have been expressed about the significance of minor histological changes of jejunal biopsy specimens (B.M.J., 1965). Further, it is of interest that one of the two cases with hookworm infestation but without any clinical symptoms and anaemia showed evidence of advanced jejunal mucosal damage (subtotal villous atrophy, Fig. 3). This is contrary to the findings of Sheehy *et al.* (1962), who failed to record intestinal abnormalities in their "asymptomatic" patient with ankylostomiasis. These discrepancies can be explained on the basis of the inherent limitations of intestinal biopsy technique in regard to the sampling of the tissue affected by focal lesions.

Chaudhuri and Saha (1964) stressed the preponderance of eosinophilic infiltration of the lamina propria of the jejunal mucosa in patients with ankylostomiasis. We have failed to substantiate this observation.

The variations in the clinical picture of ankylostomiasis is well known, and while some patients present with evidence of advanced deficiency state, others remain quite healthy. Several factors may be responsible for this. As early as 1931 Rotter suggested that cachexia observed in patients with hookworm infestation could be due to impaired absorption of nutrients, as a consequence of the atrophy of the intestinal mucosa. This statement has support from the studies of Sheehy *et al.* (1962) and of Salem and Truelove (1964). In the present study defective absorption of fat was found in 9 out of 22 patients and D-xylose absorption was poor in only three patients. The patients with absorption defects showed general features of wasting, weakness, diarrhoea, and nutritional deficiency state. The abnormal absorption tests were associated with corresponding structural abnormality in all but three patients. It may therefore be suggested that intestinal alterations in patients with ankylostomiasis influence the clinical picture, and the long-term effects of such abnormalities require further study, with special reference to tropical sprue.

The pathogenesis of intestinal damage in ankylostomiasis is not clearly understood. Parasitism (Sheehy *et al.*, 1962), associated anaemia, and malnutrition (Layrisse *et al.*, 1964) may be involved. In the present study there was no direct correlation between the degree of anaemia and the severity of intestinal damage. Rawson and Rosenthal (1960) reported that iron-deficiency anaemia in adults *per se* did not cause intestinal mucosal abnormalities. It was also noted in the present study that the nutritional status of half of the patients in whom a jejunal biopsy specimen showed evidence of structural abnormality

was similar to that of the other half of the cases who had normal histology of the jejunum. This indirect evidence suggests that anaemia and nutritional factors may not play a decisive part in the pathogenesis of intestinal reaction in hookworm infestation. Obviously there is need for further elucidation of the specific role of the parasite and associated factors in the evolution of structural damage or functional impairment of the small intestine in patients with ankylostomiasis.

Summary

Intestinal changes in 22 patients with hookworm infestation were investigated by fat-balance and D-xylose-absorption tests and intestinal biopsy studies. Jejunal biopsy specimens were abnormal in half of the cases. Increased faecal-fat excretion was present in nine cases and D-xylose absorption was poor in three. These findings indicate that intestinal damage, with associated features of malabsorption syndrome, may be frequently encountered in persons with hookworm infestation.

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Critical Electrical Stimulus which Causes Uterine Pain

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The pain associated with dysmenorrhoea or labour can be provoked by mechanical, chemical, or electrical stimuli applied to the cervix, particularly in the neighbourhood of the internal os uteri. Much of the sensory outflow of the uterus is concentrated in this area, and pain provoked in the cervix is indistinguishable from that provoked in the body of the uterus. The term "uterine pain" will therefore be used to describe pain provoked by an electrical stimulus passed through an electrode in the cervical canal. Pain so caused in a healthy woman usually begins in the midline of the abdomen about

1½ in. (3.8 cm.) above the symphysis pubis. As the stimulus is increased the pain spreads across the lower abdomen, reaching to a line drawn across it just below the level of the anterior superior iliac spines. Pain may also be felt for a short distance down the insides of both thighs. This cutaneous area of reference is innervated by the ilio-hypogastric and ilio-inguinal nerves (T 12, and L 1, and 2) (Theobald, 1941, 1949a, 1949b, 1955).

Uterine pain may be relieved either by infiltrating the parametric tissue with a local anaesthetic (Harttung, 1933; Sutherland, 1937), or by damaging the autonomic nerves in this tissue either with carbolic acid (Doppler, 1925) or with

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an 85% solution of alcohol (Young, 1932-3). It may also be relieved, sometimes permanently, by anaesthetizing the cutaneous area of reference (Theobald, 1936, 1941).

