AMBULATORY MEDICINE

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A Quick Reference for the Busy Primary Care Provider

H. Thomas Milhorn, MD, PhD

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Ambulatory Medicine:
A Quick Reference for the Busy Primary Care Provider

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Preface

Ambulatory medicine is medical care that takes place outside the hospital (outpatient care). It is the first resource for patients. Primary care providers are responsible for delivering this care. They include family physicians, internists, pediatricians, geriatricians, gynecologists/obstetricians, nurse practitioners, and physician assistants. Overall, primary care providers offer services from head to toe and from birth to death. Services include disease prevention (infectious disease prevention through immunizations, hypertension and diabetes sequelae prevention, osteoporotic fracture prevention), screenings (hypercholesterolemia, hypertension, osteoporosis, cervical cancer, lung cancer), and diagnosis and treatment of many types of illnesses (diabetes, hypertension, hypothyroidism, carpal tunnel syndrome). They also provide non-disease care, including birth control and obstetrical care. They provide education related to disease prevention and treatment, injury care (laceration repair, fracture and sprain care), counseling on many topics, including smoking cessation and weight loss, and coordination of care through subspecialists.

This book began as a manual for family medicine residents. Over time it evolved into a fairly complete coverage of most of the outpatient issues seen in their training. In response to their encouragement, I set out on the journey to convert the manual into the manuscript for this book, which was no small task. The book is seen as serving three purposes: (1) as a quick reference to use in the clinic when seeing patients, (2) as a textbook to replace the leading textbook of family medicine which is now out of print, and (3) a study guide for board examinations. I would like to thank Dr. Lee Valentine for working with Dr. Logan Rush to obtain some of the dermatology pictures. And of course, I would like the thank the EC Healthnet family medicine residents for their support and encouragement in this endeavor.

I have attempted to ensure that the medication dosages are correct; however, before using them the provider should check to determine if they are.

H. Thomas Milhorn, MD, PhD
Director of Education, EC Healthnet Family Medicine Residency Program, Meridian, Mississippi

Formerly Professor of Family Medicine, Professor of Physiology and Biophysics, and Associate Professor of Psychiatry and Human Behavior, University of Mississippi School of Medicine, Jackson, Mississippi

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CHAPTER 1

Allergy

An *allergy* is a hypersensitivity caused by exposure to a particular antigen (allergen) resulting in a marked increase in reactivity to that antigen on subsequent exposure. There are four types of hypersensitivity (allergic) reactions. Type I is anaphylactic reactions, type II is cytotoxic reactions, type III is immunocomplex reactions, and type IV is cell-mediated reactions.

Type I Hypersensitivity Reactions

- Type I hypersensitivity reactions are the most common allergic responses. IgE antibodies are produced by the immune system in response to allergens such as pollen, animal dander, insect bites, dust mites, or certain foods. In response to the antibodies, the body releases histamine and other chemicals that cause swelling and inflammation in the body tissues, with symptoms starting in seconds to minutes. Type I allergic reactions include allergic rhinitis, anaphylaxis, allergic asthma, food allergies, and skin allergies [1,2].

Allergic Rhinitis

- Allergic rhinitis is a hypersensitivity to inhaled allergens in the air. It occurs in two forms—seasonal and perennial. The seasonal form occurs in the spring, summer, and early fall when airborne pollens are at their highest levels. Perennial allergic rhinitis occurs all year long and is usually caused by home or workplace airborne pollutants. A person can be affected by seasonal forms, perennial forms, or both [3,4]. Allergic Rhinitis is discussed in Chapter 16: Otolaryngology.

Anaphylaxis

Pathophysiology

- *Anaphylaxis* is a serious, life-threatening allergic reaction which usually occurs within a few seconds or minutes after exposure to the allergenic substance. Triggers for anaphylaxis include:
  - *Food*: peanuts, tree nuts such as walnuts and pecans, fish, shellfish, cow's milk, and eggs
  - *Insect sting*: bees, wasps, hornets, yellow jackets, and fire ants
  - *Latex*: found in disposable gloves, intravenous tubes, syringes, adhesive tapes, and catheters
  - *Medications*: penicillin, aspirin, NSAIDs, and anesthesia

Signs and Symptoms

- The early signs and symptoms of anaphylaxis may be mild, such as a runny nose, skin rash, or a strange feeling. These symptoms quickly lead to more serious problems, including trouble breathing, urticaria, tightness of the throat, hoarseness, nausea, vomiting, abdominal pain, diarrhea, dizziness, hypotension, tachycardia, syncope, shock, and cardiac arrest.

