Intra-Abdominal Infection

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Preface

Ancient man ventured regularly into the cranium, made quick excursions into the chest, but invariably shunned the abdomen. And with good reason. Of all the body spaces, the journey into the abdomen is fraught with potential calamity. The cranial and thoracic cavities not only are pristine to begin with but are more apt to remain in that condition when a surgical procedure is over. The difference with the abdomen, of course, is an abundant bacterial flora, confined by the gut until unleashed by disease or operation.

During the first 50 years of this century, progress in the management of intra-abdominal infection trudged forward slowly, and the annual death rate hovered unshakably at 40 per 100,000 population. Only in recent decades has the formidable natural course of an intra-abdominal infection been favorably altered.

Today, infection within the peritoneal cavity remains a medical and surgical nemesis, but there are portents that this situation is changing. The last five years have seen remarkable advances in our understanding of the epidemiology, pathogenesis, and microbiology of intra-abdominal sepsis.

In some aspects of patient management, technological applications, such as the new noninvasive tests, have outstripped our clinical experience. As a consequence, close collaboration between physician and surgeon is essential for diagnosis and treatment.

The time is appropriate, we believe, for a new text that assembles an up-to-date interdisciplinary compendium of the laboratory and clinical knowledge concerning intra-abdominal infections. This book is written with special attention to the needs of those who treat the patient with intra-abdominal infection—the internist, the family physician, and the surgeon, as well as the medical student. It emphasizes new information, particularly that which has emerged within the last five years, in such areas as bacteriology, diagnostic methodology, antimicrobial therapy, standards for prophylaxis, and surgical management. At all times we have striven to present practical solutions for the still very serious problem of intra-abdominal infection.

Samuel Eric Wilson
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Contents

Chapter 1

Microflora of the Gastrointestinal Tract

Sydney M. Finegold

Knowledge of the normal intestinal flora encountered at various levels of the gut, as well as of modifications of this flora in various disease states and in relation to surgery and antimicrobial therapy, is valuable in dealing with intraabdominal infection. The surgeon and physician can anticipate the probable infecting organisms before receiving the patient's specific bacteriologic culture results. Unless special anaerobic culture setups, such as an anaerobic chamber or the roll-tube procedure, are used, many delicate anaerobes from the normal flora will fail to grow or will yield lower counts than can be obtained with the better techniques. Because a number of recent studies have employed such techniques in delineating normal flora, we do have good information at the present time concerning the indigenous flora of the gastrointestinal tract.

NORMAL MICROFLORA AT VARIOUS LEVELS OF THE INTESTINAL TRACT

Stomach

Normally the stomach has fewer than 10^3 organisms per milliliter and, as a rule, no obligate anaerobes. There is a direct correlation between the number of organisms present in gastric contents and the pH of that material (Figure 1-1). At a very low pH, the stomach's contents are usually sterile. Patients with achlorhydria have counts of 10^5 to 10^7 bacteria per milliliter [1]. The sparse flora that is usually encountered consists of such mouth organisms as viridans streptococci, lactobacilli, and yeasts. When the stomach is sampled at operation, salivary organisms are not uncommon because anesthesia and premedication depress gastric secretion.

Small Bowel Microflora

The proximal small bowel seldom has counts exceeding 10^4 per milliliter; most often, it shows fewer than 100 organisms per milliliter or no organisms at all. The bacteria which are found are primarily transients from the mouth, chiefly viridans streptococci and lactobacilli. Members of the Enterobacteriaceae and *Bacteroides* may also be found, but in small numbers [1].

Toward the ileum, bacterial counts increase somewhat until, in the distal and terminal ileum, counts average 10^6 or 10^7 per milliliter. Lactobacilli and streptococci are more prominent here, but *Bacteroides* and Enterobacteriaceae occur more consistently and in higher counts. In the terminal ileum, there are approximately equal numbers of aerobic and anaerobic bacteria. The distribution of viable bacteria in the small bowel is depicted in Figure 1-2.

