MEDICATION AND MASSAGE THERAPY PART II: COMMON GASTROINTESTINAL AND PAIN MEDICATIONS (4 CE Hours)

Learning objectives

- Name common medications for pain and inflammation that may require adjusted manual techniques and the reasons why.
- Name common gastrointestinal conditions in which massage may be contraindicated.
- List symptoms associated with drug toxicity.
- Explain the functions of acid-peptic drugs.
- Discuss the role of massage in relieving drug side effects.

Introduction

The following chapter introduces the pharmacological basics of drugs associated with common gastrointestinal conditions and the management of pain and inflammation. Most drugs are listed by their common scientific name and a proprietary (brand) name. An asterisk (*) denotes over-the-counter formulations, while a capitalized name in parenthesis usually refers to the proprietary name of the drug.

Drug companies give their products brand names. The U.S. Food and Drug Administration (FDA) approves the generic, shortened names by which drugs are usually known. For example:
- **Brand name:** Tylenol.
- **Generic name:** Acetaminophen.
- **Chemical name:** N-(4-hydroxyphenyl)acetamide.

Massage implications related to gastrointestinal medications and diseases

With the use of individuals taking pain medication requires extra attention to the client’s comfort and positioning. In cases where symptoms are elements of a systemic disorder, a shortened session may be appropriate.

- Dizziness, drowsiness, and postural hypotension are common side effects of many medications that can be heightened by massage. The client should sit up slowly and wait a few moments before standing. Because so many medications are associated with side effects including slight dizziness or drowsiness, be sure to assist individuals, especially the elderly, in sitting up, pausing a moment, and getting off the table.

- It is important that you are aware of all medications your client is taking, both prescription and over the counter, as multiple medications increase the potential incidence of adverse effects. Optimally timing the medication around the massage session may be critical, either ensuring that symptoms are managed effectively, or that individuals are not “masking” pain or discomfort that serves as the body’s feedback or warning mechanism. Tissues that have reduced or altered sensitivity can be injured more easily by normal use of manual techniques.

- In many cases, the health and function of the liver and kidneys are critical to maintaining therapeutic levels of medication in the blood. If normal elimination processes are compromised by renal or hepatic dysfunction, adverse effects such as fever and reddish purple bruises on the skin are early indications of drug toxicity. At any indication of drug toxicity related to any drug, massage treatments are contraindicated until the client is evaluated by a physician.

- Medication may be contraindicated in cases of oesophagitis, gastroenteritis, and/or hernia. In each case, have client consultation and approval by the doctor before massage. In case of gastritis. It is best to avoid the immediate area of the stomach, but massage of the thoracic and lumbar spine may bring relief. Light clockwise effleurage to the abdomen, to induce relaxation, may be beneficial for cases of gastroenteritis.

- In cases of heartburn, do not massage the upper abdominal area; instead downward effleurage may soothe the stomach and abdominal muscles and reduce the regurgitation of gastric juice. Massage of the affected area in individuals with peptic ulcers is contraindicated, although manipulation of the reflex areas of the lower spine and stress-reducing massage may be useful. Require a doctor’s consultation and approval before massage.

- Also obtain doctor’s approval before beginning any body work for an individual with Crohn’s disease. If approved, relaxing abdominal massage may be beneficial. In the case of irritable bowel syndrome, gentle clockwise massage may relieve some symptoms while massage of the lumbar, gluteal, and thigh muscles can help alleviate referred pain.

- Massage does not affect the absorption of antacids and anti-ulcer medications, H2-histamine drugs, or PPIs. Each of these, however, and particularly antacid medications, may cause side effects of constipation (and rarely, diarrhea). Constipation may be alleviated by working on the abdomen, in a clockwise pattern, to help stimulate peristalsis. Any time that constipation is an issue, encourage drinking water to assist intestinal motility. Side effects including diarrhea, dizziness, nausea, headache, rash, or itching should be referred to a physician.

- Antiflatulent drugs like Mylanta, as well as fiber laxatives, facilitate the release of gas pockets in the abdominal tract. Gentle abdominal massage can facilitate the process. Gentle abdominal massage can also relieve mild side effects of cramping and diarrhea from stimulant and lubricant laxatives. Any significant abdominal pain and distention, constipation, or diarrhea should be referred to a physician.

Corticosteroids cause atrophy and weaken connective tissues, including skin, fascia, ligaments, and muscle, joint capsules, bones, and tendons. When injected into joints for arthritis, steroids can induce breakdown of articular cartilage. Corticosteroids also impair the body’s ability to repair body tissues normally, resulting in longer healing periods and fragile tissue after any injury. Corticosteroids also have immunosuppressant effects that make an individual more susceptible to infection, so hand washing and being in good health are important to the client’s health and safety.

Individuals taking corticosteroids for long periods may notice changes in skin sensitivity and altered reactions to heat and cold. Normal function and sensitivity of the skin are compromised to the extent that skin rolling, friction, and wringing techniques can result in bruising and inflammation of the tissues. Any massage strokes that involve placing direct pressure or stress on tissue structures will need to be reviewed. Avoid heavy tapotement, passive forced stretching, muscle stripping, deep kneading, frictions or joint mobilization. For tissues affected by topical steroid applications, exercise caution and modify the depth of pressure when working on tissues.

Colic and constipation in infants

Results from a number of recent studies suggest that in infants with colic, massage is beneficial in dispersing gas, easing muscle spasms, and returning the digestive system to normal. Stimulation may also relieve constipation and assist digestion. Extreme caution is necessary in performing infant massage. Anyone unfamiliar with handling a baby must receive appropriate instruction before massaging. Infants are fragile and strokes must be very delicate.

Common gastrointestinal conditions

Gastrointestinal medications are used to treat a variety of disorders of the esophagus, stomach, and intestines. Disorders of the esophagus include esophagitis, an inflammation of the esophagus that may be accompanied by heartburn. Esophagitis may be caused by infection, trauma, irritation or from the ingestion of certain foods and/or acid reflux.
Disorders of the stomach and intestines include gastroenteritis, an inflammation of the intestines and stomach that may cause nausea, diarrhea, and abdominal pain. Possible causes of gastroenteritis include a viral or bacterial infection, allergic response, or exposure to irritating particles.

Peptic ulcers are ulceration of the mucosa lining of the stomach and, more commonly, the duodenum affecting about 1/10th of the U.S. population. The cause may be attributed to use of NSAIDS (nonsteroidal anti-inflammatory drugs) that include aspirin, ibuprofen, and naproxen, which account for about 20-30 percent of cases, while infection with Helicobacter pylori (H pylori) accounts for about 70-80 percent of the cases.

Acid-peptic diseases include gastroesophageal reflux, peptic ulcer (gastric and duodenal), and stress-related mucosal injury. Ulceration or mucosal erosion occurs when caustic substances (like acid, bile, and pepsin) in the gastrointestinal tract overpower the defenses of gastrointestinal mucosa (mucus and bicarbonate secretions, blood flow, prostaglandins, and cellular regeneration after injury).

Drugs used in acid-peptic disorder treatment typically do one of two things: reduce intragastric acidity or promote mucosal defense. Anti-ulcer medications reduce symptoms and encourage healing of gastrointestinal ulcers, while antisecretory ulcer medications suppress excess stomach acid production. In some cases, a material like sucralfate forms a chemical barrier over the ulcerated area, protecting it from stomach acid.

Agents that reduce intragastric acidity
Antacids: aluminum hydroxide gel*(Amphojel), calcium carbonate* (Tums), combination aluminum hydroxide and magnesium hydroxide preparations*(Maalox, Mylanta, Gaviscon), sodium bicarbonate* (baking soda, Alka Seltzer).

Antacids have a long history of nonprescription use in individuals with acid-peptic disorders, and were the primary treatment strategy until the development of H2 receptor antagonists and proton pump inhibitors. Antacids are weak bases that react with hydrochloric acid in the gut to form saltwater. Their primary function is the reduction of intragastric acidity, but they may also enhance mucosal defense through increased mucosal prostaglandin production. The acid-neutralization capacity among different antacid formulas varies widely, depending on a range of factors including rate of dissolution (pill vs. liquid, for example), gastric contents and emptying, etc.

There are three main types of antacid preparations: sodium bicarbonate, calcium carbonate, and magnesium or aluminum hydroxide.

Sodium bicarbonate reacts quickly with hydrochloric acid, producing carbon dioxide and sodium chloride, which may cause gastric distention and belching. When sodium bicarbonate is taken in high doses or by individuals with renal dysfunction, there is a potential for metabolic alkalosis due to absorption of unreacted alkali. Absorption of sodium chloride may exacerbate fluid retention, particularly in patients with hypertension, heart failure, and renal dysfunction.

Calcium carbonate is less soluble and reacts more slowly with hydrochloric acid than sodium bicarbonate, with a reaction producing carbon dioxide and calcium chloride. Use of calcium carbonate may cause gastric distention, belching, and the potential for metabolic alkalosis. Excessive doses of sodium bicarbonate or calcium carbonate with a calcium-rich diet can cause hypercalcemia, renal insufficiency and metabolic alkalosis.

Magnesium hydroxide or aluminum hydroxide react more slowly with hydrochloric acid to form magnesium chloride or aluminum chloride and water. Distension and belching do not occur, as no gas is generated by this process. Potential for metabolic alkalosis is also avoided. As unabsorbed magnesium salts may produce osmotic diarrhea and aluminum salts may produce constipation, these two items are used together in a number of proprietary medications to minimize effects on bowel movements. Because both magnesium and aluminum are absorbed and excreted by the kidneys, any individuals with renal dysfunction should not take either formulation for any length of time.

All types of antacids affect the absorption of other medications, so special care should be taken in timing medications around the use of antacids. Antacids should not be taken within two hours of tetracyclines, iraconazole, iron, and fluoroquinolones. Individuals with incidence of heartburn or dyspepsia less than three times per week may find antacids sufficient in their ability to provide rapid, short-term (1 to 2 hour) acid neutralization. (Antacids work faster than H2 antagonists but do not last as long).

Mucosal protective agents: Misoprostol (Cytotec), sucralfate, bismuth subsalicylate* (Pepto Bismol).

Gastrointestinal mucosa produces a number of prostaglandins. Mucosal prostaglandins stimulate mucus and bicarbonate secretion and mucosal blood flow. These structures act similarly to hormones in that they stimulate target cells into action, but differ from hormones in the fact that they act locally, near where they are produced.

Misoprostol is a prostaglandin analog able to inhibit acid and protect mucosal areas by stimulating mucus and bicarbonate secretion and increasing mucosal blood flow. Sucralfate is a salt that forms a viscous material that binds specifically to ulcers or areas of wear for a period up to 6 hours. It forms a physical barrier that prevents additional abrasion of the area as well as stimulating mucosal prostaglandin and bicarbonate secretion.

Little sucralfate is absorbed by the body, and so has few side effects. Usage leaves a residue of aluminum salt, causing constipation in 2 percent of the population, so should not be used for any length of time in patients with renal problems. Mucosal protective agents may interact with other medications, reducing their absorption by the body. Sucralfate is shown to be effecting in healing duodenal ulcers, but may be less effective than proton pump inhibitors. In some cases, individuals taking NSAIDS who experience dyspepsia are prescribed sucralfate.

Because peptic ulcers develop in up to 20 percent of individuals who take NSAIDS over the long-term, mucosal protective agents have been used to inhibit the incidence of NSAID-induced ulcers and ulcer-related complications significantly. However, the need for multiple doses daily and the high rate of side effects limits its use, although they may be the most appropriate course of action for individuals at high risk of NSAID complications. Ten to 20 percent of patients may experience abdominal cramping and diarrhea.

