Diarrhea is objectively defined by stool output of more than 200gm per day. A more practical definition is that of decreased stool consistency or more than 3 stools in a 24 hour period. It is useful to distinguish acute diarrhea (onset within the prior 4 weeks) from chronic diarrhea (duration greater than 4 weeks) as the differential diagnosis and management is different.

Infectious agents are responsible for most cases of acute diarrhea. Viruses are the most common cause, including Noroviruses and Rotavirus (the latter in infants and children). Nausea and vomiting often accompany diarrhea with these infections. Food poisoning caused by ingested toxins elaborated by S. aureus, B. cereus and C. perfringens is another common cause of acute diarrhea. The diarrheal illnesses caused by these viruses and bacteria are generally self-limited and require only supportive therapy. If a stool screen for occult blood and fecal leukocytes is negative, it is reasonable to provide supportive therapy and defer additional testing. If occult or gross blood is present, a stool culture should be sent. The most commonly identified bacterial pathogens are Campylobacter jejuni, Salmonella and Shigella. A single specimen is needed as these bacteria are shed continuously. If Enterohemorrhagic E. coli (EHEC) or Yersinia infection are suspected, specific culturing must be requested from the lab. E. coli 0157:H7 is the most common EHEC pathogen and generally presents with abdominal pain and bloody diarrhea in the setting of undercooked meat ingestion. It is important to recognize this organism as antibiotic treatment increases the risk of Hemolytic Uremic Syndrome and should be withheld. A new EHEC, called STEC 0104: H4, linked to produce in Germany, has sickened thousands across Europe, caused 863 cases of HUS and led to 43 deaths as of this writing. Yersinia infection may present with diarrhea and RLQ pain mimicking appendicitis or inflammatory bowel disease. A C. difficile toxin assay should be sent for nosocomial diarrhea or a history of antibiotic use within the prior 2 weeks. If parasitic disease is suspected (e.g. recent travel, day care center exposure, anal intercourse, AIDS), three stool specimens should be tested as shedding of these organisms may be intermittent.

Empiric antibiotic therapy has minimal benefit in most patients with acute diarrhea and may be harmful in patients with Salmonella or EHEC infections. However, a fluoroquinolone should be given to severely ill and immunocompromised patients without these infections. Alternatives include Azithromycin and erythromycin, particularly if fluoroquinolone resistance is suspected. Metronidazole may be initiated while awaiting toxin assay results in patients with suspected C. difficile infection. Rifamixin (Xifaxan) has shown benefit for treatment of traveler’s diarrhea caused by non-invasive E. coli.

The data for use of probiotics in acute diarrheal conditions has been mixed. Several studies and a meta-analysis have shown encouraging results for the prevention or curtailing of traveler’s diarrhea. The data for acute infectious diarrhea has been more variable, due in part to different study methodology and efficacy of different probiotic...
bacteria. Multiple lactobacillus species have shown promise and the treatment appears safe. Probiotics appear to shorten the course of acute infectious diarrhea (by viruses and bacteria) by about 17-30 hours when given in a minimal dose of 10 billion colony forming units in the first 48 hours. The use of probiotics in antibiotic associated diarrhea needs was supported by a recent meta-analysis (Jama May 8th 2012). However many of the 63 RCTs reviewed had serious methodological flaws. More study is needed. Metronidazole and vancomycin remain first line treatment for C, Difficile associated diarrhea (CDAD). A new macrolide antibiotic, Fidaxomicin (Dificid), was recently FDA approved for treatment of CDAD. When given at a dose of 200mg twice daily for 10 days, it had a cure rate similar to vancomycin 125mg po QID for ten days with a significantly lower relapse rate. A rifaximin “chaser” after a course of vancomycin in patients with multiple relapses has shown promise as has fecal bacteriotherapy and the use of probiotics such as Saccharomyces boulardii and Lactobacillus rhamnosus GG

The differential diagnosis for chronic diarrhea is extensive. The most common causes in the U.S. include irritable bowel syndrome, inflammatory bowel disease, malabsorption syndromes (e.g. lactose intolerance and celiac disease), medications and chronic infections. It is helpful to categorize the diarrhea as watery (subdivided into osmotic or secretory), inflammatory or fatty when considering the differential diagnosis. A careful history can help prioritize the differential and direct testing. Endoscopic evaluation, including colonoscopy and sometimes upper endoscopy, is frequently indicated. In difficult cases, calculation of the fecal osmotic gap and consideration of the conditions within each category can help direct additional testing. The stool osmotic gap = 290 – 2 X ([sodium] + [potassium]).