Diagnosis

- The diagnosis of anaphylaxis is clinical. Clinicians can obtain a serum tryptase level, which reflects mast cell degranulation when the clinical diagnosis of anaphylaxis is not clear; however, the result may not be readily attainable.

Treatment

- To treat anaphylaxis, the provider should remove the trigger when possible and raise the lower extremities. Give epinephrine 0.3 mg every 5–15 minutes injected into the lateral thigh as the fist-line therapy. 100% oxygen can be given by rebreathing mask. Glucagon 1 mg intramuscularly should be given first if the patient is taking a beta blocker. An intravenous bolus of two liters of normal saline is given for hypotension. Benadryl 50 mg intramuscularly or orally and a single dose of dexamethasone 6–10 mg

intravenously, intramuscularly, or by mouth should be given. After an anaphylactic episode, the patient should be monitored for a biphasic reaction for 4–12 hours. After the reaction has been successfully treated, the patient should be prescribed an epinephrine pen and instructed to wear or carry identification (bracelet or necklace) noting the condition and offending allergen. The patient should be referred to an allergist/immunologist for identification of the trigger if not known [5,6,7].

Allergic Asthma

Pathophysiology

- *Allergic asthma* is a chronic inflammatory condition in which the lungs become inflamed and the airways constricted when an allergen is inhaled. Common allergens that can cause allergic asthma include pollen, mold, dust mites, pet dander, cockroach droppings, and the presence of rodents. Common food triggers include milk, shellfish, eggs, soy products, peanuts, gluten, tree nuts, sesame seeds, and alcohol products like beer and wine.

Signs and Symptoms

- Signs and symptoms of an asthma attack, allergic or not, include wheezing, coughing, chest tightness, tachypnea, and dyspnea. The patient may have other allergic problems as well. The allergy triad is aspirin allergy, nasal polyps, and asthma.

Diagnosis

- Pulmonary function tests will improve after inhalation of a bronchodilator. The patient should be referred to an allergist for a skin prick test to identify the trigger.

Treatment

- Precipitating allergens should be avoided when possible. Pets, if a problem, should be found a new home, and the patient should stop smoking if they do so. Pest management for cockroach-infested homes is recommended. Inhaled steroids, oral leukotriene antagonists, and long-acting beta 2 agonists, as well as nasal steroids and non-sedating antihistamines, makes it possible to treat many patients with mild allergic asthma empirically. Patients with more severe allergic asthma symptoms should be referred, possibly for immunotherapy [8,9].

Food Allergy

Pathophysiology

- More than 90 percent of acute systemic reactions to food in children are from eggs, milk, soy, wheat, or peanuts, and in adults are from crustaceans, tree nuts, peanuts, or fish. Most children will outgrow the most common food allergies. Allergic eosinophilic gastrointestinal disorders are particularly prevalent in children and are thought to be caused by an IgE- and cell-mediated response to specific foods. Patients with these disorders have excess eosinophils in the mucosal and serosal layers of the portion of the gastrointestinal tract that is involved, which can range from the esophagus to the rectum.

Signs and Symptoms

- The clinical spectrum of IgE-mediated food allergies ranges from anaphylaxis to oral allergy syndrome, which is the most common food allergy. Symptoms of the oral allergy syndrome are brief, are limited to the mouth and throat, and are sometimes so mild that the patient may not seek evaluation.

Diagnosis

- The diagnosis of food allergy depends on a history of response to a particular food. Skin-prick or radioallergosorbent (RAST) tests for various foods can be done.

Treatment

- Patients with anaphylactic reactions to a food require emergent epinephrine, followed by instruction on self-administration of epinephrine in the event of future inadvertent exposures. Lessor reactions can be treated with oral diphenhydramine (Benadryl). Problem foods should be avoided. Federal law requires that food labels must state if the food contains any of the most common ingredients known to produce systemic reactions [10].

