current

DIAGNOSIS & TREATMENT

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Preface

This book is intended to serve the practicing physician as a useful desk reference on the most widely accepted technics currently available for diagnosis and treatment. It is not intended to be used as a textbook of medicine.

The wide acceptance of this book since its first appearance has been most gratifying. Annual revisions will continue to be prepared for distribution in January of each year.

Although we have dealt primarily with internal medical disorders, discussions of other disorders commonly encountered in certain other specialties are included also.

As an aid to the physician in keeping informed on new drugs, a separate section on recently introduced drugs is to be found in the appendix. Specific current references to the clinical literature and general bibliographies have been added as a guide to further reading.

The authors have drawn freely from their own published works, and much excellent tabular and graphic material has been borrowed from other sources. Due acknowledgements are given at appropriate places in the text.

The editors wish to express their sincere thanks to their associate authors for participating so effectively in this venture. It is obvious that without their cooperation and assistance this book would not have been possible.

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General Symptoms

Milton J. Chatton & Frederick H. Meyers

FEVER

The body temperature is normally subject to individual variation as well as to fluctuation due to physiologic factors. Exercise, digestion, sudden increase in environmental temperature, and excitement (e.g., medical examination) may cause a transient increase in temperature. There is a slight sustained temperature rise following ovulation during the menstrual cycle and in the first trimester of pregnancy. The normal diurnal variation may be as much as 2° F., being lowest in the early morning and highest in the late afternoon.

Careful readings with a reliable thermometer, preferably inserted for 3-5 minutes, will prevent errors in clinical interpretation and possible serious error.

Methods of Determination & Normal Adult Values

Area	Average Temp.	Range of Normal Temp.
Rectal or vaginal	99.6° F. (37.5° C.)	98.5° - 99.9° F. (37.0° - 37.7° C.)
Oral	98.6° F. (37.0° C.)	96.7° - 99.0° F. (36.0° - 37.4° C.)
Axillary	97.6° F. (36.5° C.)	95.7° - 98.0° F. (35.4° - 36.7° C.)

Types of Fevers.

The characteristics of the temperature pattern (graphic record), especially when viewed in light of other clinical findings, may be of prognostic value and a guide to the effectiveness of therapy. The older classifications of fever according to type are of limited diagnostic significance but may be useful for descriptive purposes.

A. Remittent: Fever of days' or weeks' duration with alternating periods during which temperature is normal (e.g., brucellosis or tertian malaria). Temperatures should be taken 3-4 times daily for a prolonged period (weeks to months) to demonstrate the alternating febrile and afebrile periods.

B. Intermittent: Temperature drops to normal or subnormal at least once in 24 hours (e.g., septic fevers and early tuberculosis). Temperature must be taken q.i.d. to demonstrate the variation within the day.

C. Unremittent or Continuous: Temperature never normal during 24-hour period (e.g., pneumonia, influenza). Temperature must be taken q.i.d. or, at times, every 2-3 hours to demonstrate its sustained character.

Diagnostic Considerations.

The outline below illustrates the wide variety of clinical disorders which may cause fever. Most febrile illnesses are easy to diagnose. In certain instances, however, the origin of the fever may remain obscure (FUO, PUO, or cryptogenic fever). Extensive laboratory and x-ray studies may be indicated; examination and culture of body fluids, exudates, and excretions, serologic tests, skin test, tissue biopsy, and toxicologic studies. Although fevers may be of psychogenic origin, this diagnosis should be made with extreme caution and should be based not only upon positive psychiatric criteria but after careful exclusion of the possibility of organic disease.

Clinical Classification of Causes of Fever (With Examples).

A. Infections: Viral, rickettsial, bacterial, fungal, and parasitic infections are the commonest causes of fever.

1. Generalized infections without localizing signs (e.g., septicemia).
2. Generalized infections with localizing signs (e.g., pharyngitis, scarlet fever).
3. Localized infections (e.g., pyelonephritis).

B. Diseases of Undetermined Etiology: (1) Collagen diseases (e.g., disseminated lupus erythematosus, periarteritis nodosa,

dermatomyositis, rheumatoid arthritis, rheumatic fever). (2) Other miscellaneous diseases (e.g., sarcoidosis, amyloidosis).

C. Central Nervous System Disease: Cerebrovascular accidents, head injuries, brain and spinal cord tumors, degenerative CNS disease (e.g., multiple sclerosis), spinal cord injuries.

D. Malignant Neoplastic Disease: Primary neoplasms (e.g., of thyroid, lung, liver, pancreas, and genitourinary tract). Secondary neoplasms, carcinoid.

