A cute gastroenteritis still continues to be a major health problem throughout the world. In particular, there is a significant morbidity and mortality in the lower socio-economic groups, the third world, including Asia and India.

In the poorer and developing countries up to 15% of children die from gastroenteritis before their third birthday. *(Levine and Edelman 1979).*

World-wide it is estimated that five to eight million children die annually from gastroenteritis.

In South Africa gastroenteritis remains a major cause of death in the deprived population groups. In addition the disease presents a major nosocomial problem as too often, one has seen a well child admitted to hospital for a minor surgical procedure only to fall foul of a hospital acquired gastroenteritis.

The major cause of gastroenteritis remains bacterial in the Third World and viral in the industrialised world. The isolation of specific viruses and bacteria have done much to clarify some of the confusion surrounding the etiology of gastroenteritis.

In particular the elucidation of the various pathogenic mechanisms has helped in establishing a more rational approach to the management of the disease.

The major viral causes of gastroenteritis include Rotavirus, Norwalk agent, Astrovirus, Adenovirus. Others include Coronavirus, Mini Reovirus, Calcivirus, ECHO virus and Coxsackie. The importance of other viruses is still being assessed.

The major bacterial organisms include E.Coli, Shigella, Salmonella, Campylobacter, Yersinia and Cholera. Others include Proteus, Staphylococcus, Cl. perfringens, Cl. dificile. Cl. perfringens is probably the cause of the true food poisoning.

In addition there are a host of non-infective and parasitic causes of diarrhoea which fall outside the scope of this discussion.

The one myth I would like to dispel at the outset is the association of teething and diarrhoea. The only thing that is acquired from teething is teeth. Teething does not cause temperatures, loose tummies, runny noses or any of the myriad of symptoms which have so often been ascribed to this normal physiological phenomenon.

Pathophysiology of infective diarrhoea

Of the major advances in understanding diarrhoea, the mechanisms of fluid and electrolyte loss are the most significant. There are two basic mechanisms causing diarrhoea.

Bacterial adhesion and Enterotoxin production. As late as 1960 it was demonstrated that organisms innoculated into the small intestine were rapidly removed by peristalsis. By adhering to the mucous membrane with pili, E.Coli and other organisms have been able to over-

come this important host defence mechanism.

After adherence, these bacteria produce an enterotoxin which on contact with the mucosa causes a net secretion of water and electrolytes culminating in diarrhoea, electrolyte imbalance and dehydration. There is no mucosal damage.

The normal epithelium in the small bowel can both actively absorb and secrete water and electrolytes.

Secretions may be increased by increasing cyclic AMP either by stimulating intestinal adenyl cyclase by enterotoxin, prostaglandin, or vaso intestinal peptide, or by inhibiting cyclic AMP phosphodiesterase with theophyllin. Secretions may be decreased by using prostaglandin inhibitors such as indomethacin or aspirin.

Thus, the presence of enterotoxin causes an increase in intracelullar concentration of cyclic AMP resulting in a net outflow of sodium chloride and water.

Bacterial Invasion and Cytotoxin Production. This toxin causes damage in the distal small bowel and large intestine. There may be associated invasion of the submucosa by organisms such as shigella and salmonella with resultant mucosal destruction and dysentery type stools.

Diarrhoea is thought to be due to an increased synthesis of prostaglandins which in turn causes an increased secretion of sodium chloride and water.

A third mechanism applicable to some enteropathogenic E. Coli (EPEC) is that of close mucosal adherence without invasive or enterotoxic properties. The enteropathogenic strains of E.Coli are thought to produce disease by this mechanism. This is important since it may well be associated with prolonged diarrhoea.

The role of viruses in Acute Infective Enteritis

Viral enteritis is the most common form of gastroenteritis and accounts for approximately 80% of cases in Western countries. Of these rotavirus is the most common pathogen. The disease is more prevalent in the cooler months and most commonly affects children between the ages of six months and two years.