Colonic and Fecal Microflora

Although few studies have been made of the flora of the colon, it seems to be qualitatively similar to that of feces. Estimates of the total number of

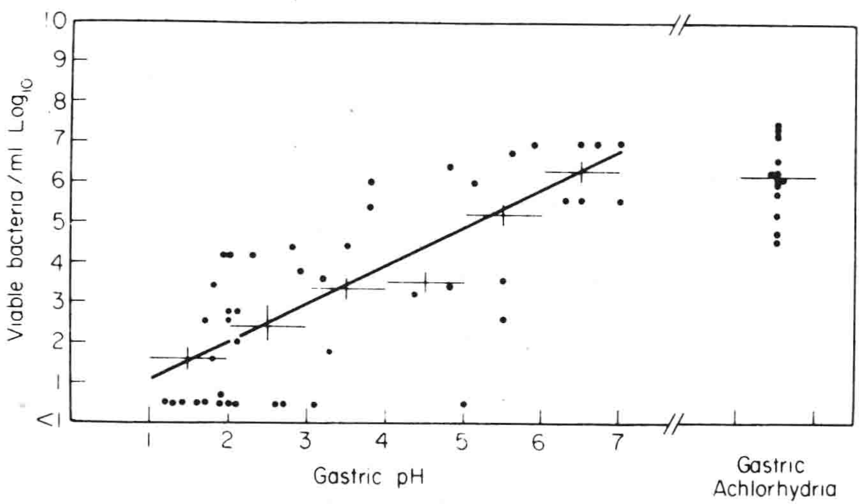

Figure 1-1 Influence of gastric pH on bacterial counts in the stomach. (*From Drasar and Hill, 1974* [1], *with permission of the authors and publisher.*)

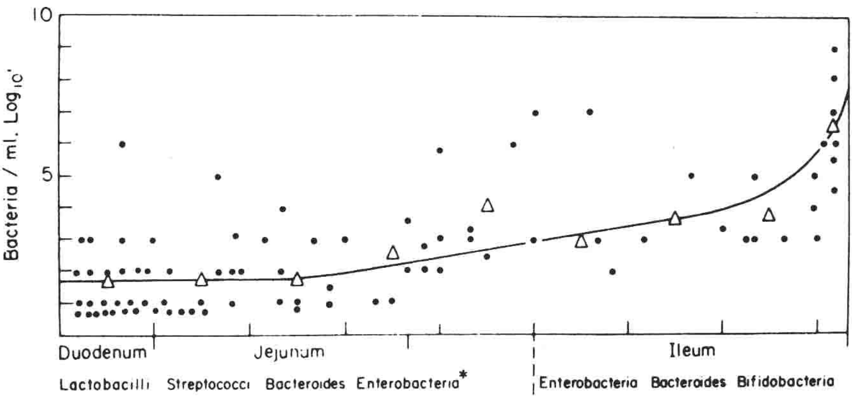

Figure 1-2 Distribution of viable bacteria in the small intestine. (*From Drasar and Hill, 1974* [1], *with permission of the authors and publisher.*)

organisms vary, some investigators suggesting that counts are higher than those in the feces [1].

Moore and Holdeman [2] have concluded that the human fecal flora may consist of more than 400 to 500 different kinds of bacteria. Because of the tremendous complexity of the fecal flora, relatively few workers have attempted to do a detailed analysis of all bacteria present [2–5]. In one study [4], the total anaerobic count was 3.79×10^{11} per gram of dry weight of feces, and the ratio of anaerobes to aerobes was over 3000 : 1. Table 1-1 lists the most prevalent species recovered in the 25 normal adults in this study. Figure 1-3 illustrates the major classes of organisms encountered in the normal fecal flora in these 25 adults, together with the range of counts and the median count for each group. Among the aerobes, species of *Bacillus* are rarely involved in infection. Among the anaerobes, *Eubacterium* and *Bifidobacterium* are nonsporeforming gram-positive anaerobic