E. Hematologic Disease: Lymphomas, leukemias, multiple myeloma, pernicious anemia, hemolytic anemias, hemorrhagic diseases (e.g., hemophilia).

F. Cardiovascular Disease: Myocardial infarction, thromboembolic diseases, bacterial endocarditis, congestive heart failure, paroxysmal tachycardias.

G. Endocrine Disease: Hyperthyroidism, pheochromocytoma.

H. Diseases Due to Physical Agents: Heat stroke, radiation sickness, trauma (e.g., surgery), crushing injuries.

I. Diseases Due to Chemical Agents: Drug reactions, anaphylactic reactions, serum sickness, chemical poisoning, pyrogen reactions (following I.V. fluids).

J. Disorders of Fluid Balance: Dehydration, acidosis.

K. Psychogenic fever.

L. Factitious fever.

Treatment.

A. Removal of the Specific Cause of the Fever: The principal problem is to determine and eradicate the cause of the fever. Symptomatic measures directed toward depression of an elevated body temperature are usually not indicated except for high, prolonged fevers.

B. Reduction of the Fever by Nonspecific Means: When the body temperature is greater than 40°C. (104°F.), particularly if prolonged, the following measures may be utilized:

1. Increased fluid intake - By oral or parenteral routes.

2. Alcohol sponges - Cooling is due to evaporation.

3. Warm or tepid baths - These cause peripheral vasodilatation.

4. Cold sponges - Provide prompt cooling of skin and psychologic relief but interfere with heat loss.

5. Ice bags - Provide local comfort, e.g., for headache.

6. Antipyretic drugs - These drugs are quite effective in reducing fever and have a simultaneous analgesic effect. They may, however, obscure the clinical picture, and may cause undesirable side effects such as sweating, nausea and vomiting, and, rarely, skin eruptions and hematologic changes. Such drugs, therefore, are to be employed cautiously in fevers due to infectious diseases and are preferably not used in the enteric fevers (e.g., typhoid fever). Acetylsalicylic acid (aspirin), 0.3-0.6 Gm. (5-10 gr.) every 4 hours p.r.n., is most commonly used. Other antipyretic analgesic drugs are listed on p. 6.

7. For reduction of very high fever [over 41.1°F. (106°F.)], see Heat Stroke.

Bennett, I.L., Jr.: Pathogenesis of fever. Bull. New York Acad. Med. **37**:440-4, 1961.

Petersdorf, R.G., & P. Beeson: Fever of unexplained origin: report on 100 cases. Medicine **40**:1-30, 1961.

Sheon, R.P., & R.A. Van Ommen: Fever of obscure origin. Diagnosis and treatment based on a series of 63 cases. Am.J.Med. **34**:486-99, 1963.

SHOCK
(Circulatory Failure or Collapse)

"Shock" is a complex and as yet incompletely understood clinical syndrome of circulatory failure - "a prolonged deficiency of blood flow" (Moore). The term is used to designate a pattern of symptoms and signs which include lowered systemic arterial pressure, tachycardia, and pale, cold skin of the face and extremities. Numerous pathophysiologic mechanisms are involved in the production of shock, such as lack of effective blood volume, alterations of cardiac output, loss of peripheral vascular tone, increased capillary permeability, and alteration of the physiochemical characteristics of the blood. Because such widely different mechanisms may result in the systemic arterial hypotension which is referred to as "shock," there is serious question concerning the desirability of retaining a catch-all term with such variable diagnostic and therapeutic meanings.

Classification.

The shock syndromes have been classified clinically according to etiology and pathophysiology as follows:

A. Neurogenic Shock (Primary, Immediate, or Psychogenic Shock, and Fainting or Syncope): This form of shock is usually vasovagal and caused by neurogenic or psychogenic factors, e.g., pain, trauma, fright, unpleasant sights, sounds, or odors, or vasodilator drugs (e.g., nitrites). Debility, asthenia, emotional instability, prolonged standing, excessive heat, alcohol, hypotensive drugs, and disorders of the autonomic nervous system predispose to neurogenic shock. The sudden autonomic overactivity results in vasodilatation or inhibition of constriction of the arterioles and rapid peripheral and splanchnic pooling of blood. Following a period of anxiety and signs of epinephrine release (tachycardia, tremors, and pallor), there is a sudden reflex vagal stimulation with decreased cardiac output, hypotension, and decreased cerebral blood flow. Although the patient usually revives promptly in the recumbent position, observation is necessary to prevent recurrence and possible progression. (See Chapter 15 for a discussion of the various types of syncope.) If the condition persists, consider other and more significant underlying causes of shock.

