Stool output and composition in the chronic non-specific diarrhoea syndrome

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SUMMARY Stool output and composition were studied in 7 children with chronic, non-specific diarrhoea syndrome and the results were compared with those of children with malabsorption due to cystic fibrosis or to bacterial overgrowth syndrome, and with stools from controls. Daily quantities of stool, fat, and total bile acids were normal in patients with chronic, non-specific diarrhoea syndrome. Faecal sodium concentration was high compared with that of controls or patients with cystic fibrosis. The extractable water phase of stools was appreciably increased in patients with chronic, non-specific diarrhoea syndrome and contained 50% of the total stool bile acids; this was also the case in patients with bacterial overgrowth syndrome. It is suggested that a secretory state of the large-bowel due to mucosal exposure of large quantities of bile salts in the extractable water phase may be contributory to the diarrhoea of chronic, non-specific diarrhoea syndrome.

The chronic non-specific diarrhoea syndrome (CNDS) is one common cause of prolonged diarrhoea in early childhood. Several clinical features including the age at onset, the normal physical development, and a positive family history can indicate this condition, but the diagnosis is essentially a negative one, based on the exclusion of other conditions able to produce chronic diarrhoea.

The cause of the syndrome is not clear. Abnormal intestinal motility, genetic predisposition, low fat intake, and prostaglandin-mediated diarrhoea have each been implicated.

The main characteristic of CNDS is the frequency and consistency of stools, but little is known about the quantity or composition of them.

We have investigated the stool output in a group of children with CNDS and compared it with the output in age-matched controls and in children with various gastrointestinal diseases. Our aim was to establish the composition of stools particularly the water, electrolyte, and bile acid excretion and distribution.

Patients

Twenty-four children were studied.

Patients with CNDS (n = 7). Their ages ranged between 18 months and 12 years. Each had 3–8 loose-to-watery bowel movements a day which had lasted from several weeks to 4 years’ duration.

Abdominal pain was a troublesome feature in 5 of them. A family history of functional intestinal disturbances was obtained in all 24 of them. Physical growth and development were normal. Routine blood tests were normal. Stools did not show pathogenic bacteria or parasites. Oral lactose tolerance test, fat balance studies, small intestinal biopsies, upper gastrointestinal follow-through, and barium enema studies were all normal.

Controls (n = 6). These were children aged between 8 and 15 years, who had been referred for investigation of abdominal pain or failure to thrive but in whom bowel movements were normal.

Cystic fibrosis (n = 6). These were aged between 10 months and 16 years; they had steatorrhoea and chronic respiratory disease, and sweat electrolyte tests had been positive.

Bacterial overgrowth syndrome (n = 5). These patients were aged between 6 months and 4 years. They had been diagnosed by culture of the upper small-bowel fluid. Two children had an underlying immune deficiency disorder and 2 others had undergone intestinal resection in the neonatal period.

Methods

Complete 72 hours’ dietary intake histories were obtained and analysed by the dietician using standard
methods. Special reference was made to the total caloric, fat, and fibre intake.

Stool collections were performed in each patient over a 72-hour period. Stool was collected free of urine. In small children this was achieved by using inverted polyethylene-lined disposable napkins and urine collectors. Stools were immediately frozen and stored at -20°C.

Stool collections were thawed, weighed, and homogenised. Duplicate 2 g aliquots of homogenate were then centrifuged at 14 000 g for one hour at 4°C in an international refrigerated centrifuge (IEC). The supernatant obtained was considered to be the extractable water phase of stool. Supernatants and pellets were weighed individually. Recovery of the initial 2-g aliquot ranged between 94.5 and 105%. Uncentrifuged homogenate samples, supernatants, and pellets from each stool collection were analysed. The concentration of sodium was measured by flame photometry after digestion with concentrated nitric acid (Analar). Total bile acids were extracted⁷ and determined enzymatically using 3-hydroxy steroid dehydrogenase.⁸ The recovery of an internal standard (¹⁴C cholic acid, Sigma Chemical Co, St Louis, Mo.) ranged between 89.7 and 95%. The recovery rate of total bile acids in the extractable water phase plus pellet ranged between 84.8 and 107% in the uncentrifuged corresponding homogenate and did not differ in the various groups of patients studied.

Quantitative stool fat excretion, measured gravimetrically⁹ in faecal homogenate, was compared with fat intake and the coefficient of fat absorption calculated using the formula: fat intake—fat output × 100/fat intake.

Results

Clinical data and stool output of patients are shown in Table 1. Although patients with CNDS had a greater number of loose, sometimes watery stools a day, the total daily quantity of stool per kg of body weight was comparable with that of controls and was far smaller than for the patients with cystic fibrosis or bacterial overgrowth syndrome. Fat output and the coefficient of fat absorption of CNDS patients were similar to those of controls. Children with cystic fibrosis or bacterial overgrowth syndrome presented with severe steatorrhoea. Total faecal bile acids were slightly increased in CNDS patients but were not significantly different from controls. Patients with cystic fibrosis or bacterial overgrowth had increased faecal bile acid losses. Stool sodium concentration was high in patients with CNDS and in conditions associated with bacterial overgrowth.

