3 PHARMACOLOGY

CORE CONCEPTS

- Explain therapeutic effects, side effects, indications, and contraindications for medications.
- Differentiate between drug tolerance and drug dependence.
- Define broad-spectrum and narrow-spectrum antibiotics.
- Discuss antibiotic resistance.
- Select common conditions requiring antifungal treatment.
- Recognize properties of nonsteroidal anti-inflammatory drugs.
- Discuss usage of non-narcotic and narcotic analgesics.
- Summarize opiate overdose and antidote treatment protocols.

INTRODUCTION

There are approximately 70 different medications in the Army's current medical equipment set kit. Combat medics must know what these medications are prescribed for and be able to reference the proper **dose** to administer. Developing a working knowledge of these medications can help ensure their safe and effective use.

PHARMACOLOGY BASICS

Simply stated, pharmacology is the science of drugs. This broad topic includes their origin, composition, appearance, chemistry, uses, physiological effects, effectiveness, toxicology, and modes of action. Combat medics focus on the clinical uses and **therapeutic effects** of drugs in human patients.

Every medication has at least three names: the chemical name, the **generic name**, and one or more **trade names** (brand names) given by the manufacturer. For example, ibuprofen is a generic name. Its chemical name is (RS)-2-(4-(2-methylpropyl) phenyl) propionic acid and it has 17 trade names, some of which include Advil (GlaxoSmithKline, Middlesex, UK), Caldolor (Cumberland Pharmaceuticals Inc, Nashville, TN), Ibutab (Zee Medical Inc, Irvine, CA), and Motrin (Johnson & Johnson, New Brunswick, NJ). Usually, the generic name is preferred.

PHARMACOLOGICAL CONSIDERATIONS

The use of a pharmaceutical product to treat a medical condition requires knowledge of the medicine, the medical condition, and the individual patient. Not all medications work equally in all people or under all conditions. Not all medications are suited for use in all patients. The prescribing medical officer (MO) must balance effectiveness and potential **side effects**. The MO must determine whether the proposed drug is appropriate for the patient and must choose the form and **dosage** of the medicine that will best achieve the desired effect. In order to achieve maximum benefit, the patient must understand the dosage instructions and be compliant with taking the drugs as directed.

Therapeutic Effects

Medications are intended to provide cures for diseases, reduce the signs of disease, and relieve symptoms. Not all drugs are curative, but all should have positive therapeutic effects. A drug's mechanism of action is the physiologic or biochemical interaction of the drug on its target (the way the drug works at the cellular or subcellular level).

Some medications have multiple therapeutic effects. For example, aspirin (acetylsalicylic acid, or ASA) is an **analgesic** that reduces inflammation, reduces fever, and reduces blood clot formation. Other drugs have

single, very specific effects. For example, some antihypertensive medications have a sole therapeutic effect of controlling high blood pressure, and **antibiotics** only treat microbial infections.

Indications

Medications are approved for use by the US Food and Drug Administration (FDA). These approved uses, or reasons the medications are administered, are the drug's indications. For example, acetaminophen is indicated for pain relief and fever reduction. Indications are located on the label or instructions for use.

Contraindications

MOs must consider whether using a drug may do more harm than good, or have undesirable effects. Some factors make the use of a particular medication in a particular patient inadvisable. These factors, called contraindications, may include things like patient age (usually pediatric or geriatric), pregnancy, immune status, allergies, and other medications. Preexisting conditions commonly result in contraindications for use. For example, aspirin is contraindicated in patients with known or suspected stomach ulcers.

Contraindications can be either relative or absolute. A relative contraindication means that a drug or treatment may harm a patient, but can still be used if the benefit outweighs the risk. An absolute contraindication means the drug is never allowed because it could cause a life-threatening condition.

If the medication cannot be used for the patient, the MO may seek available alternatives. MOs must consider effectiveness, safety, and contraindications of possible alternatives as well.

Occasionally, a drug is used "off label," or without FDA approval for a particular condition. Off-label use is not always contraindicated, but a careful risk-benefit analysis should precede such unapproved use.

Allergies

Allergic reactions are unpredictable responses to a drug that may be mild, moderate, or severe. A true allergy to a medication, while rare, contraindicates its use. Any medication can cause an allergic reaction, but some do so more frequently than others (eg, antibiotics, aspirin and other nonsteroidal anti-inflammatory drugs, sulfa drugs, **topical** and injectable medications containing iodine, and vaccines). Always ask the patient about allergies to medications before administering or dispensing them. Also, individuals with a known allergy to one drug, may be allergic to others.

Mild to Moderate Reactions

A mild to moderate allergic reaction involves a generalized body response that may persist for several hours or more, but is not progressive and does not pose a threat to life (eg, a reddened area at an injection site). Signs and symptoms of a mild to moderate allergic reaction to medication include the following:

- pruritus (itching);
- reddened skin (flush);
- swelling;
- hives (urticaria);
- watery, itchy eyes; and
- increased heart rate.