After an incubation period of 24 - 48 hours, the disease usually manifests with fever, vomiting and diarrhoea. Rotavirus infections may be associated with upper respiratory signs and symptoms and the accompanying diarrhoea may cause isotonic dehydration.

The virus is stable making for easy cross infection. Rotavirus infection may be common in the newborn period (in some series) although it may not be associated with clinical disease.

Whilst breast feeding is important in the prevention of gastroenteritis in babies,

VIRAL ENTERITIS

80% of cases in West

Rotavirus most common pathogen

Disease - children 6-24 months
- short incubation period
- upper respiratory symptoms
- diarrhoea

Mechanism - destruction of small bowel epithelium
- loss of absorptive surface
- non cyclic AMP mediated

disease patterns in neonatal rotavirus infections appear to be unrelated to the type of feed. The virus destroys small bowel epithelium resulting in a loss of absorptive surface and blunted villi. Disaccharidase production is diminished.

The mechanism of diarrhoea is therefore one of fluid and electrolyte malabsorption and is not related to the cyclic AMP mechanism. Lactose intolerance is a frequent accompaniment.

The role of E.Coli in Diarrhoea

E. Coli has been subdivided into three groups depending on the mechanism of disease production.

Enteropathogenic (EPEC). In diarrhoea due to EPEC there is a proliferation of the

Acute   infective

gastroenteritis

by Dr R. Heitner
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organism in the duodenum and upper ileum i.e. in portions of the bowel normally free of pathogenic bacteria. There is mucosal adherence and toxin production.

Enteroinvasive. The organisms cause diarrhoea indistinguishable from bacillary dysentery. Epithelial invasion is the major pathological process and toxins are involved.

Enterotoxigenic (ETEC). ETEC produces one or both of a heat stable or heat labile toxin. Both these toxins cause diarrhoea by stimulation of the adenyl cyclase system. ETEC strains have both adhesive and colonisation properties which render the organism extremely virulent.

Except for the enteroinvasive forms of the disease, E.Coli causes diarrhoea by infecting the small bowel and producing various toxins. Although the organism can be cultured from rectal swabs, its nature cannot be identified by routine techniques as these are done usually only in research laboratories. It may also be present in a carrier state in the large bowel. The presence of EPEC does not necessarily incriminate the organism as the aetiological factor.

Campylobacter Enteritis

Campylobacters are curved Gram negative rods. C.fetus is associated with acute enteritis and as with other intestinal pathogens, infections with Campylobacter do not always produce symptoms.

The disease is usually a self limiting one and has an average incubation period of three to five days.

The diarrhoea is preceded by a prodrome of fever, malaise, myalgia and colicky abdominal pain. Stools are liquid, foul smelling and may be bloody or bile stained. Diarrhoea is produced by mucosal invasion with occasional strains exhibiting an enterotoxin.

Campylobacter infections are common in black children in South Africa. Poultry and dogs are important sources. They also appear to have become the most common gastroentestinal pathogen in the United Kingdom.

Therapy of Acute Gastroenteritis

The therapy of acute gastroenteritis has been somewhat confused, mainly due to the lack of understanding of the pathogenesis of the disease. It is important to remember that gastroenteritis is a self limiting disease and that as fluid and electrolyte disturbances are the main features of the disease therapy should be primarily aimed at their correction.

Fluid and Electrolyte Replacement. In the majority of cases adequate amounts of fluid may be administered orally. Irrespective of the mechanisms of the diarrhoea a glucose electrolyte solution will be absorbed from the upper small bowel.

Glucose does not require brush border enzymes or energy for its absorption. Sodium molecules "ride piggy back" on glucose molecules thereby bypassing the cyclic AMP mechanism.

Recent work has shown that sucrose may also be used. There are numerous commercially available glucose electrolyte solutions but in emergency situations one can instruct mothers to prepare such solutions by using a teaspoon of salt plus ten teaspoons of glucose to one litre of water giving a ½ normal saline solution in glucose. Small but frequent feeds of the solution should be given to the child working on the basis of at least: 150ml/kg/24 hours for a child under one year; 120ml/kg/24 hours for a child one to two years; 100ml/kg/24 hours for older children.