Colloidal bismuth compounds like bismuth subsalicylate (Pepto Bismol) is the only bismuth compound available in the U.S. Less than 1 percent of bismuth is absorbed, with more than 99 percent of the drug eliminated in the stool. Salicylate is easily absorbed and eliminated in the urine. Bismuth coats ulcers and erosions in the same way as sucralfate, producing a protective layer against gastric juices. Bismuth may also stimulate prostaglandin, bicarbonate and mucus secretion. Bismuth subsalicylate tends to reduce bowel movement frequency and liquidity in the case of some diarrhea. Bismuth is sometimes taken before and during trips to counter potential microbial activity or increase in H pylori.

Bismuth compounds tend to blacken the stool, but have few other side effects. Liquid formulas may also darken the tongue. Bismuth compounds should only be used for short periods of time and should not be used at
all in individuals with poor renal function. Excessive or prolonged use of some bismuth compounds, but not bismuth subsalicylate, may result in symptoms of bismuth toxicity including headaches, confusion, unsteadiness, or seizures.

**H2 histamine receptor blockers [H2-receptor antagonists]**: cimetidine (Tagamet®), famotidine (Pepcid,*) nizatidine, ranitidine (Zantac). H2-receptor blockers (also referred to as H2-receptor antagonists) were once widely prescribed for acid-peptid diseases. However, since the recognition that the bacteria H pylori plays a role in ulcer disease, more and more acid-peptic conditions are being treated with proton pump inhibitors and antibacterial therapies (see below).

H2 receptor antagonists are currently primarily prescribed for the following conditions: gastroesophageal reflux disease (GERD), nonulcer dyspepsia, and for the prevention of bleeding from stress-related gastritis. Clients with heartburn or dyspepsia less than three times per week may prefer H2 antagonists to antacids. While they do not work as rapidly, H2 antagonists last for a longer period than antacids (6-10 hours vs. 1-2).

Four main H2 antagonists are in current use: cimetidine, ranitidine, famotidine, and nizatidine. Each is rapidly absorbed by the intestine. Nizatidine has little first-pass metabolism, with a bioavailability near 100 percent. Cimetidine, ranitidine, and famotidine undergo metabolism by the liver, with a bioavailability of 50 percent. Half-lives for these H2 antagonists range from about 1 to 4 hours, depending on dosage. Elimination is largely a product of hepatic metabolism and renal function. Those with poor renal and hepatic function may need an adjusted dose, with elderly individuals subject to a decline of up to 50 percent in drug clearance and limited volume of distribution.

H2 antagonists reduce basal, meal-stimulated, and histamine-stimulated acid secretion, as well as gastrin, in a linear (dose-dependent) fashion. H2 antagonists work by binding to the H2 receptor, which blocks the binding by gastrin and acetylcholine that releases histamine from ECL cells, reducing acid secretion in the process. Each of the four H2 antagonists do this in a different fashion, with H2 antagonists generally more useful in inhibiting the production of acid at night (largely a function of histamine), and less of an impact on meal-stimulated acid.

H2 antagonists may be taken before meals to reduce meal-secreted acid, but are more effective for frequent heartburn if taken 2 times per day, which usually reduces symptoms in one-half to three-fourths of subjects studied. Individuals suffering from erosive esophagitis (about one-half of those with GERD) may find some relief with H2-antagonists, but are typically directed to proton-pump inhibitors for treatment. In seriously ill individuals, H2 antagonists are used to reduce the occurrence of bleeding as a result of stress-related gastritis.

Less than 3 percent of individuals taking H2 antagonists experience side effects. Those who do may experience headaches, fatigue, constipation or diarrhea, and muscle pain. In cimetidine, specifically, long-term use or high dosages may cause lactation in women and impotence or the development of breasts in men. Cimetidine also alters drug metabolism, resulting in longer half-lives of other medications. As H2 antagonists are able to cross barriers like the placenta and are secreted in breast milk, pregnant and nursing women should not take this drug.

**Proton pump inhibitors (PPIs):** omeprazole (Prilosec) ezomeprazole (Nexium), lansoprazole (Prevacid), pantoprazole (Protonix), rabeprazole (AcipHex). PPIs have been in use since the late 1980s. They are highly effective acid-inhibiting agents used commonly for treatment of acid-peptic disorders. The five proton pump inhibitors listed above are similar in structure but each works according to a different mechanism. All proton pump inhibitors, except pantoprazole, are administered as oral doses, coated in an acid-resistant coating so it will not be destroyed by stomach-acids. Pantoprazole is administered intravenously. Once the drug is able to pass through the stomach intact, it is largely absorbed in the intestines. Due to lower bioavailability of the drug when taken with food (decreases by 50 percent), administration must be timed carefully around meals, and are most effective when taken on an empty stomach.

Proton pump inhibitors block acid secretion at the proton pump pathway. They are effective inhibitors of both meal-stimulated and fasting acid secretion, inhibiting up to 98 percent of acid secretion in a 24-hour period. Proton pump inhibitors have a relatively short half-life (1 ½ hours), but continue to have acid-inhibiting effects for up to 24 hours. In some cases, it may take three to four days for full acid-inhibiting effects to be realized. Similarly, it may take the same amount of time, after stopping dosage for acid secretion to return to normal. Proton pump inhibitors are largely metabolized by the liver and are eliminated in urine. The drug may not be appropriate for individuals with substantial liver or renal dysfunction.

Proton pump inhibitors are effective in the treatment of both non-erosive and erosive reflux disease (GERD) and its related esophageal complications, including peptic stricture or Barrett’s esophagus, and related effects outside the esophagus. One dose daily typically provides relief from symptoms and encourages healing in up to 90 percent of patients. Individuals with erosive esophagitis may experience recurrence after discontinuing proton pump inhibitors. Use of daily or twice daily dosage with proton pump inhibitors for a period of at least three months may be used to relieve non-esophageal reflux-disease-related complications and symptoms such as cough, asthma, or laryngitis.

Proton pump inhibitors assist in the healing of both duodenal and gastric ulcers, healing over 90 percent of ulcers within 8 weeks. Ulcers may be caused by H pylori or associated with the use of NSAIDs (non-steroidal anti-inflammatory drugs), like aspirin. In the case of H pylori infection, the therapeutic strategy is two-fold: to eliminate the bacteria and heal the ulcer. Elimination of the organism is produced through the proton pump inhibitor’s ability to substantially raise environmental pH in the body, allowing antibiotics to effectively combat H pylori. Proton pump inhibitors are combined with the antibiotic clarithromycin and amoxicillan (or metronidazole) to clear the infection. Use of proton pump inhibitors is typically used for up to six weeks to assure healing.

Ulcers associated with NSAID use can be effectively healed by proton pump inhibitors. In cases where NSAID use is discontinued, more effective ulcer healing occurs. While continued use of NSAID reduces the amount of healing, some positive effects are still seen. Proton pump inhibitors are used among some populations daily, to prevent potential complications from NSAID use, like bleeding or perforation. Proton pump inhibitors administered orally once or twice daily for a period of up to five days significantly reduces ulcer re-bleeding (the reoccurrence of bleeding from peptic ulcers).

Side effects of proton pump inhibitors are reported in 1-5 percent of individuals using them. Typical symptoms are diarrhea, abdominal pain, and/or headache. A reduction in acid due to proton pump inhibitor use may contribute to lowered vitamin B12 absorption from food. The reduction in acid may also produce a slightly increased risk to enteric infections like salmonella. Decreased gastric acidity tends to increase gastric bacterial concentration in individuals taking proton pump inhibitors. It also alters the absorption of some drugs that require intragastric acidity.

**Drugs for motility disorders:** cisapride (Propulsid) dolasetron (Anzemet); metoclopramide (Reglan).
Drugs that stimulate gastrointestinal motility (prokinetic agents) are useful for a number of reasons: they may enhance lower esophageal pressure in the treatment of GERD, by improving gastric passage and emptying, and may be useful in the treatment of constipation. The prokinetic activity of metoclopramide, cisapride, and domperidone is a function of cholinergic stimulation. These agents increase esophageal peristalsis, increase lower esophageal sphincter (LES) pressure and increase gastric emptying. Both metoclopramide and domperidone (see below) also provide effective anti-nausea and anti-emetic action. Cisapride also increases small bowel and colonic action. Only metoclopramide is available for use in the U.S., while domperidone is available in many other countries. Prokinetic agents are typically used together with antisecretory drugs to treat regurgitation or refractory heartburn. All three agents are useful in the treatment of GERD, but not in the case of erosive esophagitis.

Metoclopramide is used to treat individuals with delayed gastric emptying (due to surgery or diabetes) and is sometimes administered to hospitalized individuals using feeding tubes to promote movement of food from the stomach to the duodenum. Metoclopramide may also provide some relief from symptoms of chronic dyspepsia, for the prevention and treatment of emesis (nausea), and to prevent vomiting. Metoclopramide side effects are associated with central nervous system functions, with effects such as restlessness, sleepiness or insomnia, anxiety or agitation in up to 20 percent of users, and even more pronounced in elderly populations. Long-term use should be avoided, especially among the elderly.

**Laxative drugs**: bisacodyl (Dulcolax), cascara sagrada, castor oil, docusate (Colace), glycerin liquid (Fleet), lactulose (Chronicul), magnesium hydroxide (Milk of Magnesia, Epsom Salt), methylcellulose, mineral oil, polycarbophil (Equalatin), polyethylene glycol electrolyte solution (Colyte), psyllium (Metamucil), senna (ExLax).

Many people use over-the-counter laxatives instead of a high-fiber diet, adequate hydration, and exercise to maintain regularity. Laxatives work though one of four mechanisms: bulk-forming, stool softening, osmotic or stimulant laxatives. Bulk-forming laxatives cannot be digested; instead they absorb water within the body, turning into a bulky gel that stimulates peristalsis. Bulk-forming laxatives are made from plants like psyllium and methylcellulose, and synthetic fibers like polycarbophil. In the case of plant fibers, digestion can cause bloating and increased gas emissions. Stool surfactant agents, or “softeners,” allow the entry of water and lipids into the stool, softening the material. Docusate (oral or enema) is typically prescribed in hospitalized individuals to prevent constipation. Glycerin suppositories and mineral oil are also commonly used stool softeners. Mineral oil is used by some to prevent and treat constipation or impaction in children or debilitated adults. Long-term use may reduce absorption of vitamins A, D, E, and K.

Osmotic laxatives are nonabsorbable solutions that result in increased liquidity of the stool. Nonabsorbable sugars and salts, like magnesium oxide, are commonly used for the treatment of acute constipation or the prevention of chronic constipation. It should not be used long-term due to its potential for magnesium poisoning. Sorbitol and lactulose are nonabsorbable sugars used to regulate bowel movements, but because they are metabolized by bacteria in the colon, they produce side effects of cramps and increased gas. Osmotic laxatives taken in high dosages produce rapid bowel evacuation (purgatives) within a number of hours, which can be useful in cases of constipation. The most commonly used purgatives are sodium phosphate and magnesium citrate, which may cause electrolyte imbalance in elderly or frail individuals or with cardiac disease.

Polyethylene glycol (PEG) is used for colonic cleansing prior to endoscopic procedures. This solution contains a nonabsorbable, osmotically active sugar and salts that do not produce electrolyte shifts or cause the individual to retain fluids, so are safer. For the treatment or prevention of chronic constipation, small doses of PEG may be taken by mouth daily, with minimal cramping or gassy side effects.

Stimulant laxatives are also called cathartics. They are used to induce bowel movements in individuals with neuromotor impairment or bed-bound patients. Stimulant laxatives that are produced from plants, like aloe and senna, are poorly absorbed, producing bowel movement in under 12 hours (oral) and 2 hours (rectal). Long-term use causes harmless pigmentation of the colon. Castor oil is a powerful stimulant laxative hydrolyzed in the upper small intestine to form ricinoleic acid, which stimulates intestinal motility. Once commonly used, it has now fallen out of favor for purgative action.

**Drugs for the treatment of irritable bowel syndrome (IBS)**: Irritable bowel syndrome is a chronic, recurring disorder in which the individual experiences abdominal cramping and bloating with diarrhea, constipation, or both. Abdominal pain is usually associated with increased frequency of bowel movements. Treatments are typically focused on the relief of pain and normalization of bowel function.

