THE DIFFERENTIAL DIAGNOSIS OF DIARRHEA

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PREFACE

Dr. Arthur L. Bloomfield, one of medicine's most respected teachers, used to tell his interns the four questions calculated most reliably to inform the physician of his patient's daily welfare. First, have you any pain? Second, did you sleep well? Third, how is your appetite? And fourth, how are your bowels? Surely these elemental functions of the body are likely to reflect most impairments of health or happiness, as anyone who has been sick in bed will testify.

Nothing appears to the patient more clearly self-evident than the sanguine connotation of his accustomed normal bowel movements. The profligate consumption of laxatives prescribed, unprescribed, and unnecessary, from antiquity to the space age, must signify an urge as persistent as sin. It is of interest that the word "physic" has been used to mean the art of medicine, any medicine, or, specifically, a cathartic.

But if constipation is a prosaic sign of illness for a multitude, diarrhea is looked upon as a far more urgent disease in itself. Depending upon the severity of the diarrhea and the mood of the sufferer it inspires an enfeebled despair or sardonic lament almost peculiarly belonging to this affliction. It is doubtful that any other symptom has stirred its victims to invent so rich and poetic a variety of appellations, ranging from the venerable cholera morbus to the American soldier's *G.I.'s* or *screaming trots* and the traveler's *Minnesota quick-step* or *Montezuma's revenge.*

Lay concepts of diarrhea are widely variable. One fearful mother calls diarrhea the three daily solid bowel movements of

her firstborn child. A stoic farmer pays no attention to a half-dozen liquid evacuations because "they are mostly water" and have occurred from time to time without effect upon his general health. Physicians, however, are quite familiar with the normal vagaries of defecation, since their brethren are almost constantly providing them with the latest data. This book is concerned with what physicians recognize as diarrhea, with a significant decrease in the consistency of the stools, usually associated with abnormal frequency.

The physician is confronted with a disheartening number of diseases which may at one time or another be responsible for diarrhea. His speculations in a single puzzling instance may lead him into a half-dozen specialties, a circumstance of growing peril as the edifice of medicine rises higher, threatening to become a modern Tower of Babel.

It is hoped that the terms *millicurie* and *TSH* (thyroid stimulating hormone) will not render the diarrhea of thyrotoxicosis less comprehensible to all nonendocrinologists, that the new techniques for detecting malabsorption syndromes will not dim our perception of cancer of the rectum. This book is intended to unify what specialization, however necessary for thoroughness and research, tends to divide; to focus from many directions upon a single symptom. The aim is to discuss and organize in an accessible form the causes of diarrhea and to point to the means of arriving at the correct diagnosis. So large a task forbids detail as well as exhaustive exposition of other aspects of diarrhea, such as treatment and pathogenesis, apart from the inseparable connections of these topics with what must remain our central theme, the differential diagnosis of diarrhea.

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Sherman M. Mellinkoff, M.D.

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AN APPROACH TO THE DIFFERENTIAL DIAGNOSIS OF DIARRHEA

In many diseases diarrhea is ordinarily a cardinal feature; yet a small number of patients with the same disease will complain of other symptoms, while diarrhea is either mild or absent. In sprue, for instance, the stools may be very frequent and watery, and diarrhea is the rule, but a few patients with sprue complain of some other symptom, such as muscular cramps (due to hypocalcemia), while the stools are infrequent and difficult to pass.

Conversely, there are diseases in which diarrhea is seldom seen, or, if present at all, it is mild. But an occasional patient with one of these illnesses which are not regarded as "diarrheal diseases" will have diarrhea out of proportion to the usual manifestations of his condition. Thus, cirrhosis of the liver, notorious for a host of other troubles, is sometimes responsible for marked diarrhea.

This variability of diarrhea in etiologically unrelated disorders creates great difficulties in differential diagnosis. The diagnosis is sometimes clarified by focusing attention upon the diarrhea and by considering the generic or specific causes of loose stools which could possibly be related to the other manifestations of the individual patient's illness.

The ensuing chapters of this book describe the diagnostic features of a great many illnesses in which diarrhea may occur. The reader may seek characteristics of specific disorders or groups of disorders by chapter headings or subheadings. He may wish to compare the illness of his own patient with the picture recorded under a particular title, and perhaps to see what must be done to verify or exclude a certain diagnostic possibility. There are many cross references, and the index is often necessary to locate different aspects of a given topic.

In this chapter, however, no specific disease is discussed, or even mentioned, except as an illustration of some wider tenet that spans a number of separate entities. The purpose is to provide in skeleton form a general approach to the problem of diarrhea, to answer such questions as these:

In which *category* does the patient's diarrhea belong?

What steps are necessary to arrive at the correct *classification*?