The composition of the extractable water phase is shown in Table 2. Stools of patients with CNDS had a high percentage of extractable water (28.7 ± 6.2%). This was exceeded only by the diarrhoeal stools of those with bacterial overgrowth syndrome

### Table 1 Clinical features and stool composition in the various groups of patients

<table>
<thead>
<tr>
<th>Groups</th>
<th>Age (years)</th>
<th>Faecal output (g/kg per 24h)</th>
<th>Faecal fat (g/24h)</th>
<th>Coefficient of fat absorption (%)</th>
<th>Faecal bile acids (µmol/kg per 24h)</th>
<th>Sodium (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls (n = 6)</td>
<td>4.7 ± 5.4</td>
<td>5.2 ± 3.8</td>
<td>3.4 ± 1.6</td>
<td>94.3 ± 4.6</td>
<td>16.6 ± 3.3</td>
<td>1.5 ± 0.6</td>
</tr>
<tr>
<td>CNDS (n = 7)</td>
<td>5.0 ± 4.2</td>
<td>6.2 ± 4.1</td>
<td>2.8 ± 1.1</td>
<td>94.6 ± 4.0</td>
<td>23.0 ± 10.1</td>
<td>2.6 ± 1.5</td>
</tr>
<tr>
<td>Cystic fibrosis (n = 6)</td>
<td>7.4 ± 5.8</td>
<td>9.9 ± 3.5*</td>
<td>16.1 ± 6.8***</td>
<td>66.9 ± 13.8***</td>
<td>74.5 ± 29.1***</td>
<td>3.9 ± 2.1*</td>
</tr>
<tr>
<td>Bacterial overgrowth syndrome (n = 5)</td>
<td>2.3 ± 1.2</td>
<td>23.8 ± 17.1***</td>
<td>6.0 ± 4.4</td>
<td>74.8 ± 20.0</td>
<td>41.1 ± 18.3***</td>
<td>1.2 ± 0.4</td>
</tr>
</tbody>
</table>

Values are mean ±SD.

*P < 0.05, **P < 0.01, ***P < 0.001 compared with controls.

CNDS = chronic non-specific diarrhoea syndrome.

### Table 2 Composition of extractable water phase obtained by centrifugation of 2 g stool homogenate

<table>
<thead>
<tr>
<th>Groups</th>
<th>Quantity</th>
<th>Bile acids</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ml/2 g homogenate</td>
<td>%</td>
</tr>
<tr>
<td>Controls (n = 6)</td>
<td>0.24 ± 0.1</td>
<td>10.7 ± 6.6</td>
</tr>
<tr>
<td>CNDS (n = 7)</td>
<td>0.54 ± 0.1**</td>
<td>28.7 ± 6.2***</td>
</tr>
<tr>
<td>Cystic fibrosis (n = 6)</td>
<td>0.20 ± 0.1</td>
<td>9.2 ± 6.2</td>
</tr>
<tr>
<td>Bacterial overgrowth syndrome (n = 5)</td>
<td>1.0 ± 0.9*</td>
<td>40.9 ± 31.2*</td>
</tr>
</tbody>
</table>

Values are mean ±SD.

*P < 0.05, **P < 0.01, ***P < 0.001 compared with controls.

CNDS = chronic non-specific diarrhoea syndrome.
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(40.9 ± 31.2%). Bile acid content of the extractable water phase was high in CNDS (2.58 ± 2.0 μmol) accounting for 50.0 ± 17.5% of the total bile acid in the respective stool homogenate. This unusual distribution of bile acid was an outstanding feature of the group of CNDS patients. A similar tendency was also observed in patients with bacterial overgrowth syndrome (28.6 ± 9.5%) but to a lesser degree. Patients with cystic fibrosis had a much higher daily total faecal bile acid output (74.5 ± 29.1 μmol/kg) and concentration (3.9 ± μmol/g faeces). Yet, the distribution between the solid and extractable water phase was similar to that of the controls.

The correlation between the total daily stool output and the respective calculated quantity of extractable water within the various conditions is shown (Fig. 1). It is evident that the daily quantity of extractable water is not directly related to the total daily stool output. In controls the quantity of water present in the extractable water phase is low, the ratio of extractable water per total daily stool being 0.19. This is also the case in patients with cystic fibrosis (ratio = 0.10). Patients with CNDS have a high ratio of 0.32 but the diarrhoea differs quantitatively from the secretory type associated with bacterial overgrowth in which both daily stool losses and amounts of extractable water are very high (ratio = 0.52).