IBS may be associated with recurrent abdominal cramping, pain, and/or diarrhea/constipation cycle. IBS may be may be stress-induced or exacerbated. In some cases, gentle clockwise massage may be helpful in reducing symptoms; massage of the lumbar, gluteal, and thigh muscles may reduce referred pain.

Individuals suffering from constipation can use fiber supplements to soften the stools, but this may result in excessive bloating and gas, increasing abdominal discomfort. Instead, osmotic laxatives are often used to soften and increase stool frequency. Individuals experiencing diarrhea may find loperamide (see below) offers some relief, reducing urgency and frequency of bowel movements.

**Anticholinergic drugs**: atropine, belladonna alkaloids tincture, dicyclomine, glycopyrrolate (Robinit), l-hycosamine (Anaspaz); methscopolamine (Pamime); propantheline; scopolamine; tridihexethyl (Pathilon).

Anticholinergic medications block or slow nerve impulses at parasympathetic nerve endings. This prevents muscle contraction and gland secretion in the organs involved. These medications are thought to slow the action of the bowel and relieve spasms (antispasmodic) through relaxation of the muscles. Dicyclomine and hycosamine are sometimes considered antispasmodics, but typically relieve abdominal pain through anticholinergic activity (small and large bowel spasms are not typically associated with IBS). These anticholinergic properties sometimes increase gastrointestinal motility and secretion, and reduce bowel movement frequency and liquidity. These medications are used infrequently due to the incidence of side effects including visual disturbances, urinary dysfunction, and constipation.

**Antidiarrheal drugs**: bismuth subsalicylate (Pepto Bismol), difenoxin (Motofen), diphenoxylate (Lomotil), kaolin/pectin (Kaopectate), loperamide* (Imodium).

Colloidal bismuth compounds, like bismuth subsalicylate, are classified as both antidiarrheals and mucosal protective agents. Antidiarrheals are typically used to control chronic diarrhea caused by irritable bowel syndrome (IBS) or inflammatory bowel disease (IBD). In general, antidiarrheal drugs should only be used in cases of mild to moderate diarrhea, and should not be used by individuals with blood in their stool, a high fever, or other condition that might cause systemic toxicity or worsen the pre-existing condition. They should not be used by individuals with diarrhea that worsens after administration of any antidiarrheal drug.

Two main opioids are used as anti-diarrheal agents: loperamide and diphenoxylate. Both
 Elite duration of transit time in the colon. Afferent neutrons inhibiting colonic motility, fact that it blocks 5-HT3 receptors on enteric hepatic metabolism and is excreted in urine. Last much longer. Alosetron is subject to life of 1½ hours, with effects that typically bioavailability near 55 percent, and a half-life from 4 to 9 hours and undergo substantial hepatic metabolism. While all are substantial hepatic metabolism. While all are

Alosetron is a powerful 5-HT3 antagonist that works by inhibiting 5-HT3 receptors in the gastrointestinal tract, minimizing visceral afferent pain and intestinal motility. Alosetron is approved for individuals with severe IBS with diarrhea. Alosetron is highly specific to the 5-HT3 receptor that is rapidly absorbed from the gastrointestinal tract with a bioavailability near 55 percent, and a half-life of 1½ hours, with effects that typically last much longer. Alosetron is subject to hepatic metabolism and is excreted in urine. Alosetron inhibits distention-induced sensory and motor reflex activation as well as central response to visceral stimulation due to the fact that it blocks 5-HT3 receptors on enteric afferent neurons inhibiting colonic motility, particularly in the left colon, and increasing the duration of transit time in the colon.

While alosetron is currently approved for the treatment of women experiencing IBS with diarrhea as the primary symptom, efficacy in use among men has not been supported by research data. Among women, about one-half of individuals taking alosetron find relief from pain or discomfort and a reduction in bowel movements compared with 30–40 percent of individuals treated with placebo. Because alosetron is associated, in rare cases, with gastrointestinal toxicity, it should be discontinued if constipation occurs (about 30 percent of users). In very rare cases (1 out of 1000 users), constipation has resulted in complications requiring hospitalization or surgery, and ischemic colitis in as many as 3 out of 1000 users. Due to the seriousness of these side effects, alosetron is only approved in women with diarrhea-prone IBS who have not responded to other strategies and are aware of the risks. Alosetron appears to have no significant interactions with other drugs.

Tegaserod is a partial serotonin 5-HT4 receptor agonist with a similar structure to serotonin. Tegaserod has a bioavailability of about 10 percent and should be taken before meals, as food can further reduce its bioavailability. About 2/3 of the drug is excreted virtually unchanged in fecal matter, while 1/3 is eliminated as a metabolite in the urine. Tegaserod should not be used by individuals with hepatic or renal dysfunction.

Research suggests that stimulation of 5-HT4 receptors on mucosal afferent nerve fibers triggers the release of neurotransmitters, stimulating the peristaltic reflex (bowel contraction and bowel relaxation) and promoting gastric emptying, increasing movement through the small and large bowel. Stimulation of the 5-HT4 receptors also leads to increased liquidity of the stool.

Tegaserod was recently approved for the treatment of IBS associated with constipation. Tegaserod appears to reduce pain and bloating, increases the number of bowel movements while decreasing stool hardness compared to the placebo. Diarrhea occurs in less than 10 percent of users within the first few days of treatment, but normalizes in the majority of individuals. Headaches may be another side effect. There are no known drug interactions.

Nausea is an uneasiness of the stomach that often accompanies the urge to vomit, but doesn’t always lead to vomiting. Vomiting is the forcible voluntary or involuntary emptying (“throwing up”) of stomach contents through the mouth. Some triggers that may result in vomiting can come from the stomach and intestines (infection, injury, and food irritation), the inner ear (dizziness and motion sickness), and the brain (head injury, brain infections, tumors, and migraine headaches).

Various stimuli that affect nausea and vomiting come together in an area in the brain known as the vomit (or emetic) center in the medulla. This “center” is not a discrete nucleus, but a complex array of coordinated neurons. The vomit center receives input from four major areas: the GI tract, the chemoreceptor trigger zone, the vestibular apparatus, and the cerebral cortex. Each of these four areas responds to certain types of stimuli, modulated by specific neurotransmitters that bind specific receptors. Identification of increasing numbers of neurotransmitters has been associated with the development of antiemetic agents that have affinity for specific receptors, with combinations causing a variety of different mechanisms, and effects. Ondansetron, granisetron, dolasetron are 5-HT3 antagonists approved for prevention and treatment of nausea and vomiting. Each has powerful antiemetic properties mediated primarily through peripheral 5-HT3 receptor blockade on intestinal vagal afferents, in the vomiting center, and chemoreceptor trigger zone. Ondansetron, granisetron and dolasetron have a half-life from 4 to 9 hours and undergo substantial hepatic metabolism. While all are excreted by renal and hepatic elimination, dose reduction for elderly individuals or those with renal insufficiency is generally not necessary. People with liver dysfunction may require dose reduction in the case of ondansetron. All agents tend to slow esophageal and gastric motility and increase colonic transit time. 5-HT3 receptor antagonists are increasingly being used to prevent and treat postoperative nausea and vomiting as well as nausea and vomiting in patients treated with radiation therapy due to their relative lack of serious adverse side effects. Symptoms may include headache and dizziness, as well as constipation, in some cases. Each of the three agents discussed above produce a small but significantly extended QT interval (an abnormality in the heart’s electrical system) that is most pronounced with dolasetron. These drugs should not be used by individuals experiencing prolonged QT intervals or with other medications that might also extend the QT interval.
Research data shows no significant drug interactions. All three discussed above experience hepatic metabolism but do not seem to affect the metabolism of other drugs. Other drugs, however, may reduce hepatic elimination of the 5-HT3 receptor antagonists, changing the half-life value.

**Motion sickness**

While most anticholinergic and H1 antihistamine agents have weak antiemetic activity, they may be particularly useful in preventing motion sickness. Their use, however, may be limited by the presence of side effects, including sleepiness, dizziness, dry mouth or urinary retention. Diphenhydramine and dimenhydrinate are histamine H1 antagonists with both antiemetic and sedating effects. Meclizine is less sedating, and may be used for prevention of motion sickness and cases of vertigo. Hyoscine (scopolamine) is one of the most effective treatments for the prevention of motion sickness. Incidence of anticholinergic effects from oral administration are reduced significantly by administration in the form of a transdermal patch.

**Anti-inflammatory drugs used in gastrointestinal disease [Drugs used to treat inflammatory bowel disease (IBD)]:** balsalazide (Colazal), budesonide (Entocort), hydrocortisone (cortenema), mesalamine (Asacol), olsalazine (Dipentum), sulfasalazine (Azulfidine), infliximab (Remicade).

Inflammatory bowel disease (IBD) is the general name for diseases that cause inflammation in the small intestine and colon. Inflammatory bowel disease (IBD) refers to two distinct disorders: Crohn’s disease and ulcerative colitis. The cause and progression of both is still largely unknown. Crohn’s disease (regional enteritis) is a condition of inflammation of the mucosa in the large intestine, and more commonly, the ileum of the small intestine. Accumulation of scar tissue may lead to poor absorption of nutrients, with symptoms including abdominal pain, diarrhea, nausea, and fever. The cause is unknown, but there may be a genetic component or predisposition.

Ulcerative colitis is a disease that causes inflammation and sores (ulcers) in the lining of the rectum and colon. Ulcers form where the inflammatory process has killed the cells that usually line the colon, then bleed and produce pus. Inflammation in the colon also causes the ileum of the rectum and sigmoid colon to empty frequently, causing diarrhea. It can be difficult to distinguish between ulcerative colitis and Crohn’s disease. Crohn’s disease differs because it causes inflammation deeper within the intestinal wall and can occur in other parts of the digestive system including the small intestine, mouth, esophagus, and stomach.

In cases of IBD, always require a doctor’s consultation and approval before massage; relaxing abdominal work may be beneficial.

Aminosalicylates [5-aminosalicylic acid (referred to as 5-ASA)] have been used effectively for years to treat IBD. For aminosalicytes to work, they must be absorbed topically, rather than systemically, into the diseased gastrointestinal areas. As much as 80 percent of 5-ASA may be absorbed from the small intestine, not reaching its target area. Four formulations have been developed that deliver the drug to specific segments of the small bowel or the colon. They are sulfasalazine, balsalazide, olsalazine, and a variety of types of mesalamine.

Three of these drugs, sulfasalazine, balsalazide, and olsalazine contain 5-ASA bound by an azo bond. This characteristic significantly reduces absorption of the drug by the small intestine. Once it reaches the terminal ileum and colon, naturally occurring bacterial action releases active 5-ASA from the drug at concentrations powerful enough to be available to the terminal ileum and colon. There are also a number of 5-ASA compounds formulated to reach diseased areas in the small or large bowel, which are referred to as mesalamine. Pentasa, asacol, Rowasa, and Canasa target this area through oral coated formulations, enema, and suppositories.

While these drugs have been successful inducing and maintaining remission in ulcerative colitis, their efficacy in Crohn’s disease is not as pronounced. Much of the benefit of the drug is tied to its ability to maintain high concentrations of the drug at the targeted site of action. Of the four, sulfasalazine has the highest incidence of adverse effects, with up to 40 percent of individuals using the drug unable to tolerate amounts necessary to be therapeutic. Common side effects include stomach upset, nausea, headaches, and myalgia. Hypersensitivity can result in fever, dermatitis, pancreatitis, and anemia, among a range of other serious conditions. The other 5-ASA compounds are far more easily tolerated, with adverse effects similar to individuals taking placebo.

Olsalazine may stimulate diarrhea in 10 percent of users.