Table 1-1 Most Prevalent Species in Fecal Flora of 25 Normal Subjects on Western Diet

Eubacterium lentum	*Clostridium bifermentans*
Bacteroides distasonis	*Bacteroides ovatus*
Escherichia coli	*Eubacterium combesi*
Bacteroides vulgatus	*Peptococcus prevotii*
Bacteroides fragilis	*Acidaminococcus fermentans*
Streptococcus faecalis	*Clostridium perfringens*
Clostridium ramosum	*Streptococcus lactis*
Bacillus sp	*Klebsiella* sp
Bacteroides fragilis group, other	*Streptococcus mitis*
Peptostreptococcus intermedius	

Source: Modified from Finegold et al., 1975 [4].

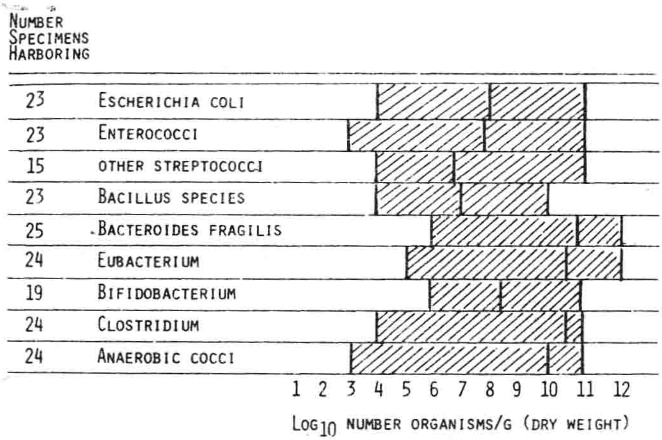

Figure 1-3 Predominant fecal flora from 25 normal adult subjects. The length of the block represents the range, the vertical lines the median counts. (*From Finegold, 1977* [6], *with permission of the publisher.*)

bacilli which are relatively nonpathogenic. A further indication of the complexity of this type of fecal study is that the clostridial isolates from the 25 subjects included 35 separate known species plus 20 other groups of *Clostridium* that have a number of features in common. These groups may represent individual species, but they are distinct from previously described species in this genus.

Although the *Bacteroides fragilis* group (including *B. fragilis, B. distasonis, B. vulgatus, B. ovatus,* and *B. thetaiotaomicron*) is the dominant group of organisms in the normal bowel flora, *B. fragilis* itself (the most pathogenic member of the group, commonly found as an important pathogen in intra-abdominal infection [6]) is isolated less frequently from feces than are certain other members of the group (Table 1-1). Another important pathogen in intra-abdominal infection is *Clostridium perfringens*. This organism occurs in significant numbers in the large bowel but not normally in the stomach or small intestine. It does occur consistently in feces (and therefore in the colon) as noted by Collee [7] and Sapico et al. [8]. In one study [8], 36 of 43 adult subjects yielded *C. perfringens* in feces. The counts were $\geq 10^5$ per gram of stool in 21 of these subjects, more than 10^3 but fewer than 10^5 per gram in an additional 12, and $\leq 10^3$ in the remaining three subjects that yielded the organism.

Persistence of Specific Types of Bacteria

For the most part, the bowel flora appears to be a stable self-regulating system. Minor components of the fecal flora vary considerably in count on repeated sampling, probably reflecting the unavailability of effective selective media for these particular types of organisms. Nonetheless, it has been noted that the variation between multiple samples from an individual is much less than between samples from different individuals [9]. The rate of multiplication of the intestinal bacteria is very low, and bacteria in the colon must be adapted for this low growth rate and for maximal utilization of substrates.

