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October 1986

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PREFACE

The Specialized Bibliography Series is a part of the larger effort to facilitate exchange of information and to establish an information network in the field of diarrhoeal diseases -- an effort being carried out by the International Diarrhoeal Disease Information Service and Documentation Centre (DISC) of the ICDDR,B. The present issue, the eleventh of the series, includes citations of 368 papers (172 abstracted) on chronic diarrhoeal diseases. This is a subject of high current importance, and the reason for selecting the topic is explained in the Introduction.

This is a selective bibliography on the topic. The bibliography was compiled from the resources available at the ICDDR,B Library/DISC, and it is possible that inadvertent omissions may have occurred.

We hope the present bibliography will contribute towards generating greater interest and awareness in this field, and will facilitate user access to existing knowledge. Copies of the articles cited in this bibliography are available from the ICDDR,B Library/DISC to interested persons/organizations. We will consider this attempt successful if the bibliography helps diarrhoeal disease researchers and practitioners' interest.

M Shamsul Islam Khan

Head, Library and Publication Branch
International Centre for Diarrhoeal
Disease Research, Bangladesh

ACKNOWLEDGEMENTS

The activities, services and programs of the International Diarrhoeal Disease Information Service and Documentation Centre are supported by the International Development Research Centre, Canada and the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B). ICDDR,B is supported by countries and agencies which share its concern about the impact of diarrhoeal diseases on the developing world. Current major donors giving assistance to ICDDR,B are: Arab Gulf Programme, Australia, Bangladesh, Belgium, Canada (Canadian International Development Agency, the International Development Research Centre, and World University Service of Canada), the Ford Foundation, Japan, Norwegian Agency for International Development, Saudi Arabia, Swedish Agency for Research Co-operation with Developing Countries, Switzerland, United Kingdom, United Nations Children's Fund, United Nations Development Programme, United States Agency for International Development, and World Bank.

Publication of this bibliography was made possible by a special grant from the International Development Research Centre, Canada.

CONTENTS

INTRODUCTION

Considerable research efforts have been devoted to the field of diarrhoeal disease over the past decades, providing new knowledge on the etiology, pathophysiology, effective management and prevention of this illness. This has led to substantial reduction in diarrhoea-related morbidity and mortality. Alongwith the breakthrough made with acute diarrhoea, the associated problems in persistent diarrhoea have surfaced. Current research is yet to evolve appropriate conclusions on its definition, clinical picture, and physiopathology. An array of terminologies, such as chronic diarrhoea, persistent diarrhoea, intractable diarrhoea, prolonged diarrhoea, post-gastroenteritis syndrome, tropical sprue, weanling diarrhoea, are presently used to identify this illness. Its duration varies from two weeks to four weeks, according to the nature of definition used.

The incidence rate and the magnitude of the havoc caused by persistent diarrhoea on public health in the developing countries have not been quantitatively estimated. The etiologies of persistent diarrhoea in the more developed western countries are few, their mechanisms and management being already known, although the cause and pathophysiology of this condition in children of poor households in less developed countries are definitely more intricate, being inter-webbed with several factors, which call for further research. Preliminary findings from current studies indicate that some factors, such as repeated attacks of acute diarrhoea, bloody mucoid type of diarrhoea, inappropriate use of antibiotics, cow's milk protein allergy, etc., may contribute significantly to the degree of severity and the duration of diarrhoeal episodes. The role of fecal contamination, repeated infections, infestation by multiple parasite loads and even malnutrition need to be ascertained. Community-based prospective research on cohorts of children suffering from acute diarrhoea may lead to a better understanding of its cause and may assist in working out prevention measures and appropriate cures. Many studies on this subject are already underway.

The purpose of this bibliography is to collate information on relevant literature and to provide researchers in this field with a ready reference source book so that a planned approach can be devised for research on this important clinical problem.

A M Molla, MD, PhD

International Centre for Diarrhoeal
Disease Research, Bangladesh

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The Author Section contains citations arranged alphabetically by the first author and then by the title of paper. Co-authors' names also appear in alphabetical order alongwith a cross-reference to the first author (e.g. Adams FG see Lamont CM). This will facilitate a search by co-authors' names.

Efforts have been made to present abstracts with all available information regarding the study's nature and objective, method(s) used, and the major findings and conclusions.

The bibliography is in English. A title in parenthesis indicates that the paper is in another language.

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Adler M, Quenon M, Schoutens-Serruys E. [The coprologic examination. Its interpretation in cases of chronic diarrhea]. Acta Gastroenterol Belg 1981 Jan-Feb;44(1-2):56-61

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Agarwal DK see Agarwal VK

Agarwal RG see Sarin LR

Agarwal VK, Agarwal DK, Srivastva AC, Gupta SC, Nigam DK, Pandey RC. Some observations of chronic diarrhoea - laboratory, radiological and histological study. II. Indian Pediatr 1979 Sep;16(9):791-6

This study was undertaken to assess the various radiological, histological and biochemical changes in chronic diarrhoea. Twenty-five children with chronic diarrhoea and another 25 normal children, admitted to the Sarojini Naidu Children Hospital, were selected for this study. Some 16 cases (64%) had moderate anemia, while mild anemia was detected in 4 cases (16%). Anemia in 3 diarrhoea cases (12%) and 2 normal cases (8%) showed normal levels of hemoglobin. Ascaris and Ankylostoma were observed in 24% of diarrhoea and 16% of normal cases respectively. In stools of 64% of the cases, one or other types of bacteria were grown. Escherichia coli was the commonest organism (40%), followed by Klebsiella and Salmonella 16% and 8% respectively. In 44% cases of chronic diarrhoea, the radiological picture of the chest was suggestive of primary complex. The high incidence of primary complex was found because chronic diarrhoea lowered the general body resistance and made the child more susceptible to various infections. Total serum protein and albumin showed low levels. Slight rise in gamma globulin and fall in beta globulin fractions were observed. Serum calcium and phosphorous levels were low in all the cases. Steatorrhea was present in 92% of those with chronic diarrhoea. Sixteen cases (64%) of chronic diarrhoea had D-xylose values less than 0.75 g/5 h. About 84% of chronic cases showed malabsorption (mucosal edema). Most cases (72%) had abnormal jejunal histology. In 64% of the cases, Giardia was isolated from jejunal fluid. The findings were in close conformity with the findings of other studies.

Aggarwal KC see Walia BNS

Ahmed MU, Sarker NC, Haque E, Hasan MA. Chronic diarrhoeal diseases in adults (a preliminary report). Bangladesh Med Res Counc Bull 1976 Jun;2(1):8-11

Akhter MH, Sabir M, Bhide NK. Possible mechanism of antidiarrhoeal effect of berberine. Indian J Med Res 1979 Aug;70:233-41

Berberine, an alkaloid derived from the plant, Berberis aristata, is of a definite value in gastroenteritis. Some pertinent experiments were carried out to explain its mechanisms. Ipomoea turpethumrval, a purgative, was used to induce purging in dogs. Berberine (0.06-20 mg/kg) given orally prolonged the latent period and reduced frequency and severity of purging. Oral administration of 1.25-5 g/kg magnesium sulfate produced dose-dependent purging in adult rats. Berberine in doses of 0.3-30 mg/kg did not reduce it between the two drugs. The results were unable to show any significant difference in the treatment of various chronic diarrhoeas between loperamide and codeine phosphate at this stage in the analysis.

Alam MN, Islam N, Shamsuddin M. Ulcerative colitis in Bangladesh. Bangladesh Med Res Counc Bull 1975 Oct;1(2):103-9

In a one-year study during 1974-1975, 100 cases of chronic diarrhoea with no apparent cause were investigated in Dhaka, Bangladesh. After obtaining a detailed clinical history, a complete physical examination, stool examination, proctosigmoidoscopic and barium enema examinations, and rectal biopsy were performed. Fifty-seven of the patients (51 males) fulfilled the diagnostic criteria of ulcerative colitis. The histology revealed edema and infiltration of the lamina propria with chronic inflammatory cells. The epithelium was intact and crypt abscesses were not found in any of these cases. Forty-one of these 57 patients were treated for acute amebic dysentery during the initial episodes of their illness. Since the attack of acute amebic dysentery is liable to produce post-dysenteric ulcerative colitis, it is possible that ulcerative colitis exists in this country in at least two forms—idiopathic and post-dysenteric. It is also suggested that many of the cases labeled as chronic intestinal amebiasis are probably cases of post-dysenteric ulcerative colitis.

Albano O see Gasbarrini G

Alexander FW. Chronic diarrhoea of unknown cause with response to steroids. Proc R Soc Med 1973 Nov;66(11):1067-8

This is a case report of a 6-year-old Pakistani boy, born in London, who developed chronic diarrhoea. The initial diagnosis was tuberculous peritonitis, and the patient received anti-tuberculous drugs. After 3 months in hospital, his weight had fallen, and copious diarrhoea continued despite a disaccharide-free diet. Prednisolone was given empirically (7.5 mg 8 hourly), which resulted in dramatic improvement in the number and the quality of the stools. The patient was maintained on prednisolone for 2 months, after that the dose was reduced and eventually stopped. Diarrhoea again occurred one week later so that prednisolone was restarted. The diarrhoea improved, and he remained well on 2.5 mg of prednisolone twice daily. When prednisolone was stopped for a second time, the boy continued to gain weight and showed improved appetite, but had 1 to 2 soft stools per day. The patient showed signs of malabsorption as indicated by a low-serum iron and serum folate and a high-fecal fat excretion. Despite normal levels of immunoglobulins, the

patient's repeated response to steroids suggests an immunological disorder that needs further investigation.

Alioto RL see Mir GN

Allen G, Watkinson G. A double-blind comparison of loperamide with codeine in the treatment of unremitting diarrhoea. In: Gough D, ed. The control of diarrhoea in clinical practice. London: The Royal Society of Medicine, 1978:35-40. (Royal Society of Medicine International Congress and Symposium series, 5)

This study involves a double-blind comparison of loperamide with codeine in the treatment of unremitting diarrhoea. Twenty-three patients were given 2 mg of loperamide or 30 mg of codeine phosphate marked as drug A or drug B. Each patient recorded the time of defecation, their stool consistency and the time of ingestion of the drug A or B. During the investigation, some laboratory tests were carried out, such as peripheral hematology and regular inspection of blood urea, electrolytes, and liver function tests at intervals of 0.4 and 9 weeks. There were only marginal differences between loperamide and codeine treatment. Though loperamide was more effective, the difference did not reach the required 95% level of probability. There was a correlation between the rating of severity of the diarrhoea by the patient and the objective measurement of diarrhoea and also significant and positive correlation between the number of capsules taken and the severity of diarrhoea. There were no significant side-effects in either group. Neither objective measurement in the form of stool frequency and consistency nor the semi-quantitative linear analogue scale measurements were adequate to resolve the differences between the two drugs. The results were unable to show any significant difference in the treatment of various chronic diarrhoeas between loperamide and codeine phosphate at this stage in the analysis.

Alos Alminana M see Peris Vidal A

Altomare E see Gasbarrini G

Amador A see Vazquez B

Ament ME, Barclay GN. Chronic diarrhea. Pediatr Ann 1982 Jan;11(1):124-31

Ament ME. Management of chronic diarrhea with parenteral nutrition and enteral infusion techniques. Pediatr Ann 1985 Jan;14(1):57-60

Ament ME see Heyman MB

Ana CAS see Fordtran JS

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Anderson CM see Challacombe DN

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Antes G, Igl W, Gebauer A, Kruis W. [Ultrasonics as an aid in the diagnosis of a case of chronic diarrhea]. ROFO 1982 Jul;137(1):112-3

Aparisi Ibanez M see Peris Vidal A

Arasu TS, Wyllie R, Fitzgerald JF. Chronic diarrhea in infants and children. Am Fam Physician 1979 Apr;19(4):87-94

A useful clinical classification of chronic diarrhoea is based on the character of the stool - watery, fatty, or bloody. Pathophysiologic mechanisms include osmotic and secretory diarrhoeas, bacterial overgrowth leading to excess colonic bile acids and fatty acids, defective anion exchange systems, mucosal damage and abnormal motility and transit. Evaluation may require hospitalization. Antidiarrhoeal agents are not used. Antibiotics are generally not indicated. Parenteral hydration and feedings of special formulas are carefully monitored. (Author's abstract)

Araya M see Brunser O

Arora NK, Bhan MK, Ghai OP. Protracted diarrhea of infancy: its aetiology and management in 25 patients. Indian Pediatr 1981 Jun;18(6):373-8

A prospective study of infants with protracted diarrhoea with special reference to etiology and response to a hypoallergenic chicken meat-based formula was performed. Twenty-five infants, aged below 1 with diarrhoea of more than 2 weeks' duration referred to the All-India Institute of Medical Sciences, New Delhi, India, formed the subjects of this study. Etiological factors were identified in 19 (76%) of the 25 infants suffering from protracted diarrhoea seen over a period of eight months. Secondary disaccharide intolerance (32%) and milk-protein intolerance (24%) were the commonest etiological factors. Fifty percent of the latter patients were intolerant to soy protein. Radiological evidence of pneumonia was found in 5 infants. Four infants died - a mortality rate of 16% in the series. Of the remaining 21 infants, 18 were successfully treated with enteral feeding with a hypoallergenic chicken meat-based formula and 3 with a soy protein-based formula.

Arora NK see Bhan MK

Attach EB see Olambiwonnu NO

Auricchio S, Cucchiara S, D'Antonio AM, De Titis G, De Vizia B, Follo D, Iaccarino E. Gastrointestinal allergy or intolerance to multiple foods in severe chronic diarrhea in early infancy. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:425-34

Auricchio S. Peptide digestion and absorption in the small intestinal mucosa during acute and chronic diarrhea. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:179-91

Awori NW, Rees PH, Roy AD. Causes of chronic diarrhoea in Kenya and their relationship to ulcerative colitis. East Afr Med J 1972 Aug;49(8):604-13

This paper identifies the causes of chronic diarrhoea in Kenya and their relationship with ulcerative colitis. A group of patients with chronic diarrhoea at the Kenyatta National Hospital, Nairobi, were included in the 18-month study. Through stool examination and other investigations, many causes of chronic diarrhoea were mentioned, which include ulcerative colitis, amebic dysentery, malabsorption syndrome, granulomatous colitis, carcinoma of

rectum, schistosomiasis (mansoni), tuberculosis of the small intestine and others. Four cases of ulcerative colitis were recorded, of which two had a total colectomy and ileo-rectal anastomosis. Some uncommon conditions were also detected. These additional cases of ulcerative colitis in tropical Africa are discussed in relation to the true prevalence of the disease. Diagnostic and surgical aspects of ulcerative colitis were also considered. Steroids and salazapyrin were used in the treatment of ulcerative colitis in the first instance; if these drugs failed to control the disease, a survey was advised. It is concluded that ulcerative colitis should be considered in all cases of dysentery in which organisms cannot be demonstrated. Carcinoma of the colon is not common in East Africa, but it may present as a chronic diarrhoea.

Aynsley-Green A, Bloom SR. The role of hormones in the pathophysiology of acute and chronic diarrhea. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:289-306

Azczurowna M see Swicowa K

Babb RR. Coffee, sugars, and chronic diarrhea: why a dietary history is important. Postgrad Med 1984 Jun;75(8):86-7

Patients with chronic diarrhoea should carefully be questioned about their diets. A correlation may be found between gastrointestinal symptoms and the ingestion of coffee, milk, or sugars, such as sorbitol and fructose. This report, therefore, stresses the importance of a thorough dietary history. It was found that 15 of the 100 patients referred to a physician in the USA because of chronic diarrhoea were drinking more than 10 cups of coffee a day. Diarrhoea ceased in 4 when this excessive intake was stopped. It is suggested that if diarrhoea resolves after lactose has been removed from the diet, the patient undoubtedly has a lactose deficiency. Sorbitol has been reported to cause diarrhoea when ingested in doses of over 50 g/day. Another study revealed that after ingesting 50 g of 10% fructose, 6 of the 16 healthy volunteers showed poor intestinal absorption and complained of cramps and diarrhoea. Thus, if the offending agent can be identified and withdrawn from the diet, the diarrhoea may stop.

Bader JP, Benhamon JP, Caroli J, et al. [How to find the cause of nonparasitic chronic diarrhea]. Presse Med 1965 Oct 30;73:2617-9

Balistreri WF. Bile-acid-induced intestinal dysfunction: implications to protracted infantile diarrhea and malnutrition. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:347-64

Ball JA see Kingham JG

Ballesteros Bermudez J see Burgos Courlaender C

Bampoe V see Maffei HVL

Banchini G see Gregori G

Banterle C see Gasbarrini G

Baquero M see Lopez-Brea M

Barbara L see Gasbarrini G

Barber DC see Read M

Barbezat GO, Clain JE, Halter F. A double-blind trial of loperamide in the treatment of chronic diarrhoea. S Afr Med J 1979 Mar 24;55(13):502-3

The effect of a double-blind randomized treatment regimen with loperamide in 40 patients (16 males and 24 females) with chronic nonspecific diarrhoea of at least 3 weeks' duration, was studied. The mean age of these patients was 46 years (range 5-81 years). Thirty-one of the patients were affected during a diarrhoea epidemic in a western Cape Town, South Africa, and no specific etiologic agent could be isolated from their stools. All other antidiarrhoeal medication was withheld throughout the trial, but other non-related therapy was permitted. The patients were randomly treated with either 2 mg of loperamide or with tablets of identical composition. The initial dose was one tablet twice a day, which was increased to one tablet 4 times a day, and then to two tablets 4 times a day when no clear improvement in stool frequency was seen. This treatment was continued for a week. Of the 19 patients who had received loperamide, 17 responded well, while two were recorded as treatment failures. Among the 19 patients who received placebo, 7 responded to treatment and 12 showed no response. This difference is highly significant (x^2 =11, 31; p<0.001). During the second week of treatment, the patients given loperamide recovered satisfactorily and compared to those given placebo; the response to treatment in the loperamide group was far better. Results of this study showed that loperamide was an effective antidiarrhoeal agent in patients with chronic nonspecific diarrhoea.

Barbulescu V see Popescu V

Barclay GN see Ament ME

Barness LA. Chronic diarrhea in children. Postgrad Med 1979 Feb;65(2):163-6, 168-9

Pathogenic and clinical features of chronic diarrhoea in children are described. Several mechanisms have been implicated as causes of diarrhoea. Chronic diarrhoea results in malnutrition, malabsorption and other complications. Less common causes include inflammatory responses, enzyme deficiencies, metabolic, anatomic and physiologic abnormalities, and endocrine disorders. Ingestion of excess calories may also cause diarrhoea. The use of antibiotics sometimes causes an inflammatory response in the bowel. Escherichia coli strains are often responsible for diarrhoea through production of enterotoxins. Alterations in prostaglandins or acetyl choline levels may cause chronic diarrhoea, while parasites like Giardia may also cause diarrhoea. Chronic diarrhoea accompanies immunoglobin deficiency. The recommended hydrating solution consists of 75 to 90 mEq/l of sodium chloride administered parenterally with 40 mEq/l of potassium in case of dehydration due to diarrhoea. Oral replacement of fluids can be increased gradually. Severe chronic diarrhoea may require hyperalimentation with parenteral aminoacids, sugar, and fat. Nonspecific treatment includes a diet of clear liquids with elimination of milk, cereals, and vegetables. Medications containing atropine or morphine should be avoided in treatment of diarrhoea. Diagnosis of the underlying cause of chronic diarrhoea is desirable before definite treatment is begun, and physical examinations should be done carefully. Stools should be examined, and sweat tests should be made. Various laboratory tests should be carried out to rule out cystic fibriosis, anatomic and inflammatory

abnormalities, and celiac diseases. Treatment should be directed to the underlying disease.

Bartlett JG see Sutphen JL

Bartnik W see Butruk E

Becker S see Black RE

Beer WH, Fan A, Halsted CH. Clinical and nutritional implications of radiation enteritis. Am J Clin Nutr 1985 Jan;41(1):85-91

In this study, the pathophysiology and nutritional significance of post-radiation enteritis were evaluated in patients with chronic diarrhoea. A subgroup of five patients with malabsorption and malnutrition was studied in California, USA. Eight patients (7 female and 1 male), aged 40 to 79 years, received pelvic radiation for gynecologic or testicular malignancy. Each patient complained of chronic diarrhoea. Steatorrhea was found in 7. The radiology of the small bowel was normal in all but 2 patients. Jejunal mucosal histology was normal in 4 biopsies, while 3 biopsies showed mild to moderate plasma cell infiltrates of the lamina propria. The levels of mucosal lactase and sucrase were decreased in 6 and 3 biopsies respectively. Fasting levels of breath hydrogen were greater than 10 ppm in 3 patients. The baseline and post-lactose breath hydrogen level was reduced by oral antibiotic therapy in 1 patient. The mean intakes of energy and nitrogen were similar among the 3 regimens, whereas mean carbohydrate intake was greater and fat was less during each elemental diet as compared to the oral diet. Fecal fat excretion decreased by formula liquid diets: "Vivonex-HN" was superior in digestibility of energy, nitrogen and carbohydrate, but resulted in decreased utilization of protein. The net effect of these processes was a 3-fold greater retention of absorbed N_2 with "Criticare-HN" than with "Vivonex-HN". The reasons of this phenomena are still unclear and need further investigation.

Befus AD see McDermott MR

Begemann F. [Lactase deficiency as cause of chronic recurrent diarrhea]. Med Klin 1972 Feb 18;67:233-9

Beier LV see Sazanova NE

Benhamou JP see Bader JP

Benincori N see Businco L

Bergman L, Djarv L. A comparative study of loperamide and diphenoxylate in the treatment of chronic diarrhoea caused by intestinal resection. Ann Clin Res 1981;13(6):402-5

The antidiarrhoeal effects of loperamide and diphenoxylate were compared in a double-blind crossover study in 29 adult patients with chronic diarrhoea due to intestinal resection in Sweden. Most of the subjects had had surgery for Crohn's disease which was in a stable and nonactive phase during the study. Loperamide (2 mg) and diphenoxylate (2.5 mg) (with atropine 0.025 mg) were presented as identical capsules. Each was administered for a minimum duration of 25 days, with other medications kept unchanged throughout the study. The

number of capsules required to control diarrhoea was significantly smaller in the loperamide group than in the diphenoxylate group ($p<0.01$). Loperamide was also superior to diphenoxylate in reducing the number of stools and improving the fecal consistency. Loperamide was preferred by 19 patients; 5 preferred diphenoxylate, while 5 did not find any difference. The preference for loperamide was statistically significant ($p=0.011$). Loperamide was recommended as the drug of choice in the symptomatic treatment of chronic diarrhoea.

Berrettini WH see Weiss KJ

Berrut C, Loizeau E. [Chronic diarrhea: current aspects]. Ther Umsch 1984 Sep;41(9):618-24

Bhan MK, Arora NK, Khoshoo V, Ghai OP. Chronic diarrhea in infants and children. Indian J Pediatr 1985 Sep-Oct;52(418):483-95

Bhan MK, Khoshoo V, Arora NK, Sood D, Kumar R, Stinzing G. In vitro immunological tests for diagnosis of milk protein allergy in infants with protracted diarrhoea. In: Programme, papers and abstracts of Third Asian Conference on Diarrhoeal Diseases, Bangkok, 10-14 Jun 1985:277

The inhibition of leukocyte migration through production of leukocyte migration inhibition factor was measured following in vitro challenge with B-lactoglobulin in 90 infants with protracted diarrhoea, 16 normal infants, 12 malnourished infants and 16 infants with acute gastroenteritis. Twelve infants with protracted diarrhoea fulfilled Goldman's clinical criteria for milk-protein intolerance, 63 had lactose malabsorption and 15 had no etiological findings. The mean index of migration inhibition in clinically milk allergic infants (58.8 ± 11.98) was higher than in normal controls (8.25 ± 3.91; $p<0.05$). Migration inhibition index greater than 20% (mean ±3SD in normal infants) was considered a positive assay. The assay was positive in all 12 cases of milk-protein allergy and in 4 of the remaining 78 cases of protracted diarrhoea. The assay was negative in all patients with gastroenteritis and malnutrition. These results suggest that this immunological assay is a sensitive test for diagnosis of milk-protein allergy.

Bhan MK see Arora NK

Bhave SA, Pandit AN, Agarkhedkar SR. Protracted diarrhea and its management. Indian Pediatr 1983 Mar;20(3):173-8

The study had two aims: to evaluate diets in chronic diarrhoea, and to establish a methodology for management of diarrhoea within the framework of facilities easily available in India. Of the 569 diarrhoea cases hospitalized in a children's ward over 20 months, 56 (10.9%) had protracted diarrhoea, 2 had diarrhoea from birth, and, in the others, diarrhoea had started acutely. Associated illnesses and abnormalities were present in 18 (32.14%). Definitive causes could be established only in 26 of the 56 (47.7%) cases. Of these, 20 were due to secondary disaccharide intolerance. Three diets were evaluated for dietetic management. The results showed that chicken-based and rice/dal-based diets were significantly better than a calcium caseinate-based diet. Overall mortality was 23.2%. Achievement of a positive nutritional balance in management of diarrhoea is stressed.

Bhide NK see Akhter MH

Bienenstock J see McDermott MR

Bierla J see Socha J

Binder HJ. New approaches to antidiarrheal therapy. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:437-43

Bittner K, Korbas J. [Saccharose intolerance as a cause of chronic diarrhea in an 8-month-old infant]. Wiad Lek 1969 Aug 1;22:1433-5

Bjorck I see Suthutvoravut U

Black RE, Brown KH, Becker S. Effects of diarrhea associated with specific enteropathogens on the growth of children in rural Bangladesh. Pediatrics 1984 Jun;73(6):799-805

Black RE, Brown KH, Becker S. Malnutrition is a determining factor in diarrheal duration, but not incidence, among young children in a longitudinal study in rural Bangladesh. Am J Clin Nutr 1984 Jan;39(1):87-94

Diarrhoea and malnutrition are common in developing country young children, and a reciprocal relationship has been postulated with diarrhoea leading to malnutrition and malnutrition predisposing to diarrhoea. To investigate the importance of malnutrition as a diarrhoea-determining factor, data were analyzed from a longitudinal community-based study done at two rural villages in the ICDDR,B's Matlab field research area. A total of 197 children, aged 2 to 48 months, classified by nutritional status according to a variety of anthropometric indicators, were evaluated prospectively for incidence, duration and etiology of diarrhoea. For those aged under 24 months, the mean diarrhoea duration in the lowest weight-for-length group (less than 80% of the National Center for Health Statistics standard) was 56% longer than the duration for children who were at least 90% of the standard. However, children of differing nutritional status had similar diarrhoeal incidences. Diarrhoea duration, including that associated with enterotoxigenic Escherichia coli and Shigella, increased progressively as nutritional status indicators worsened. Duration and incidence of diarrhoea for those aged over 24 months did not vary with nutritional status. It is suggested that nutritional interventions alone are unlikely to reduce high diarrhoeal incidence, but that efforts to improve nutritional status may positively affect duration of diarrhoea and its unfavorable nutritional consequences.

Blake PA see Osterholm MT

Blaser MT. Brainerd diarrhea: a newly recognized raw milk-associated enteropathy [editorial]. JAMA 1986 Jul 25;256(4):510-11

Bloom SR see Aynsley-Green A

Boda M see Varkonyi A

Boedeker EC. Mechanisms of adherence of Escherichia coli to enterocytes: their possible role in intractable infant diarrhea. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:329-45

Boedeker EC. Vaccines and other approaches to the prevention of intractable

infant diarrhea by the prevention of intestinal colonization. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:477-93

Bogoniowska Z see Kulesza E

Boland CR. Mucin glycoproteins in chronic ulcerative colitis: peanut lectin binding in human and nonhuman primate colons. Dig Dis Sci 1985 Dec;30(12 Suppl):S147-53

This paper reports results from work in humans and preliminary data from the marmoset species model. Eighteen patients with chronic ulcerative colitis, involving the entire colon, and 3 species of marmoset that spontaneously developed chronic ulcerative colitis in captivity, were studied. Whereas fluorescein isothiocyanate-conjugated peanut agglutinin does not bind to glycoconjugates in normal colonic mucosa, 11 of the 18 rectal biopsies demonstrated labeling in the epithelial cells by this lectin. In all, the 17 animals studied, the labeling occurred in the supranuclear cytoplasm, a region that appeared to correspond to the Golgi apparatus. During the 4-year period of follow-up, 7 neoplastic incidents occurred among these 18 high-risk patients: 6 cases of dysplasia in colonoscopic biopsies, and one case of invasive adenocarcinoma. The correlation between peanut agglutinin-labeled rectal biopsies and the subsequent development of neoplasia was not statistically significant. Thus, a larger cohort is necessary to evaluate the predictive value of this approach. One patient in whom rectal goblet cell mucin was labeled by fluorescein isothiocynate-peanut agglutinin developed carcinoma in the transverse colon 2 years after the initial biopsy. Three patterns of labeling of colonic epithelium by fluorescein isothiocyanate-peanut agglutinin were observed in the marmoset colons; in 16 of 49 (33%), either trace or no labeling was observed, while in 11 of 49 (22%), an intermediate degree of labeling of the supranuclear cytoplasm was found. In 22 of 49 (45%), a much greater amount of labeling in the supranuclear cytoplasm by fluorescein isothiocyanate-peanut agglutinin was seen. A portion of the Oedipus marmosets with colitis spontaneously developed carcinoma of the colon. The presence of intermediate or marked labeling in non-neoplastic colonic mucosa was significantly more likely among the 17 animals in which cancer was also present (16/17) than among the 32 animals in which cancer did not occur (17/32; $p<0.01$). Similarly, labeling by fluorescein isothiocyanate-peanut agglutinin was significantly more likely to occur in Oedipus colons than in the 2 non-Oedipus species (83% vs 45%; $p<0.02$). The Oedipus-cancer colons were significantly more likely to be markedly labeled by peanut agglutinin than were Oedipus - no cancer colons (76% vs 25%; $p<0.02$). Thus, although the cancer-associated glycoconjugate recognized by fluorescein isothiocyanate-peanut agglutinin is not specific for neoplastic colonic epithelium, its appearance in the premalignant colon may be important in assessing the relative risk of cancer.

Bolin TD. Use of oral sodium cromoglycate in persistent diarrhoea. Gut 1980 Oct;21(10):848-50

Twenty adult patients with persistent diarrhoea participated in a double-blind randomized trial of oral sodium cromoglycate and placebo in Australia. The dosage of oral sodium cromoglycate was 200 mg four times daily. Eight patients noted significant benefit from the use of sodium cromoglycate with a reduction in frequency and firmer consistency of their motions. The beneficial response to sodium cromoglycate did not correlate with the presence of other atopic

diseases, a history of food intolerance, or the presence of lactase deficiency. The finding of symptomatic improvement in 40% of the patients, who had in the past tried a multitude of symptomatic measures, suggests that oral sodium cromoglycate has a role to play in treating persistent diarrhoea without an obvious organic cause. The results also suggest that some patients with diarrhoea of unknwon cause may have food allergy as a major contributing cause for their diarrhoea.

Bo-Linn GW, Vendrell DD, Lee E, Fordtran JS. An evaluation of the significance of microscopic colitis in patients with chronic diarrhea. J Clin Invest 1985 May;75(5):1559-69

The study was undertaken to examine colonic biopsy specimens in a blinded fashion, comparing biopsy results from patients with microscopic colitis with biopsy specimens from subjects in two control groups. This analysis revealed that colonic mucosa from six patients with microscopic colitis was in fact abnormal. Their mucosa contained an excess of both neutrophils and round cells in the lamina propria, cryptitis, and reactive changes. These and other differences were statistically significant. Colonic absorption, measured by the steady state nonabsorbable marker perfusion method, was severely depressed in the patients. Mean water absorption rate was 159 ml/h in normal subjects and was reduced to only 26 ml/h in six patients with microscopic colitis. Results of net and unidirectional electrolyte fluxes and of electrical potential difference suggest that colonic fluid absorption was abnormal, because of reduced active and passive sodium and chloride absorption and because of reduced Cl/HCO_3 exchange. Small intestinal fluid and electrolyte absorption was abnormally reduced in two of the six patients, suggesting the possibility of coexistent small intestinal involvement in some of these patients. It is concluded that nonspecific inflammation of colonic mucosa is associated with a severe reduction of colonic fluid absorption, and that the latter probably contributes to the development of chronic diarrhea. (Modified author's abstract)

Bo-Linn GW see Fordtran JS

Bombardieri G see Innocenti P

Bondue H. [The contribution and limitations of the Schilling test in the evaluation of chronic d iarrhoeas]. Acta Gastroenterol Belg 1981 Jan-Feb;44 (1-2):62-6

Book LS see Hill RR

Booth IW, Harries JT. Electrolyte therapy in acute and chronic diarrhea. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984: 457-67

Booth IW, Harries JT. Regulatory mechanisms of secretory diarrhea and electrolyte imbalance in acute and chronic diarrhea in infancy. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:307-17

Borisova LI see Daletskaia GV

Borzani M see Roggero P

Bowie MD. Total parenteral nutrition in the malnourished child. S Afr Med J 1976 Oct;50(42):1721-3

Seventeen infants (mean age 3.3 months, mean weight 3.4 kg), hospitalized in Cape Town with chronic diarrhoea, were subjected to total parenteral nutrition after exclusion of the other factors known to cause diarrhoea. The mean percentage of expected weight-for-age of these infants was 52%. The average duration of diarrhoea before commencement of intravenous (i.v.) nutrition was 30 days. The i.v. fluid contained Amigen 5%, glucose 50%, Ca gluconate 10%, KCl 15%, intralipid 10% and $MgSo_4$. Two routes of administration were used — a central venous catheter was used on 12 infants, and peripheral veins were used in 5. Eleven of the 17 infants were successfully treated for the diarrhoea, and it was possible for the patients to return to oral feeds. At least 14 days of i.v. nutrition were necessary before the reintroduction of oral feeds could be attempted. There were 6 deaths -- all in the group using central venous catheter. Complications, such as candidiasis, septicemia, sloughed scalp and forearm, were noted. They were related to the manner of administering the infusate. No metabolic complications were encountered. Total parenteral nutrition has a part to play in the treatment of protracted diarrhoea in infancy, but it should be considered much earlier in the course of the disease so that safer peripheral venous routes can be used.

