

Difficult Diagnosis

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PREFACE

A book entitled *Difficult Diagnosis* was written by H. J. Roberts, M.D., and published by W. B. Saunders Company in 1958. This new book differs from the previous work in two important ways: First of all, medicine is now, a quarter-century later, so much more complex that no single author could write an authoritative, comprehensive volume spanning virtually all specialty areas. Second, whereas Roberts discussed literally hundreds of clinical entities, it has now become necessary to limit the number of topics in order to discuss each in adequate depth.

Roberts' original preface stated one reason why he undertook the writing: "I needed a book like this in my own practice." So do I. This work describes the diagnostic approach to a selected group of challenging clinical problems. The topics of the chapters that follow have been chosen to represent the most enigmatic clinical presentations, without regard for the frequency of their occurrence in practice. The topic list represents areas—amenorrhea, purpura, jaundice, chronic urticaria, and delayed puberty are just a few—that have frequently prompted me to make a trip to the library or seek consultation. In each instance, the chapter has been written by an expert on that topic, with data recorded more or less according to a standard format. The approach is one that I have found useful in practice: an overview of the problem, a directed medical history with high-payoff questions, a physical examination focused on specific areas, laboratory investigations that include the latest technology, and a systematic, sometimes algorithmic, analysis of clinical data.

Difficult Diagnosis is intended for use by the primary care physician and by the specialist who encounters patients with problems outside his or her field of expertise. The problems discussed in this book transcend traditional specialty lines; that is, the patient with facial pain may be seen by the neurologist, neurosurgeon, otolaryngologist, or oral surgeon, as well as by the family physician. For this reason, the topics are listed alphabetically rather than by specialty or organ system. The focus is on diagnosis, and information regarding therapy is included only when it may facilitate diagnosis, e.g., the use of a trial of progesterone in amenorrhea.

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ABDOMINAL PAIN, ACUTE

JOSEPH L. BYRNE □ ARTHUR A. VERCILLO □ SYED N. ZAMAN

□ SYNONYMS: Pain in the abdomen, belly pain

BACKGROUND

Definition and Origins

Abdominal pain describes a sensation of malaise or discomfort related to the abdominal cavity. Difficulty in establishing a precise diagnosis arises from the fact that an enormous number of disease entities produce abdominal pain. Abdominal pain can be caused by any of three broad categories of disease: intra-abdominal disease, referred pain from localized extra-abdominal disease, and systemic disease.

Intra-abdominal Disease

Critical to the establishment of the diagnosis of abdominal pain is an understanding of the mechanisms of abdominal pain. There are essentially two types of abdominal pain, which derive from the neurologic anatomy of the abdomen.

Visceral Pain. The abdominal viscera and the visceral peritoneum that envelops them are supplied by a paucity of nerve endings mediated through the splanchnic nerves. In addition, the innervation is multisegmental and overlapping, so that visceral pain is not well localized. The visceral pain fibers respond to increased intraluminal pressure and not to direct stimuli such as crushing and burning. Owing to the poor localization, obstruction or distension of almost any hollow viscera initially manifests as vague discomfort in the central portion of the abdomen. An example of this vagueness is the periumbilical pain produced by initial distension of the appendiceal lumen in early appendicitis.

Parietal Pain. The parietal peritoneum is supplied by somatic afferent nerves that can precisely localize adjacent inflammatory processes. For example, as appendicitis progresses to transmural inflammation, precise localization of pain to the right lower quadrant occurs as the parietal peritoneum is irritated.

Referred Pain from Extra-abdominal Disease

Abdominal pain due to extra-abdominal disease is common because central pathways for afferent neurons are shared. Thus, severe angina and other primary thoracic diseases may manifest as abdominal pain. Similarly, severe retroperitoneal disease,

such as rupture of an aortic aneurysm, often causes abdominal pain. Table 1 presents the most common causes of referred abdominal pain.

Embryologic considerations are also important in the diagnosis of abdominal pain. For example, the common origin of the testicle and kidney explain the presentation of ureteral colic as sharp testicular pain.

Systemic Disease

Presenting symptoms of a variety of systemic illnesses include acute abdominal pain. These illnesses are listed in Table 2.

