Hookworm disease and duodenal ulceration

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EDITORIAL COMMENT This study suggests that hookworm disease does not predispose an individual to develop duodenal ulceration.

The first documented case of duodenal ulcer reported from India (White, 1892) had shown on necropsy a perforated duodenal ulcer and large number of hookworms near the lesion, and White suggested that possibly those parasites were a causative factor in duodenal ulceration in tropical countries. In a group discussion on peptic ulcer held in 1959 under the auspices of the Indian Council of Medical Research, the possible association of hookworm infestation and duodenal ulcer was pointed out by many observers, and it was felt that in regions where hookworm infestation was common duodenal ulcer was seen more frequently.

Hookworms attach themselves to the mucosa of the jejunum, duodenum, and upper part of the ileum and thrive on the host's blood, producing iron-deficiency anaemia. How could they induce duodenal ulceration? The secretion of gastric acid and the resistance of the duodenal mucosa are two important factors in the genesis of ulcer. Chatterjea (1963) noted that although gastric acid secretion, as assessed by a fractional test meal, was reduced in iron-deficiency anaemia, in the presence of hookworms the acid secretion was stimulated. Floch and Thomassen (1963), using submaximal histamine stimulation, frequently found depression of acid output in these cases. There is hardly any report on the quantitative assessment of gastric acid secretion in hookworm anaemia.

Hookworm anaemia may be associated with radiological abnormalities of prominent mucosal folds, irritability and spasm of the duodenum (Hodes and Keefer, 1945), and these changes are thought to be suggestive of 'duodenitis' (Ostrow and Resnick, 1959), but the relationship of these changes to duodenal ulceration is not clear.

The present investigation deals with the radiological appearances of the stomach and duodenum and the assessment of gastric acid secretion with the augmented histamine test (Kay, 1953) in hookworm infestation associated with anaemia.

MATERIAL AND METHODS

Radiological investigation was done with non-flocculable barium in 55 cases of hookworm disease. All were adult males and had haemoglobin values less than 8 g. %.

The hookworm ova load was determined by Stoll's method (1923) by which stools collected during 24 hours were weighed. Three g. of the faeces was added to 45 ml. of 0.1 N NaOH in a thick glass tube and thoroughly mixed to make a uniform suspension. This was facilitated by adding a few glass beads, closing the mouth with a rubber stopper, and shaking vigorously. Exactly 0.15 ml. of the emulsion was removed by a measuring pipette and placed on a large slide, 7.5 × 5 cm.; a cover slip, measuring 22 × 40 mm., was then put over it. All the eggs in the preparation were counted, including a few which had escaped below the cover slip. The ova count per day was calculated as the number of eggs in the preparation × 100 × weight of a 24-hour collection of faeces. An ova count per 24 hours was preferred because an ova count per gram of faeces would not take into account the amount of faeces passed by the patient.

Forty-one patients with hookworm disease were included for the assessment of acid secretion. To evaluate precisely the significance of alterations in gastric acid output, 22 normal subjects and seven cases of anaemia due to blood loss from causes such as bleeding piles were also investigated. The normal subjects had no abdominal symptoms and belonged to the same geographical area and socioeconomic status as the cases of anaemia. Most of these came to the hospital for minor surgical procedures and all of them had haemoglobin values over 13 g. %.

The mean age was 28.9 years (S.D. 9.31) in normals; 35.9 years (S.D. 10.73) in hookworm anaemia and 33.2 years (S.D. 10.6) in other cases of anaemia. The mean weight was 48.4 kg. (S.D. 5.8) in normals, 44.8 kg. (S.D. 5.9) in cases of hookworm disease and 46.2 kg. (S.D. 5.5) in cases of iron-deficiency anaemia due to bleeding piles.

The mean haemoglobin value was 4.46 g. (S.E. 0.24) in cases of hookworm disease and 8.32 g. (S.E. 0.99) in cases of anaemia not due to hookworm.

The technique of the augmented histamine test was the same as that described by Marks (1961) using histamine acid phosphate in a dose of 0.04 mg./kg. body weight under antihistaminic cover. The acidity was determined

by titrating the gastric contents with freshly prepared 0·1N sodium hydroxide using phenolphthalein as indicator (pH 8·3 to 8·5) as already described elsewhere (Goyal, Gupta, and Chuttani, 1966). The coefficient of variation (Hill, 1961) in duplicate tests was 9·16% for maximal acid output (M.A.O.) and 16·6% for basal acid output (B.A.O.).

