense argentophilia or were very pale. Some appeared to have no

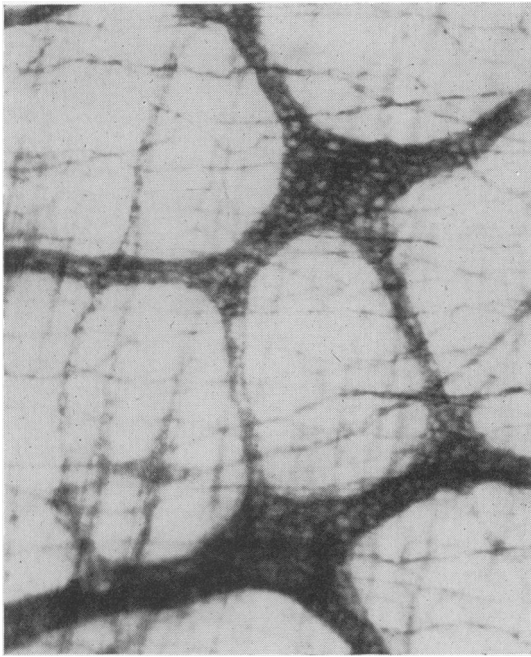


FIG. 1. *The normal myenteric plexus of the rabbit demonstrated by a cholinesterase technique to show the layout of the primary neurones. $\times 90$.*

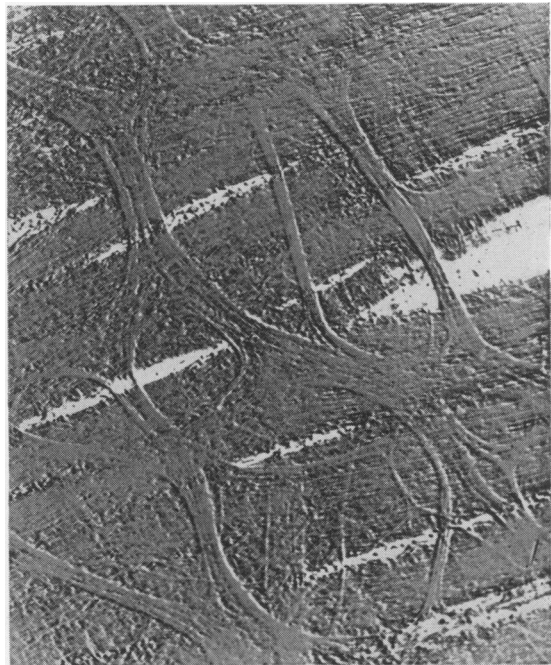


FIG. 2. *A whole mount of the muscle coats of the sigmoid colon of a neonate to show that the layout in the human is the same as that in the animal. Schofield $\times 50$.*

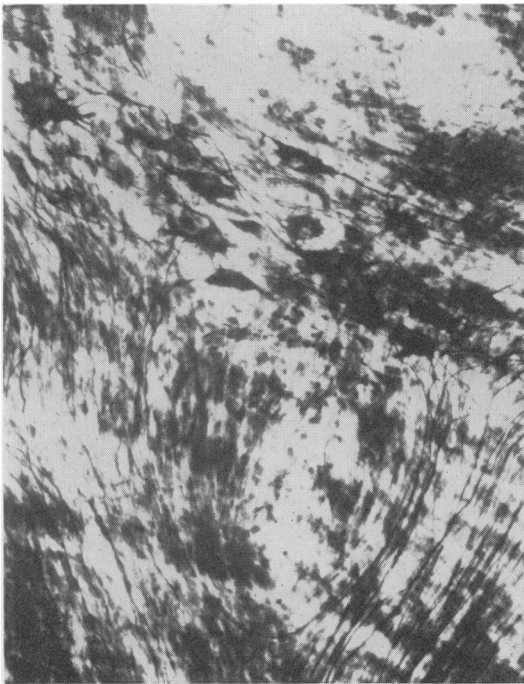


FIG. 3. *The normal myenteric plexus in the human showing a group of neurones and a number of axons running in various directions. Schofield $\times 86$.*



FIG. 4. *A section from the aganglionic segment of case 1 showing the arrangement of unmyelinated fibres. Schofield $\times 86$.*