Incidence and Causes

Abdominal pain was the chief presenting complaint in one out of every 20 emergency room patients seen recently in a large medical center.³ Interestingly, the most common final diagnosis in this study was abdominal pain of unknown cause (41.3 per cent). The next three most common diagnoses were also nonsurgical: gastroenteritis (6.9 per cent), pelvic inflammatory disease (6.7 per cent), and urinary tract infection (5.2 per cent). The most common surgical disease, appendicitis, was observed in only 4.3 per cent of cases. This study highlights the facts that the majority of patients presenting with abdominal pain have nonsurgical disease and that often no specific

Table 1. MOST COMMON CAUSES OF REFERRED ABDOMINAL PAIN

Location	Disorders
Cardiothoracic	Pericarditis Pleuritis Pneumonia Acute myocardial infarction
Abdominal wall	Rectus sheath hematoma Muscle strain
Retroperitoneal	Renal colic Renal infarct Ruptured abdominal aortic aneurysm
Pelvic	Mittelschmerz Endometriosis

2 □ ABDOMINAL PAIN, ACUTE

Table 2. SYSTEMIC ILLNESSES CAUSING ABDOMINAL PAIN

Metabolic	Acute porphyria Uremia Diabetic ketoacidosis Addisonian crisis
Hematologic	Sickle cell anemia Leukemia
Toxic	Heavy metal poisoning Bacteria (staphylococcus, tetanus) Drug effects Insect bite reactions

diagnosis is made. Statistics, however, are no consolation to the individual patient, and the burden of proof lies on the diagnostician first to exclude a life-threatening, surgically treatable illness as the cause of abdominal pain. The challenge, therefore, in diagnosis of the acute abdomen is to separate those patients with conditions that require diagnosis in a matter of minutes if treatment is to be successful such as leaking aortic aneurysms, from the overwhelming number of patients with benign conditions for which the diagnostic process can proceed in a leisurely fashion.

HISTORY

A carefully taken history remains the cornerstone of diagnosis of the acute abdomen. Table 3 summarizes the key points to address in history taking. The history should record the exact time of onset. Pain that awakens the patient from sleep is often of serious import. Of similar importance is the subsequent temporal pattern of the pain. For example, as illustrated in Figure 1, one can often separate the pain caused by obstruction of a hollow viscus, which recurs in waves, from that caused by perforation of a viscus, in which a crescendo of severe pain is often followed by regression. The waxing-and-waning pattern of pain from obstruction of a hollow viscus can often

Table 3. KEY POINTS OF HISTORY IN ACUTE ABDOMINAL PAIN

Pain:
Time of onset
Pattern of recurrence
Pattern of radiation
Character
Provocative and palliative features
Character of emesis?
Syncope?
Menstrual history

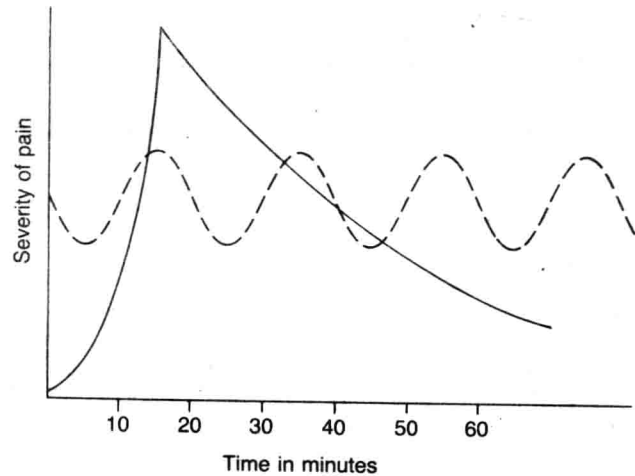


Figure 1. Temporal sequence of abdominal pain as a guide to diagnosis. Solid line indicates pattern in perforated viscus. Dotted line indicates pattern in obstruction of hollow viscus.

be quite similar, whether the viscus involved is part of the gastrointestinal tract, the biliary tract, or the genitourinary tract. The interval of freedom from pain may be helpful in localizing the site of obstruction in the gastrointestinal tract, because the interval between cramping pains is longer if the site of obstruction is more distal.⁴

The pattern of radiation of pain is another key feature in the history. Radiation to the shoulder implies irritation of the diaphragm with pain referred via the phrenic nerve. It may suggest perforated ulcer with diaphragmatic irritation, splenic rupture or infarct, or liver abscess. Pain radiating to the back is typical of pancreatitis, penetrating peptic ulcer, and rupture of abdominal aortic aneurysms.

The character of the pain may be helpful. For example, the dull, fixed pain of pyelonephritis may often be distinguished from the tearing pain of a leaking aortic aneurysm.

Provocative and palliative features are noteworthy. For example, biliary colic and intestinal angina are typically aggravated by eating, whereas the pain of peptic ulcer is relieved by the neutralizing effect of a meal. Pain aggravated by urination may suggest appendicitis irritating the right ureter or a pelvic abscess in proximity to the bladder.

