Chapter 1

Gastrointestinal disorders

A. Peptic ulcer disease

Clinical synopsis

Peptic ulcer disease (PUD) is a general term describing a group of acid-peptic disorders of the upper gastrointestinal (GI) tract including the esophagus, stomach, and duodenum. A peptic ulcer is defined as a circumscribed loss of tissue or break that occurs in the GI mucosa extending through the GI tract smooth muscle. There is an imbalance between gastric acid and pepsin and mucosal defense factors, including prostaglandins, which protect the stomach by increasing the production of gastric mucus and reducing the production of gastric acid.

There are three types of peptic ulcers: gastric ulcer, which occurs in the stomach; duodenal ulcer, which occurs in the duodenum; and esophageal ulcer, which occurs in the esophagus. Most peptic ulcers are asymptomatic; however, the more commonly seen symptoms in symptomatic ulcers are midepigastric pain, dyspepsia (indigestion), nausea, fullness, nocturnal pain, anorexia, and weight loss. One of the distinguishing features of gastric ulcer is the presence of stomach pain after eating. When pain occurs hours after eating or on an empty stomach accompanied with pain at night, it is duodenal ulcer (Peters *et al.* 2010). The classical epigastric pain in a duodenal ulcer occurs when acid is produced and secreted in the absence of food in the stomach.

The Dentist's Quick Guide to Medical Conditions, First Edition. Mea A. Weinberg, Stuart L. Segelnick, Joseph S. Insler, with Samuel Kramer.

Table 1.1 Medications for peptic ulcer disease and gastroesophageal reflux disease.

Generic drug	Brand name
Proton pump inhibitors (PPI)	
Dexlansoprazole	Dexilant
Esomeprazole	Nexium
Lansoprazole	Prevacid
Omeprazole	Prilosec
Pantoprazole	Protonix
Rabeprazole	AcipHex
Histamine-2 receptor antagonists (H2RAs)	
Cimetidine	Tagamet
Famotidine	Pepcid
Nizatidine	Axid
Ranitidine	Zantac
Prostaglandin supplements	
Misoprostol (prevention of gastric and duodenal ulcers due to nonsteroidal anti-inflammatory drugs)	Cytotec
Protective barrier drug	
Sucralfate (for healing of duodenal ulcers, not gastric ulcers)	Carafate
Gastrointestinal stimulant drug	
Metoclopramide	Reglan

The two most common causes of PUD are chronic nonsteroidal anti-inflammatory drugs (NSAIDs) use and *Helicobacter pylori* (*H. pylori*), a Gram-negative bacterium, which resides in the GI mucosal lining and in certain individuals can erode the mucosa resulting in ulceration. Even though the majority of duodenal ulcers are caused by *H. pylori*, only 5–10% will develop ulcers (Malfertheiner *et al.* 2009; Peters *et al.* 2010). The definitive diagnosis of PUD is generally made by an upper GI endoscopy (Peters *et al.* 2010).

Diagnostics/lab values

If it is certain that the ulcer is not caused by chronic NSAID use, a blood test to detect the presence of *H. pylori* antibodies is a noninvasive test. Although the test has high sensitivity and specificity when lab serology is used, it cannot discriminate if it is a current infection or previous exposure. Additionally, IgG testing may be positive for many years after treatment and eradication of the bacteria. Saliva can also be used but there is low sensitivity and specificity (Meurer and Bower 2002). Urea breath test (UBT) and fecal antigen test are the other preferred methods for diagnosing the presence of *H. pylori* before administration of antibiotic and antisecretory drugs (Peters *et al.* 2010). The UBT is utilized to confirm the eradication of *H. pylori*. Recurrence of *H. pylori* infection usually is defined by a positive result on urea breath or stool antigen testing six or more months after documented successful eradication therapy (Ables *et al.* 2007).

Medications

Management of PUD can differ depending upon whether the etiology is NSAID use or *H. pylori* infection. Antibiotics are used to eradicate *H. pylori* infection. Proton pump inhibitors (PPIs) and histamine-2 receptor antagonists (H_2RAs) provide quick pain relief and accelerated healing of the ulcer (Table 1.1). H2 receptor blockers reduce histamine-stimulated gastric acid secretion by competitively inhibiting

H_2 receptors on the parietal cells in the stomach. These agents have a limited effect on gastric acid secretion after food ingestion and are effective in healing ulcers in 6–12 weeks. Antacids are used for the treatment of dyspepsia. PPIs provide rapid symptomatic relief with accelerated healing of duodenal ulcers, thus providing the most rapid symptom relief and highest percentage of esophageal healing of all agents used in gastroesophageal reflux disease (GERD) management. They are the drug of choice for patients with frequent daily symptoms, patients with moderate to severe GERD symptoms, patients not responding to H_2RAs, and patients with complicated disease, including Barrett's esophagus and esophagitis.