RESULTS

RADIOLOGICAL ABNORMALITIES Fifty-five patients with hookworm anaemia were investigated radiologically. Twenty-three of these complained of abdominal pain which was usually sharply localized in the epigastrium but had an indefinite relationship with food. Periodicity of the pain was unusual. Only one out of 55 showed duodenal deformity and diverticulum. Commonly observed changes were prominence of mucosal folds in the stomach and duodenum. There was no significant difference in the radiological appearances in patients with or without epigastric pain. However, irritability of the duodenum was more frequently seen in cases with abdominal pain (Table I).

GASTRIC ACID SECRETION The patients with hookworm disease secreted a mean of 27·98 ml. of gastric

TABLE I
RADIOLOGICAL ABNORMALITIES IN STOMACH AND DUODENUM
IN HOOKWORM DISEASE

	Cases with Abdominal Pain	Cases without Pain	All Cases
<i>Oesophagus</i>			
Normal	23 (100%)	32 (100%)	55 (100%)
<i>Stomach</i>			
Normal	14 (61%)	19 (59%)	33 (60%)
Prominent mucosal folds	8 (35%)	12 (38%)	20 (36%)
Pyloric spasm	1 (4%)	1 (3%)	2 (4%)
<i>Duodenum</i>			
Normal	16 (70%)	23 (72%)	39 (71%)
Prominent mucosal folds	4 (17%)	7 (22%)	11 (20%)
Irritable bulb	3 (13%)	1 (3%)	4 (7%)
Deformity with diverticulum	0 (0%)	1 (3%)	1 (2%)
Totals	23 (100%)	32 (100%)	55 (100%)

TABLE II GASTRIC ACID SECRETION (MEAN $\pm$ S.E.) UNDER BASAL CONDITIONS AND AFTER MAXIMAL HISTAMINE STIMULATION							
Group	No. of Cases	B.A.O./Hour		M.A.O./Hour		$\frac{\text{B.A.O.}}{\text{M.A.O.}} \times 100$	
		Volume (ml.)	Acid (mEq.)	Volume (ml.)	Acid (mEq.)		
Normals	22	59·73 $\pm 5·29$	3·01 $\pm 0·30$	153·38 $\pm 7·97$	15·01 $\pm 0·96$	20·24 $\pm 1·40$	
Hookworm anaemia	41	27·98 $\pm 1·98$	1·06 $\pm 0·12$	85·90 $\pm 6·92$	7·57 $\pm 0·82$	14·96 $\pm 0·94$	
Iron-deficiency non-hookworm anaemia	7	32·84 $\pm 4·62$	1·17 $\pm 0·21$	86·14 $\pm 11·13$	7·72 $\pm 1·05$	15·04 $\pm 2·19$

FIG. 1. Gastric acid secretion under basal conditions and after histamine stimulation. Each dot represents an individual patient.

juice with 1·06 mEq. HCl per hour under basal conditions. This was significantly less than that in normal subjects ($P < 0·05$). The acid secretion in hookworm anaemia was not significantly different from that in cases of anaemia due to blood loss caused otherwise than by hookworm infestation (Table II).

After maximal histamine stimulation, patients with hookworm anaemia secreted a mean of 7·57 mEq. HCl per hour which was significantly less than 15·01 mEq. produced by normal subjects ($P < 0·05$) and was similar to that seen in cases of iron-deficiency anaemia not due to hookworms.

The mean value of basal to maximal acid output in normal subjects was 20·24% (S.E. 1·40) compared with 14·96% (S.E. 0·93) in cases of hookworm anaemia and 15·04% (S.E. 2·19) in those of anaemia without hookworms. The difference in this ratio between normals and anaemic subjects was significant ($P < 0·05$ in both instances).

OVA LOAD AND HAEMOGLOBIN LEVEL There was no correlation between ova output per 24 hours in the faeces and the haemoglobin level. The coefficient of correlation (r) was 0.127 ($P > 0.05$, not significant).