Hartley et al. [10] studied *Escherichia coli* isolates from 13 individuals sampled at intervals over several weeks or longer. The strains which were isolated were serotyped. The individuals studied showed a spectrum of stability of various serotypes of *E. coli,* some individuals showing persistence of the same serotype for extended periods of time, others showing various serotypes on different occasions.

PROBLEMS IN THE STUDY OF BOWEL FLORA

New Techniques for Recovery of Fecal Microflora

It was formerly thought that 30 to 40 percent of the wet fecal mass consisted of bacteria. In a key study reported by Stephen and Cummings [11], however, bacteria accounted for 55 percent of the total solids of feces. Their technique included repeated vigorous agitation with detergent and high-speed centrifugation for separation of the microflora from dietary fiber residue and soluble substances.

Recovery of Fastidious Organisms

Highly specialized media and/or techniques are required to demonstrate organisms with unusual growth requirements. Using such specialized approaches, one may demonstrate in the human bowel or feces methane-producing bacteria [3], anaerobic sarcinae [3], spirochetes [12], sulfate-reducing bacteria [13], and cellulose digesters [14]. Approaches using other substrates and perhaps other culture techniques would undoubtedly reveal additional types of organisms not detectable by the more conventional cultural procedures.

Selective Media

Efficient selective media exist for many different organisms of interest in the colon [3–5]. Selective media not only facilitate recovery of organisms from such complex mixtures as exist in feces, but may actually ensure recovery of organisms present in small numbers, organisms that would otherwise be overgrown by the more predominant flora. Although we do have good selective media for a few species of *Clostridium,* such as *C. difficile* and *C. paraputrificum,* there is a real need for additional selective media for members of this genus. We also need selective media for anaerobic cocci and streptococci and for members of the genus *Eubacterium*.

Mucus-Associated Flora

Microorganisms closely associated with the gastrointestinal epithelium in the mucus layer (rather than free in the lumen) have been studied extensively in various animal models and are known to exist in healthy humans as well. These organisms presumably would be of major importance, but our knowledge of them in humans is still quite sketchy.

Preparations of the human stomach have revealed numerous spiral-shaped bacteria attached to the epithelium and deep in foveae [15]. Gram-negative and gram-positive bacteria have been noted in mucus on the mucosal epithelium of jejunal biopsies. Microorganisms have also been found to be associated with the mucus on the epithelium of the ileum and colon. In most cases, the detected bacteria associated with the mucus layer are gram-positive. In the colon, only anaerobic gram-positive cocci can be seen. However, they are present in enormous numbers, forming relatively thick layers on the colonic epithelium [15].

MODIFICATION OF INTESTINAL FLORA BY VARIOUS FACTORS

Race

There is no evidence that race per se is a determinant of bowel flora. Differences in flora in populations from various parts of the world and with different racial backgrounds may be explained by factors other than race, such as nutritional state, dietary habits, and sanitary practices.

Age

At birth, the human gastrointestinal tract is sterile. Soon afterward, however, there is colonization of the gastrointestinal tract, including the meconium. Under the influence of breast feeding, a stable microflora develops in the colon within 3 to 4 days. Typically, more than 99 percent of the flora consists of *Bifidobacterium,* often a special type (D IV), which is said not to occur in nature except in breast-fed babies [16]. Less than 1 percent of the fecal flora is made up of coliforms, enterococci, and aerobic lactobacilli. Staphylococci are frequently present, but in very small numbers. There are few or no *Bacteroides, Clostridium, Proteus, Veillonella,* or other putrefactive bacteria. Bottle-fed babies have a different flora, as will be discussed in the next section. Gorbach et al. [9] compared the fecal flora of individuals 20 to 39, 40 to 69, and 70 to 100 years of age. They found that older subjects tended to have larger numbers of coliforms in their stools. "Anaerobic lactobacilli" were more numerous in the younger age group than in the 70- to 100-year-old subjects. Fungi, however, were less common in the age group 20 to 69 years.