For NSAID-induced peptic ulcer, an H_2 antagonist or PPI is prescribed. Antacids are recommended for the epigastric pain. Antibiotics are not prescribed.

Management of non–NSAID-induced peptic ulcer that is positive to *H. pylori* includes systemic antibiotics and H_2 antagonists or PPIs. Over the years, resistance to antibiotics is emerging. The goal of treating ulcers is the elimination of *H. pylori*, which will increase healing of the ulcer, improve symptoms, and reduce recurrence. Although the management of *H. pylori* is being continuously investigated, currently, the accepted protocol for *H. pylori* eradication (Box 1.1) is quadruple or triple therapy; usually, it is triple therapy. The drawback of therapy is low adherence because of the vast number of medications that have to be taken for 14 days; *H. pylori* cannot be eradicated with just one antibiotic or medication.

Helicobacter pylori has been found in dental biofilms, and its appearance varies from one site to another in the oral cavity (Kilmartin 2002). Individuals with gastric *H. pylori* were positive for oral *H. pylori* also (Anand *et al.* 2006). Other studies have found that patients with the presence of *H. pylori* in dental plaque had a greater prevalence of gastric infection (Lui *et al.* 2009). It has been theorized that antibiotics used to eliminate gastric *H. pylori* do not eliminate *H. pylori* in dental plaque and can be a source of future reinfection (Anand *et al.* 2006).

Dental drug–drug interactions/adverse reactions

Common dental drug-peptic ulcer disease drug interactions are listed in Table 1.2.

Oral adverse reactions of medications/disease (McGrath *et al.* 2008)

Common oral adverse reactions of medications/disease are:

- Antacids and bismuth can cause black hairy tongue.
- Metronidazole can cause a metallic taste in the mouth.
- Clarithromycin can cause a metallic taste in the mouth.
- Tetracycline can cause black hairy tongue.
- GERD can cause erosion of enamel.

Box 1.1 Therapy for *H. pylori* Management (http://www.fpnotebook.com/GI/ID/HlcbctrPylr.htm; Ables *et al.* 2007; Chey and Wong, 2007; Peters *et al.* 2010).

Quadruple Therapy

- Metronidazole (Flagyl) 250 mg four times a day +
- Tetracycline 500 mg four times a day +
- Bismuth subcitrate (Pepto-Bismol) 525 mg four times a day +
- Antisecretory drug (up to 6 weeks): omeprazole (Prilosec) 20 mg twice a day OR esomeprazole 20–40 mg daily OR lansoprazole (Prevacid) 20 mg twice a day OR pantoprazole (Protonix) 40 mg twice a day OR rabeprazole (Aciphex) 20 mg twice a day

Triple Therapy

- Amoxicillin 500 mg twice a day
- Clarithromycin (Biaxin) 1000 mg twice a day
- Metronidazole (Flagyl) 500 mg twice a day (only use if allergic to penicillin)
- Prevpac is a combination product containing pantoprazole, clarithromycin, and amoxicillin.

Table 1.2 Dental drug–drug interactions (www.rxlist.com; Peters *et al.* 2010).

Prescribing dental drug	Peptic ulcer disease drug	Management
Ketoconazole	Proton pump inhibitors, histamine-2 receptor antagonists	Not as effective in a less acidic stomach environment
Doxycycline, tetracycline (if it is not being prescribed as quadruple therapy)	Antacids (e.g., Mylanta, Maalox, and Gelusil contain aluminum hydroxide), calcium tablets, zinc, iron	Antacids that contain di- or trivalent ions (Mg^{2+}, Ca^{2+}, Al^{3+}) bind to and form an insoluble complex with tetracyclines, which will decrease the absorption *rate* of these antibiotics. Thus, antacids should not be given concurrently with these antibiotics but 1–2 h before or after taking the antibiotics. Kaolin (in Kaopectate) binds to the tetracycline molecule and decreases the absorption rate of the antibiotic. Do not take Kaopectate together with tetracycline. It is best to wait 1–2 h before or after taking kaolin or the antibiotic.
Ciprofloxacin (Cipro)	Antacids, calcium tablets, zinc, iron	Di- or trivalent ions (Mg^{2+}, Ca^{2+}, Al^{3+}) containing antacids bind to and form an insoluble complex with fluoroquinolones, which will decrease the absorption *rate* of these antibiotics. Thus, antacids should not be given concurrently with these antibiotics but 1–2 h before or after taking the antibiotics.

