Hydroxyproline excretion in infantile gastroenteritis

R. H. J. BEGENT AND H. P. LAMBERT

From the Department of Communicable Diseases, St. George's Hospital, Blackshaw Road, London SW17

Summary

Total hydroxyproline/creatinine ratio (THP:Cr) was measured in random urine specimens from 18 infants with gastroenteritis. THP:Cr was sometimes increased during the acute phase of the illness and the reasons for this are discussed. Seven patients failed to thrive after the acute phase and THP:Cr was low in all of these. The test appears to be a sensitive indicator of the onset of failure to thrive, and it is suggested that it may be of value in the management of these patients.

Infantile gastroenteritis is sometimes followed by persistent diarrhoea and failure to thrive. This is often attributed to malabsorption caused by carbohydrate intolerance (Clarke et al., 1964; Burke et al., 1965; Lifshitz et al., 1971; Bartrop and Hull, 1973). The condition may persist for weeks or months with growth failure and cachexia. Management usually involves the administration of various synthetic diets, and accurate assessment of the response to these would be of use in deciding their therapeutic value in each individual case.

Hydroxyproline is largely a breakdown product of collagen, and its rate of excretion is used as a measure of the rate of collagen turnover. Total hydroxyproline excretion has been shown to be a sensitive indicator of growth rate in normals (Younoszai et al., 1967; Zorab et al., 1970; Wharton et al., 1973) and various types of growth failure (Whitehead, 1965; Wharton et al., 1972; Teller et al., 1973).

The purpose of this investigation was to measure total hydroxyproline excretion, expressed as total hydroxyproline:creatinine ratio (THP:Cr), in cases of failure to thrive after gastroenteritis and to determine whether it is a useful indicator of progress.

Methods

Failure to thrive was defined as persistence of diarrhoea and failure to gain weight for 10 days after the onset of gastroenteritis in infants. THP:Cr was measured serially in random samples of urine from 18 inpatients with gastroenteritis. Thirteen patients were studied in the acute phase; 11 of these recovered uneventfully, but two failed to thrive. A further five patients failed to thrive but were not examined in the acute phase. Each patient was compared with a normal control whose age did not differ from his own by more than 15%. Patients and controls abstained from meat and gelatin for 24 hours before samples were collected. The specimens were placed in store at −20°C within two hours of voiding.

Urinary total hydroxyproline was measured by the method of Goverde and Veenkamp (1972). A hot air oven with a fan giving uniform internal temperature was used for the hydrolysis stage. The means of duplicate total hydroxyproline measurements were taken, and these were in the range 0·17–30·7 mmol/l. Standard deviations of the means were 0·2–6 mmol/l, mean 0·38 mmol/l. Urinary creatinine was measured by the method of Bonsnes and Tausky (1945) modified for the Technicon AutoAnalyzer. THP:Cr was expressed as millimoles hydroxyproline per mole of creatinine.

Results

THP:Cr in nine of the 13 patients seen in the acute phase rose to levels exceeding the 90th centile for normals established by Wharton et al. (1972). The peak occurred four to nine (median 5) days from the onset of symptoms. When the highest values seen in the 13 patients were compared with their controls, using the paired t test, they were found to be significantly higher (p < 0·01). The individual values and ages of this group are shown in Table 1.
Table 1  Aages and levels of urinary total hydroxyproline/creatinine ratio (THP:Cr) in patients with gastroenteritis seen during the acute phase