Bowie MD see Hill ID

Bowie MD see Mann MD

Boyle JT see Fisher SE

Boyne LJ, Kerzner B, McClung HJ. Chronic nonspecific diarrhea: the value of a preliminary observation period to assess diet therapy. Pediatrics 1985 Oct;76 (4):557-61

Eighteen children with chronic nonspecific diarrhoea were evaluated prospectively to determine "basal" fat consumption and the response of their diarrhoea to diets containing either 25% or 50% of total calories as fat. In the observation period, prior to initiating any alteration in dietary fat content, diarrhoea subsided. Only five of the 18 patients had a low-fat intake (less than 27% of total calories) at the outset of the study, and spontaneous resolution of the diarrhoea precluded an assessment of the effect of altering fat intake on stool frequency. Therefore, a preliminary observation period, in which details of the diarrhoea are documented, is essential to evaluate any treatment modality for this poorly defined condition. (Modified author's abstract)

Branski D. [Diagnosis and treatment in case of chronic diarrhea in children]. Harefuah 1979 Jan 1;96(1):34-6

Branski D. Specific etiologies of chronic diarrhea in infancy. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:107-145

Brassinne A see Dreze C

Brey OA, Garner EPR, Twycross RG, Wells D. Duodenal diverticulosis and chronic diarrhoea. Br Med J 1971 Jan 23;1(5742):211-2

This paper describes duodenal diverticulosis and chronic diarrhoea in two

patients. In case 1, a 61-year-old patient, who had several attacks of pancreatitis over a 2-year period and later developed intermittent diarrhoea, was studied. During continuous diarrhoea for 2 years, he lost 30 lbs in weight. Examination showed nothing abnormal apart from generalized wasting. Hemoglobin was 12.0 g/100 ml. He had a megaloblastic anemia. After 2 intramuscular injections of 1 mg of cyanocobalamin, the diarrhoea gradually ceased, and the hemoglobin rose to 14.3 g/100 ml. Four months later, the diarrhoea returned but responded to weekly injections of 1 mg of cyanocobalamin. He remained well for six months. In case 2, a woman aged 73, who had passed up to 12 semi-formed stools a day for 20 years, was studied. She lost 14 lbs in weight and had anorexia, nausea, abdominal discomfort and occasional vomitng for 2 weeks. She was pale and dehydrated. Her serum potassium concentration was 2.7 mEg/l and hemoglobin was 8.5 g/100 ml. A three-day fecal fat excretion was 3.2 g/day. After treatment with intramuscular cyanocobalamin weekly and oral folic acid 15 mg daily, her hemoglobin level rose to 14 g/100 ml, and the diarrhoea had ceased. The results of the lactose and galactose-glucose tests indicated an associated hypolactasia. Two duodenal diverticula were shown. The variable response of different patients to vitamin B_{12} shows the essential interaction of several components in the production of the malabsorption syndrome.

Brook CGD see Maffei HVL

Brown IL see Mills PR

Brown KH see Black RE

Brown MR see Smalley JR

Brown RS see Gunn T

Brunser O, Araya M. Damage and repair of small intestinal mucosa in acute and chronic diarrhea. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:31-55

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Buisseret P. Drugs for chronic diarrhoea [letter]. Br Med J 1980 Apr 19;280 (6221):1089

Bujanover Y, Sullivan P, Liebman WM, Goodman J, Thaler MM. Cholestyramine treatment of chronic diarrhea associated with immune deficiency syndrome. Clin Pediatr 1979 Oct;18(10):630-3

This paper describes the treatment of chronic diarrhoea associated with immune deficiency syndrome with cholestyramine. A 5-year-old boy was admitted to the University of California Medical Center, USA, with a 7-month history of recurrent diarrhoea. He had 3 to 10 watery bowel movements daily and had respiratory infection when aged 5 months, and also had immunodeficiency disease, hypogammaglobulinemia and deficient T-cell at the age of one. One month prior to admission, diarrhoea with associated dehydration which recurred after an upper respiratory tract infection. On admission, he was afebrile, and tests showed the following: hemoglobin 9.4 g/dl; negative stool examination (bacteria, fungi, ova, and parasites); T-cell rosettes 45% (normal 65%); phyothemagglutinin and MLC responses, 10% of normal. Candida albicans at the

villus surface with many organisms invading mucosal epithelial cells were observed by electron microscopy. Disaccharides activity was normal. Duodenal aspirate revealed a large number of yeast forms. The diarrhoea was treated with an elemental formula (Vivonex) and oral mycostatin. The diarrhoea responded only to cholestyramine, 12 g daily, but antimycotic therapy failed. Cholestyramine was discontinued after 6 months with prompt recurrence of diarrhoea. The pattern of recurrence and improvement off and on cholestyramine, respectively, was repeated thrice thereafter. No organisms were present in duodenal aspirate. The complexing of resin with C. albicans may have occurred and contributed to the resolution of diarrhoea. Cholestyramine can produce significant side-effects, if used generally in nonspecific diarrhoeas. The patient responded to repeated courses of cholestyramine resin given over a six-month period.

Bukhave K, Rask-Madsen J. An approach to evaluation of local intestinal PG production and clinical assessment of its inhibition by indomethacin in chronic diarrhea. Adv Prostagl Thromb Res 1980;8:1627-31

Prostaglandin (PG) E_2 levels in fasting jejunal secretions of man were measured to define a simple index of intestinal PG production and to study possible variations of this index in relation to changes in the physiologic state. Seventeen healthy volunteers and 77 patients with chronic alcoholism, irritable bowel syndrome, or celiac disease were studied in Denmark. The normal range of PGE_2 in fasting jejunal secretions of healthy volunteers was 0-205 pg/ml. All patients with alcoholism had PGE_2 levels within the normal range. Although most patients with irritable bowel syndrome had PGE_2 levels within the normal range, significantly elevated values were observed in 2 patients classified as irritable bowel syndrome 1 and in 10 patients classified as irritable bowel syndrome 3. Following treatment with indomethacin (75 to 125 mg/day), PGE_2 concentrations decreased to normal levels. In all patients with celiac disease, a marked rise in PGE_2 concentrations was observed. Other patients in complete remission on a gluten-free diet had significantly lower ($p<0.005$) PGE_2 levels, but never reached the normal range. Indomethacin therapy in 6 patients classified as irritable bowel syndrome 3, with a history of diarrhoea and significantly raised PGE_2 level, resulted in a 50%-decrease in stool volumes and frequencies of bowel movement within 72 h. Withdrawal of indomethacin caused a severe relapse. Subsequently, a double-blind randomized multiple crossover study was carried out in two patients classified as irritable bowel syndrome 3. All placebo periods were correctly defined by the patient with a raised PGE_2 level, thus showing that indomethacin was effective in preventing PGE_2-mediated diarrhoea in this patient ($p<0.005$). The other patient with normal PGE_2 level did not show a defined period. The investigation suggests that determination of luminal PGE_2 levels provides a simple and reproducible index of intestinal PG production which may be used for studies on pathophysiologic mechanism and as an approach to rational therapy. PGE_2 measurements also give a more sensitive measure of inflammatory activity in celiac disease.

Bukhave K, Rask-Madsen J. Prostaglandins and chronic diarrhoea: methodological problems. Scand J Gastroenterol 1979;14(Suppl 53):67-71

Since prostaglandins (PG) are effectively degraded in the lungs, the determination of the arteriovenous difference in PGE_2 levels offers a unique opportunity to check the validity of a sample collection. To determine the arteriovenous difference in circulating PG levels, the isotope derivative

technique was applied to rat plasma for measurements of PGE_2. No arteriovenous difference was observed when blood was collected without precautions to avoid in vitro PG production in the sampling tube. In contrast, collection of blood during blockade of the in vitro PG synthesis by indomethacin resulted in significantly lower levels in the atrial plasma (60±20 pg/ml; n=8; $p<0.02$) and a peripheral arterial level away from zero. Fasting is characterized by high peripheral concentrations of free fatty acids. Therefore, the PGE_2 precursor, arachidonic acid, was measured in mixed arterial and venous blood revealing significantly different ($p<0.01$) plasma concentrations in fed (12.0±3.4 µM; n=7) and fasted aminals (6.8±1.6 µM; n=7). A significant difference in PGE_2 levels of right atrial plasma from fed and fasted rats was observed without the use of in vitro indomethacin blockade (210±70 pg/ml; n=4, and 330±35 pg/ml; n=4 respectively). No significant difference between fasted (90±35 pg/ml; n=5) and fed (60±20 pg/ml; n=9) animals could be demonstrated, if indomethacin was infused into the catheter during the sampling procedure ($p>0.05$). It is suggested that the higher level of PGE_2 (without indomethacin) in fasted rats reflects that of arachidonic acid plasma level. The data on PGE_2 levels in the rat demonstrate that determination of primary PGs in circulating blood includes a series of artifacts primarily due to the in vitro production of PGs. The available methods for the determination of primary PG and PG metabolites are discussed.

Bukhave K see Rask-Madsen J

Bulgarelli R, Grossi Bianchi ML. (Allergy to cow's milk in chronic infantile diarrhea. Its treatment). Minerva Diet 1963 Oct-Dec;3:149-63

Bunjes R see von Muhlendahl KE

Burgos Courlaender C, Ballesteros Bermudez J. [Trichocephalus as cause of chronic diarrhea in children. Treatment of it with hexylresorcinol enemas]. Rev Kuba Med Trop 1960 Jan-Mar;16:1-7

Burkinshaw JH see Thornton AA

Burrows CF. Chronic diarrhea in the dog. Vet Clin North Am 1983 Aug;13(3): 521-40

A specific understanding of the cause of chronic diarrhoea in dog is essential to ensure a specific therapy. A specific diagnosis is based on an understanding of the pathophysiology of diarrhoea, on a carefully taken history, and on the logical application of appropriate diagnostic or gastrointestinal function tests. This article describes how the logical and sequential application of this knowledge can be used to diagnose the cause of chronic diarrhoea. It is suggested that, once the disorder has been localized, a specific diagnosis can be made by specific gut function studies, by a logical therapeutic trial, or in the large bowel diarrhoea, by colonoscopy and biopsy. The possibility of referral of problem cases should never be excluded. It is also indicated that symptomatic therapy cannot be a substitute for more appropriate and more logical treatment which will achieve a specific cure.

Businco L, Benincori N, Cantani A, Tacconi L, Picarazzi A. Chronic diarrhea due to cow's milk allergy. A 4-to 10-year follow-up study. Ann Allerg 1985 Dec;55(6):844-7

Butler T, Middleton FG, Earnest DL, Strickland GT. Chronic and recurrent

diarrhea in American servicemen in Vietnam: an evaluation of etiology and small bowel structure and function. Arch Intern Med 1973 Sep;132:373-7

Seventy previously healthy American soldiers in Vietnam, aged 18 to 26 years, had diarrhoea of at least 2 weeks' duration with no evidence of infection with Entamoeba histolytica or Shigella species. These patients were studied to clarify the causes of diarrhoea and to characterize its effect on the structure and function of the small intestine. D-xylose excretion was less than 5.0 g in 40 of the 64 patients tested (63%). Fecal fat excretion was elevated in 21 of the 26 patients with a mean of 12.7 g/day. The Schilling test result was abnormal in 14 of the 29 patients (48%), and the mean excretion was 9.1%. These results showed that there was a high incidence of malabsorption. Jejunal biopsy revealed jejunitis in 10 patients; their D-xylose absorption and vitamin B_{12} excretion levels were significantly lower than those of patients without jejunitis ($p<0.05$). Fourteen patients had bacterial contamination of the jejunum, and 11 patients harbored the intestinal helminths, hookworm, or Strongyloides stercoralis. Seventy percent of the patients with jejunitis harbored Giardia lamblia, while only 29% of those without jejunitis had this Parasite ($p<0.05$). All patients with helminths showed improvement as did most of the patients with giardiasis treated with quinacrine hydrochloride. The frequent occurrence of intestinal parasites and the favorable responses in 91% of the patients to regimens that included appropriate antiparasitic drugs suggest that intestinal parasitosis, especially giardiasis, was a common cause of diarrhoea in these patients. Jejunal biopsy can be recommended in patients who did not promptly show any improvement with symptomatic or antiparasitic therapy.

Butruk E, Bartnik W. [Results of treating chronic diarrhea with loperamide in patients with functional intestinal disorders]. Pol Tyg Lek 1979 Mar 12;34 (11):437-8

Cacciarelli A see Holmes R

Cacciatore L see Giardina MF

Calvin RT, Klish WJ, Nichols BL. Disaccharidase activities, jejunal morphology, and carbohydrate tolerance in children with chronic diarrhea. J Pediatr Gastroenterol Nutr 1985;4(6):949-53

Eighty-eight children, aged 1 month to 16 years with chronic diarrhoea, were examined in Texas, USA, for their carbohydrate tolerance, small bowel morphology, and specific disaccharidase activities. The aim was to determine whether disaccharidase enzymatic activity is related to villus height. The findings showed that 65-78% of all abnormal biopsy samples had specific disaccharidase activities that fell within the normal range. Comparisons of the means of the groups with milder degrees of mucosal injury with those of more severe injury without gluten-sensitive enteropathy showed no significant difference. Clinical disaccharide tolerance data showed that 85% of the children with abnormal lactase activity had clinical lactose intolerance. Only 40% of cases with abnormal sucrase activity, however, demonstrated sucrose intolerance. Thus, specific enzyme activity did not correlate with disaccharidase tolerance. The incidence of lactose intolerance increased with decreasing villus height in patients with normal lactase activity. Jejunal mucosal disaccharidase enzyme activities were found not to correlate with mucosal morphology, and respective disaccharidase specific activities were found to be poor predictors of clinical carbohydrate tolerance.

Camarero C see Lopez-Brea M

Cameron DG, Warner HA, Szabo AJ. Chronic diarrhea in an adult with hypokalemic nephropathy and osteomalacia due to a functioning ganglioneuroblastoma. Trans Am Clin Climatd Assoc 1967;78:205-17

Cameron DG, Warner HA, Szabo AJ. Chronic diarrhea in an adult with hypokalemic nephropathy and osteomalacia due to functioning ganglioneuroblastoma. Am J Med Sci 1967 Apr;253:417-24

Cameron DJS see Candy DCA

Campana AO, de Andrade DR, Tovar JW, Neves DP. [Electrolyte changes determined by intestinal lavages utilized in the preparation of colons for radiological examination, in patients with chronic diarrhea]. Rev Assoc Med Bras 1961 Apr; 7:108-13

Campbell CB see Cowen AE

Campbell MA see Smalley JR

Candy DCA, Leung TSM, Marshall WC, Harries JT. Increased adhesion of Escherichia coli to mucosal cells from infants with protracted diarrhoea: a possible factor in the pathogenesis of bacterial overgrowth and diarrhoea. Gut 1983 Jun;24(6):538-41

Mucosal adhesion of bacteria has been studied in 8 infants, aged 3 to 44 weeks with protracted diarrhoea and malnutrition, using a buccal epithelial cell technique. Ten children with acute diarrhoea, 13 healthy infants and 10 healthy adults were examined as controls. A known non-adhesive strain of Escherichia coli (O1:K1:H7), adhered to a significantly greater ($p<0.001$) proportion of buccal epithelial cells from patients with protracted diarrhoea (18-96%), compared to children with acute diarrhoea (0-24%), healthy infants (0-41%), and healthy adults (0-8%). Also, enterobacteria, isolated from the jejunum or stools of patients with protracted diarrhoea, adhered to far greater numbers of their own buccal epithelial cells compared with those of healthy adults. The seven strains of enterobacteria were negative when tested for CFA/I and CFA/II production. Thus, adhesion was not mediated by CFA/I or CFA/II. The results suggest that bacterial adhesion may play an important role in the pathogenesis of protracted diarrhoea. It is speculated that malnutrition and/or genetic predisposition may influence the adhesive properties of mucosal cells.

Candy DCA, Larcher VF, Cameron DJS, Norman AP, Tripp JH, Milla PJ, Pincott JR, Harries JT. Lethal familial protracted diarrhoea. Arch Dis Child 1981 Jan;56 (1):15-23

Twenty-four children with severe protracted diarrhoea from 10 families, in which at least one sibling was affected, have been reported. The siblings in 2 families were from first-cousin marriages, both parents of the siblings in one family had unaffected children from previous marriages, and the mother of the siblings in another family had a normal daughter from a previous marriage. Mean birthweight was 3.03 kg. Each patient had presented at one of 3 hospitals (2 in the UK, 1 in Australia) during the 14-year study period. The onset of diarrhoea was seen on the first day of life in 12 infants, sometime during the

first 17 days in 10, and at 13 weeks and at 1 year and 6 days in the remaining 2 patients. In all cases, the diarrhoea was 'cholera-like'. Investigations failed to show any of the established causes of protracted diarrhoea. Twenty-one (87.5%) infants died after an illness that had lasted between 12 days and over 6 years, despite periods of prolonged intravenous feeding and the administration of a wide variety of pharmacological agents, including steroids, antibiotics, disodium cromoglycate, prostaglandin synthetase inhibitors, beta-blockers, antihistamines, cholestyramine, nonspecific antidiarrhoeal agents, and vitamin B_{12}. The 2 patients who recovered appeared to do so spontaneously. Eleven of the 21 patients who died were below their birth-weights at death. Fourteen (58.3%) had extra-gastrointestinal or gastrointestinal-related abnormalities. Steady-state perfusion studies were performed in the proximal jejunum of 2 patients, and in the colon of 1, to define the pathophysiological mechanism operating in the genesis of their diarrhoea. In both patients, the proximal jejunum was in a net secretory state with respect to water; fructose and glucose absorption was impaired from varying intraluminal concentrations, and transmural potential difference was reduced. These observations suggest that, in these 2 patients, the diarrhoea resulted from small intestinal secretion of fluid and electrolytes overwhelming the reabsorptive capacity of a normal colon. Although this series of serious protracted diarrhoea does not represent a single disease entity, the familial pattern suggests an autosomal recessive mode of inheritance for at least one of the conditions.

Candy DCA, Larcher VF, Tripp JH, Harries JT, Harvey BAM, Soothill JF. Yeast opsonisation in children with chronic diarrhoeal states. Arch Dis Child 1980 Mar;55(3):189-93

Four children with protracted diarrhoea and severe illness of undetermined cause, and with defective yeast opsonisation have been reported from London, UK. Plasma infusions improved the opsonising function in all 4 and the diarrhoea in 3. This immunological abnormality was assessed in 100 sequential patients with chronic diarrhoea associated with various gastrointestinal disorders. Fifty-two of them had protracted diarrhoea and failure to thrive of undetermined cause. Twenty-six had 'toddler diarrhoea', 8 had celiac disease, and 5 had chronic inflammatory bowel disease (3 ulcerative colitis and 2 Crohn's disease). Nine children had other disorders. Twelve (23%) of the 52 patients with protracted diarrhoea and failure to thrive had defective opsonisation, while the defect was present in only one child with toddler diarrhoea and in one with Crohn's disease. Thus, the defect was more frequent ($p<0.05$) in the first group compared with the toddler diarrhoea group or the remaining patients, in whom the frequency (4%) was similar to that (5%) in healthy populations. No pathogenic bacteria or Giardia sp. were recovered from duodenal juice or stools. It is suggested that determination of yeast opsonisation index should be an integral part of the investigation of children with protracted diarrhoea. Plasma infusions can be an effective form of treatment.

Cantini A see Businco L

Capano G see Pignata C

Caprio P see Gregori G

Cariloo J see Ramirez-Mayans JA

Caroli J see Bader JP

Carrazza FR, Gopalakrishna GS, Sperotto G, Nichols BL. Net acid balance in infants with diarrhea and carbohydrate intolerance. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:163-78

Castillo-Duran C see Rodriguez A

Cataland S see Kidd GS

Catassi C, Pasquini E, D'Angelo G, Coppa GV, Giorgi PL. Serum carotene level and 1-hr blood xylose test in the evaluation of children with chronic diarrhoea. Ital J Gastroenterol 1986 Jun;18(3):166-8

The aim of this study was to compare the usefulness of serum carotene level with that of the 1-h blood xylose test in the diagnostic evaluation of 75 children with chronic nonspecific diarrhoea and 17 children with active gluten-sensitive enteropathy. The age range was 5 months to 9 years (mean age - 20 months). The study was performed during July 1981-July 1983. The results of the 1-h blood xylose test were in accordance with the final diagnosis in 85% of the children with chronic nonspecific diarrhoea and in 79% of the children with gluten-sensitive enteropathy. The serum carotene level accorded with the final diagnosis in 92% of the children affected with chronic nonspecific diarrhoea and in 83% of the children suffering from gluten-sensitive enteropathy. These results suggest that the diagnostic accuracy of serum carotene level is at least equal to that of the 1-h blood xylose test for the screening of gluten-sensitive enteropathy. The main advantages of the serum carotene test are the low cost and the simplicity of the dosage technique. (Modified author's abstract)

Cattan D see Gouerou H

Cattan R see Ligny G

Challacombe DN, Richardson JM, Rowe B, Anderson CM. Bacterial microflora of the upper gastrointestinal tract in infants with protracted diarrhoea. Arch Dis Child 1974 Apr;49(4):270-7

The aerobic and anaerobic bacterial microflora of the upper gastrointestinal tract in 7 infants, aged under 4 months with chronic diarrhoea, 7 under-5 children with post-operative diarrhoea and 1 aged 7 months with acute diarrhoea, were studied in the UK. The results were compared with a group of control infants without diarrhoea. The duodenal juice of patients with protracted diarrhoea was rarely sterile and was characterized by an increase in numbers and types of microorganisms. The mean of the total organism count was 7.3 $\log_{10}$/ml in infants with chronic diarrhoea and 6.4 $\log_{10}$/ml in the post-operative infants. Although coliforms were present in the gastric juice of the controls (6 of 13), they were more frequently isolated from the chronic diarrhoea (6 of 7) and post-operative patients. Five of the seven duodenal samples from chronic diarrhoea patients had coliforms (all Escherichia coli), while 6 of the 7 duodenal samples from post-operative cases had coliforms (5 had E. coli). In individual patients, the same serotypes of E. coli were found throughout the intestinal tract. This suggests that factors unrelated to impaired peristalsis could also contribute to the presence of these organisms in the duodenum. The presence of E. coli in the duodenum may be as important to the etiology of protracted diarrhoea, as it is to acute diarrhoea.

Chandra RK, Pawa RR, Ghai OP. Disaccharide intolerance in the aetiology of chronic and/or recurrent diarrhoea in young children. Indian J Med Res 1969 Apr;57(4):713-7

The results of screening tests and loading studies on 192 young children with chronic and recurrent diarrhoea are reported. Chronic diarrhoea was defined as the duration of an episode that exceeded 2 weeks, and recurrent if there were more than 3 episodes in 3 months. Of the 192 children, 63 showed a fecal pH below 6. Forty-nine children exhibited abnormal sugar tolerance tests. Daily fecal fat excretion exceeded 6 g in 9 (steatorrhea) of the 23 patients. D-xylose excretion was very low in 5 of the 18 children. Enteropathogenic bacteria (Escherichia coli) were isolated from 3 children, while 2 had Giardia lamblia. Three children showed flat absorption curves for monosaccharide load. All the 49 patients with abnormal sugar tolerance test responded well when fed with diets low in carbohydrates, e.g. disaccharides. It appeared that the acquired disaccharide intolerance was a significant factor in the etiology of chronic and recurrent diarrhoea in young children.

Chang TW see Sutphen JL

Chaptal J, Jean R, Dossa D, Meylan P, Guillaumot R, Morel G, Vernier M, Kesch. [Chronic diarrhea, neither infectious nor parasitic, in infants]. Arch Franc Pediatr 1962 Apr;19:463-79

Charoenkwan P see Eksaengsri P

Chatterjee H. Chronic diarrhoeas in adults. J Indian Med Assoc 1977 Dec 1;69 (11):259-61

This report describes chronic diarrhoea in adults. Among the cases of chronic diarrhoea admitted in the School of Tropical Medicine in Calcutta, India, malabsorption and irritable colon were commonly found. Passage of 3-10 soft motions per day was observed. The age group was 20-55 years for both sexes. The duration of diarrhoea varied from 6 months to 30 years. In cases of prolonged diarrhoea, no severe malnutrition was seen. Giardia intestinalis was present in 10% and ova of hookworm in 8% of the cases examined. The patients improved when put on a low-residual diet, avoiding leafy vegetables, seeds, and scales. In severe cases, nonspecific anticholinergic drugs were effective. There are many causes of malabsorption syndrome, but the exact causes are not known. The treatment is by broad spectrum antibiotics, folic acid, and non-residual diet. Idiopathic steatorrhea or non-tropical sprue is due to gluten sensitivity. It was noted that, for sometime after an attack of infective diarrhoea, the patients did not tolerate milk due to temporary deficiency of certain intestinal enzymes which are involved in digestion and absorption of milk. Milk should not be taken for a month during treatment of diarrhoea. For irritable colon, the treatment is by non-residual diet, anticholinergic drugs, tranquilisers and probing into the prevailing socioeconomic problems. In cases of acute ulcerative colitis, the diet should be non-residual with supplementation of vitamins, proteins, and minerals. Often salicylazosulpha-pyridine controls the diarrhoea in milk-induced cases. In more severe cases, corticohopin or corticosteroids are added. Tuberculosis of the intestine is discussed. In case of chronic bacillary dysentery, metronidazole (400-mg tablet 3 times a day for 8 days) is very effective.

Chatterjee H, Adhikari GN. Clinical and radiological aspects of chronic diarrhoeas. J Indian Med Assoc 1984 Jun;82(6):194-6

A composite study, based on clinical and radiological investigations in 59 chronic diarrhoea patients hospitalized in Calcutta, India, is reported. Of the 374 barium meal studies, 120 showed radiological features suggesting malabsorption. Only 59 (50%) of the latter, however, were suffering from chronic diarrhoea. Twenty-nine of these chronic diarrhoea patients showed both biochemical and radiological signs of malabsorption; in 30, there was no biochemical evidence, although radiological features were characteristic of malabsorption. Among the malabsorbers, again, only half had steatorrhea. The degree of fat absorption impairment was directly related to the combined lesions in jejunum and ileum with dilatation as a constant feature. In steatorrhea, the maximum ileal dilatation was 55 mm and minimum 20 mm. Clinical malnutrition was almost absent.

Chernoff R, Dean JA. Medical and nutritional aspects of intractable diarrhea. J Am Diet Assoc 1980 Feb;76(2):161-9

Chopra K, Dua N, Saha K. Chronic diarrhoea: etiology, secretory immunoglubins and role of colostrum as a therapeutic agent. In: Proceedings of the Seminar of the Commonwealth Society, London, 1985:1-5

The etiology and secretory immunoglobulin profile of chronic diarrhoea and the role of colostrum as a therapeutic agent were prospectively studied in 60 Indian children, aged between 9 months and 3 years. On admission, 93.3% of the patients were malnourished; 35% showed grade I, 28.33% grade II, and 27.27% grade III malnutrition. Enteropathogenic Escherichia coli were isolated from 40% of the patients and Giardia lamblia from another 10%. Twenty percent of the cases had ascariasis. Mean stool IgA levels in chronic diarrhoea was 11.57±1.09 mg/g of dry stool. In normal controls, it was 2.13±3.56 mg/g. The difference was significant ($p<0.001$). Mean serum IgA in patients with chronic diarrhoea (136.07±45.0 mg%) was significantly higher ($p<0.001$) than that of controls (86.86±31.18 mg%). The patients were divied into 3 equal treatment groups to receive antidiarrhoeal agents (group A), 20 ml of colostrum daily for 7 days (group B) or colostrum plus antidiarrhoeal agents (group C). Response to therapy as judged by the cessation of diarrhoea was 42.10% in group A, 23.52% in group B and 41.77% in group C. The study highlights the beneficial role of colostrum in the treatment of diarrhoea and the importance of breast feeding in the prevention of diarrhoeal diseases in the developing countries.

Christie DL see Clausen CR

Chronic diarrhea associated with raw milk consumption - Minnesota. MMWR 1984 Sep 21;33(37):521-2, 527-8

[Chronic diarrhea. Symposium held on 17 and 18 October 1980]. Acta Gastroenterol Belg 1981 Jan-Feb;44(1-2):7-87

Ciampolini M, Savini P, Olivieri V. [Effects of correction of eating behavior and metabolic consumption on diarrhea, subcutaneous tissue, growth and hemoglobin in 18 children with a specific chronic diarrhea]. Minerva Pediatr 1981 Nov 30;33(22):1081-7

Cichowicz-Emmanuelli E. Chronic non-specific diarrhea of infancy. Boll Assoc Med P R 1982 May-Jun;74(5-6):178-81

Cichy W see Socha J

Clain JE see Barbezat GO

Clark JH see Fitzgerald JF

Clarke JT, Quillian W, Shwachman H. Chronic diarrhea and failure to thrive due to intestinal disaccharidase insufficiency. Pediatrics 1964 Dec;34(6):807-13

This paper reports the case of an infant who was born after approximately 32 weeks' gestation, with a birth weight of 2 lbs and 6 oz. The infant had chronic diarrhoea due to suspected generalized disaccharidase insufficiency. The clinical condition of the patient improved following the removal of lactose and sucrose from the diet. The fermentative and acidic stool with free lactose and lactic acid also improved. To maintain proper hydration and blood pH, almost continuous intravenous fluids were given, with supplementary potassium bicarbonate and an occasional transfusion. Parenteral antibiotics (kanamycin plus penicillin) were administered because of suspected sepsis. The patient developed abdominal distension and expired on the 16th day of hospitalization, at the age of three and a half months. The infant was too ill to undergo direct assay of intestinal mucosal tissue for disaccharidase activity or for challenge with offending sugars. Post-mortem tissue assay revealed less than 10% of normal activity for lactase (beta-galactosidase), sucrase, maltase, and isomaltase in the intestinal mucosa.

Claude R, Tournier C. [A study of CM 422 in acute and chronic diarrhea in adults]. Med Chir Dig 1980;9(1):83-5

Clausen CR, Christie DL. Chronic diarrhea in infants caused by adherent enteropathogenic Escherichia coli. J Pediatr 1982 Mar;100(3):358-61

Enteropathogenic Escherichia coli (ETEC) (0111:K58:H-) was isolated from the small bowel of two infants, aged 5.5 months and 15 months with chronic diarrhoea in Washington, USA. The isolates adhered to tissue culture cells in densely packed aggregates. Small bowel biopsy revealed acute inflammatory changes and focal adherence by large numbers of ETEC 0111. The pattern of adherence was unique and found in only 11 of the 196 enteric isolates of E. coli. All of the adherent E. coli were in serogroups 0111 and 0119. The study reinforces evidence that infection with certain ETEC strains may result in serious diarrhoea; the pathogenic mechanism appears related to dense colonization of intestinal tissue. The adherent strains can be detected by tissue culture assay.

[Clinico-pathologic conference. Chronic diarrhea in a 43-year-old female]. Internist 1981 Nov;22(11):694-704

Clune S see Holmes R

Coale MS, Robson JRK. Dietary management of intractable diarrhea in malnourished patients. J Am Diet Assoc 1980 May;76(5):444-50

Patients with protein-calorie malnutrition frequently have a flattened intestinal mucosa, which gives rise to diarrhoea and malabsorption. Repletion of nutritional status is essential for repair of the gut tissue and clinical improvement of diarrhoea and malabsorption. Rapid enteral refeeding, however, may cause severe setbacks in progress. This paper presents a gradual three-stage enteral feeding protocol for nutritional rehabilitation which is

effective in treating patients with chronic diarrhoea that is induced or exacerbated by protein-calorie malnutrition. For tube feeding (stage I), formulations containing calcium caseinate, medium-chain triglycerides and water, were outlined. A continuous infusion was indicated. The recommended progression and rates of flow of the tube-feeding formula were specified. After completion of the tube-feeding protocol, adult patients should be challenged with a bolus feeding (stage II) of a high-protein, high-calorie, milk shake mixture. Solid feedings (stage III) are begun when the patient tolerates previously introduced feedings, and when protein status is improved. Patients should closely be monitored for progress on the diet. Evaluation should include daily weighing, number and volume of bowel movement, and stool pH.

