

Title: Study of Acute Diarrhea in Thais

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Objective:

1. To define histologic changes in the upper small bowel during acute diarrhea.
2. To measure the degree of malabsorption occurring during acute diarrhea, and the extent of recovery 1-3 months later.

Methods:

Twenty-one adult male patients with acute diarrhea were admitted from the emergency room of Chulalongkorn Hospital to the renal-metabolic study ward of the same institution between 11 March and 29 June 1966. After an initial evaluation, the patients were kept at bed-rest, fed adlibitum, and started on supportive measures: intravenous fluids, and antispasmodic drugs if abdominal cramping was present. Antibiotics were not used, although many of the patients had taken them before admission. The mean duration of diarrhea after admission was 2 days. A bacteriologic diagnosis was made in 10 patients as follows: Shigella sp. 5, Salmonella sp. 4, and Vibrio cholera, El tor, 1. Stool examination for intestinal parasites was positive in 14 of the 21 patients (5 patients with two parasites): Hookworm 6, Entamoeba histolytica cysts 5, trophozoites 2, Trichuris 3, Ascaris 2, and Giardia 1.

The following studies were attempted during the first few days after admission: small intestine biopsy, 25 g xylose excretion test, Schilling test (vitamin B₁₂ absorption), fecal fat analysis (during a daily dietary supplement of 75 g of butter fat), and gastric analysis after maximal histamine stimulation. On admission, blood was drawn for B-carotene, total cholesterol, albumin and globulin, and CBC. Eleven patients returned 4-11 weeks later for follow-up studies. Jejunal biopsies were carried out with a Crosby or a Carey capsule after x-ray verification of the location of the capsule. All specimens were fixed in 10% neutral buffered formalin and examined with a stereomicroscope, magnification x 20. Tissue was embedded in paraffin and sections cut at 7 microns. Hematoxylin and eosin and MacCallum-Goodpasture stains were done in all cases. Azure-eosin and PAS stains were done on selected material. All biopsies were examined without knowledge of the clinical situation and reviewed later with clinical information available.

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Results:

In 16 of the 21 patients an adequate jejunal biopsy was obtained during the acute illness. The villus pattern as observed through the dissecting microscope did not differ from the Thai norm. All specimens displayed to some degree the histologic abnormalities previously described in Thai people¹. In addition, 6 of the 17 patients had considerable edema of the villus tips and polymorphonuclear leucocyte infiltration of the gut epithelium. No correlation could be shown between the presence of these acute changes and the type of agent demonstrated by bacteriologic methods.

Six of the patients had large numbers of eosinophils in the lamina propria. One of the six also had acute inflammatory changes near the villus tips. All of these patients also had intestinal parasites. A comparison made after knowledge of the stool bacteriologic findings suggested that the intestinal lymphoid follicles were much more prominent in patients with Salmonella sp. than in those with Shigella sp. or, those in whom no isolation was made.

No bacteria were seen in the gut epithelium or lamina propria in any of the patients. Follow up biopsies from 4 patients failed to reveal significant changes when compared to their biopsies obtained during acute diarrhea.

The 5-hr. urine d-xylose excretion in 20 patients during acute diarrhea averaged 4.56 ± 1.21 g. In all patients at follow-up, the excretion was significantly higher, 6.06 ± 1.29 g. When the data from the 11 following-up patients are paired with their values in the acute period, the excretion is likewise significantly higher ($p=0.05$).

Because of the difficulties of collecting a twenty-four hour urine specimen during acute diarrhea, the Schilling test was carried out satisfactorily in only 7 patients. In 4, excretion was below 7.5%, a value generally considered the lower limit of normal. Follow-up studies were carried out in two patients and were normal in both (34%, 21%).

Fecal fat excretion was measured in 15 patients acutely, and averaged 3.10 ± 2.16 g/day. Only one patient excreted over 5 g/day (7.7 g), the upper limit of normal. Follow-up studies were carried out in 5 subjects, and averaged 1.89 ± 7.72 g/day. None were above 5 g/day. When the data from the 5 patients who were studied during both the acute and follow-up period are paired, there is no significant difference between the two sets of observations.

Paired serum B-carotene values were available from the acute (74.9 ± 35.8 μ g%) and follow-up (103.0 ± 27.7 μ g%) periods in seven patients. This increase noted during follow-up was not significantly higher. Paired serum cholesterol values in the same number of patients were, however, significantly greater ($P=0.01$) during the following-up period (191 ± 29 mg%) when compared to the value obtained acutely (154 ± 29 mg%). Serum albumin, available in acute and follow-up patients in only 5 instances, averaged 3.33 ± 0.68 g% acutely and 4.31 ± 87 g% in the follow-up period, a significantly higher value ($P=0.01$).

No difference was noted in paired values between mean serum globulin in the acute phase (2.57 ± 0.45 g%) and in the follow-up period (2.45 ± 0.62 g%).

Hemoglobin was normal (over 13.0 g%) in all 21 patients acutely except in three who had values of 11.0, 12.5, and 12.6 g%. Follow-up values in the nine patients in whom hemoglobin was measured were all normal.

Gastric analysis following maximal histamine stimulation was carried out in twelve patients. In five, maximum acid production was 20 units or less in the acute period. Only one patient in the follow-up period, originally with low acid production was re-tested, and he was found to have normal acid production.

Discussion:

The dissecting microscope appearance of the jejunal mucosa was not strikingly different from that seen in normal Thais. No change was noted between acute and recovery biopsy specimens in patients so studied. The enteritis observed with the standard light microscope is qualitatively similar to that described earlier in human biopsy material. We were unable to establish morphologic criteria which could distinguish various etiologic agents. In contrast to various experimental diarrheas, we did not observe granulomatous lesions, epithelial ulceration or tissue invasion by bacteria. The absence of the latter, however, cannot be established with assurance by the techniques employed. Fluorescent antibody techniques might well be more fruitful.

Moderate impairment of xylose absorption was noted in many of the patients during the acute period of diarrhea, however, all had returned to normal at the time of follow-up. This finding confirms other work² on acute diarrhea done in East Pakistan, with the exception that persistent xylose malabsorption was noted in a few of the patients in the latter study. Vitamin B₁₂ absorption, impaired in 4 out of 7 patients in the acute phase of diarrhea, is generally considered to be a reflection of ileal absorptive capacity. Since most bacterial diarrheas (cholera excepted) are thought to affect the terminal ileum and colon, it is not surprising that impaired Vitamin B₁₂ absorption occurred with such frequency. Fecal fat excretion was normal in all but one of 15 patients tested during acute diarrhea, and was likewise normal in all 5 tested at follow-up. This test is a rather crude measure of intestinal function, and becomes impaired only when major gastro-intestinal disease processes, such as celiac sprue or cystic fibrosis of the pancreas, are present. The absence of steatorrhea in acute diarrhea is thus consistent with the mild nature of the disease in our patients.

Low gastric acid production in acute diarrhea is previously unreported. Unfortunately, follow-up studies were not available to find out if gastric secretion returned to normal. The validity of this observation, furthermore, is lessened by the fact that fluoroscopic placement of the nasogastric tube to ensure complete collections was not done, and that small amounts of blood were present in some specimens, which might also account for a lowered acid production. Nevertheless, the observation is quite interesting since gastric acid is known to be a major bactericidal defense mechanism and if achlorhydria can be shown to exist before diarrhea occurs it, may point to a new mechanism in the pathogenesis of bacterial diarrhea.