B. Gastroesophageal reflux disease

Clinical synopsis

GERD is one of the most common chronic conditions of the upper GI tract. In GERD, there is a reflux or "backing up" of gastric contents from the stomach into the esophagus, which generally occurs in many individuals without causing any complications and damage to the mucosal lining of the esophagus. The most common complaint or symptom is heartburn, but the individual may also complain of epigastric pain.

If the acidic gastric contents stay in contact for prolonged periods of time with the mucosal tissue of the esophagus, a form of GERD called reflux esophagitis will develop, which is characterized by inflammation of the esophagus due to excessive acid reflux. Acid reflux into the oral cavity may cause the development of tooth erosion, particularly on the palatal surfaces of the maxillary incisors. Esophagitis results from excessive reflux of gastric juices rather than excessive acid secretion in the stomach as seen in PUD. Other complications from GERD include dysphagia (difficulty in swallowing) and esophageal ulcers.

Medications

Antacids are primarily used in the treatment of dyspepsia (indigestion or heartburn). Antacids are basic salts that dissolve in gastric acid secretions and neutralize some but not all gastric hydrochloric acid and have a greater effect of increasing the pH in the duodenum than in the stomach. Antacids neutralize or reduce the *acidity* of gastric juices, but they do not affect the rate or amount of gastric acid secretion by the stomach cells and do not prevent ulcer recurrence. Rather, antacids are usually used to relieve occasional duodenal ulcer symptoms or GERD on an as-needed basis by the patient.

The first-line drug therapy for GERD is antacids and a nonprescription H_2RA such as famotidine (Pepcid) or a PPI such as omeprazole (Prilosec). Given the chronic nature of GERD and the high recurrence rates if acid suppressive therapy is discontinued, long-term maintenance therapy is appropriate and indicated for most patients.

Lab tests

There are no specific laboratory tests for GERD that dentists need to know for dental treatment.

Medications: Drugs used to treat GERD include the following

- Antacids
- H_2RAs
- PPIs

Dental notes: PUD and GERD

1. There are no precautions or contraindications with epinephrine and antacids, H_2RAs, or PPIs.
2. Note all drug–drug interactions that can occur with medications used for PUD/GERD.
3. If a patient requires an antibiotic for a dental infection and since the patient is already taking amoxicillin and clarithromycin, the dose of these antibiotics should not be increased but rather a different class of antibiotic should be prescribed such as clindamycin.
4. Question the patient regarding the use of OTC and prescription NSAIDs (e.g., Advil and Aleve) and antacids. Avoid recommending or prescribing NSAIDs in patients with a previous history or current history of peptic ulcers/GERD.
5. Avoid prescribing steroids in patients with PUD.
6. Remember to ask patients if they are taking any OTC medications for their ulcer or GERD. Many of these medications are available OTC (e.g., antacids, Tagamet, and Prilosec).
7. Patients that have GERD and are taking only antacids should not take tetracycline or doxycycline concurrently with the antacid; wait for 1–2 h.
8. Black hairy tongue due to antacids, bismuth subsalicylate, and tetracycline is temporary and will disappear when the medications are stopped.
9. Patients with gastroesophageal reflux may present with oral symptoms, including burning mouth and tooth erosion. In fact, GERD is a differential diagnosis for burning mouth symptoms.
10. Place the patient in a semi-supine position in the dental chair.
11. Recommend reducing acid content in the mouth with sodium bicarbonate mouthrinse.
12. Recommend to apply in-office fluoride and possible prescription for home-applied fluoride for GERD patients.

C. Irritable bowel syndrome

Clinical synopsis

Irritable bowel syndrome (IBS) is a noninflammatory condition that consists of chronic or recurrent GI symptoms that are diagnosed only clinically without any specific laboratory test or any biological cause. IBS causes a dysregulation in the functions of the intestinal motor, sensory and central nervous systems resulting in altered bowel habit (American Gastroenterology Association 2002). The main GI and non-GI symptoms include diarrhea, bloating, constipation, and increased urinary frequency. Irritable bowel symptoms can also be associated with other conditions such as ulcerative colitis (UC) or Crohn's disease (CD) (Ringel and Drossman 2000).

The clinical diagnosis of IBS is usually based on the Rome criterion, which requires the presence of abdominal pain or discomfort to make a definitive diagnosis of IBS (Thompson *et al.* 2000). Additionally, the biopsychosocial approach melds the physiologic and psychosocial aspects to the overall diagnosis (Drossman *et al.* 1997; Ringel and Drossman 2000).