The first accounts concerning the relief of visceral pain by anaesthetizing the cutaneous area of reference were conflicting, the more so because physiologists at that time maintained that sensory nerves did not travel in sympathetic pathways. Daniélopoulou and Hristidé (1923) claimed to have prevented the onset of anginal pain by anaesthetizing the second and third left dorsal nerves, and similar results were obtained by Weiss and Davis (1928). Morley (1931) stated that shoulder pain, provoked during abdominal operations (under regional anaesthesia) by irritating the dome of the diaphragm with a gauze swab, could either be abolished or relieved by anaesthetizing the skin area to which it was referred. On the other hand, direct stimulation of the phrenic nerve was found to cause shoulder pain whether the supraclavicular cutaneous nerves were anaesthetized or ablated by block dissection (Woollard, Roberts, and Carmichael, 1932; Doran and Hall Ratcliffe, 1954). Lewis (1942) and others refused to believe that visceral pain could be relieved by anaesthetizing the cutaneous area of reference.

Theobald (1941, 1946) suggested that the divergence between the results obtained by Morley on the one hand and by Woollard *et al.* on the other was to be attributed to the difference in the intensity of the stimulus they severally applied (see also Doran and Hall Ratcliffe, 1954). Whereas he could relieve the pain of dysmenorrhoea or that of early labour by infiltrating either the ilio-hypogastric and ilio-inguinal nerves or the autonomic nerves in the parametrium with a local anaesthetic, he could not so relieve pain caused by cauterizing the cervical canal with a stick of AgNO_3 , a treatment which proved very successful in the treatment of dysmenorrhoea.

The purpose of this communication is to report a precise method for measuring the electrical stimulus which when passed through an electrode in the cervical canal causes pain, and the degree to which pain so caused can be relieved by infiltrating the ilio-hypogastric and ilio-inguinal nerves with lignocaine (Xylocaine) (Bryant, Menzies, and Theobald, 1964).

Method

Attempts to do this were made some years ago (Theobald, 1949b), but until the advent of the transistor and the consequent development of the battery-operated circuit this was impossible to carry out with complete safety to the patient. The present pulse-generator is housed in a small perspex box, with a switch to turn on the current. It has two controls, one of which regulates pulse width and the other pulse frequency. The circuit is operated by two tapped 22½-volt dry batteries so as to maintain 12 volts at the patient electrodes. As the maintenance of this voltage is dependent on tissue-resistance the voltage applied to the tissues must be adjusted by choosing the appropriate taps.

The circuit is shown in Fig. 1. Transistors tr 1 and tr 2

FIG. 1.—Circuit of the pulse generator.

operate as an on/off switch, so that when the voltage at point *a* falls sufficiently below point *b*, due to the charging of the 2.5 mfd condenser, the electronic switch closes, discharging this condenser through the pulse-width control and simultaneously short-circuiting the two 750-ohm resistances. When the voltage across the condenser has fallen almost to zero the switch reopens, the voltage at point *b* returns to its original level almost instantaneously, and the cycle is repeated. Thus at point *b* a repetitive rectangular pulse recurs with an amplitude of $4\frac{1}{2}$ volts. This pulse switches the power transistor tr. 3, so that the required output voltage is delivered at the patient electrodes. A 1-ohm resistance of high accuracy is connected in series with these electrodes and to the signal terminals of an oscilloscope, so as to show simultaneously the voltage (V), current (I), pulse frequency, and pulse width. Since $I = \frac{V}{R}$ (R represents resistance), the use of a dual-beam oscilloscope makes it simple to deduce the electrical resistance of the cervical tissue, for the same amount of current passes through the one-ohm resistance as through the cervix.

The electrodes.—Many different electrodes have been devised and tried, and the best for the purpose so far made is illustrated in Fig. 2, A. It consists of a nylon rod of 5mm. diameter which is bored through its centre to take a polyethylene catheter for recording uterine activity. On each side is a groove cut to accommodate a piece of watchspring. The electrode is introduced with modified uterine plugging forceps.

FIG. 2.—The two drawings on the left and centre (A) illustrate the watch-spring electrode. The photograph on the right (B) shows the smaller silver-solder electrode. The irregular shadow is retained to indicate its cylindrical shape.

When it is removed the electrode springs fly apart and make firm but limited contact with the cervical walls. If the subject be a nullipara a smaller nylon rod of 4 mm. diameter is used. Wires are led up the grooves, and a bead of silver solder on each side takes the place of the watchspring. The wires are fixed in position with araldite, which also insulates them (Fig. 2, A and B).