Severe Reactions

Anaphylaxis refers to a life-threatening hypersensitivity reaction to an **antigen**; it is the most severe of allergic reactions. Even mild initial allergic reactions may progress to anaphylaxis without warning. There are a number of common medications that cause anaphylaxis (anaphylactic shock), including antibiotics, aspirin, vaccines, and medications containing iodine (topical and injectable). Signs and symptoms include:

- airway compromise that may include hoarseness, stridor, edema, rhinorrhea, and wheezing;
- low blood pressure;
- tachycardia, chest pain, and tightness;
- nausea, vomiting, abdominal cramping, and diarrhea;
- itching, hives, swelling of the face, neck, and extremities; and
- **angioedema**.

Patients should remain in the treatment area for 20 minutes following injections because of the possibility of a severe reaction that must be treated immediately.

Side Effects

Pharmaceutical agents often have negative effects or actions in addition to the desired actions. Every medication, over-the-counter (OTC) and prescription, has numerous potential side effects. Most drugs affect more than one system of the body, so the drug target site probably is not the only site of action. For example, ibuprofen may relieve muscle strain, but may also upset the stomach (especially if taken without food).

Although many side effects are minor and tolerable, others may outweigh the benefits of the drug and be severe enough for the patient to discontinue the medication. Some side effects may be life threatening. The drug label describes when the patient should seek emergency medical care or medical advice for side effects. Patients must be advised of potential interactions before taking any medication.

> **Note:** Do not confuse side effects with allergic reactions. Severe allergic reactions are medical emergencies. Symptoms of severe allergic reactions include hives, difficulty breathing, and swelling of the tongue, throat, lips, or face.

Drug Interactions

Drugs may modify the action of one or more other drugs by altering, increasing, or decreasing the expected effects. Drug interactions are common and may be intentional or unintentional. The risk of unintended interactions increases with the number of different drugs a patient uses. Interactions also occur when drugs are used along with dietary supplements (eg, vitamins or herbals), foods, or alcohol. Factors such as age, gender, weight, certain disease states, and genetic predispositions also affect drug interactions.

If a patient is taking more than one drug, or is taking supplements, MOs and pharmacists should check for interactions and evaluate the safety of combining them. Advise patients of potential interactions before administering any medication.

> **Note:** The responsibility of correctly and safely dispensing medications remains with the combat medic, even when administering a medication directed by a supervising health care provider.

Drug Tolerance

Many drugs become progressively less effective over time because the patient's body reacts less to the drug. This happens at the cellular level when the drug is metabolized more quickly, the body produces fewer receptors to the drugs, or the existing receptors become desensitized. When tolerance develops, MOs typically prescribe a higher dose (or a different medicine) to produce the original desired effect. Diphenhydramine is an example of a common medication that may result in tolerance. Drug tolerance is not the same as drug addiction; however, some drugs that produce tolerance are also potentially addictive (eg, **opioids**).

Drug Dependence

Drug dependence occurs when a person becomes reliant on a medication to help them function or feel normal. Soldiers who are prescribed certain formulary medications (eg, **narcotics**) may be at risk of developing dependence, so caution is always required. Susceptibility, or risk of developing dependence, varies among individuals. There are two aspects of dependence: psychological and physical. Though often discussed as separate entities, they most often occur together and may not be distinguishable in practice.

Psychological dependence is characterized by persistent cravings for a substance or a strong belief that it is needed. There are many withdrawal symptoms of psychological dependence, including anxiety, mood swings, sleep disruption, and poor judgement. Many psychotropic medications (eg, some antidepressants) are associated with psychological dependence.

Physical (or physiological) dependence is a state where the body has developed a need for the substance. It is characterized by physical withdrawal symptoms such as nausea, vomiting, diarrhea, body aches, and seizures. Physical dependence commonly occurs with chronic use of a tolerance-producing drug and can occur even when drugs are taken as prescribed. Some pain-relieving drugs such as narcotics (eg, opioids) are associated primarily with physical dependence.

Check on Learning

1. Define mechanism of action as it pertains to medications.
2. Define indications as they pertain to medications.
3. What is the difference between a relative and an absolute contraindication?
4. List seven signs and symptoms of a severe allergic reaction to a medication.

DOSAGE FORMS

Manufacturers produce medications in a variety of forms. These dosage forms (or unit doses) contain a mixture of active ingredients and inactive additives manufactured into a form that delivers medication to sites of action in the body. Dosage forms may be configured in a variety of ways, depending on factors such as physical characteristics (eg, liquid or solid), **route** of administration (eg, oral, topical, injectable), patient characteristics (eg, infant or adult), stability requirements (shelf life), and even aesthetic considerations. Each dosage form has advantages and disadvantages, and specific drugs are often available in more than one form. Similarly, drugs may not be available for every method of administration. Dosage forms are commonly classified by their physical forms.

Solids

Solid form drugs are administered orally. They are very common and have many benefits. They are easy to mass produce with uniform doses. Stability of the active ingredient, enveloped in a solid form, may be superior to that of other dosage forms. Although solid oral medications are convenient for consumers, they have the disadvantage of being difficult for some to swallow. There is also a lag time between taking the medication and experiencing its effects because it must be broken down in the small intestine before being absorbed into the bloodstream for transport to the target site. Common examples of solid medications taken orally are aspirin, ibuprofen, and acetaminophen.