OVA LOAD AND ACID SECRETION The coefficient of correlation (r) between the ova count per 24 hours and the maximal acid output was 0.023 ($P > 0.05$, not significant).

HAEMOGLOBIN LEVEL AND ACID SECRETION There was no correlation between the haemoglobin level and the acid output. The coefficient of correlation (r) between haemoglobin level and basal acid output was 0.132 ($P > 0.05$, not significant) and between haemoglobin and maximal acid output 0.065 ($P > 0.05$, not significant).

ABDOMINAL PAIN AND ACID SECRETION Of 41 subjects with hookworm anaemia, whose acid secretion was investigated, 11 complained of upper abdominal pain or discomfort. The gastric acid secretion in these cases was compared with those without pain but with comparable haemoglobin and ova load (Table III). The acid secretion values after histamine stimulation were significantly higher in patients with abdominal pain than those without pain ($P > 0.05$).

TABLE III

ACID SECRETION IN CASES OF HOOKWORM DISEASE WITH AND WITHOUT ABDOMINAL PAIN

Component of Acid Secretion	Cases with Abdominal Pain	Cases without Pain	Value for P
B.A.O. (mEq./h.)	Mean 1.07 S.E. $\pm$ 0.22	0.81 $\pm$ 0.14	> 0.05
M.A.O. (mEq./h.)	Mean 10.44 S.E. $\pm$ 2.23	5.43 $\pm$ 0.78	< 0.05
B.A.O. $\times$ 100	Mean 11.78 S.E. $\pm$ 1.99	14.98 $\pm$ 1.69	> 0.05

COMMENTS

The significance of the prominent mucosal folds and spasm and irritability of the duodenum in the absence of duodenal ulceration on radiological examination is an unsettled issue. Some observers (Ostrow and Resnick, 1959) considered them as suggestive of 'duodenitis', while others (Fraser, Pitman, Lawrie, Smith, Forrest, and Rhodes, 1964) have refrained from applying a pathological term to the radiological appearances. Beck, Kahn, Lacerte, Solymar, Callegarini, Geokas, and Phelps (1965) have shown the existence of duodenitis as a distinct clinical pathological entity without radiological

abnormalities. However, there is no doubt that in many subjects prominent duodenal folds are associated with gastric acid hypersecretion (Fraser and his colleagues, 1964) particularly under the basal state (Marks, Selzer, Louw, and Bank, 1961; Chuttani and Goyal, 1966). Some of these may lead on to duodenal ulcer a few years later (Whitby, 1958).

Some cases of hookworm anaemia, particularly advanced ones, show increased gastro-duodenal rugosity on radiological examination (Hodes and Keefer, 1945). Thirty per cent of our patients showed prominence of mucosal folds or irritability or spasm of the duodenum. But there was no evidence of hypersecretion of gastric acid in these cases. In fact, the acid production was reduced, both under basal conditions and after histamine stimulation. The depression of basal acid output, being out of proportion to the depression of histamine, stimulated acid secretion. These observations are in contrast with those of Raju and Narielvala (1965) who reported radiological evidence of 'duodenitis' in all their cases of hookworm infestation without iron-deficiency anaemia. They also found basal hypersecretion of acid in these cases and suggested that 'duodenitis' and basal hypersecretion produced by the hookworms might lead on to duodenal ulceration. Our observations appear to indicate that hookworms, by producing iron-deficiency, in most cases they infest also cause the stomach to produce less acid and thus reduce the chances of duodenal ulceration. The cases of hookworm anaemia with increased gastro-duodenal rugosity are not comparable with the reported cases of prominent gastro-duodenal mucosal folds associated with hypersecretion of gastric acid (Ostrow and Resnick, 1959; Whitby, 1958).

Leslie and Tovey (1955) did not find a higher incidence of duodenal ulcer in cases of hookworm infestation compared with those without hookworms. Only one case out of 55 showed duodenal ulcer in this study. Conversely, investigations of proved duodenal ulcer cases have not shown a higher incidence of hookworm infestation than was found in cases without ulcer (Leslie and Tovey, 1955; Raghavan, 1962).

The cause of abdominal pain in hookworm disease is not clear. There was no difference in the prevalence of duodenal abnormalities on radiological examination in cases with and without abdominal pain. However, an irritable duodenal bulb was more often seen in patients who complained of abdominal pain. It would be of interest to note that patients with hookworm disease with abdominal pain secreted significantly more acid after maximal histamine stimulation than those without pain. The significance of this finding is not clear at present.