How does one proceed when the cause of the diarrhea is puzzling?

The History

As in most branches of medicine, a good history is usually the most important factor in making a diagnosis. Obviously this is not the place to review the entire art of history taking,[1–3] which in a puzzling case of diarrhea is frequently the key, not only to the diagnosis, but also to the treatment according to an old and generally reliable formula:

$$\frac{1}{\text{Case history}} = R_x$$

The more detailed and painstaking the history, the less treatment is usually required. Often new drugs or more drugs are prescribed because an inadequate history has concealed the correct diagnosis.

There are no short cuts to completeness and the sympathetic ear. A patient may not, for instance, be aware of any relationship between his diarrhea and his attitude toward his father, and may deny the association if asked directly in the first interview, but

in a thorough family history the physician may clearly find the connecting links. If he skips the family history, or lightly skims it, no number of x-rays and blood chemistries will ever compensate for this omission, nor will any tranquilizer cure the illness.

Apart from thoroughness and the kindly acceptance that silently encourages the patient to talk, a few aspects of the history specifically relating to diarrhea are important. Some of these, pertaining to the differentiation of psychogenic and so-called "organic" diarrhea, are discussed at greater length in Chap. 11. Here, however, are listed a few questions the history should answer together with their meaning:

1. *How long has the diarrhea been present?* The answer to this question is not always obtained easily. A patient may say that he has had diarrhea for one day, but similar difficulties may have beset him several times in the past. Certain types of diarrhea frequently come and go, for example, ulcerative colitis, psychogenic diarrhea, and amebic colitis. Others are characterized by few if any relapses once the acute illness, for example, shigellosis, has subsided.

2. *Do the bowel movements awaken the patient from sound slumber?* While there are, of course, exceptions, certain illnesses, even when severe, do not ordinarily rouse the patient from sleep; for example, psychogenic diarrhea. In other forms of diarrhea the stools may appear exclusively during the waking hours, but if the illness is at all severe, the bowel movements usually awaken the patient at least once each night, and often with critical urgency. Examples of the latter type are ulcerative colitis, acute salmonella dysentery, and regional enteritis.

3. *What do the stools look like?* The patient's description may be deceiving, but more often it is of help. Ulcerative colitis that has been present for any length of time is very likely to produce bright red blood in the stools, while in psychogenic diarrhea, regional enteritis, or sprue, for instance, the stools are most often free of red blood. Stools that contain recognizable pieces of eggs, meat, or butter suggest pancreatic exocrine insufficiency. Stools that are very large and bulky and pale in color suggest some type of malabsorption syndrome, while frequent watery squirts

are more characteristic of a colonic disease. Large amounts of mucus in the stools may be seen in many diseases, including mucous colitis (a form of psychogenic diarrhea), ulcerative colitis, cancer of the colon, and villous adenoma of the colon, but mucus is unlikely to be a prominent feature of the stools in sprue.

4. *Where is the discomfort or pain accompanying or preceding the urge to defecate?* Periumbilical or right lower quadrant pains suggest small bowel disease, such as regional enteritis or sometimes psychogenic hyperperistalsis in the small bowel. Lower abdominal pain with diarrhea suggests disease of the large bowel, and rectal or sacral pain may indicate inflammation, obstruction, or dysfunction of the rectum or rectosigmoid. Complete absence of pain with diarrhea may occur in many diseases, but is more characteristic of noninflammatory disorders, such as sprue, than of mucosal irritation, such as that seen in ulcerative colitis or arsenic poisoning. Unremitting pain, in contrast to pain related to eating or defecating, is often present by the hour in gallstone colic, by the day in pancreatitis, and for weeks or months in various abdominal malignancies. Absolutely constant pain for years is usually hysterical.

5. *How is the appetite?* Certain diarrheal diseases are apt to produce anorexia, for example, severe ulcerative colitis involving more than the terminal segment, abdominal malignancies, and bacillary dysentery. Other diarrheal diseases, such as benign adult pancreatic steatorrhea, are often accompanied by a ravenous appetite. "A very poor appetite" associated with weight gain or stubborn obesity is usually a neurotic complaint, unless edema or ascites are present. The diurnal variation in appetite is often worth exploring, from meal to meal and from day to day.[4] Many organic diseases, such as hepatitis or partial obstruction of the stomach, are characterized by maximum appetite in the morning and progressive loss of appetite with each meal. Anorexia or nausea in the morning, with a good appetite later in the day, is common among alcoholics and overly anxious or depressed patients. Severe anorexia that alternates with an excellent appetite according to changes in the patient's occupation or environ-

ment is usually related to emotional disturbances. A stubbornly poor appetite which appears in an affable patient accustomed to good health is commonly a symptom of cancer.