Coffman J. Data base for weight loss and chronic diarrhea. VM SAC 1981 Jan; 76(1):95-9

Coffman J. Data base for weight loss and chronic diarrhea-2. VM SAC 1981 Feb; 76(2):225-30

Cohen S, Mathis R, Walker WA. Chronic nonspecific diarrhea: role of dietary management in control. Pediatr Res 1978;12:432

Cohen S, Lake AM, Mathis RK, Walker WA. Perspectives on chronic nonspecific diarrhea: dietary management. Pediatrics 1978 May;61(5):808-9

This paper reviews the role of dietary intake in the cause and management of chronic nonspecific diarrhoea. Observations suggest a role of inadequate dietary fat — one that normally would delay gastric emptying and slow intestinal transit. The clinical experience indicates that a significant subset of patients, classified as having chronic diarrhoea, have symptoms that are dietarily, often iatrogenically, induced. A complete dietary history, with an otherwise normal history and results of physical examination, may help the pediatrician to determine those patients who may benefit from increased quantities of dietary fat (preferably polyunsaturated) to slow intestinal transit time and treat the diarrhoea gradually.

Cohen SA, Hendricks KM, Eastham EJ, Mathis RK, Walker WA. Chronic nonspecific diarrhea: a complication of dietary fat restriction. Am J Dis Child 1979 May; 133(5):490-2

Chronic nonspecific diarrhoea is a frequent cause of prolonged diarrhoea in childhood. Typical diagnostic features include onset by 30 months of age, normal growth and development, and diarrhoea with more than 2 weeks' duration. It usually follows gastroenteritis or an acute infection and is often associated with a low intake of dietary fat. This paper reports the cases of 5 patients who experienced this condition following dietary manipulation to prevent the occurrence of atheromatous coronary artery disease. Once daily dietary fat (primarily polyunsaturated) intake was raised to 30 to 50% of the total calories consumed, diarrhoea abated in each of the five patients within 5 to 28 days. When they resumed their low-fat diet, the symptoms of diarrhoea recurred in each instance. Delayed gastric emptying and altered intestinal motility, caused by an increased fat intake, may account for the cessation of diarrhoea in the cases under study. The results also indicate that diminished dietary fat cannot only prolong post-infectious diarrhoea, but can also induce a state of chronic diarrhoea without evidence of malabsorption.

Cohen SA, Hendricks KM, Mathis RK, Laramee S, Walker WA. Chronic nonspecific diarrhea: dietary relationships. Pediatrics 1979 Oct;64(4):402-7

Chronic nonspecific diarrhoea is the most common cause of prolonged diarrhoea without failure to thrive. Although it is most common in the 6-36-month-olds, chronic nonspecific diarrhoea may persist until 54 months of age. Forty-four outpatients with this syndrome, seen at a hospital in Boston, USA, had complete dietary histories. These patients were divided into 4 groups according to their daily fat and caloric intake and to their responses to dietary modifications. Although the patients with chronic nonspecific diarrhoea had statistically fewer bowel movements per day than did those with other causes for diarrhoea ($p<0.001$), the consistency of stools from both groups was not different. All 4 groups of patients with chronic nonspecific diarrhoea had significantly less fat ($p<0.05$) in their diets at the time of presentation than did the 10 non-chronic nonspecific diarrhoea patients. In 3 of the groups, daily fat consumption was increased, irrespective of the adequacy of their initial intakes. In all 38 patients in these groups, this dietary modification was associated with the resolution of symptoms. The fourth group, with initially normal dietary fat ingestion, did not respond to diet therapy. The overall success rate of the regimen in this patient population was 82%. The 3 groups had an increase in caloric intake during the treatment period. The protein intake in each group of patients was normal on the initial diet and did not increase during treatment. There was no difference in other dietary constituents during treatment. Thus, carbohydrate, fiber, and caloric contents of the diets did not play a role as significant as fat intake. The study showed that a lack of appropriate dietary fat might be of importance in the prolongation of diarrhoea in patients with chronic nonspecific diarrhoea syndrome. Based on this initial study, a therapeutic trial of increased dietary fat and diminished carbohydrate is recommended for patients fulfilling the currently accepted criteria for chronic nonspecific diarrhoea.

Cole CR see Rogers WA

Colle E see Gunn T

Collins OD, 3d see Peterson HD

Cook RA, Tappe JP. Chronic enteritis associated with Edwardsiella tarda infection in Rockhopper penguins. J Am Vet Med Assoc 1985 Dec 1;187(11): 1219-20

Cooke WT see Cooper BT

Cooper BT, Holmes GKT, Ferguson R, Thompson R, Cooke WT. Proceedings: chronic diarrhoea and gluten sensitivity. Gut 1976 May;17(5):398

Copeland L. Chronic diarrhea in infancy. Am J Nurs 1977 May;77(3):461-3

Coppa GV see Catassi C

Corazza GR see Gasbarrini G

Corbett C, Holdsworth D. The effect of loperamide in chronic diarrhoea: comparison with placebo, pilot comparison with other antidiarrhoeal agents, and effect on small bowel transit time. In: Gough D, ed. The control of diarrhoea

in clinical practice. London: The Royal Society of Medicine, 1978:15–20 (Royal Society of Medicine International Congress and Symposium series, 5)

This two-part study was designed to assess the effectiveness of loperamide in chronic diarrhoea by a double-blind crossover comparison with placebo, and a pilot study was carried out comparing loperamide with codeine phosphate and diphenoxylate. The effect of loperamide on small bowel transit time was also studied. Patients with diarrhoea of more than three months' duration and requiring symptomatic treatment were entered to the trial. The 12 patients in the first part of the trial took loperamide as 2 mg capsules/twice daily, and this dose was gradually increased until control of diarrhoea was achieved. The number of capsules taken until diarrhoea stopped was noted. Loperamide or a placebo of identical appearance were then given for 3 weeks each on a double-blind randomized crossover basis. In the second part of this study, patients were given codeine phosphate or diphenoxylate for 2 weeks each, the drugs being dispensed as identical capsules containing 30 mg of codeine phosphate or 2.5 mg of diphenoxylate. One to 3 capsules were given daily, and this dose was increased until diarrhoea stopped. Loperamide produced better control than 150–180 mg of codeine phosphate or 10–15 mg of diphenoxylate daily. Ease of control was not affected by the course of the diarrhoea. Mean small bowel transit time before treatment was 61.4±5.6 min and was prolonged by loperamide to 106.4±8.9 min ($p<0.001$). The patients in whom control of diarrhoea could not be achieved with other antidiarrhoeal agents was achieved with loperamide.

Corbett CL see Palmer KR

Correa O see Weidenslaufer A

Cosnes J, Gendre JP, Le Quintrec Y. [Chronic radiation enteritis. II. General consequences and prognostic factors]. Gastroenterol Clin Biol 1983 Aug-Sep;7 (8-9):671-6

Cosnes J see Gendre JP

Cowen AE, Campbell CB. Symptomatic therapy for chronic diarrhoea: a comparison of the effects of codeine phosphate and diphenoxylate hydrochloride. Med J Aust 1973 Apr 28;1(17):842-3

In this study, a small group of patients with daily diarrhoea for over 6 months were studied, and the symptomatic effect of codeine phosphate was compared with that of diphenoxylate hydrochloride in their treatment and recovery. Ten patients with chronic diarrhoea, attending a gastroenterology outpatient clinic and whose diarrhoea lasted for more than 6 months, were included in the study. The first, second, fifth and sixth weeks were control periods when no therapy was given. During the 3rd and 4th weeks and again during the 7th and 8th weeks, tablets were administered in a double-blind manner. There was no significant difference in the daily fecal weight during the 3 study periods. No changes occurred in the underlying disease process, and no placebo effect was apparent even in patients with functional diarrhoea. A statistically significant reduction in stool frequency was achieved with both tablets, diphenoxylate hydrochloride (2.5 mg) and atropine sulphate (0.025 mg) (lomotil) (tablet A) and codeine phosphate (7.5 mg) and atropine sulphate (0.025 mg) (tablet B). There was no significant difference in the observed effects among patients between the 2 therapeutic regimes. This study showed that codeine

phosphate and diphenoxylate hydrochloride were equally effective in reducing frequency of bowel movements in patients with chronic persistent diarrhoea. Side-effects from both drugs were relatively few. Because of the possibility of addiction with both codeine phosphate and opium derivatives, diphenoxylate hydrochloride is suggested to be safer for long-term management of chronic diarrhoea.

Creamer B, Dutz W, Post C. Small-intestinal lesion of chronic diarrhoea and marasmus in Iran. Lancet 1970 Jan 3;1(7636):18-20

The small intestines of 11 infants, whose ages ranged from two and a half to six and a half months and who had died of chronic diarrhoea and marasmus in an orphanage in Shiraz, Iran, were examined at necropsy. Gross abnormalities were found throughout most of the small bowel in every case. In 3 cases, there were moderate changes in villus structure - convolutions and, on the crest of mucosal folds, long low ridges throughout the duodenum and jejunum with convolutions and some leaf-shaped villi in the ileum. The rest showed severe changes, the mucosa on the crest of mucosal folds being flat with the faint outline of a convoluted pattern. In between the folds, there were long low ridges lying on the transverse axis of the bowel. On histological examination, the abnormal bowel was very similar to that seen in the coeliac syndrome or tropical sprue. The findings suggested that malabsorption was present in this syndrome.

Cucchiara S see Auricchio S

Dahlqbvist A see Suthutvoravut U

Dahms BB see Marino LR

Daletskaia GV, Ekisenina NI, Kamenetskaia BI, Borisova LI, Deino GI. [Emotional-vegetable disorders in chronic diarrhea] Sov Med 1983;(9):14-7

D'Angelo G see Catassi C

D'Antonio AM see Auricchio S

D'Hoore-Braun E see Juhe H

David VH, Lisewski G, Marx I. [On problems of absorption disorders in chronic enteritis. A contribution to the malabsorption syndrome]. Dtsch Gesundh 1967 Mar 2;22:385-95

Chronic enteritis is histologically characterized by a broadening or fusion of the small intestinal villi, with a simultaneous infiltration of the villus stroma by plasma cells, lymphocytes and occasionally by eosinophils. Electron microscopy revealed changes in endoplasmatic reticulum, mitochondriae and Golgi field, and modifications of both brush border microvilli and of epithelial cells' terminal web. The digestive-resorptive surface of the epithelial cells of the top of the villi, which normally is considerably enlarged by microvilli development, may be reduced to values below 10% in chronic enteritis. At the same time, the enzymatic activities of the disaccharidases, peptidases, etc., are decreased. In most cases, the changes are only focifom, their degree varying in individual cells. The histologic and electron microscopic findings in chronic enteritis are very similar to those of the primary and secondary

malabsorption syndrome, constituting a special case of secondary malabsorption. Invariably, the plasma membrane of the epithelial cell microvilli, responsible for the digestive-resorptive process, is the decisive region. It is of lesser importance for the clinical and morphological picture of the malabsorption syndrome, whether the latter is primarily or secondarily affected by an injury. The clinical picture of chronic nonspecific enteritis depends on the injury's quantitative extent.

Davidson GP, Robb TA, Kirubakaran CP. Bacterial contamination of the small intestine as an important cause of chronic diarrhea and abdominal pain: diagnosis by breath hydrogen test. Pediatrics 1984 Aug;74(2):229-35

A modified breath hydrogen test with improved sensitivity and reliability was used as a part of the investigative assessment of children with chronic diarrhoea and abdominal pain. Unsuspected bacterial contamination of the small intestine was indicated by breath hydrogen testing in 9 patients, aged 2 to 34 months during physical examination for chronic diarrhoea and abdominal pain in Adelaide, Australia. Elevated bacterial counts of questionable significance were found in duodenal aspirates before and after antibiotic treatment. Deconjugated bile acids were not detected in duodenal juice from any patient. The duodenal mucosal architecture as viewed by both light and electron microscopy was normal in all patients. This may indicate that the site of colonization was distal to the biopsy site. Breath testing indicated lactose malabsorption in all patients, and 4 of the 5 patients tested also malabsorbed sucrose. The duodenal mucosal disaccharidase levels in all patients were within normal range except for sucrose depression in 2 patients. The lactase-sucrase ratio was greatly elevated (0.80 ± 0.36) in 8 patients, and they were significantly different from those of 16 normal subjects (0.40 ± 0.16; $p<0.01$). Dietary restriction alone did not cause complete cessation of symptoms, whereas all patients responded dramatically to oral antibiotic therapy, which led to complete resolution of symptoms within 24 h. When patients were well, the lactase-sucrase ratio had returned to normal in those tested, and all 9 had normal lactose and lactulose breath hydrogen tests. Unsuspected bacterial contamination of the small intestine, which is easily detected using the breath hydrogen test, may be more commonly associated with chronic diarrhoea in children than previously realized. Bacterial overgrowth may be the reason for continuing symptoms and may represent one of the causes or consequences of chronic diarrhoea. In such cases, therapy should be directed at removing the contamination. This study demonstrates the value of breath hydrogen test in the small intestine of children. The breath hydrogen test is simple, rapid, noninvasive, and obviates the need for duodenal intubation or anaerobic culture facilities for the diagnosis.

Davidson GP, Robb TA. Children with chronic diarrhoea and altered disaccharidase ratio who respond to sucrose withdrawal [letter]. Lancet 1982 Aug 7;2(8293):325

Davidson M, Wasserman R. The irritable colon of childhood (chronic nonspecific diarrhea syndrome). J Pediatr 1966 Dec;69(6):1027-38

This report summarizes a number of features that were observed in a group of children with chronic nonspecific diarrhoea syndrome who were managed without restrictions in diet. Case histories of 186 children were examined retrospectively at an American hospital. In 90% of the cases, despite management without medication or dietary restrictions, the diarrhoea stopped by

to 39 months of age. Only 3 to 4 bowel movements per day were passed during attacks, while about 10% of the patients reported more than 6. Between the initial visit and clearing of symptoms, the children did no worse, and frequently better than with various treatments with drugs or restrictive dietary regimens. Limited number of laboratory studies, the clinical pattern and character of stools, and the normal growth and development of the children indicate that this benign condition is not caused by gastrointestinal infection nor is it a form of malabsorption. There appears to be a strong relationship between this condition of children and the functional difficulty of adults which is known as the irritable colon syndrome. This relationship is discussed.

Dawson AM see Kingham JG

De Andrade DR see Campana AO

De Angelis GL see Gregori G

De Cree J see Verhaegen H

De Marco F see Giardina MF

De Ritis G see Pignata C

De Titis G see Auricchio S

De Vizia B see Auricchio S

De Vizia B see Pignata C

Dean JA see Chernoff R

Deckelbaum RJ see Weizman Z

Deino GI see Daletskaia GV

Delforge M see Dreze C

Dervichian M see Gouerou H

Desai HG. Chronic diarrhea in adult population in Bombay: a review. Indian J Med Sci 1967 Apr;21:240-9

Desideri D see Gasbarrini G

Dicke WK see Kamer JH

Dive C see Melange M

Diver-Haber A see Jonas A

Djarv L, Sjodahl R. Elimination of loperamide in patients treated for chronic diarrhoea. Drugs Exp Clin Res 1981 Feb;7(1):25-30

The elimination kinetics of loperamide were studied in Sweden in 10 adult

patients treated for chronic diarrhoea with therapeutic doses of the drug. Plasma concentrations were determined with a specific radioimmunoassay method. The plasma concentrations of loperamide on the mornings of day 4, 5 and 6 were 2.2±1.3, 1.8±1.2, and 2.4±1.9 ng/ml respectively. The clinical response observed in the treated patients suggests that a plasma concentration of 2 ng/ml can be considered to be within the therapeutic range. The elimination constant was -0.018 to -0.092. The mean plasma half-life was 16.2±6.2 when elimination from steady-state was followed. It is suggested that the influence of diarrhoea on absorption of drugs and binding of loperamide to orosomucoid may be the reasons for a prolonged half-life. To control chronic diarrhoea in patients with a reduced response to antidiarrhoeal drugs, a high initial dose, followed by a low maintenance dose, is suggested.

Djarv L see Bergman L

Djupri L see Sutjiningsih

Dobrzanska A, Rowecka-Trzebicka R, Socha J, Stodulski J, Wozniewicz B. [VIPoma as a cause of chronic diarrhea in a 3-year-old boy]. Pediatr Pol 1983 Jan;58 (1):103-7

Dobrazanska A see Socha J

Dodge J. Chronic non-specific diarrhoea in children. In: Gough D, ed. The control of diarrhoea in clinical practice. London: The Royal Society of Medicine, 1978:31-4. (Royal Society of Medicine International Congress and Symposium series, 5)

This study describes a double-blind crossover trial of loperamide compared with placebo in their efficacy in antidiarrhoeal agents. Sixteen children with persistent diarrhoea were included in the study whose ages ranged from 6 to 56 months (median 22.5), and the duration of their diarrhoea ranged from 2 to 56 months (median 18). Initially, loperamide syrup, in a concentration of 0.2 mg/ml, was given in increasing doses, until the control of diarrhoea was achieved or the predetermined maximum dose of 0.12 mg/kg was reached. After a five-day interval, loperamide hydrochloride syrup or a matching placebo was given at the previous dosage for five days. The alternative drug or placebo was given for a final five-day period. The stool frequency and character of the stools was recorded by the parents. The severity of diarrhoea was measured accordingly. The statistical analyses pertain only to the 12 patients whose records were complete for the three phases of the study. Three of the four withdrawal cases had a good response to loperamide. It was seen from the results that most marked effect was upon consistency of stools, although there was a decrease in the frequency with which they were passed. No side-effects were observed in those on loperamide, but one patient had a poor appetite while on placebo. Loperamide was thus found effective in children with chronic nonspecific diarrhoea.

Domschke W see Ruppin H

Donovan EJ. A diagnostic approach to chronic diarrhea. Dis Colon Rectum 1969 Sep-Oct;12:364-70

Donowitz M see Kidd GS

Dossa D see Chaptal J

Dreze C, Delforge M, Brassinne A, Herve P, Lombard R, Jacquet N. [Chronic diarrhea or steatorrhea as inaugural and revealing manifestation of a Zollinger-Ellison syndrome]. Acta Gastroenterol Belg 1980 May-Jun;43(5-6): 187-208

Dua N see Chopra K

Duquesne Perez F see Robbio Troyano L

Durand P, Martino AM. [Chronic intestinal disorders caused by deficiencies of digestive enzymes. Considerations on diarrhea caused by deficiency of lactase activity]. Minerva Diet 1961 Sep;1:79-81

Durrani HA see Kotwal MR

Duthie HL see Read M

Dutton PV see Furnell JR

Dutz W see Creamer B

Dwyer J see Glassman M

Eastham EJ see Cohen SA

Eckstein R see Oertel H

Edkins S see Nelson R

Eichenberger JR, Hadorn B, Schmidt BJ. A semi-elemental diet with low osmolarity and high content of hydrolyzed lactalbumin in the treatment of acute diarrhea in malnourished children. Arq Gastroenterol (S. Paulo) 1984 Jul-Sep; 21(3):130-5

Attempts were made in Brazil to speed up the recovery of children suffering from acute diarrhoea by using a semi-elemental diet formulated to suit the reduced absorption capacity of the damaged intestinal mucosa of the children. Thirty-eight infants, aged 1 to 11 months with moderate to severe malnutrition and severe acute or subacute diarrhoea, were randomly divided into two groups. Twenty patients formed the study group who received the semi-elemental diet with an osmolality of 302 mOsm/l, a low-lactose content and a relatively high content of lactalbumin hydrolysate (1 g/100 ml). Eighteen patients received available proprietory formulas or diluted cow's milk with added carbohydrates, and served as controls. The results showed that the children given the semi-elemental diet had a better average weight gain during the first 3 weeks of hospitalization compared to the control group. The children receiving semi-elemental diet also required a smaller number of intravenous rehydration drips. It is, therefore, suggested that the components of the semi-elemental diet formula should be made available to pediatricians involved in the care of infants with chronic diarrhoea.

Ekisenina NI, Krums LM, Iosava LI, German GP, Lorie NIu. [Pathogenetic principles in treating chronic diarrhea]. Ter Arkh 1981;53(2):55-8

Ekisenina NI see Daletskaia GV

Eksaengsri P. Chronic diarrhoea in children. Southeast Asian J Trop Med Public Health 1982 Sep;13(3):502

Forty cases of chronic diarrhoea in children, admitted to the Children's Hospital, Bangkok during 1979-1980, were analysed. Twenty-two cases (55%) were aged under three months. Most of them were poor, bottle-fed and malnourished. Infection was the most common cause; five cases had no identifiable cause. Secondary lactase deficiency was found in 12 cases. The treatment consisted of enteral (diluted normal formula, Prosobee and Pregestimil) and/or parenteral feeding. The mean duration of treatment was 18.3 days, with the mortality rate of 20%. (Modified author's abstract)

Eksaengsri P, Harikul S, Charoenkwan P. Two reported cases of chronic diarrhoea. In: Programme, papers and abstracts of Third Asian Conference on Diarrhoeal Diseases, Bangkok, 10-14 Jun 1985:275

Two rare cases of chronic diarrhoea, caused by ganglioneuroblastoma and nesidioblastoma, were reported. The first case was an 11-month-old girl who had chronic diarrhoea and right axilla mass for 2 and 1 months respectively. On examination, she was cachectic, severely dehydrated and had hirsutism. Her face and extremities were flushed. Two rubbery masses about 2 and 5 cms in diameter were palpated at her right axilla and left inguinal regions. Biopsy of the masses was compatible with ganglioneuroblastoma, a tumor which secretes vasoactive intestinal peptide. The second case was a 5-month-old girl who had intermittent diarrhoea since birth. She was admitted 6 times to the hospital because of this problem. Salmonella E was occasionally found in her stool specimens. On her last admission, when she was 5 months old, she had a very stormy course, complicated by hypoglycemia, pneumonia, sepsis and intravascular coagulation defect. The autopsy revealed that she had nesidioblastosis of the pancreas which could explain the clinical course of her chronic diarrhoea.

Engelhardt J see Jansen-Goemans A

Ernest DL see Butler T

Escribano Montaner A see Peris Vidal A

Evans GW see Krieger I

Familiades J see Ghisolfi J

Fan A see Beer WH

Farrell MK see Rothbaum RJ

Farthing MJG. Giardiasis: pathogenesis of chronic diarrhea and impact on child growth and development. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:253-67

Feliciani M see Gasbarrini G

Ferenci P, Lochs H, Potzi R. [Clinical results with loperamide in the treatment of chronic diarrhoea of varied aetiology]. Wien Klin Wochenschr 1982 Mar 19;94(6):148-50

Ferguson R see Gooper BT

Ferrer Calvete J, Tomas M, Galmes J, Prieto F. [Chronic diarrhea with selective IgA deficit associated with Turner's syndrome]. An Esp Pediatr 1982 Jun;16(6):459-63

Fiasse R see Mainguet P

Fiasse R see Melange M

Filipowicz-Ulewicz J see Swicowa K

Filler RM see Shwachman H

Fischer D, Labayle D, Kemeny F. [Microscopic colitis: a possible cause of chronic diarrhea? (letter)]. Gastroenterol Clin Biol 1985 May;9(5):452

Fisher SE, Leone G, Kelly RH. Chronic protracted diarrhea: intolerance to dietary glucose polymers. Pediatris 1981 Feb;67(2):271-3

Prior to the fall of 1978, the commercial elemental formulation Pregestimil (Mead Johnson) contained simple glucose as the major source of carbohydrate. To decrease the formula osmolality, this was then replaced by glucose polymers. This paper reports the case of a 7-week-old American male infant recovering from chronic protracted diarrhoea who was unable to tolerate glucose polymers, but thrived on the "old" glucose-containing Pregestimil formulation. On two occasions during treatment, glucose polymers caused diarrhoea with the presence of stool-reducing substances. The symptoms resolved when an equivalent mass of simple glucose was substituted, indicating that monosaccharide absorption was adequate. Osmolality of the formulation was, therefore, not a problem. The patient's glucose polymer intolerance was accompanied by an insult of intestinal mucosal injury with resultant chronic diarrhoea and secondary malnutrition. These latter conditions were shown to be associated with transient pancreatic insufficiency, and decreased brush-border enzyme activity. The patient's congenital hypothyroidism could have been a contributing factor in the initial stages of his problem. The child did well when his diet was changed to Nutramigen (Mead Johnson) plus proprietary strained baby foods. At 10 months of age, his height and weight were at the fifth to tenth percentile.

Fisher SE, Boyle JT, Holtzapple P. Chronic protracted diarrhea and jejunal atrophy in an infant: cimetidine-associated stimulation of jejunal mucosal growth. Dig Dis Sci 1981 Feb;26(2):181-6

This paper reports the case of a black male infant hospitalized in the USA, with massive chronic protracted diarrhoea beginning in the first week of life, and continuing unabated until its death at 21 months. An unusual jejunal mucosal lesion was noted, characterized by severe mucosal atrophy, round cell inflammation, and markedly decreased crypt mitotic activity. Anti-intestinal antibodies were found in the patient's serum. Cimetidine was administered for 4 months in an attempt to increase endogenous gastrin secretion and to stimulate mucosal growth. Thirty-minute post-prandial serum gastrin levels were higher during cimetidine therapy (mean$\pm$SEM=663$\pm$115 pg/ml). These values were significantly higher than the 3-h fasting levels during therapy ($p<0.01$). Coincident with the cimetidine therapy, the jejunal mucosa showed progressive histologic improvement. The index of crypt mitotic activity steadily rose; pretreatment mitotic activity was 1.3 (mitoses/100 crypt cells), mid-study 3.3, and end of the study 4.5. There was a direct correlation between 30-min

post-prandial serum gastrin and mitotic activity ($r=0.989$, $p<0.005$). In the last 1½ months of cimetidine treatment, the pre-existing renal disease worsened, and serum creatinine level rose to >3 mg/dl. The patient died of renal failure one month after the cessation of cimetidine administration. At autopsy, the small bowel had returned to an atrophic state. It is proposed that cimetidine may have influenced on jejunal mucosal growth, possibly through meal-stimulated hypergastrinemia. It is also speculated that an immunologic reaction may have perpetuated the symptoms in this patient.

Fitzgerald JF, Clark JH. Chronic diarrhea. Pediatr Clin North Am 1982 Feb;29 (1):221-31

This paper discusses the pathogenic mechanisms in diarrhoea, including osmotic and secretory diarrhoeas, bacterial overgrowth, defective anion exchange systems, mucosal damage, and dysmotility. A useful clinical classification of chronic diarrhoea is based on the character of stool - watery, fatty, or bloody. It was emphasized that a complete history and a thorough physical examination are essential for the evaluation and diagnosis, while hospitalization is often necessary for a complete evaluation. A detailed diagnostic approach to the problem of chronic diarrhoea has been outlined. A list of the causes of chronic diarrhoea, classified according to the stool characteristics, has also been provided.

Fitzgerald JF see Arasu TS

Fleischli DJ. Chronic diarrhea. JAMA 1967 Mar 20;199(12):925-7

This paper describes a case of chronic diarrhoea, involving a 47-year-old woman, who was hospitalized with complaints of intermittent cramps and diarrhoea during the past year. A typical attack lasted three to four days and consisted of 5 to 10 episodes. Her stools had mucus but no blood. Between attacks, she was asymptomatic for periods of two to three weeks. Sigmoidoscopy revealed several 5 mm discrete shallow ulcers near the rectosigmoid junction. Giardia lamblia cysts were found in her stool. After a 10-day course of succinylsulfathiazole, her symptoms subsided. Sigmoidoscopy, three months later, showed normal mucosa without ulcers. Almost four months after her first admission, she returned with similar complaints of cramps and diarrhoea. Sigmoidoscopy showed edematous mucosa but no ulceration. A barium enema study was done. The day following the barium enema, prednisone therapy of 40 mg daily was started. Two weeks after admission, the patient underwent a dilatation and curettage, which revealed a benign endometrial polyp as the cause of intermittent vaginal bleeding. This caused severe lower abdominal pain. A series of roentgenograms showed progressive dilatation of the colon with marked thickening of the wall suggestive of pseudopolyps. Finally, small bowel obstruction or very severe adynamic ileus, in addition to the process in the colon, was found. Toxic amebic ulcerative colitis was suggested. This was the first case recorded in the laboratory of amebic ulcerative colitis, involving the entire colon and stimulating idiopathic ulcerative colitis.

Flores A see Sutphen JL

Follo D see Auricchio S

Fontana G see Gasbarrini G

Fordtran JS, Ana CAS, Morawski SG, Bo-Linn GW, Schiller LR. Pathophysiology of chronic diarrhoea: insights derived from intestinal perfusion studies in 31 patients. Clin Gastroenterol 1986 Jul;15(3):477-90

Fordtran JS see Bo-Linn GW

Fordtran JS see Harford WV

Fordtran JS see Read NW

Forfang JC see Osterholm MT

Forouzandeh B see Mir-Madjlessi SH

Francis DEM see Larcher VF

Fulton WF. An instructive problem in chronic diarrhea. Am J Gastroenterol 1962 Jan;37:85-6

Fung W-P, Kho KM. The importance of milk intolerance in patients presenting with chronic (nervous) diarrhoea. Aust NZ J Med 1971 Nov;1(4):374-6

This is the first report of milk intolerance in patients presenting with chronic (nervous) diarrhoea in Singapore. Nineteen patients, aged 19 to 53 years with chronic (nervous) diarrhoea, were screened for milk intolerance by lactose barium study and/or lactose tolerance test. Eighteen patients were intolerant to milk, showing that lactase deficiency is a very important etiological factor in chronic (nervous) diarrhoea in Singapore. After the withdrawal of milk, symptoms improved in 17 cases and completely cleared up in 11. A simple lactose barium study is adequate as a screening test for milk intolerance. If radiology is not possible, a lactose tolerance test would be adequate, and estimation of lactase in the jejunal mucosa is not necessary for routine clinical practice.

Furnell JR, Spiers AL, Dutton PV. Chronic non-specific diarrhoea [letter]. Arch Dis Child 1985 Oct;60(10):994

Galambos JT, Hersh T, Schroder S, Wenger J. Loperamide: a new antidiarrheal agent in the treatment of chronic diarrhea. Gastroenterology 1976 Jun;70(6): 1026-9

This paper describes the action of loperamide, an antidiarrhoeal agent used commonly in the treatment of chronic diarrhoea. Twenty-seven patients (median age 44.5 years) with chronic diarrhoea due to Crohn's disease (8), ulcerative colitis (4), short bowel syndrome (3), and idiopathic (functional) causes (5) participated in a multi-phase study (open, double-blind, and long-term open) on the effects of loperamide hydrochloride. In the open phase of the study, loperamide effectively relieved symptoms of diarrhoea in 21 of the 27 patients at a median daily dose of four capsules (range 2 to 8 capsules). The median number of stools dropped from eight (range 2 to 30) in the initial relapse period to two stools (range 4 to 30) after 1 month of treatment ($p=0.0001$). Loperamide effectively improved diarrhoea in 5 patients who were previously poorly controlled with other antidiarrhoeal agents. All 10 of the patients during the double-blind phase on loperamide confirmed the positive results of the open phase. The consistency of stools improved from soft to normal after

14 to 40 days on loperamide. All but one of the 9 patients, who received placebo during the double-blind phase, relapsed between 2 and 15 days (median 4 days) of treatment. The relapsed placebo patients were controlled by loperamide in the third phase of the study. After the double-blind phase, all 18 patients were treated in a long-term open phase with their predetermined optimum individual dose (2 to 8 capsules, median 4 capsules) for 6 to 18 months. The median number of stools remained 2 a day, and the median consistency of stools was normal. The diarrhoea in 6 patients did not improve with loperamide. Four of the 27 patients had abdominal cramps and pain during loperamide treatment. Loperamide has been found useful in the treatment of chronic diarrhoea.

Galbert MW. Chronic diarrhea with ganglioneuroblastoma. Clin Pediatr 1971 Aug;10:476-9

Galian A see Gouerou H

Gall DG, Hamilton JR. Chronic diarrhea in childhood: a new look at an old problem. Pediatr Clin North Am 1974 Nov;21(4):1001-17

Gallagher ND, Harrison DD, Wyatt JV, Skyring AP. Sodium conservation by the small intestine in a patient with chronic ileostomy diarrhoea. Gut 1969 Mar;10(3):202-5

Galmes J see Ferrer Calvete J

Gardey RH see Rider JA

Gardner FH. Nutritional management of chronic diarrhea in adults. JAMA 1962 Apr 14;180(2):147-52

Chronic diarrhoea in the adult may be associated with a variety of nutritional deficiencies. These deficiencies are often found with abnormal anatomic changes or mucosal alteration of the small bowel. This paper discusses the impairment of electrolyte vitamin and mineral absorption and general nutritional depletion, e.g. steatorrhea and azotorrhea. These deficiencies can be produced by several mechanisms. Bacterial reactions that initiate chronic diarrhoea are related mostly to anatomical lesions that allow areas of stasis for an excessive proliferation of the normal bowel bacterial flora. Such cul-de-sacs may impair nutrition by (1) bacterial competition for nutrients, or by (2) producing toxic elements that irritate the bowel mucosa and decrease absorption of all foodstuffs. Antibiotic therapy is, therefore, important to improve nutritional status of patients with anatomical defects. Impaired fat absorption may be associated with pancreatic insufficiency. In such cases, enzyme replacement with pancreatic extracts is a well-known practice. Available diagnostic procedures permit the physician to classify bowel disorders that may be treated by surgical correction, antibiotics, or specific dietary programs.