For treatment, see p. 480.

B. Hypovolemic Shock (Secondary, Delayed, Prolonged, Oligemic, Hemorrhagic, Traumatic, or Surgical Shock): In this form of shock there is a true diminution of blood volume due to loss of whole blood or plasma from the circulation. Compensatory vasoconstriction reduces the size of the vascular bed and may temporarily maintain the BP, but if fluid is not replaced immediately hypotension occurs and the tissues become progressively more anoxic. Since the vascular space is the smallest of the body fluid compartments, even a moderate sudden loss of circulating fluids can result in severe and sometimes irreversible damage to vital centers. Rapid loss of 50% of blood volume is usually fatal.

Hypovolemic shock may result from (1) loss of whole blood by hemorrhage due to external or internal injuries, (2) loss of whole blood through nontraumatic internal hemorrhage (e.g., bleeding peptic ulcer, ruptured varices), (3) loss of blood and plasma in extensive fractures and crushing injuries, (4) loss of plasma and hemolysis of red cells in extensive burns, (5) loss of plasma into serous body cavities (e.g., peritonitis), (6) loss of plasma due to nephrotic syndrome, or (7) dehydration with electrolyte imbalance.

Debility, malnutrition, senility, hypotensive drugs (e.g., coronary vasodilators), local anesthetics, general anesthetics, and adrenocortical insufficiency all predispose to hypovolemic shock.

The classical signs of pallor, coldness, cyanosis, sweating, tachycardia, and arterial hypotension may appear suddenly and often represent fully-developed shock. Since advanced shock is often refractory to even the most vigorous anti-shock therapy, early recognition or anticipation of shock is imperative.

C. Shock Due to Infection (Septic, Endotoxic, or Exotoxic Shock): The peripheral vascular collapse which follows the toxemia of overwhelming infection is characterized by an initial vasoconstriction followed by (or alternating with) vasodilatation, with venous pooling of blood. There is often a direct toxic action on the heart and adrenals. Shock should always be suspected when the febrile patient has chills, pallor, tachycardia, a moist skin, hypotension, and hyperpnea, especially if no other cause of shock is evident. Septic shock occurs more often in the very young and very old. It may be obscured by ineffective antibiotic therapy.

D. Cardiogenic Shock: Shock due to ineffective circulation associated with inadequacy of cardiac output may occur in myocardial infarction, severe tachycardia, and other serious cardiac arrhythmias; pulmonary embolism, cardiac temponade, or terminal congestive failure.

E. Allergic Shock: See Anaphylactic Reactions.

Treatment of Hypovolemic (Secondary) Shock.

A. Emergency Measures:

1. Place patient in the "shock position" (recumbent with head lower than the rest of the body) unless he has a head injury.

2. Maintain an adequate airway. If dyspnea or cyanosis is present, administer oxygen by nasal catheter or mask. Ensure adequate ventilation by mouth-to-mouth breathing. Pull out the tongue; remove dental plates from the mouth and mucus from the nose and mouth.

3. Keep the patient comfortably warm. Avoid chilling (to prevent heat loss), and excessive externally applied heat, which will further dilate the peripheral vessels.

4. Control pain (particularly if severe) promptly by the use of appropriate first aid measures and analgesic drugs. Give morphine sulfate, 10-30 mg. ($\frac{1}{6}$-$\frac{1}{2}$ gr.) subcut. for pain, but remember that subcut. absorption is poor in patients in shock. In case of severe pain, morphine sulfate, 10-15 mg. ($\frac{1}{6}$-$\frac{1}{4}$ gr.) I.V., may be used to greatest advantage. **Caution:** Do not give morphine to unconscious patients, patients who have head injuries, those with respiratory depression, or those without pain.

Avoid overdosage with morphine; substitute barbiturates and salicylates for sedation and analgesia whenever possible.

5. Allay apprehension by reassuring word and action. Pentobarbital sodium (Nembutal®), 0.1 Gm. (1½ gr.) orally, or 0.13 Gm. (2 gr.) subcut. or by rectal suppository, may be of value. Avoid "tranquilizing" drugs because of their undesirable hypotensive effect.