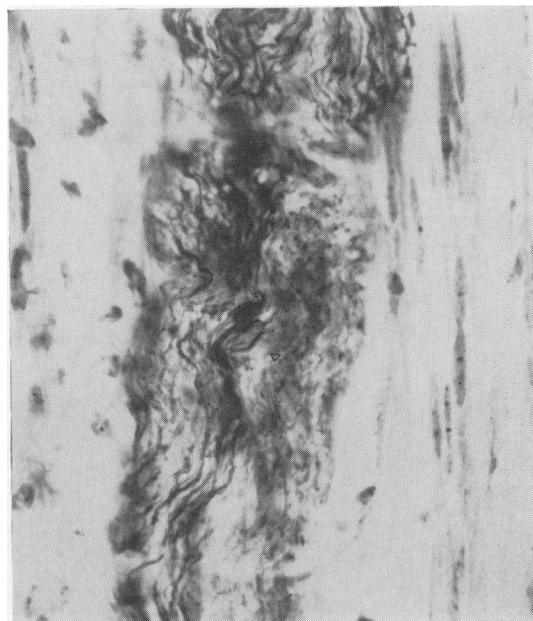
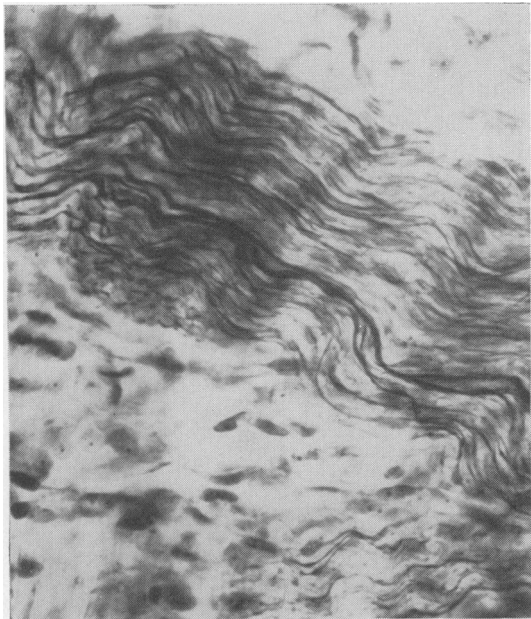


FIG. 5. A section of an unmyelinated nerve bundle to show the large number of fine axons it contains. Schofield $\times 350$.

FIG. 6. A similar section from the junction zone in case 1. The fibres on the right of the bundle are beginning to break up. Schofield $\times 350$.

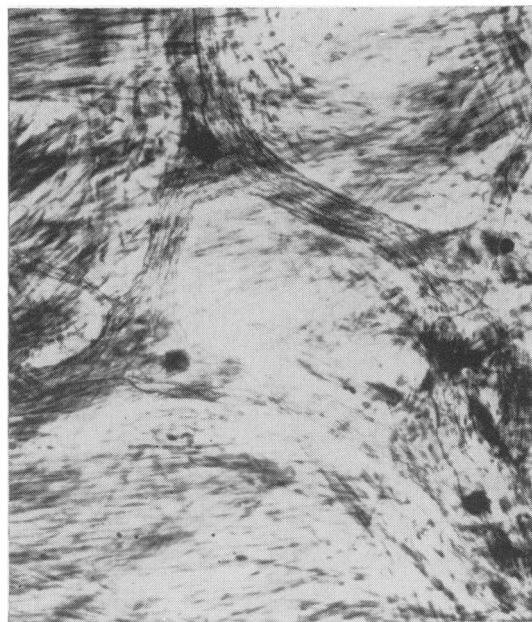


FIG. 7. A group of very abnormal neurones, only one of which has an axon. Schofield $\times 350$.

FIG. 8. A portion of the unmyelinated network of case 1. Rather poorly formed neurones are present in the angles, one of which has a definite axon. $\times 86$.