Garner EPR see Brey OA

Gasbarrini G, Corazza GR, Feliciani M, Albano O, Stufano N, Altomare E, Fontana G, Valpiani D, Scuro LA, Vantini I, Vaona B, Barbara L, Miglioli M, Banterle C, Desideri D, Manto M. Comparison of lidamidine HCl and loperamide in the symptomatic treatment of chronic diarrhoea. Ital J Gastroenterol 1986 Jun;18 (3):155-8

The efficacy of lidamidine HCl, a new drug with proposed alpha-2-adrenergic activity, was compared with that of loperamide in 59 patients with chronic diarrhoea of more than 3 months' duration (at least 3 or more bowel movements per day). The administration of any other antidiarrhoeal drugs, antispasmodics, anticholinergics, antibiotics and cholestyramine was suspended. Identical capsules, containing 2 mg of active principles, were used for both lidamidine HCl and loperamide. After two days of observation only and without any pharmacological treatment, each patient was assigned at random to one of the two treatment groups. The initial dose was 1 capsule given thrice a day. Of the 59 patients, 29 were treated with lidamidine HCl and 30 with loperamide. During the first week of treatment, the number of stools decreased from 5.81±0.69 to 3.63±0.33 ($p<0.01$ vs baseline) in the lidamidine HCl group and from 4.91±0.43 to 2.75±0.42 ($p<0.01$ vs baseline) in the loperamide group. At the end of the first week of dosage adjustment for both drugs, the treatment proved to be effective in 77% of the patients treated with lidamidine HCl and in 83% of those treated with loperamide, with a reduction in the number of daily bowel movement by over one-third. Only 5 patients in the loperamide group and 6 in the lidamidine HCl group were considered treatment failures. After suspension of both drugs, the number of bowel movements increased again but not significantly. The results of the study showed that lidamidine HCl and loperamide had comparable effects in the pharmacological treatment of chronic diarrhoea of both organic and functional origin. Lidamidine HCl was shown to be well tolerated, side-effects being minor and self-limiting.

Gazdzik W see Kulesza E

Gebauer A see Antes G

Gemer O, Zaltzein E, Gorodischer R. Absorption of orally administered gentamicin in infants with diarrhea. Pediatr Pharmacol 1983;3(2):119-23

While oral gentamicin in infantile diarrhoea is recommended by some authors, almost no information is available concerning the gastrointestinal absorption of gentamicin in infants when small intestinal mucosa is damaged. Therefore, plasma gentamicin concentration was measured for the first time in 14 infants, aged 6 weeks to 16 months hospitalized in Israel with prolonged severe diarrhoea and on treatment with oral gentamicin (mean dose: 17 mg/kg every 8 h). Plasma gentamicin levels were determined serially following the oral dose. Although marked individual and erratic temporal variations existed, average plasma gentamicin concentrations were low and stable (0.3±0.12 µg/ml). Duration of diarrhoea and plasma gentamicin concentrations were positively correlated ($Y=0.59$, $p<0.05$), indicating that the morphological and functional changes in the intestinal mucosa of infants with prolonged diarrhoea allow the absorption of the polar gentamicin molecule.

Gendre JP, Cosnes J, Le Quintrec Y. [Chronic radiation enteritis. I. Intestinal malabsorption. Anatomo-functional correlates]. Gastroenterol Clin Biol 1983 Aug-Sep;7(8-9):664-70

Gendre JP see Cosnes J

George DE. Chronic diarrhea in infants and children. Am Fam Physician 1984 May;29(5):280-8

Georgescu M see Popescu V

German GP see Ekisenina NI

Ghadimi R see Mir-Madjlessi SH

Ghai OP see Arora NK

Ghai OP see Bhan MK

Ghai OP see Chandra RK

Ghai OP see Walia BNS

Ghishan FK, Soper RT, Nassif EG, Younoszai MK. Chronic diarrhea of infancy: nonbeta islet cell hyperplasia. Pediatrics 1979 Jul;64(1):46-9

The case of a white male infant, who developed refractory watery diarrhoea at the age of 2 weeks, is described. Its stool frequency increased to 15 to 20 per day and his weight decreased gradually. Dietary manipulations did not affect its diarrhoea. At 3½ months of age, oral feedings were discontinued, and a central venous catheter was inserted to maintain nutrition intravenously. Despite no oral intake, the patient continued to pass 400 to 600 g of watery loose stools daily. A vasoactive intestinal peptide (VIP)-producing tumor was suspected, and an exploratory laparatomy was performed at the age of 7½ months. A tissue specimen from the tail of the pancreas showed non-beta islet cell hyperplasia arranged in clumps, with surrounding chronic inflammatory cells. VIP levels were elevated in plasma and pancreatic tissue. After 95% pancreatectomy, plasma VIP levels dropped to normal. Hypokalemia, described in adult patients with VIP-producing pancreatic tumors and refractory watery diarrhoea, was not a significant problem in this infant. Post-mortem findings showed atrophic small bowel mucosa and marked fatty degeneration of the liver. This is the first report on the association of refractory watery diarrhoea with elevated levels of plasma VIP and pancreatic islet non-beta cell hyperplasia in the pediatric age group.

Ghishan FK see Greene HL

Ghisolfi J, Olives JP, Familiades J, Rives JJ, Rives-Tocaven M. [Chronic diarrhea in nonspecific colopathies in children. Trial of etiological classification]. Arch Fr Pediatr 1983 Aug-Sep;40(7):531-6

Giannella RA. Chronic diarrhea in travelers: diagnostic and therapeutic considerations. Rev Infect Dis 1986 May-Jun;8(Suppl 2):S223-6

Although the epidemiology, etiology, and pathophysiology of travelers' diarrhoea are well understood, the long-term consequences of this syndrome are poorly appreciated. Many people struck with travelers' diarrhoea do not completely recover, but rather develop one of several chronic diarrhoeal syndromes. In some patients, an episode of travelers' diarrhoea seems to unmask a pre-existent, underlying gastrointestinal disorder. The frequency of these complications and the magnitude of this problem are unknown. The differential diagnosis, diagnostic workup, and treatment of such patients have been outlined; unfortunately, many patients with chronic diarrhoea elude diagnosis, and treatment is problematic. Some of the questions that must be answered include the following: (1) What is the magnitude of the problem of chronic diarrhoea following travelers' diarrhoea?, (2) What is the natural

history of patients with this syndrome?, (3) Which individuals are most likely to develop a chronic diarrhoeal syndrome, and can they be identified in advance?, (4) Are new etiologic agents involved in these chronic diarrhoeal syndromes? Answers to these questions will require well-organized, multicenter studies of a large number of travelers to various locales. (Author's abstract)

Giardina MF, Matarazzo M, Cacciatore L, De Marco F. Ticlopidine can cause chronic diarrhoea [letter]. Lancet 1984 Feb 18;1(8373):407

Gibbs JO see Rider JA

Giger DK see Penn RG

Gillin FD see Smith PD

Giorgi PL see Catassi C

Giri IW see Soeparto P

Glassman M, Grill B, Gryboski J, Dwyer J. High incidence of hypogammaglobulinemia in infants with diarrhea. J Pediatr Gastroenterol Nutr 1983;2(3):465-71

Quantitative immunoglobulin estimations were done on 136 children, aged under 3, referred to an American hospital for chronic or severe diarrhoea between 1977 and 1981. Thirty-one patients (22.8%) had serum immunoglobulin levels below the 5th percentile for age. Twenty-four of these 31 patients (77.4%) had normal to near-normal serum immunoglobulin levels by before reaching three years of age, and 15 of them were categorized as having transient hypogammaglobulinemia of infancy. This condition was thought to be a rare disorder; only 27 patients with this problem were reported prior to 1978. The results also suggest that the IgG levels noted in patients with a transient deficiency of IgA had also been partially supressed by whatever mechanism was responsible for the maturation delay producing low levels of IgA. The mechanism responsible for both the hypogammaglobulinemia and the diarrhoea are unclear. Patients with transient hypogammaglobulinemia were younger at presentation (mean age 8.3 months) and at the onset of their diarrhoea (3.1 months) than those with chronic diarrhoea but normal immunoglobulins (18.2 and 8.2 months respectively). Males and females were equally affected. The diarrhoea of infants with transient hypogammaglobulinemia and its variance were responsive to the elimination from the diet of milk, soy, and gluten. While the etiology of the diarrhoea remained obscure, significant problems outside the gastrointestinal tract did not occur. Circumstantial evidence suggests that the failure to produce normal amounts of IgG and IgA may result from a lack of some aspect of T cell helper function essential for the genetic switching of immature B cells. Increased numbers of B cells carrying IgM receptors were noted in some of the patients with transient hypogammaglobulinemia.

Goldgar CM, Vanderhoof JA. Lack of correlation of small bowel biopsy and clinical course of patients with intractable diarrhea of infancy. Gastroenterology 1986 Mar;90(3):527-31

To assess the value of small bowel biopsy in determining the prognosis of intractable diarrhoea of infancy, a retrospective comparison of the clinical

course and small bowel histology of infants with intractable diarrhoea was made. Small bowel biopsy specimens of 19 infants (11 males), aged 0 to 6 months at the onset of their diarrhoeal symptoms, were examined blindly, and a score reflective of the severity of injury for each biopsy specimen was derived. Biopsy scores were correlated with the duration of nutrition support required in the treatment of each patient. The correlation between the total biopsy score and the clinical course variables was not significantly different from zero. Thus, no correlation could be found between the severity of the small bowel mucosal injury on biopsy and the clinical course of the patient. In general, the data refute the clinical use of the small bowel biopsy as a therapeutic guide or prognostic indicator for the course of the disorder. Small bowel biopsy should not, therefore, be used to advise parents on the possible duration of intractable diarrhoea of infancy.

Goldman H. Acute versus chronic colitis: how and when to distinguish by biopsy [editorial]. Gastroenterology 1984 Jan;86(1):199-201

This editorial highlights the findings of Surawicz and Belic (1984) which suggests that rectal mucosal biopsy can be used to distinguish acute and chronic colitis in a high proportion of cases. Seven histologic features noted in the rectal mucosal biopsy specimens proved to be highly discriminant. Some features are indicative of chronic colitis either of the ulcerative or Crohn's type. Granulomas and basally located giant cells, although more common in chronic colitis and in Crohn's disease, can be seen in acute disorders, such as serious infections. Basal lymphoid aggregates have been noted in chronic colitis. One or more of these discriminant features are present in 79% of the cases of chronic irritable bowel syndrome. The appearance of superficial acute inflammation or giant cells in the face of normal crypt architecture is highly suggestive, but not diagnostic of acute colitis. Biopsy can be done as early as 3 or 4 weeks after the onset of symptoms. If the biopsy specimen is completely normal, e.g. no element of crypt distortion or atrophy, no sign of epithelial regeneration or Paneth cell metaplasia, the patient then has self-limited colitis. The patient of irritable bowel syndrome would show crypt irregularity or evidence of persistent inflammation. The presence of continuous inflammation with a longer duration would secure the diagnosis of chronic ulcerative colitis. In Crohn's disease, the disorder tends to be more often focal. In any clinical situation, one must collect all available information to establish an exact etiology of the disease. It is concluded that the technique used by Surawicz and Belic can serve as a standard for future structural studies.

Goldman H <u>see</u> Perlmutter DH

Goldschmidt B. Microscopic stool-gazing, a guide to the cause and cure of chronic and recurrent diarrhoea in children. S Afr Med J 1966 Feb 26;40(9):191-5

Microscopic examination of the fresh, warm stool is a helpful procedure in defining the cause of chronic and recurrent diarrhoea in children. It has been suggested that the examination should be performed by the clinician himself, which will enable him to make an immediate diagnosis and consequently institute an appropriate treatment at an early stage. This report also outlines and illustrates the common microscopic findings. It is indicated that infection often initiates malnutrition and may also be responsible for its continuation. The severe cases of kwashiorkor and marasmus can be remedied after treatment is

initiated with suggestive guidelines made available from an early microscopic examination of the patient's stools.

Goldsmith RS. Chronic diarrhea in returning travelers: intestinal parasitic infection with the fluke Metagonimus yokogawai. South Med J 1978 Dec;71(12): 1513-5

An unusual infection with the parasite, Metagonimus yokogawai, was acquired by a 60-year-old American woman traveling in the orient. Diarrhoea began abroad and recurred at intervals, until she was seen 1½ years later. Stool examinations resulted in the recovery of many small operculated ova, 25.9 to 30.0 μ long and 15.5 to 18.0 μ wide. Morphologically, they were suggestive of an intestinal heterophyid fluke infection. Treatment with hexylresorcinol failed to eradicate the infection. The patient was then treated with 5 ml of tetrachloroethylene in the morning after an overnight fast. Ten adult worms in various stages of disintegration were recovered from the stool, which led to a specific diagnosis of metagonimiasis. After treatment, the patient became free of symptoms, and she remained coprologically negative for the parasite at follow-up visits over the next 2 years. The diagnostic, therapeutic, and clinical features of metagonimiasis and related intestinal fluke infections have been reviewed. It is concluded that metagonimiasis and related intestinal fluke infections should be considered as a possible cause of persistent diarrhoea in travelers returning from endemic areas abroad.

Gomez-Orozool L see Ortega Gomez H

Goodman J see Bujanover Y

Gopalakrishna GS see Carrazza FR

Gore RM see Gould RJ

Goriup U, Shmerling DH. [Dietary therapy of intestinal diseases in childhood]. Ther Umsch 1978;35(8):673-8

The dietary management of intestinal enzyme deficiencies, such as lactase and sucrase-isomaltase deficiency and that of the major malabsorptive states, such as celiac disease and cow's milk protein intolerance, consists in the exclusion of the offending nutrient from the diet, which should otherwise remain nutritionally as adequate as possible. The practical aspects of these diets are described in detail. General nutritional support is indicated for catabolic patients with chronic inflammatory bowel diseases (ulcerative colitis and Crohn's disease) and with exocrine pancreatic insufficiency. This is best achieved with elemental diet or parenteral nutrition. (Modified author's abstract)

Gorodischer R see Gemer O

Gouerou H, Redelsperger P-Y, Galian A, Dervichian M, Pappo E, Cattan D. [Chronic ulcerative jejunoileitis with malabsorption]. Gastroenterol Clin Biol 1977 Jun-Jul;1(6-7):561-70

The case of a 61-year-old female patient, suffering from chronic ulcerative jejunoileitis with malabsorption, is reported. Villus atrophy was limited to the areas close to ulcerations. In this patient, malabsorption was not

improved by a gluten-free diet. The topography of the mucosal atrophy and the inefficiency of a gluten-free diet provide arguments to distinguish jejunoileitis with malabsorption from celiac disease.

Gould RJ, Gore RM. A large colonic intraluminal mass in a young man with chronic diarrhea. JAMA 1983 Nov 18;250(19):2675-7

Gracey M. Antibiotic and antiparasitic therapy in chronic diarrhea. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984: 469-76

Gracey M. Chronic diarrhoea in protein-energy malnutrition. Paediatr Indones 1981 Nov-Dec;21(11-12):235-9

This review describes chronic diarrhoea in protein-energy malnutrition (PEM). Studies have shown that bacterial contamination of upper intestinal secretions is common in malnourished children. Bacterial overgrowth in the proximal gut can produce a wide range of clinical effects, including steatorrhea, carbohydrate malabsorption, hypoproteinemia, vitamin B_{12} deficiency, and can also be associated with macrocytic anemia and iron deficiency. In malnutrition, these problems may operate with recurrent and chronic gastrointestinal infections damaging the intestinal mucosa. Toxigenic Escherichia coli present in the gastrointestinal tract in malnourished children produce toxins which interfere with the intestinal absorption of fluids and electrolytes. There are significant differences between the appearance of gastrointestinal mucosa in tropical and non-tropical regions. The changes in the gastrointestinal tract due to diarrhoea associated with malnutrition include thinning of the gut wall, marked flattening and broadening of the intestinal villi, inflammatory infiltration of the lamina propria and alteration of the enterocytes from columnar to cuboidal or aquamous loss of secretion of hydrochloride acid in the upper intestine. These could contribute to the heavy bacterial populations in the upper gut of malnourished children. The possible contributions of impaired digestion and absorption, increased mucosal and transmucosal losses and the role of intraluminal factors are uncertain. Disaccharide deficiency, rickets, and vitamin E deficiency are also associated with PEM as seen in studies done at Ethiopia, Thailand and in the Middle East. Anemia in 10% of the malnourished children has been reported. Further studies on the effects of PEM on the gastrointestinal mucosa should be carried out.

Gracey M. The intestinal microflora in malnutrition and protracted diarrhea in infancy. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:223-36

Gracey M, Stone DE. Small-intestinal microflora in Australian aboriginal children with chronic diarrhoea. Aust NZ J Med 1972 Aug;3(2):215-9

The small intestinal microflora were studied for the first time in a series of 18 Australian aboriginal children with a history of chronic diarrhoea. All except one of these children were aged under 24 months. Eleven Caucasian children, most of whom were hospitalized due to chronic diarrhoea, served as controls. All specimens of small intestinal contents, obtained by pernasal intubation, were cultured under identical conditions. Among aboriginal children, there was a generalized and marked increase in oral-type and fecal-type aerobes isolated from the small intestinal contents. The mean count

of oral-type organisms was 10^6/ml and of fecal-type organisms was $8x10^5$/ml in aboriginal children not receiving antibiotics. In patients receiving antibiotics, the mean colony count of oral-type organisms was $5x10^6$/ml and of fecal-type organisms was $5x10^4$. Anaerobes were isolated only rarely in patients and controls. A prominent feature was the high isolation rate of Candida and coagulase-negative Staphylococci. It is suggested that unsuspected bacterial contamination of the small bowel contributes to the common problem of malabsorption and malnutrition in Australian aboriginal children.

Gracey M, Henderson R. The use of a carbohydrate-free feeding formula in Australian aboriginal children with chronic diarrhoea. Aust Paediatr J 1974 Jun;10(3):164-7

A newly devised carbohydrate-free feeding formula (CF1. Nestle) was used in 48 aboriginal infants and children with malnutrition and diarrhoeal illnesses. It was effective in rapidly reducing diarrhoea in most patients, and in some requiring intravenous feeding, it was a useful additional source of calories. One disadvantage of CF1 was its restricted caloric content. Although diarrhoea ceased promptly, weight gain was slow until additional calories were added in the form of glucose. Such a formula should prove useful in malnourished children with diarrhoea, and a simple, standardized regime is put forward for trial in areas where medical and nursing supervision is in short supply. It is proposed that in the first 48 h, CF1 should be given alone; glucose should then be added in second daily increments of 1%, up to 6%.

Graham GG. Chronic 'diarrhea' and diet [letter]. Am J Dis Child 1980 May;134 (5):526

Graham GG see MacLean WC, Jr.

Grand RJ see Motil KJ

Grand RJ see Sutphen JL

Grannell J see Santoscoy G

Greenberger NJ. A diagnostic approach to the patient with a chronic diarrheal disorder. J Kans Med Soc 1978 Jun;79(6):257-6

Greene H see Parker P

Greene HL, Ghishan FK. Excessive fluid intake as a cause of chronic diarrhea in young children. J Pediatr 1983 Jun;102(6):836-40

This paper describes how excessive fluid intake causes chronic diarrhoea in young children. Studied were 105 outpatients with chronic diarrhoea reporting to the Gastrointestinal and Nutrition Unit of the Vanderbilt Children's Hospital at Nashville, Tennesse, USA. Eighty-five patients did not have any clinical or laboratory evidence of malabsorption by routine tests. In 40 of the patients, chronic nonspecific diarrhoea was diagnosed on the basis of the characteristic features of this illness. An outpatient study evaluated fecal output, dietary energy-protein intake and non-protein fluid intake. Patients were separated into two groups whose fluid intakes were highly different: group A, 196±32 ml/kg.day and group B, 91±15 ml/kg.day ($p<0.001$). The non-protein fluid intake was then reduced to 90 ml/kg.day with no change in diet. Evaluation at two weeks and again at six to eight weeks showed a decrease in

stool frequency (from 4 to 10 per day to 0 to 3 per day) and an increase in stool consistency in all patients in group A, but no significant change in stool patterns in group B. When fluids are prescribed in the management of diarrhoea, attention should be given to the volume of intake as well as to the mixture. A close cause-and-effect relationship was seen between excessive fluid intake and some cases of chronic nonspecific diarrhoea.

Gregori G, de Angelis GL, Caprio P, Banchini G. [Use of oral bacteria therapy in childhood during acute enteritis and functional chronic diarrhea. Clinical experience]. Acta Biomed Ateneo Parmense 1985;56(1):23-6

There are some theoretical reasons to give an oral bacterial therapy when intestinal ecosystem changes its composition. The authors would verify the clinical effectiveness or oral bacterial therapy during acute and functional chronic diarrhoea, even if the course of the illness does not become shorter, oral bacterial therapy moreover may be useful in reducing the risk of having casual carries of pathogenic agents and may restore an intestinal ecosystem previously modified by antibiotic therapy. (Author's abstract)

Grill B see Glassman M

Grill B see Gryboski JD

Groll A. Symposium on diarrhea. 3. Investigation of chronic diarrhea. Can Med Assoc J 1977 Apr 9; 116(7):742-4

An investigation of diarrhoea, occurring in patients without liver, biliary or gastric disease, is reported. The presence of fresh blood or mucus in stool was indicative of rectal or colonic disease. Focal areas of discrete erythema with minute ulceration suggest Crohn's disease. Certain histologic features may allow differentiation between pseudomembranous colitis, ischemic colitis, Crohn's disease, and ulcerative colitis. Barium enema and rectal biopsy are the critical investigations for establishing a diagnosis in such cases. Steatorrhea was demonstrated by the daily output of stool fat occurring with a normal diet, which contains 80 to 100 g of fat per day. Both radiographic study and biopsy of small bowel for such cases are to be performed. Pancreatic insufficiency is associated with severe steatorrhea and protein loss into the stool. Clinical features of pancreatic insufficiency are discussed. Pancreatitis was usually associated with carbohydrate intolerance or overt diabetes mellitus. Endoscopic retrograde cholangiopancreatography may differentiate between carcinoma and chronic pancreatitis in selected patients. Vitamin B_{12} malabsorption in chronic pancreatic insufficiency is also discussed. The approach to the investigation of diarrhoea should be logical and systematic, based on the results of sequential investigations.

Grossi Bianchi ML see Bulgarelli R

Gruttner R, Lucking Th. Chronic diarrhoea following partial resection of the small bowel. Acta Paediatr Scand 1971 May;60(3):366-7

Surgical intervention was necessary on a normally developed girl aged 2½ years, due to ileus, caused by strangulation of a diverticulum of Meckel. The terminal ileum, the cecum and the appendix, 20 cm in length altogether, had to be resected. Following the surgery, the girl immediately developed severe diarrhoea and no longer gained in height or weight. Celiac disease was

suggested as the introduction of a gluten-free diet was followed by marked improvement in diarrhoea. Antibodies against gluten could be demonstrated in the blood. A detailed examination 2 years later did not point to any of the chronic intestinal malabsorption syndromes. All resorption tests performed were normal. Steatorrhea could not be demonstrated. Oral loading with gluten was followed by diarrhoea. Oral biopsies, following the oral gluten loading, did not show pathognomonic changes of the intestinal mucosa resembling those of gluten intolerance. Two months later, oral loading with milk protein resulted in abdominal pain and partly mushy stools, but steatorrhea could not be seen. The renewed oral biopsy showed partial and subtotal villus atrophy. Following a gluten- and milk-free diet, marked improvement of diarrhoea occurred. It was not possible to determine whether the pathogenesis of this disease was influenced by bacterial migration from the colon to the small intestine or by disturbances in bile salt reabsorption.

Gruttner R see Lucking T

Gryboski J see Glassman M

Gryboski JD, Hillemeier AC, Grill B, Kocoshis S. Bismuth subsalicylate in the treatment of chronic diarrhea of childhood. Am J Gastroenterol 1985 Nov;80(11):871-6

This study determines the value of Pepto-Bismol (bismuth subsalicylate) in the treatment of chronic diarrhoea of childhood and to establish an effective dosage for children and infants. Twenty-nine infants with chronic diarrhoea were admitted to a double-blind, parallel clinical trial. About 14% of the patients showed gastrointestinal allergy to milk and to soy proteins. Fourteen patients were assigned to the placebo formulation group and 15 to the bismuth subsalicylate formulation group. Stool transit times varied from 3 to 30 h and showed no consistent change to either therapeutic programs. Children in the bismuth subsalicylate group gained weight steadily during the study. The baseline number of stools was higher ($p<0.05$) in the bismuth subsalicylate group than in the placebo group. The stools became more firm following bismuth subsalicylate therapy than after placebo therapy ($p<0.01$). Bile acid excretion increased during therapy with both bismuth subsalicylate and placebo. The bismuth subsalicylate formulation gave better response ($p<0.01$) in the clinical treatment of diarrhoea. The stool cultures of the patients revealed no enteric pathogens. In the Schilling's test, the abnormal results in 20% of the patients suggest terminal ileal dysfunction and a choleretic mechanism for their diarrhoea. The dosages used in this study were safe as well as effective. The results suggest that bismuth subsalicylate in the dosage employed is useful in the therapy of chronic childhood diarrhoea.

Gryboski JD. Chronic diarrhea. Curr Probl Pediatr 1979 Mar;9(5):1-52

Gryboski JD, Walker WA. Chronic nonspecific diarrhea syndrome (irritable colon of childhood). In: Gryboski JD, Walker WA, eds. Gastrointestinal problems in the infant. Philadelphia: Saunders, 1983:576-7

Gryboski JD, Kocoshis S. Immunoglobulin deficiency in gastrointestinal allergies. J Clin Gastroenterol 1980 Mar;2:71-6

Multiple gastrointestinal allergies were studied in 98 infants and children. Combined sensitivities were milk and soy in 61, soy and gluten in 34, and milk

and gluten in three. Two clinical groups became apparent: those infants with early diarrhoea (1-6 months of age) with strong family history of atopy or food allergies and without prior intestinal infection; and those children up to age 3 years who developed chronic diarrhoea and gastrointestinal sensitization after an acute viral or bacterial gastroenteritis. Transient or "late turn-on" immunoglobulin disorders were present in nearly half of the milk-allergy infants studied, and in nearly a third of the entire group. Such a high incidence of immunoglobulin abnormalities has not been previously reported in children with allergic gastroenteritis. (Author's abstract)

Guandalini S see Pignata C

Guarino A see Pignata C

Guillaumot R see Chaptal J

Gullner HG. [Chronic diarrhea caused by abuse of laxative (letter)]. Dtsch Med Wochenschr 1985 Feb 1;220(5):197-8

Gunn T, Brown RS, Pencharz P, Colle E. Total parenteral nutrition in malnourished infants with intractable diarrhea. Can Med Assoc J 1977 Aug 20; 117(4):357-60

Gupta SC see Agarwal VK

Gupta SC see Pande RC

Gupte SP, Mehta S. Chronic diarrhoea - an etiological study. Indian Pediatr 1970 Nov;7:625-7

Gupte SP. Chronic diarrhoea and marasmus [letter]. Lancet 1970 Oct 3;2(7675): 725

Gupte SP see Perkash A

Gupte SP see Walia BNS

Gutierrez C see Weidenslaufer A

Hadorn B see Eichenberger JR

Halpin TC see Marino LR

Halsted CH see Beer WH

Halter F see Barbezat GO

Hamamoto H see Takanashi T

Hamborg B see Kittang E

Hamilton JR. Nutritional therapy of chronic diarrhea. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:535-40

This paper examines some current theoretical considerations in the nutritional

management of children with severe chronic diarrhoea. The pathophysiological characteristics of idiopathic chronic diarrhoea are discussed. It was found that breast feeding and hygienically prepared foods can reduce the incidence and severity of the illness as seen in many parts of the world. In the active treatment of affected patients, specific foods can seldom be identified as important causative factors, but adequate, balanced nutritional intake is undoubtedly an important component of the treatment of chronic infantile diarrhoea. Nutrients, both macro and micro, may favorably affect intestinal renewal and differentiation, thereby hastening intestinal repair. The enteric route should be used for nutrients if at all possible, and a variety of products and techniques are available to optimally utilize the existing absorptive function. Feedings should be adjusted according to the individual child's intestinal status and tolerance. Total parenteral nutrition carries certain risks, but provides a powerful tool for sustaining the severely affected babies.

Hamilton JR see Gall DG

Haque E see Ahmed MU

Hardjadinata D see Sutjiningsih

Harford WV, Krejs GJ, Ana CAS, Fordtran JS. Acute effect of diphenoxylate with atropine (lomotil) in patients with chronic diarrhea and fecal incontinence. Gastroenterology 1980 Jan-Mar;78(3):440-3

This study attempted to assess the effects of a 3-day therapy with placebo which was compared with treatment with diphenoxylate and atropine (lomotil) in 15 patients with chronic diarrhoea and fecal incontinence. All patients were admitted to a clinical research center. The patients were then crossed over to the alternate medication. They were placed on a regular diet, except in one case where lactose-free diet was used. After taking a complete history and performing physical examinations, the patients were put in a double-blind manner on lomotil or placebo. Sphincter and continence studies were carried out. Lomotil had no statistically significant effect on rectal or anal sphincter pressures or on continence to a solid sphere or to saline that was infused into the rectum. Lomotil significantly reduced stool weight and stool frequency. There were three notable exceptions among the patients with pancreatic insufficiency and ulcerative colitis. Twelve patients, who received 4 tablets per day, showed qualitatively same results as did the entire group. Basal and squeeze pressure was 39 and 96 mmHg on placebo compared with 41 and 94 on lomotil ($p>0.6$ and $p>0.3$ respectively). Three of the patients were incontinent during the 7-day experiment (all on placebo). The results in 15 patients revealed that lomotil therapy reduced average stool weight and average stool frequency by 44 and 55% respectively. During lomotil therapy, the patients received a daily dose of 0.1 to 0.2 mg of atropine, present in lomotil tablets. This small dose of atropine could have contributed to the observed effect or observed lack of effect of lomotil. These results suggest that temporary or intermittent therapy with lomotil and related drugs may benefit patients with chronic diarrhoea and fecal incontinence.

Hargrove MD, Jr. see Netchvolodoff KV

Harikul S see Eksaengsri P

Harries JT see Booth IW

Harries JT see Candy DCA

Harries JT see Larcher VF

Harrison DD see Gallagher ND

Harvey BAM see Candy DCA

Hasan MA see Ahmed MU

Heim T. Requirements and utilization of macronutrients in enteral and parenteral nutrition in acute and chronic diarrhea. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:541-57

This chapter discusses the theoretical and practical aspects of nutritional support to patients with acute and chronic diarrhoea with particular emphasis on protein, energy and macronutrient requirements. It is concluded that oral-rehydration and maintenance therapies have beneficial effects in the routine clinical management of infants and children with acute diarrhoea. Nutritional adequacy with these therapies can, however, be achieved only in well-nourished infants and children who have enough energy reserves to cover their maintenance metabolism during the oral maintenance therapy. If the diarrhoea lasts more than 2 weeks, i.e. becomes protracted, nutritional management becomes a principal part of the therapy, and treatment is generally based on dietary manipulation. If oral feeding (with either customary or elemental diet) fails, supplemental parenteral nutrition offers a feasible means to deliver the needed increases in caloric and macronutrient supply.

Hemming VG see Hill RR

Henderson R see Gracey M

Hendricks KM see Cohen SA

Henochowicz S. Chronic diarrhea and weight loss in a patient with common variable immunodeficiency. Ann Allergy 1986 May;56(5):382-3, 410-3

Herbst JJ see Hill RR

Herbst JJ see Wender EH

Herman S see Maffei HVL

Hernandez Marco R see Peris Vidal A

Hersh T see Galambos JT

Herve P see Dreze C

Heyman MB, Paterno VI, Ament ME. Campylobacter colitis: a cause of chronic diarrhea in children. West J Med 1982 Sep;137(3):243-5

The cases of a 7-month-old girl with chronic diarrhoea producing blood-streaked feces and a 13-year-old girl with crampy abdominal pain and bloody diarrhoea are reported from the USA to document the existence of chronic Campylobacter

colitis in infants and children and its response to treatment. Malabsorption was absent in these cases indicating that the small bowel mucosal damage was either limited or absent. The findings of leukocytes and blood in the feces, colitis with inflamed friable mucosa on sigmoidoscopic examination, and inflammatory reaction with crypt abscesses and mucus depletion on histologic examination of rectal biopsy specimens were similar to those of adult cases of Campylobacter colitis. Cultures of stool specimens from the proctosigmoidoscopic examination grew C. jejuni and were negative for other enteric pathogens. The 7-month-old girl was treated successfully with erythromycin (50 mg/kg of body weight.day) for 10 days, while the 13-year-old girl improved gradually without antibiotic therapy. Erythromycin proved to be an effective antimicrobial agent and was considered one of the drugs of choice for the treatment of Campylobacter infections. It is concluded that Campylobacter enterocolitis should be considered in the differential diagnosis of infants with chronic diarrhoea, especially if gross blood is present in the feces. A sigmoidoscopic examination would be helpful in obtaining stool specimens for isolation of pathogens and for evaluating the state of patients. However, a fresh stool specimen is adequate for the diagnosis of C. jejuni, if cultured appropriately.