Pills

Pill is a common term for many solid oral medications, but more specifically, it describes a round, solid form of medication that is broken down into a solution in the stomach. For example, aspirin is commonly manufactured in pill form.

Tablets

Tablets are the most common dosage form across all types. They come in many shapes and have diverse physical properties (Figure 3-1). They are very familiar in oblong or circular (wafer-like) forms, but may also be spherical or oddly shaped. Tablets dissolve in the stomach or small intestines. They are frequently coated and may be manufactured as caplets (elongated tablets coated for easier swallowing), or as enteric-coated tablets (tablets that pass through the stomach unchanged and are dissolved and absorbed in the small intestines). Enteric-coated medications should not be chewed or crushed because that will destroy the special coating that prevents them from dissolving in the stomach. Chewable or effervescent tablets are examples of uncoated tablets. Throat lozenges (or troches) are sweet, mucilaginous tablets that dissolve slowly in the mouth. Some tablets are scored (indented or marked to allow a person to break the tablet into halves or quarters).

Figure 3-1. Tablet dosage forms. Photograph by Carnfinwen. Reproduced from Pixabay. https://pixabay.com/photos/pills-pill-pharmacy-anxieties-2397455/

Capsules

Capsules are drug forms that contain a solid (eg, powder), oil, or liquid medication enclosed in a soft or hard gelatin or polymer coating (Figure 3-2). Capsules are mostly tasteless and odorless and they are relatively easy to swallow. They must be administered whole to achieve the desired result. In particular, sustained-release and timed-release capsules cannot be divided or crushed. Capsules are usually more expensive than tablets.

Figure 3-2. Capsule dosage form. Photograph by Heung-Soon. Reproduced from Pixabay. https://pixabay.com/photos/pill-capsule-medicine-pharmacy-4099839/

Powders

Powders are dry preparations with a uniform mix of medications. They are often mixed with liquids and are mostly delivered orally; however, some powders are applied topically. Nutritional supplements, such as protein powders, are a familiar example.

Semisolids

These semisolid dosage forms are applied to skin or mucous membranes. They may have local or systemic effects.

- Ointment—a viscous, oil-based semisolid mixture applied to the skin (eg, nitroglycerin ointment to prevent angina).
- Gel—an aqueous solution that liquefies on contact with skin, dries into a thin film, and is easily removed (eg, some OTC gels for treating muscle pain).
- Cream—a semisolid emulsion of water and oil that is easy to apply to skin (eg, lidocaine cream).
- Lotion—an aqueous or alcohol preparation for skin that dries quickly after application. Lotions can soothe, protect, cleanse skin, or act as an astringent (eg, camphor-glycerin-alcohol-water astringent lotion).
- Paste—a mixture of powder and ointment (eg, zinc oxide paste).

Liquids

Liquid medications can come in a variety of forms, many of which must be shaken before use to ensure equal distribution of the drug throughout the formulation (Figure 3-3). Liquids are typically administered orally or by injection.

Figure 3-3. An oral medication formulated as a liquid. Photograph by frolicsomepl. Reproduced from Pixabay. https://pixabay.com/photos/anxieties-medicines-syrup-pharmacy-342448/

Solutions

A liquid containing a dissolved medication is a solution. Sugar dissolved in water is a household example of a solution. There are three common solutions used in medicines. An alcohol solution that is sweet, aromatic, and designed to be taken orally is an **elixir**. A solution consisting of medication dissolved in a concentrated solution of sugar and water is a **syrup**. A solution of the soluble constituents of vegetable compounds that act as drugs is a **fluid extract**.

Suspensions

Undissolved drugs, finely divided and mixed into liquids, are **suspensions**. They may consist of one or more drugs in a single suspension. Shake suspensions before administering them to mix the liquid with the solid portions of the medication that settled at the bottom of the container. A household example of a suspension is a mixture of flour and water.

Figure 3-4. A suppository dosage form. Photograph by Marco Verch. Reproduced from Flickr. https://www.flickr.com/photos/30478819@N08/49175691543

Suppositories

A suppository is a drug mixed with a lubricated substance and molded to insert into body cavities such as the rectum or vagina (Figure 3-4). Suppositories are solid at room temperature, but dissolve quickly and release medication when inserted and warmed by body heat. This useful dosage form can rapidly exert both local and systemic effects.

Transdermal Patches

Transdermal patches (or topical disks) are medicated, adhesive patches placed on skin (Figure 3-5). The medication is absorbed through the skin and

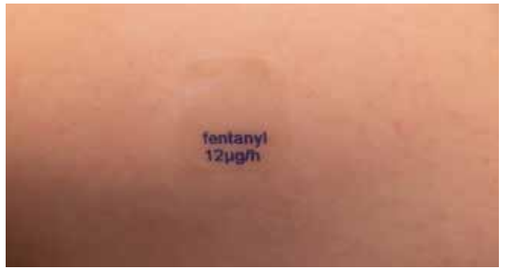

Figure 3-5. A fentanyl transdermal patch. Photograph by Daniel Tahar. Reproduced from Wikimedia Commons. https://commons.wikimedia.org/wiki/File:A_generic_fentanyl_transdermal_patch,_with_a_release_rate_of_12mcg_per_hour,_applied_to_the_skin_(cropped).jpg

into the bloodstream, providing a slow, controlled release of therapeutic agents. They increase compliance because patients do not have to remember dosing instructions and they are particularly useful in patients who cannot take oral medications (unconscious or nauseated). Transdermal patches are used to deliver substances such as analgesics, estrogen, nicotine, and nitroglycerin.