Osmotic diarrhea is characterized by diarrhea that stops with fasting and a large osmotic gap (greater than 125mOsm/kg). The most common exogenous causes of osmotic diarrhea include ingestion of magnesium-containing antacids (e.g. Mylanta, Maalox), laxatives containing poorly absorbed anions (e.g. phosphate, sulfate, citrate), sugar free candies and gum (e.g. contain sorbitol, mannitol) and nonabsorbable fats (e.g. Olestra). Endogenous causes of osmotic diarrhea include congenital lactose and fructose intolerance. Acquired forms of osmotic diarrhea include transient lactase deficiency following gastroenteritis, pancreatic insufficiency and celiac disease.

Secretory diarrhea is typically large volume and persists with fasting. The stool osmotic gap is small (less than 50mOsm/kg). Exogenous causes include stimulant laxatives containing bisacodyl or senna, many medications (e.g. prostaglandins, theophylline, colchicine), and dietary secretagogues (e.g. ethanol, caffeine and colas). Endogenous causes include conditions leading to bile acid malabsorption such as Crohn’s ileitis, small bowel resection and bacterial overgrowth. Hormone-producing tumors (e.g. VIPoma, gastrinoma) are rare causes of secretory diarrhea.

Inflammatory diarrhea is typically mucoid and bloody and often associated with tenesmus, abdominal pain and fever. Common causes include chronic infections (e.g. C.difficile, amebiasis, TB and parasitic infections), inflammatory bowel disease, radiation or chemotherapy-induced mucositis, and colonic ischemia. Stool samples usually test positive for blood and fecal leukocytes. Testing for fecal leukocytes has limited sensitivity (70%) and specificity (50%). In the future, it may be replaced by assessment of fecal calprotectin as a more reliable way to distinguish inflammatory from noninflammatory causes of chronic diarrhea. This zinc and calcium binding protein is
released by neutrophils and monocytes in a number of inflammatory conditions, including inflammatory forms of diarrhea.

Fatty diarrhea is characterized by floating stool, often with fat droplets. The diagnosis can be made by qualitative stool testing (e.g. stool Sudan III stain) or by quantitative testing. The classic quantitative test, the 72 hour fecal fat collection, is uncommonly performed as it is cumbersome and the results not highly reproducible. An abnormal result is excretion of greater than 7 grams of fat in a 24 hour period (on a high fat diet). New, less cumbersome methods, such as the acid steatocrit, have shown fairly good correlation with the quantitative fecal fat collection. This test involves separation of a fecal homogenate into separate lipid, water and solid phases using centrifugation. The lipid component is then measured. Near infrared reflectance analysis (NIRA) is a novel method for evaluating fat malabsorption that appears to be as accurate as the 72 hour fat collection and allows simultaneous measurement of fecal fat, carbohydrates and nitrogen on a single stool sample. The use of NIRA is growing in Europe and starting in the U.S. It may become the method of choice for assessing fat malabsorption in the future. The most common causes of fatty diarrhea include pancreatic insufficiency, Crohn’s disease, short bowel syndrome and bacterial overgrowth.

The history is directed towards characterizing the stool as watery, bloody or fatty. It is also helpful for prioritizing the differential diagnosis and distinguishing organic from functional etiologies. Indicators of a functional etiology include a long duration of symptoms (e.g. greater than one year) with lack of significant weight loss, the absence of nocturnal diarrhea, straining with defecation and the absence of dehydration or hypokalemia.

Initial laboratory testing should include CBC with differential, electrolyte panel, total protein and albumin, thyroid function tests and sedimentation rate. Markers of malabsorption such as iron studies, vitamin B12, folate and Prothrombin time should also be considered as well as a sprue serology (e.g. tissue transglutaminase antibody). Initial stool testing should include fecal occult blood testing, fecal leukocytes, C. difficile toxin (if antibiotic history) and stool culture, three samples for ova and parasites and an ELISA for Giardia antigen. Pathogens that can be associated with chronic diarrhea include C. difficile, Campylobacter, Aeromonas, Pleisiomonas, Ameba, Giardia, Cryptosporidium, Cyclospora and Whipple’s disease.

