INFECTIVE DIARRHOEA

THESIS

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By

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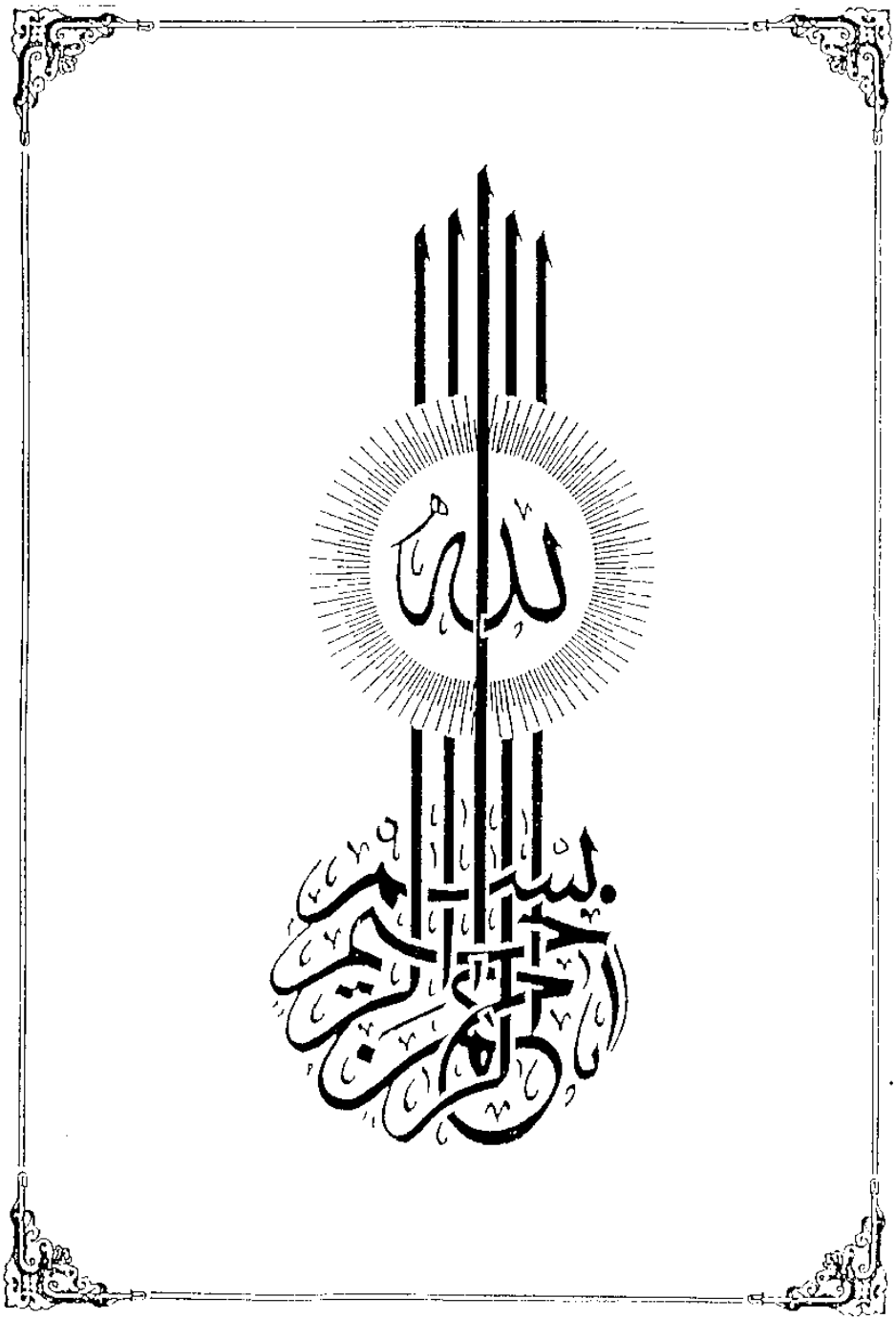

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INTRODUCTION

Acute diarrheal disease is a wide spread disease and is one of the most common problems throughout the world. It is one of the main causes of high morbidity and mortality rates in infants and children (Palmer et al., 1957). In nurseries and neonatal wards it occurs both sporadically and as epidemics that can be prolonged, with high morbidity and mortality (Boyer et al., 1975).

It is a disease characterized by diarrhea which may or may not be associated with passage of mucus and blood. Hippocrates distinguished diarrhea from dysentery by associating diarrhea with the frequent passage of liquid stools, and dysentery with the passage of bloody stools (Bradford et al., 1969).

In 1928 Fisher considered that bacteria played no role in the etiology of the disease. Hess (1930) wrote "it is my belief, that in most cases there is an underlying infection of the gastro-intestinal tract".