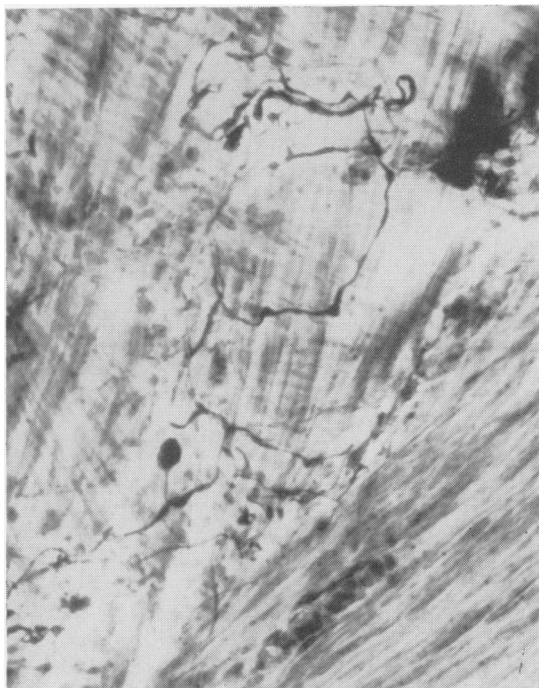


FIG. 9. An area from the junctional area of case 2. It shows a totally irregular network and the presence of a large retraction ball. $\times 250$.

axons, others had short branches which were irregular in thickness and random in direction (Fig. 7). In some cases one could see these neurones lying among the bundles of unmyelinated fibres (Fig. 8). A number of rather thick axons were seen pursuing a convoluted course, often singly or in the neighbourhood of other axons but not forming any definite anatomical bundle. Fibres ran into the muscle and then curved back again; some had retraction balls and others showed gross irregularity in calibre (Fig. 9). However, the important feature of the whole proximal part of the specimen was the complete lack of the normal anatomical pattern, right up to the cut edge.

DISCUSSION

During the development of the parasympathetic system axons grow out from the preganglionic neurones situated either in the vagal nuclei or in the sacral cord, and some time later ganglion cells migrate along these nerves to form the myenteric and other plexuses (Kuntz, 1920). In Hirschsprung's disease the unmyelinated fibres contain large amounts of cholinesterase (Niemi, Kouvalainen, and Hjelt, 1961) much more than the normal adult plexus,

which makes it unlikely that they are sympathetic in origin. It is possible that they are the remains of the original parasympathetic outflow which occurred in foetal life and that their orderly replacement by the migrating ganglion cells has not occurred. The appearances in the intermediate zone where neurones can be seen lying at the junction of the unmyelinated branches as well as the similarity of their pattern to the normal innervation suggests that the unmyelinated trunks act as a guide to the migrating neurones. After the ganglion cells have arrived, matured, and produced axons, these trunks may partially disappear leaving only the adult extrinsic nerve supply.

The function of the normal myenteric plexus is presumably to coordinate the peristaltic wave although segmentation can occur in its absence.

The muscle coats of the gut are arranged in two spirals, the inner a tight one, being responsible for cephalic contraction, and the outer, an open one for caudal relaxation. Carey (1921), who originally described the anatomy, considered that a peristaltic wave could occur as a result of this arrangement and no nervous influence was necessary. However, in the animal in which the myenteric plexus has been destroyed by anoxia, it has been noted that the peristaltic wave does not cross the denervated area although segmentation may occur (Hukuhara, Kotani, and Sato, 1961). The plexus is necessary for coordinated peristalsis. This will be impaired not only when ganglion cells are absent but when the anatomy of the plexus is disorganized. The unmyelinated bundles do not appear to have muscular branches so that they cannot have much effect on muscle function. In the absence of ganglion cells the inner coat, which is presumably stronger than the outer coat, appears to be in a state of chronic contraction both in Hirschsprung's disease and in the experimental animal (Hukuhara *et al.*, 1961). However, the function of the gut above the physiological obstruction may be important in the production of clinical symptoms, particularly where the aganglionic segment is short. Hukuhara *et al.* (1961) point out that there is normal gut above the aganglionic segment, and, although the peristaltic wave does not pass, faeces do get through, pushed by those above. In Hirschsprung's disease there is poor innervation for some considerable distance above the contracted segment and therefore the faeces collect in the dilated segment and progress no further.

It would appear that in these cases the migration of neurones from the central nervous system has been incomplete and the resultant plexus disorganized. The clinical picture is produced by the physiological obstruction of the aganglionic segment combined with inefficient peristalsis in the part of the colon proximal to it.

SUMMARY

Two cases of Hirschsprung's disease are described showing a reduction in ganglion cells, many of which are abnormal, the presence of unmyelinated nerve trunks, and a gross disorganization of the myenteric plexus throughout the dilated segment.