Gases

This group of dosage forms includes inhalers and aerosols. **Nebulizers** (Figure 3-6), pressurized metered-dose aerosols, or powder aerosols administer medications by the respiratory route. This route is common for management and treatment of respiratory conditions such as asthma.

Figure 3-6. A nebulizer mask. Photograph by James Heilman, MD. https://commons.wikimedia.org/wiki/File:Nebulizer.JPG

ANTIBIOTICS

An antibiotic is a chemical compound that kills, inhibits, or stops the growth of microorganisms such as bacteria, fungi, and protozoa. Most frequently they are indicated for treatment or prevention of bacterial infections. There are more than 150 antibiotics developed to help in the fight against infectious diseases and they have saved millions of lives.

Categories and Types of Antibiotics

All antibiotics fall into one of two categories: broad spectrum or narrow spectrum. Broad-spectrum antibiotics are effective against a wide range of organisms. For example, ampicillin is a broad-spectrum antibiotic that is effective against numerous gram-negative and gram-positive bacteria. Broad-spectrum antibiotics are useful for treating infections with more than one pathogen, or for treating infections before the pathogen is identified. Narrow-spectrum antibiotics are effective against only a few microorganisms and should be used in a targeted manner for identified pathogens. Antibiotics in both categories are used to treat or prevent infections prior to surgery. Broad-spectrum antibiotics are better suited for combat environments, unless specific infectious agents are known. Narrow-spectrum antibiotics are most suited for treating known pathogens. Many different broad-spectrum and narrow-spectrum antibiotics are available. Local standard operating procedure will guide their selection and use.

Antibiotics are also grouped into classes (types), each with its own chemical composition, use, mode of action, and potential side effects. The following are common classes of antibiotics, with representatives (generic names) for each:

- beta-lactam—penicillin, amoxicillin, cephalexin;
- macrolide—erythromycin, azithromycin;
- tetracycline—tetracycline, doxycycline;
- aminoglycoside—gentamicin, neomycin; and
- fluoroquinolone—ciprofloxacin, levofloxacin.

Some patients are allergic to specific types of antibiotics (eg, penicillin allergies are common); those antibiotics are contraindicated in such patients.

Antibiotic Dosage Forms

Antibiotics that are applied directly on the skin, the mucous membrane of the conjunctiva, or the nasopharynx are known as topical antibiotics. Uses include treatment for skin diseases, wound management, burns, and conjunctivitis. Topical antibiotics are easy to use and generally noninvasive. Absorption through mucous membranes is rapid. Examples of topical antibiotics include bacitracin (minor skin infections), mupirocin (impetigo), besifloxacin (conjunctivitis), and silver sulfadiazine (burns).

Oral antibiotics typically are taken by mouth over a course of time (usually 7–10 days). Oral antibiotics are the oldest method of administration and have a number of advantages that make them the preferred route. Oral antibiotics are easy to administer and are the safest, most convenient, and most economical route of administration. With all of their benefits, oral antibiotics also have limitations and disadvantages. Administration requires a conscious and cooperative patient. Irritation of the gastrointestinal mucosa may cause vomiting. Also, when compared to other routes, they have a much slower absorption rate. Examples of oral antibiotics include levofloxacin, streptomycin, and the combination drug sulfamethoxazole and trimethoprim.

Note: All medications have side effects and it is your responsibility to know the side effects for all medications you administer.

For treatment of severe illness and injury in patients who are unconscious or uncooperative, or who cannot tolerate oral antibiotics, the preferred route is intravenous (IV). IV antibiotics have a much faster and more predictable absorption rate, which makes them ideal for emergencies. The fast absorption rate can also be problematic, since allergic reactions occur more quickly and more severely than with oral administration. Intravenous access is a requirement for IV antibiotics; therefore, administration is more difficult and may induce anxiety in patients who have a fear of needles. IV antibiotics can also cause tissue necrosis if administered incorrectly. Examples of IV antibiotics include cefazolin and ertapenem.

Antibiotic Resistance

Antibiotic-resistant bacteria appeared soon after penicillin was introduced in the 1940s. Over the years, overuse and misuse of antibiotics have caused problems with their effectiveness. Antibiotics are frequently used for conditions or infections that are not caused by bacteria (eg, viral infections). They are also heavily used in agriculture to prevent animal disease. Antibiotic resistance reduces the capability of some drugs to treat certain bacteria effectively. It is a growing concern because we rely heavily on antibiotics in modern medicine and many bacteria are now resistant to commonly used antibiotics. For example, methicillin-resistant *Staphylococcus aureus* (MRSA) was once seen only in hospitals, but now it appears in the wider community. These types of infections are relatively common in the military.