**Glucocorticoids:** betamethasone (Celestone), cortisone, dexamethasone (Decadron), Hydrocortisone or cortisol (Cortef), hydrocortone, methylprednisolone (Medrol), prednisolone, (Prelone), prednisone (Metocorten), tramacinolone (Kenacort).

Glucocorticoids/corticosteroids are used to treat a wide variety of conditions and diseases, such as joint pain, cancer, asthma and allergies. The oral and injected types of corticosteroids form a major part of treatment plans for many chronic pain conditions. Many inflammatory conditions, such as rheumatoid arthritis and gout, are first treated with nonsteroidal anti-inflammatory drugs (NSAIDs). If these drugs do not control the symptoms, corticosteroids are often the next line of treatment.

Corticosteroids are a group of anti-inflammatory drugs similar to the hormone cortisol produced in the body. Corticosteroids reduce the inflammation associated with many diseases, including many forms of arthritis. They can be taken in a variety of forms, such as pills, injections, inhalers, nasal sprays, topical creams, drops, ointments, enemas, foams and suppositories. Most corticosteroids are available only with a physician’s prescription. However, your client may use topical creams that are available over the counter.

Glucocorticoids, like prednisone and prednisolone, are useful in their ability to inhibit production of inflammatory cytokines and chemokines, reducing the expression of inflammatory molecules. Hydrocortisone enemas are used to maximize effects in the targeted tissue of the rectum and sigmoid colon, and minimize systemic absorption. A controlled-release formula (Entocort) releases the drug in the distal ileum and colon.

Glucocorticoids are used to treat moderate to severe active inflammatory bowel disease. Higher dosages risk significantly higher incidence of adverse effects. Oral dosage of prednisone or prednisolone is typically taken daily, once an individual responds to the initial therapy (usually a period of up to two weeks). Dosage is minimized to limit the risk of adverse effects. In very ill patients, intravenous administration may be common. IBD involving the sigmoid colon or rectum is primarily administered rectally to minimize systemic absorption.

Orally administered budenoside is slightly less effective than prednisolone in the treatment of active mild or moderate Crohn’s disease affecting the ileum and proximal colon. While achieving slightly less clinical remission, it has significantly fewer side effects. Once remission is achieved, doctors often abandon glucocorticoids in favor of aminosalicylates.

Corticosteroids can have a wide variety of serious side effects – particularly when oral forms of the drug are taken for long periods of time. These include acne, weight gain, loss of bone density associated with osteoporosis and decrease in immune response. Many types of medication can interfere with corticosteroids. Corticosteroids are different from the banned
Elite

Oral and intravenous:
Include:
Common side effects of corticosteroids
benefits with a physician before taking them.
Corticosteroids are strong medications.
body tissue as if it were an outside invader.
inflammation when they react to normal
Some autoimmune disorders also trigger
system (such as prostaglandins) that
production of substances in the immune
Corticosteroids work by blocking the
is the body’s normal response to outside
problems, the adrenal glands produce more
cortisol, which helps the body to cope with
the stress. When the stress disappears, cortisol
production returns to normal.

Cortisol also suppresses inflammation, which
is the body’s normal response to outside
invaders, such as bacteria.

Corticosteroids work by blocking the
production of substances in the immune
system (such as prostaglandins) that
trigger allergic and inflammatory reactions.
Some autoimmune disorders also trigger
inflammation when they react to normal
body tissue as if it were an outside invader.
Corticosteroids are strong medications.
Although they have proven to be helpful in
treating many medical disorders, they have
side effects that can be serious. Your client
should have discussed the potential risks and
benefits with a physician before taking them.

Common side effects of corticosteroids
include:

- Oral and intravenous:
  - Suppression of the immune system
    increasing likelihood for infection.
  - Bone loss, which may lead to or
    exacerbate osteoporosis.
  - Cartilage damage after repeated
    injections.
  - Acne.
  - Weight gain.
  - Mood swings.
  - Delayed growth (in children).
  - Blurred vision.
  - Frequent urination.
  - Increased thirst.
  - Increased appetite.
  - Indigestion.
  - Flushing of face or cheeks.

- Ointments/drops:
  - Eye infection.
  - Eye pain.
  - Gradual blurring or loss of vision.
  - Nausea/vomiting.

- Inhaled corticosteroids:
  - Sore mouth or throat, hoarseness.
  - Coughing.
  - Thrush (fungus infection in the mouth).
  - Decrease in bone thickness.
  - High blood pressure in the eye or fluid
    buildup in the eye.

- Nasal spray corticosteroids:
  - Increased chance of bruising.
  - Skin or muscle wasting.
  - Weight gain or fluid retention.
  - Decrease in bone density.
  - Damage to bones and bone cells
    (avascular osteonecrosis).
  - Increased blood pressure.
  - Increased risk of ulcer.
  - Increased risk of eye complications (e.g.
    glaucoma, cataracts).

- Topical corticosteroids:
  - Skin blisters filled with blood.
  - Itching or burning skin.
  - Increased skin sensitivity.
  - Numbness in the fingers.
  - Increased chance of bruising.
  - Raised red spots on the skin.

- Enemas/foams/suppositories:
  - Burning or itching of skin.
  - Diarrhea.
  - Infection.
  - Rectal bleeding.
  - Sensation of pins and needles.

- Pastes:
  - Infection.
  - Irritation, such as burning, itching,
    blistering or peeling.

Some side effects of corticosteroid drugs
are considered more dangerous, though rare.
An individual should immediately contact a
physician if they experience any of these side
effects:

- Blindness.
- Unusual confusion or excitement.
- Hallucinations.
- Mental depression.
- Eye pain.
- Irregular heartbeat.
- Bloody stool.
- Unusual increase in hair growth.
- Vomiting.

**Drug or other interactions with corticosteroids**

Clients who seek your advice should instead be urged to consult their physician before taking any additional prescriptions, over-the-counter medications, nutritional supplements, herbal medications or certain foods. Of particular concern to individuals taking corticosteroids:

- Diuretics (water pills) can cause the diuretic to be less effective and may increase the loss of potassium.
- Heart medications can increase the risk of having an irregular heartbeat or other problems by decreasing the amount of potassium in the blood.
- Cyclosporine (used for autoimmune disorders, in addition to preventing transplanted organ rejection) can cause seizures when taken with some corticosteroids.

- Anti diabetic agents or insulin (used to treat diabetes) can increase glucose (blood sugar) levels when taken with corticosteroids.
- Medicines containing potassium (used to treat high blood pressure) can interfere with potassium levels in the blood.
- Medicines containing sodium can cause the body to retain excess sodium and water, which can cause high blood sodium, high blood pressure and excess body water.
- Licorice (candy made from the licorice plant’s root) can increase the effects of corticosteroid medications.
- Antacids (counteracts stomach acidity) can decrease the effectiveness of some corticosteroids.
- Anticonvulsants (used to treat seizures) can decrease the effectiveness of some corticosteroids.
- Phenylbutazone (used to treat fever and pain) can reduce the effectiveness of corticosteroids.
- Aminoglutethimide (used to treat some kinds of tumors) can reduce the effectiveness of corticosteroids.
- Griseofulvin (used to treat skin infections) can reduce the effectiveness of corticosteroids.
- Ephedrine may decrease the effectiveness of nasal corticosteroids.
- Ritodrine (used to stop premature labor) can cause serious side effects when taken with corticosteroids.
- Rifampin (antibacterial drug used to treat tuberculosis) may decrease the effectiveness of nasal corticosteroids.
- Barbiturates (group of drugs used as sedatives) can decrease the effectiveness of some corticosteroids.
- Mitotane (used to treat cancers that affect the adrenal cortex) can decrease the effectiveness of some corticosteroids.
- Amphoter cin B by injection (used to treat fungal infections) can decrease the amount of potassium in the blood.

**Purine analogs: Purine anti-metabolites with immunosuppressive properties**

Azathioprine and 6-mercaptopurine are anti-metabolites with immunosuppressive properties and long half-lives. Therapeutic benefits of treatment are not realized for as long as 17 weeks for IBD. Therapeutic mechanisms of purine analogs are not understood, but appear to result in inhibition of cell reproduction. Both azathioprine and 6-mercaptopurine are used to treat ulcerative colitis and Crohn’s disease. More than one-half of all patients with active disease achieve remission within six months of treatment, and maintain remission in most cases. Individuals who rely on long-term glucocorticoid use to manage their disease
Digestive enzymes: Pancrelipase (Cotazym, Pancrease, Viokase); oral formula contains lipase, protease, and amylase activity. Pancreatic dysfunction may be caused by cystic fibrosis, chronic pancreatitis, or pancreatic surgery. When pancreatic enzymes do not function normally, fats and proteins are not properly digested, leading to a variety of deficiencies and weight loss. Supplements containing a mixture of amylase, lipase, and proteases are the primary form of treatments for pancreatic enzyme deficiency. The two main preparations are pancreatin, with low concentrations of lipase and proteolytic enzymes, and pancrelipase, a much stronger preparation which is no longer in clinical use.

Pancrelipase is available in two coated forms, necessary for oral administration, as gastric acids render pancrelipase enzymes inactive. Nontoxic coated preparations (Cotazym, Viokase) should be taken with acid suppression therapy, such as proton pump inhibitor or H2 agonist, to reduce acid in the stomach. Encapsulated formulations such as Creon and Pancrease or Ultrace contain acid-resistant properties and do not require concomitant acid suppression therapy. Pancrelipase is usually administered along with food in a range of formulations that have varying amounts of lipase, amylase, and protease. Most pancreatic enzyme supplements are well tolerated when swallowed (not chewed, due to risk of oropharyngeal mucositis). High doses may cause abdominal pain and diarrhea. Side effects may include increased levels of uric acid and renal stones.

**Drugs that dissolve gallstones:** Monoctanoin (Mocctanin); Ursodiol (Actigall) Ursudio, or ursodeoxycholic acid, is a bile acid used to dissolve cholesterol gallstones and reduce hepatic cholesterol secretion. Side effects include diarrhea.

**Pain and inflammation: The body’s immune response**

The immune response involves the activation of cells in the body, in response to foreign organisms or matter, resulting in an acute or chronic inflammatory condition. In some cases, the outcome is beneficial to the host. In other cases, the response itself is damaging to the host.

Arthritis is a general term for conditions that affect the joints and surrounding tissues. Joints are places in the body where bones come together, such as the knees, wrists, fingers, toes, and hips. The two most common types of arthritis are osteoarthritis and rheumatoid arthritis.

Osteoarthritis (OA) is a painful, degenerative joint disease that often involves the hips, knees, neck, lower back, or the small joints of the hands. OA usually develops in joints that are injured by repeated overuse from performing a particular task or playing a favorite sport, or from carrying around excess body weight. Eventually this injury or repeated impact thins or wears away the cartilage that cushions the ends of the bones in the joint. As a result, the bones rub together, causing a grinding sensation. Joint flexibility is reduced, bony spurs develop, and the joint swells.

Usually, the first symptom of OA is pain that worsens following exercise or immobility. Treatment usually includes analgesics, topical creams, or nonsteroidal anti-inflammatory medications (known as NSAIDs); appropriate exercises or physical therapy; joint splinting; or joint replacement surgery for seriously damaged larger joints, such as the knee or hip.

Rheumatoid arthritis (RA) is an autoimmune inflammatory disease that usually involves various joints in the fingers, thumbs, wrists, elbows, shoulders, knees, feet, and ankles. An autoimmune disease is one in which the body releases enzymes that attack its own healthy tissues. In RA, these enzymes destroy the linings of joints. This causes pain, swelling, stiffness, malformation, and reduced movement and function. People with RA also may have systemic symptoms, such as fatigue, fever, weight loss, eye inflammation, anemia, subcutaneous nodules (bumps under the skin), or pleurisy (a lung inflammation).

Most people with arthritis will use pain management strategies at some time. Regardless of the cause, pain management strategies are similar for people with osteoarthritis and rheumatoid arthritis. These strategies are included in the following chart.