There is also a rating for the severity of pain, and management is based on this severity. For example, if the symptoms are mild, then only dietary and lifestyle changes and patient education are recommended. Moderate symptoms most likely will require medications and psychological therapy. Severe symptoms may require the addition of antidepressants (Olden and Schuster 1997; Engstrom and Goosenberg 1999).

Medications

The pharmacologic management of IBS poses a therapeutic challenge since there are multiple symptoms, sometimes nonspecific, that cannot be managed with just a single drug. Most of the medications used to manage IBS have not changed in the past few decades and are aimed at controlling the abdominal pain and bloating, constipation, and diarrhea (Engstrom and Goosenberg 1999). The following are the medications indicated for IBS:

- Antimotility drugs such as loperamide (Imodium) and adsorbents such as bismuth salicylate (Pepto-Bismol, Kaopectate) indicated for diarrhea
- Bile acid sequestrant such as cholestyramine (Questran powder) indicated for diarrhea from excess bile acids and could cause constipation
- Laxatives for constipation. Chronic laxative use may lead to hypokalemia.
- Antispasmodic/anticholinergics: dicyclomine (Bentyl), chlordiazepoxide/clidinium bromide (Librax), phenobarbital, hyoscyamine, atropine, scopolamine (Donnatal), and hyoscyamine (Levsin) indicated for abdominal cramping pain and bloating
- Tricyclic antidepressants (TCAs) such as amitriptyline (Elavil) or selective serotonin reuptake inhibitors are for the psychological component of the IBS
- Nonnarcotic analgesics are indicated for pain relief as narcotic analgesics increase the incidence of constipation.

Probiotics are live organisms formulated from bacteria found in the GI tract. The rationale for its use is based on the theory that endogenous intestinal microflora play a crucial role in the pathogenesis of disorders such as IBS and UC (Quigley 2007). Probiotics are intended to restore the normal intestinal flora that may have been altered in the disease state due to stasis and reduced colonic transit time (Boynton and Floch 2013). Common encountered dental drug interactions are listed in Table 1.3.

Table 1.3 Dental drug–drug interactions (www.drugs.com; www.rxlist.com).

Dental drug prescribed	Irritable bowel syndrome drug	Management
Acetaminophen/ hydrocodone; acetaminophen/ codeine; acetaminophen/ oxycodone	Bismuth subsalicylate (Kaopectate; Pepto-Bismol)	Can increase blood levels or adverse reaction of either medication. Severe abdominal cramps or bloating can occur. Use with caution or substitute another analgesic.
Doxycycline, tetracycline	Bismuth subsalicylate (Kaopectate; Pepto-Bismol)	May decrease the effect of doxycycline; space dosing 2–3 h apart.
Penicillins	Cholestyramine (Questran)	When administered concurrently reduces rate of absorption. Separate doses 1–2 h apart.
Epinephrine in local anesthetic	Tricyclic antidepressants (TCAs)	TCAs inhibit the reuptake of norepinephrine via the NE reuptake pump allowing NE to stay in the synapse helping to relieve antidepressant symptoms. Epinephrine works similar to TCAs, through the reuptake pump. So, when the reuptake pump is not working, there will be enhanced accumulation of epinephrine (EPI) and norepinephrine (NE) in the synapse resulting in hypertension and cardiac arrhythmias. Epinephrine is NOT contraindicated but just the amount has to be limited to two cartridges of 1:100,000. Levonordefrin is CONTRAINDICATED. This drug–drug interaction DOES NOT occur with selective serotonin reuptake inhibitors

Dental notes

- Since patients with IBS may be taking numerous medications for their symptoms, it is important to ask at every dental visit what prescription and OTC drugs they are taking.
- Remember to limit the amount of epinephrine to two cartridges of 1:100,000 if the patient is taking a TCA.
- Avoid codeine and derivatives including hydrocodone and oxycodone if the patient is already constipated from IBS.

D. Inflammatory bowel disease (CD and UC)

a. Crohn's disease

Medical synopsis

CD is a chronic condition that can occur anywhere in the entire GI tract from the oral cavity to the rectum; however, the lower part of the small intestine is mostly affected (Ganda 2013). Chronic

inflammation occurs with increased number of white blood cells (WBCs) in the lining of the duodenum resulting in ulceration. Chronic blood loss can lead to the development of anemia. Symptoms of CD include chronic diarrhea, abdominal pain, weight loss, fever, and nausea/vomiting.