Profuse ongoing diarrhoea and/or intractable vomiting despite adequate fluid replacement are indications for hospitalisation and not for opium derivatives, diphenotylate, loperamide, or any other anticholinergic drug.

The role of antibiotics

The use of antibiotics is controversial and has been the subject of many trials with many anecdotal experiences being reported. Since the great majority of cases of gastroenteritis are viral there can be no benefit from the use of antibiotics. In fact there are potential hazards with the indiscriminate use of these drugs e.g. the administrations of such drugs may lull the practitioner into a false state of security and divert his attention from the main objective of therapy, that is fluid and electrolyte replacement.

The widespread use of such agents is probably the major cause in the emergence of antibiotic resistant bacteria.

The use of antibiotics may create carrier states.

What of the child in whom a specific bacterial organism has been isolated or is strongly suspected? Let us discuss some of these more common bacterial pathogens.

Salmonella. Excluding typhoid and paratyphoid fever, which are systemic illnesses, salmonella is a veritable pathogen that instills fear into the heart of many clinicians.

Salmonellae are organisms that are capable not only of attaching themselves to mucosal cells but also of penetrating the mucosa into the lamina propria.

Polymorphoneuclear leukocytes become activated and ingest these organisms. In systemic salmonellosis killing is however not always achieved and the organism may actually replicate within the phagocyte to be liberated at a distal site with the death of this cell.

There is no doubt that this form of invasive and systemic salmonellosis requires antimicrobrial therapy. Salmonella organisms also have the phenomenon of microbial persistance.

ANTIBIOTICS

Dangers
- false sense of security
- antibiotic resistance
- carrier states

SALMONELLA

organism invades
⬇
poly activation - ingestion
⬇
incomplete intracellular killing
⬇
poly migratien
⬇
organism's liberation
⬇
microbial persistance

In vitro, antibiotics may enter the polymorphoneuclear leucocyte but may only retard the growth of the organism and cause it to remain in a stationery phase. On withdrawal of the antibiotic, bacterial multiplication once again resumes. This phenomenon may account in part for the carrier states which persist after a bout of salmonella gastroenteritis.

Antibiotics have no effect on the duration of the illness and actually prolong the duration of positive stool cultures. A recent double blind trial in 44 children with salmonella enteritis using placebo, amoxicillin, or ampicillin showed that not only

do neither of these drugs provide any benefit to the patient with uncomplicated gastroenteritis but the use substantially increases the risk of bacteriologic or systemic relapse.

E.Coli. Most children with E.Coli diarrhoea will recover with prompt fluid and electrolyte therapy. Antibiotic therapy is seldom if ever needed. However as discussed previously some E. Coli do not fall into these traditional entero-invasive, enterotoxic or enteropathic groups of diarrhoea, but rather into the entero-adhesive mechanism. Under these circumstances appropriate antibiotic therapy is indicated.

ROLE OF E. COLI

A. Enteropathogenic (EPEC)

- Proliferation of organism in small bowel
- Mucosal adherence
- Toxin

B. Entero-invasive

- Epithelial invasion and toxin

C. Enterotoxigenic (ETEC)

- ETEC extremely virulent
- Toxins
- Cyclic AMP mediated

Shigella. The use of antibiotics in Shigellosis is also open ended, with opinion evenly divided. Antibiotics have been shown to be effective in reducing the duration of symptoms and also possibly shortening the period of post-infective carriage. In the majority of patients the disease is mild and self limited. There is also a high risk of transferrable antibiotic resistance.

These factors tend to mitigate against the use of antibiotics. In Shigellosis one would consider the use of antibiotics in the presence of severe disease. the drug of choice being ampicillin or trimethoprim and sulphamethoxazole should there be ampicillin resistance. There is no indication for oral non-absorbable antibiotics.