This chart provides an overview of some of the similarities and differences between osteoarthritis (OA), and rheumatoid arthritis (RA). Some individuals with these conditions may have a different experience or may require a different medical approach to manage their disorder(s).
For mild to moderate pain, your client may use non-opioid (non-narcotic) drugs like acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs), such as aspirin and ibuprofen, which can be purchased over-the-counter (without a prescription). Moderate to severe pain may require opioids (also known as narcotics) such as morphine, fentanyl, hydromorphone, oxycodone, and codeine, which require a prescription. Physicians sometimes prescribe nonopioids along with opioids for moderate to severe pain.

Many anti-inflammatory medications are nonopioid analgesics, like aspirin, available without a prescription, and doctors find them appropriate for the treatment of acute and chronic effects. People with inflammation should be treated for both relief from pain and to slow or limit damage to the tissues that is the underlying cause. Nonsteroidal anti-inflammatory drugs (NSAIDs) can reduce inflammation for varying lengths of time.

**Massage implications related to medications for pain and inflammation**

Working with individuals taking pain medication requires extra attention to the client’s comfort and positioning. Swollen tissues should be elevated to encourage drainage. Use supports and pillows to cradle body parts comfortably and safely. In cases where pain and inflammation are symptoms of a systemic disorder, a shortened session may be appropriate. Individuals in severe pain may not be able to tolerate any additional stress on their tissues.

Dizziness, drowsiness, and postural hypotension are common side effects of many medications that can be heightened by massage. The client should sit up slowly and wait a few moments before standing. Because so many medications are associated with side effects including slight dizziness or drowsiness, be sure to assist individuals, especially the elderly, in sitting up, pausing a moment, and getting off the table.

It is important that you are aware of all medications your client is taking, both prescription and over-the-counter, as multiple medications increase the incidence of their adverse effects. Timing the medication, optimally, around the massage session may be critical, either ensuring that pain medication is kicking in at the appropriate time or is not “masking” pain that serves as the body’s feedback mechanism. Tissues that have reduced or altered sensitivity can be more easily injured from normal use of manual techniques.

In many cases, the health and function of the liver and kidneys are critical to maintaining therapeutic levels of medication in the blood. If normal elimination processes are compromised by renal or hepatic dysfunction, adverse effects such as fever and reddish purple bruises on the skin are early indications of drug toxicity. At any indication of drug toxicity related to any drug, massage treatments are contraindicated until the client is evaluated by a physician.

Drugs that alter blood-clotting mechanisms predispose users to bruising, so extra care should be used with clients taking anticoagulants, platelet inhibitors, aspirin, and other NSAIDs. Petriissage, for example, may cause bruising in an individual taking any of these medications. Massage techniques like deep kneading, ischemic compressions, and cross fiber frictions may need to be modified or avoided. While these techniques do not damage normal healthy connective tissue, they may produce bruising and inflammation in those taking medications that alter blood clotting.

Massage therapists should not perform any techniques that create inflammation or damage tissue. In any case where pain perception may be altered, feedback mechanisms for pressure and intensity of massage are not reliable because medications may alter normal pain responses that act as warning signs of potential injury to the tissues during massage treatment. Techniques or modalities that would normally cause some discomfort are more easily tolerated than they should be. A client, for example, may have a more normal range of motion, or movement without the level of pain and discomfort usually associated with the same amount stress on their tissues. As anti-inflammatories and analgesics are primarily used to relieve pain, therapists should reduce the intensity of the massage, in general, until the client’s comfort and safety is assured.

Assessing individuals using topical anti-inflammatories or analgesics may be difficult in that these body tissues may appear healthier and more resilient than they actually are. Practitioners who are unaware of the medication may be more aggressive than is appropriate or required, with greater risk of bruising.

Be aware that any complaint of gastrointestinal pain and discomfort among individuals using NSAIDS is significant, as these medications can cause ulcers and bleeding of the gastrointestinal tract, both of which can become life-threatening if not addressed. If the client has been diagnosed and is being treated for these side effects, abdominal massage and hydrotherapy are contraindicated until the condition has resolved. Corticosteroids cause atrophy and weaken connective tissues, including skin, fascia, ligaments, and muscle, joint capsules, bones, and tendons. When injected into joints for arthritis, steroids can induce breakdown of articular cartilage. Corticosteroids also impair the body’s ability to repair body tissues normally, resulting in longer healing periods and fragile tissue after any injury. Corticosteroids also have immunosuppressant effects which may exacerbate the client’s condition.
effects that make an individual more susceptible to infection, so hand washing
and being in good health are important to the client’s health and safety.

Individuals taking corticosteroids for long periods may notice changes in skin sensitivity
and altered reactions to heat and cold. Normal function and sensitivity of the skin are
compromised to the extent that skin rolling, friction, and wrinkling can result in bruising and inflammation of the tissues. Any massage strokes that involve placing direct pressure or stress on tissue structures will need to be reviewed. Avoid heavy tapotement, passive forced stretching, muscle stripping, deep kneading, frictions or joint mobilization. For tissues affected by topical steroid applications, exercise caution and modify the depth of pressure when working on tissues.

Nonsteroidal anti inflammatory drugs (NSAIDs): aspirin, acetylsalicylic acid, celectoxib (Celebrex), choline salicylate (Arthroman), diclofenac (Voltaren), diflunisal (Dolobid), etodolac (Lodine), fenoprofen (Nalfon), flurbiprofen (Ansaid), ibuprofen (Motrin, Advil*), indomethacin (Indocin), ketoprofen (Orudis), ketorolac (Toradol), magnesium salicylate (Doan’s Pills), meclofenamate sodium, mefenamic acid (Ponstel), meloxicam (Mobic), nabumetone (Relafen), naproxen (Aleve*, Naprosyn); ocyaprozin (Daypro), piroxicam (Feldane), rofecoxib (Vioxx) withdrawn, salicylsalicylic (Disalcid), sodium salicylate, sulindac (Clinoril), suprofen (Profenal), tolmetin (Tolectin), valdecoxib (Bextra) withdrawn.

The NSAIDs include a large and chemically diverse group of drugs that possess analgesic, anti-inflammatory, and antipyretic (fever-reducing) properties. There are dozens of NSAIDs on the market, with new ones constantly becoming available. Some can be purchased as over-the-counter preparations, but larger doses of those drugs or other preparations are available only by prescription.

NSAIDs span a number of chemical categories, with a range of different pharmacokinetics and pharmacodynamics. The anti-inflammatory abilities of NSAIDS are a function of their ability to inhibit the production of prostaglandins, which are responsible for producing inflammation and pain. Prostaglandins are a powerful hormone-like substance, derived from arachidonic acid, found in many body tissues and produced in response to trauma. Prostaglandin production may alter blood pressure, metabolism and smooth muscle activity. NSAIDs have a number of potentially serious side effects. The most common is irritation of the stomach. NSAIDs are very useful in treating joint pain, swelling, and muscle pain. Although all NSAIDs appear to work in the same way, not every one has the same effect on every person. Individuals should use only one NSAID at any given time. Most NSAIDS are an appropriate treatment for rheumatoid arthritis, psoriatic arthritis, and arthritis associated with inflammatory bowel disease (IBD); osteoarthritis, sprains and strains. Originally, aspirin was the only choice of NSAID. Now many other effective NSAIDs exist, many without the most common negative side effects of aspirin.

The most common side effect from NSAIDs is stomach upset or indigestion, especially in older patients. Taking NSAIDs with food or milk or immediately following a meal lessens the chance of this occurring. Some NSAIDs products are less likely to upset the stomach. NSAIDs also prevent platelets (blood cells that help blood clot after an injury) from working correctly. When platelets don’t function as they should, bleeding is more difficult to stop. NSAIDs can also irritate the stomach and cause bleeding. Stools that are darker than normal or unusual bruising, are both signs of bleeding, and a client who experiences these should be referred to a doctor. Other side effects include kidney problems and stomach ulcers.

NSAIDs should be used only under CLOSE physician supervision if a client: ♦ Has asthma. ♦ Has liver problems. ♦ Has heart problems. ♦ Has kidney problems.

There are three types of NSAIDs: Salicylates (acetylated, such as aspirin, and non-acetylated), the traditional NSAIDs, and COX-2 selective inhibitors. All NSAIDs are gastric irritants, although newer formulations cause less gastric acid, in general, than aspirin. All newer NSAIDs are analgesic, anti-inflammatory, and antipyretic, and most [except the COX-2-selective agents and non-acetylated salicylates (see below) inhibit platelet aggression.

Aspirin (acetylsalicylic acid, ASA Bayer)
Commonly known as aspirin, acetylsalicylic acid is this country’s most widely used drug, both singularly and in combination with many prescription and patent medicines. Used for many different aches and pains, aspirin can injure the stomach, interfere with the absorption of several vitamins (especially C, K, and folic acid), and pose a special risk for pregnant women and patients with ulcers.

NSAIDs and the role of cyclooxygenase inhibition
NSAIDs work to block the effect of an enzyme called cyclooxygenase. This enzyme is critical in the body’s production of prostaglandins. It is prostaglandins that cause swelling and pain in a condition such as arthritis or bursitis. Therefore, by interfering with cyclooxygenase, you decrease the production of prostaglandins, and decrease pain and swelling associated with this condition.

However, prostaglandins also have other important functions in the body. One type of prostaglandin (there are many varieties) helps line the stomach with a protective fluid (called gastric mucosa). When the production of this protective fluid is diminished, some people are at risk for developing stomach ulcers.

Aspirin’s anti-inflammatory effects are due to its nonselective inhibition of both cyclooxygenase (COX) forms. Aspirin is a more potent inhibitor of both prostaglandin synthesis and platelet aggregation than other salicylic acid derivatives. The differences in activity between aspirin and salicylic acid are thought to be due to the acetyl group on the aspirin molecule. This acetyl group is responsible for the inactivation of cyclooxygenase via acetylation.

In general, immediate release aspirin is nearly completely absorbed from the gastrointestinal (GI) tract. Following absorption, aspirin is hydrolyzed to salicylic acid with peak plasma levels of salicylic acid occurring within 1-2 hours of dosing. The rate of absorption from the GI tract is dependent upon the dosage form, the presence or absence of food, gastric pH (the presence or absence of GI antacids or buffering agents), and other physiologic factors. Enteric-coated aspirin products are unevenly absorbed from the GI tract.

Salicylic acid is widely distributed to all tissues and fluids in the body including the central nervous system (CNS), breast milk, and fetal tissues. The highest concentrations are found in the plasma, liver, renal cortex, heart, and lungs. The protein binding of salicylate is concentration-dependent, i.e., nonlinear. An early sign of salicylic overdose (salicylism) is tinnitus (ringing in the ears). Aspirin is rapidly hydrolyzed in the plasma to salicylic acid such that plasma levels of aspirin are essentially undetectable 1-2 hours after dosing. The elimination of salicylic acid follows zero order pharmacokinetics; (i.e., the rate of drug elimination is constant in relation to plasma concentration). Renal excretion of unchanged drug depends upon urine pH. Following therapeutic doses, approximately 10 percent is found excreted in the urine as salicylic acid, 75 percent as salicyluric acid, and 10 percent phenolic and 5 percent acyl glucuronides of salicylic acid.

Aspirin affects platelet aggregation by irreversibly inhibiting prostaglandin cyclooxygenase. This effect lasts for the life of the platelet and prevents the formation...
of the platelet-aggregating factor. Non-acetylated salicylates (see below) do not inhibit this enzyme and have no effect on platelet aggregation. At somewhat higher doses, aspirin reversibly inhibits the formation of prostaglandin I2 (prostacyclin), which is an arterial vasodilator and inhibits platelet aggregation.

At higher doses, aspirin is an effective anti-inflammatory agent, partially due to inhibition of inflammatory mediators via cyclooxygenase inhibition in peripheral tissues. Studies suggest that other mediators of inflammation may also be suppressed by aspirin administration, although the precise mechanism of action has not been explained. It is this nonspecific suppression of cyclooxygenase activity in peripheral tissues following large doses that leads to its primary side effect of gastric irritation.