![Graph 1: Daily total faecal and extractable water phase output in the various groups of patients. Asterisk indicates statistical significance of total stool output; P indicates comparison of extractable water.](image1)

![Graph 2: Stool bile acid excretion expressed as concentrations (μmol/g of homogenate and extractable water phase) and total daily loss (μmol/kg per 24h homogenate and extractable water) in the various groups of patients. Statistical comparison as for Fig. 1.](image2)
The bile acid concentration and daily outputs in stool homogenates and extractable water are compared in Fig. 2. It is evident that the bile acid concentration of the extractable water in CNDS (1.26 ± 1.0 μmol/ml) even exceeds conditions with faecal bile acid loss such as bacterial overgrowth syndrome (0.32 ± 0.1 μmol/ml) or cystic fibrosis (0.48 ± 0.1 μmol/ml). The daily output of bile acid in extractable water of CNDS patients (11.7 ± 7.1 μmol/kg per day) is high and resembles cases associated with bacterial overgrowth syndrome (11.0 ± 5.0 μmol/kg per day).

We tried to establish whether a direct correlation exists between the daily quantity of extractable water and its bile acid content. No such correlation was found in controls, or in patients with cystic fibrosis or CNDS. Only stools of patients with bacterial overgrowth syndrome showed a trend towards a positive correlation between the two variables (r = 0.79) but the numbers were too small to reach statistical significance. No significant correlation was found between bile acid concentration and stool output or sodium concentration in any of these conditions.

The dietary intakes of patients were analysed and compared, special emphasis being given to fat and fibre intake. The food intake calculated per kg each day in the various groups of children is shown in Table 3. No significant differences were noted.

**Discussion**

The separation of stools into a solid pellet and water by centrifugation had been attempted previously in normal adults, in patients with ileal disease, and in children after operation for Hirschsprung's disease and the technique is well known. Our results in normal children regarding quantity and compartmentalisation of stool into pellet and extractable water are similar.

We found that children with CNDS have normal daily quantities of stools but moderately increased electrolyte and bile acid concentration compared with controls. The most remarkable finding was the significantly increased quantity of extractable water which contained 50% of the total faecal bile acid output.

Data on the physical state of bile acids in stools are taken from studies in adults. Under normal conditions, bile acids are strongly absorbed to solids. Normal found only 10–20% of bile acids present in the extractable water phase separated by centrifugation. Patients with ileal disease and faecal bile acid loss were found to have appreciable amounts of bile acids in the supernatant ranging between 0.7 and 18 mmol, whereas controls had no supernatant at all.

Our study indicates that high concentrations and daily outputs of bile acid are not necessarily distributed in the extractable water phase nor are they associated with watery diarrhoea. This is best illustrated by the group of patients with cystic fibrosis.

Increased faecal passage of water and electrolytes is often found in cases of malabsorption due to bacterial overgrowth. There is the production of known secretagogues such as bacterial toxins and metabolites of bile salts and fats. Associated increased aboral myoelectric activity probably enhances the abnormal stool losses.

Certain similarities between patients with bacterial overgrowth syndrome and CNDS were observed. Both groups had watery diarrhoea, high extractable water content, and comparable daily bile acid output present in the extractable water phase. However the total daily stool and bile acid loss in CNDS patients was only slightly raised and did not reach the levels present in patients with bacterial overgrowth syndrome.

The causal relationship between the quantity and bile acid content of water phases in the individual patient remains unresolved. It seems that in patients with bacterial overgrowth syndrome or CNDS the colon is exposed to large quantities of bile salts present in a soluble form and therefore easily accessible to the mucosal surface. Bile acids are known inhibitors of sodium and water absorption in both the small- and large-intestine. The lack of direct correlation between bile acid concentration and sodium and water loss indicates that perhaps a specific component of bile salts rather than the total bulk may be determinant. Previous studies have indicated that the total amount of chenodeoxycholic acid entering the colon, irrespective of its physical state, is important in the diarrhoea of ileal dysfunction.

A secretory epithelium of the distal small-bowel with increased sensitivity to bile acid perfusion has been reported in 6 adults with the irritable bowel syndrome, a condition considered the counterpart...
of CNDS in children. This is further supported by increased levels of adenylate cyclase and (Na\(^+\)K\(^-\)) ATP-ase in children with toddler’s diarrhoea.\(^{17}\) It seems therefore that the abnormal distribution of bile salts in the colonic content of patients with CNDS induces an abnormal handling of water and electrolyte by the mucosa of the large-bowel\(^{18}\) and consequently in the production of loose watery stools. The cause for these alterations is not clear. Dietary fibres are known to have a profound effect on daily stool weight and transit time.\(^{19}\) The capacity of stools to hold water is also directly related to the quantity of the unabsorbed fibre content.\(^{10}\) Assuming that a low daily fibre intake is responsible for the alteration of stool composition in CNDS, we compared the dietary intake of these patients with that of controls and patients with gastrointestinal diseases, and found them equal. The digestibility of dietary fibres was not determined and the possible influence of colonic bacterial metabolism on fibre breakdown was not considered.\(^{20}\)

Further efforts will have to be directed towards a better understanding of altered bile salt excretion in patients with CNDS.

References


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