The timing and character of associated emesis are important. In appendicitis, pain almost invariably precedes emesis. Emesis of gastric contents with bile staining may occur with biliary colic, ureteral colic, or proximal small bowel obstruction. The emesis of feculent material is virtually pathognomonic of distal small bowel obstruction.

Syncope in association with abdominal pain may suggest hypotension and severe blood volume loss as seen in ruptured aortic aneurysms, ectopic pregnancy, or ruptured spleen. A menstrual history is critical in women; amenorrhea suggests

ectopic pregnancy, and pain in midcycle suggests mittelschmerz.

Previous medical history should be completely evaluated. Alcohol abuse is important in gastritis, peptic ulcer, and pancreatitis. Prior abdominal surgery is of obvious importance. It is worth noting that adhesions from previous surgery are one of the three most common causes of bowel obstruction in the adult, hernia and neoplastic lesions being the remaining two causes.

PHYSICAL EXAMINATION

General observation of the patient is critical to the rapid assessment of the severity of the illness. Pallor, lethargy and cool, cyanotic extremities may suggest imminent hypovolemic shock from blood loss. Likewise, a patient with diffuse peritonitis usually lies extremely still because of pain with any motion, but a patient with ureteral colic often is writhing in pain.

Routinely, the temperature, pulse, and respiratory rate should be recorded, although they are highly variable as indices of the severity of acute abdominal pain. Abnormal vital signs are helpful in targeting patients with significant disease. However, it is not uncommon to see perforated appendicitis, for example, with entirely normal vital signs, including temperature.

The abdominal examination should include the traditional activities of inspection, palpation, percussion, and auscultation. *Inspection* may reveal the restricted respiratory motion seen in advanced peritonitis or, occasionally, the visible pulsation of an aortic aneurysm. Maintenance of thigh flexion indicates psoas abscess or appendicitis. *Palpation* should detect areas of maximal tenderness, muscle guarding, and masses. Organomegaly should be sought, and special attention should be directed to the inguinal rings and femoral triangles for hernial defects or incarcerated masses. Table 4 suggests diagnoses that may be suggested by localization of findings on palpation. *Percussion* of the abdomen is valuable in assessing whether abdominal distension is liquid, as in ascites, or tympanitic, as in the presence of bowel obstruction or perforated viscus. Loss of the liver dullness usually noted in the right upper quadrant suggests free intraperitoneal air from a perforated viscus. Exquisite tenderness to light percussion is a reliable indicator of peritonitis and should replace more heavy-handed methods of searching for "rebound" tenderness. A distended bladder, which should be detected by percussion, may establish that the abdominal pain is secondary to prostatic obstruction, a not uncommon diagnosis in the elderly male. *Auscultation* is probably the least helpful mode of examination. Traditionally, the silent abdomen has been considered pathogno-

Table 4. DIAGNOSES OF THE ACUTE ABDOMEN ACCORDING TO LOCALIZATION OF FINDINGS ON PALPATION

Localization	Likely Diagnoses
Right upper quadrant	Acute cholecystitis Hepatitis Hepatomegaly due to congestive heart failure Peptic ulcer Retrocecal appendicitis Right lower lobe pneumonia Carcinoma of hepatic flexure of colon Right pyelonephritis Hepatic abscess
Left upper quadrant	Gastritis Splenic rupture Left pyelonephritis Myocardial ischemia Left lower lobe pneumonia Splenic infarct
Right lower quadrant	Appendicitis Regional enteritis (Crohn's) Ectopic pregnancy Torsion or rupture of right ovarian cyst Meckel's diverticulitis Psoas abscess Endometriosis Cecal carcinoma
Left lower quadrant	Diverticulitis Carcinoma of left colon Ectopic pregnancy Torsion or rupture of left ovarian cyst Psoas abscess Endometriosis

monic for diffuse peritonitis, and the high-pitched borborygmi of peristalsis pathognomonic for mechanical intestinal obstruction. In reality, active peristalsis often persists despite extensive peritonitis, and the late stages of mechanical obstruction may be associated with a silent abdomen. Auscultation of an abdominal bruit may suggest arterial insufficiency, but ruptured aneurysms and ischemic bowel are often found in the absence of bruit.

Certain physical signs used traditionally in the abdominal examination may be helpful. They are as follows.

Psoas test: With the patient lying on the left side, forced extension of the right hip will cause pain if the psoas muscle is irritated by an inflamed appendix.