6. Parenteral fluid therapy - **Replace and maintain adequate blood volume.** The need may be determined by the history, vital signs, hematocrit, and, when available, blood volume studies. The clinical determination of effective blood volume may be difficult and is subject to considerable variation. There is no single technic or rule by which to judge the fluid requirements. Response to therapy is a valuable index. Selection of the replacement fluid which is most appropriate to the individual case is based upon consideration of what type of fluid has been lost (see pathophysiology, above), the availability of the various solutions, laboratory facilities, and, to a lesser extent, expense.

(1) Saline or glucose solutions - Give immediately 500 ml. sodium chloride injection or 5-10% dextrose injection, or 200 ml. of 5% saline solution (may be given rapidly I.V. while making preparations for plasma, serum albumin, or whole blood). Plasma, serum albumin, and whole blood exert a more sustained increase in blood volume through the colloidal osmotic pressure effect than do dextrose or electrolyte solutions.

(2) Whole blood - Whole blood may sometimes be of value in the treatment of severe or refractory shock even in the face of an apparently good hematocrit figure; this is because of the misleading effect of hemoconcentration. (a) For impending shock, administer 250-500 ml. of blood immediately and follow closely clinically and with hematocrit and blood volume studies to determine need for further plasma. (b) For early or advanced shock, administer 500 ml. whole blood immediately and repeat with 500 ml. every half hour up to a total of 2 L., depending upon the presence of continued hemorrhage, clinical course, and hematocrit and blood volume findings. If shock persists, the prognosis is very poor.

(3) Plasma or serum albumin - Any of the various plasma preparations, such as lyophilized or reconstituted plasma, may be employed. Plasma is usually readily procurable, may be rapidly set up for administration, and does not require preliminary blood typing. The quantity of plasma to be given depends upon the stage of shock and the response to therapy, based upon both clinical and laboratory studies.

(4) Plasma expanders - Fairly effective plasma substitutes for emergency treatment of shock are now available. These agents have high molecular weights, high oncotic pressures, and the necessary viscosity, but they have not proved to be as useful as plasma. They have the added advantage of not causing infectious hepatitis. Dextran injection (Expandex®, Gentran®, Plavlolex®) is a water-soluble biosynthetic polysaccharide available as a solution in isotonic saline for I.V. use. Give 500-1000 ml. at a rate of 20-40 ml./minute. Use cautiously in patients with cardiac or renal insufficiency. Anaphylactoid reactions have been reported. In order to avoid hemodilution, the dosage should not exceed that which maintains the systolic BP at about 85 mm. Hg.

7. Vasopressor drugs - These agents are most effective in hypotensive shock without associated decrease in blood volume (e.g., spinal anesthesia or overwhelming intoxications), although they are of at least transient value in severe shock due to any cause. Their use in myocardial infarction is controversial. They should not be used in lieu of more physiologic measures or specific treatment of the cause of shock. In many instances it is doubtful whether the BP elevation produced by the vasopressor drugs has either a beneficial or detrimental effect upon the underlying disturbance. (For example, the actual influence of the altered peripheral resistance on the blood supply to vital organs is incompletely understood.) Dosage levels for the various agents are empiric and must be carefully adjusted according to patient response (BP and pulse). The use of autonomic blocking agents (the reverse of the vasopressin drugs) has been suggested in order to provide maximum blood flow to vital tissues rather than to simply maintain BP, but they have not been widely accepted for this purpose and the matter is controversial.

(1) Levarterenol bitartrate (Levophed®), 4-16 mg. (4-16 ml. of 0.2% solution) in 1 L. of glucose I.V. Avoid extravasation (may cause tissue necrosis and gangrene). Constant supervision with regular determination of BP is essential. With concentrations greater than 4 mg./L., an inlying catheter is required.

(2) Phenylephrine hydrochloride (Neo-Synephrine®), 0.5 mg. I.V., or 5 mg. I.M., or by slow I.V. infusions of 100-150 mg./L. of glucose.

(3) Mephentermine sulfate injection (Wyamine®), 5-20 mg. at a rate of 1 mg./minute by continuous I.V. infusion of a 0.1% solution in 5% dextrose in water; or 15-20 mg. I.M.

(4) Metaraminol bitartrate (Aramine®), 2-10 mg. I.M., or 15-100 mg. in 250-500 ml. of 5% dextrose, or 0.5-5 mg. I.V.

(5) Methoxamine hydrochloride (Vasoxyl®), 15 mg. I.M., or 5 mg. I.V., or 35-40 mg. in 250-500 ml. of 5% dextrose by slow I.V. infusion.