Skin Allergies

Skin allergies include angioedema, atopic dermatitis, and urticaria.

- *Angioedema* is edema of the deep dermis and subcutaneous tissues due to increased capillary permeability. It is usually an acute event, but sometimes it is chronic (lasting greater than six weeks). It is a reaction caused by exposure to a drug (angiotensin-converting enzyme inhibitors), venom, dietary substances, pollen, or animal dander allergens. It can be idiopathic [11,12].
- *Atopic dermatitis* (eczema) is a chronic relapsing and remitting inflammatory disease caused by a complex interaction of immune dysregulation, epidermal gene mutations, and environmental factors that disrupts the epidermis, causing intensely pruritic skin lesions.

Repeated scratching triggers a self-perpetuating itch-scratch cycle [13].

- *Urticaria* is an allergic reaction that involves the more superficial layers of the skin. It is caused by immunoglobulin E- and non-immunoglobulin E-mediated mast cells and basophils which release histamine and other inflammatory mediators. Although typically benign and self-limited, urticaria can be a symptom of anaphylaxis [12,14].
- Angioedema, atopic dermatitis, and urticaria are discussed in Chapter 3: Dermatology.

Type II Hypersensitivity Reactions

- Type II hypersensitivity reactions occur when IgG or IgM antibodies bind with antigens on cell surfaces. This causes a chain of reactions that activates the complement system leading to cell death. Symptoms occur in minutes to hours of exposure to the allergen. Type II allergic reactions include autoimmune hemolytic anemia, autoimmune neutropenia, Goodpasture syndrome, Grave' disease, immune thrombocytopenia, and myasthenia gravis [1,15].

Autoimmune Hemolytic Anemia

- Autoimmune hemolytic anemia is caused by autoantibodies that react with red blood cells at temperatures ≥ 37°C (warm antibody hemolytic anemia) or < 37°C (cold agglutinin disease). Hemolysis is extravascular [16]. Autoimmune hemolytic anemia is discussed in Chapter 7: Hematology.

Goodpasture Syndrome

Pathophysiology

- *Goodpasture syndrome* is a combination of glomerulonephritis and alveolar hemorrhage due to antiglomerular basement membrane (anti-GBM) antibodies. The circulating anti-GBM antibodies bind to basement membranes, fix complement, and trigger a cell-mediated inflammatory response. Patients with Goodpasture syndrome may have both pulmonary hemorrhage and glomerulonephritis or either one separately.

Signs and Symptoms

- Hemoptysis is the most prominent symptom of Goodpasture syndrome; however, hemoptysis may be absent in up to a third of patients with alveolar hemorrhage. Instead, they may have infiltrates on chest X-ray with or without respiratory distress. Other common symptoms include cough, dyspnea, fatigue, fever, hematuria, and weight loss. However, up to 40% of patients with Goodpasture syndrome do have gross hematuria. Pulmonary hemorrhage may precede renal manifestations by weeks to years.

Diagnosis

- Serum anti-GBM antibody level should be obtained. This is followed by renal biopsy when anti-GBM antibodies are negative. Antineutrophil cytoplasmic antibodies (ANCA) testing is positive in 25% of patients with Goodpasture syndrome. Immunofluorescence staining of renal or lung tissue classically shows linear IgG deposition along the glomerular or alveolar capillaries.

Treatment

- Treatment of Goodpasture syndrome includes emergency referral for plasma exchange, corticosteroids, and cyclophosphamide [15].

Graves' Disease

- *Graves' disease* is a common cause of an excessive production of thyroid hormones. It is an autoimmune disorder caused by antibodies to TSH receptors on the thyroid gland [17]. Graves' disease is discussed in Chapter 5: Endocrinology.

Immune Thrombocytopenia Purpura

- *Immune thrombocytopenia Purpura (ITP)* is an illness in which unusually low levels of platelets lead to purpura. In this disorder, the immune system produces antiplatelet antibodies which attach themselves to the surface of platelets as if the platelets were foreign substances. The spleen recognizes these platelets as abnormal and removes them from the circulation [18]. ITP is discussed in Chapter 7: Hematology.