Technique

The electrode having been inserted and connected to the box terminals, a rectangular pulse, monitored by an oscilloscope, is passed through the cervix. The amplitude is held as near to 12 volts as possible, and the pulse frequency at about four a second. The pulse width is started at 0.1 msec. and is gradually increased until pain is felt, and then

rapidly reduced to its starting width. This is repeated several times. The point at which pain is appreciated is remarkably constant for each individual on any specific occasion. Pain provoked by the current disappears immediately the current is switched off, and there is no measurable time lag between switching it on and pain apperception.

It was not always possible to maintain precisely the desired amplitude with batteries, especially while varying both the pulse frequency and its width, but it was estimated that a pulse width of 9 msec. at 10 volts caused approximately the same degree of pain or discomfort as one of 7 msec. at 15 volts. The most precise information was obtained when the voltage and pulse frequency were kept constant and only the pulse width was altered.

The pulse width at which pain was first appreciated having been determined, the ilio-hypogastric and ilio-inguinal nerves on either side were infiltrated with some 10 ml. of a 1% solution of lignocaine containing 0.01 mg. adrenaline in each ml. It takes at least 10 minutes for this infiltration to become fully effective. After this has occurred the electrical stimulus is again passed through the cervix.

Results

The resistance of the cervical tissue was found to be very low and usually varied between 50 and 150 ohms. The current passing through the tissue was of the order of from 50 to 150 mA, and tended to fall after the machine had been running for a few minutes, presumably owing to polarization, which could be prevented by frequent reversal of the current.

We have made 15 studies in nine women, five of whom were referred because of severe dysmenorrhoea, for which they had all undergone various and unavailing treatments, including, in one woman, presacral neurectomy. Women who suffer no pelvic discomfort during the menstrual cycle can tolerate a rectangular pulse of 15 volts, with a frequency of five a second and a width of 10 msec. On the other hand, each of the five women who had severe dysmenorrhoea felt pain when the pulse width was 0.4 msec. or less. On one occasion the voltage had to be lowered to 5 before the pain associated with a pulse width of 0.2 msec. could be tolerated. After the above-mentioned nerves had been infiltrated with lignocaine the patients could usually tolerate a fivefold, and sometimes even a twentyfold, increase in the pulse width before pain was again appreciated.

Discussion

It has been shown that the passage through the cervix uteri of a precise electrical stimulus causes uterine pain, and that the required intensity varies more than fiftyfold from patient to patient. Pain so caused, up to a certain intensity, can be completely relieved by infiltrating the ilio-hypogastric and ilio-inguinal nerves with a local anaesthetic, but beyond this intensity the pain recurs and is referred to the same area of skin, although it is completely anaesthetic. This allows the concept of a measurable value for true uterine pain, and one also for the cutaneous nerve impulses which "summate" with those from the uterus.

Dysmenorrhoea, however caused, would appear to be associated with a lowered threshold to uterine pain, but it by no means follows that the woman is more sensitive than normal to pain arising in other parts of her body. It has been claimed that dysmenorrhoea can be cured either by temporarily anaesthetizing or by overstimulating the nerve pathways concerned (Theobald, 1941, 1946, 1955, 1965), and the few cases we have studied would suggest that it is possible to raise the electrical threshold of the uterus to pain (see also Lenzi and Andreani, 1955). We conclude that we have provided a measurable basis for the clinical postulates made a quarter of a century ago.

Summary

Pain indistinguishable to the woman from dysmenorrhoea can be provoked by chemical, mechanical, or electrical stimuli applied to the endocervix. Pain so caused, up to a certain intensity, can be relieved by anaesthetizing the ilio-hypogastric and ilio-inguinal nerves. A precise method for measuring the effective electrical stimulus to the cervix which causes pain, and the amount by which it can be increased before anaesthetization of the ilio-hypogastric and ilio-inguinal nerves becomes ineffective for its relief, has been described. This pain comes almost immediately the effective current is switched on, and disappears immediately it is switched off.

Women with dysmenorrhoea have a much lower threshold to cervical pain thus caused than do women who have painless periods. In the former group the threshold to such pain may be increased twentyfold by anaesthetizing the above-named nerves. This technique is valuable in the study of uterine pain, and the results indicate where skin electrodes should be placed in order to induce labour with an electric current.

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