B. Specific Measures:

1. Hemorrhage and anemia - Although plasma is usually given as an emergency measure in shock complicating hemorrhage, acute anemia must be corrected by replacement with whole blood to prevent hypoxia. It is the hemorrhage, not the BP, which requires treatment. The quantity of whole blood to be given will depend upon clinical response, hematocrit, and, when available, blood volume studies.

2. Anoxia (or hypoxia) - Oxygen may be indicated for hypoxia due to disorders such as cardiac failure and pneumonia. However, the patient in impending shock is apprehensive, and the mask or tent may increase his apprehension.

3. Dehydration - Administer 500-1000 ml. of sodium chloride injection or 5% dextrose injection, I.V. or by hypodermoclysis as needed. As soon as the patient can swallow, give fluids by mouth. Unless there is specific clinical or biochemical evidence of sodium deficiency, avoid administration of more than 1 L. of saline solution on the first day. Subsequent parenteral fluids may be given as dextrose solutions (see Chapter 2).

4. Adrenocortical failure - Adrenocortical steroid therapy has been found to be effective in shock-like states associated with serious medical emergencies. Although steroid treatment is most specifically applicable to shock of Addison's crisis, it may also be of spectacular value in certain acute allergic emergencies and overwhelming intoxications. Give hydrocortisone sodium succinate (Solu-Cortef®) (or equivalent), 100-300 mg. as a 5% solution in sterile water or isotonic saline solution, rapidly I.V. Subsequent doses of 50 mg. may be given as required. Doses of 500-1000 mg. daily for 3-5 days may be necessary.

5. Cardiac failure - Digitalis and other drugs for treatment of cardiac failure are indicated only for those patients with pre-existing or presenting evidence of cardiac failure. Use parenteral fluids cautiously and avoid sodium-containing solutions. Digitalis is of no value in shock due to any other cause.

6. Infection - Immediate measures should be taken to combat infection, if present. Early recognition is important. Initiate bacteriologic studies immediately and before therapy, if possible. Overwhelming infections are capable of producing sufficient metabolic changes in the body tissues to predispose to shock. Institute preliminary broad-spectrum antibiotic therapy until bacteriologic studies reveal the identity of the organism. "Prophylactic" antibiotics are of doubtful value and may even be harmful, except when the hazard of infection is great (e.g., extensive burns). Give hydrocortisone or its equivalent in doses of 250-500 mg. I.V. every 8-12 hours for 3 days, and supportive measures such as oxygen, pressor drugs, and parenteral fluids.

C. Evaluation of Therapy: Constant observation of patient is imperative. The pulse, respiration, temperature (rectal), and BP should be taken immediately and every 15-30 minutes or oftener thereafter until peripheral circulation has definitely improved.

1. Rapid recovery - If vital signs return rapidly to normal, keep the patient under close observation but withhold further antishock therapy. Check vital signs every half-hour. Determine hematocrit if there is any suspicion whatever that shock persists. Remember that hemoconcentration usually precedes BP and pulse changes. After eliminating potential or existing shock-producing factors, the patient may be managed expectantly until it is reasonably certain that the danger has passed.

2. Delayed recovery - If the vital signs remain abnormal for even a brief period after initial measures have been taken, or if there is evidence of progression of peripheral circulatory failure, institute further vigorous antishock therapy. Blood hemoglobin, RBC, and hematocrit should be determined immediately for a base-line, and should be repeated as often as necessary to evaluate the results of therapy.

Greisman, S.E.: The physiologic basis for vasopressor therapy during shock. Ann. Int. Med. **50**:1092-1114, 1959.

Irving, D.W., & E. Corday: Recognizing compensated shock. Am.J.Cardiol. **8**:611-61, 1961.

Rushmer, R.F., Van Citters, P., & D.L. Franklin: Shock: a semantic enigma. Circulation **26**:445-59, 1962.

Schneider, P.B.: Orthostatic hypotension. Arch.Int.Med. **110**:240-8, 1962.

Shoemaker, W.C.: Recent additions to the knowledge of the cause and management of shock. S.Clin.North America **42**:3-13, 1962.

Symposium on mechanisms of shock. Joint meeting of sections on anesthesiology and on experimental medicine and therapeutics of the American Medical Association. J.A.M.A. **181**:866-84, 1962.

Weil, M.H.: Adrenocortical steroid for therapy of acute hypotension. Am.Practitioner **12**:162-8, 1961.

Weil, M.H., & W.W. Spink: The shock syndrome associated with bacteremia due to gram-negative bacilli. Arch.Int.Med. **101**: 184-93, 1958.