Hill HR, Book LS, Hemming VG, Herbst JJ. Defective neutrophil chemotactic responses in patients with recurrent episodes of otitis media and chronic diarrhea. Am J Dis Child 1977 Apr;131(4):433-6

Fourteen patients, who have had repeated episodes of otitis media and chronic diarrhoea, were evaluated to ascertain whether any defect in the host defense mechanism could account for the unusual incidence of infection. The clinical and immunologic data obtained from these patients are described. Each of these patients had serious problems in neutrophil granulocyte chemotaxis. The mean chemotactic index of the patients was 21±6, while that of 25 age-matched and non-age-matched controls was 62±10. Patients with chronic diarrhoea without a history of recurrent infection had normal chemotactic function in each instance. In addition, patients with acute and chronic otitis media without diarrhoea had normal or increased chemotactic indices. Other neutrophil functions, lymphocyte T-cell populations, immunoglobulins, and complement components were normal in the patients. Serum IgE levels were also normal. The presence of a defect in neutrophil chemotaxis in the patients with recurrent otitis media and chronic diarrhoea suggests that the phagocyte may play an important role in protection of the mucosal surfaces of the respiratory and gastrointestinal tracts. This work indicates that normal patients with acute or chronic middle ear infections also have normal or increased polymorphonuclear leukocyte chemotactic function. Thus defective chemotaxis in the patients with recurrent otitis media and chronic diarrhoea does not appear to be the result of infection, per se.

Hill ID, Mann MD, Bowie MD. Successful management of persistent diarrhoea in infants. S Afr Med J 1980 Aug;58:241-3

Ten infants, aged 1.5 to 7 months and hospitalized in Cape Town, South Africa with persistent, dehydrating diarrhoea, were given a combination of gentamicin, metronidazole, and cholestyramine. The drugs were administered in the following dosage: (i) gentamicin - 50 mg/kg.day in 6 divided doses orally for 3 days (maximum 360 mg/day); (ii) metronidazole - 100 mg 8-hourly orally for 5 days; and (iii) cholestyramine - 1 g 6-hourly for 5 days. Daily stool weights were recorded before and during treatment, and in all cases, there was a marked

decrease in the severity of diarrhoea. A decrease in the intravenous fluid requirement and a noticeable improvement in the general well-being of the infants accompanied the decrease in severity of diarrhoea in all cases. No clinical evidence of adverse effects of the medications was noted. The results demonstrate that this combination of drugs provides a safe and effective therapy for persistent diarrhoea in infants.

Hill ID see Mann MD

Hillemeier AC see Gryboski JD

Hillman HS. Chronic diarrhoea and the pancreas. Med J Aust 1964 Aug 22;2: 296-8

Hirschhorn N, Vincent D. Cost of workup for chronic diarrhea [letter]. Postgrad Med 1977 Oct;62(4):40-3

Hlubner G see Oertel H

Hoberman LJ see Martin DL

Hock CW. Chronic diarrhea. Med Times 1960 Mar;88:320-3

Hock CW. Observations on the use of sorboquel in chronic diarrhea. Am J Dig Dis 1960 Nov;5:971-4

Holdsworth CD see Palmer KR

Holdsworth D see Corbett C

Holman GH see Jarrett EC

Holmes GKT see Cooper BT

Holmes R, Clune S, Cacciarelli A, Yang SS. Chronic diarrhea and failure to thrive [clinical conference]. J Pediatr 1983 Sep;103(3):491-5

This paper describes chronic diarrhoea of a premature infant and its failure to thrive. At the age of one month, the infant began to have diarrhoea, and when 24 months, she had 15 motions per day. Occult blood was detected in the stool. Small bowel examination showed dilution of barium (hypersecretion) in distal small bowel. There was no confirmation that this patient had hereditary fructose intolerance or fructose malabsorption when she was hospitalised at the age of 11 months. A diagnosis of "irritable bowel syndrome" was made at the age of 2 years. The child was not growing at a normal rate. This child's history of watery diarrhoea suggests that she had disaccharide malabsorption. The child was malabsorbing carbohydrate and fat secondary to intestinal cell injury. The D-xylose test yielded abnormal results, while fecal pH was also low. This child showed signs and symptoms consistent with celiac disease. Her normal results at the oral lactose tolerance test contradicted the diagnosis made. In summary, the child had a malabsorptive syndrome consistent with sucrase-isomaltase deficiency; however, celiac disease could not be excluded. The biopsied specimen was a portion of distal duodenal mucosa with occasional Brumer glands. Villi were short, broad, and distorted, and the crypts were elongated. The ratio of villus height to crypts was 1:1, whereas the ratio is

4:1. The small intestinal mucosa showed mucosal atrophy with no lactase, sucrase and palatinase activities. The patient's 5-year-old sister was admitted to the same hospital in New York, USA, and her small bowel biopsy showed normal intestinal histology, but with the sucrase-isomaltase deficiency. The familial occurrence was consistent with the autosomal recessive inheritance of sucrose-isomaltase deficiency while also having crypt hyperplastic villus atrophy.

Holt H. [Aspects of differential diagnosis and diagnostic errors in chronic diarrhea. Verner-Morrison syndrome, gluten induced enteropathies, laxative abuse]. Dtsch Gesund 1972 Nov 16;27:2178-81

Holtzapple P see Fisher SE

Huibregtse K see Tytgat GN

Hull BL. Differential diagnosis of chronic diarrhea in cattle. J Am Vet Med Assoc 1972 Dec 1;161(11):1291-2

Chronic diarrhoea in cattle includes chronic parasitism, chronic bovine viral diarrhoea-mucosal disease, the malabsorption syndrome, Johne's disease, and lymphosarcoma. Although history and clinical examinations may be helpful in the differential diagnosis of chronic diarrhoea, laboratory examinations are often necessary for the final diagnosis. Chronic parasitism, chronic bovine viral diarrhoea-mucosal disease, and malabsorption syndrome usually affect cattle aged under 2, while Johne's disease and lymphosarcoma are usually confined to cattles aged under 2. The procedures for the differential diagnosis of these diseases have been outlined in this report.

Hyams JS, Leichtner AM. Apple juice; an unappreciated cause of chronic diarrhea. Am J Dis Child 1985 May;139(5):503-5

Chronic nonspecific diarrhoea remains a common pediatric problem. Previous reports have suggested disordered small intestinal motility, food intolerances, dietary fat restriction, and excessive fluid consumption as possible contributory factors. The authors recently encountered a subset of children with chronic nonspecific diarrhoea, in whom nonexcessive apple juice intake seemed to cause their diarrhoea. Five children between the ages of 13 and 31 months with a history of chronic diarrhoea (of 3 to 11 months' duration), seen at Hartford (Conn) Hospital between January and June 1984, formed the basis of this report. They represent approximately 15% of all children younger than 5 years of age with chronic diarrhoea, who were seen in the outpatient pediatric gastroenterology clinic during this period. All of these patients had histories of watery stools (2 to 8 per day), normal growth and development, and unremarkable physical examinations. A significant (>10 ppm) increase over the baseline in the breath hydrogen concentration was observed in all of the study patients, following ingestion of 240 ml of apple juice. The rise in the breath hydrogen concentration was seen as early as 30 min and as late as 120 min after ingestion of the juice. In these subjects, ingestion of apple juice disclosed evidence of significant carbohydrate malabsorption by breath hydrogen testing, and each subject developed diarrhoea following the challenge. Withdrawal of apple juice from the diets of these subjects was curative in all cases. Before embarking on an expensive and time-consuming evaluation for chronic nonspecific diarrhoea in otherwise healthy children, a brief restirction of apple juice intake may be warranted.

Iaccarino E see Auricchio S

Iacob C see Popescu V

Idiopathic chronic ulcerative enteritis [editorial]. Lancet 1980 Nov 22;2 (8204):1118-9

Igl W see Antes G

Ingomar CJ, Mullertz S, Terslev E. Chronic diarrhoeas in infancy and childhood. I. D-xylose tolerance test. Arch Dis Child 1964 Feb;39:79-84

Ingomar CJ, Terslev E. Chronic diarrhoeas in infancy and childhood. II. Enzyme content of duodenal juice. Arch Dis Child 1967 Jun;42(223):289-93

Innocenti P, Rossi L, Bombardieri G. [Clinical effectiveness of difenoxine in patients with acute and chronic diarrhea]. Boll Chim Farm 1983 Dec;122(12): S64-S8

Iosava LI see Ekisenina NI

Islam N see Alam MN

Israsena S see Manatsathit S

Iwanczak F. [Results of cholestyramine treatment of chronic infantile diarrhea]. Pol Tyg Lek 1981 Apr 13;36(15):525-8

Jacob E see Lim P

Jacquet N see Dreze C

Jansen-Goemans A, Engelhardt J. Intractable diarrhea in a boy with vasoactive intestinal peptide-producing ganglioneuroblastoma. Pediatrics 1977 May;59(5): 710-6

Janukwicz K see Zychowicz C

Jarrett EC, Holman GH. Chronic diarrhea in infancy with resultant disaccharide malabsorption. J Med Assoc Georgia 1966 May;55:170-3

This paper presents two chronic diarrhoea cases (Negro male and female infants) with intestinal disaccharidase deficiencies implied by abnormal disaccharide tolerance tests. The related literature are briefly reviewed, revealing that the disaccharide-splitting enzymes are localized in the brush border of the small bowel's lining cells. Diagnosis and treatment methods are discussed, including a simple test for fecal-reducing sugar determination.

Jaskiewicz K see Swicowa K

Jaspar HH see Sengers RC

Jean R see Chaptal J

Jewell D see Vessey M

Johnson A see Olambiwonnu NO

Jonas A, Diver-Haber A. Stool output and composition in the chronic, non-specific diarrhoea syndrome. Arch Dis Child 1982 Jan;57(1):35-9

Stool output and composition, in regard to water, electrolyte, and bile acid excretion and distribution, was studied in 7 patients with chronic nonspecific diarrhoea syndrome. The results were compared with those of 6 children with cystic fibrosis, 5 with bacterial overgrowth and 6 controls. Seventy-two-hour urine-free stools were collected and stored at -20°C until analysis. The stools' extractable water phase was determined; and fecal fat, bile acid, bile salt and electrolytes were determined, both from the supernatant and the pellets. The extractable water content of chronic nonspecific diarrhoea syndrome was higher (28.7±6.2%), and this was exceeded by those with bacterial overgrowth syndrome (40.9±31.2%). Patients with cystic fibrosis and bacterial overgrowth had increased bile acid loss (74.5±29.1% and 41.1±18.3% respectively). The absorption coefficient of fat was lowest in cystic fibrosis (66.9%), followed by bacterial overgrowth syndrome (74.8%). The stool sodium content in chronic nonspecific diarrhoea syndrome and bacterial overgrowth was 27.7±5.9 and 44.8±31.9 mmols/l respectively. The authors suggest that, in chronic nonspecific diarrhoea syndrome and bacterial overgrowth, the colon is exposed to large quantities of bile salts present in soluble form, that are easily accessible to the mucosal surface. Bile salts thus inhibit sodium and water absorption in both conditions, contributing to increased stool output.

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Kidd GS, Donowitz M, O'Dorisio T, Cataland S, Newman P. Mild chronic watery diarrhea-hypokalemia syndrome associated with pancreatic islet cell hyperplasia: elevated plasma and tissue levels of gastric inhibitory polypeptide and successful management with nicotinic acid. Am J Med 1979 May;66(5):883-8

This paper reports a mild chronic watery diarrhoea-hypokalemia syndrome associated with pancreatic islet cell hyperplasia. A 46-year-old patient with depression, hypokalemia and a 13½-year history of watery diarrhoea was admitted to a medical center in Washington DC, USA, in August 1976. Sigmoidoscopy and colonoscopy with multiple biopsies disclosed no abnormalities. A lactose tolerance test gave normal results. Stool cultures were negative for ova and parasites. Watery diarrhoea was present throughout the tenure of hospitalization. Treatment with methylprednisolone, both at 12 mg and 35 mg daily, decreased but did not stop the diarrhoea. An exploratory laparatomy revealed a nodular area in the tail of the pancreas, and a 75%-distal pancreatectomy was performed. There was an increased number of irregularly shaped islet cells in the pancreas. Three months postoperatively, the diarrhoea continued. Gastric pH was 4.5. After 3 months of treatment with nicotinic acid, the patient had normal stools with an occasional episode of watery diarrhoea lasting for one to two days. Hormonal analyses were carried out. Purified gastric inhibitor polypeptide induces intestinal secretion, but its mechanism of action is not known. Nicotinic acid may be useful in the treatment of chronic diarrhoeal diseases.

Kingham JG, Levison DA, Ball JA, Dawson AM. Microscopic colitis - a cause of chronic watery diarrhoea. Br Med J 1982 Dec 4;285(6355):1601-4

Microscopic colitis - a cause of chronic watery diarrhoea - is reported in this paper. Six patients with severe watery diarrhoea were found to have microscopic total colitis. Their ages ranged from 39 to 62 years, and diarrhoea was present for 3 months to 25 years at the time of diagnosis. None had any abnormality detectable by conventional tests used to diagnose inflammatory bowel disease - namely, barium radiology and endoscopy. The diagnosis could only be made by microscopic examination of biopsy specimens from the apparently normal colon. Anemia, raised erythrocyte sedimentation rate, hypokalemia and hypoalbuminemia were common findings. Small bowel function was normal in all, though 3 patients had jejunal lesions of uncertain relevance but seemingly unrelated to the diarrhoea. The five patients were given anti-inflammatory drugs which brought a satisfactory response with improvement of the diarrhoea and the colonic inflammation and also achieved a return to normal of the abnormal laboratory findings. Microscopic colitis is responsible for a proportion of cases of intractable diarrhoea of obscure origin when rectal and colonic biopsies are advised to be performed.

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Kittang E, Hamborg B, Schjonsby H. Absorption of food cobalamins assessed by

the double-isotope method in healthy volunteers and in patients with chronic diarrhoea. Scand J Gastroenterol 1985 May;20(4):500-7

To make a food preparation containing radioactively labeled cobalamins, rabbits were given repeated injections with ^{57}Co-labeled cyanocobalamin. The liver was removed, homogenized, and fried for 1 min or boiled for 30 min. Of the radioactivity in the fried homogenate, 41.7% was recovered in the centrifuged supernatant compared with 50.8% in the boiled homogenate. The radioactivity in the supernatants had a molecular size close to that of free ^{57}Co-labeled cyanocobalamin. Forty-two percent of the radioactivity in the whole homogenate had been incorporated into 5-deoxyadenosyl-, 10% into methyl-, and 16.5% into hydroxy-cobalamin. To assess the validity of a double-isotope method for measuring the intestinal absorption of doses of the ^{57}Co-labeled liver cobalamins, $^{51}CrCl_3$ was used as a non-absorbable marker. In 14 healthy volunteers, the correlation coefficient between the absorption, measured by the double-isotope technique and the fecal excretion test, was highly significant ($r=0.96$, $p<0.005$), and there was only a small variation in the $^{57}Co/^{51}Cr$ ratio in successive stool collections. In 11 patients with chronic diarrhoea, there was a significant correlation between the absorption, measured by the double-isotope technique and the fecal excretion test ($r=0.92$, $p<0.005$), but in some patients, there was considerable variation in the $^{57}Co/^{51}Cr$ ratio in successive stool collections.

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Krieger I, Evans GW, Zelkowitz PS. Zinc dependency as a cause of chronic diarrhea in variant acrodermatitis enteropathica. Pediatrics 1982 Jun;69(6):773-7

Reported here are the observations in two siblings with variant acrodermatitis enteropathica who responded to treatment with pancreatin (viokase) or with high doses of zinc. These two patients were compared with three other patients with acrodermatitis enteropathica at a children's hospital in Michigan, USA. The case one, a young child, had chronic diarrhoea at the age of 6 months. When aged one, the diarrhoea ceased with viokase and showed rapid weight recovery during the next two months. A younger brother with the same symptoms was admitted to the hospital, and both children were placed on a regimen of zinc sulfate. Improvement was obtained with doses of 60 mg of zinc per day. Zinc therapy was later discontinued after which the diarrhoea reappeared. Upon reinstitution of zinc sulfate therapy at 10 mg of zinc per day, the diarrhoea ceased. Zinc therapy was subsequently increased to 50 mg per day. The patient was then well and gained weight at a normal rate. The case two, the brother of the first case, developed diarrhoea at the age of 3 months. The child was treated with zinc sulfate given 40 mg per day; he showed improvement in stool frequency and quantity, and the rate of average weight gain was 510 mg per month over four months. During treatment, its plasma zinc level was 153 µg/100 ml. Improvement was seen on a regimen of 25 mg of zinc per day; later, he was given 50 mg of zinc per day. Zinc was withdrawn at 25 months of age, and the child was admitted to the Childrens' Hospital of Michigan, USA. Culture of duodenal aspirate showed no enteropathogenic organisms. A skin test for Candida showed positive. The analysis of picolinic acid in blood was carried out. The role of picolinic acid in human metabolism remains to be defined. The effectiveness of viokase in these cases was not explained fully.

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Larcher VF, Shepherd R, Francis DEM, Harries JT. Protracted diarrhoea in infancy: analysis of 82 cases with particular reference to diagnosis and management. Arch Dis Child 1977 Jul;52(7):597-605

Eighty-two infants, aged under 1 presenting with protracted diarrhoea during a

6-year study period, were analyzed in the UK, with particular attention to the differential diagnosis and to the management of those patients in whom a specific diagnosis could not be established. A diagnosis was established in 59 (72%) patients (category 1), the commonest diagnoses being celiac disease (33.2%), secondary disaccharide intolerance (12.2%), and cow's milk protein intolerance (11.3%). Other causes of protracted diarrhoea included conditions, such as primary sucrase-isomaltase deficiency, Shwachman's syndrome, ulcerative colitis, ganglioneuroma, defective opsonization, and staphylococcal pneumonia. A surgical cause for protracted diarrhoea was found in 3 patients. Despite intensive investigation, a diagnosis could not be established in 23 (28%) infants (category 2). Age of onset of symptoms in this patient group tended to be earlier than the category 1 patients, and 6 (7%) presented with diarrhoea dating from their birth. Of particular interest in these 6 patients was the high incidence of extraintestinal anomalies, and of those who had died after protracted diarrhoea dating from birth. Four of these 6 infants died, accounting for a mortality of 5% for the whole series. The remaining 17 (21%) patients in category 2 presented at varying intervals after birth having previously been in good health. The mean age of onset of the diarrhoea was 4.9 weeks (range 1-18 weeks). The mode of onset was usually acute diarrhoea with or without vomiting. A chicken-based feeding regimen, containing comminuted chicken, "Gastrocaloreen" (a glucose polymer) and "Prosparol" (an emulsion of long-chain triglycerides), was a highly effective form of dietary treatment in all 17 infants with protracted diarrhoea since birth of undetermined cause. The mean duration of hospitalization and weight gain was 29 weeks and 29 g per day respectively. It was speculated that, in a proportion of affected patients, an acute infective action renders the small intestine susceptible to intolerance of foreign proteins and/or bacterial colonization. This sequence of events is important in the pathogenesis of the diarrhoea and malnutrition. Malnutrition, whether primary or secondary to infection, probably plays an important pathophysiological role.

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Ligny G, Troupel S, Renault H, Cattan R. [Contribution to the study of the absorption of glucides and lipids in chronic diarrhea]. Arch Mal Appar Dig 1962 Sep;51:969-91

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Magnesium levels in accessible tissues were estimated in 7 patients with chronic diarrhoea. Cases 5, 6, and 7 had clinical and biochemical evidence of malabsorption, the etiology being chronic Salmonella (Group C) enteritis, tuberculous enteritis, and chronic pancreatitis respectively. The cause of diarrhoea in cases 1, 2, and 3 could not be established with thorough clinical and laboratory investigations. Case 4 was found to have clear-cut evidence of ulcerative colitis radiologically and sigmoidoscopically. Two patients (cases 1 and 7) received all their magnesium replacement parenterally, and they had repeat muscle biopsies after repletion. Three patients (cases 3, 5, and 6) had exacerbation of diarrhoea with oral magnesium, and replacement was unlikely to be adequate notwithstanding the magnesium infusions they received initially while in the ward. The average daily protein intake of the patients ranged between 20 and 40 g. Six patients were found to have reduced skeletal muscle magnesium, presumably as a consequence of previous magnesium losses in the stool, aggravated by inadequate intake. Five of these deficient patients had bone biopsies, all of which revealed normal magnesium levels. Only 1 of the deficient patients had a low magnesium level in serum, serum ultrafiltrate, and the erythrocyte. Low skeletal muscle potassium was present in 4, and hypocalcemia in 3, of the 6 patients with low skeletal muscle magnesium. Magnesium therapy alone corrected hypocalcemia in all cases and restored skeletal muscle potassium in 2 patients in whom this was re-estimated. Clinical features, consisting mainly of signs of neuromuscular

hyperexcitability, were present in magnesium-deficient patients only, and, in those patients with normocalcemia, were probably due directly to magnesium deficiency. The great majority of these clinical features were eliminated with magnesium therapy alone. (Modified author's abstract)

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Lindquist B, Meeuwisse GW. Chronic diarrhoea caused by monosaccharide malabsorption. Acta Paediatr 1962 Nov;51:674-85

A girl, born in Sweden, presented with a form of intestinal malabsorption, not previously described, causing chronic diarrhoea since her birth. The sugar balance studies, the sugar loading tests and the intubation studies indicated that the mechanism of this condition was a selective disturbance of the absorption of the monosaccharides-glucose and galactose. The intubation studies revealed that the production of trypsin and lipase in response to a test meal was probably within normal limits, while the amylase concentration was somewhat decreased. The clinical picture was almost the same as that found in conditions of deficiency of disaccharide-splitting enzymes. The difference, however, was that the patient failed to improve on a diet based on glucose as the carbohydrate. In contrast, on a similar diet based on fructose, the diarrhoea disappeared. The implications of the different findings are discussed, and it is proposed that the condition of the patient be called monosaccharide malabsorption.

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Linevsky YV. [Disorders of dipeptidase activity of the small intestine in chronic enteritis and their treatment]. Klin Med (Mosk) 1977;55:54-8

The glycyl-l-leicindipeptidase activity of biopsized mucosa homogenates from the small intestine's antral portion was studied in 169 patients with chronic enteritis during the disease exacerbation period, and in 122 of them after 3-4-days' treatment. The small intestine's dipeptidase formation was depressed both in the presence and absence of morphological changes in its mucosa detectable by photo-optical microscopy. Compared to photo-optical microscopy, studying small intestine dipeptidase production is the most sensitive test to diagnose chronic enteritis. Complex treatment of chronic enteritis stimulated dipeptidase production. Nerobol produced a stimulating effect on small intestine dipeptidase production. Prednisolone, enteroceptol and furazolidone produced no such effect.

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Liston TE. Clostridium difficile toxin associated with chronic diarrhea and failure to gain weight. Clin Pediatr 1983 Jun;22(6):458-60

The role of Clostridium difficile toxin in chronic diarrhoea and the resultant failure to gain are summarised. Two young children are described in whom chronic diarrhoea was associated with the presence of C. difficile toxin. A male infant, aged 4 months, who experienced otitis media, responded to a 10-day course of oral amoxicillin. He was evaluated twice for irritability and loose stools attributed to viral gastroenteritis. His diarrhoea continued with fluid loss, but stools contained no blood, and he gained 896 g in weight in nine months. The tested stool samples contained no enteric pathogens. The C.

difficile toxin assay using specific neutralisation technique showed positive. The child had regular formula during the illness; the stools were negative for the reducing substances. The diarrhoea ceased when treatment was begun with oral vancomycin (30 mg/kg.day) in 4 divided doses for 10 days. In another case, a male infant, aged 4 months, was admitted for hematochezia. His stools contained no pathogenic organisms or reducing substances, and it was thought to have allergic gastroenteropathy. After a few days on soy formula, the child developed chronic diarrhoea and fussiness. The C. difficile toxin assay was positive. Oral vancomycin at a dose of 30 mg.kg.day in 4 divided doses for 10 days stopped the diarrhoea. The child gained 2,212 g in weight in the next 120 days. C. difficile infection should be considered in the evaluation of young children with diarrhoea who fail to gain weight, even in the absence of prior antibiotic treatment.

Lloyd-Still JD. Chronic diarrhea of childhood and the misuse of elimination diets. J Pediatr 1979 Jul;95(1):10-3

Present dietary practices to treat chronic, recurrent diarrhoea and any side-effects or long-term health complications of dietary manipulations were prospectively studied in 108 children referred for outpatient evaluation. Most of the children did not have a serious underlying disorder. Elimination diets (milk-free, egg-free, wheat-free) were widely prescribed for treatment of chronic diarrhoea and were given for longer intervals than originally recommended. Elimination diets sometimes resulted in inadequate caloric intake and failure to thrive. Wheat (gluten)-free diets were prescribed for more than one month in 64 (59%) children without a specific diagnosis having been made. Thus, elimination diets frequently are misused, and prolonged adherence to such diets may result in nutritional damage. Indiscriminate use of wheat-free diets to treat chronic diarrhoea may mask the diagnosis of celiac disease and may partly explain the low incidence of this disorder in the USA.

Lo CW, Walker WA. Chronic protracted diarrhea of infancy: a nutritional disease. Pediatrics 1983 Dec;72(6):786-800

Chronic protracted diarrhoea of infancy, a nutritional disease, is well known. Occasionally, it becomes protracted, leading to a cycle of malabsorption, malnutrition, and failure to thrive. This paper is a review on the recent scientific findings on the etiology, pathogenesis, diagnosis and laboratory investigation of chronic protracted diarrhoea in infancy. Prevention and management aspects are also discussed. A number of causes of chronic diarrhoea in infancy have been identified and discussed, including post-infectious enteritis, celiac sprue, cow's milk allergy, and parasitic infection. Celiac sprue was observed to be related to wheat in the diet. Cow's milk allergy may be due to early exposure to cow's milk protein at a time when there is excessive intestinal antigenic uptake of macromolecules. Giardiasis may also cause chronic diarrhoea; Entamoeba histolytica can also cause chronic dysentery or diarrhoea. In this work, the case fatality rate was 27%. Metronidazole is suggested for dysentery and amebiasis. Shigella, Salmonella, Escherichia coli, Yersinia enterocolitica, and Campylobacter fetus are the most common causative agents of infectious diarrhoea in children. Viral gastroenteritis causes structural abnormalities similar to those found with celiac disease, villus atrophy, crypt hypertrophy, and inflammation infiltrate. The resulting diarrhoea may involve several mechanisms, including osmotic and secretory diarrhoea, bacterial overgrowth, and disordered motility. Diagnosis of chronic diarrhoeal disease should include a careful dietary history and attention to

signs of malnutrition and tests for specific malabsorption. Management is directed at providing adequate nutrition through oral elemental diets or total parenteral nutrition. Therapeutic efforts should concentrate on nutritional rehabilitation through appropriate oral elemental formulas or total parenteral nutrition. Prevention of the original causes can most effectively be implemented by encouraging breast feeding.

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Loeb H, Mozin MJ. Prevention of chronic diarrhea: nutritional implications. J Pediatr Gastroenterol Nutr 1983;2(Suppl 1):S328-34

This paper reports the experiences of treating diarrhoea with a dietetic approach which involved systematic and very early use of a semi-elemental diet in concentrations which were rapidly increased. This approach allowed prevention of the development of chronic diarrhoea in several patients and obviated the need for total parenteral nutrition. A diet, providing 150 kcal/kg.day for 150 ml/kg.day, was used by 25 infants who had an apparently intractable diarrhoea. The average daily weight gain was about 20 g, and the average period of diet therapy in the hospital was ±30 days. On the basis of these results, a ready-for-use formula, "Alfare", was developed. This formula was used in a successive series of 48 infants suffering from severe chronic diarrhoea. The average daily weight gain was about 25 g, and the average duration of administration of the diet in the hospital was about 25 days. The effectiveness of Alfare in the treatment of extreme cases of chronic diarrhoea was examined in another series of 15 infants, aged 26 days to 4.5 months. All the infants were malnourished, and the diarrhoea was considered as resistant to the usual forms of orally administered treatments. Most of the children showed an ascending weight curve. In another study, pasteurized human milk preserved through deep-freezing proved to be inferior to Alfare in both acute and chronic diarrhoea, probably because of its high lactose content and higher osmolarity.

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MacLean WC, Jr., Lopez de Romana G, Massa E, Graham GG. Nutritional management of chronic diarrhea and malnutrition: primary reliance on oral feeding. J Pediatr 1980 Aug;97(2):316-23

This paper focuses on effective oral treatment in chronic diarrhoea and malnutrition. The course of 61 infants, aged from 1.8 to 27 months and hospitalized in Lima, Peru for treatment of chronic diarrhoea and malnutrition, was reviewed. Thirty children had marasmus, 18 kwashiorkor, and 13 marasmic kwashiorkor. After initial rehydration, infants were managed with a predominantly oral nutrition regimen using a formula based on whole protein (casein), vegetable oil (80:20 blend of soybean-cottonseed oil), glucose, and sucrose. Intravenous fluids were required for 38 infants (62%) for a median duration of 6 days, principally for the delivery of antibiotics. Amino acids were added to the infusion in 7 instances. The formula was initially fed at 25 kcal/kg.day in a volume sufficient to meet the fluid requirements, usually 125 to 150 ml/kg.day, based on appetite, urine volume, and urine-specific gravity. Intake was increased 26 kcal/kg.day every other day, until steady weight gain ensued provided that stool output did not exceed 100 to 150 g/day alongwith improved stool character. On the average, children were tolerating 75 kcal/kg.day by the end of 8 days in the hospital. Infants with marasmus and marasmic kwashiorkor reached a maximum intake of 151±21 kcal/kg.day after 5 weeks of treatment. Weight gain had been occurring for 2 weeks prior to this time. Infants with kwashiorkor were purposely not advanced post 75 kcal/kg.day until edema had cleared; a maximum intake of 135±16 kcal/kg.day was reached at 5 weeks. Mean initial serum concentration in these infants with kwashiorkor was 1.8±0.3 g/dl and required 20±13 and 53±24 days respectively to exceed 2.0 and 3.6 g/dl. Fourteen (23%) of the 61 infants died. Six were moribund on arrival and died within the first 3 days. Of the remaining 8, sepsis was thought to be the cause of death in 6 and pneumonia in 2. The average length of stay in the hospital for survivors was 185±71 days and did not vary with diagnosis. The data indicate that once infection is controlled, infants with chronic diarrhoea and malnutrition can be successfully managed primarily by enteral feeding without resorting to parenteral alimentation.

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intolerance, detected by the hydrogen breath test, in infants and children with chronic diarrhoea. Arch Dis Child 1977 Sep;52(9):766-71

This paper describes lactose intolerance, as detected by the breath hydrogen test, in infants and children with chronic diarrhoea. Twenty-three patients, aged 2 months to 13 years with diarrhoea of more than 2 weeks' duration, were studied. A further 8 children with suspected or proven celiac disease were also investigated. Six children, aged 5 months to 5 years without diarrhoea, served as controls. The breath hydrogen test was compared with the histology of the jejunal mucosa, mucosal lactase estimations, a lactose tolerance test, symptoms during the test, and follow-up after starting a lactose-free diet. Of these six children, no hydrogen concentration was detected in 4, while the fifth produced a very low level of doubtful significance. The last child had an early rise and fall of hydrogen, suggestive of small bowel colonization, which was proved by the culture of jejunal juice. Sixteen of the 23 patients produced hydrogen after lactose ingestion. Three patients had higher levels of breath hydrogen of more than 40 ppm, while one with a hydrogen concentration of 25 ppm showed symptoms in 24 h after the test. All 12 patients with peak hydrogen of 24 ppm improved on lactose-free diet with complete resolution of symptoms. The 4 patients with celiac disease became free of gastrointestinal symptoms after 6 months (or more) on a gluten-free diet; three of them had mild lactose intolerance and one had partial villus atrophy despite 8 years on apparent gluten exclusion. The breath hydrogen test gives a useful prognostic guide to the efficacy of a lactose-free diet in the treatment of chronic diarrhoea in children.

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Mainguet P, Fiasse R. Double-blind placebo-controlled study of loperamide (imodium) in chronic diarrhoea caused by ileocolic disease or resection. Gut 1977 Jul;18(7):575-9

Loperamide was compared with a placebo in a double-blind crossover study of 21 patients with chronic diarrhoea caused by ileocolic disease or resection. Eighteen of the 21 patients completed the trial. Each patient was treated with loperamide or placebo and when switched to the alternate medication in the subsequent treatment period. The median duration of loperamide treatment period was 37 days and of placebo 16.5 days ($p<0.001$). The frequency, consistency and weight of the stools were superior during loperamide treatment as compared with the placebo. The median dose of loperamide was 6 mg. Carmine transit time was found to be longer during administration of loperamide. Eight patients reported side-effects (nausea, vomiting, abdominal pain, and distension). Alleviation of diarrhoea was more effective with loperamide than with the placebo. Gastrointestinal side-effects were few and comparable during both treatment periods. As the effect of loperamide in the patients was to prolong the reduced transit time acquired by diarrhoea, the drug should prove to be useful in patients with intestinal resections or with extensive regional enteritis.