Myasthenia Gravis

- *Myasthenia gravis* is an autoimmune disorder in which antibodies attack the receptors that respond to the neurotransmitter acetylcholine at the neuromuscular junction, thus interrupting normal functioning and causing episodes of muscle weakness [19,20]. Myasthenia gravis is discussed in Chapter 12: Neurology.

Type III Hypersensitivity Reactions

- Type III hypersensitivity reactions involve IgG and IgM antibodies which bind with antigens to form immunocomplexes that settle on organ tissues. The body's attempt to remove these complexes damages the underlying tissue. Symptoms begin several hours after exposure. Type III allergic reactions include systemic lupus erythematosus, rheumatoid arthritis, and serum sickness [1,2].

Systemic Lupus Erythematosus

- *Systemic lupus erythematosus (SLE)*, usually just called lupus, is an autoimmune disease that affects many systems, including dermatologic, musculoskeletal, renal, neuropsychiatric, hematologic, cardiovascular, pulmonary, and reproductive systems [21]. Lupus is discussed in Chapter 22: Rheumatology.

Rheumatoid Arthritis

- *Rheumatoid arthritis (RA)* is a chronic, inflammatory, autoimmune disorder in which diverse immune cells are involved. These include T cells, B cells, macrophages, and dendritic cells. In some people, in addition to joints, the condition can damage the skin, eyes, lungs, heart, and blood vessels [22]. Rheumatoid arthritis is discussed in Chapter 22: Rheumatology.

Serum Sickness

Pathophysiology

- The mechanism of *serum sickness* consists of exposure to an antigen (often a large protein) that leads to formation of an antigen-antibody complex. The immune complex load becomes too high to be excreted from the body, causing deposition in joints, tissues, and vascular endothelium. It also leads to activation of the complement pathway, which prompts mast cell and basophil degranulation with vasoactive amine release. The deposition of immune complexes and release of inflammatory mediators (histamine, serotonin) leads to the common symptoms of urticarial rash, joint pain, and fever. Classically, serum sickness is linked to antivenom for snake bites.
- A serum sickness-like reaction is thought to result from a non-protein drug binding to a serum protein to make a complete antigen. The newly formed antigen then forms an antigen-antibody complex. These complexes mimic the inflammatory cascade and symptomatic response of a true serum sickness reaction. Serum sickness-like reactions have been linked to medications such as allopurinol (Zyloprim), certain antibiotics, bupropion (Wellbutrin), hydralazine (Apresoline), phenytoin (Dilantin), and methimazole (Tapazole).

Signs and Symptoms

- Common manifestations of serum sickness include fever, pruritic rash (not involving mucosal membranes), and arthralgia of the metacarpophalangeal joints, knees, wrists, ankles, and shoulders. These symptoms occur 7–14 days after exposure to the offending agent and can occur more promptly if there has been previous exposure. Urticaria is the most common symptom. Less common symptoms include headache, gastrointestinal bloating, cramps, diarrhea, and nephropathy.

Diagnosis

- Workup of serum sickness includes CBC with differential (leukocytosis or leukopenia, eosinophilia, or mild thrombocytopenia), erythrocyte sedimentation rate (ESR) and CRP (usually slightly elevated), urinalysis for proteinuria, urine for hematuria and active sediment, BUN, and creatinine (may be transiently elevated), and C3, C4, CH50 (depressed due to complement consumption).

Treatment

- The offending agent should be discontinued, which leads to spontaneous resolution within several weeks. Low-grade fever and/or arthralgias are treated with acetaminophen (Tylenol) or NSAIDs. Antihistamines are used to treat urticarial symptoms.
- Patients with more severe disease (temperature ≥ 38.5°C, severe arthralgias, extensive rashes) should be referred. These more severe cases are usually treated with a short course of prednisone (Deltasone) 40–60 mg by mouth daily. Intravenous agents may be needed for some patients [methylprednisolone (Solu-Medrol) 1–2 mg/kg in one or two divided doses intravenously]. Some physicians recommend tapering corticosteroids over two weeks to avoid rebound symptoms. Plasmapheresis or plasma exchange is a treatment option used to eliminate immune complexes from the body [23].

