Intestinal biopsy in childhood*

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The current policy in this department is to utilize small intestinal biopsy early in the course of investigation of children with suspected malabsorption (Townley, 1971). Also, we have not been unduly hesitant to perform intestinal biopsy in research studies, after the procedure and its risks have been explained to parents (Barnes and Townley, 1973). Others have raised doubts about the safety (Partin and Schubert, 1966; Sheldon and Tempany, 1966) and the ethical aspects of intestinal biopsy in childhood, and we are glad to justify our current policy. We here report our experience with intestinal biopsy in 1172 children carried out in the 4-year period 1968–72, and also describe the technique we use.

Biopsy technique

Preparation of patient. Any patient with a significant degree of malnutrition is given intramuscular vitamin K the day before biopsy is to be done to correct any prothrombin deficiency consequent to malabsorption.

Most biopsies are carried out on outpatients. Parents are given printed sheets which outline what the procedure involves and what the risks are. The sheets also list symptoms which might indicate the presence of a complication of biopsy and parents are urged to contact the department should any of these symptoms develop after the procedure. They are requested to give the child only clear fluids by mouth on the morning biopsy is to be done. Patients are brought to the hospital usually between 8 and 10 a.m. They receive premedication of oral quinalbarbitone (Seconal) and metoclopramide (Maxolon), in the doses shown in Table I, about 1 hour before the planned time of biopsy.

Many school-age children can tolerate biopsy without sedation. In those who seem temperamentally suitable, we omit quinalbarbitone but

TABLE I
Premedication oral doses for intestinal biopsy

Age (mth)	Quinalbarbitone* (mg)	Metoclopramide (ml)
6–12	50–75	2–3
12–24	100	3–5
Over 24	150	5–10

*Dosage is reduced for undersized or anaemic children.

spray the pharynx with 10% lignocaine solution a few minutes before starting the procedure.

Parents of children who have been given a sedative are encouraged to stay with the child until he falls asleep. They may then either go off for refreshments or, if they specially desire, stay with the child while the biopsy is performed.

Biopsy instrument and tubing. A Watson paediatric capsule* with a port of 2 mm diameter is used. We have modified our capsule by slightly enlarging the hole at the base to accommodate a particular type of cardiac catheter tubing (Kifa, red) which has the advantage of being radio-opaque, readily guided, and resistant to biting.

Biopsy procedure. The patient is supine with his arms held by an assistant to 'splint' his head. The operator depresses the patient's tongue, and pushes the biopsy capsule into the pharynx. The capsule is then advanced by pushing in more tubing, until some resistance is felt. The position of the capsule and tubing is then checked fluoroscopically. Occasionally the capsule will be found already in the duodenum, more commonly in the pyloric region, but at times it will be in the fundus with a coil of tubing. In the last event, the tubing is withdrawn until the capsule is at the cardia, the patient is rolled semiprone onto his right side, and the tube advanced again.

*In the 'Personal practice' series of articles authors are invited to give their own views on some current practical problem.

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Usually within a few minutes of the capsule reaching the pyloric antrum it will pass into the duodenum. Its passage may be accelerated by gently pushing the tubing at the mouth, and by manual pressure on the abdominal wall just below the greater curvature.

When the capsule reaches the fourth part of the duodenum the tubing is cleared by the slow injection of a few ml air. Very gentle intermittent suction is then applied until a drop or two of intestinal fluid appears at the nozzle of the syringe. Vigorous suction on the 20 ml syringe is then applied to 'fire' the spring-loaded knife. The capsule is then withdrawn.

Specimens. The biopsy specimen is spread out on nylon mesh with the mucosal surface uppermost and examined with a dissecting microscope. It may be divided into two or more pieces to allow for estimation of disaccharidase levels, as well as for histological examination.

A drop of the intestinal juice from the tubing is examined microscopically for the presence of vegetative forms of *Giardia lamblia*.

The results of dissecting microscopy of the mucosal specimen and of microscopy of the intestinal juice are conveyed to the parents. If a diagnosis of coeliac disease or giardiasis has been made, appropriate management can be initiated before the patient leaves the hospital. The patient is usually able to leave within 1 hour of biopsy being performed.

Patients. In a 4-year period starting from October 1968, 1172 patients underwent 1247 intestinal biopsies for diagnostic reasons. The patients were all referred for investigation of suspected malabsorption, failure to thrive, or chronic or recurrent diarrhoea. Repeat biopsies were carried out in children in whom results of the first biopsy were of dubious diagnostic significance.

The numbers of patients in different age ranges were: under 6 months 101, 6 to 12 months 199; 12 to 24 months 473, over 24 months 474. The youngest patient was 3 weeks old.

The 1172 patients included 37, all over 4 years of age, in whom a previous diagnosis of coeliac disease had been made elsewhere without confirmation by biopsy. These patients had all been treated with a gluten-free diet for months or years. They were all placed on a normal diet for at least 4 weeks before undergoing biopsy.

Disaccharidase estimations. A portion of the biopsy specimen was used to determine lactase,

sucrase, isomaltase, and maltase levels in 830 of the 1172 patients, using a modification of the method of Dahlqvist (1964).

Complications

Specimens were obtained in less than 15 minutes in over 90% of cases. The average screening time was less than 1 minute. Only one serious complication occurred. This was melaena in a 14-month-old boy who was admitted to hospital for observation. His bleeding settled spontaneously and transfusion was not required. One other child was admitted to hospital for observation because of several episodes of vomiting after his biopsy: his symptoms subsided uneventfully within 24 hours of the procedure.

In one 8-year-old boy a specimen was not obtained because the capsule could not be passed through the pylorus. Our usual routine had been altered in this instance, in that biopsy was attempted just before the patient was due to have his tonsils removed, when he had been premedicated with morphine and atropine. A specimen was obtained readily from this boy at a later date after the more usual premedication.