PAIN

Pain is usually sharply localized in disorders of superficial structures and peripheral (spinal or cranial) nerves, and diffuse or poorly localized in disorders of deeper structures. Deep pain may be "referred" to other areas of the body (e.g., shoulder pain in gallbladder disease). The reaction to pain, a function of the higher centers, is extremely variable and influenced by many factors.

It is important to determine, whenever possible, the primary etiology (e.g., infection, toxins) and the pathogenesis (e.g., inflammation, ulceration, distention, anoxia, spasm) of pain. In most disorders it is possible to determine both the etiology and pathogenesis of pain (e.g., pleurisy associated with pneumococcic pneumonia); in other instances it is not possible to determine either (e.g., trigeminal neuralgia).

The relief of pain is achieved by removal of the primary cause (e.g., cure of infection), neutralization of the effect of the stimulus (e.g., antacids for hyperacidity of peptic ulcer), and, when these are not feasible, by dulling or obliteration of the sense of pain (e.g., palliative narcotics for terminal cancer). The psychic relief of pain by hypnosis has been repopularized as a means of analgesia in a wide variety of disorders. It is essential that hypnosis be administered by a professional person who has received special training in this field.

The hazards of administering analgesics without first attempting to establish a diagnosis cannot be overemphasized (e.g., acute abdominal pain). Analgesics, particularly narcotics, may mask the symptoms of serious acute or chronic illness.

Pain may be treated nonspecifically with drugs, physical measures (e.g., heat, cold, immobilization), or surgery (e.g., nerve resection, chordotomy). Narcotic analgesics should be avoided unless nonnarcotic drugs (in adequate dosage) would be ineffective. When narcotics are required, the relatively less addictive drugs (e.g., codeine) should be employed first. One should prescribe the lowest effective dosage of narcotics and discontinue as soon as possible.

Because psychic or emotional factors may greatly influence the pain threshold, it is important to consider the "placebo" role of all therapeutic measures for the control of pain. Pharmacologically inactive drugs may be surprisingly effective in alleviating the pain of organic as well as functional disorders.

Nonnarcotic Analgesics.

A. Salicylates: The salicylate drugs are antipyretic, analgesic, antirheumatic, and uricosuric; useful in relieving myalgias, neuralgias, arthralgias, headaches, and dysmenorrhea. Untoward reactions are usually mild, consisting of dizziness and dyspepsia, but large doses may cause tinnitus, deafness, blurring of vision, nausea and vomiting, diarrhea, diaphoresis, headache, and delirium. In sensitive patients, salicylates may cause urticarias and acute laryngeal edema.

1. Acetylsalicylic acid (aspirin or ASA), plain, buffered, or enteric-coated, 0.3 Gm. (5 gr.) tablets. Ordinary dosage is 0.3-0.6 Gm. (5-10 gr.) every 4 hours p.r.n.; 0.3 Gm. (5 gr.) every 2-3 hours is said to be more effective and to cause fewer untoward reactions. Aspirin may cause gastrointestinal irritation and bleeding; this may be reduced by administration of the drug on a full stomach or with 1/2-1 tsp. of baking soda or other antacid. Peptic ulceration has been attributed to aspirin, but this point remains controversial. Buffered aspirin usually available contains only small amounts of antacid, and the incidence of side effects and the blood levels achieved are not appreciably different than with ordinary aspirin. The enteric coated preparation is slower acting, but it prevents gastric irritation and is also useful for those patients who might be skeptical of the analgesic value of "ordinary aspirin." In certain cases it may be necessary to administer powdered aspirin rectally in a thin starch paste.

2. Sodium salicylate, plain or enteric-coated, 0.3-0.6 Gm. (5-10 gr.) every 4 hours p.r.n.

3. Acetylsalicylic acid compound (APC) contains aspirin, phenacetin, and caffeine. It is given as 1-2 tablets every 3-4 hours p.r.n. No advantage of this combination over ordinary aspirin has been conclusively demonstrated. The amounts of phenacetin ingested by habitual users of this combination cause serious renal damage.

4. Methyl salicylate (wintergreen oil) - For external use as a 10% oil or ointment applied over sore muscles or joints. Because of long-standing usage these "liniments" appear to have therapeutic value - largely on a psychologic basis.

B. Acetophenetidin (phenacetin), 0.3 Gm. (5 gr.) every 3-4 hours, may be employed in case of salicylate intolerance; in general, however, this drug is more toxic than other nonnarcotic analgesic preparations, and prolonged or excessive use is not advised. Its principal use is in analgesic combinations (e.g., APC).