Resistance occurs when an antibiotic fails to kill all of the bacteria it targets and the surviving bacteria become resistant to that particular drug (and frequently to other antibiotics, as well). This drug-resistant bacteria is a "super bug." Doctors may prescribe a stronger antibiotic, but the bacteria quickly evolve to withstand the more potent drug as well, perpetuating a cycle in which increasingly powerful drugs are required to treat infections. To reduce the development of resistance, the full course of antibiotics should always be completed, regardless of whether the patient feels better before finishing all the medication. Do not save antibiotics for later use or use someone else's prescription.

Check on Learning

5. What is an antibiotic?
6. What is the difference between broad-spectrum and narrow-spectrum antibiotics?
7. What are the advantages of oral antibiotics?

ANTIFUNGALS

Antifungal medications are used to treat fungal infections, known as mycoses. Mycoses are generally named based on the location of the infection and they can affect superficial, cutaneous, or subcutaneous areas of the skin. The route of the medication (topical, oral, or IV) will depend largely on the location and extent of the infection. Factors that contribute to the appearance and extent of fungal infections include high humidity and hormonal or immune system abnormalities.

Prevention includes keeping skin clean and dry, proper hand washing, avoiding infected individuals, and maintaining good hygiene. Fungal infections are contagious, so it is important to wash any area that may have come in contact with contaminated surfaces or others who may be infected. Common mycoses include ringworm, scalp infection (a form ringworm), athlete's foot, and jock itch.

Tinea corporis, also known as ringworm, is a superficial fungal infection that can appear anywhere on the body. The name is derived from its appearance (a raised ring at the center of the infection). Individuals living in crowded, humid conditions are more susceptible, as are those who participate in contact sports, particularly wrestling. The extent of the infection will determine course of treatment for ringworm. Topical OTC antifungal medications include clotrimazole, ketoconazole, fluconazole, and undecylenic acid. Oral antifungals such as griseofulvin may also be used. In more severe cases, a systemic IV medication (amphotericin B) may be needed for fungal infections that show resistance to other drugs.

Tinea capitis is a fungal infection of the scalp characterized by severe itching, raised ring-like appearance, and bald patches on the affected area. Treatment for this form of fungal infection is identical to that of tinea corporis.

Tinea pedis, also known as athlete's foot, is a fungal infection that affects the feet, particularly the toes and the webbing of the toes. Treatment for athlete's foot includes topical OTC antifungals (eg, clotrimazole) or oral prescription antifungals (eg, terbinafine hydrochloride or griseofulvin). Fungal nail infections are similar to athlete's foot. These infections can be treated with topical OTC medications or an oral prescription drug (eg, itraconazole or terbinafine hydrochloride).

Tinea cruris, also known as jock itch, is a fungal infection of the groin characterized by itching, burning, and a reddish appearance. Jock itch is more common in males, but can also occur in females. Topical antifungals are the preferred course of treatment for tinea cruris in males. Treatment for fungal infection caused by *Candida albicans* (vaginal yeast infection) includes tioconazole (ointment or suppository).

Check on Learning

8. What is the location of tinea corporis?
9. What is the location of tinea capitis?
10. What is the location of tinea pedis?

ANTIHISTAMINES

Histamines and leukotrienes are immune system substances released by the body in response to sensitivity to certain foreign antigens. Mild to moderate allergy symptoms represent physiological overreactions to a foreign invader. Histamines are physically active substances found in plant and animal tissues. They are released from mast cells in the human body and contribute to stimulation of gastric secretions, dilation of capillaries, constriction of bronchial smooth muscles, and decrease in blood pressure. Leukotrienes are fatty molecules of the immune system that contribute to inflammation in asthma and bronchitis patients.

Antihistamines are a class of drugs that combat the histamine release during an allergic reaction by blocking the action of the histamine on the tissue. Antihistamines do not stop the formation of histamine, nor do they stop the allergic reaction between the body's antibodies and the foreign substance, but they do protect tissues from some of its effects. Side effects associated with antihistamines include drowsiness, dry mouth, urine retention in men, and increased heart rate. Newer, non-sedating antihistamines are generally thought to be less effective. Antihistamines provide only temporary relief and must be used frequently to control symptoms. Prolonged use may result in undesirable effects.

Some example of antihistamines include, fexofenadine, diphenhydramine, loratadine, and cetirizine. Antihistamines should be prescribed with great caution in a combat environment and when the patient is returned to duty (consider if the patient will drive or operate machinery). Treatment for mild to moderate allergic reactions may also include bronchodilators to relieve lung symptoms. Cortisone preparations and other anti-inflammatory agents may have cooling and antiseptic effects and reduce itching and other symptoms.

Check on Learning

11. What are the effects of histamines on the body?
12. Do antihistamines stop the production of histamines?
13. What are some side effects associated with antihistamines?