Endoscopic evaluation is usually warranted. In general, colonoscopy is the preferred test, especially for individuals over the age of 45, with iron deficiency or suspected Crohn’s disease. In selected patients, upper endoscopy may be helpful to rule-out sprue or Whipple’s disease.

In cases of chronic diarrhea that defy diagnosis, it is helpful to first ensure that one has carefully assessed for common problems overlooked, including lactose intolerance, fecal incontinence and medication-induced diarrhea. The osmotic gap should be calculated if not previously assessed.

A laxative screen should be obtained to uncover inadvertent or surreptitious laxative use. Some experts have suggested early consideration and assessment for factitious diarrhea to help limit other expensive testing. This opinion is based on data suggesting that factitious diarrhea accounts for 20% of cases evaluated at tertiary referral centers. Factitious diarrhea may be dilutional (osmolality less than 290), osmotic or secretory. A laxative screen should include urine assessment for anthraquinones (e.g. senna, cascara, rhubarb and aloe), phenolphthalein (use banned in the U.S.) and bisacodyl
(e.g. Dulcolax, Correctol). Stool assessment for phosphate and magnesium should be performed. Repeat analysis may be required as well as a hospital admission for controlled evaluation.

In difficult cases of secretory diarrhea, plasma peptide secretagogue levels should be measured, including VIP, gastrin, glucagon and calcitonin. A 24 hour urine collection is a sensitive test for carcinoid. CT scan imaging should be performed to look for pancreatic neoplasm, intestinal lymphoma and tuberculosis. In the appropriate setting, mesenteric angiography (CT or MRA) should be considered to assess for mesenteric ischemia.

In difficult cases of inflammatory diarrhea, plasma peptide secretagogue levels should be measured, including VIP, gastrin, glucagon and calcitonin. A 24 hour urine collection is a sensitive test for carcinoid. CT scan imaging should be performed to look for pancreatic neoplasm, intestinal lymphoma and tuberculosis. In the appropriate setting, mesenteric angiography (CT or MRA) should be considered to assess for mesenteric ischemia.

In difficult cases of secretory diarrhea, plasma peptide secretagogue levels should be measured, including VIP, gastrin, glucagon and calcitonin. A 24 hour urine collection is a sensitive test for carcinoid. CT scan imaging should be performed to look for pancreatic neoplasm, intestinal lymphoma and tuberculosis. In the appropriate setting, mesenteric angiography (CT or MRA) should be considered to assess for mesenteric ischemia.

In difficult to diagnose cases of inflammatory diarrhea, a small bowel follow-through can assess for inflammatory bowel disease involving this region. Capsule endoscopy is playing an increasingly important role in assessing small bowel pathology. If a qualitative fecal fat assessment like the Sudan stain indicates fat malabsorption, several tests are available to assess for pancreatic insufficiency: Pancreatic imaging can be obtained to look for evidence of chronic pancreatitis; MRI/MRCP is proving capable of providing detailed information regarding pancreatic parenchymal and ductal morphology that rivals ERCP in sensitivity. Promising non-invasive tests for pancreatic insufficiency include stool fecal elastase or chymotrypsin measurement and the urine Pancreolauryl test (also known as the Fluorescein Dilaurate test). Alternatively, gauging a patient’s response to a trial of pancreatic enzymes can help to discern clinically significant exocrine pancreatic insufficiency.

The evaluation of chronic diarrhea is often time-consuming (and expensive). Therapeutic interventions should be employed during the evaluation to improve quality of life. Opiates such as Loperamide, Lomotil and tincture of Opium drops (DTO) have proven effective in many cases. Cholestyramine is a nonspecific binding agent and also binds excess bile, ameliorating diarrhea by several mechanisms. An empiric trial of antimicrobial therapy may be pursued to ascertain if bacterial overgrowth is perpetuating chronic diarrhea. Finally, Octreotide can often control even severe cases of chronic diarrhea.

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