SUMMARY

Radiological investigation was done in 55 patients with hookworm anaemia. Only one showed duodenal deformity and diverticulum. Radiological abnormalities of prominence of mucosal folds and pyloric spasm were seen in 40% of the cases and similar changes in the duodenum were seen in 30% of these cases. There was no difference in the radiological abnormalities in cases with and without abdominal pain.

Basal acid secretion and acid output after maximal histamine stimulation as well as the percentage of maximal secretory capacity of the stomach under basal conditions was reduced in cases of hookworm anaemia. These patients with abdominal pain produced significantly more acid after histamine stimulation than those without pain.

It is argued from these findings that favourable circumstances for the development of duodenal ulcer do not exist in cases with hookworm anaemia.

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REFERENCES

- Beek, I. T., Kahn, D. S., Lacerte, M., Solymar, J., Callegarini, U., Goekas, M. C., and Phelps, E. (1965). 'Chronic duodenitis'. A clinical pathological entity? *Gut*, 6, 376-383.
- Chatterjea, J. B. (1963). Some aspects of iron-deficiency anemia in India. In *Iron Metabolism*, pp. 219-239, edited by F. Gross. An international symposium sponsored by Ciba. Springer, Berlin.
- Chuttani, H. K., and Goyal, R. K. (1966). Assessment of gastric acid secretion. *Lancet*, 1, 819-820.
- Floch, M. H., and Thomassen, R. W. (1963). Gastritis in hookworm disease. *Amer. J. dig. Dis.*, 8, 128-134.
- Fraser, G. M., Pitman, R. G., Lawrie, J. H., Smith, G. M. R., Forrest, A. P. M., and Rhodes, J. (1964). The significance of the radiological finding of coarse mucosal folds in the duodenum. *Lancet*, 2, 979-982.
- Goyal, R. K., Gupta, P. S., and Chuttani, H. K. (1966). Gastric acid secretion in Indians, with particular reference to the ratio of basa to maximal acid output. *Gut*, 7.
- Hill, A. B. (1961). *Principles of Medical Statistics*, 7th ed. p. 90. The Lancet, London.
- Hodes, P. J., and Keefer, G. P. (1945). Hookworm disease, a small intestinal study. *Amer. J. Roentgenol.*, 54, 728-742.
- Indian Council of Medical Research (1959). Proceedings of the group discussion on *Problem of Peptic Ulcer*, pp. 16-72. New Delhi.
- Kay, A. W. (1953). Effects of large doses of histamine on gastric secretion of HCl: an augmented histamine test. *Brit. med. J.*, 2, 77-80.
- Leslie, H., and Tovey, F. I. (1955). Relation of hookworm infestation with duodenal ulcer. *J. Indian med. Ass.*, 25, 548-551.
- Marks, I. N. (1961). The augmented histamine test. Editorial. *Gastroenterology*, 41, 599-603.
- , Selzer, G., Louw, J. H., and Bank, S. (1961). Zollinger-Ellison syndrome in a Bantu woman, with isolation of gastrin-like substance from the primary and secondary tumors. I. Case report. *Gastroenterology*, 41, 77-86.
- Ostrow, J. D., and Resnick, R. H. (1959). Hyperchlorhydria, duodenitis and duodenal ulcer: a clinical study of their interrelationships. *Ann. Intern. Med.*, 61, 1303-1328.
- Raghavan, P. (1962). Epidemiology and clinical behavior of peptic ulcer in Bombay, India. *Gastroenterology*, 42, 130-143.
- Raju, S., and Narielvala, F. M. (1965). Study of gastric acid secretion in hookworm duodenitis. *Gut*, 6, 540-544.
- Stoll, N. R. (1923). Investigations on the control of hookworm disease. XV. An effective method of counting hookworm eggs in feces. *Amer. J. Hyg.*, 3, 59-70.
- Whitby, J. (1958). Dyspepsia with negative X-ray findings. (Abstr.) *Brit. med. J.*, 2, 313.
- White, J. C. (1892). Perforating ulcer of the duodenum. *Ibid.*, 1, 1359.