EPINEPHRINE

Anaphylaxis is an immediate life threat and must be addressed as soon as it is identified. Treatment for an anaphylactic reaction includes securing the airway, administering supplemental oxygen with positive pressure ventilations (if necessary), and administering epinephrine 0.3 to 0.5 mg (1:1,000 solution) intramuscular (IM) or subcutaneous (SC) for an adult. Epinephrine may be repeated every 5 to 10 minutes if symptoms continue or recur. The MO may also prescribe antihistamines (diphenhydramine 25–50 mg IM or IV), corticosteroids (methylprednisolone sodium succinate 125 mg IV), and a normal 500 cc saline bolus.

Note: Epinephrine is the first-line treatment for anaphylaxis.

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

Nonsteroidal anti-inflammatory drugs (**NSAID**s) are drugs with analgesic (pain-killing), antipyretic (fever-fighting), and anti-inflammatory (swelling-reducing) effects. NSAIDs are indicated for patients in mild to moderate pain, febrile patients, and patients with tissue inflammation. They are commonly prescribed to reduce inflammation of arthritis, tendinitis, bursitis, and other body tissues. To alleviate pain, they should be tried prior to using narcotics if the situation warrants. Examples include aspirin, ibuprofen, and naproxen. Acetaminophen is not an anti-inflammatory drug, so it is not considered an NSAID, even though it relieves pain and reduces fever.

Side effects of therapeutic doses of NSAIDs include:

- gastric irritation (epigastric discomfort or stomach ache),
- heartburn,
- nausea,
- lack of appetite,
- prolonged clotting time in some (eg, aspirin),
- high-pitch tinnitus,
- vertigo, and
- deafness.

Overdose and toxicity are concerns with NSAIDs. Although hearing and balance problems are generally temporary or curable, permanent damage can occur from ototoxicity. Toxic doses also greatly elevate body temperature, resulting in hyperthermia. This is in direct contrast to the effects of therapeutic doses. Behavioral side effects of overdose may include central nervous system stimulation followed by depression, agitation, and confusion. This may be followed by stupor and coma. Respiratory stimulation may proceed to the point of hyperventilation, followed later by respiratory depression.

Hypersensitivity (an undesirable overreaction of the immune system) is a serious complication of NSAID use. Aspirin may cause hypersensitivity and exacerbate asthma symptoms. Also, aspirin and other NSAIDs are extremely hard on the stomach lining. With prolonged use, they may cause peptic ulcers with resultant gastric bleeding. NSAIDs may cause acute renal failure, so encourage patients taking them to drink adequate fluids.

Note: Aspirin and ibuprofen are contraindicated for military members in combat because they inhibit blood clotting.

Warning: Do not give aspirin to children! Aspirin may cause **Reye's syndrome**.

Check on Learning

14. What are the signs and symptoms of NSAID toxicity?
15. Why is aspirin not recommended for military personnel in combat?
16. What are the properties of NSAIDs?

ANALGESICS

Medications intended to relieve pain are known as analgesics. Analgesics are typically divided into two groups: narcotic and non-narcotic. Generally, the patient's pain level will determine the type of analgesic required for relief. Non-narcotic analgesics (indicated for mild to moderate pain) include meloxicam and acetaminophen. Narcotic analgesics (indicated for moderate to severe pain) include morphine, fentanyl, and ketamine.

Non-narcotic Analgesics

For patients who are experiencing mild to moderate pain, a non-narcotic analgesic such as meloxicam or acetaminophen is recommended. These are useful in combat situations for conscious and lucid casualties

who are still able to fight. Give meloxicam 15 mg per os (by mouth) daily. The recommended dosage for acetaminophen is two 500 mg caplets per os every 8 hours. As with any medication, patients should be monitored for adverse reactions. High doses of meloxicam can cause serious gastrointestinal issues and high doses of acetaminophen can cause liver damage if given for an extended period of time or in patients with known liver disease. Document every dose given and the time it was administered.

Narcotic Analgesics

Severely injured patients (eg, those with operational and combat injuries, traumatic amputations, ballistic injuries, severe burns, or crush injuries) experiencing moderate to severe pain require narcotic analgesics. All opioid analgesics can be addictive, so limit use to casualties in moderate or severe pain only, as described below.

Caution: Respiratory depression can occur with repeated doses of narcotic analgesics, as can nausea or vomiting.

Morphine

Morphine is indicated for severe pain. Morphine causes constriction of the pupils and inhibits pupillary reactions; therefore, using pupillary response for trauma casualty assessment is an unreliable vital sign for assessment of head injuries.

Contraindications for morphine include morphine allergies and altered mental status. Some soldiers may claim to have an allergy to morphine and will either develop a rash or experience nausea, vomiting, or pruritus (itching) when morphine is administered. In combat, these soldiers can still take morphine. The soldiers who have had a previous anaphylactic reaction to morphine must be identified early in the predeployment process and have other injectable pain medications supplied for their use. The specific type of alternate medication to carry and administer will depend on the area of deployment and the decision of the MO.

Morphine is administered in an initial dose of 5 mg slow IV push over 1 to 2 minutes. Dilute the 5 mg dose in 5 mL normal saline prior to IV administration. Repeated doses of morphine IV may be given every 5 minutes. Most adults will experience pain relief at a total dose of 10 to 20 mg, although higher doses may be required. Document every dose given, including the time of administration. Monitor the casualty closely for adverse effects.