Campylobacter. Most patients with Campylobacter disease do well without antibiotics. In fact, by the time the laboratory report has been obtained, the need for antibiotic medication has, in most instances, passed. However, in severely ill patients erythromycin stereate is a convenient and safe form of therapy, but its efficacy is still in doubt.

Cholera. Cholera has become an epidemic disease in South Africa and should always be considered in the differential diagnosis of severe watery diarrhoea. It may present with catastrophic

diarrhoea and dehydration, convulsions and hypoglycaemia.

Fluid replacement is of paramount importance. The antibiotic of choice is tetracycline in a dose of 10 mgms/kg six hourly. Other antibiotics although not as efficacious include furazolidine and chloromycetin.

In summary therefore, there are very few indications for antibiotic therapy in gastroenteritis, i.e. S.Typhi and Paratyphi; Systemic Salmonellosis; Cholera; Immunologically compromised host such as the neonate, the child with malnutrition, the patient on immunotherapy; Extra-gastrointestinal sepsis - septicaemia, pneumonia; Severe Shigellosis; Prolonged E. Coli enteritis.

Maintenance of nutrition

Gastroenteritis is associated with impaired nutrition due to both large nitrogen losses in the stools and decreased food and calorie intake. The decreased intake is due to anorexia caused by the illness and to dietary restrictions imposed by the doctor.

Whilst in a well fed child this temporary disruption should not be of any great importance, in the malnourished child or the child who already has chronic diarrhoea a bout of acute gastroenteritis may be sufficient to precipitate the child into an acute state of kwashiorkor. It is important then to ensure that children with gastroenteritis are fed as soon as possible and that dietary restrictions are limited to as short a time as possible.

Lactose intolerance frequently complicates gastroenteritis especially that caused by rotavirus. These children will usually tolerate a lactose free formula early on and should remain on a lactose free diet for approximately a week. Lactose intolerance may usually be diagnosed at the bedside with a diagnostic stick.

A loose stool with a pH of less than 6 will strongly suggest carbohydrate intolerance. The diagnosis may be confirmed by testing the stool against Benedict's reagent which will show positive for reducing substances.

In children in whom diarrhoea has gone on for more than the usual few days, because of the vital factor of nutritional maintenance, Drs. Bowie, Mann and Hill in Cape Town created the "Cape Town Cocktail". This is composed of gentamycin given as 50mgs/kg/day in six divided doses orally for three days, metronidazole 100mgs, eight-hourly for five days, and cholestyramine 1 grm. six-hourly for five days. This cocktail coupled with dietary manipulation has radically shortened cases of prolonged acute diarrhoea, curtailed protein loss, and minimised hospital stay.

It is postulated that Cholestyramine acts

MAINTENANCE OF NUTRITION

1Gastro-enteritis is associated with impaired nutrition
a) Nitrogen losses in stools
b) Dimishes intake
c) Imposed dietary restrictions

Danger: Acute malnutrition!

DIETARY MANIPULATION

Lactose intolerance

Cape Town Cocktail-:

Gentamycin 50mg/kg/day (6 hourly x 3 days)

Metronidazole 100mg 8 hourly x 5 days

Cholestryamine 1gm 6 hourly x 5 days

by binding toxins and also free bile salts which have been deconjugated by the presence of bacteria in the small bowel. The role of the antibacterial agents is not completely clear.

Paralysing agents

One of the important protective mechanisms of the gut is peristalsis which by increasing transit time diminishes mucosal contact time with any pathogen. Drugs such as diphenoxylate-atropine and loperamide are potentially hazardous.

By slowing intestinal transit, intestinal colonisation by the pathogens may be encouraged with exacerbation of the disease. In shigellosis, particularly because the invasion of the intestinal tissue is important in the pathogenesis, prolongation of the contact time between the organism and epithelial cells by inhibition of peristalsis will promote increased mucosal penetration by bacteria and enhance the severity of the disease.

In addition these drugs may lead to the development of a megacolon — a recognised complication of shigellosis.