C. Colchicine: See Gouty Arthritis.

D. Phenylbutazone (Butazolidin®) or Oxyphenbutazone (Tandearil®): See Gouty Arthritis.

E. Dextro Propoxyphene (Darvon®) and Ethoheptazine (Zactane®): Although related chemically to other narcotics, these drugs are less potent in all respects. Side effects are uncommon (dizziness, epigastric pain, nausea) and addiction is not a problem, but the claim that these drugs are comparable to codeine has been disproved. Their principal use is in patients who are allergic to or who cannot tolerate aspirin. They are also dispensed in combination with aspirin compound (Darvon Compound®, Zactirin®) every 4-6 hours p.r.n. No narcotic prescription is required.

Narcotic Analgesics.

The narcotic analgesics alter the perception of pain by their effects on the CNS. They are indicated for the relief of pain which is too intense to be controlled with nonnarcotic drugs or when pain is of a type not relieved by the salicylates (e.g., visceral pain).

The narcotics are also mildly sedative in small doses; larger doses produce sleep, stupor, and respiratory depression. They are addictive and should be used cautiously and with careful attention to federal and state laws. Except for codeine, they should not be used for chronic illnesses except when necessary for the control of otherwise intractable pain in terminal illness.

Addiction is discussed in Chapter 16.

The specific treatment of intoxication with these drugs is discussed in Chapter 28.

The standard drugs and their congeners are discussed below.

Note: Always use the least potent narcotic drug which will control the pain, i.e., aspirin is preferable to codeine, codeine to meperidine, and meperidine to morphine.

A. Morphine: This drug is the most valuable of the potent narcctics for general clinical use. It causes CNS depression which results in powerful analgesia associated with sedation, euphoria, and hypnosis; selective respiratory center depression, and dulling or abolition of the cough reflex. It increases intracranial pressure and causes spasm of biliary and ureteral smooth muscle. Morphine is useful for relief of acute or prolonged severe pain, especially pain arising from disorders which are of less than 10-14 days' duration. The drug may be valuable in the treatment of severe cardiac dyspnea (e.g., pulmonary edema or cardiac asthma of "left ventricular failure"). It is a commonly used and valuable preoperative drug. Morphine is contraindicated in morphine sensitivity, bronchial asthma, undiagnosed surgical abdominal disease, liver disease, hypothyroidism, morphinism, head injury, Addison's disease, and whenever vomiting may be dangerous. Untoward reactions include hypnosis (may be undesirable), respiratory depression, nausea and vomiting, severe constipation, allergic responses (urticaria, pruritus, and anaphylactoid reactions). The addiction tendency is great.

1 Morphine sulfate, 8-15 mg. ($^1/_8$-$^1/_4$ gr.) orally or subcut. In cases of severe agonizing pain, especially pain associated with impending neurogenic shock (e.g., acute pancreatitis), it may be given slowly in 5 ml. physiologic saline I.V. It is probable that only increased duration of effect is gained by increasing the dose above 10 mg.

2. Morphine adjuncts - Belladonna alkaloids, such as atropine and scopolamine, in dosages of 0.3-0.6 mg. ($^1/_{200}$-$^1/_{100}$ gr.) subcut. administered simultaneously with morphine, may reduce some of the untoward effects of morphine. The phenothiazine tranquilizers may enhance the analgesic effect.

B. Morphine Congeners: A number of drugs equivalent to morphine but offering no advantages are available. Claims of fewer side effects should be regarded with scepticism.

The following subcut. doses are equivalent to 10 mg. of morphine: dihydromorphinone (Dilaudid®), 2 mg.; levorphanol (Levo-Dromoran®), 2 mg.; oxymorphone (Numorphan®), 1 mg.; phenazocine (Prinadol®), 1 mg.; piminodine (Alvodine®), 7.5 mg.

C. Methadon (Dolophine®): Methadon, 5-10 mg. subcut., provides analgesia similar to that achieved with morphine. The onset is slower and the effect is more prolonged. It has powerful addictive properties. The only situation in which methadon is preferred is in the institutional treatment of addiction; withdrawal symptoms are ameliorated if methadon is first substituted for heroin or whatever opiate the addict has been taking.

D. Meperidine (Demerol®): 50-100 mg. orally or I.M. (not subcut.) every 3-4 hours provides analgesia and causes less intense side effects than morphine. It is also less addictive than morphine, but addiction to meperidine is nevertheless very common.