Note: Due to the adverse effects of morphine on the respiratory system, fentanyl is preferred over morphine in a combat environment.

Fentanyl

Fentanyl is an opioid pain medication used for moderate to severe pain in casualties who are alert and conscious. Fentanyl "lollipops" are most commonly used in combat settings for quick pain relief. Fentanyl is also useful for patients with known morphine allergies; however, it is contraindicated in patients with altered mental status or allergies to the medication (or any of its components). Exercise caution when administering fentanyl to a patient who has already been given morphine, since this combination can increase the chances of respiratory depression and adverse narcotic side effects.

Fentanyl is administered transbuccally (absorbed through the mucosal lining of the cheeks) via an 800 μg (micrograms) lozenge. To avoid an overdose, tape the lozenge to the patient's finger. When pain is relieved, the patient's finger will move away from their mouth. Reassess patients every 15 minutes for early recognition of serious side effects or respiratory depression.

Ketamine

Patients with possible cardiorespiratory depression may be given ketamine, a very potent analgesic that is mainly used as a general anesthetic. It is indicated for controlling moderate to severe pain. Ketamine can cause hallucinogenic terrors, so it is contraindicated in patients with history of schizophrenia and in patients under 3 years old. A nasal spray formulation of ketamine (10 mg) is in development for soldiers. It reportedly will not have abuse potential and will be easier to administer.

High doses ranging from 50 to 100 mg (or 0.5–1.0 mg/kg) IM or intranasal (IN) can dissociate conscious thought from sensory input (including pain). The dosage can be repeated every 20 to 30 minutes (IM or IN) or every 20 minutes (IV) as needed to control pain or until the patient develops **nystagmus**. The half-life for ketamine is 2.5 hours. Patients given a single high dose will have approximately 30 minutes duration of dissociation.

At low doses of 30 mg (or 0.3 mg/kg) slow IV or intraosseous (IO) push over one minute, ketamine relieves pain twice as fast as morphine. The dosage can be repeated every 20 minutes as necessary to control severe pain, or until the casualty develops nystagmus.

Note: Ketamine requires slightly more time and expertise to administer than fentanyl, but avoids the risk of cardiorespiratory depression.

Check on Learning

17. Acetaminophen can cause damage to what organ in high dosages?
18. What are the contraindications for fentanyl?
19. What are the contraindications for ketamine?
20. What is the dose for fentanyl?

ANTIDOTE

The potential for overdose exists in any patient who is administered a potent opiate narcotic, such as morphine. Respiratory depression is a sign of overdose and is a life threat. If overdose is suspected, the **opiate** antagonist, naloxone, is used to reverse the effects of the narcotic. Naloxone binds to the same receptors in the central nervous system that opiates normally attach to, blocking the narcotic from binding to the same receptors. Naloxone has no absolute contraindications for use and minimal side effects. It may induce narcotic withdrawal symptoms (eg, nausea, vomiting, and tachycardia). Emergency administration of the antidote outweighs the potential side effects of the medication.

Typical dosage and administration of naloxone involve slow IV push 0.4 to 2.0 mg over 1 to 2 minutes (IM or SC), which may be repeated 3 or 4 times. The recommended dosage for effective management of suspected opiate overdose is up to 10 to 20 mg. When administered via IV, an immediate positive response is usually realized within 1 to 2 minutes and the duration of action is 1 to 2 hours. Since the half-life of morphine is 2 to 4 hours and the half-life of naloxone is 1 to 2 hours, naloxone effects may wear off earlier than morphine and patients could lapse back into respiratory depression. Accordingly, naloxone should be adjusted to the patient's respiratory status rather than their level of consciousness and patients must be continually monitored for relapse.

Check on Learning

21. Subsequent doses of naloxone should be administered with consideration to what?
22. List the side effects associated with naloxone.

SUMMARY

Every day, combat medics use the principles of pharmacology in their patient care roles, whether consciously or subconsciously. Whether in a garrison environment with a team of health care providers, or working independently in a combat setting, knowledge of pharmacology improves patient outcomes by affecting treatment decisions. Within your scope of practice, you must use your full knowledge to provide high-quality, competent, and compassionate medical care.