A study by Portnoy evaluated 80 children with gastroenteritis to assess the efficacy of diphenoxylate-atropine mixture, kaolin pectin alone or in combination. None of these agents had any effect on the frequency of bowel movement, weight of the faeces passed or the water content of the stools.

Finally, diphenoxylate-atropine is potentially a toxic substance. A month old white child, 4,650 kgs, developed gastroenteritis. She was seen by her doctor and 2,5ml of diphenoxylate-atropine was prescribed four–hourly. Two days later the patient developed choking spells and lethargy. The drug was discontinued for approximately 18 hours and restarted in the same dosage for ongoing diarrhoea.

Over the next two days the child became progressively more lethargic and difficult to arouse. She was finally admitted to hospital in a coma and respiratory failure.

Even with accidental overdose of relatively small amounts of the drug (six tablets for a two year old child) respiratory and cardiac arrest have occured. In this particular drug although the quantity of atropine per unit dose is small for adults, children will sometimes develop symptoms of atropinism. In children the line between therapeutic doses and potentially toxic doses is very narrow.

As a result of the reporting of numerous cases of poisoning, the American FDA has revised the literature in diphenoxylate-atropine and the drug is now contra-indicated in children under the age of two years. In addition, like digoxin, it is hoped to make this drug available in a bottle with a graduated dropper. These appear to be extreme measures for a drug which is not really indicated in gastroenteritis.

Binding agents

The time honoured kaolin and pectin mixtures have also come under review and it may come as a surprise that not only are they potentially dangerous, but they are totally ineffective. If one recalls the mechanisms of diarrhoea production it is obvious that these drugs play no role in diminishing intestinal secretions, Kaolin and pectin are adsorbant and binding agents.

When administered both the doctor and the parent may be lulled into a false sense of security at seeing some improvement by noting less frequent and possibly more well formed stools. This is false since the patient continues to pour fluid into his bowel lumen which is then sequestrated, and one may be faced with a severely dehydrated child whose mother quite correctly informs you that the child has not passed a single stool.

Cholestyramine has been used on its own or in combination with the "bowel cocktail". Unconjugated bile acids provoke increased secretions from both the small and large bowel. In patients with bacterial overgrowth in the terminal ileum particularly due to E.Coli there is both an increased rate of bile acid deconjugation and an impaired rate of bile salt reabsorption resulting in an increased amount of unconjugated bile in the colon. Neutralising these bile salts by binding them to cholestyramine has proved to be of some value.

The use of Aspirin and Indomethacin

In well controlled studies these drugs have been found to be of therapeutic value by inhibiting prostaglandin formation and inhibiting the formation of cyclic AMP, thereby diminishing intestinal secretions. On their own however, these drugs are not without significant side effects and until further studies have been done, their routine use in gastroenteritis is not recommended.

In summary, the therapy of gastroenteritis is now clear and may be divided into:

- The prevention of fluid loss and correction of fluid and electrolyte abnormalities.
- Antibiotic therapy in specific cases.
- Dietary manipulation and the maintenance of nutrition.
- The cessation of diarrhoea.

The indications for hospital admission are: persistent vomiting; inadequate fluid intake; dehydration; acidosis; the immunologically compromised host; the child with malnutrition or impending malnutrition.

Finally, I would like to end with a short poem by Professor Hendrickse of Liverpool who in these few words, says it all.

> *Babies who have D & V*
> *Shrivel and fail to wee*
> *When this happens, then we oughta*
> *Fill them up with salt and water.*
>
> *When they are shocked, they will only last*
> *If you give them plasma fast,*
> *After that you must proceed*
> *According to your patient's needs.*
>
> *If the salt is high and water low*
> *Keep your IV weak and slow*
> *Play it cool don't lose your wits*
> *For rushing things will bring on fits.*
>
> *But when the sodium is rather low*
> *That's the time to have a go*
> *With stronger stuff at greater speed*
> *To make up losses and daily needs.*

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