Enteric Infection

MECHANISMS, MANIFESTATIONS AND MANAGEMENT

Edited by
M. J. G. Farthing

and

G. T. Keusch

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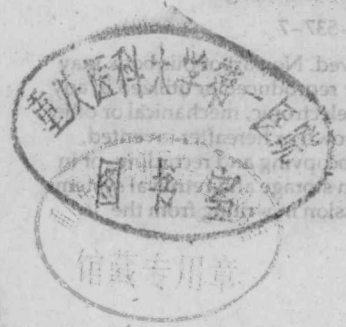

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Foreword

One of the greatest achievements of medicine during the past few decades has been the virtual conquest of cholera. As a result of the application of knowledge of intestinal transport of fluid and electrolytes, of fluid balance, of immunology and of the morphology of the gut in health and disease, an epidemic affliction which often had a high mortality has been reduced to manageable proportions. At the same time it has been increasingly recognized that intestinal infection is globally one of the most important conditions that affects mankind, particularly the young, in the harsh socio-economic conditions of the poorer nations of the earth.

In the laboratories of basic scientists, vitally important discoveries have been made on the relationship of glucose to electrolyte transport, on the significance of adenylate cyclase in fluid secretion by the gut, and on how toxins elaborated by bacteria may alter the normal function of the enterocyte. The use of modern techniques of molecular and cell biology has made it possible to identify and clone some of these toxins. In the future molecular fingerprinting seems likely to revolutionize both bacterial taxonomy and methods of diagnosis. In addition, hitherto unrecognized bacterial and viral pathogens have been isolated using modern techniques of electron microscopy and new methods of cultivation of bacteria in the laboratory have also played an important role in leading to advances.

Understanding of both humoural and cellular immunity, the result of intense laboratory investigation in recent decades, has greatly increased our understanding of how intestinal infection occurs, and biochemical studies of the complex substances which mediate the binding and attachment of a bacterium or virus to a gut cell have been of equal importance. Parasitic infection has also provided a fertile field for study, representing an important proportion of intestinal infection worldwide. Nor should epidemiological studies be forgotten since in attempting to combat gut infection in any community, it has proved essential to build up an important body of community based research.

These advances, which have involved basic scientists, epidemiologists, clinicians, microbiologists, health administrators and many others have taken place at a whirlwind pace which has often made it difficult for any individual to comprehend what has been happening in this important field of medicine, particularly those whose approach has been necessarily focused on one particular area of research or practice. There has therefore been an urgent need for experts to come together to create a synthesis of current knowledge, bringing

together the work of many different disciplines, so that individual scientists, clinicians and health workers may be enabled to obtain a comprehensive survey of the current scene. It is this synthesis that Michael Farthing and Gerald Keusch have so successfully achieved in this book.

Sir Christopher Booth
London, September 1988

Preface

During the past 20 years there has been a dramatic increase in clinical interest and scientific endeavour directed towards infectious diseases of the intestinal tract. These diseases have for centuries been one of the major causes of death in the developing world and key contributors to malnutrition and growth failure in infants and young children. Even with the potentially life-saving intervention of oral rehydration therapy for the early treatment of dehydration the prevalence of these organisms and diarrhoeal disease attack rates remain unchanged.

Many new intestinal microbial pathogens have been recognized during the last two decades, including *Campylobacter jejuni*, Enteroadherent *E. coli*, *Campylobacter pylori*, *Cryptosporidium* sp. and a variety of diarrhoea viruses such as rotavirus and enteric adenoviruses. Increase in foreign travel has highlighted the relevance of enteric pathogens for those living predominantly in the industrialized world, while AIDS has presented clinicians with a new spectrum of intestinal infectious diseases, many of which have devastating consequences for the sufferer. Thus, with the appearance of an abundance of new enteropathogens, the increasing diversity of the clinical impact of these infections together with the meteoric rise in the laboratory investigation of these organisms, it seemed timely to produce a book which brought together both the clinical and basic science aspects of microbial disease of the gut. We have not attempted to be encyclopaedic, but have concentrated on those pathogens about which there is important new information, irrespective of whether they are well known or newly described. The contributors to this volume are internationally known and experts in the field about which they write.

We hope that this mix of basic science and clinical medicine will make the volume useful to clinicians, particularly those working in the fields of infectious diseases and gastroenterology who may want to update their knowledge about the scientific underpinning of their specialty, to laboratory scientists who wish to broaden their perspective on the clinical aspects of intestinal infection, and to students of biology, medicine and microbiology.