Contraindications of aspirin
Allergy: Aspirin is contraindicated in people with known allergy to nonsteroidal anti-inflammatory drug products and in patients with the syndrome of asthma, rhinitis, and nasal polyps. Aspirin may cause severe urticaria, angioedema, or bronchospasm (asthma).

Reye's syndrome: Aspirin should not be used in children or teenagers for viral infections, with or without fever, because of the risk of Reye's syndrome with concomitant use of aspirin in certain viral illnesses.

Alcohol warning: People who consume three or more alcoholic drinks every day should be counseled by their doctor about the bleeding risks involved with chronic, heavy alcohol use while taking aspirin.

Coagulation abnormalities: Even low doses of aspirin can inhibit platelet function leading to an increase in bleeding time. This can adversely affect people with inherited (hemophilia) or acquired (liver disease or vitamin K deficiency) bleeding disorders.

Gastrointestinal side effects: GI side effects include stomach pain, heartburn, nausea, vomiting, and gross GI bleeding. Although minor upper GI symptoms, such as dyspepsia, are common and can occur anytime during therapy, physicians should remain alert for signs of ulceration and bleeding, even in the absence of previous GI symptoms. Physicians should inform patients about the signs and symptoms of GI side effects and what steps to take if they occur.

Peptic ulcer disease: People with a history of active peptic ulcer disease should avoid using aspirin, which can cause gastric mucosal irritation and bleeding.

Renal failure: Avoid aspirin in people with severe renal failure (glomerular filtration rate less than 10 mL/minute).

Hepatic insufficiency: Avoid aspirin in people with severe hepatic insufficiency.

Sodium restricted diets: People with sodium-retaining states, such as congestive heart failure or renal failure, should avoid sodium-containing buffered aspirin preparations because of their high sodium content.

Aspirin has been associated with elevated hepatic enzymes, blood urea nitrogen and serum creatinine, hyperkalemia, proteinuria, and prolonged bleeding time.

Drug interactions
Angiotensin converting enzyme (ACE) inhibitors: The hyponatremic and hypotensive effects of ACE inhibitors may be diminished by the concomitant administration of aspirin due to its indirect effect on the renin-angiotensin conversion pathway.

Acetazolamide: Concurrent use of aspirin and acetazolamide can lead to high serum concentrations of acetazolamide (and toxicity) due to competition at the renal tubule for secretion.

Anticoagulant therapy (heparin and warfarin): People on anticoagulation therapy are at increased risk for bleeding because of drug-drug interactions and the effect on platelets. Aspirin can displace warfarin from protein binding sites, leading to prolongation of both the prothrombin time and the bleeding time. Aspirin can increase the anticoagulant activity of heparin, increasing bleeding risk.

Anticonvulsants: Salicylate can displace protein-bound phenytoin and valproic acid, leading to a decrease in the total concentration of phenytoin and an increase in serum valproic acid levels.

Beta blockers: The hypotensive effects of beta blockers may be diminished by the concomitant administration of aspirin due to inhibition of renal prostaglandins, leading to decreased renal blood flow, and salt and fluid retention.

Diuretics: The effectiveness of diuretics in people with underlying renal or cardiovascular disease may be diminished by the concomitant administration of aspirin due to inhibition of renal prostaglandins, leading to decreased renal blood flow and salt and fluid retention.

Methotrexate: Salicylate can inhibit renal clearance of methotrexate, leading to bone marrow toxicity, especially in the elderly or renal impaired.

Nonsteroidal anti-inflammatory drugs (NSAIDs): The concurrent use of aspirin with other NSAIDs should be avoided because this may increase bleeding or lead to decreased renal function.

Oral hypoglycemics: Moderate doses of aspirin may increase the effectiveness of oral hypoglycemic drugs, leading to hypoglycemia.

Uricosuric agents (probenecid and sulfinpyrazone): Salicylates antagonize the uricosuric action of uricosuric agents.

Carcinogenesis, mutagenesis, impairment of fertility: Administration of aspirin for 68 weeks at 0.5 percent in the feed of rats was not carcinogenic. In the Ames Salmonella assay, aspirin was not mutagenic; however, aspirin did induce chromosome aberrations in cultured human fibroblasts. Aspirin inhibits ovulation in rats. (See Pregnancy.)

Pregnancy: Pregnant women should only take aspirin if clearly needed. Because of the known effects of NSAIDs on the fetal cardiovascular system (closure of the ductus arteriosus), use during the third trimester of pregnancy should be avoided. Salicylate products have also been associated with alterations in maternal and neonatal hemostasis mechanisms, decreased birth weight, and with perinatal mortality.

Labor and delivery: Aspirin should be avoided 1 week prior to and during labor and delivery because it can result in excessive blood loss at delivery. Prolonged gestation and prolonged labor due to prostaglandin inhibition have been reported.

Nursing mothers: Nursing mothers should avoid using aspirin because salicylate is excreted in breast milk. Use of high doses may lead to rashes, platelet abnormalities, and bleeding in nursing infants.

Pediatric use: Pediatric dosing recommendations for juvenile rheumatoid arthritis are based on well-controlled clinical studies.

Side effects
Many adverse reactions due to aspirin ingestion are dose-related. The following is a list of adverse reactions that have been reported in the literature.

General: Fever, hypothermia, thirst.

Cardiovascular: Dysrhythmias, hypotension, tachycardia.

Central nervous system: Agitation, cerebral edema, coma, confusion, dizziness, headache, subdural or intracranial hemorrhage, lethargy, seizures.

Fluid and electrolyte: Dehydration, hyperkalemia, metabolic acidosis, respiratory alkalosis.
Interstitial nephritis, papillary difficulty perceiving tinnitus.

Hyperglycemia.

Hypoglycemia (in children), angioedema, asthma, bronchospasm, laryngeal edema, urticaria.

Musculoskeletal: Rhabdomyolysis.

Metabolism: Hypoglycemia (in children), hyperglycemia.

Reproductive: Prolonged pregnancy and labor, stillbirths, lower birth weight infants, antepartum and postpartum bleeding.

Respiratory: Hyperpnea, pulmonary edema, tachypnea.

Special senses: Hearing loss, tinnitus. People with high frequency hearing loss may have difficulty perceiving tinnitus.

Urogenital: Intersitial nephritis, papillary necrosis, proteinuria, renal insufficiency and failure.

Nonacetylated salicylates: magnesium salicylate (Doan’s pills) sodium salicylate, and salicylate (Disalcid).

All nonacetylated salicylates are useful anti-inflammatories, although they may be less effective analgesics than aspirin. There are significantly less effective than aspirin as cyclooxygenase inhibitors, so are more desirable when cyclooxygenase inhibition is not wanted, which is the case in individuals with asthma, bleeding tendencies and renal dysfunction. Individuals taking nonacetylated salicylates should be monitored for serum salicylate levels.

In the past several years, some newer medications have come on the market that are commonly referred to as COX-2 inhibitors. All NSAIDs work against cyclooxygenase (COX). Traditional NSAIDs (e.g. Ibuprofen, Motrin, Aleve) work against both COX-1 and COX-2. COX-1 and COX-2 are both types of cyclooxygenase enzymes that function in the body. The new medications (which included Celebrex, Vioxx, and Bextra, among others) only work against COX-2, and allow COX-1 to function normally.

Because COX-1 is more important in producing the protective lining in your gut (gastric mucosa), these newer NSAIDs are believed to have less of a risk of causing stomach ulcers. That said, the newer NSAIDs have not been shown to work any better against the COX-2 enzyme. Therefore, the COX-2 inhibitors have the benefit of possibly having fewer side effects, but not necessarily better relief from symptoms.

**COX-2 selective inhibitors ( Coxibs):**

- celecoxib (Celebrex)
- etoricoxib, meloxicam.

COX-2 inhibitors achieve inflammation reduction by selectively blocking the COX-2 enzyme, which obstructs the production of the prostaglandins (chemical messengers) that cause the pain and swelling of arthritis inflammation. COX-2 inhibitors do not block the COX-1 enzyme, making them uniquely different from traditional NSAIDs.

Cyclooxygenase-1 (COX-1) is an enzyme normally present in a variety of areas of the body, including sites of inflammation and the stomach. The COX-1 enzyme of the stomach produces certain chemical messengers (called prostaglandins) that ensure the natural mucus lining which protects the inner stomach. Common anti-inflammatory drugs like aspirin block the function of the COX-1 enzyme along with another enzyme, COX-2. Inflammation is reduced when the COX-1 enzyme is blocked, but the protective mucus lining of the stomach is also reduced. This reduction in the stomach lining can cause stomach ulceration and bleeding from the stomach and intestines.

Cyclooxygenase-2 (COX-2) also produces these chemical messenger molecules, but the COX-2 enzyme is located specifically in areas of the body that are responsible for inflammation, and not in the stomach. A COX-2 inhibitor blocks the enzyme and inflammation is reduced. Since the COX-2 enzyme does not affect the normal function of the stomach or intestinal tract, medications that selectively block COX-2 do not present the same risk of injuring the stomach or intestines. However, they do cause a significant increase in cardiovascular risk such as stroke or heart attack.

COX-2 plays a significant role in the development of various symptoms and conditions, including fever, inflammation, and pain. Its role in other conditions, such as cancer and Alzheimer’s dementia, also is being investigated.

**Vioxx and Bextra**

The common anti-inflammatory drugs (like aspirin, ibuprofen, and naproxen) all act by blocking the action of both the COX-1 and COX-2 enzymes. Blocking the COX-2 enzyme impedes the production of the prostaglandins that cause the pain and swelling of arthritis inflammation.

Their selective action provides the benefits of reducing inflammation without irritating the stomach. While these drugs pose an advantage in comparison to previous anti-inflammatory drugs because their mechanism of action carries nowhere near the risk of stomach ulceration and bleeding, the fact that they can cause cardiovascular risks (a side effect of some of the COX-2 NSAIDs is an increase in the risk of heart attacks and strokes, especially when they are used at higher doses) was sufficient for the FDA to recall COX-2 inhibitors Vioxx and Bextra.

Because of these reports, Merck, the company that makes Vioxx, voluntarily took it off the market in September 2004. On April 7, 2005, Vioxx was recalled because of the potential cardiac risks that were found in a recent study of this drug. In the study, patients who regularly took Vioxx for a period of 18 months or longer had an increased risk of cardiac events, such as heart attack and stroke. Pfizer withdrew Bextra from the market at the FDA’s request due to similar cardiovascular risks and reports of serious skin rashes in some people. In addition, the FDA stated that Bextra had no clear advantage over traditional NSAIDs for pain control.

**Celecoxib (Celebrex)**

The COX-2 inhibitor Celebrex is currently still on the market and is now taking the place of former prescriptions of Bextra and Vioxx. Although widely expected that COX-2 inhibitors will be of great value to people with arthritis and variety of pain conditions, the increased risk of heart attacks and strokes has caused many to seek alternatives to COX-2 inhibitors. However, in April 2005, an FDA alert warned that Celebrex has been linked to an increased risk of serious cardiovascular (CV) events (such as heart attack or stroke) which appears to be a risk shared by all medicines called non-steroidal anti-inflammatory drugs (NSAIDs) (excluding aspirin).

The FDA requested that the package insert (labeling) for all NSAIDs, including Celebrex, be revised to include a “boxed” or serious warning to highlight the potential increased risk of CV events, and the well known risk of serious, and potentially life-threatening, stomach bleeding. FDA has also requested that the package insert for all NSAIDs be revised to state that people who have just had heart surgery should not take these medicines.