E. Meperidine Congeners: Alphaprodine (Nisentil®), 60 mg. subcut., and anileridine (Leritine®), 50 mg. subcut., are equivalent to meperidine, 100 mg., except that their duration of action is shorter.

F. Dihydrocodeinone and Dihydrohydroxycodeinone: These narcotics are present in

many combinations and are frequently misused because the names suggest a similarity to codeine. Both are more potent and more addictive than codeine.

G. Codeine: Codeine is pharmacologically similar to morphine but is less potent. Codeine diminishes the cough reflex and decreases bowel motility (constipating). It is preferred to morphine for relief of moderate degrees of pain because it is much less habit-forming and causes fewer untoward reactions (urticaria, nausea and vomiting, pruritus, dermatitis, anaphylactoid reactions).

1. Codeine phosphate, 8-65 mg. (1/8-1 gr.) orally or subcut. every 3-4 hours p.r.n. If 65 mg. (1 gr.) is ineffective, use stronger narcotics, since larger doses of codeine are attended by increasing side reactions without increasing analgesia.

2. Codeine in dosages ranging from 8-65 mg. (1/8-1 gr.) is often used in combination with acetylsalicylic acid or ASA compound. The dosage is one tablet orally 3-4 times daily as necessary. In such mixtures codeine is the active ingredient; the aspirin is added for convenience in prescribing.

DeKornfeld, T.J., Lasagna, L., & T.M. Frazier: A comparative study of five proprietary analgesic compounds. J.A.M.A. **182**:1315-8, 1960.

Murphree, H.B.: Clinical pharmacology of potent analgesics. Clin. Pharmacol. & Therap. **3**:473-504, 1962.

Reynolds, T.B., & H.A. Edmondson: Chronic renal disease and heavy use of analgesics J.A.M.A. **184**:435-44, 1963.

ALLERGIC DISORDERS

Allergic disorders may be manifested by generalized systemic reactions or by localized reactions in any organ system of the body. The reactions may be acute, subacute, or chronic, and may be caused by an endless variety of offending agents (antigens). Many of the obscure or so-called idiopathic disorders are considered to have a possible allergic origin.

Allergic Reactions in Otherwise Nonallergic ("Normal") Individuals.

Development of sensitization through contact with the antigen is more or less apparent. These reactions occur in a large percentage of "normal" individuals without evident hereditary predisposition. The diagnosis may be readily confirmed by appropriate skin testing or therapeutic trial **(caution).**

1. Serum sickness.
2. Drug anaphylaxis.
3. Dermatitis venenata.
4. Tuberculous sensitization.

Atopic Disorders.

These "natural or spontaneous" allergies occur in about 10% of the population, often with a family history of the same or a similar disorder. Antigenic etiology is much more obscure than in the case of the "normal" allergies. Determination of the allergens is much more difficult since complete reliance cannot be placed upon clinical history, skin tests, or elimination diets. Eosinophilia is characteristic but not pathognomic of atopic disorders.

1. Hay fever (allergic rhinitis).
2. Eczema.
3. Urticaria.
4. Angioneurotic edema.
5. Allergic purpura.
6. Allergic migraine.
7. Allergic asthma.
8. Anaphylactic reactions.

Anaphylactic Reactions (Anaphylactic Shock).

Anaphylactic reactions are the immediate shock-like and frequently fatal reactions which occur within minutes after administration of foreign sera or drugs. Although there is occasionally no history of previous exposure to the foreign substance, these acute reactions undoubtedly represent induced hypersensitivity. Anaphylactic reactions may occur following the injection of sera, penicillin and other antibiotics, and practically all repeatedly administered parenteral therapeutic agents. **Note:** For this reason, sensitizing drugs should not be administered indiscriminately by oral, topical, or parenteral routes. Emergency drugs should be available whenever injections are given.

Symptoms of anaphylaxis include apprehension, paresthesias, generalized urticaria or edema, choking sensation, cyanosis, wheezing, cough, incontinence, shock, fever, dilatation of pupils, loss of consciousness, and convulsions; death may occur within 5-10 minutes.

A. Emergency Treatment:

1. Epinephrine solution, 1 ml. of 1:1000 solution (1 mg.) I.M. stat., repeated in 5-10 minutes and later p.r.n. If the patient does not respond immediately, give 0.1-0.4 ml. of 1:1000 solution diluted in 10 ml. saline **slowly** I.V.

2. Place in shock position. Keep warm.

3. Maintain adequate airway.

4. Diphenhydramine hydrochloride (Benadryl®), aqueous, 5-20 mg. I.V., after epinephrine if necessary.