KEY TERMS AND ACRONYMS

Analgesic. A pain reliever that does not cause loss of consciousness.
Anaphylaxis. An acute allergic reaction to an antigen (eg, venom from a bee sting) to which the body has become hypersensitive.
Angioedema. Diffuse swelling that may start with the lips, hands, feet, or mucous membranes, and sometimes progresses to the airway, causing difficulty breathing.
Antibiotics. Chemical compounds that inhibit or kill the growth of microorganisms, such as bacteria, fungi, and protozoa.
Antigen. A foreign substance that produces an immune response in the body. Examples include viral and bacterial components or products, some food proteins, venom, and pollen.
Astringent. A substance that causes tightening of soft tissues, such as skin.
Dosage. The calculation or administration of the proper amount, number, and frequency of doses. Often used interchangeably with dose.
Dose. The amount (quantity) of medication administered. Often used interchangeably with dosage.
Emulsion. A blend of liquids that do not mix together, but where one component is dispersed in fine droplets in another. For example, oil and vinegar dressing after thorough shaking.
Elixir. An alcohol solution that is sweet and aromatic.
Fluid extract. A solution of the soluble constituents of vegetable compounds that act as medications. Each milliliter of the drug represents 1 gram of medication.
Generic name. The official chemical name for a drug.
Mechanism of action. A predictable chemical reaction that determines how a drug works at the cellular or subcellular level. This is observed as expected responses in the body that indicate the drug is working.
Narcotic. A sleep-inducing drug that relieves pain. The term is usually associated with opiates.
Nebulizer. A medical device that dispenses liquid respiratory medication by dispersing it with pressurized oxygen. The patient breathes the resulting fine spray or mist into the lungs.
NSAID. Nonsteroidal anti-inflammatory drug.
Nystagmus. A condition where eyes move rapidly and uncontrollably. Movements may be side to side, up and down, or circular. Vertical nystagmus might be a sign of serious brain injury.
Opiate. A drug derived from alkaloids produced by the opium poppy. The major biologically active opiates found in opium are morphine and codeine.
Opioid. Specifically refers to synthetic narcotics that are similar to opiates, such as heroin and hydrocodone. However, the term is often used to include opiates and synthetic narcotics.
Reye's syndrome. A rare, but serious condition that damages the brain and liver. It was seen more often in the past, when children were given aspirin to alleviate symptoms of a viral illness.
Route. The means of access for medication delivery, or how the medication is administered.
Side effects. Negative effects or actions other than the desired actions.
Suspension. One or more drugs finely divided and mixed into a liquid without dissolving.
Syrup. Medication dissolved in a concentrated solution of sugar and water.
Therapeutic effects. The expected positive effect of a drug.
Topical. A medication designed to be applied to the body surface (eg, skin or eyes).
Trade name. The official brand name of a drug produced by a specific company.

CHECK ON LEARNING ANSWERS

1. Define mechanism of action as it pertains to medications.

   How the drug works. Certain responses are expected in the body and can also be described as predictable chemical reactions.

2. Define indications as they pertain to medications.

   The reason the medication is administered.

3. What is the difference between a relative and an absolute contraindication?

   A relative contraindication is when the medication or treatment may harm the patient but can still be administered if the benefit outweighs the risk. An absolute contraindication means that the drug or treatment could cause a life-threatening condition and is never allowed.

4. List seven signs and symptoms of a severe allergic reaction to a medication.

   Any seven of the following: airway compromise that may include hoarseness, stridor, edema, rhinorrhea, and wheezing; low blood pressure; tachycardia; chest pain and tightness; nausea; vomiting; abdominal cramping; diarrhea; itching; hives; and angioedema.

5. What is an antibiotic?

   A chemical compound that inhibits or kills the growth of microorganisms, such as bacteria, fungi, or protozoa.

6. What is the difference between broad-spectrum and narrow-spectrum antibiotics?

   Broad-spectrum antibiotics are effective against a wide range of microorganisms, whereas narrow-spectrum antibiotics are effective against only a few or specific microorganisms. Broad-spectrum antibiotics are better suited for combat environments unless the specific infection is known.

7. What are the advantages of oral antibiotics?

   They are generally safe, convenient, economical, and are easy to administer.

8. What is the location of tinea corporis?

   The body.

9. What is the location of tinea capitis?

   The head.

10. What is the location of tinea pedis?

    The feet.

11. What are the effects of histamines on the body?

    Stimulate gastric secretions, dilate capillaries, constrict bronchial smooth muscles, and decrease blood pressure.

12. Do antihistamines stop the production of histamines?

    No. They block the action of histamines on tissues.

13. What are some side effects associated with antihistamines?
    Drowsiness, dry mouth, urine retention in men, and increased heart rate.
14. What are the signs and symptoms of NSAID toxicity?
    Hyperthermia, behavioral effects, respiratory stimulation, and high-pitch tinnitus.
15. Why is aspirin not recommended for military personal in combat?
    It contributes to prolonged clotting times, which may cause excessive bleeding.
16. What are the properties of NSAIDs?
    Analgesic, anti-inflammatory, and antipyretic.
17. Acetaminophen can cause damage to what organ in high dosages?
    The liver.
18. What are the contraindications for fentanyl?
    Altered mental status or allergy to the medication or its components.
19. What are the contraindications for ketamine?
    Children under 3 and patients with a history of schizophrenia.
20. What is the dose for fentanyl?
    800 μg.
21. Subsequent doses of naloxone should be administered with consideration to what?
    The patient's respiratory level.
22. List the side effects associated with naloxone.
    Nausea, vomiting, and tachycardia.

SOURCES

Kizior, RJ, Hodgson K. *Saunders Nursing Drug Handbook*. Elsevier Health Sciences; 2019.

National Association of Emergency Medical Technicians; American College of Surgeons Committee on Trauma. *PHTLS: Prehospital Trauma Life Support*. 9th ed. Jones & Bartlett Learning; 2020.