The role of bacteria in production of outbreaks of gastroenteritis has long been known (Topley and Wilson, 1966).

Viruses have also been isolated and transmitted during epidemics of diarrhea (Budding and Dodd, 1944).

A viral etiology for diarrhea was logically suspected when it was repeatedly demonstrated that in over one half of moderate or severe cases of acute diarrhea no bacterial pathogen could be incriminated (Cramblet and Siewers, 1965).

El-Diwany et al. (1960) showed that pathogenic bacteria could be isolated from only 12% of all diarrheal cases examined. Parasitic infestation has been incriminated. These cases are characterized by prolonged diarrhea (Valsov, 1966).

Increased numbers of normal bowel flora, particularly of Candida albicans, were reported to be present in the upper small intestine of adults and children with diarrhoea (Cohen et al., 1967).

The frequency of positive cultures for bacteria or viruses from the stools varies directly as the assiduity with which these organisms are looked for.

Positive bacterial cultures vary from 4 to 62 percent (Connor and Barrett-Connor, 1967). Similarly, rates of positive virus culture vary from none to as high as 31 percent,

the commoner viruses being Echo, poliovirus, coxsackie and the adenoviruses.

Gastro-enteritis is the biggest killer in the developing countries (Labib, 1972). It is necessary to stress that gastro-enteritis is a dangerous disease. The real incidence of the disease is difficult to assess, since in most countries only the severe cases are notified (Topley and Wilson, 1966). As a rule, the incidence of diarrhoea is inversely related to general hygienic standards, rather than to particular factors, such as the quality of the drinking water or the prevalence of flies (Zijl, 1966). Besides poor standards of personal and household hygiene, the most important predisposing factor is malnutrition which enhances both the susceptibility to, and the severity of the infantile gastro-enteritis (Cruickshank et al., 1975).

In our country, post natal deaths constitute 81% of infant mortality in Egypt, gastro-enteritis causes 55% of these deaths. The infant mortality rate in Egypt was found to be 92.3/1000 as compared with 1/1000 in U.S.A. and England (Labib, 1972). Gastro-enteritis is a disease of summer. The highest incidence occurs during summer (Labib, 1972).

Guinena (1972), reported a morbidity rate of gastro-enteritis in infants and children up to 53.3% in Egypt specially in June, July, August and September. In Egypt, 1972, Labib, reported that the highest incidence of gastro-enteritis occurs in the sixth to the ninth months after birth, where foreign food is introduced to the infant diet. Infection occurs much more frequently in artificially fed than in the wholly breast fed babies. The nutritional factors are responsible for most of the serious consequences of gastro-enteritis in infancy.

Prevension of infective diarrhoea is by improvements of water supplies and sanitation and the development of vaccines conferring long-lasting protection against the major enteric pathogens

Young children in developing countries have several episodes of diarrhoea each year (Mata, 1978; Kamath et al., 1969). Since these episodes are caused by a wide variety of bacterial, viral and parasitic agents (Black et al., 1980), identification of the types of diarrhoea that are most likely to result in death is vital for vaccine development.

The aim of vaccination against enteric pathogens is to substantially reduce diarrhoeal morbidity and mortality in

developing countries. The vaccine must be administered within the first 6 months of life.

Acute diarrheal disease an ubiquitous clinical syndrome of diverse and frequently unidentifiable etiology, presents with loose stools and often fever as the most common manifestations. While it may include specific infectious diseases such as cholera, shigellosis, salmonellosis, amebiasis, enteropathogenic Escherichia coli infections, or acute viral gastroenteritis, it also may be caused by other viruses or helminths or protozoa. A variety of other organisms of low pathogenicity also may be etiologically associated when present in large numbers, especially if there are modifying conditions such as poor nutrition, metabolic abnormalities, concurrent disease, or unaccustomed environmental stresses.

Recognition of specific enteritis may rest entirely upon clinical and epidemiological grounds because of the difficulty in identifying specific infectious agents, especially in developing areas where undifferentiated diarrheal disease is most prevalent, where multiple infections and concurrent disease are more common, and where facilities for clinical and laboratory differentiation are limited. Identification of the causative infectious agent(s) should be attempted whenever possible.

Viral gastroenteritis comprises at least two distinct entities with considerable clinical similarity, but distinct epidemiological differences.

Epidemic viral gastroenteritis tends to occur in community-wide outbreaks, sporadic viral gastroenteritis principally affects children in limited outbreaks. They are presented separately.