The Physical Examination

Careful and complete examination of every patient is, of course, routine. A few points sometimes overlooked in connection with diarrhea are listed here:

1. Real *fever*, confirmed by feeling the hot skin or taking the temperature, even in a neurotic patient, suggests an inflammatory or neoplastic disease, such as regional enteritis or a lymphoma. Oral temperature up to 99.8°F, or sometimes even a little higher, may occur in the absence of organic disease, however, and should not be accepted as positive proof that diarrhea is not psychogenic. Similarly, a short bout of genuine fever in diarrhea of long duration may add up to nothing more than influenza in a patient with an afebrile type of diarrhea. On the other hand, a patient who complains of diarrhea and who has been seen with "the flu" eight or nine times a year may well be suffering from regional enteritis or ulcerative colitis.

2. Signs of considerable *weight loss, edema, vitamin deficiency, anemia, tetany*, or a *hemorrhagic diathesis* are common in malabsorption syndromes (Chaps. 7 and 8).

3. A *protuberant abdomen* that is not commensurately tympanitic, without shifting dullness in the flanks, is often found in patients with sprue, and under these circumstances an x-ray of the abdomen taken with the patient standing will frequently reveal multiple air-fluid levels in dilated loops of the small bowel.[5]

4. *Arthritis* is common in ulcerative colitis, regional enteritis, and Whipple's disease.

5. It is also common to find in regional enteritis or ulcerative colitis various other types of "hypersensitivity reactions", such as *iritis, erythema multiforme, pyoderma gangrenosum*, or *erythema nodosum*.

6. Proctosigmoidoscopy, which is almost always a part of the physical examination in a patient with diarrhea, is discussed in Chaps. 2 and 5. This examination very often enables one to make

a diagnosis that is otherwise elusive. A friable rectal mucosa may be the only sign of ulcerative colitis; or what appears to be ulcerative colitis sometimes turns out on biopsy of the mucosa to be, in fact, amebiasis.

Laboratory Examinations

Very few laboratory procedures are profitable as a matter of routine. Every patient with diarrhea should, of course, have a blood count, including careful perusal of the blood smear, a urinalysis, and inspection of the stool for gross characteristics (mentioned above). When the doctor himself looks at a 24-hr stool collection, he sometimes finds that the patient's description has been misleading. The character of the feces may have changed so slowly that the patient failed to observe their remarkable bulk, or stools described dramatically as large and watery may actually be unimpressive to the objective observer. In addition there should be microscopic examination for white and red cells and for ova and parasites, and a chemical test, such as the guaiac reaction, for occult blood. Screening or definitive tests for malabsorption syndromes are found in Chaps. 7 and 8. A serum carotene concentration as a screening procedure is inexpensive to determine and is often very low in sprue, even in the absence of severe malnutrition.

Other laboratory procedures or x-rays should be performed to answer specific questions which are raised by the history or physical examination.

Classification of Diarrheal Diseases

There are, of course, many ways of classifying diarrheal diseases, and each physician may wish to work out his own diagnostic approach. Fundamentally most cases of diarrhea result from a relatively few generic types of physiological disorders:

1. Propulsion of normal enteric contents too rapidly because of
   a. Abnormal nervous impulses (as in psychogenic diarrhea or mecholyl poisoning)
   b. Abnormal chemical influences upon motility (as in carcinoid syndrome, Addison's disease, thyrotoxicosis, etc.)

   c. *Irritation of the bowel* (as in castor oil ingestion, ulcerative colitis, pericolic abscess, amebiasis, uremic colitis, etc.), or
   d. *Loss of colonic storage* (as in destruction of the anal sphincter, ileostomy, etc.)
2. Impaired digestion of food because of
   a. *Loss of reservoir function of the stomach* (as in dumping syndrome)
   b. *Pancreatic disease*
   c. *Insufficient length of small bowel,* or
   d. Possibly *abnormal secretion of HCl,* as in some cases of Zollinger-Ellison syndrome (Chap. 6)
3. Abnormal absorption of adequately digested food because of
   a. *Liver disease*
   b. *Small-bowel disease* (anatomical or chemical; Chap. 7), or
   c. *Mesenteric obstruction* (as in carcinomatosis or tuberculosis)

Some causes of diarrhea may belong simultaneously in more than one of the above categories. For example, a form of ulcerative colitis (so-called "ileocolitis") may produce diarrhea by inflammatory irritation of the colon and at the same time cause a malabsorption syndrome through involvement of a substantial portion of the terminal small bowel or through concomitant liver disease. Or a lymphoma of the small bowel may create propulsive dysfunction by infiltration of the bowel or narrowing of it, and also cause a malabsorption syndrome.

In other cases of diarrhea, such as the Zollinger-Ellison syndrome or hepatic disease without steatorrhea, the pathogenesis of the loose stools is not clear.