Oral features (Engstrom and Goosenberg 1999)

- The oral cavity especially the gingiva and buccal mucosa may appear to be swollen. In severe attacks, there may be oral candidiasis (thrush) and aphthous ulcerations.
- Patients may be deficient in vitamin B12 due to malabsorption. Orally this may manifest as glossitis, oral candidiasis, erythematous mucositis, and pale oral mucosa (Pontes *et al*. 2009).
- Bleeding may be a problem due to abnormal liver function; evaluate the patient's CBC and liver function test profile before dental treatment (Ganda 2013).

Diagnosis/lab tests

Diagnosis of CD is based on signs and symptoms, computed tomography (CT) or MRI, and endoscopy with biopsy. The disease severity is categorized into mild to moderate, moderate to severe, or severe to fulminant (American College of Gastroenterology *et al.* 1997).

Medications

Medications indicated in the treatment of CD include anti-inflammatories and antibiotics (American College of Gastroenterology *et al.* 1997).

For mild to moderate CD:

1. Oral 5-aminosalicylate (e.g., mesalamine, sulfasalazine) is a bowel-specific anti-inflammatory class of drugs that are metabolized by the normal flora in the bowel, which allows for the drug to work at the site of inflammation.
2. Metronidazole is prescribed when patients do not respond to oral aminosalicylate drugs. Metronidazole is antibacterial as well as anti-inflammatory and is recommended in the treatment of *Clostridium difficile* infections.

For moderate to severe CD:

1. Systemic corticosteroids (e.g., prednisone and methylprednisolone)
2. Immunosuppressant or immunomodulator drugs (e.g., 6-mercaptopurine, azathioprine, and cyclosporine). The CBC and absolute neutrophil count should be reviewed before starting dental treatment (Ganda 2013).
3. Anti–tumor necrosis factor (anti-TNF) drugs [e.g., adalimumab (Humira), infliximab (Remicade), and certolizumab (Cimzia)] reduce the synthesis of elevated TNF, thus reducing inflammation. Indicated for patients that do not respond to other drugs.
4. Antibiotics such as tetracycline, clarithromycin, ciprofloxacin, or metronidazole for intestinal infection.
5. Antidiarrheal medications [e.g., loperamide (Imodium), diphenoxylate (Lomotil), and bismuth subsalicylate (Kaopectate)]
6. Hydration: The patient may need to use the restroom frequently.

For severe to fulminant CD:

1. Hospitalization
2. Parenteral steroids and antibiotics

Dental notes

- Patients on long-term systemic steroids may present with steroid-induced diabetes mellitus, which is a risk factor for periodontal diseases. The patient's periodontal condition should be closely monitored.
- Epinephrine is synthesized and secreted by the adrenal medulla and can safely be used in patients taking a systemic steroid such as prednisone.
- Cyclosporine, an immunomodulator, may cause gingival enlargement. As long as the patient is taking this drug, there will be gingival enlargement. Meticulous plaque control is important. In severe cases, periodontal surgery may be indicated to excise the gingival overgrowth; however, it will recur as long as the patient continues to take cyclosporine.
- Avoid prescribing codeine or derivatives including hydrocodone and oxycodone if the patient is taking an antidiarrheal medication.
- Some patients may take omega-3 fatty acids, which may increase the risk of bleeding. Caution should be used when performing invasive dental procedures.
- Metronidazole may cause a metallic taste in the mouth. Do not prescribe an alcoholic mouthrinse while the patient is taking metronidazole.
- A significant adverse reaction to anti-TNF drugs is *oral tuberculosis* and oral candidiasis (thrush)/oral ulcers (www.rxlist.com). The oral cavity infrequently becomes a site for extrapulmonary tuberculosis; however, if it happens clinically it may show ulcerated lesions on the tongue, gingiva, and palate. Diagnosis is confirmed by biopsy, histopathology, sputum, and immunology (Nanda *et al.* 2011). Treatment of extrapulmonary tuberculosis is the same as for pulmonary tuberculosis (Ferguson and McCormack 1993).
- If the patient is taking tetracycline, clarithromycin, ciprofloxacin, or metronidazole and concurrently has a dental infection and requires an antibiotic, do not increase the dose of the current antibiotic but rather prescribe a different antibiotic. Remember that tetracycline and clarithromycin are bacteriostatic, so prescribing clindamycin would be appropriate since it is also bacteriostatic. If the patient is taking metronidazole, which is bactericidal, then penicillin, which is also bactericidal, would be appropriate. Hence, if the patient is taking a bacteriostatic antibiotic, it is contraindicated to prescribe a bactericidal antibiotic and vice versa.
- The adrenal cortex normally produces and secretes cortisol, an endogenous hormone, in the body. When exogenous steroids (e.g., prednisone and methylprednisolone) are taken, the adrenal gland shuts off. In the normal, nonstressed person, about 20–30 mg of cortisol is produced per day, which is equivalent to about 5–7 mg of prednisone. Cortisol is released in a highly irregular manner with peak secretion in the early morning, which then tapers out in the late afternoon and evening. When a person is stressed, cortisol production is increased to about 50–300 mg/day. Cortisol functions to regulate energy by selecting the right type and amount of substrate (carbohydrate, fat, or protein) that is needed by the body to meet the physiological demands that are placed upon it. Cortisol mobilizes energy by moving the body's fat stores (in the form of triglycerides) from one area to another or delivering it to hungry tissues such as working muscles. During stressful times, higher levels of cortisol are released, which has been associated with several medical conditions including suppressed thyroid function and hyperglycemia; however, when taking exogenous steroids, the person's endogenous production is stopped and there may not be enough endogenous cortisol to handle the body's stressful demands. For this reason, in the past, patients on long-term systemic steroid have been advised to take supplemental glucocorticoids. *A medical consultation is necessary before any additional steroids are prescribed.*
- An "older" theory concerning the need for steroid supplementation in patients taking steroids was called the "rule-of-twos," which stated that if the patient was currently on 20 mg of cortisone (equivalent to 5 mg prednisone) daily for 2 weeks or longer within the past 2 years, then it was necessary to give supplemental steroids to prevent an adrenal crisis.