Epidemic viral gastroenteritis:

1. Identification:

Epidemic viral gastroenteritis is usually a self-limited mild disease which often occurs in outbreaks and which is characterized by a spectrum of clinical symptoms which may include nausea, vomiting, diarrhea, abdominal pain, malaise, low grade fever or a combination thereof. Clinical features usually last 24-48 hours.

The virus may be identified in preparations made from stools of ill individuals by immune electron microscopy. Serologic evidence of infection also may be demonstrated by immune electron microscopy, using a particle-positive stool filtrate as antigen.

2. Occurrence:

Probably world wide, occurs in outbreaks most often but may also occur sporadically.

3. Infectious agent:

The 27 nm particle, a parvovirus-like agent, has recently been suggested as the etiologic agent on the basis of immune electron microscopy.

4. Reservoir:

Man is the only known reservoir.

5. Mode of transmission:

Unknown, possibly by fecal-oral route.

6. Incubation period: 24-48 hours.

7. Period of communicability:

During acute stage of disease and possibly shortly thereafter also.

Sporadic viral gastroenteritis:

1. Identification: A sporadic severe gastroenteritis of infants and young children, characterized by diarrhea, with or without vomiting, patients usually febrile, has recently been associated with a reovirus-like 70 nm particle.

Deaths from acute gastroenteritis associated with the reovirus-like agent in this young age group have been reported occasionally. Milder forms of gastroenteritis due to this agent probably also occur, but most studies have dealt with hospitalized infants and young children. The virus is identified by electron microscopic examination of preparations made from stools from ill patients. Serologic evidence of infection can be demonstrated by the complement-fixation and/or indirect immunofluorescent techniques.

2. Occurrence: Probably world-wide, occurs sporadically, and also in outbreaks.

3. Infectious agent: The 70 nm reovirus-like agent (also designated arbivirus, rotavirus and duovirus) has been shown to be the etiologic agent of a large percentage of severe diarrhea of infants and young children.

4. Reservoir: Probably humans, role of animals unknown.

5. Mode of transmission: Unknown, possibly fecal-oral or fecal respiratory route(s).

6. Incubation period: Probably less than 48 hours.

7. Period of communicability: Maximum excretion of virus particles on 3rd. or 4th. day after onset of symptoms as determined by electron microscopy. The agent is rarely detectable after the 8th. day.

BACTERIAL AGENTS CAUSING DIARRHOEA

Clostridium Difficile

C. difficile is a gram-positive, obligate anaerobic rod. It was described as early as 1935 by Hall and O'Toole and was considered non-pathogenic for humans until recently (Bartlett & Larson, 1978).

C. difficile is difficult to isolate, therefore selective medium is used. The bacteria are very vulnerable on the strongly selective medium, and all suspected colonies had to be subcultivated on non-selective media as soon as possible. The characteristic odour of the bacterium is useful for the diagnosis.

C. difficile can be isolated from stools from 2% of healthy individuals (adults) (Nord & Heimdahl, 1979).

Investigations in recent years have showed that some antimicrobial agents given for certain period are commonly complicated by the occurrence of clostridium difficile diarrhea (Bartlett et al., 1979; George et al., 1980) and relatively high counts of toxigenic C. difficile are present in the feces of patients with C. difficile-induced diarrheal disease. Antimicrobial agents ppt. diarrhea and pseudomembranous enterocolitis (PMC) commonly due to different bacteria, e.g. staphylococcus spp., Pseudomonas spp., and Proteus spp. (Bartlett & Gorbach, 1977).

Recently (Larson et al. (1978) & Bartlett et al. (1978) suggested that in many cases, toxin producing clostridia can

cause PMC. Clostridium difficile has especially been associated with PMC (Bartlett et al., 1979).

C. difficile toxin has been detected in feces from 98% of patients with PMC and in 15% of patients with antibiotic-induced diarrhoea without signs of PMC (Bartlett et al., 1979).

The epidemiology of C. difficile-induced diarrheal disease is obscure. The nature of the alterations in the intestinal tract that predispose to overgrowth or acquisition of C. difficile and the source(s) from which C. difficile gains access to the bowel are unknown.

It is possible that the only important source of C. difficile is endogenous, in the gastrointestinal tract or other body site of some individuals, and that the organism proliferates when the normal milieu of the bowel is altered by antimicrobial therapy.

Alternatively, the major source for enteric infection with C. difficile may be exogenous.

Finally, it is conceivable that both endogenous and exogenous sources of C. difficile are important reservoirs.

Endogenous carriage of C. difficile has not been studied with highly selective culture media. C. difficile was isolated from the stools of 4 of 10 healthy infants is one study (Hall & O'Toole, 1935) and 10 of 22 healthy infants in another (Snyder, 1940). In detailed studies