Obturator test: With the patient supine, rotation of the hip joint with the thigh flexed may cause pain if the obturator muscle is irritated by a pelvic appendicitis.

Murphy's sign: Deep inspiration during deep palpation in the right upper quadrant will cause pain if the gallbladder is distended or inflamed.

Grey Turner's sign: Flank discoloration by subcutaneous hematoma may be seen in advanced cases of hemorrhagic pancreatitis.

Careful pelvic and rectal examinations are mandatory in all cases of acute abdominal pain.

DIAGNOSTIC STUDIES

Complete blood count and urinalysis are the first-line tests useful in acute abdominal pain. It should be emphasized that a normal hematocrit is the rule in early hemorrhage, even of extensive proportions, because equilibration takes hours to occur.

The white blood cell (WBC) count is notoriously inaccurate for identifying acute surgical conditions in the abdomen. In a representative sample of surgical explorations focusing on appendicitis, patients with appendicitis or another surgical condition did have, on the average, higher white blood cell counts than patients with nonsurgical disease, but significant numbers of patients in both surgical groups had white blood cell counts less than 10,000 cells/mm³.⁵ On the other hand, 55 per cent of the patients with nonsurgical disease had white blood cell counts exceeding 10,000 cells/mm³.

Urinalysis may confirm a diagnosis of urinary tract infection. Red cells are usually, but not invariably, present in cases of ureteral calculi. Urinalysis for human chorionic gonadotropin (hCG) is helpful if ectopic pregnancy is suspected.

Amylase determinations may be made if pancreatitis is suspected, but normal amylase levels may be seen in advanced pancreatitis, usually in the setting of chronic pancreatitis with an extensively damaged pancreas. Many other acute abdominal conditions, including cholecystitis, ischemic bowel, and perforated or obstructed bowel, may cause elevations in the serum amylase level. The urine amylase level may be elevated even in the face of normal serum amylase levels; however, amylase elevations are seen in such a wide variety of diseases that their diagnostic value is limited.

Radiographs of the abdomen should be taken in two planes, one either decubitus or upright, so that air-fluid levels can be detected. Air-fluid levels suggest mechanical bowel obstruction but are also found in paralytic ileus due to other abdominal disorders. Free air from a perforated viscus may be better seen on an upright chest film. Calcification noted in the region of the pancreas indicates chronic pancreatitis. Blunting of the psoas shadows is seen in massive hemorrhage or abscess formation. Gallstones, appendicoliths, and ureteral calculi should be sought.

It should not be inferred that every patient with abdominal pain needs radiography. Patients clearly suffering from abdominal catastrophes

should undergo prompt surgical exploration without the hazardous delays imposed by these additional tests. Also, as noted previously, the majority of patients with abdominal pain prove not to have serious illness, and the cost effectiveness of routine abdominal films has been demonstrated to be quite low.⁶ Often a simple trial of observation and careful follow-up can avoid the costs of multiple radiographs.

Special radiographic studies have a limited role in diagnosis of the acute abdomen. An intravenous pyelogram may be used to confirm the diagnosis of ureteral calculus if suggested by the history, physical findings, and urinalysis results. Barium studies in the setting of acute abdominal pain should be discouraged, because they may be dangerous if a viscus is already perforated and they may obscure the findings of subsequent, urgent evaluations such as ultrasonography and angiography. Ultrasonography may be useful to demonstrate gallstones and has the advantages of being safe and simple and of not introducing contrast media into the abdomen.

Radioisotopic scanning of the biliary tree is being used increasingly to determine whether the cystic duct is blocked, a better sign of acute cholecystitis than the mere presence of gallstones, which may in fact be asymptomatic. Intravenous cholangiography has virtually disappeared from the diagnostic armamentarium.

Arteriography may be useful if superior mesenteric artery embolus or thrombosis is suspected. Ischemic bowel, which is being recognized more often as the elderly population increases in size, is a difficult diagnosis to make. Again, the premature administration of barium precludes the use of arteriography. This procedure is not necessary in cases of suspected ruptured abdominal aortic aneurysm, and the best diagnostic measure if such a diagnosis is suspected is emergency laparotomy.

Laparoscopy has been suggested as a useful diagnostic tool, particularly in menstruating females, in whom it is often difficult to distinguish between appendicitis and pelvic disease.⁷ This procedure, however, has not gained widespread popularity in the diagnosis of acute abdominal pain, even in the female population. The distinction between appendicitis and pelvic disease can usually be made via combined surgical and gynecologic consultation and occasionally by the addition of pelvic ultrasonography or barium enema. Barium enema is most helpful if it demonstrates a filling defect in the cecum, suggesting an appendiceal mass, but the disadvantages of any barium study in the setting of acute abdomen are real and must be weighed carefully before the procedure is ordered.