Adrenal crisis is associated with a stressful event that is caused by the failure of cortisol levels to meet the body's increased requirements for cortisol and is primarily a mineralocorticoid steroid deficiency, not a glucocorticoid deficiency. Mineralocorticoids (e.g., aldosterone) maintain the level of sodium and potassium in the body. Adrenal crisis, a medical emergency that occ*urs very rarely in dental patients,* is characterized by abdominal pain, weakness, hypotension, dehydration, and nausea and vomiting (Khalaf *et al.* 2013). It has been concluded in clinical studies that *patients on long-term steroid drugs do not require supplemental "steroid coverage*" for routine dentistry, including minor surgical procedures under profound local anesthesia with adequate postoperative pain control (Miller *et al.* 2001). The low incidence of significant adrenal insufficiency precludes the addition of supplemental steroids (Gibson and Ferguson 2004). For major oral/periodontal surgery under general anesthesia, supplemental steroids may be required depending upon the dose of steroid and duration of treatment. It is important to obtain a medical consultation from the patient's physician.

The final conclusion is that adrenal crisis is a rare event in dentistry, especially for patients with secondary adrenal insufficiency who develop this condition from taking steroids for common medical conditions. Most routine dental procedures, including nonsurgical periodontal therapy (scaling and root planing) and restorative procedures, can be performed without glucocorticoid supplementation.

- See Tables 1.2 and 1.3 for dental drug interactions.

b. Ulcerative colitis

Clinical synopsis

UC is a chronic condition causing inflammation and ulceration of the mucosa of the colon. It usually begins in the rectum and may involve various lengths of the colon over time or at the same time (Engstrom and Goosenberg 1999). The etiology is unclear, and it is diagnosed by positive WBC and bacteria in the stool, sigmoidoscopy, colonoscopy, barium enema, and X-rays. If the patient has recently taken antibiotics, the stool should be tested for the presence of *Clostridium difficile*. Stress, NSAIDs, and some antibiotics (e.g., penicillin, erythromycin, and quinolones such as ciprofloxacin) have been reported to cause inflammatory bowel disease (Singh *et al.* 2009).

Lab tests

UC is diagnosed based on the presence of WBCs and bacteria in stool samples. UC can occur as a result of recent antibiotic exposure with the development of *Clostridium difficile* (Engstrom and Goosenberg 1999). Additionally, a signoidoscopy or colonoscopy is performed to determine the extent of the colitis (Engstrom and Goosenberg 1999). Other diagnostic tools include X-rays and barium enema.

There are no laboratory values that are important for dentistry. Iron deficiency may result from the chronic blood loss. Additionally, hypokalemia and hypoalbuminemia may occur. Also, there may be abnormal liver function tests.

Medications

Management of UC depends on the severity of the disease and is very similar to the drugs prescribed for CD (Lichenstein *et al.* 2009; Lichenstein 2011). There is no curative pharmacological treatment, and drugs are used to induce and maintain remission (Gledhill and Bodger 2013). The following drugs are used in the management of mild to moderate UC (American College of Gastroenterology *et al.* (1997); Kornbluth and Sachar 2010).