Prior to the recall of Cox-2 painkillers, these drugs were aggressively marketed as being more effective than traditional painkillers and less likely to cause gastrointestinal side effects associated with older NSAIDs like ibuprofen and naproxen. The studies used to develop this marketing pitch have been highly scrutinized since new studies have found evidence to the contrary. Thousands of injured consumers worldwide have filed lawsuits against the makers of these painkillers. In the United States, consumers who allegedly suffered serious Vioxx side
effects have filed at least 7,000 lawsuits against Merck. Hundreds more Bextra side effect victims have filed similar lawsuits against Pfizer.

**COX-2 inhibitor benefits and risks**
Currently, the only available COX-2 inhibitor NSAID is Celebrex. The FDA concluded that the benefits of Celebrex outweighed the potential risks but in addition to patient warnings with each prescription, encouraged patients and their physicians to discuss these risks when Celebrex is prescribed. The FDA also advised patients to use the lowest effective dose of Celebrex to control their pain and to use it only as long as necessary.

In addition, the FDA now requires the addition of more specific information about the risks for stomach irritation and ulcers, skin rashes, and a possible increase in risk for cardiovascular events with prescription and nonprescription forms of traditional or non-selective NSAIDs except aspirin. NSAIDs are contraindicated after coronary artery bypass surgery. Although all NSAIDs have the potential to cause high blood pressure and worsen congestive heart failure, to date, studies have not clearly shown that the traditional NSAIDs cause an increase in heart attacks and strokes that were seen with some of the COX-2 NSAIDs. More research is needed to understand if some or all of the traditional NSAIDs also increase the risk of these events.

People should not take Celebrex if they:
- Have had an allergic-type reaction to sulfa medicines.
- Have had asthma, hives or allergic-type reactions after taking aspirin or other NSAID (nonsteroidal anti-inflammatory drugs) medicines. People also may have aspirin-sensitive asthma, which means aspirin can cause severe narrowing of the airway (bronchospasm) and even death. Since this type of reaction also has occurred after taking NSAIDs, Celebrex should not be given to aspirin-sensitive patients.
- Are pregnant, especially during the last 3 months.

Celebrex and other NSAID medicines can cause serious problems such as:
- **Stomach ulcers that bleed.** The chance of this serious prob-lem increases the longer a person takes Celebrex, but it can also happen suddenly. If it does, the person should stop taking Celebrex and call a health care professional right away. Symptoms include a burning stomach pain, black bowel movements that look like tar, or vomit that looks like blood or coffee grounds.
- **Liver damage.** Some of the warning signs of liver damage are nausea, vomiting, tiredness, loss of appetite, itching, yellow coloring of skin or eyes, “flu-like” symptoms and dark urine. If this happens, a person should stop taking Celebrex and call a health care professional right away.
- **Kidney problems** that include sudden kidney failure or worsening of existing kidney problems.
- **Fluid retention** (holding of water in the body) and swelling. Fluid retention can be a serious problem for people with high blood pressure or heart failure.

In addition to the serious side effects listed above, some common, but less serious side effects with Celebrex may include:
- Headache.
- Indigestion.
- Upper respiratory tract infection (a “cold”).
- Diarrhea.
- Sinus inflammation.
- Stomach pain.
- Nausea.

**NSAID side effects in general include:**
- **Gastrointestinal:** Dyspepsia, heartburn, epigastric distress, and nausea; less frequently, vomiting, anorexia, abdominal pain, GI bleeding, and mucosal lesions. Misoprostol (Cytotec), a synthetic prostaglandin that inhibits gastric acid secretion, may be given to prevent GI intolerance. It prevents gastric ulcers and their associated GI bleeding in people receiving NSAIDs.
- **Genitourinary:** Fluid retention, reduction in creatinine clearance, and acute tubular necrosis with renal failure.
- **Hepatic:** Acute reversible hepatotoxicity.
- **Cardiovascular:** Hypertension and moderate to severe noncardiogenic pulmonary edema.

- **Hematologic:** Altered hemostasis through effects on platelet function.
- **Other:** Skin eruption, sensitivity reactions, tinnitus, and hearing loss.

**Pregnancy and lactation**
NSAIDs should be avoided during the first trimester and just before delivery; they may be used cautiously at other times during pregnancy. NSAIDs appear in breast milk and should be used cautiously by breastfeeding mothers.

**Nonselective COX inhibitors**
Approximately 17 million Americans take nonsteroidal anti-inflammatory drugs (NSAIDs) daily for treatment of pain or inflammation. These drugs are nonselective inhibitors of the enzymes cyclooxygenase (COX) 1 and 2, which convert arachidonic acid to prostaglandins. Unfortunately, they are also associated with serious adverse gastrointestinal effects, such as gastritis, dyspepsia, gastroduodenal ulcers, perforations, and bleeding. Endoscopic studies have shown that within one week of starting NSAID therapy, more than 30 percent of patients will have gastric erosions or ulcers, and within one year, approximately 3 percent will have significant gastrointestinal bleeding. As many as 15,000 deaths each year have been attributed to NSAID use in the United States.7

**Acetic acid NSAIDs**
Diclofenac (Cataflam, Voltarren): Relatively nonselective as a COX inhibitor, adverse effects occur in about 20 percent of users, include symptoms of gastrointestinal distress, bleeding, and ulceration. Used post-surgically in certain operations.

Etodolac (Lodine): Somewhat more COX-2 selective than most NSAIDs may cause less gastric toxicity in relation to ulcer disease that other nonselective NSAIDs.

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Indomethacin (Indocin): A powerful nonselective COX inhibitor that may also decrease T-cell proliferations. Useful for rheumatic conditions and can reduce gingival inflammation in an oral rinse administration. At higher dosages, one-third of users have reactions requiring discontinuing the drug. Side effects include abdominal pain, diarrhea, gastrointestinal hemorrhage, and pancreatitis. Headache is experienced in up to one-quarter of users and is associated with dizziness, confusion, and depression. May interact with other medications. Should not be used in individuals with nasal polyps or angioedema, as it may precipitate an asthma attack.

Propionic acid NSAIDs
Fenoprofen (Nalfon): Most associated with rare toxicity of interstitial nephritis among all the NSAIDs. Other side effects include nausea, dyspepsia, peripheral edema, rash, central nervous system and cardiovascular effects, and tinnitus. Drug interactions.

Flurbiprofen (Ansaid): Extensive hepatic metabolism; comparable in strength to aspirin in studies with rheumatoid arthritis and osteoarthritis; available in a topical form; effective after surgery; side effects similar to other NSAIDS, with slightly more pronounced adverse effects including ataxia or tremors.

Ibuprofen (Motrin, Advil): Oral ibuprofen is often prescribed in low doses, at which it has analgesic, but not anti-inflammatory effects. Topical cream and liquid gel forms may be more effective for absorption into flesh and muscle. Gastrointestinal irritation and bleeding occur less frequently than with aspirin. Use of aspirin and ibuprofen together may decrease overall anti-inflammatory effects. Therefore, treatment with ibuprofen in individuals with increased cardiovascular risks may limit the heart protecting effects of aspirin. Contraindicated in individuals with nasal polyps, angioedema, and bronchospastic reactivity to aspirin. Has also been associated with rash, pruritus, tinnitus, dizziness, headache, and fluid retention. Renal difficulties occur (as with all NSAIDS) but very rarely.

Ketoprofen (Orudis): Ketoprofen nonselectively inhibits COX and lipoxygenase, but is similar to the other NSAIDs in its effectiveness for the treatment of rheumatoid arthritis and osteoarthritis. Adversely affects the gastrointestinal tract and central nervous system.

Naproxen (Nasprosyn, Aleve): Naproxen availability is 41 percent higher in women than in men and is effective for rheumatologic conditions in a slow release formula, topical preparation and as an eye-wash. Over the counter use of naproxen is associated with two times greater incidence of gastrointestinal bleeding than that of over-the-counter use of ibuprofen. Beyond normal NSAID-associated effects, rare cases of allergic pneumonitis, leukocytoclastic vasculitis and pseudopopyphrya are associated with use.

Oxaprozin (Daypro): The major difference between this drug and other NSAIDS like it is its very long half-life, permitting dosage in a once-a-day formulation.

Fenamate NSAIDs
Meclofenamate sodium, mefenamic acid (Ponstel) inhibit both COX and phospholipase A2. Meclofenamate has similar side effects to other NSAIDS, with slightly higher incidence of abdominal pain and diarrhea. It also enhances the effect of oral anticoagulants and is contraindicated in pregnancy. Mefamic acid is less effective than aspirin as an anti-inflammatory, but is considerably more toxic. It should not be used for a period over one week.

Napthylalkanone NSAIDs
Nabumetone (Relafen): Nabumetone is the only nonacid NSAID currently available. Its half-life is greater than 24 hours, permitting a once-daily dose. It may be slightly less damaging to the stomach than other NSAIDS, but is more expensive, which may be prohibitive in larger dosages. Like naproxen, nabumetone has been reported to cause photosensitivity and pseudopopyphyrya in some users.

Oxicam NSAIDs
Piroxicam (Feldene): Has a long half-life, permitting once a day dosage. At high concentrations, this COX inhibitor also inhibits leukocyte migration, decreases oxygen radical production and inhibits lymphocyte function. Toxicity includes gastrointestinal symptoms in 20 percent of users, and other adverse effects including headache, dizziness, tinnitus, and rash. Peptic ulcer and bleeding can occur at higher dosages, at a rate more than nine times that of other NSAIDS.

Diflunisal (Dolobid): Although it is derived from salicylic acid, it is not reduced to salicyclic acid or salicylate. Clearance is dependent on renal function and hepatic metabolism, and dosages should be limited in users with renal impairment. It is considered particularly effective for pain in cases of bone metastases and dental surgery.

Ketorolac (Toradol): Used for systemic use primarily as an analgesic, rather than an anti-inflammatory, although it does have typical NSAID anti-inflammatory properties. Most typically given intramuscularly or intravenously after surgery, but an oral dose is available. When combined with an opioid, it can decrease the amount of opioid required by a much as 25-50 percent. Toxicities are similar to other NSAIDS, with renal toxicity perhaps more common with chronic use than that of other NSAIDS.

Sulindac (Clinoril): Along with its use for rheumatic disease, it may have implications for inhibiting the growth of certain cancers. Like diclofenac, may cause elevated serum aminotransferases more than most other NSAIDS.

In most cases, the choice of an NSAID is based on risk of toxicity and cost-effectiveness. In general, the gastrointestinal and renal side effects of ketorolac limit its use. On a toxicity index, indomethacin and meclofenamate were associated with the greatest toxicity, while salsalate, aspirin, and ibuprofen were least toxic of all the non-selective COX inhibitors. For users with renal dysfunction, nonacetylated salicylates may have fewer side effects. Fenoprofen is used less because it is associated with interstitial nephritis. Two nonselective NSAIDS, diclofenac and sulindac, are more associated with liver function abnormalities than any other NSAIDS. In most cases, physicians seek a good fit between an individual’s needs and sensitivities and an NSAID that best suits those needs.

Acetaminophen (Tylenol)
Acetaminophen is a drug with antipyretic and analgesic effects similar to those of aspirin and NSAIDS, but with limited anti-inflammatory or antirheumatic effects. It is used to treat mild to moderate pain. Unlike aspirin and related drugs, acetaminophen is not irritating to the stomach. While people rarely have any side effects from the usual dose of acetaminophen, liver and kidney damage may result from using large doses of this medicine every day for a long time, or drinking alcohol with the usual dose. Even moderate amounts of alcohol can produce liver damage in people taking acetaminophen.

Acetaminophen is administered orally with absorption associated with the rate of gastric emptying. Peak blood concentrations usually occur within one-half to one hour. In large doses, a highly active metabolite is associated with acetaminophen’s toxicity to the liver and kidneys. The half-life of this drug is two to three hours and is generally unaffected by renal function. With large doses or in the case of liver disease, the half-life duration may double.