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Manto M see Gasbarrini G

Marino LR, Dahms BB, Halpin TC. Chronic diarrhea and neutropenia not associated with pancreatic insufficiency: a non-Shwachman-Diamond entity. J Pediatr Gastroenterol Nutr 1983 Aug;2(3):559-62

Findings of six children, initially referred for evaluation of Shwachman-Diamond syndrome with chronic diarrhoea and neutropenia, were found to have no evidence of pancreatic insufficiency. During June-December 1980, 125 children with chronic diarrhoea were evaluated by the gastroenterology unit at a children's hospital in Cleveland, Ohio, USA. Due to growth failure and neutropenia, six children were hospitalized for further studies. Five of the six children with chronic diarrhoea and neutropenia were male. The age range of those studied was 2-26 months. There was a seasonal predilection for illness in the spring. All children had a mild respiratory illness prior to the onset of diarrhoea. Fever did not exceed 38.5°C rectally. The children had 10-20 loose stools per day with no blood. They were treated with formula change to a lactose-free soy-protein formula; their stool examinations for pH and reducing substances were abnormal (pH 5.5, and reducing substances 1%) in each patient. Steatorrhea was found in one case (by 72-h fecal fat). Stool cultures were negative for bacterial pathogens, ova, and parasites. Neutrophil count in six children was <1,500. Iron deficiency anemia was found in four, while two showed myeloid arrest. In all patients, there was increased cellularity in the lamina propria. Half of the patients had an increased mitotic index at the bases of intestinal glands. One child had a small bowel ulcer. All children had complete resolution of the diarrhoea and neutropenia by 6-month follow-up, and there was no recurrence of neutropenia at one year. In conclusion, the association of neutropenia with chronic diarrhoea and failure to thrive is not necessarily indicative of the Shwachman-Diamond syndrome. Children with this clinical presentation should undergo evaluation, including a 72-h fecal fat analysis.

Markiewicz A see Zahorska-Markiewicz B

Marquez LA see Sampayo RR

Marshall WC see Candy DCA

Martin DL, Hoberman LJ. A point source outbreak of chronic diarrhea in Texas: no known exposure to raw milk [letter]. JAMA 1986 Jul 25;256(4):469

Martinez F see Weidenslaufer A

Martino AM see Durand P

Marx I see David VH

Massa E see MacLean WC, Jr.

Maszewaka-Kuzniarz K, Sonta-Jakimczy KD. [Chronic enteropathy in infants due to feeding with cow milk formulas]. Pol Tyg Lek 1972 Sep 11;27:1444-6

Mata L, Urrutia JJ, Simhon A. Infectious agents in acute and chronic diarrhea of childhood. In: Lebenthal E, ed. Chronic diarrea in children. New York: Raven Press, 1984:237-52

This work describes the agents of acute and chronic diarrhoea of childhood. Enterotoxigenic Escherichia coli (ETEC) and rotaviruses stand out as the main agents associated with acute diarrhoea. In the National Childrens' Hospital in Costa Rica, chronic diarrhoea is the main cause of death being also associated with severe protein-energy malnutrition (PEM) in children. The agents found in chronic diarrhoea are generally the same as those diagnosed in acute diarrhoea, but their relative frequency varies. Shigella and parasites, especially Giardia and Entamoeba histolytica, are more prominent in poor urban and rural children. E. coli, Campylobacter, Yersinia among others are often also responsible for chronic diarrhoea. Coronaviruses provided to be associated with chronic diarrhoea in India. Persistence of Shigella infection in small children is also discussed. A retrospective analysis of agents in acute and chronic diarrhoea was carried out. Results showed the presence of pathogens in the following manner: 41% had single infections, 14% had double, and 3.7% had triple infections. The multiple pathogenic organisms were found in the stools of children with severe PEM and diarrhoea in studies done in Guatemala. Observations indicated that chronic diarrhoea does not occur in infants who are breast-fed from birth. Administration of allergenic food with early weaning, failure of the host to cope with infection, failure to diagnose the exact causal agent with other reasons, all contribute towards establishing chronic diarrhoea. Multinational collaborative studies on the infectious etiology of acute and chronic diarrhoea are recommended.

Matarazzo M see Giardina MF

Mathis RK see Cohen SA

Matseshe JW, Phillips SF. Chronic diarrhea: a practical approach. Med Clin North Am 1978 Jan;62(1):141-54

Many patients who present with chronic diarrhoea are not found to have an important organic disease. This review presents a logical and practical approach for treatment based on a definition of chronic diarrhoea, brief consideration of the relevant pathophysiology, and a scheme for the clinical evaluation of patients. The history, the physical examination and the initial laboratory tests should lead to a provisional diagnosis, with respect to the organic or functional origin, and the location of disease in the small or the large bowel. Tests used to investigate chronic diarrhoea may include further macroscopic, microscopic, and bacterial examination of stools; proctosigmoidoscopy; blood tests; barium enema; specific tests of malabsorption, inflammatory bowel diseases, carcinoma of the large bowel, parasitic infections, and metabolic disorders; and determination of serum

concentration of gastrointestinal hormones. Specific causes of chronic diarrhoea, including functional diarrhoea, irritable colon, inflammatory bowel disease, large bowel carcinoma, amebic colitis, giardiasis, metabolic disorders, and gastrointestinal hormone-producing tumors, are discussed. Functional diarrhoea is common, and these patients are no less susceptible to severe disease than is the rest of the population. Treatment of various forms of chronic diarrhoea is also outlined.

Maur PR see Rothbaum RJ

Meeuwisse GW see Lindquist B

Mehrotra TN see Pande RC

Mehta PJ see Kokal KC

Mehta S. Investigative approach towards chronic diarrhoea in infants and children. Indian Pediatr 1977 Apr;14(4);303-8

Mehta S see Gupte SP

Mehta S see Walla BNS

Mehta SR see Sarin LR

Melange M, Vanheuverzwyn R, Fiasse R, Dive C. [A study of the anorectal motricity: its value in chronic diarrhea]. Acta Gastroenterol Belg 1981 Jan-Feb;44(1-2):76-82

Mendeloff AI. Chronic diarrheas: a diagnostic approach. Med Sci 1962 Apr 10;11:596-608

Meroni RJ see Sampayo RR

Merrick MV see Ludgate SM

Merritt RJ see Thomas DW

Metz G see Maffei HVL

Meuwissen SG see Tijtgat GN

Meuwissen SG see Tytgat GN

Meylan P see Chaptal J

Michaux HR. A mutton and rice diet for treating chronic diarrhea in the dog. J Am Vet Med Assoc 1966 Aug;149:296-7

Middleton FG see Butler T

Miglioli M see Gasbarrini G

Milla PJ see Candy DCA

Mills PR, Brown IL, Watkinson G. Idiopathic chronic ulcerative enteritis.

Report of five cases and review of the literature. Q J Med 1980 Spring;49 (194):133-49

Mills PR see Lamont CM

Milloy PT see Osterholm MT

Mir GN, Alioto RL. A semichronic diarrheal model. J Pharmacol Methods 1982;7: 115-20

A method of producing semi-chronic diarrhoea in rats by producing a state of lack of absorption of lactose is presented. Male and female (140-160 g) rats (Sprague-Dawley, Wistar, and Long-Evans) were used. When fed a combination of 50% lactose and 50% commercially available feed, the rats were subjected to continuous diarrhoea, which lasted for 96 h or more. At the same time, the animals continued gaining body weight. Long-Evans rats of both sexes and the female Wistar rats were more sensitive in producing watery diarrhoea than the other rats. The relative lack of the enzyme lactose in the rat results in the accumulation of lactose in the gut and probably by an osmotic effect, sets up conditions for the passage of a watery diarrhoea. Various combinations of lactose and commercially available feeds were tried. It was observed that rats functioned without any ill effects (e.g. body weight loss) and produced consistent diarrhoea with the above mentioned combination. The effects of morphine, diphenoxylate, and loperamide were studied in the female Wistar rats at 5, 10, and 20 mg/kg on 24 and 48 h diarrhoeas respectively. All 3 drugs were effective in this model. Loperamide was the most effective, followed by diphenoxylate and morphine. Thus, a lactose-rich diet-induced diarrhoea in rats may be a useful diarrhoeal model of extended duration, particularly for testing the long-term antidiarrhoeal activity of potential drugs.

Mirescu M see Popescu V

Mir-Madjlessi SH, Forouzandeh B, Ghadimi R. Ulcerative colitis in Iran: a review of 112 cases. Am J Gastroenterol 1985 Nov;80(11):862-6

From 1973 to 1982, 112 cases of chronic ulcerative colitis were diagnosed and followed up in Tehran, Iran, and the findings were compared with those reported from other countries. The study group was comprised of 40% males and 60% females. The mean age of onset of chronic ulcerative colitis was 31.8 years. Bloody diarrhoea and crampy abdominal pain were the most common symptoms and were present in 84% of the cases, while 9% of the patients had constipation and 30% had fever. Weight loss (32%), anemia (49%), distal colitis (42%), substantial colitis (22%), and total colitis (28%) were also seen. Chronic ulcerative colitis was mild in 54.5% of the patients, moderate in 36.5% and severe in 9%. Various complications, e.g. colonic or rectal strictures, pseudopolyp, anal fissure, colon cancer, liver cirrhosis, and perianal abscess, occurred in the patients. Only chronic ulcerative colitis-specific treatment resulted in remission. Of the 112 cases, 105 were given salicylazofulfapyridine, either alone or in combination with adrenal steroids. The overall mortality rate was 9%. Nearly one-third of the patients were subjected to surgery for hemorrhoids or anal fissures. The demographic and clinical findings in the patients corresponded to those reported from other developing countries. Skin lesions, such as erythema nodosum and pyoderma gangrenosum, were absent. A low incidence of colorectal cancer in chronic ulcerative colitis has been reported. The pathogenesis of chronic ulcerative

colitis is unknown, and the influences of life-style, socioeconomic factors and emotional stress on its development are matters of controversy. The rarity of Crohn's disease in Iran is noted.

Moeller HC see Rider JA

Moore L see Mann MD

Morawski SG see Fordtran JS

Morawski SG see Read NW

Morel G see Chaptal J

Morrison L see Sanders DY

Morton RE see Reisman T

Mosca F see Roggero P

Moses LG see Premchander KV

Motil KJ, Grand RJ. Nutritional management of inflammatory bowel disease. Pediatr Clin North Am 1985 Apr;32(2):447-69

This paper reviews the epidemiology and etiology of malnutrition and growth failure in inflammatory bowel disease. Chronic inflammatory bowel disease represents two intestinal disorders of childhood: ulcerative colitis and Crohn's disease. Because of the clinical significance of the symptoms associated with these diseases, nutritional considerations have a major impact in the therapeutic management of inflammatory bowel disease in childhood. Individual nutrient deficiencies may occur in children, but more frequently there is generalized protein-energy malnutrition, complicated by progressive growth retardation. The etiology of malnutrition in inflammatory bowel disease is multifactoral and may be due to inadequate dietary intakes, excessive intestinal losses, malabsorption, and increased nutrient requirements. Malabsorption or its complications are more common in patients with long-standing Crohn's disease and weight-for-age deficits. The indications for nutritional intervention in inflammatory bowel disease include the provision of primary nutritional support during active inflammatory disease, the treatment of individual nutrient deficiencies, and the reversal of malnutrition and growth arrest. Nutritional disorders and their complications in chronic inflammatory bowel disease can be prevented by monitoring appropriate anthropometric and laboratory indices and by promptly instituting enteral or parenteral nutritional rehabilitation when indicated.

Moxey PC see Trier JS

Moylan FMB. Aluminum hydroxide in the symptomatic treatment of infants with chronic diarrhea. J Pediatr Gastroenterol Nutr 1983 May;2(2):295-8

Two neonates with milk intolerance and two older infants, one with acute gastroenteritis and the other with prolonged malnutrition, developed chronic diarrhoea. Despite bowel rest, total parenteral nutrition, and alterations in the protein and carbohydrate content of the milk preparations used, every

attempt to feed them resulted in diarrhoea. All four patients were given aluminum hydroxide because of its bile salt-binding activity and its tendency to cause constipation. Coincident with its administration the diarrhoea stopped, and the enteral feedings were successfully reinstituted. The only complication seen was the development of constipation in two of the infants; this responded to lowering of the dose of the aluminum hydroxide. (Author's abstract)

Mozin MJ see Loeb H

Mullertz S see Ingomar CJ

Munir M. Protracted diarrhea in infants and young children: a clinical evaluation with special reference to the role of infection. Paediatr Indones 1982 May-Jun;22(5-6):89-98

Clinical evaluation of protracted diarrhoea was done for children hospitalized at the Gunung Wenang Hospital, Manado, Indonesia between 1977 and 1980. Of the 1,186 diarrhoea cases, 49 (4%) were diagnosed as protracted diarrhoea. The 49 cases were subdivided into 3 main categories: acute onset of protracted diarrhoea without failure to thrive (16 cases), chronic recurrent diarrhoea with failure to thrive (10 cases), and chronic recurrent diarrhoea without failure to thrive (2 cases). Malaria played an important role in 10 cases of failure to thrive with protracted diarrhoea, and in 3 acute onset of prolonged diarrhoea cases without failure to thrive. Amebiasis was found in 3 cases of acute onset of prolonged diarrhoea. Escherichia coli was found in 8 cases of acute onset of prolonged diarrhoea without failure to thrive, in 2 cases of acute onset of prolonged diarrhoea and failure to thrive, in 1 case of prolonged diarrhoea in multiple congenital malformation and failure to thrive, and in 1 case of chronic recurrent diarrhoea in colostomy and failure to thrive. Although only a very small number of diarrhoeal cases belonged to protracted diarrhoea, acute infection was the most common underlying cause, i.e. malaria was found in 10 cases, congenital malformation in 2, meningitis in 1, and CMEP in 2 cases, Marked anemia was found in all cases, and 4 patients with severe anemia needed blood transfusions. Six of the 49 cases evidenced a marked vitamin A deficiency, and as such, a high dose of vitamin A was recommended for all protracted diarrhoea cases. Dietary treatment was stressed as an important aspect in the management of protracted diarrhoea.

Murphy GM see Nelson R

Nash TE see Smith PD

Nassif EG see Ghishan FK

Nelson R, Murphy GM, Edkins S, Richardson JM, Anderson CM. A new procedure for the study of malabsorption and chronic diarrhoea of undermined aetiology in infancy and childhood. Gut 1973 May;14(3):427

A comprehensive test of pancreatic function, bile salt metabolism, and small intestinal bacterial flora, that requires a single duodenal intubation, has been developed. Intubation of duodenum and stomach was performed after a fast of more than 5 h. Duodenal fluid was collected for 30 min fasting, for 30 min after intravenous pancreozymin, and for a further 30 min after secretion. Two hours after pancreozymin, a test meal of measured composition, containing 1 g

fat/kg of body weight was instilled directly into the stomach. Duodenal contents then were collected for 60 min. This procedure was applied to patients with malabsorption and diarrhoea of unknown etiology. Results were presented and their clinical value discussed.

Netchvolodoff CV, Hargrove MD, Jr. Recent advances in the treatment of diarrhea. Arch Intern Med 1979 Jul;139(7):813-6

Recent advances in the treatment of diarrhoea, both acute and chronic, are discussed. Often treatment is not indicated in individuals who have acute diarrhoea that improves spontaneously in one or two days. Treatment is indicated if the diarrhoea causes a large volume of fluid loss, is severe from the onset, is accompanied by blood in the stool, or persists without improvement for more than 24 h. Parenteral and oral fluid replacements, drugs that decrease intestinal motility, and antibiotic therapy for specific microorganisms are also discussed. An exact diagnosis is essential for proper management of patients with chronic diarrhoea. A complete history and physical examination, stool examination for blood, leukocytes, parasites, and fat, proctoscopic examination, roentgenograms of the stomach, small intestine, and colon are required for almost all patients. Although treatment of patients with functional diarrhoea is difficult, drugs, such as diphenoxylate hydrochloride and anticholinergic agents, may provide partial symptomatic relief. Causes, diagnoses and therapy in different types of organic diarrhoea are also outlined in this review paper.

Neves DP see Campana AO

Newman F see Kidd GS

Nichols BL see Calvin RT

Nichols BL see Carrazza FR

Nigam DK see Agarwal VK

Nitulescu M see Popescu V

Noerasid H see Soeparto P

Norman AP see Candy DCA

O'Donnell AM, Orsi M. Feeding of children with protracted diarrhea in developing countries. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:521-33

O'Dorisio T see Kidd GS

Oertel H, Eckstein R, Hlubner G, Wiebecke B, Riess H, Paumgartner G. [Chronic diarrhea in an Arab patient with acquired immuno-deficiency syndrome (AIDS)]. Internist (Berlin) 1985 Nov;26(11):712-6

Olambiwonnu NO, Johnson A, Adeniyi A, Adeyokunnu A, Attah EB. Diabetes mellitus associated with chronic diarrhoea in an infant. E Afr Med J 1976 Jul;53(7):407-10

Olives JP see Ghisolfi J

Olivieri V see Ciampolini M

Orsi M see O'Donnell AM

Ortega G'omez H, Symes Gracia I, Gomez-Orozco L. [Chronic diarrhea caused by allergy to cow's milk]. Alergia 1979 Jan;26(1):5-11

Osterholm MT, MacDonald KL, White KE, Wells JG, Spika JS, Potter ME, Forfang JC, Sorenson RM, Milloy PT, Blake PA. An outbreak of a newly recognized chronic diarrhea syndrome associated with raw milk consumption. JAMA 1986 Jul 25;256(4):484-90

A previously undescribed chronic diarrhoea syndrome affected 122 residents of Brainerd, Minn, USA, between December 1983 and July 1984. The illness lasted at least one year for 75% of the case-patients and was characterized by acute onset, marked urgency, a lack of systemic symptoms, and a failure of response to antimicrobial agents. Clinical and laboratory data indicate that the diarrhoea was caused by a secretory mechanism. Consumption of raw milk from a single dairy was associated with illness (odds ratio, 28.3; 95% confidence interval, 9.0 to 89.0). A median incubation period of 15 days was determined for seven case-patients. Possible secondary transmission was noted in one family. Extensive laboratory examination did not identify an etiologic agent. Outbreaks or sporadic cases of a similar illness have occurred in at least seven states; the outbreaks were less extensively investigated, and findings were not published, but raw milk consumption was common in the affected persons. This illness appears to represent a previously unrecognized but important clinical entity and public health problem. The etiology and effective therapy for this illness must be determined by further studies of sporadic cases and outbreaks. (Author's abstract)

Ottredi ML see Roggero P

Owyang C. Treatment of chronic secretory diarrhea of unknown origin by lithium carbonate. Gastroenterology 1984 Sep;87(3):714-8

This paper reports the treatment of chronic secretory diarrhoea of unknown origin with lithium carbonate. A 49-year-old woman was admitted to the University of Michigan Medical Center in November 1981. She complained of a watery diarrhoea, weight loss, and weakness. Multiple stool tests for ova leukocytes and parasites were negative. The patient excreted 1-3 l of stool per day. A 72-h fecal fat collection gave a value of 6.4 g/24 h. She had chronic gastritis. Basal acid output was 2 mEq/h and maximal acid output 5.5 mEq/h. Barium studies of the esophagus, stomach, small bowel and colon were normal, and the breath hydrogen test was also normal. Hypergastrinemia was observed. Various pharmacotherapy with diphenoxylate hydrochloride, indomethacin, and prednisone were tried on the patient without any significant result. She was then started on oral lithium carbonate at doses of 300 mg every 12 h. Within 48 h, her stool volume decreased from 2 to 0.5 l. On the fourth day, her diarrhoea had stopped. She was maintained on this treatment for 3 months. The patient remained asymptomatic for 15 months after discontinuation of treatment with lithium carbonate. In this case, the possibility of the infection by an unidentified microorganism cannot be excluded. The effect of lithium carbonate on intracellular cyclic adenosine 3',5'-monophosphate may be responsible for its antisecretory effect in the intestine.

Pacht M. [Chronic diarrhea in infants caused by malabsorption of sugars]. Dapim Refuiim 1966 Jan-Jun;25:152-8

Pague C. [Initial clues in the diagnosis of chronic diarrhea in children]. Maroc Med 1971 Nov;51:670-1

Palmer FB see Wender EH

Palmas S. [Therapy of acute and chronic diarrhea in adults. I). Clin Ter 1979 Mar 15;88(5):517-39

Palmas S. [Therapy of chronic diarrhea in adults. II]. Clin Ter 1979 Mar 31;88(6):639-56

Palmer KR, Corbett CL, Holdsworth CD. Double-blind cross-over study comparing loperamide, codeine and diphenoxylate in the treatment of chronic diarrhea. Gastroenterology 1980 Dec;79(6):1272-5

The findings of a comparative double-blind crossover study with loperamide, codeine, and diphenoxylate in the treatment of chronic diarrhoea are reported. Thirty patients with diarrhoea participated in the experiment. Before entry, 5 patients were taking codeine at mean daily doses of 90.0±9.5 mg, and their mean stool frequency was 2.6±0.4. Ten patients were taking loperamide, 5.2±2.5 mg per day, and they had 3.0±0.2 stools per day, while 2 patients took diphenoxylate. Mean daily stool frequency for all patients was 4.9±0.4 (range 1-9). Each patient underwent three randomized treatment periods of 4 weeks' duration. Patients were instructed to increase the daily dose gradually, until control was achieved or side-effects became intolerable. Stool frequency, consistency, urgency and incontinence were then compared when a stable dose was reached. Nine of the 20 patients had occasional fecal incontinence. There was no significant difference between either the number of capsules taken per day or the stool frequency in each of the treatment periods. Treatment with diphenoxylate was associated with smaller percentage of solid stools than either loperamide or codeine. There were significantly more complaints of urgency while taking diphenoxylate than the other two ($p<0.05$). Ten patients complained of side-effects during treatment with loperamide, 12 with codeine, and 12 with diphenoxylate. The total number of complaints was greater for diphenoxylate than for loperamide and codeine. When effects on the central nervous system were considered, the difference between loperamide and diphenoxylate was more marked. Finally, 8 of the 25 patients expressed a preference for loperamide, 7 for codeine, and 5 for diphenoxylate. Two mg of loperamide was equivalent in constipating activity to 45 mg of codeine phosphate. A similar dose was also indicated by other workers. Diphenoxylate was less effective in the control of urgent cases because of poor patient tolerance. Both codeine and loperamide were found to be superior to diphenoxylate in terms of improving stool consistency, relieving urgency, and incidence of side-effects.

Pancaldi R see Shmerling DH

Panchatcharam M see Premchander KV

Pande RC, Rajvanshi VS, Gupta SC, Mehrotra TN. Enteropathogenic serotypes of Escherichia coli isolated from sporadic cases of acute diarrhoea and gastroenteritis and chronic diarrhoea in Allahabad. Indian J Med Res 1973 Nov;61(11):1588-93

The present study was undertaken to determine the serotypes prevalent in sporadic cases of acute diarrhoea and gastroenteritis and chronic diarrhoea in and around Allahabad, India. Feces from 120 cases of acute infantile diarrhoea and gastroenteritis and 34 cases of chronic diarrhoea were studied for enteropathogenic Escherichia coli (EPEC). Stool samples or rectal swabs showing distinct fecal staining from infants, aged under 2, were obtained from patients attending S N Children Hospital, Allahabad. By using nine EPEC antisera, it was possible to type 79% of the strains, isolated from acute diarrhoea and gastroenteritis and 39% from the cases of chronic diarrhoea. E. coli serotype 026 was the commonest organism associated with acute infantile diarrhoea and gastroenteritis and chronic diarrhoea. Eight of the 120 cases of acute infantile diarrhoea and gastroenteritis and of the 34 cases of chronic diarrhoea were found to be associated with serotype 0126. This serotype has been isolated only rarely from the cases of infantile diarrhoea in India. (Modified author's abstract)

Pande RC, Rajvanshi VS, Mehrotra TN, Gupta SC. Phage typing of enteropathogenic serotypes of Escherichia coli from sporadic cases of acute chronic diarrhea and gastroenteritis in Allahabad. Indian J Med Res 1976 Jun;64(6):841-6

Pandey RC see Agarwal VK

Pandit AN see Bhave SA

Pap Z, Kemeny G, Lakatos M, et al. [Histomorphological changes in chronic diarrheas in infants and young children (study of 72 enteral biopsies)]. Pediatria (Bucur) 1970 Jul-Aug;19:335-42

Pappo E see Gouerou H

Parker P, Stroop S, Greene H. A controlled comparison of continuous versus intermittent feeding in the treatment of infants with intestinal disease. J Pediatr 1981 Sep;99(3):360-4

Two feeding regimens -- continuous intragastric feedings and intermittent oral feeding — were compared with each other in 9 infants, aged under 6 months with protracted diarrhoea and malnutrition and 2 infants, aged 3 and 7 months with surgically created short bowel. The dietary formula was mixed locally using Portagen as the base and adding other ingredients to achieve the desired mixture of carbohydrate, fat, protein, and minerals. Continuous nasogastric feeding caused significant increase in internal balance of the major nutrients, whereas intermittent feedings resulted in negative or only slightly positive internal balance. The improvements in internal balance from intermittent to continuous feeding in diarrhoeic infants was noticeable. There was a significant increase ($p<0.001$) in body weight during the continuous feeding (168±16 g/72 h) as compared to the intermittent feeding (-171±26 g/72 h). The fecal weight was significantly greater ($p<0.001$) during the period of intermittent bolus feeding. Similar improvements in internal balance were seen in the two infants with short bowel. During continuous infusion feedings, both patients demonstrated maximum weight gain and 31 to 48% decrease in fecal weight. The infant with the most compromised bowel had the most impressive response. The results suggest that improved internal balance can be achieved with continuous feeding in infants with chronic diarrhoea and malnutrition or with short bowel syndrome.

Pasquini E see Catassi C

Paterno VI see Heyman MB

Paterson ID. The use of loperamide for treatment of "difficult to manage" chronic diarrhoea in adults. J Int Med Res 1977;5:459-61

An open study of loperamide hydrochloride in 7 patients with chronic diarrhoea, who were inadequately controlled by previous antidiarrhoeal therapy, has been reported from England. The trial comprised 3 distinct periods. In period 1 (1 week), all antidiarrhoeal therapy was withdrawn to provide baseline data. In period 2 (3 weeks), the patients were given loperamide hydrochloride as 2 mg capsules at a dosage of 2 capsules daily in the morning, followed by one after each loose stool (up to a maximum of 8 capsules per day). Individualized dose of the drug was administered as a regular daily dose in period 3 (8 weeks). There was a significant ($p<0.05$) decrease in the stool frequency on loperamide treatment. The consistency of stools was also normalized by loperamide therapy. The mean daily dosage of loperamide was 1.9 and 2.2 capsules, respectively, in periods 2 and 3. Most patients were able to eat a normal diet after treatment. No side-effects were reported. It is concluded that loperamide may be effective in the control of chronic diarrhoea.

Paumgartner G see Oertel H

Pawa RR see Chandra RK

Pelemans W, Vantrappen G. A double blind crossover comparison of loperamide with diphenoxylate in the symptomatic treatment of chronic diarrhea. Gastroenterology 1976 Jun;70(6):1030-4

The symptomatic antidiarrhoeal efficacy of loperamide was compared with that of diphenoxylate in a double-blind crossover study of 23 adult patients, aged 24 to 63 with chronic diarrhoea of various etiologies. Identical opaque capsules, each containing either 2 mg of loperamide or 5 mg of diphenoxylate plus 0.05 mg of atropine sulphate, were supplied to patients, and a flexible dosage schedule was employed. In the group of 17 patients who were evaluated by means of stool frequency and consistency, both loperamide ($p=0.001$) and diphenoxylate ($p=0.006$) effected significant improvements. However, loperamide was significantly superior ($p=0.01$) to diphenoxylate in this respect, even at a 2.5-fold lower dose level. Nine patients reported adverse experiences - 4 in the diphenoxylate treatment period, 3 in the loperamide period, and 2 in both periods. The study indicates that loperamide is an orally effective antidiarrhoeal agent capable of controlling or significantly reducing chronic diarrhoea of diverse origin.

Pencharz P see Gunn T

Penn RG, Giger DK, Knoop FC, Preheim LC. Plesiomonas shigelloides overgrowth in the small intestine. J Clin Microbiol 1982 May;15(5):869-72

The case of an 83-year-old male, who had chronic diarrhoea and protein malnutrition, associated with Plesiomonas shigelloides overgrowth in the small intestine, is presented. This overgrowth was related to achlorhydria and small bowel diverticula. P. shigelloides was isolated from the stool culture. A duodenal aspirate grew $3x10^8$ P. shigelloides organism per ml. All stool and

duodenal isolates of P. shigelloides were tested for their ability to produce enterotoxic activity. Cell-free culture supernatants, prepared from these isolates, were consistently negative in the infant mouse and cultured adrenal cell assay for enterotoxic activities. The patient was given intravenous hydration, parenteral vitamin B_{12}, and a 7-day course of tetracycline, 250 mg four times a day, orally. The patient responded satisfactorily to tetracycline, to which this unusual isolate was susceptible in vitro. This report documents for the first time the association of P. shigelloides with the small bowel overgrowth syndrome. The results suggest that correct identification and determination of the antimicrobial susceptibility of P. shigelloides in the setting of small bowel overgrowth will help determine appropriate therapy.

Perazzani M see Roggero P

Peris Vidal A, Hernandez Marco R, Escribano Montaner A, Aparisi Ibanez M, Alos Alminana M. [Zinc balance in malnourished children given prolonged total parenteral feeding]. An Esp Pediatr 1986 Feb;24(2):111-7

Perkash A, Gupte SP. Blood and bone-marrow patterns in chronic diarrhoea in children. Indian J Pediatr 1971 Aug;38:326-30

Perlmutter DH, Leichtner AM, Goldman H, Winter HS. Chronic diarrhea associated with hypogammaglobulinemia and enteropathy in infants and children. Dig Dis Sci 1985 Dec;30(12):1149-55

To define the gastrointestinal manifestations and small intestinal structure and function in a group of infants with chronic nonspecific diarrhoea and hypogammaglobulinemia, 55 such patients were identified retrospectively from a population of 518 children (10.6%) evaluated for chronic diarrhoea over a 6-year period during 1976-1981 in the USA. To assess the importance of the immunoglobulin deficiency as an independent variable, 85 children similar to the study group, but having normal immunoglobulin levels, served as controls. All the study patients had IgG levels 2.0 SD (or more) below the mean values for age. Patients with biochemical evidence of protein loss (enteropathy or nephropathy) were excluded. Small intestinal histology was abnormal in 50% of the patients with hypogammaglobulinemia who had undergone biopsy, a significant difference when compared to 23% in controls ($p<0.05$). Of the 34 biopsies, 12 were consistent with healing enteritis, four with acute enteritis, focal or mild, and one with diffuse severe active enteritis. Carbohydrate malabsorption, and infection with Giardia lamblia or Clostridium difficile occurred in 34% and 24% of the patients tested respectively. Patients with hypogammaglobulinemia had a significantly higher prevalence of carbohydrate malabsorption ($p<0.005$) as well as infections with G. lamblia and C. difficile ($p<0.01$). The results suggest that immunoglobulin determination in children, who would otherwise carry a diagnosis of chronic nonspecific diarrhoea, identifies a group with hypogammaglobulinemia, having an increased incidence of treatable intestinal dysfunction or infection, and a spectrum of small intestinal histologic abnormalities.

Peterson HD, Collins OD, 3d. Chronic diarrhea and failure to thrive secondary to ganglioneuroma. Arch Surg 1967 Dec;95:934-6

Petrescu CT see Popescu V

Pettersson T, Selroos O. [Chronic diarrhea in domestic giardiasis]. Nord Med 1971 Jan 21;85:78-80

Phillips SF see Matseshe JW

Phuapradit P, Varavithya W. Treatment of chronic diarrhoea with galantase. Southeast Asian J Trop Med Public Health 1982 Sep;13(3):503

Galantase, a synthetic lactase, was used in the management of 8 patients who suffered from chronic diarrhoea of 26.8±15.4 days' duration. Seven of these 8 patients also had poor nutritional status. Prior to treatment with galantase, 3 of the 6 patients, who had been receiving non-lactose milk, did not gain weight. When non-lactose milk was substituted by full-strength humanized or cow's milk plus galantase, no significant change in stool frequency was observed in these 8 patients. All except one of these patients gained weight. One patient developed osmotic diarrhoea after discontinuation of galantase. Galantase may be used to substitute non-lactose milk in the management of patients with chronic diarrhoea associated with lactose intolerance. The duration of administration of galantase depends on the severity and duration of diarrhoea in each patient.

Picarazzi A see Busino L

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Pincott JR see Candy DCA

Podlesny J see Kulesza E

Poley JR. Causes of chronic diarrhea in infants and children. Postgrad Med 1970 Dec;48(6):143-7

This paper discusses the causes of chronic infantile diarrhoea and their diagnosis. A reliable feeding history of the patient helps diagnosis by enabling the physician to put the newer diagnostic tests to their optimal use. In addition, growth data should be obtained whenever possible. The symptoms and diagnosis of various types of dietary proteins and carbohydrates are discussed. Both chronic ulcerative colitis and Crohn's disease may be associated with chronic or recurrent diarrhoea. It is suggested that careful proctoscopy and X-ray study of the intestine may assist in differentiating ulcerative colitis from Crohn's disease. The use of drinking water, containing a significant amount of sulfates in infant formula, may also lead to diarrhoea which can be severe, and being usually watery. The World Health Organization, therefore, recommends that water with a sulfate content of more than 400 mg/l is unsafe for infant feeding.