MJGF
GTK
October 1988

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CHAPTER ONE

Global impact and patterns of intestinal infection

M. J. G. Farthing
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1.1 INTRODUCTION

Infectious diseases of the gastrointestinal tract continue to cause major problems throughout the world, especially in infants and children. They are of special concern in the developing nations where they have an unacceptably high morbidity and mortality. It has been estimated that there are at least 500 million episodes of diarrhoea each year resulting directly or indirectly in 5–10 million deaths in preschool children. Many of these deaths are directly due to dehydration, and therefore potentially preventable. In parts of the world where oral rehydration therapy has been successfully implemented mortality of children from acute diarrhoeal disease has fallen dramatically. We still have to face the reality, however, that the pathogens responsible for diarrhoea remain as entrenched as ever in these environments. Thus, oral rehydration therapy is only a treatment for established disease and not a cure or a measure to eradicate infections. To reduce the frequency of diarrhoeal disease, international health agencies, governments and health workers must continue to develop strategies to reduce the prevalence of enteropathogens in high-risk communities and to introduce measures to prevent or reduce access of these pathogens to their human hosts.

Infectious diseases are only one of the many conditions that afflict the human gastrointestinal tract but in terms of morbidity and mortality their importance greatly exceeds that of other common intestinal diseases including gastrointestinal malignancy, non-specific inflammatory bowel disease and other relatively uncommon malabsorptive conditions such as coeliac disease (Table 1.1).

1.2 CLINICAL PATTERNS OF GASTROINTESTINAL INFECTION

Infectious diarrhoeal disease has three major clinical presentations: (1) acute watery diarrhoea, (2) acute or chronic diarrhoea with blood (dysentery) and (3) chronic or protracted diarrhoea with or without intestinal malabsorption. It is important to distinguish these different types of presentation clinically, because there are important implications with regard to diagnosis and management. Some of the important pathogens responsible for these different types of infective diarrhoea are shown in Table 1.2.

As a clinical rule it is less critical to pursue a precise microbiological diagnosis in patients with acute watery diarrhoea than it is to classify the illness into the first of the three categories noted above. The vast majority of such

Table 1.1 World morbidity and mortality of some intestinal diseases

Disease	*Estimated morbidity (thousands/year)*	*Estimated mortality (thousands/year)*
Diarrhoeal disease	3 000 000–5 000 000	5000–10 000
Amoebiasis	1500	7–10
Schistosomiasis	20 000	600–1000
Colorectal cancer		500

Table 1.2 Patterns of Gastrointestinal infection

1. Acute watery diarrhoea	Enterotoxigenic *Escherichia coli*
	Vibrio cholerae
	non-cholera vibrios
	bacterial food poisoning (see Table 1.5)
	Rotavirus, Norwalk virus
	Cryptosporidium spp.
2. Dysentery	*Shigella* spp.
	Enteroinvasive *E. coli* (EIEC)
	Verotoxin-producing *E. coli* (VTEC)
	Salmonella spp.
	Campylobacter jejuni
	Entamoeba histolytica
3. Chronic diarrhoea/malabsorption	*Giardia lamblia*
	Strongyloides stercoralis
	tropical sprue
4. Anorectal symptoms	see Table 1.3
5. Dysphagia	*Candida albicans*
	Herpes simplex virus
	Cytomegalovirus
Dyspepsia	*Campylobacter pylori*

infections are self-limiting and require only supportive therapy in the form of oral or, in very severe cases, intravenous rehydration therapy. In a cholera-endemic area, however, it can be argued that a precise diagnosis should be made (and this is easily done by darkfield microscopy) since the duration of hospital stay and intravenous fluid requirements due to severe dehyration would be significantly diminished by the addition of oral antibiotics, to the treatment regimen. Similarly, patients receiving or who have recently completed a course of broad-spectrum antibiotics and who develop watery or bloody diarrhoea should be suspected of having *Clostridium difficile* infection, and the diagnosis pursued by faecal toxin assay and/or culture, for this would result in proper and prompt treatment with oral vancomycin or metronidazole. In patients with dysentery, however, one can make a strong case for attempting to make a clear diagnosis in each case (or at least attempt to exclude infective or inflammatory conditions that might require specific therapy) because the specific treatment is so different.

Most infections due to *Shigella sonnei*, *Salmonella enteritidis* spp., *Campylobacter jejuni*, *Yersinia enterocolitica*, enteroinvasive *Escherichia coli* serotypes and Verotoxin-producing *E. coli* are self-limiting conditions without antimicrobial therapy, but others, particularly due to *Shigella dysenteriae* 1 or *Entamoeba histolytica*,