1. Oral 5-aminosalicylate (e.g., mesalamine and sulfasalazine) is a bowel-specific anti-inflammatory class of drugs that are metabolized by the normal flora in the bowel, which allows for the drug to work at the site of inflammation.
2. Topical mesalamine enema (foam or suppository) or hydrocortisone (enema or foam)
3. Oral corticosteroids (e.g., prednisone and methylprednisolone)
4. Immunosuppressant or immunomodulator drugs (e.g., 6-mercaptopurine, azathioprine, and cyclosporine)
5. Metronidazole is prescribed when patients do not respond to oral aminosalicylate drugs. Metronidazole is antibacterial as well as anti-inflammatory and is recommended in the treatment of *Clostridium difficile* infections.
6. Omega-3 fatty acids have an anti-inflammatory action and are used in the management of active UC but not when the patient is in remission.
7. Anti-TNF drugs [e.g., adalimumab (Humira), infliximab (Remicade), and certolizumab (Cimzia)] reduce the synthesis of elevated TNF thus reducing inflammation. These drugs are indicated in severe refractory CD.
8. Newest therapy: Integrin antagonists (e.g., vedolizumab) inhibit leukocyte adhesion which inhibits inflammation. This drug is used to induce remission in UC (Gledhill and Bodger 2013).

Dental drug–drug interactions

- Mesalamine + NSAIDs [e.g., ibuprofen and naproxen sodium (Aleve)] may increase the risk of renal reactions. It is best to avoid both the drugs. Recommend or prescribe another analgesic.

Oral features

- The oral cavity especially the gingiva and buccal mucosa may appear to be swollen. In severe attacks, there may be oral candidiasis (thrush) and aphthous ulcerations. Oral aphthous ulcers occur in about 10% of patients with UC and usually will disappear when the disease is in remission.
- Patients may be deficient in vitamin B12 due to malabsorption. Orally this may manifest as glossitis, oral candidiasis, erythromatous mucositis, and pale oral mucosa (Pontes *et al*. 2009).
- Bleeding may be a problem due to abnormal liver function; evaluate the patient's CBC and liver function test profile before dental treatment (Ganda 2013).

Key notes

Key notes are the same as for CD. See the dental notes given earlier.

1. In addition, clindamycin should be prescribed with caution in patients with colitis or regional enteritis.

E. Diverticular disease

Clinical synopsis

Diverticular disease is divided into diverticulitis and diverticulosis. Diverticular disease is a condition where herniation of the mucosa of the colon occurs communicating with the muscle layer of the colon rather than the entire layers of the bowel wall, which is a congenital condition (Wilkins *et al.* 2013). It usually occurs in individuals over the age of 50 (Engstrom and Goosenberg 1999). Diverticular disease includes diverticulosis and diverticulitis, which are the same except that inflammation and diverticulum perforation are present in the latter and it is usually a more severe condition

than diverticulosis. In the USA, by the age of 80, approximately 70% of individuals have diverticulosis (Shaheen *et al*. 2006).

Diverticulosis is usually asymptomatic, and individuals go through life maybe not even knowing that they have the disease, but some clinical signs and symptoms that can occur include constipation, abdominal pain in lower left abdomen, and flatulence. In about 15–40% of patients, there is an accompanied diverticular (lower GI) bleeding (Engstrom and Goosenberg 1999).

Dental features

There are no corresponding oral lesions associated with diverticular diseases.

Diagnosis/lab values

CT is recommended for the diagnosis of diverticulosis and determining the extent and severity of the disease. Colonoscopy is recommended 4–6 weeks after resolution of symptoms for patients with complicated disease (Wilkins *et al.* 2013).

Medications

Treatment for diverticular disease is based on the presence of symptoms (Boynton and Floch 2013). For uncomplicated or asymptomatic diverticular disease, the only treatment is to increase fiber in the diet, which increases the bulk of stool, lowers colonic pressure, and increases transit time through the colon (Engstrom and Goosenberg 1999). For symptomatic diverticulitis, additional therapy includes bowel rest, antibiotics, analgesics, anticholinergic and antispasmodic agents (for some patients), and surgery (for selected cases) (Boynton and Floch 2013).

In colonic diverticulosis, the content of the colon is static, which can ultimately cause a bacterial overgrowth and result in a chronic mucosal inflammation (Ventrucci *et al*. 1994; Colecchia *et al*. 2003; Boynton and Floch 2013). Rifaximin (Xifaxan), a poorly absorbed antibiotic, is recommended for this condition. Since it is poorly absorbed into the bloodstream, it remains in the GI tract longer which allows for its efficacy. Rifaximin can also be used in IBS. There are no documented dental drug interactions with rifaximin. Mesalamine is prescribed for the anti-inflammatory effect.