The pathogenesis of the condition and its relation to the normal function of the myenteric plexus is discussed.

I am grateful to Mr. I. P. Todd for permission to use his case records and to Dr. Basil Morson for giving me

the material. The photographs were taken by Mr. Peter Crocker.

REFERENCES

- Carey, E. J. (1921). Studies on the structure and function of the small intestine. *Anat. Rec.*, **21**, 189-215.
- Hukuhara, T., Kotani, S., and Sato, G. (1961). Effects of destruction of intramural ganglion cells on colon motility; possible genesis of congenital megacolon. *Jap. J. Physiol.*, **11**, 635-640.
- Kuntz, A. (1920). The development of the sympathetic nervous system in man. *J. comp. Neurol.*, **32**, 173-229.
- Niemi, M., Kouvalainen, K., and Hjelt, L. (1961). Cholinesterases and monoamine oxidase in congenital megacolon. *J. Path. Bact.*, **82**, 363-366.
- Schofield, G. C. (1960). Experimental studies on the innervation of the mucous membrane of the gut. *Brain*, **83**, 490-512.
- Whitehouse, F. R., and Kernohan, J. W. (1948). Myenteric plexus in congenital megacolon. *Arch. intern. Med.*, **82**, 75-111.

The April 1967 Issue

THE APRIL 1967 ISSUE CONTAINS THE FOLLOWING PAPERS

- Hepatic biochemistry KEITH S. HENLEY
- Psychogenic vomiting and hypokalaemia OSCAR W. HILL
- Ocular complications of ulcerative colitis F. A. BILLSON, F. T. DE DOMBAL, G. WATKINSON, and J. C. GOLIGHER
- Observations on the incidence and cause of anaemia in ulcerative colitis T. P. ORMEROD
- Transition from symptomatic diffuse spasm to cardio-spasm PHILIP KRAMER, LAURAN D. HARRIS, and ROBERT M. DONALDSON, JR
- Oesophageal sensitivity to Mecholyl in symptomatic diffuse spasm PHILIP KRAMER, BERTRAM FLESHLER, EDMUND MCNALLY, and LAURAN D. HARRIS
- ABO blood group and secretor status in stomal ulcer M. J. S. LANGMAN, R. DOLL, and R. SARACCI
- Pre- and post-operative symptoms of patients with stomal ulcers J. HOWEL JONES and M. J. S. LANGMAN
- Effects of gastric surgery upon gastric emptying in cases of peptic ulceration K. G. BUCKLER
- Side effects of carbenoxolone sodium: a study of ambulant therapy of gastric ulcer R. D. MONTGOMERY
- An evaluation and comparison of the early and late results of standardized Polya gastrectomy DONALD KEMP
- Use of $^{51}\text{CrCl}_2$ in the diagnosis of protein-losing enteropathy J. A. WALKER-SMITH, A. P. SKYRING, and S. P. MISTILIS
- Recovery, reproducibility, and usefulness of polyethylene glycol, iodine-labelled rose bengal, sulphobromophthalein, and indocyanine green as non-absorbable markers WILLIS C. MADDREY, HAROLD A. SEREBRO, HELEN MARCUS, and FRANK L. IBER
- Cytology of islet tumours and hyperplasias associated with the Zollinger-Ellison syndrome C. CAVALLERO, E. SOLCIA, and R. SAMPIETRO
- Rectal stricture due to ischaemia following ruptured ectopic gestation J. F. CURR
- Epidemiological study of peptic ulcer in the south of India and the ulcer change S. L. MALHOTRA
- Colo-rectal anastomosis with a suturing apparatus in resection of the rectum and colon A. N. RYGICK, G. M. JUCHVIDOVA, V. L. RIVKIN, CH. F. GUREEVA, and JU. M. MILITAREV
- An application of transintestinal intubation to the study of the colon A. TORSOLI, P. ARULLANI, and C. CASALE
- Methods and techniques*
New methods of studying intestinal transit times R. P. ROSSWICK, R. D. STEDEFORD, and BRYAN N. BROOKE
- An improved technique of perfusion of the stomach for the study of gastric secretion in the rat G. A. PISSIDIS and C. G. CLARK
- Gastroenterological Society of Australia

Copies are still available and may be obtained from the PUBLISHING MANAGER,
BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE W.C.1., price 18s. 6d.