Poley JR. Chronic diarrhea in infants and children. I. South Med J 1973 Sep;66:1035-49

Poley JR. Chronic diarrhea in infants and children. II. South Med J 1973 Oct;66:1133-41

Poley JR. The small bowel mucosa in disease states characterized by chronic

diarrhea: observations by scanning electron microscopy. Scan Electron Microsc 1983;(pt 3):1293-306

Poley JR. Ultrastructural topography of small bowel mucosa in chronic diarrhea in infants and children: investigations with the scanning electron microscope. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:57-105

Pongpunlert W see Poovorawan P

Poovorawan P, Pongpunlert W, Reinprayoon S, Sensirivatana R. Chronic diarrhea in infants from salmonellosis. Chulalongkorn Med J 1984 May;28(5):497-505

The incidence and mortality rates of chronic diarrhoea due to Salmonella infection were examined in young infants. During an outbreak of Salmonella infection in a Thai hospital (1977-1980), 26 of the 71 chronic diarrhoea cases were identified as salmonellosis. Salmonella was detected in the initial stool culture in 10 cases. The remaining 16 were found during the course of diarrhoea occurring at the hospital. Low birth weight neonates were prone to this infection. There was no difference between the mortality rates in the salmonellosis group (11.5%) and the overall chronic diarrhoea group (12.7%).

Popescu V, Iacob C, Mirescu M, Stanescu M, Lordachescu F, Georgescu M, Barbulescu V, Radoi E, Petrescu CT, Nitulescu M. [Chronic diarrheic diseases with disaccharide intolerance. Anatomo-clinical correlates]. Rev Pediatr Obstet Gynecol 1978 Oct-Dec;27(4):297-312

Popescu V. [Treatment of chronic diarrhea by antiperistaltic inversion of a jejunal loop]. Chirurgia 1973 Aug;22:741-5

Popescu V see Priscu R

Posada OR, Kurdian M. [Study of the absorption of orally administered glucose in chronic diarrhea and in gastroectomized patients]. Prensa Med Argent 1965;52:1967-70

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Potzi R see Ferenci P

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Premchander KV, Sundaravalli N, Panchatcharam M, Ranganathan G, Moses LG, Raju VB. Pattern of sugar intolerance in children following chronic or recurrent

diarrhoea: a preliminary report. Indian Pediatr 1976 Mar;13(3):177-86

The incidence of sugar intolerance in children following chronic or recurrent diarrhoea was examined in India. One hundred children, aged 0 to 7 years, were studied, while 20 children served as controls. One-third of the cases came from middle and high income groups and the remaining were from a low income group. The incidence was highest in the 4-to-9-month age group. The characteristic stool appearance was small, frothy, watery, yellowish, and acid smelling in majority of the cases. The stool pH ranged from 5 to 6. Reducing substance in the stool was more than 2% in majority of the cases. Combined intolerance to glucose, galactose, and lactose was most common. Lactose tolerance test was diagnostic in all 36 cases, and radiological study was diagnostic in 43 cases. Therapeutic measures were taken up depending on the nutritional status of the patients. In undernourished children, after exclusion of offending sugar for 3 to 4 weeks, honey and Casilan feeds (100 cal/kg) were given. After 4 weeks, the offending feeds were introduced gradually. Many of the difficult cases, especially those with malnutrition, were given intravenous plasma 20 ml/kg at weekly intervals. Re-introduction of milk or offending feed was successful by 2 months in majority of the patients. In this study, the mortality rate was 18%.

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Priscu R, Popescu V. [Chronic diarrhea caused by carbohydrate intolerance (diarrhea caused by deficiency of disaccharidase and by disorders of aldose transfer)]. Pediatria (Bucur) 1974 May;23:193-204

Puletti EJ see Rider JA

Pyrikova IA see Sazanova NE

Quenon M see Adler M

Quillian W see Clarke JT

Radoi E see Popescu V

Raju VB see Premchander KV

Rajvanshi VS see Pande RC

Ramirez-Mayans JA, Carriloo J, Rivera-Echegoyen M. [Intestinal biopsy in children with chronic diarrhea. Study of 100 cases]. Bol Med Hosp Infant Mex 1983 Nov;40(11):632-7

Ranganathan G see Premchander KV

Rask-Madsen J, Bukhave K. Prostaglandins and chronic diarrhoea: clinical aspects. Scand J Gastroenterol 1979;14(Suppl 53):73-8

This paper reviews the literature on the biological actions of prostaglandins (PG) with respect to the role of PGE and PGF in the pathogenesis of diarrhoea. The review is largely concerned with physiological aspects which are particularly relevant to the therapeutic application of PG synthetase inhibitors in the treatment of chronic and relapsing diarrhoea. PGs are

synthesized in virtually every organ including the small intestine. The E-type appears to elicit secretion of salt and water, while the F-type seems to promote intestinal motility — at least in pathological conditions; but a physiological role has not yet been defined for either of them. Since the effect on transepithelial on transport is similar to that produced by cholera toxin, the adenylate cyclase cyclic adenosine 3',5'-monophosphate (cAMP) system has been implicated in the mechanism of PG action. Although PGE mimics the effects of cholera toxin and cAMP, not all experimental observations are explicable in terms of the theory which links PGs to cAMP. Only pharmacological concentrations (10^{-6}-10^{-4}M) have been shown to activate intestinal adenylate cyclase, and the action of PGE on cAMP concentrations is additive to that of cholera toxin. On the other hand, a dose-dependent relationship between exogenous PGE_2 and changes in ionic movements has been demonstrated in the short-circuited human jejunum *in vitro* during blockage of endogenous PG-biosynthesis with indomethacin (threshold response at 10^{-11} M; half maximal response at 10^{-9}M). Important therapeutic implications are suggested by the successful treatment of the diarrhoea observed in the irradiation syndrome, specific food intolerance, irritable bowel syndrome, Crohn's disease, ulcerative colitis, and intestinal pseudo-obstruction with specific PG-synthetase inhibitors, such as indomethacin, aspirin and related drugs, or nutmeg. PGs also appear to be involved in the pathogenesis of diarrhoea in pancreatic cholera, the carcinoid syndrome, and medullary carcinoma of the thyroid. Effects have been made in assaying primary PG levels in peripheral plasma for clinical use. The demonstration of a marked *in vitro* production during the sampling procedure seems to explain the conflicting data in accordance with the known ability of the lungs to remove the majority of PGs from circulation. However, local PG-release is reflected in the intestinal secretions which may be sampled for analysis without laborious precautions.

Rask-Madsen J *see* Bukhave K

Read M, Read NW, Barber DC, Duthie HL. Effects of loperamide on anal sphincter function in patients complaining of chronic diarrhea with fecal incontinence and urgency. Dig Dis Sci 1982 Sep;27(9):807-14

The study was undertaken to investigate the effect of loperamide (4 mg tds) on the continence to a standard volume of rectally infused saline and anorectal manometry in 26 patients (10 male and 16 female), aged between 24 and 82 years (mean =45±18 years), complaining of chronic diarrhoea complicated by fecal incontinence and severe urgency. Each patient was treated for one week with loperamide (4 mg tds) and for one week with an identical placebo in a double-blind crossover trial. Results showed that, as well as its established effects of improving stool consistency and reducing stool weight, frequency and episodes of incontinence and severe urgency, loperamide also significantly improved continence to a standard volume of rectally infused saline. This action was associated with an increase in the maximum basal sphincter pressure, an increase in the rectal volume required to abolish recovery of the rectoanal inhibitory reflex, and a reduction in rectal compliance. These results also suggest that loperamide may have a specific action on the anal sphincter, which may aid continence in patients who complain of diarrhoea and fecal incontinence. (Modified author's abstract)

Read MG *see* Read NW

Read NW, Krejs GJ, Read MG, Ana CAS, Morawski SG, Fordtran JS. Chronic diarrhea of unknown origin. Gastroenterology 1980 Feb;78(2):264-71

This report examines 27 patients with severe chronic diarrhoea for which extensive investigations carried out at different institutions in the USA had failed to reveal a diagnosis. The patients were studied by standard diagnostic methods as well as by careful fecal analysis and perfusion of jejunum (23 patients), ileum (19), and colon (12). Three tests of anal sphincter function were performed if the patient gave a history of fecal incontinence. Stool weight was normal in 6 patients, greater than 500 g/24 h in 10, and in excess of 1000 g/24 h in 4. Average bowel movement frequency varied from 2 to 19/day. There was a positive but relatively weak correlation between movement frequency and stool weight ($p<0.01$). Although many were suspected of having pancreatic cholera syndrome, this diagnosis could not be established in a single patient. The most common diagnosis that could be established was surreptitious ingestion of drugs (laxatives in 7 patients and diuretics in 2). Other specific diagnoses included ulcerative colitis (2), allergy to beef (1), and bacterial overgrowth of the small intestine (1). Thus a specific diagnosis was established in 13 patients. The remaining 14 were assigned to various descriptive categories. Eight had findings suggestive of irritable bowel syndrome, and 2 had anal sphincter dysfunction. The other 4 undiagnosed patients had severe secretory (3 patients) or osmotic (1 patient) diarrhoea. Follow-up interviews, carried out 6 months to 6 years after discharge in 20 patients, failed to reveal evidence of a cause for diarrhoea that had been overlooked during the study. The importance of a search for surreptitious drug ingestion and accurate measurement of bowel movement frequency and stool weight was emphasized. Intestinal perfusion was not of any major diagnostic value in any of the 27 patients.

Read NW see Read M

Redelsperger P-Y see Gouerou H

Rees PH see Awori NW

Reinprayoon S see Poovorawan P

Reisman T, Morton RE, Rogers AI. Gastroenterology: a hypothetical case of chronic diarrhea incorporating a management self-test. Postgrad Med 1976 Feb;59(2):203-10

Chronic diarrhoea may be a manifestation of any of the several local and systemic disorders. A thorough history and physical examinations of a patient with this complaint are mandatory. Appropriate laboratory and radiological studies should be obtained after the attending physician has outlined a rational approach to the problem. This paper reports a hypothetical case of chronic diarrhoea in which questions concerning management are interposed at points in the workup where they would arise in practice. The questions and answers should enable the physicians to formulate a rational approach to the diagnosis and treatment of chronic diarrhoea.

Renault H see Ligny G

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Rider JA, Moeller HC, Gibbs JO, Gardey RH, Puletti EJ. The symptomatic treatment of chronic diarrhea. Curr Ther Res 1962 Feb;4:25-30

Riess H see Oertel H

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Robbio Troyano L, Lopez Lorenzo S, Seijo Hernandez JL, Duquesne Perez F. [Chronic diarrhea and polyparasitosis] Rev Cubana Med Trop 1982 Sep-Dec;34(3):341-5

Robles E see Trier JS

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Rodriguez A, Soto G, Torres S, Venegas G, Castillo-Duran C. Zinc and copper in hair and plasma of children with chronic diarrhea. Acta Paediatr Scand 1985 Sep;74(5):770-4

A study was carried out to evaluate the nutritional status in children with chronic diarrhoea with specific regard to levels of zinc and copper and to establish the relationship between these deficiencies in zinc and copper in the body and the degree of intestinal malabsorption. Nineteen children with chronic diarrhoea were studied. Jejunal biopsies showed severe villus atrophy in eight cases which showed evidence of malabsorption syndrome. Duration of clinical diarrhea was 10.8±6.5 and 12.9±8.3 months in patients with and without malabsorption respectively. Patients without malabsorption were harboring Giardia lamblia in 2 cases, G. lamblia and Ascaris lumbricoides in 5 and G. lamblia and Trichuris trichiura in 3. In both groups with chronic diarrhoea, plasma zinc levels were lower than those seen in the healthy control group. The hair zinc levels were also lower in both groups with diarrhoea. The plasma copper levels were similar in both groups, but were lower than that of both control groups ($p<0.01$). Hair copper level in the malnourished control group was also slightly lower. Significant depletion of zinc and copper was found in both groups with chronic diarrhoea. A positive correlation was found between plasma zinc levels and plasma carotene concentrations after carotene overload ($r=0.62$, $p<0.01$). There was a significant correlation between post-overload plasma carotene and hair copper levels. In this study, the relationship between zinc and copper deficiencies in intestinal malabsorption was clearly established. Chronic diarrhoea in children appeared to be accompanied by zinc and copper depletion, due to malabsorption, or in conjunction with a decrease in dietary intake.

Roenprayoon S see Manatsathit S

Rogers AI see Reisman T

Rogers WA, Stradley RP, Sherding RG, Powers J, Cole CR. Simultaneous evaluation of pancreatic exocrine function and intestinal absorptive function in dogs with chronic diarrhea. J Am Vet Med Assoc 1980 Dec 1;177(11):1128-31

The N-benzoyl-L-tyrosyl-p-aminobenzoic acid (BT-PABA):xylose test was evaluated

in 5 clinically normal dogs, 5 dogs with pancreatic exocrine insufficiency, and 7 dogs with intestinal malabsorption. A solution of BT-PABA (1 g/100 ml) and d-xylose (10 g/100 ml) was given orally (5 ml/kg of body weight) to dogs in each group. Plasma PABA curves were decreased in dogs with pancreatic exocrine insufficiency and intestinal malabsorption ($p<0.05$), but were the lowest in dogs with pancreatic exocrine insufficiency compared with clinically normal dogs. Xylose values in dogs with malabsorption were decreased ($p<0.05$), compared with clinically normal dogs. Dogs with pancreatic exocrine insufficiency had plasma xylose values that were intermediate to values in clinicaly normal dogs and dogs with intestinal malabsorption. Results of BT-PABA:xylose testing were compared with results of sodium PABA:xylose testing to determine whether decreased PABA values, obtained by the BT-PABA:xylose test, were caused by free PABA malabsorption or by maldigestion of BT-PABA. The sodium PABA:xylose test was performed in dogs from each group by oral administration of a solution (5 ml/kg) of sodium PABA (0.372 g/100 ml) and d-xylose (10.0 g/100 ml). Plasma PABA values, obtained by the sodium PABA:xylose test, were similar in each group. Thus, different PABA values, obtained by the BT-PABA:xylose test, were not caused by PABA malabsorption. Xylose values were similar to values obtained by the BT-PABA:xylose test. It is concluded that: (1) the BT-PABA:xylose test is a practical test for detecting maldigestion or malabsorption in the dog; (2) dogs with intestinal malabsorption may have functional pancreatic exocrine insufficiency; and (3) decreased plasma PABA values, obtained by BT-PABA:xylose testing, are not caused by malabsorption of free PABA. (Modified author's abstract)

Roggero P, Mangiaterra V, Mosca F, Ottredi ML, Perazzani M, Borzani M. [Ultrastructual morphological evaluation of the intestinal epithelium in subjects with gluten intolerance, giardiasis, chronic diarrhea and intestinal lymphangiectasil]. Minerva Pediatr 1982 Feb 28;34(4):161-8

Role of dietary fat in chronic non-specific diarrhoea in childhood. Nutr Rev 1980 Jul;38(7):240-2

Rollo JL see Ulshen MH

Romero M see Santoscoy G

Rosenberg IH, Solomons NW, Schneider RE. Malabsorption associated with diarrhea and intestinal infections. Am J Clin Nutr 1977 Aug;30(8):1248-53

An episode of diarrhoea causes weight loss and temporary cessation of growth in infants and children. Diarrhoea is accompanied by malabsorption of sugars, nitrogen, fats, and micronutrients. This review article examines the regularities with which diarrhoeal diseases of different etiologies produce malabsorption, and the possible mechanisms whereby infectious diarrhoea may produce a transient, but significant malabsorption syndrome. Also discussed are possible nutritional implications of malabsorption in diarrhoea. The nutritional costs of malabsorption may pose a major threat if diarrhoea becomes chronic or recurrent. The hydrogen breath test for carbohydrate malabsorption does not require intubation or blood drawing. This test can be used in children to help clarify the importance of carbohydrate intolerance in the duration and perpetuation of acute diarrhoea and intestinal bacterial overgrowth.

Rossi L see Innocenti P

Rossi TM, Lebenthal E. Pathogenic mechanisms of protracted diarrhea. Adv Pediatr 1983;30:595-633

Rothbaum RJ, Maur PR, Farrell MK. Serum alkaline phosphatase and zinc undernutrition in infants with chronic diarrhea. Am J Clin Nutr 1982 Mar;35(3):595-8

Ill infants and children need zinc replacement in total parenteral nutrition solutions, but assessment of these needs and total body zinc status is difficult. Seven infants with severe diarrhoea initially given 80 to 100 µg/kg.day of elemental zinc developed systemic zinc deficiency as indicated by an acrodermatitis-like skin rash and low serum alkaline phosphatase. Serum zinc levels were borderline low only in conjunction with hypoalbuminemia. Daily urinary zinc excretion was normal. With increased zinc supplementation of 200 to 300 µg/kg.day, the rash healed and serum alkaline phosphatase rose to normal levels for age. The activity of the metalloenzyme alkaline phosphatase accurately reflects total body zinc status in infants. With diarrhoeal illness, infants need high dose zinc supplementation to replace considerable stool losses. (Author's abstract)

Rowe B see Challacombe DN

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Ruppin H, Kachel G. [Chronic diarrhea: etiopathogenesis, diagnosis and therapy]. Med Monatsschr Pharm 1984 May;7(5):133-41

Ruppin H, Domschke W. [Chronic diarrhea. New aspects of diagnosis and therapy]. Fortschr Med 1981 Oct 15;99(39):1583-8

Sabir M see Akhter MH

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Salomon H. Salt free diet in acute and chronic diarrhea. Indian Med Gaz 1939;74:268-70

Sampayo RR, Meroni RJ, Marquez LA. [A non-milk food lacking gluten, lactose and saccharose for the treatment and diagnosis of some chronic diarrheas in childhood]. Arch Argent Pediatr 1965;63:418-21

Sanders DY, Sinal SH, Morrison L. Chronic salmonellosis in infancy. Clin Pediatr 1974 Aug;13(8):640-3

The cases of 3 infants (age: 8 weeks, 3 weeks and 13 days), who presented with

chronic diarrhoea associated with Salmonella group C infections, have been reported from the USA. Salmonella was found in the blood culture of the first infant, in both blood and stool culture of the second infant, and in the stool culture of the third infant. One mother had positive stool culture for Salmonella, while another had serum agglutinins to Salmonella group C somatic antigen in a titer of 1:160. All 3 mothers gave a history of mild diarrhoea during late pregnancy. It was, therefore, most likely that all 3 infants were infected from maternal sources. The infants were successfully treated with intravenous ampicillin. It is recommended that the possibility of chronic salmonellosis should be included in the differential diagnosis of infants with chronic diarrhoea and failure to thrive even if signs of infection are obscure. As the organism may be excreted intermittently, repeated stool cultures may be needed to establish the diagnosis. Appropriate antibiotic therapy alongwith hydration and general supportive care can be beneficial in young infants with persistent symptoms of Salmonella-associated gastroenteritis.

Sanghavi NG see Shah CP

Santoscoy G, Grannell J, Romero M. Treatment of chronic diarrhea with amoxicillin. J Infect Dis 1974 Jun;129(Suppl):S228-30

The efficacy of amoxicillin in the treatment of chronic bacterial diarrhoea was studied in patients of two low-socioeconomic groups at Guadalajara, Mexico, among whom chronic diarrhoea was endemic. Fifty-seven patients (36 females), aged 6 months to 72 years, were treated for a four-day period. The dose regimens were: 25-50 mg/kg.day for children aged under 2, 125 mg every 8 h for children aged 2 to 5, 250 mg every 8 h for children aged above 5, and 250-500 mg every 8 h for the adults. Fifty-five (96%) patients were asymptomatic within 72 h, and 36 (70%) within 48 h. Stool cultures were negative in 49 and positive in four. Four patients, all cleared of symptoms within 48 h, failed to appear for stool culture analysis. Thus, the medication was effective in 92% of the patients evaluated microbiologically. Two patients with septicemia due to Escherichia coli and two with Citrobacter infections were not cured. In one very severe Shigella infection, 1,500 mg of amoxicillin was given every 6 h, and the patient was cured clinically and microbiologically without incident. There was no side-effect attributable to the medication.

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Sarin LR, Mehta SR, Agarwal RG, et al. Aetiology of chronic diarrhoea. J Indian Med Assoc 1967 Mar 16;48:266-8

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Satjadibrata K see Soeparto P

Saulsbury FT, Winkelstein JA, Yolken RH. Chronic rotavirus infection in immunodeficiency. J Pediatr 1980 Jul;97(1):61-5

To investigate the role of rotavirus as a cause of diarrhoea in immunodeficient children, the characteristics of rotavirus infection in 23 children, aged 4 months to 18 years with a variety of primary immunodeficiency diseases, were

studied in the USA. Control subjects consisted of 46 healthy children with acute gastroenteritis, aged under 3, and 39 normal children without gastrointestinal symptoms, aged 6 months to 16 years. Stools and sera were tested for rotavirus using the enzyme-linked immunosorbent assay and enzyme-linked fluorescent assay respectively. Four immunodeficient patients had diarrhoea during the study period, and all had rotavirus infection; rotavirus was not detected in the stools of the 19 asymptomatic immunodeficient patients nor was it found in 39 asymptomatic control children, while 22 of the 46 control subjects with diarrhoea had rotavirus infection. One immunodeficient patient with X-linked gammaglobulinemia and one with severe combined immunodeficiency had chronic, symptomatic rotavirus infection with prolonged diarrhoea and fecal excretion of rotavirus for over 6 weeks. The other two immunodeficient patients had acute, self-limited gastroenteritis with disappearance of rotavirus within 12 days. Eight control infants with rotavirus infection eliminated the virus from their stools in periods ranging from 2 to 12 days. Rotavirus antigen was detected in the sera of 3 of the 4 immunodeficient patients. None of the 14 control infants tested had rotavirus antigen in their sera. The results suggest that chronic rotavirus infection may account for some instances of chronic diarrhoea in the immunodeficient patient, and that antibody contributes significantly to the host's defense against rotavirus.

Savilahti E, Simell O. Chronic non-specific diarrhoea. Arch Dis Child 1985 May;60(5):452-6

Recurrent, unexplained diarrhoea is a common intestinal complaint in children, aged 6 months to 3 years. Twenty-seven children, aged under 3 with unexplained, intermittent diarrhoea, were followed up until the age of 5 in Helsinki, Finland. Their diarrhoea began at the mean age of 9 months (range 4 to 16 months) and was resolved in 21 children by 3 years of age. Seventeen family members, out of 75 in 13 families, reported prolonged gastrointestinal symptoms. Twelve children had had infantile colic before the onset of diarrhoea. Fifteen children were given antibiotics as treatment for otitis media. In 6 patients, diarrhoea was caused by food allergy (allergy to fresh vegetables and cow's milk). Episodes of diarrhoea persisted in 4 of these 6. Twenty-one children had unexplained diarrhoea, which resolved in 19. Nutritional deficiencies were rare: only one child had iron deficiency. All the children had had 2 or more episodes of diarrhoea without fever lasting from 2 days to 2 weeks. There was a significant ($p<0.001$) reduction in relative weights between ages 1 and 2 years. At 5 years of age, 6 patients continued to have episodes of diarrhoea, and abdominal pains, headaches, and atopy which occurred more commonly in them than in the general population. They had a lower relative weight (mean (SD) 6.3 (7.6)%) than patients without diarrhoea (mean (SD) 3.5 (7.5)%). It is suggested that there are 2 major subgroups among children with recurrent diarrhoea - children with food allergy and those who react to environmental stresses with a variety of somatic symptoms.

Savini P see Ciampolini M

Saxena S see Sareen D

Sazanova NE, Vernacheva LN, Beier LV, Pyrikova IA. [Diagnosis of the chronic diarrhea syndrome in young infants and preschoolers]. Pediatria 1985 Jun;(6):40-2

Schiller LR see Fordtran JS

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Schjonsby H see Kittang E

Schmidt BJ see Eichenberger JR

Schmueli A see Weizman Z

Schneider RE see Rosenberg IH

Schoutens-Serruys E see Adler M

Schretlen ED see Sengers RC

Schroder S see Galambos JT

Schuermans V see Verhaegen H

Schwartz HJ see Weiss KJ

Schwarz RP, Ulshen MH. Pseudomembranous colitis presenting as mild, chronic diarrhea in childhood. J Pediatr Gastroenterol Nutr 1983;2(3):570-3

Two female children, aged 11 months and 8 years, were admitted to the North Carolina Memorial Hospital, USA, with mild, chronic diarrhoeal illness. Sigmoidoscopic and histologic findings revealed typical pseudomembranous colitis in both cases, which responded to therapy. The 11-month-old girl received 0.5 g of cholestyramine therapy four times a day and total parenteral nutrition, while the 8-year-old girl was treated with 250 mg of vancomycin four times daily. While variation in the severity of pseudomembranous colitis is recognized, the subtle, chronic presentation exemplified by these cases has not previously been well described. It is suggested that for patients with chronic diarrhoea, even when mild, the presence of fecal leukocytes calls for sigmoidoscopy or colonoscopy to look for the typical findings of pseudomembranous colitis. If present, specific therapy could then be initiated.

Scuro LA see Gasbarrini G

Seijo Hernandez JL see Robbio Troyano L

Selroos O see Pettersson T

Sengers RC, Stadhouders AM, Jaspar HH, Schretlen ED, van Munster RJ. Chronic mild diarrhoea, stunted growth and neuromuscular abnormalities. Eur J Pediatr 1978 Mar 13;127(3):211-7

Sensirivatana R see Poovorawan P

Shah BR see Shah CP

Shah CP, Shah BR, Sanghavi NG, Shah NB. Malabsorption in chronic diarrhoea. Indian Practioner 1972 Dec;25(2):537-41

The etiological pattern of chronic diarrhoea was prospectively studied with

particular reference to malnutrition. Eighty patients, hospitalized at Baroda, India with diarrhoea for more than 6 weeks, were examined. Eighteen (22%) patients had primary malabsorption, 16 (20%) had intestinal tuberculosis, and 7 had nutritional diarrhoea with normal absorption. Etiology was obscure in 9 patients. In 67 (84%), there was overall malnutrition, in 59% clinical avitaminosis, and in 53% hypoalbuminemia. Thirteen had malabsorption associated with other diseases, e.g. intestinal tuberculosis (8), diabetes mellitus (2), ulcerative colitis (1), ankylostomiasis (1), and thyrotoxicosis (1). Seven patients had an evidence of clinical and biochemical malnutrition without malabsorption, and they responded well to vitamin B complex, iron and protein therapy. In such cases, their illness was termed as nutritional diarrhoea. It was found that the deficiency of vitamins, iron, protein, and folic acid is more common than that of calcium, phosphorus, potassium and B_{12} deficiencies in chronic diarrhoea.

Shah NB see Shah CP

Shah SN see Kotwal MR

Shamsuddin M see Alam MN

Shann F. Metronidazole for chronic diarrhoea in children. Papua New Guinea Med J 1979 Dec;22(4):98-100

Shapiro BG. Chronic diarrhea caused by bread intolerance. S Afr Med J 1962 Sep 29;36:818-21

Shee CD, Pounder RE. Loperamide, diphenoxylate, and codeine phosphate in chronic diarrhoea. Br Med J 1980 Feb 23;280(6213):524

The antidiarrhoeal activity of loperamide, diphenoxylate, and codeine phosphate was examined in an outpatient trial involving 11 patients with chronic diarrhoea in the UK. The patients received four successive courses of treatment, each lasting a fortnight. The treatment was double-blind and given in a predetermined random order. The results showed that for treating chronic diarrhoea, codeine phosphate (30 mg) was equivalent to loperamide (2 mg) or diphenoxylate (5 mg). All 3 drugs were well tolerated, and no serious side-effect was reported. It is suggested that, if there is no hazard of addiction or accidental overdosage, codeine phosphate may be the drug of choice, being cheap as well.

Shepherd R see Larcher VF

Sherding RG see Rogers WA

Shi BP, Shi YM, Lin LY, Bu HD. The radiation of the He-Ne laser on acupoints in treatment of infantile chronic diarrhea in 93 cases. J Tradit Chin Med 1985 Jun;5(2):89-91

Shi YM see Shi BP

Shiner M see Maffei HVL

Shmerling DH, Pancaldi R. Differential diagnosis of malabsorption syndrome and chronic diarrhea in infants and children. Schweiz Rundschau Med 1981;70(42): 3-8

Shmerling DH see Goriup U

Shwachman H, Filler RM, Khaw K-T. A new method of treating malnourished infants with severe chronic diarrhoea. Acta Paediatr Scand 1970;59:446-7

A newly devised technique of total parenteral nutrition was used in the treatment of 5 infants, aged 56 to 150 days with severe malnutrition secondary to chronic diarrhoea. The infants failed to respond to the usual medical measures, including intravenous therapy. These infants had a similar history of onset of diarrhoea and vomiting shortly after birth, inability to tolerate formula, no fever except for 1 patient with a diagnosis of otitis media. Laboratory tests performed gave a variety of negative results. Oral feedings were instituted gradually, first with clear solutions and the initial formula given was a special preparation, which was composed of glucose, M.C.T., casein hydrolysate, starch, plus vitamins and minerals. Serial intestinal biopsies were performed in 4 infants. At the beginning of the special therapy on 3 infants and on several subsequent occasions, histologic changes were noted in all cases with grade 2 to 3 villus atrophy. There was also a reduction in activity of lactase, maltase and sucrase. This secondary deficiency persisted in 3 patients, and in case 5, the intestinal mucosa and the disaccharides returned to normal when tested 3 months after the institution of therapy. Clinical improvement in all cases was remarkable.

Shwachman H see Clarke JT

Sibthorpe G. Chronic diarrhoea due to Strongyloides stercoralis. Med J Aust 1961 Oct 7;48(2):599

Sidhu JK see Walia BNS

Simell O see Savilahti E

Simhon A see Mata L

Sinal SH see Sanders DY

Sinatra FR see Thomas DW

Sithicharoenchai P see Manatsathit S

Sivokhina IK, Mamedova LD. [Dietotherapy in chronic enteritis and colitis in a hospital]. Vopr Pitan 1982 Jul-Aug;(4):73-4

Sjodahl R see Djarv L

Skyring AP see Gallagher ND

Smalley JR, Klish WJ, Brown MR, Campbell MA. Chronic diarrhea associated with Campylobacter. Clin Pediatr 1982;21(4):220

This is a report of a 20-month-old Caucasian child with chronic diarrhoea of many months' duration, from whose stools Campylobacter was isolated. She had 1 to 5 stools per day which were watery and voluminous. Stool culture grew Campylobacter fetus, and she was treated with oral erythromycin (200 mg twice a day) for 7 days. Her diarrhoea resolved, and after 9 months when examined again she reported of having no further diarrhoea. The patient demonstrated

that chronic diarrhoea can be secondary to Campylobacter infections. Although, in general, an infectious cause of chronic diarrhoea in childhood is unlikely, it is suggested that the stools from such children be examined for Campylobacter.

Smalley JR, Klish WJ, Campbell MA, Brown MR. Use of psyllium in the management of chronic diarrhea of childhood. J Pediatr Gastroenterol Nutr 1982;1(3):361-3

To evaluate the response of patients with chronic nonspecific childhood diarrhoea to psyllium bulk agents and to assess the role of diets in its treatment, 23 children, aged 11 to 31 months with the clinical diagnosis of chronic nonspecific diarrhoea, were studied in New York, USA. In these children, all other etiologies of chronic diarrhoea had been ruled out. The children were treated first with an unrestricted diet, including milk for 1 week, and if no response was seen, they were then treated with psyllium bulk agents (1 tablespoon twice a day) for 2 weeks. Twenty (87%) patients responded to this therapy. Seven patients responded to an unrestricted diet only, and 13 responded to psyllium. Only 3 (13%) patients did not respond. Most children were on a restricted diet at presentation. However, only 6 of the 23 patients were actually on a low-dietary fat intake. Since only 2 of them responded to an increase of fat in the diet, it is suggested that low-dietary fat intake has no etiological role. Treatment with normalization of the diet and psyllium bulk agents seem to be an effective mode of therapy for chronic nonspecific childhood diarrhoea.

Smith A see Vessey M

Smith DH. Tropical diseases. 5. Chronic diarrhoea in the tropics including amoebiasis. Nurs Times 1968 Apr 19;64:527-30

Smith PD, Gillin FD, Spira WM, Nash TE. Chronic giardiasis: studies on drug sensitivity, toxin production, and host immune response. Gastroenterology 1982 Oct;83(4):797-803

A 27-year-old white American patient with persistent symptomatic giardiasis for 2½ years, despite seven separate courses of either quinacrine or metronidazole, was cured by combined quinacrine and metronidazole therapy. To investigate the mechanism of the patient's diarrhoea and his response to this infection, Giardia lamblia was isolated and cultured for the following examination: (a) parasite drug sensitivity; (b) possible enterotoxin production by the parasite; and (c) the patient's humoral and cellular immune responses to the organism. The patient's organism was not more resistant than 3 other isolates as measured by inhibitory and lethal concentration indices. This suggests that chronicity of his infection was not due to the organism having unique properties of drug resistance. The organism was more sensitive to combined quinacrine and metronidazole than to either drug alone. Therefore, combined quinacrine and metronidazole should be tried in patients in whom infection persists after at least one course of each drug administered separately. G. lamblia trophozoites did not produce enterotoxin, capable of stimulating water and electrolyte secretion. The patient produced intestinal immunoglobulin A. In addition, circulating immunoglobulin G anti-G. lamblia antibodies were present during his prolonged infection. His lymphocyte response to a crude extract of G. lamblia suggests that the antigen recognition phase of his cellular immune response was intact. Peripheral blood mononuclear cells from the patient exhibited reduced cytotoxicity for G. lamblia in vitro.

This may have contributed to the persistence of the patient's infection, and it should be suspected in other patients with chronic giardiasis.