Diagnostic yield

Diagnoses made by histological examination or microscopy of duodenal juice are shown in Table II. Abnormalities of disaccharidases, excluding those attributable to coeliac disease or giardiasis, are shown in Table III. 'Partial sucrase deficiency'

TABLE II
Abnormal microscopical findings in 1172 patients

Giardiasis	154
Coeliac disease	123
Intestinal lymphangiectasis	4
Tropical sprue	1
Abnormal fat accumulation in mucosal epithelium	1
Total	283 (24% of 1172)

TABLE III
Disaccharidase abnormalities in 830 patients excluding patients with coeliac disease or giardiasis

Isolated lactase deficiency	27
Generalized disaccharidase depression	28
Sucrase-isomaltase deficiency (virtual absence)	6
Partial sucrase-isomaltase deficiency (sucrase less than lactase)	51
Total	112 (10% of 1172)

refers to children whose mucosal lactase level in contrast to the usual pattern, exceeded the sucrase level. The clinical significance of this finding will be discussed elsewhere (J. D. Mitchell and R. R. W. Townley, unpublished observations). Thus an abnormal finding was uncovered in a total of 34% of the 1172 patients.

Of the 37 patients previously diagnosed elsewhere as having coeliac disease without confirmation by biopsy, 13 had mucosal changes of coeliac disease, but 24 had normal histological findings.

Discussion

The diagnostic value of any investigation must be weighed against the discomfort and risks to the patient. Our experience here has been that intestinal biopsy can be carried out in childhood with little or no distress to patients, and will provide useful specific diagnostic information in a significant proportion. We found an abnormal result in 34% of our patients, and in addition, the negative findings in 24 of the 37 patients previously diagnosed on clinical grounds as having coeliac disease were of obvious importance. Anderson, Gracey, and Burke (1972) studied a similar group of patients by biopsy after at least 6 weeks on a normal diet and found a comparable proportion (15/22) with normal mucosal histology.

We cannot be certain that a diagnosis of coeliac disease has been finally excluded in the 24 patients with normal biopsy findings only 4 weeks after the reintroduction of dietary gluten, since others have found that histological abnormalities may not become apparent for up to 2 years (Meeuwisse, 1970; J. R. Hamilton, personal communication, 1971). However, we suspect, as did Anderson *et al.* (1972), that the majority of our patients will not develop mucosal changes with time. We intend to repeat investigation of these patients in the future. Even in the remaining patients with normal findings, the results were often helpful to reassure parents, and to diminish the need for other investigations.

Our current approach to investigation of children with possible malabsorption, using intestinal biopsy early, and usually as an outpatient procedure, has evolved with our increasing conviction of its safety and the recognition that biopsy provides a degree of diagnostic sensitivity superior to other tests of intestinal absorption. We, like others (Benson, Kowlessar, and Sleisenger, 1964; MacDonald, Dobbins, and Rubin, 1965) have seen a number of children with normal fat balance results but with mucosal changes quite characteristic of coeliac disease. Many centres perform barium studies

routinely in the investigation of suspected malabsorption in childhood, but we have found such studies to be much less rewarding than intestinal biopsy. Since the average amount of radiation we use in performing intestinal biopsy is less than that involved in a barium meal and follow-through, we feel that biopsy should precede barium studies and that it will often provide information that renders further radiological investigation unnecessary.

We regard the risk of intestinal biopsy as comparable to that of intravenous pyelography, but regard its diagnostic return as being greater.

Our approach to investigation of children with malabsorption has been endorsed by parents whose children have been investigated previously elsewhere. Often such investigation has involved admission to a large hospital for weeks or even months. These parents are naturally biased, but without exception have been grateful for the rapid and precise diagnostic information which intestinal biopsy has provided. Many have asked why similar facilities were not available in the other centres.

We have been at a loss to answer this question but we hope that the results of our experience reported here might dispel some of the antipathy to intestinal biopsy in childhood. Our students and residents may be disappointed that patients with coeliac disease are rarely seen around the wards these days, but the patients and their families do not share this disappointment.

REFERENCES

- Anderson, C. M., Gracey, M., and Burke, V. (1972). Coeliac disease. Some still controversial aspects. *Archives of Disease in Childhood*, **47**, 292.
- Barnes, G. L., and Townley, R. R. W. (1973). Duodenal mucosal damage in 31 infants with gastroenteritis. *Archives of Disease in Childhood*, **48**, 343.
- Benson, G. D., Kowlessar, O. D., and Sleisenger, M. H. (1964). Adult celiac disease with emphasis upon response to the gluten-free diet. *Medicine (Baltimore)*, **43**, 1.
- Dahlqvist, A. (1964). Method for assay of intestinal disaccharidases. *Analytical Biochemistry*, **7**, 18.
- MacDonald, W. C., Dobbins, W. O., and Rubin, C. E. (1965). Studies of the familial nature of celiac sprue using biopsy of the small intestine. *New England Journal of Medicine*, **272**, 448.
- Meeuwisse, G. W. (1970). Diagnostic criteria in coeliac disease. (Discussion, European Society for Paediatric Gastroenterology.) *Acta Paediatrica Scandinavica*, **59**, 461.
- Partin, J. C., and Schubert, W. K. (1966). Precautionary note on the use of the intestinal-biopsy capsule in infants and emaciated children. *New England Journal of Medicine*, **274**, 94.
- Sheldon, W., and Tempany, E. (1966). Small intestinal peroral biopsy in coeliac disease. *Gut*, **7**, 481.
- Townley, R. R. W. (1971). Diagnosis and treatment of coeliac disease in childhood. *Medical Journal of Australia*, **1**, 696.

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