Type IV Hypersensitivity Reactions

- Type IV hypersensitivity reactions are mediated by T cells that provoke an inflammatory reaction against exogenous or endogenous antigens. The T cells becomes sensitized and activated. These cells then release

cytokines and chemokines. These reactions are also called delayed allergic reactions because symptoms manifest days after contact with the allergen. Type IV allergic reactions include allergic contact dermatitis, DRESS syndrome, and tuberculin reactions [1,2].

Allergic Contact Dermatitis

- With *allergic contact dermatitis*, a foreign substance comes into contact with the skin and is linked to skin protein, forming an antigen complex that leads to sensitization. Upon re-exposure of the epidermis, the sensitized T cells initiate an inflammatory cascade, causing skin changes. A common cause of allergic contact dermatitis is exposure to urushiol, a substance in the sap of rhus plants (poison ivy, oak, sumac) [24]. Allergic contact dermatitis is discussed in Chapter 3: Dermatology.

DRESS Syndrome

Pathophysiology

- *DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms) syndrome* is an uncommon, severe drug reaction characterized by an extensive skin rash in association with visceral organ involvement, lymphadenopathy, eosinophilia, and atypical lymphocytosis. It may be fatal. There may be a genetic component [25].

Signs and Symptoms

- The prodromal phase of DRESS syndrome is often characterized by nonspecific symptoms such as fever, malaise, and lymphadenopathy. The drug eruption starts as a maculopapular rash that may progress to a coalescing erythema. Additional findings include purpura, infiltrated plaques, pustules, exfoliative dermatitis, and target-like lesions. Facial edema is striking and is present in most cases. Fever is typically ≥ 101.3°F. Other signs and symptoms depend on the organ systems involved (liver, pancreas, kidneys, lungs, heart).

Diagnosis

- DRESS syndrome should be suspected in a patient who received a new drug treatment in the previous 2–8 weeks and presents with an acute cutaneous eruption associated with systemic involvement, such as fever, lymphadenopathy, eosinophilia, or abnormal organ function tests. Laboratory tests include CBC, liver function tests, kidney function tests, cardiac enzymes, amylase and lipase, viral serology (HHV-7, HHV-8, EBV, CMV), and hepatitis A, B, and C tests.

Treatment

- Treatment of DRESS syndrome is based on the severity of skin and organ involvement. Patients with widespread rash and severe systemic symptoms should be hospitalized for evaluation and treatment. The most severe of these may need admission to the ICU [25].

Tuberculin-Type Hypersensitivity Reaction

- *Tuberculin-type hypersensitivity reaction* can be seen after intradermal injection of purified protein derivative (PPD). The reaction produces measurable local induration and swelling that is typically measured in millimeters between 48–72 hours after the injection. The tuberculin test is a method to diagnose tuberculosis infection, even if the disease is latent (see Chapter 8: Infectious Disease) [26,27].

Other

Allergic Medication Reactions

Pathophysiology

- *Allergic medication reactions* may fall in any of the four allergy classes discussed above, depending on the medication:
- *Type I (IgE mediated reaction)*
  - Drug-IgE complex binds to mast cells. Then clinical manifestations occur, consisting of- urticaria, angioedema, bronchospasm, pruritus, GI symptoms, and/or anaphylaxis. Manifestations occur minutes to hours after drug exposure, depending on the route of administration. A medication that can cause this type of reaction is β-lactam antibiotics.
- *Type II (cytotoxic reaction)*
  - Specific IgG or IgM antibodies are directed at drug-hapten coated cells, which causes hemolytic anemia, neutropenia, or thrombocytopenia. The timing of the reaction is variable. Medication examples include penicillin (hemolytic anemia) and heparin (thrombocytopenia).
- *Type III (immune complex reaction)*
  - Antigen-antibody complexes are formed, which causes serum sickness, vasculitis, or drug fever. Symptoms occur 1–3 weeks after drug exposure. Medication examples include penicillin (serum sickness), sulfonamides (vasculitis), and azathioprine (drug fever).
- *Type IV (delayed, cell mediated reaction)*
  - Activation and expansion of a drug-specific T cell takes place, which causes contact dermatitis or