Generally, however, from a diagnostic point of view, diarrhea is of three types:

1. *Of short duration,* in which case the diagnosis may be clear or speculative, but which, in either case, is not a lasting problem. Examples: acute viral diseases (Chap. 4), ingestion of unripe fruit, and the "touristas" (Chaps. 3 and 9).

2. *Of long duration,* in which the history, physical examination, or routine laboratory procedures point to one or more of the broad categories listed above, or in the table of contents of

Table 1-1. CONDITIONS AMONG ADULTS CAUSING DIARRHEA AS CHIEF COMPLAINT WHICH WERE NOT DIAGNOSED FOR THREE OR MORE MONTHS PRIOR TO THEIR APPRAISAL AT THE U.C.L.A. MEDICAL CENTER IN 5-YEAR PERIOD

Present diagnosis*	Diagnoses entertained previously	Present diagnosis suspected on basis of	Diagnosis established by	Types of treatment used	Result
Psychoneurosis, spastic colon (Chap. 11)	Ulcerative colitis, regional enteritis, cancer, diverticulitis, pancreatitis, sprue, adhesions	History, physical examination	History and objective studies to rule out organic possibilities	Psychotherapy of different types	Variable, poor to excellent
Ulcerative colitis (Chap. 5)	"Nervous diarrhea" or psychoneurosis	History, stool examination	Proctosigmoidoscopy, x-rays of colon, or rectal mucosal biopsy	Improved nutrition, rest, supportive psychotherapy, local or systemic steroids, colectomy	Variable, poor to excellent
Regional enteritis (Crohn's disease) (Chap. 5)	"Nervous diarrhea" or psychoneurosis	History, physical examination	Small bowel x-ray and/or laparotomy	Improved nutrition, rest, supportive psychotherapy, surgery	Variable, poor to excellent
Cancer of the colon (Chap 6)	Psychoneurosis, spastic colon, diverticulitis	History, physical examination	Proctosigmoidoscopy, barium enema x-ray	Surgical resection	Fair to excellent
Nontropical sprue (gluten-sensitive type) (Chaps. 7 and 8)	"Nervous diarrhea," regional enteritis, hypoparathyroidism, cancer, Addison's disease, "colitis"	History, physical examination, serum carotene, small bowel x-rays	Response to gluten-free diet or small-bowel mucosal biopsy or both; steatorrhea documented before therapy	Gluten-free diet	Excellent
Dumping syndrome plus psychoneurosis (Chaps. 7, 9, and 11)	Dumping syndrome, malabsorption syndrome	History	History, quantitative fecal fat, response to therapy, exclusion of other illnesses	Psychotherapy and various measures to improve nutrition	Poor to excellent

Diverticulitis (Chap. 5)	Psychoneurosis, cancer adhesions	History, physical examination	Barium enema x-rays or surgical resection	Measures to prevent constipation, periodic antibiotics, surgery	Good to excellent
Whipple's disease (Chap. 7)	Sprue, "collagen disease," cancer, psychoneurosis	History, physical examination	Small-bowel biopsy	ACTH, antibiotics	Temporary remission
Massive jejunal diverticulosis (Chap. 7)	Nontropical sprue	Plain upright films of abdomen	Small-bowel x-rays	Antibiotics	Fair
Primary biliary cirrhosis (Chaps. 7, 9)	Sprue, psychoneurosis	History, physical examination	Operative cholangiogram and liver biopsy	Symptomatic and supportive	Poor
Amyloidosis of small bowel (Chap. 7)	Psychoneurosis	Long-standing rheumatoid arthritis, quantitative fecal fat indicating steatorrhea	Biopsy of rectal mucosa	Symptomatic, nutritional support	Fair
Steatorrhea of unknown cause (Chaps. 7, 8)	"Sprue"	Failure to respond to gluten-free diet; documentation of steatorrhea	Laparotomy, small-bowel biopsy	Supportive	Poor
Gastroileal fistula (inadvertent, surgical) (Chap. 7)	Psychoneurosis, dumping syndrome	History, physical examination	G.I. series	Surgical and supportive	Excellent
Gastrocolic fistula (due to benign gastric ulcer) (Chaps. 5, 7)	Gastric ulcer, psychoneurosis	History, physical examination, quantitative fecal fat	Barium enema	Surgical	Excellent
Cancer of pancreas (Chaps. 6, 7)	Psychoneurosis	Quantitative fecal fat establishing diagnosis of steatorrhea	Laparotomy	Surgical	Poor
Carcinoma of jejunum (Chap. 6)	Psychoneurosis, sprue	History of periumbilical pain and symptoms of obstruction	Small-bowel x-rays	Resection	Palliative