<table>
<thead>
<tr>
<th>Name</th>
<th>Sex</th>
<th>Age</th>
<th>Urinary THP:Cr (mmol/mol)</th>
<th>Control 90th centile for normals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>RM</td>
<td>F</td>
<td>1 mth</td>
<td>665</td>
<td>362</td>
</tr>
<tr>
<td>TJ</td>
<td>F</td>
<td>4</td>
<td>404</td>
<td>43</td>
</tr>
<tr>
<td>MG</td>
<td>F</td>
<td>5</td>
<td>462</td>
<td></td>
</tr>
<tr>
<td>RP</td>
<td>M</td>
<td>6</td>
<td>268</td>
<td>238</td>
</tr>
<tr>
<td>TP</td>
<td>M</td>
<td>9</td>
<td>235</td>
<td></td>
</tr>
<tr>
<td>MD</td>
<td>F</td>
<td>14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LH</td>
<td>M</td>
<td>14</td>
<td>735</td>
<td></td>
</tr>
<tr>
<td>PM</td>
<td>M</td>
<td>18</td>
<td>330</td>
<td></td>
</tr>
<tr>
<td>SH</td>
<td>M</td>
<td>24 yr</td>
<td>95</td>
<td></td>
</tr>
<tr>
<td>NL</td>
<td>F</td>
<td>24</td>
<td>202</td>
<td>356</td>
</tr>
<tr>
<td>MA</td>
<td>M</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MH</td>
<td>M</td>
<td>3</td>
<td>67</td>
<td>85</td>
</tr>
<tr>
<td>KU</td>
<td>F</td>
<td>6</td>
<td>102</td>
<td>104</td>
</tr>
</tbody>
</table>

Conversion: SI to traditional units—THP:Cr 1 mmol/mol = 1.15 mg/g

THP:Cr was found to be lower than the paired controls in every case of failure to thrive, the difference being statistically significant using the paired t test (p < 0.01). THP:Cr was also lower than the 10th centile for normals (Wharton et al., 1972) in each case. The individual values and ages of this group are shown in Table 2. The lowest values were recorded between five days and 10 weeks (median 16 days) after the onset of gastroenteritis.

Table 2  Urinary total hydroxyproline/creatinine ratios (THP:Cr) in patients failing to thrive after gastroenteritis and later in the same patients when thriving

<table>
<thead>
<tr>
<th>Name</th>
<th>Age at onset of symptoms</th>
<th>Lower limit of normal THP:Cr (mmol/mol) for age</th>
<th>THP:Cr for failure to thrive</th>
<th>Thriving</th>
</tr>
</thead>
<tbody>
<tr>
<td>JO</td>
<td>7 days</td>
<td>434</td>
<td>217, 338</td>
<td>712</td>
</tr>
<tr>
<td>JH</td>
<td>2 weeks</td>
<td>573</td>
<td>377, 388</td>
<td>1887, 1380</td>
</tr>
<tr>
<td>WH</td>
<td>8</td>
<td>408</td>
<td>322</td>
<td>494, 611, 527, 1210</td>
</tr>
<tr>
<td>MF</td>
<td>3 months</td>
<td>303</td>
<td>46</td>
<td>485</td>
</tr>
<tr>
<td>VV</td>
<td>3</td>
<td>303</td>
<td>75</td>
<td>273*, 234*</td>
</tr>
</tbody>
</table>

*These specimens were taken three months after the first when the lower limit of normal THP:Cr would be 186 mmol/mol.

Conversion: SI to traditional units—THP:Cr: 1 mmol/mol = 1.15 mg/g

In five patients, THP:Cr was measured during the period of failure to thrive and later when the patient was gaining weight. The levels were significantly higher in the convalescent group (p < 0.05 using the paired t test). Figure 1 shows two cases of failure to thrive in which high readings during the acute phase were followed by low readings at the start of the period of failure to thrive.

In two patients, THP:Cr was measured just before they started to thrive. The ratios were low during failure to thrive and rose to normal when only a small weight gain had occurred (Fig. 2).

Figure 3 shows THP:Cr in 19 normal South London children superimposed on the 10th and 90th
serial specimens should be collected at the same time of day. The normal values for Bristol children (Wharton *et al.*, 1972) were estimated on random specimens of urine.