Unlike NSAIDS, acetaminophen does not have anti-inflammatory properties, so does not affect uric acid levels and platelet function. Patients allergic to aspirin, unable to take salicylates, individuals with hemophilia, a history of peptic ulcer, or those with aspirin-associated bronchospasms should not take acetaminophen. It is also often used in children with viral infections. Larger doses may cause
dizziness, excitement, and disorientation. Early symptoms of hepatic damage include nausea, diarrhea, vomiting, and abdominal pain. There have also been rare cases of renal damage.

The exact mechanism of action of acetaminophen is not known. Acetaminophen relieves pain by elevating the pain threshold, that is, by requiring a greater amount of pain to develop before it is felt by a person. It reduces fever through its action on the heat-regulating center of the brain. Specifically, it tells the center to lower the body’s temperature when the temperature is elevated.

Acetaminophen is used for the relief of fever as well as aches and pains associated with many conditions. Acetaminophen relieves pain in mild arthritis but has no effect on the underlying inflammation, redness and swelling of the joint. If the pain is not due to inflammation, acetaminophen is as effective as aspirin. It is as effective as the non-steroidal anti-inflammatory drug ibuprofen in relieving the pain of osteoarthritis of the knee.

Acetaminophen is metabolized (eliminated by conversion to other chemicals) by the liver. Therefore drugs that increase the action of liver enzymes that metabolize acetaminophen (e.g. carbamazepine, isoniazid, rifampin) may decrease the action of acetaminophen. The potential for acetaminophen to harm the liver is increased when it is combined with alcohol or drugs that also harm the liver. When used appropriately, side effects are rare. The most serious side effect is liver damage due to large doses, chronic use or concomitant use with alcohol or other drugs that also damage the liver.

Acetaminophen is excreted in breast milk in small quantities. However, acetaminophen use by the nursing mother appears to be safe. Acetaminophen has been used in all stages of pregnancy.

**Medications for inflammation**

For pain caused by swelling, glucocorticoids or steroids, like prednisone, may be useful, but because of the toxicity associated with their effects, their use has been limited, in general, to treatment for acute flare-ups of the joints. For long-term use, the NSAIDS now have the primary role in treatment.

People who take corticosteroids for painful conditions such as osteoarthritis and rheumatoid arthritis may get them in the form of injections. For people with one painful joint (e.g., knee), an injection can provide pain relief and reduce swelling. Corticosteroids injected directly into a joint can concentrate the medication where it is needed and avoid potential problems such as an upset stomach. However, continued injections into specific joints may eventually damage the cartilage in the joint.

People taking corticosteroids should never stop taking them abruptly because they can experience serious side effects. A physician can provide a schedule for safely discontinuing the use of corticosteroids. Most corticosteroids are available only with a physician’s prescription. However, some low-strength topical creams are available over the counter.

Corticosteroids are extremely helpful as short-term relief for many chronic pain conditions. They are some of the most powerful medicines available to fight inflammation. However, long-term use of corticosteroids may lead to numerous side effects. Some of the strongest side effects are associated with the oral and intravenous forms of corticosteroids, which are used for pain. Physicians may try to minimize the side effects by prescribing as low a dose as possible for pain relief and by using corticosteroids for severe pain only.

For further information, refer to the section under Gastrointestinal Medications (corticosteroids), above.
MEDICATION AND MASSAGE
THERAPY PART II:
COMMON GASTROINTESTINAL AND
PAIN MEDICATIONS
FINAL EXAMINATION QUESTIONS

Select the best answer for each question and complete your test online at www.ilmassagece.com.

1. Which of the following statements regarding corticosteroids is false?
   a. Corticosteroids cause atrophy and weaken connective tissues, including skin, fascia, ligaments, and muscle, joint capsules, bones, and tendons.
   b. Corticosteroids also enhance the body’s ability to repair body tissues, resulting in shorter healing periods and less fragile tissue after any injury.
   c. Corticosteroids also have immunosuppressant effects that make an individual more susceptible to infection, so hand washing and being in good health are important to the client’s health and safety.
   d. Individuals taking corticosteroids for long periods may notice changes in skin sensitivity and altered reactions to heat and cold.

2. Which of the following statements about acid-peptic diseases is false?
   a. Acid-peptic diseases include gastroesophageal reflux, peptic ulcer (gastric and duodenal), and stress-related mucosal injury.
   b. Ulceration or mucosal erosion occurs when caustic substances (like acid, bile, and pepsin) in the gastrointestinal tract overpower the defenses of gastrointestinal mucosa (mucus and bicarbonate secretions, blood flow, prostaglandins, and cellular regeneration after injury).
   c. Drugs used in acid-peptic disorder treatment typically do one of two things: reduce intragastric acidity or promote mucosal defense.
   d. Antacids have no history of nonprescription use in individuals with acid-peptic disorders.

3. Which of the following is not one of the three main types of antacid preparations?
   a. Sodium bicarbonate.
   b. Colloidal bismuth.
   c. Calcium carbonate.
   d. Magnesium or aluminum hydroxide.

4. Which of the following statements about H2 receptor antagonists is false?
   a. H2 receptor antagonists are currently prescribed for the following conditions: gastroesophageal reflux disease (GERD), nonulcer dyspepsia, and for the prevention of bleeding from stress-related gastritis.
   b. While they do not work as rapidly, H2 antagonists last for a longer period than antacids (6-10 hours vs. 1-2).
   c. More than 10 percent of individuals taking H2 antagonists experience side effects.
   d. Half-lives for these H2 antagonists range from about 1 to 4 hours, depending on dosage.

5. Which of the following is not one of the four main H2 antagonists in current use?
   a. Cimetidine.
   b. Ranitidine.
   c. Famotidine.
   d. Lamotidine.

6. Which of the following statements about proton pump inhibitors (PPI) is false?
   a. PPIs have been in use since the late 1980s.
   b. They are highly effective acid-inhibiting agents used commonly for treatment of acid-peptic disorders.
   c. All proton pump inhibitors, except rabeprazole, are administered intravenously.
   d. Proton pump inhibitors are largely metabolized by the liver and are eliminated in urine.

7. Which of the following statements about proton pump inhibitors and ulcers is false?
   a. Proton pump inhibitors assist in the healing of both duodenal and gastric ulcers, healing over 90 percent of ulcers within 8 weeks.
   b. Ulcers may be associated with the use of glucocorticoids.
   c. In the case of H pylori infection, the therapeutic strategy is two-fold: to eliminate the bacteria and heal the ulcer.
   d. Elimination of the organism is produced through the proton pump inhibitor’s ability to substantially raise environmental pH in the body, allowing antibiotics to effectively combat H pylori.

8. Which of the following statements about metoclopramide is false?
   a. Metoclopramide is used to treat individuals with delayed gastric emptying (due to surgery or diabetes).
   b. It is sometimes administered to hospitalized individuals using feeding tubes to promote movement of food from the stomach to the duodenum.
   c. Metoclopramide may also provide some relief from symptoms of chronic dyspepsia, for the prevention and treatment of emesis (nausea), and to prevent vomiting.
   d. Long-term use of metoclopramide is encouraged.

9. Laxatives work though all of the following mechanisms, except:
   a. Bulk-forming.
   b. Stool softening.
   c. Analgesic.
   d. Osmotic.

10. Stimulant laxatives are also called:
   a. Cathartics.
   b. Purgatives.
   c. Softeners.
   d. Constipators.

11. Which of the following statements about stool surfactant agents is false?
   a. They allow the entry of water and lipids into the stool, softening the material.
   b. Atropine (intravenous) is typically prescribed in hospitalized individuals to prevent constipation.
   c. Glycerin suppositories and mineral oil are also commonly used stool softeners.
   d. Long-term use of mineral oil may reduce absorption of vitamins A, D, E, and K.
12. Which of the following statements about laxatives is false?
   a. Many people use over-the-counter laxatives instead of a high-fiber diet, adequate hydration, and exercise to maintain regularity.
   b. Bulk-forming laxatives cannot be digested; instead, they absorb water within the body, turning into a bulky gel that stimulates peristalsis.
   c. Osmotic laxatives are absorbable solutions that result in decreased liquidity of the stool.
   d. Polyethylene glycol (PEG) is used for colonic cleansing prior to endoscopic procedures.

13. Which of the following statements about anti-diarrheal drugs is false?
   a. Colloidal bismuth compounds, like bismuth subsalicylate, are classified as proton pump inhibitors (PPI).
   b. Anti-diarrheals are typically used to control chronic diarrhea caused by irritable bowel syndrome (IBS) or inflammatory bowel disease (IBD).
   c. Anti-diarrheal drugs should only be used in cases of mild to moderate diarrhea, and should not be used by individuals with blood in their stool, a high fever, or other condition that might cause systemic toxicity or worsen the pre-existing condition.
   d. Two main opioids are used as anti-diarrheal agents: loperamide and diphenoxylate.

14. Which of the following statements about vomiting or nausea is false?
   a. Nausea is an uneasiness of the stomach that always leads to vomiting.
   b. Some triggers that may result in vomiting can come from the stomach and intestines (infection, injury, and food irritation), the inner ear (dizziness and motion sickness), and the brain (head injury, brain infections, tumors, and migraine headaches).
   c. Various stimuli that affect nausea and vomiting come together in an area in the brain known as the vomit (emetic) center in the medulla.
   d. The vomit center receives input from four major areas: the GI tract, the chemoreceptor trigger zone, the vestibular apparatus, and the cerebral cortex.

15. Which of the following statements about inflammatory bowel disease (IBD) is false?
   a. IBD is the general name for diseases that cause inflammation in the small intestine and colon.
   b. IBD refers to two distinct disorders: Crohn’s disease and ulcerative colitis.
   c. The cause and progression of both Crohn’s disease and ulcerative colitis is well known.
   d. Crohn’s disease (regional enteritis) is a condition of inflammation of the mucosa in the large intestine, and more commonly, the ileum of the small intestine.

16. Which of the following statements about ulcerative colitis is false?
   a. Ulcerative colitis is a disease that causes inflammation and sores (ulcers) in the lining of the rectum and colon.
   b. Ulcers form where inflammation has killed the cells that usually line the colon, then bleed and produce pus.
   c. Inflammation in the colon also causes the colon to empty frequently, causing diarrhea.
   d. It is not difficult to distinguish between ulcerative colitis and Crohn’s disease.

17. Which of the following statements about aminosalicylates (5-ASA) is false?
   a. Aminosalicylates have been used effectively for years to treat IBD.
   b. For aminosalicytes to work, they must be absorbed systemically, rather than topically, into the diseased gastrointestinal areas.
   c. As much as 80 percent of 5-ASA may be absorbed from the small intestine, not reaching its target area.
   d. There are also a number of 5-ASA compounds formulated to reach diseased areas in the small or large bowel, which are referred to as mesalamine.

18. Which of the following statements about glucocorticoids/corticosteroids is false?
   a. Corticosteroids are a group of anti-inflammatory drugs similar to the hormone cortisol produced in the body.
   b. Corticosteroids reduce the inflammation associated with many diseases, including many forms of arthritis.
   c. They can be taken in a variety of forms, such as pills, injections, inhalers, nasal sprays, topical creams, drops, ointments, enemas, foams and suppositories.
   d. Most corticosteroids are available over the counter.

19. Oral forms of corticosteroids taken for a long time can have a wide variety of side effects, including all the following except:
   a. Acne.
   b. Weight loss.
   c. Loss of bone density associated with osteoporosis.
   d. Decrease in immune response.

20. Which of the following statements about cortisol is false?
   a. Corticosteroids are synthetic versions of the natural hormone cortisol, which is chemically related to the natural hormones produced by the body’s adrenal glands, located at the top of each kidney.
   b. Cortisol plays an important role in controlling salt and water balance in the body and regulating carbohydrate, fat, and protein metabolism.
   c. Cortisol also suppresses inflammation, which is the body’s normal response to outside invaders, such as bacteria.
   d. When the body becomes stressed from infection, trauma, surgery, or emotional problems, the adrenal glands stop producing cortisol.