Upper gastrointestinal endoscopy has undoubtedly increased the accuracy of diagnosis of peptic ulceration. Unfortunately, it is expensive and un-

comfortable. Often in cases of acute peptic ulcer, the patient can be treated empirically initially, and when the condition has proved to be stable over the course of 48 to 72 hours, the diagnosis can be made by barium swallow.

Although rare, Meckel's diverticula often contain ectopic gastric mucosa that will specifically take up certain radioisotopes. This test may be useful in cases of obscure, recurrent abdominal pain.

ASSESSMENT

An accurate diagnosis is essential in acute abdominal pain because so many of the diseases involved are treated quite safely if diagnosed early yet have catastrophic consequences if there is undue delay in diagnosis. In a study of 1,000 consecutive emergency room evaluations for abdominal pain, 11 patients were erroneously discharged and on return were found to have acute surgical problems.³ Eight of the 11 were found ultimately to have acute appendicitis, and three to have intestinal obstruction. In this section, discussion focuses on these two problem areas of diagnosis and also on selected other diagnoses that are troublesome to the clinician.

Acute Appendicitis

As noted, appendicitis remains the most common cause for error in diagnosis of acute abdominal pain. The diagnosis is most often missed in three specific groups:

1. Children 1 to 14 years of age, in whom the diagnosis at surgery is usually mesenteric adenitis, a syndrome of abdominal pain caused by mesenteric lymph node enlargement usually on the basis of an upper respiratory viral illness. Yaijko and Steel⁸ noted that 50 per cent of patients found to have mesenteric adenitis at surgery gave a history of recent upper respiratory infection, and that the WBC count was less than 12,500 cells/mm³ in 75 per cent of cases. The peak incidence of mesenteric adenitis was between 11 and 20 years of age in the study, whereas the peak incidence of appendicitis is between 16 and 25 years of age.

2. Women 10 to 29 years of age, in whom the diagnostic error is most often made by confusing appendicitis with pelvic inflammatory disease.

3. The elderly, who demonstrate a less dramatic physiologic response to serious illness. Many elderly patients with advanced appendicitis have no fever or leukocytosis and only minimal abdominal tenderness.

How, then, can one best avoid overlooking appendicitis? One should pay careful attention to the history, which in appendicitis begins with

crampy periumbilical pain (visceral pain) and is followed by localization to the right lower quadrant as transmural inflammation proceeds, irritating the parietal peritoneum (parietal pain). The pain should be followed by nausea, emesis, or, at the least, anorexia. Localized tenderness in the right lower quadrant remains the key physical finding. Normal urinalysis and the presence of leukocytosis are confirmatory signs, but as emphasized before, a normal WBC count by no means excludes the diagnosis. Rarely will the plain film of the abdomen demonstrate a fecalith. Perhaps the key point is that diagnostic laparotomy in cases of strongly suspected appendicitis remains the most reasonable course. Hospitals that maintain rates for negative exploration results for appendicitis that are less than 10 per cent are probably overconservative in the use of laparotomy and may well expose their patient population to the hazards of perforated appendicitis.

Bowel Obstruction

This diagnosis probably accounts for a common cause of error in diagnosis owing to its wide variety of clinical presentations. Silen⁹ analyzed the causes of bowel obstruction by incidence; his results are summarized in Table 5. Careful questioning regarding a change in bowel habit (common in colonic neoplasms) and identification of previous abdominal surgery are the two key points in history taking. Physical examination may not demonstrate abdominal distension if the obstruction is high and the bowel is decompressed by vomiting. Again, palpation of all hernial orifices and a careful rectal examination with stool guaiac test for occult blood are necessary. The plain films of the abdomen also can be unremarkable in proximal obstruction.

Laparotomy

A good summary of common diagnostic pitfalls is given in the study by Yaijko and Steel⁸ of 178 patients in whom laparotomy revealed no abnor-

Table 5. CAUSES OF BOWEL OBSTRUCTION

Cause	Incidence (%)
Hernia	41
Adhesions	29
Intussusception	12
Cancer	10
Volvulus	4
Miscellaneous	4

(Data from Silen W. Cope's early diagnosis of the acute abdomen. 15th ed. New York: Oxford University Press, 1979:149. Reprinted with permission.)