It is often difficult to interpret small weight changes in children failing to thrive because of minor alterations in fluid balance. It is necessary to observe progressive weight gain over several days before it can be confidently stated that growth is restored. THP:Cr has potential advantages in giving early evidence of restored growth because it gives an indication of growth rate at a point in time. This is illustrated in Fig. 2 where the THP:Cr ratios were low during failure to thrive and rose to normal when there was still clinical doubt whether growth was restored on the basis of weight recordings. At this time one patient was only 25 g above the weight on admission (1800 g) and 100 g above the lowest weight. The other patient was 125 g above the weight on admission (4800 g) and 150 g above the lowest weight. The investigation may also be valuable in the early recognition of patients who fail to thrive after gastroenteritis, as shown by the low THP:Cr illustrated in Figure 1.

Formal and repeated tests of intestinal function are often impossible or inappropriate in these frail infants. Treatment is largely empirical, and several different synthetic diets may have to be tried in an individual patient before growth is restored. The results suggest that THP:Cr, being a more sensitive indicator of growth rate than weight measurements, may enable earlier selection of an effective diet.

The pathogenesis of failure to thrive after gastroenteritis is not well understood. A reduction in protein synthesis or an increase in catabolism might be important. Although we did not measure 24-hour hydroxyproline excretion, it seems likely that the low THP:Cr is caused by reduced hydroxyproline excretion. Since hydroxyproline is largely a breakdown product of collagen, the results suggest no significant increase in the catabolism of this protein. A failure of synthesis seems more likely.

High levels of THP:Cr were sometimes seen in the acute phase of gastroenteritis and are not easily explained. It seems unlikely that tissue collagen could be broken down fast enough to provide this rapid rise and fall in hydroxyproline excretion. The catabolism of hydroxyproline-containing plasma proteins, such as the complement component C1q (Reid *et al.*, 1972), seems a more plausible explanation. Alternatively, reduced creatinine excretion would result in increased THP:Cr. We have not yet explored these possibilities. In any event, the findings give useful background knowledge when following individual patients with gastroenteritis from the start of their illness.

---

**Fig. 2** Two patients showing low levels of THP:Cr when failing to thrive followed by a rise to normal before a definite weight gain is seen. The 10th centiles for normals are taken from Wharton *et al.* (1972).

---

**Discussion**

The use of random specimens of urine has obvious practical advantages over 24-hour collections in infants. THP:Cr in 24-hour specimens of urine has been shown to be a more accurate measure of growth rate than total hydroxyproline alone (Allison *et al.*, 1966), and further studies have shown a reasonable correlation of this ratio in random specimens with that in 24-hour collections (Howells *et al.*, 1967; Younoszai *et al.*, 1969). However, Mautalen (1974) has pointed out that hydroxyproline excretion and THP:Cr in adults is subject to diurnal variation and has questioned the validity of measurements on random specimens. Reviewing this controversy, Wharton (1974) noted that the variations in THP:Cr in children were small enough to make measurements on single specimens adequate for clinical purposes. As an added safeguard, he suggested that...
Hydroxyproline excretion in infantile gastroenteritis

Failure to thrive after gastroenteritis is often a serious condition and management may be hampered by difficulties in assessment of progress. It is suggested that THP:Cr may be a useful indicator of progress and that a larger study is justified.

We are grateful to the Medical Research Committee of St. George’s Hospital which supported this work, and to the Department of Chemical Pathology for performing the creatinine assays.

We also thank the nursing staff of St. George’s Hospital, the staff of the Patrick Doody Clinic, who collected most of the specimens, and not least the children and their parents.

References


Younoszai, M. K., Andersen, D. W., Filer, L. J., Jr.,


Reports and Bulletins prepared by the Association of Clinical Biochemists

The following reports and bulletins are published by the Association of Clinical Biochemists. They may be obtained from The Publishing Department, British Medical Journal (ACB Technical Bulletins), B.M.A. House, Tavistock Square, London WC1H 9JR. Overseas readers should remit by British Postal or Money Order.