Socha J, Dobrzanska A, Rowecka K, Cichy W, Bierla J, Stodulski J, Wozniewicz B. Chronic diarrhea due to VIPoma in two children. J Pediatr Gastroenterol Nutr 1984 Jan;3(1):143-8

This paper describes vasoactive intestinal polypeptide-secreting tumors (VIPoma) in two boys. In case 1, a 7-year-old boy, who had chronic diarrhoea and hypokalemia for 6 years, was studied. His stool volumes ranged from 105 to 1,500 g with daily frequency from one/two to several. Na and K concentrations in stool ranged from 136.2 mEq/l (Na) and 84 mEq/l (K) to very low ones, e.g. 1.11 mEq/l (Na) and 3.12 mEq/l (K). At the age of 3, he had dextral nephrolithiasis for which he was treated surgically. Corticosteroids gave a transient remission. During the last 2 years of the patient, his condition was relatively balanced with a high-potassium diet and potassium supplementation. Following his death, a postmortem examination revealed a left adrenal gland tumor, 4 cm in diameter. The tumor appeared with hemorrhagic foci at the section. Microscopically ganglioneuroma was shown. In case 2, a patient with a milder course of disease was reported. The volume of his stool ranged from 50 to 600 g with one/two to six bowel movements in 24 h. High levels of VIP in serum suggest that diarrhoea was due to VIPoma as in case 1. A large left adrenal mass was shown by computed tomography. The tumor was removed by surgery which was 4x4 cm in size. Ganglioneuroma was shown. After surgery, the patient's potassium level returned to normal, watery diarrhoea caused and noradrenaline level had also decreased. Post-operative serum VIP concentration was 5 pmol/l. For 2 years, the patient has been progressing well. Serial serum VIP measurements may be useful as a diagnostic test as well as for monitoring the effects of therapy and for predicting the appearance of tumors.

Socha J see Dobrzanska A

Socha J see Kulesza E

Soeparto P, Noerasid H, Satjadibrata K. Carbohydrate intolerance in infants with chronic recurrent diarrhea. Paediatr Indones 1977 May-Jun;17:153-60

Forty-eight infants, aged 1 month to 2 years with chronic recurrent diarrhoea, were examined for sugar intolerance in Indonesia. Intolerance to lactose was found in 14 patients (29.2%), while one of them had intolerance to glucose as well. Positive stool cultures were obtained from 14 patients. Enteropathogenic Escherichia coli was encountered most frequently, followed by Salmonella and Pseudomonas. Many of the lactose-intolerant patients, whose stool cultures were negative, showed an increased number of leukocytes in their stools, suggesting some form of enteric infection. In severe diarrhoeal diseases, there may be a cycle of upper small bowel infection, impaired carbohydrate absorption, and bacterial catabolism of the unabsorbed sugars leading to diarrhoea, and a further proliferation of bacteria in the intestines. To break the vicious cycle, lactose intolerance is one of the factors to be considered in treating patients with chronic diarrhoea.

Soeparto P, Subijanto MS, Noerasid H. Prolonged diarrhoea following acute gastroenteritis. Paediatr Indones 1982 May-Jun;22(5-6):83-8

Eighty-four children, most aged under 1 with prolonged diarrhoea (continuing

for more than 7 days), were studied for stool pathogens, as well as fat and sugar malabsorption. The illnesses' clinical courses were also evaluated. In most cases, the diarrhoea lasted 10-25 days. Of the infants, 53.6% excreted intestinal pathogens: Escherichia coli (31%), Salmonella sp. (17.9%), Staphylococcus aureus (10.7%), and E. coli aggl neg. (1.2%). Lactose intolerance and gross fat malabsorption accounted, respectively, for 5% and 41.7% of infants with prolonged diarrhoea.

Soeparto P, Giri IW. Small bowel morphology in chronic infantile diarrhoea. Paediatr Indones 1982 Sep-Oct;22(9-10):195-9

Soeparto P see Sutjiningsih

Solomons NW see Rosenberg IH

Sonta-Jakimczy KD see Maszewaka-Kurniarz K

Sood D see Bhan MK

Soothill JF see Candy DCA

Soper RT see Ghishan FK

Sorenson RM see Osterholm MT

Soto G see Rodriguez A

Sperotto G see Carrazza FR

Spiers AL see Furnell JR

Spika JS see Osterholm MT

Spira WM see Smith PD

Srivastava AC see Agarwal VK

Stadhouders AM see Sengers RC

Stanescu M see Popescu V

Stauffer JQ, Levine WL. Chronic diarrhea related to Endolimax nana response to treatment with metronidazole. Am J Dig Dis 1974 Jan;19(1):59-63

Two cases of chronic diarrhoea related to infestation with Endolimax nana are reported from the USA. Both the patients were male; one was aged 48 and the other 19. They are orally treated with metronidazole (250 mg) three times a day for 10 days. Both cases showed a favorable response to metronidazole therapy. The second case, however, had a relapse of diarrhoea a week after his initial improvement. The relapse was associated with reappearance of the E. nana cysts and required a second course of therapy with metronidazole before the cysts were entirely eliminated from his stools. It is suggested that this ameba may occasionally cause diarrhoea in man, and treatment of the symptomatic individual is warranted when other causes of diarrhoea have been excluded.

Stinzing G see Bhan MK

Stocchi F. [Clinical diagnosis of chronic diarrhea]. Policlinico 1971 Apr 1;78:288-97

Stodulski J see Dobrzanska A

Stodulski J see Socha J

Stone DE see Gracey M

Stradley RP see Rogers WA

Strickland GT see Butler T

Strobel CT see Ackerman NB, Jr.

Stroop S see Parker P

Stufano N see Gasbarrini G

Subijanto MS see Soeparto

Suharjono see Sunoto

Sullivan P see Bujanover Y

Sundaravalli N see Premchander KV

Sunoto, Suharjono, Mangiwa J, et al. Lactose intolerance in chronic diarrhea among Indonesian children. Paediatr Indones 1971 Sep-Oct;11(5):1-6

Suthutvoravut U, Tontisirin K, Varavithya W, Valyasevi A, Bjorck I, Dahlqvist A. Wheat extract and milk mixture as a milk substitute for children with milk intolerance. J Diarrhoeal Dis Res 1984 Sep;2(3):168-72

A mixture of milk with wheat extract and oil known to provide a low-lactose and high-energy formula, was evaluated for its efficacy in 28 malnourished patients, aged 3-18 months, who had diarrhoea of 3-30 days' duration. The patients were assigned alternately in equal numbers into the study and control groups. The experimental formula was a mixture of wheat extract, powdered whole milk and corn oil, while the control diet was an infant formula. The lactose contents of the experimental and control formulae were, respectively, 1.1 and 7.2 per 100 ml. Both formulae had equal amounts of fat, and almost identical amounts of carbohydrates and protein. After rehydration with intravenous or oral electrolyte solutions for 12-24 h, patients were fed full-strength experimental formula (20 kcal/oz) or diluted infant formula (10 kcal/oz). The concentration of infant formula was increased gradually to 20 kcal/oz, according to clinical response determined by daily weight, and stool frequency and consistency. Eleven of the 14 patients in the study group and 10 of 14 in the control group recovered completely from diarrhoea. The mean duration of diarrhoea after treatment was 3.2 days for the study group and 5.3 days for the controls ($p<0.01$). Daily energy intake was higher in the study group ($p<0.001$). The results suggest that wheat extract, mixed with whole milk and vegetable oil, is beneficial as a milk substitute in the management of chronic diarrhoea in children with milk intolerance.

Sutjiningsih, Soeparto P, Salim H, Hardjadinata D, Djupri L. Cow's milk

protein-sensitive enteropathy (CMPSE) in infant with chronic diarrhea. Paediatr Indones 1982 Jan-Feb;22(1-2):23-31

Cow's milk protein-sensitive enteropathy is recognized as a significant cause of chronic infantile diarrhoea. Six cases of cow's milk protein-sensitive enteropathy as diagnosed by biopsy studies, combined with clinical symptoms admitted to the Paediatric Ward of Dr Soetomo Hospital, Surabaya, Indonesia, were studied. All infants were aged between 2 months and 1 year and had suffered from chronic diarrhoea for two weeks or more before admission, five of whom developed failure to thrive. The infants tolerated Progestimil, a protein hydrolysate. On challenge with cow's milk formula 3 to 4 weeks later, three developed transient diarrhoea. Small bowel biopsy, taken 3 to 4 weeks after a cow's milk-free diet, showed either a normal or mildly abnormal mucosa, but subsequent biopsies, taken 48 h after the reintroduction of a cow's milk formula, showed increased mucosal damage in all 6 infants. No pathogenic microorganism was isolated from the infants' stools. Stool examinations for ova and parasites were also negative. After a lactose challenge, lactose intolerance was not found among these infants. The present series indicates the cow's milk protein-sensitive enteropathy occurs in Indonesia.

Sutphen JL, Grand RJ, Flores A, Chang TW, Bartlett JG. Chronic diarrhea associated with Clostridium difficile in children. Am J Dis Child 1983 Mar;137 (3):275-8

The role of Clostridium difficile toxin in chronic noncolitic diarrhoea was examined in a series of infants and young children repeatedly exposed to antibiotics. The cases were derived from a retrospective review of a referral clinic population in Boston, USA. C. difficile toxin was associated with chronic diarrhoea without classic symptoms of colitis in seven children aged 7 weeks to 7 years. All patients had received antibiotics. In 2 patients, the onset of diarrhoea occurred during the antibiotic therapy; in 5, it occurred from 2 days to 1 month after therapy. Six of the seven patients treated with vancomycin hydrochloride showed improvement. After treatment, 4 patients suffered relapses, and three required further therapy. One patient had four relapses. During all clinical relapses, toxin reappeared in the stool, the recovery being associated with its disappearance. Sixteen family contacts were examined, nine (56%) of whose stools showed positive cultures. The results document C. difficile as a probable cause of chronic diarrhoea in childhood and emphasize its infectious potential. The data suggest that children, like adults, may exhibit a spectrum of disease ranging from obvious colitis to a mild chronic diarrhoea.

Suwanakul P see Manatsathit S

Swicowa K, Szczurowna M, Filipowicz-Ulewicz J, Zamojski G, Zoltowska A, Jaskiewicz K. [Problems of the etiology and pathogenesis of chronic diarrheal syndromes in infants]. Pediatr Pol 1982 Nov;57(11):897-902

Swicowa K, Szczurowna M, Ulewics-Filipowicz J, Zamojski G. (Treatment of chronic diarrhea syndromes in infants). Pediatr Pol 1983 Mar;58(3):271-5

Symes Gracia I see Ortega G'omez H

Szabo AJ see Cameron DG

Szabo I see Varkonyi A

Szczurowna M see Swicowa K

Tacconi L see Businco L

Takanashi T, Katoh T, Takeda H, Tokuoka T, Hamamoto H, Kitamura K. The absorption of digitoxin in patients with acute and chronic diarrhea. Jpn Circ J 1978 Jul;42(7):849-53

Takeda H see Takanashi T

Tandon BN, Tandon HD, Prakash O. A study of chronic colonic diarrhoea and dysentery. I. Clinical, endoscopic and coprological study. Indian J Med Res 1966 Jul;54(7):623-8

The prevalence of chronic colonic diarrhoea and dysentery, and the relative frequency in irritable colon syndrome, nonspecific diarrhoeal colitis, ulcerative colitis, amebic colitis and bacterial colitis, were examined at the gastroenterology clinic of the All-India Institute of Medical Sciences Hospital at New Delhi, India. Various laboratory aids and their uses in the diagnosis of these colonic disorders were also assessed. The incidence of colonic disorders presenting as chronic diarrhoea and dysentery was 15.8% of all the gastroenterological problems recorded at the clinic during the 1.5-year study period. Nonspecific condition accounted for 86.5% of the cases, which included irritable colon syndrome (25.4%), nonspecific diarrhoeal colitis (24.8%), and nonspecific ulcerative colitis (26.3%). Only 13.5% of the cases had specific colitis comprising of amebic infestation in 11.4%, Shigella flexneri infection in 1.6% and mixed amebic and bacillary infection in 0.5% of the patients. A rather low incidence of amebic and bacillary forms of colitis recorded in this work may be due to the selective type of urban population investigated at the clinic. The results emphasize that nonspecific colonic disorders are frequent causes of bowel disturbance in North India, and all the cases need not be indiscriminately treated with repeated courses of antibacterial and antiamebic drugs. The limitations of the clinical picture, sigmoidoscopic examination, and barium enema studies for providing definitive labels to the colonic disorders make coprological investigation of great diagnostic importance. The plan for a specific diagnosis of amebic colitis has been outlined.

Tandon BN see Tandon HD

Tandon BN see Walia BNS

Tandon HD, Prakash O, Tandon BN. A study of chronic colonic diarrhoea and dysentery. II. Rectal biopsy study. Indian J Med Res 1966 Jul;54(7):629-35

Rectal biopsy study was used in patients with several types of colonic diarrhoeal and dysenteric disorders to assess the utility of this method as a guide to etiologic diagnosis and treatment and to study the correlation of histopathological changes with disease severity. One hundred and fifteen patients, representing classic ulcerative colitis, milder forms of ulcerative colitis, nonspecific diarrhoea colitis and irritable bowel syndrome, were studied in India. The biopsies in the classic ulcerative colitis group showed histopathological changes which correlated well with the clinical severity and sigmoidoscopic findings. Where present, the ulcer bed was covered with a thick fibrino-purulent inflammatory exudate. The crypts were markedly irregular in size, shape, orientation and spacing. Cryptitis or crypt abscesses were seen

in 23 of the 39 cases. The biopsies in milder ulcerative colitis showed a range of pathologic changes from near normal to those of confirmed ulcerative colitis. There was a distinct increase in cellularity of the lamina propria. Eosinophils were seen in significantly large numbers. Cryptitis and crypt abscesses were seen in 8 of the 25 cases. Some increase in the cellularity of lamina propria was common in specific colitis. The inflammatory cells included a large number of polymorphs. The changes were much milder in nonspecific diarrhoeal colitis and mildest in irritable bowel syndrome. It was difficult to identify precise boundaries between normal and abnormal rectal mucosa. A personal experience of studying normal rectal biopsies is, therefore, considered essential. Crypt abscess is not considered to be of primary significance in causing lesions in ulcerative colitis, although a secondary role in extension of the lesions cannot be denied. Despite a considerable overlap of changes seen in a variety of patients, the rectal biopsy may still be a useful adjunct to the diagnosis of diarrhoeal and dysenteric disorders. It is also considered valuable in predicting the future clinical course and prognosis, and in a follow-up of treatment in such cases.

Tandon HD see Tandon BN

Tappe JP see Cook RA

Terslev E see Ingomar CJ

Thaler MM see Bujanover Y

Thomas DW, Sinatra FR, Merritt RJ. Random fecal alpha-1-antitrypsin concentration in children with gastrointestinal disease. Gastroenterology 1981 Apr;80(4):776-82

To compare random fecal alpha-1-antitrypsin concentrations in normal subjects with those of children with various gastrointestinal illnesses, 115 subjects (59 males) were evaluated at a hospital in California, USA. The subjects included 39 controls, and patients with chronic inflammatory bowel disease (20), chronic diarrhoea (18), acute gastroenteritis (17), allergic gastroenteropathy (5), chronic pancreatic exocrine insufficiency (4), acute gastrointestinal bleeding (4), nonspecific colitis (4), celiac disease (3), and intestinal lymphangiectasia (1). Mean fecal alpha-1-antitrypsin for the controls was 0.98±0.17 mg/g lyophilized stool. All children with celiac disease, allergic gastroenteropathy, lymphangiectasia, nonspecific colitis, acute gastrointestinal bleeding, and 19 of the 20 patients with active chronic inflammatory bowel disease had fecal alpha-1-antitrypsin concentrations >2.6 mg/g dry stool (mean of the controls ±2 SD). These disorders have all been previously documented to cause protein-losing enteropathy by ^{51}Cr-labeled albumin excretion tests. Gross or occult blood was observed only in those subjects with colitis or isolated gastrointestinal bleeding. The other study patients had normal fecal alpha-1-antitrypsin excretion when compared with controls. Serial fecal antitrypsin concentrations paralleled disease activity and clinical response to therapy. A weak statistical correlation was observed between fecal alpha-1-antitrypsin and serum albumin values (n=63, r=0.40, and p=0.05). However, 24% of the patients with high fecal alpha-1-antitrypsin concentration was not hypoalbuminemic, indicating that hepatic secretory protein synthesis can compensate for mild degrees of excessive enteric protein loss. It is concluded that determination of random fecal alpha-1-antitrypsin concentration may be a convenient and reproducible method for screening in

various gastrointestinal mucosal disorders associated with abnormal transmucosal serum protein loss.

Thompson R see Cooper BT

Thornton AA, Burkinshaw JH, Kawerau E. Chronic diarrhea relieved by lactose-free diet. Proc R Soc Med 1962 Nov;55:979-81

Tijtgat GN, Meuwissen SG, Huibregtse K. Loperamide in the symptomatic control of chronic diarrhoea; double-blind placebo-controlled study. Ann Clin Res 1975 Oct;7(5):325-30

Fifteen patients (6 men and 9 women; age range 20-66 years) with persistent diarrhoea of varying etiology were selected for an open trial of loperamide (2 mg capsules). The optimal daily dose for substantial reduction of the diarrhoea ranged from two to seven capsules. Eleven patients showed a significant improvement in stool consistency, a highly significant decrease in stool frequency, and a decrease of abdominal cramps. One ileostomy patient with abundant ileostomy output and intermittent leaking of the ileostomy appliance at night experienced a substantial reduction of the stoma output with virtual disappearance of soiling accidents at night. Loperamide appeared to be ineffective in two patients with cholerrheic diarrhoea, in one patient with laxative-induced diarrhoea and in one patient with probable nervous diarrhoea. The 11 successfully treated patients then entered a double-blind placebo-controlled trial for 10 days or until relapse, the daily dose being identical to the optimal one previously determined in the open phase of the study. The drug was well tolerated. Because of its considerable efficacy and low side-effect liability, loperamide has to be considered a promising drug in the treatment of chronic diarrhoea. (Modified author's abstract)

Tokuoka T see Takanashi T

Tomas M see Ferrer Calvete J

Tomkins A. Nutritional status and severity of diarrhoea among pre-school children in rural Nigeria. Lancet 1981 Apr 18;1(8225):860-2

The influence of pre-existing malnutrition in the severity of diarrhoea was investigated by assessing the attack rate and duration of diarrhoea in 343 children, aged 6 to 32 months at the beginning of the rainy season in a northern Nigerian village. There were 1.4 attacks of diarrhoea per child during the rainy season. The frequency of diarrhoea had not increased in underweight (<75% weight/age) or stunted (<90% height/age) children, but those who were wasted (<80% weight/height) experienced 47% more episodes of diarrhoea than those who were not wasted ($p<0.02$). The 343 children as a group spent 10.5% of the time with diarrhoea during the 3-month rainy season. Diarrhoea lasted 33% longer in those who were underweight compared with those well-nourished ($p<0.01$), and 37% longer in the stunted compared with well-nourished children ($p<0.01$). The most striking effect was the 79% increase in the duration of diarrhoea in those who were wasted compared with the well-nourished ($p<0.001$). The results showed that nutritional status related more to duration of diarrhoea than to the number of attacks, and emphasize that the wasted child is particularly at risk of more frequent and protracted episodes of diarrhoea.

Tontisirin K see Suthutvoravut U

Torres S see Rodriguez A

Tournier C see Claude R

Tovar JW see Campana AO

Townley RRW. The management of chronic or recurrent diarrhoea in childhood. Postgrad Med J 1969 Feb;45:135-46

Based on the experiences with patients of predominantly Caucasian stock drawn from communities with good living standards living in a temperate climate, an approach to the management of childhood diarrhoea is outlined. Since the causes of diarrhoea are so diverse, a comprehensive clinical history is always required, but certain aspects of the history need to be given special attention. The patient's growth progress deserves careful scrutiny. During clinical examination, special attention should be given to the patient's abdomen, and the clinician should inspect one or more of the patient's stools. When the clinical features are sufficiently characteristic of a disease entity to allow a confident provisional diagnosis, then the investigatory procedures that will most definitively confirm that diagnosis should be carried out without delay. Tests, such as microscopy, hematology, stool culture, tests for stool-reducing substances, and stool pH have been recommended. More complex investigatory procedures, including the tests for intestinal absorption, radiological tests, small intestinal biopsy, the sweat test and pancreatic enzyme estimations, have also been discussed. The diagnosis and treatment of some of the clinical syndromes that may cause diarrhoea have been outlined.

Trier JS, Moxey PC, Schimmel EM, Robles E. Chronic intestinal coccidiosis in man: intestinal morphology and response to treatment. Gastroenterology 1974 Aug;66(5):923-35

This report describes chronic intestinal coccidiosis in man and response to treatment. A 58-year-old male with chronic diarrhoea was admitted to Boston Veteran Administration Hospital in the USA in 1963. He described episodic diarrhoea of more than 20 years when first evaluated 7 years before his diagnosis was documented. He had diarrhoea, fever, eosinophila, malabsorption, and weight loss. A severe mucosal lesion of the small intestine, characterized by shortened villi, hypertrophied crypts, and infiltration of the lamina propria and round cell, was associated with the intestinal coccidial infestation. The intracellular stages of both the asexual and sexual cycles of Isospora belli were observed with an electron microscope. The mechanism by which the invading parasite produces mucosal lesion is not clear. Observations suggest that therapy with pyrimethamine and sulfadiazine was associated with prompt disappearance of coccidial infestations and gradual reversion of mucosal histology to normal. The patient remained asymptomatic without evidence of intestinal coccidial reinfestation for 3 years. Similar treatment is recommended for other patients with intestinal coccidiosis.

Tripp JH see Candy DCA

Troupel S see Ligny G

Truchot R see Levrat M

Tucker VL, Wilmore D, Kaiser CJ, Lauer RM. Chronic diarrhea and alkalosis. Pediatrics 1964 Nov;34(6):601-8

The case of a 13-month-old Caucasian male infant, hospitalized in Kansas, USA with severe diarrhoea and alkalosis which started in the first month of life, is reported. Three balance studies were carried out on the infant. The patient excreted frequent, profuse, watery stools containing large quantities of chloride, sodium, and potassium. The urine was quite hypotonic. The second part of the first balance study demonstrated the water-electrolyte changes, which occurred as the child was rehydrated with parenteral fluids containing approximately 5 mEq of KCl and 7 mEq of NaCl per kg of body weight per day. Sufficient amounts of electrolytes were also provided in the diet. Thus, the body electrolyte and water could be maintained in a physiological range. This, however, did not affect the volume, frequency, or content of the stools. The patient was considered similar to the 2 cases of congenital alkalosis with diarrhoea described earlier. An investigation of causes of the patient's metabolic abnormality was attempted. Exploratory laparatomy failed to demonstrate an anatomical lesion. The only findings were dilated terminal ileum and nonspecific hyperplasia of mesenteric lymph nodes. No abnormal endocrinopathy could be demonstrated. In one of the three lactose tolerance tests, the patient failed to hydrolyze lactose. The absence of lactase activity in the duodenum was confirmed by a peroral duodenal biopsy. Such transient lactose deficiency in association with chronic or acute diarrhoea usually resolves when the underlying problem is corrected. It was, therefore, considered unlikely that the inability to hydrolyze lactose was the intrinsic defect in this child.

Tumen HJ. Differential diagnosis of chronic diarrhea. J Einstein Med Cent 1964 Apr;12:92-7

Twycross RG see Brey OA

Tytgat GN, Huibregtse K, Meuwissen SG. Loperamide in chronic diarrhea and after ileostomy: a placebo-controlled double-blind cross-over study. Arch Chir Neerl 1976;28(1):13-20

The constipating effect of loperamide was evaluated in patients with chronic diarrhoea of various origins, and in patients with total colonic resections and permanent ileostomy. Loperamide (2-mg capsule) was given to 15 patients, aged 20 to 66 years with long-standing chronic diarrhoea of varying etiology in the Netherlands. The optimum daily dose for substantial reduction of diarrhoea ranged from 2 to 7 capsules. Loperamide was successful in controlling diarrhoea in 11 of the 15 patients. In the successfully treated patients, a statistically significant amelioration of stool consistency ($p<0.05$) and stool frequency ($p<0.01$), and a trend towards a lessening of abdominal cramps ($p<0.1$) were found. Loperamide failed in 2 patients with cholera-like diarrhoea, 1 with laxative-induced diarrhoea, and 1 with diarrhoea of unknown etiology. The 11 successfully treated patients then entered a double-blind placebo-controlled trial for 10 days or until relapse, the daily dose being identical to the optimal dose determined in the open phase. The investigator was able to assess the code correctly in 10 of the 11 patients ($p<0.01$). Loperamide was well tolerated, and only one patient complained of nausea and vomiting during the double-blind trial. Twenty ileostomy patients, aged 25 to 73 years, volunteered for the evaluation of the inhibitory activity of loperamide on small intestinal peristalsis in a double-blind placebo-controlled crossover study. Daily fecal outputs were significantly lower ($p<0.001$), and the median daily ileostomy output decreased by 22% in the loperamide period, as compared with the drug-free study phase. Sixteen of the 20 patients guessed the code correctly, while 4 were uncertain, although their fecal weights were lower with

loperamide. Two patients spontaneously reported an increased urinary production during loperamide, while most of the others did so upon questioning. Many patients experienced an improvement in their ileostomy care and soiling accidents. Because of the effectiveness, low side-effects and lack of toxicity of loperamide, the drug has been considered promising in the symptomatic treatment of chronic diarrhoea, and advantageous in the care of ileostomy.

Ulshen MH, Rollo JL. Pathogenesis of Escherichia coli gastroenteritis in man - another mechanism. N Engl J Med 1980 Jan 10;302(2):99-101

The case of a 7-week-old female infant, hospitalized in North Carolina, USA with chronic diarrhoea and Escherichia coli overgrowth in the small intestine, is reported. The patient's diarrhoea persisted despite total parenteral nutrition. Aerobic and anaerobic cultures of the duodenal aspirates, collected after 2 weeks, grew only E. coli sensitive to both gentamicin and colistin. Assays for E. coli heat-labile toxin, heat-stable toxin and invasiveness were negative. On light microscopy, the villi were moderately blunted, and there was crypt hypertrophy. Electron microscopy of the duodenal mucosa showed regions of normal mucosa interrupted by mucosa with adherent organisms, consistent with Gram-negative bacilli. The adherent organisms displaced the microvilli, although the subjacent terminal web appeared normal. Disaccharidase activity was low in all enzymes studied (lactase, sucrase, maltase, and palatinase). Rectal biopsy showed an unremarkable surface epithelium, except that necrotic granulocytes were noted in some of the crypts. The lamina propria was broadened and contained an inflammtory infiltrate similar to that in the jejunum. The infant was given oral colistin (15 mg/kg.day). Five days latter, diarrhoeal stools with occult blood persisted, with evidence of a diffuse enteritis. Treatment with a 10-day course of intravenous gentamicin (7 mg/kg.day) was successful. The results suggest that the pathogenic mechanism of the illness produced by this E. coli was unlike those previously described in man.

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Varkonyi A, Boda M, Szabo I. The importance of cow's milk protein intolerance in chronic diarrhoea of children. Acta Paediatr Hung 1983;24(2):169-74

Thirty-five cases (16 males) with cow's milk protein intolerance were studied during a 5-year-period in Szeged, Hungary. The diagnosis was based on the regression of clinical symptoms after elimination of cow's milk from the diet and their recurrence after milk challenge. Milk challenge was usually done twice with 5 to 10 ml/kg of pasteurized cow's milk. The most common symptoms were diarrhoea, failure to thrive, and vomiting. Intestinal biopsy was carried out in 28 patients; three patients were re-biopsied after milk challenge. Partial villus atrophy was observed in 2 of these 3 patients. In the third case, scanning electron microscopy disclosed cellular edema and microvillus destruction. It is concluded that cow's milk protein intolerance is a transitory illness limited to a certain age. Its diagnosis is an everyday problem which rests on the history, the clinical symptoms and on the response to a cow's milk challenge after a cow's milk-free diet is given for a certain period. Intestinal biopsy is justifiable only if exclusion of celiac disease is necessary for a correct diagnosis.

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The effectiveness of loperamide in the treatment of acute, subacute and chronic diarrhoeas of various etiologies has been studied by many workers, but it is

questionable whether, in addition to rehydration, alongwith the maintenance of electrolyte balance and dietary treatment, a pharmacological adjunct is really necessary. An anti-peristalic agent or water-absorbent therapy may be dangerous by masking water losses into the bowel. A further argument against the use of loperamide is that it may induce ileus in children. In the Children's Hospital of the Free University in Berlin, a one-year-old patient, who was given a single therapeutic dose (0.045 mg/kg) of loperamide, had a paralytic ileus with stool retention for 7 days. On the fifth day, surgery had to be considered. Less severe symptoms were seen after an overdose (1.4 mg/kg) in another patient, aged 17 months. Loperamide previously was recommended by the manufacturers for use in children without any age limit; since 1977, it has been recommended for use in those aged over 2 in Germany.

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Walia BNS, Gupte SP, Mehta S, Aggarwal KC. Chronic diarrhoea in North Indian children. Indian J Med Res 1971 Sep;59(9):1448-53

To assess the role of etiological factors in causing chronic diarrhoea in infancy and childhood, 200 patients, aged under 14, were studied in India. The investigations included microscopic examination of stool, stool culture, daily fecal fat excretion, D-xylose test, sweat chloride estimation, and pre-oral jejunal biopsy. Sigmoidoscopy and lactose tolerance tests were performed when indicated. Giardia intestinalis was recovered from the stools of 26% cases and Entamoeba histolytica from 4.5%. Various helminths, such as Ascaris lumbricoides, Ankylostoma duodenale, Trichuris trichiura, and Strongyloides stercoralis, were isolated from the stools of 14% of the patients. Bacterial pathogens were encountered in 8% of the total cases of chronic diarrhoea. Chronic diarrhoea was associated with steatorrhea in 31.5% cases. The prominent causes were celiac disease (18.5%), cystic fibrosis (6.5%), and endemic tropical sprue (3%). Seven cases of steatorrhea could not be classified by their cause. In 11.5% cases, the exact cause of diarrhoea could not be established. It is recommended that a detailed history of illness and a thorough microscopic examination be carried out to provide useful clues to exclude the infective group and suspect the presence of steatorrhea. The next step is a 3-day stool fat excretion study.

Walia BNS, Sidhu JK, Tandon BN, Ghai OP. Etiology of chronic diarrhoea in north Indian children. J Trop Med Hyg 1967 Dec;70(12):303-6

To determine the relative incidence of various etiological factors responsible for producing chronic diarrhoea in North Indian children, 95 consecutive unselected patients, aged under 14, were investigated. Eighty percent of the patients had diarrhoea of more than 3 months' duration and 60% had been ailing for more than 1 year. Infections and infestations were responsible for producing chronic diarrhoea in 56.9% of the patients. Giardiasis alone was found in 32 of them, and steatorrhea was detected in 10 of these 32 (34%). The children with giardiasis were successfully treated with mepacrine, 100 to 300 mg daily for seven days. There were 3 cases of amebiasis which responded to specific anti-amoebic treatment. Pathogenic bacteria were found in 9 patients. These included pathogenic Escherichia coli (3 patients), Shigella sp. (2), Citrobacteria (3), and Pseudomonas pyocyaneus (1). All these 9 cases responded to specific antibacterial therapy. Steatorrhea was responsible for chronic diarrhoea in 25 patients. The fecal fat excretion ranged from 7.9 g to 43 g per day. In the miscellaneous group, ulcerative colitis was found in one

patient, while the cause of diarrhoea remained undetermined in 15. All had severe growth failure, weight loss, wasting, and anemia. Their diet was grossly inadequate with regard to protein and caloric intake. Their diarrhoea was controlled with the introduction of a diet rich in protein and calories content.

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Eighteen infants with severe prolonged diarrhoea were fed successfully by continuous drip enteral feedings with an elemental diet. The mean weight gain was 6.4±0.7 g/kg.day, using a solution containing up to 87 kcal/dl at volumes up to 260 ml/kg.day. No cardiovascular or metabolic abnormalities occurred. Advantages of the continuous drip regimen were demonstrated by an adaptation phase with a plateau or even a decline in body weight in 12 patients, with weaning from continuous periodic feedings without changing the total caloric or volume intake. Continuous drip feeding provides an alternative for total parenteral nutrition in patients with severe prolonged diarrhoea and intolerance to even an elemental diet given as periodic feedings. (Author's abstract)

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Yakubu AM, Sathiakumar N. Chronic diarrhoea in Nigerian children. J Diarrhoeal Dis Res 1985 Sep;3(3):145-8

To study the etiology of chronic childhood diarrhoea among Nigerian children, 142 patients, aged 6 months to 5 years with diarrhoea for at least one month, were evaluated. Enteropathogenic agents were identified in stools of 90 (63%) patients. Giardia lamblia and Entamoeba histolytica were most commonly detected, representing 41 and 23% respectively of all parasitic pathogens. In 4 children with negative stool microscopy, chronic diarrhoea was associated with primary lactose intolerance in two, and with abdominal tuberculosis in two. During the period of treatment, 13 (9%) of the study children died. These results indicate that early detection and treatment of amebiasis and giardiasis is a useful approach in the treatment of chronic diarrhoea among children.

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