Dental drug–drug interactions

- Mesalamine + NSAIDs [e.g., ibuprofen and naproxen (Aleve)] may increase the risk of renal reactions. It is best to avoid both the drugs. Recommend or prescribe another analgesic.

Dental notes

1. Avoid prescribing codeine in patients with diverticular disease to prevent further constipation.
2. Avoid recommending or prescribing NSAIDs to patients taking mesalamine.

F. Acute pancreatitis

Clinical synopsis

Acute pancreatitis is primarily caused by alcoholism and alcohol abuse and gallstones. Other factors include genetic, autoimmune, damage or injury to the pancreas, Reyes syndrome, cystic fibrosis,

hyperparathyroidism, and hypertriglyceridemia (Banks and Freeman 2006). Most cases are treated in the hospital and will probably not be seen in the dental office.

G. Celiac sprue

Clinical synopsis

Celiac sprue or celiac disease is a genetic/autoimmune disease of the small intestine.

Medications

None. Gluten-free diet is the only effective treatment.

Dental drug–drug interactions

Since treatment is solely through change of diet with a gluten-free diet, there are no drug–drug interactions relating to dentistry.

Dental notes

- There may be affected dental enamel defects in patients, especially children, with celiac disease. Enamel defects include tooth discoloration (white, yellow, or brown), enamel pitting, and a mottled or translucent appearance to the teeth. These tooth defects are usually seen on the incisors and molars. If all other systemic diseases are ruled out, referral to a gastroenterologist is recommended (Malahias *et al*. 2009)
- Celiac disease may be associated with an increased incidence of recurrent aphthous ulcers, atrophic glossitis, dry mouth, and squamous cell carcinoma.

H. Pseudomembranous colitis

Clinical synopsis

Clostridium difficile-associated diarrhea (CDAD) or pseudomembranous colitis has been reported with the use of nearly all antibacterial agents, not only clindamycin but almost any broad-spectrum antibiotic, and may range in severity from mild diarrhea to fatal colitis. CDAD may or may not be due to antibiotic usage. Antibiotic-associated diarrhea may be constant and watery/bloody diarrhea (new onset of more than three partially formed or watery stools per 24 h period). Treatment with antibacterial agents alters the normal flora of the colon leading to the overgrowth of *C. difficile*, which produces toxins A and B. There is an increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and usually require hospitalization. CDAD must be considered in all patients who present with diarrhea following antibiotic use; however, not all diarrhea associated with antibiotic use are positive for *C. difficile* (McFarland *et al*. 1994; Fordtran 2006). Careful medical history is necessary since CDAD has been reported to occur over 2 months after the administration of antibacterial agents. If CDAD is suspected or confirmed, the offending antibiotic is discontinued and appropriate fluid and electrolyte management, protein supplementation, antibiotics, or surgical intervention may be required. The most important first step in the treatment of mild cases is to immediately discontinue the antibiotic. Treatment of more severe cases involves the

administration of antibiotics. The choice of initial antibiotic therapy depends on the severity of the presenting disease and whether the GI tract is functioning. Primary treatment will usually be with oral metronidazole or oral vancomycin; vancomycin is reserved to hospital patients who do not respond to metronidazole. Vancomycin is actually the only treatment that is FDA approved (Fekety 1997; Fordtran 2006; Gerding *et al.* 2008).

Lab values

Patients with *C. difficile* colitis often have elevated WBC counts and, in severe colitis, the WBC counts can be very high (20,000–40,000).

Management to prevent antibiotic-associated Clostridium difficile *infection*

- To help avoid antibiotic-related diarrhea, it is recommended to all patients to eat yogurt (containing live and active cultures such as Kefir, Dannon, or Yoplait). *Approximately 4–8 ounces of yogurt should be taken twice daily while on the antibiotic. Yogurt should be taken at least 2 h before or 2 h after the antibiotic.* If diarrhea does not stop, the patient should discontinue the antibiotic and call emergency services.
- The patient should not take antidiarrheal medications because it is advantageous to eliminate the bacterial toxins. *Pseudomembranous colitis symptoms could appear after a few doses or from 2 to 9 days or even months after the start of antibiotic therapy; it could happen at any time while taking the antibiotic.*
- If a patient has reported on their past medical history and hospitalization due to pseudomembranous colitis (*C. difficile*), caution should be used in the antibiotic prescribed. Most likely the patient has already been on antibiotics. In dentistry, in most cases, a broad-spectrum antibiotic is unnecessary; always start with a narrow-spectrum antibiotic such as penicillin V rather than amoxicillin in non–penicillin-allergic patients. Consultation with the patient's physician is recommended.

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