SCIENTIFIC REPORTS (price £1.00/$2.00 each)

3 Automatic dispensing pipettes: an assessment of 35 commercial instruments September 1967 P. M. G. BROUGHTON, A. H. GOWENLOCK, G. M. WIDDOWSON, and K. A. AHLQUIST

4 An evaluation of five commercial flame photometers suitable for the simultaneous determination of sodium and potassium March 1970 P. M. G. BROUGHTON and J. B. DAWSON

SCIENTIFIC REVIEWS (price £1.00/$2.00 each)

1 The assessment of thyroid function March 1971 F. V. FLYNN and J. R. HOBBES

2 Renal function tests suitable for clinical practice January 1972 F. L. MITCHELL, N. VEALL, and R. W. E. WATTS

3 Biochemical tests for the assessment of fetoplacental function May 1975 C. E. WILDE and R. E. OAKLEY

4 Test of exocrine pancreatic function March 1977 A. H. GOWENLOCK

TECHNICAL BULLETINS (price £1.00/$2.00 each)

9 Determination of urea by AutoAnalyzer November 1966 RUTH M. HASLAM

11 Determination of serum albumin by AutoAnalyzer using brom cresol green October 1967 B. E. NORTHAM and G. M. WIDDOWSON

13 An assessment of the Technicon Type II Sampler Unit March 1968 B. C. GRAY and G. K. MCGOWAN

14 Atomic absorption spectroscopy: an outline of its principles and a guide to the selection of instruments May 1968 J. B. DAWSON and P. M. G. BROUGHTON

15 A guide to automatic pipettes (2nd edition) June 1968 P. M. G. BROUGHTON

16 A guide to automation in clinical chemistry May 1969 P. M. G. BROUGHTON

17 Flame photometers: a comparative list of 17 instruments readily available in Britain August 1969 P. WILDE

19 Spectrophotometers: a comparative list of low-priced instruments readily available in Britain May 1970 C. E. WILDE and P. SEWELL

20 Quantities and units in clinical biochemistry June 1970 P. M. G. BROUGHTON

21 Filter fluorimeters: A comparative list of 18 instruments September 1970 H. BRAUNSBERG and S. S. BROWN

22 Bilirubin standards and the determination of bilirubin by manual and technicon AutoAnalyzer methods January 1971 BARBARA BILLING, RUTH HASLAM, and N. WALD

23 Interchangeable cells for spectrophotometers and fluorimeters September 1971 S. S. BROWN and A. H. GOWENLOCK

24 Simple tests to detect poisons March 1972 B. W. MEADE et al.

25 Blood gas analysers May 1972 K. DIXON

26 Kits for enzyme activity determination September 1972 S. B. ROSALKI and D. TARLOW

27 Assessment of pumps suitable for incorporation into existing continuous flow analytical systems November 1972 A. FLECK et al.

28 Routine clinical measurements of transferrin in human serum September 1973 K. DIXON

29 Control materials for clinical biochemistry (5th edition) September 1973 J. F. STEVENS

30 Notes on the quality of performance of serum cholesterol assays September 1973 S. S. BROWN

31 Determination of uric acid in blood and in urine July 1974 R. W. E. WATTS

32 A survey of amino acid analysers readily available in the United Kingdom September 1974 J. E. CARLYLE and P. PURKISS

33 Definitions of some words and terms used in automated analysis November 1974 A. FLECK, R. ROBINSON, S. S. BROWN, and J. R. HOBBES

34 Measurement of albumin in the sera of patients January 1975 LINDA SLATER, P. M. CARTER, and J. R. HOBBES


36 Factors influencing the assay of creatinine November 1975 J. G. H. COOK
Hydroxyproline excretion in infantile gastroenteritis.

R H Begent and H P Lambert

_ J Clin Pathol_ 1977 30: 630-634
doi: 10.1136/jcp.30.7.630

Updated information and services can be found at:
http://jcp.bmj.com/content/30/7/630

**Email alerting service**

These include:

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/