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MARCUS A. KRUPP
MILTON J. CHATTON

1978

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By

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CURRENT MEDICAL DIAGNOSIS & TREATMENT 1978

From inability to let well alone; from too much zeal for the new and contempt for what is old; from putting knowledge before wisdom, Science before Art and cleverness before common sense; from treating patients as cases, from making the cure of the disease more grievous than the endurance of the same, Good Lord deliver us.

—Sir Robert Hutchison

Preface

Current Medical Diagnosis & Treatment 1978 is intended to serve the practicing physician as a useful desk reference on widely accepted technics currently available for medical diagnosis and treatment. It is not intended to be used as a textbook of medicine. Specific current references to the clinical literature and general bibliographies are included as a guide to further study.

The book has been revised annually since its first appearance in 1962, and its wide acceptance has been most gratifying. The evaluation of new medical concepts and advances in diagnosis and treatment has been a constant challenge. Particularly difficult are the editorial decisions to delete familiar or traditional methods in favor of the new. Medical progress and space limitations are the deciding factors.

Enthusiasm for new methods has had to be weighed carefully against pragmatic considerations such as availability, feasibility, and safety. Priority of emphasis has been given to conservative diagnostic and treatment methods which have survived critical analysis. It is beyond the scope of this volume to fully discuss many interesting current controversial aspects of diagnosis and treatment.

Although we have dealt primarily with internal medical disorders, discussions of other disorders commonly encountered in certain other specialties are also included. Special chapters on medical genetics, cancer chemotherapy, and immunologic disorders are intended to serve as medically oriented introductory discussions of these fields with important clinical implications for patient care.

The widespread dissemination of this book overseas both in translation and in its English language editions has been a continuing source of satisfaction to all of us who have worked on it over the years. A Spanish edition is available from El Manual Moderno (Mexico City), an Italian edition from Piccin Editore (Padua), a Serbo-Croation edition from Savremena Administracija (Belgrade), a Portuguese edition from Atheneu Editora (São Paulo), a German edition from Springer-Verlag (Heidelberg), and a Japanese edition from the Maruzen Company (Tokyo). An English edition for distribution in Asia is printed in Tokyo by Maruzen, and a Middle East edition (in English) is available under the imprint of Librairie du Liban (Beirut).

The editors wish to express their sincere thanks to their associate authors for participating so effectively in this venture, and to the many students and physicians who have contributed suggestions and criticisms for this and previous editions. We continue to solicit comments and recommendations for future editions.

Marcus A. Krupp
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January, 1978

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General Symptoms

Milton J. Chatton, MD

FEVER

Fever was well known to the ancients as an important manifestation of illness, but it remained for modern medical science to provide a better understanding of the significance of body temperature variations in health and in disease. As the large number of specific causes of fever were being identified over the past century, interest also turned toward the pathophysiology of fever. It is now known that the thermoregulatory center is in the hypothalamus, which, in disease, is acted upon by fever-producing (pyrogenic) substances of either exogenous (eg, microbial) or endogenous (host tissue) origin. In turn, blood warmed by the fever triggers the hypothalamus to dissipate heat by peripheral (cutaneous) dilatation and sweating and by control of the shivering mechanism.

Fever may also occur when body metabolic heat production or environmental heat load exceeds normal heat loss capacity, or when there is impaired heat loss.

The body temperature is normally subject to individual variation as well as to fluctuation due to physiologic factors, eg, exercise, digestion, sudden increase in environmental temperature, and excitement. 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 1° C, being lowest in the early morning and highest in the late afternoon.

Careful readings with a reliable thermometer will prevent errors in clinical interpretation. Oral temperatures may be unreliable in "mouth-breathers" or in patients who are uncooperative, debilitated, or in shock. Rectal or vaginal temperatures are taken in these circumstances.

The average normal oral body temperature is 37° C (range 35.9–37.2° C), or 98.6° F (range 96.8–99.3° F). The normal rectal or vaginal temperature is 0.5° C (1° F) higher than the oral temperature, and the normal axillary temperature is correspondingly lower.

It is not known if fever plays any beneficial role in the body defense mechanism. In the preantibiotic era, fever was employed with limited success as nonspecific therapy for chronic infections. Markedly elevated or prolonged fevers may result in profound metabolic disturbances. Fever per se may also alter the metabolism and disposition of drugs used for the treatment of the diverse diseases associated with fever. Prolonged elevation of rectal temperature over 41° C (106° F) may result in permanent brain damage; when the rectal temperature is over 43° C (109° F), heat stroke occurs and death is common.

The characteristics of the temperature pattern (graphic record), especially when viewed in the light of other clinical findings, may be of diagnostic and prognostic value and may serve as a guide to the effectiveness of therapy.

The degree of fever does not necessarily correspond to the severity of the illness. Acute benign viral infections, for example, may be associated with high fever, whereas there may be a relatively minimal fever in much more serious disorders. In general, the febrile response tends to be greater in children than in adults; in elderly persons, the febrile response is less marked than in younger adults. A sudden fall in temperature in the febrile patient is not necessarily a favorable sign; unless there is a corresponding improvement in the patient's well-being, it may portend a serious complication such as shock.

Diagnostic Considerations

The outline below illustrates the wide variety of clinical disorders that may cause fever. Most febrile illnesses are due to common infections, are short-lived, and are relatively easy to diagnose. In certain instances, however, the origin of the fever may remain obscure ("fever of undetermined origin," FUO) after careful diagnostic examination. Meticulous history-taking (including history of exposure to infection, travel, drugs), careful physical examination, extensive laboratory and x-ray studies, and even exploratory surgical procedures may be required (see Chapter 21).

In about 40% of cases, the cause of FUO is infectious disease. About 20% of cases of FUO are due to neoplastic disease; about 15% are due to connective tissue disease; and the remainder are due to miscellaneous causes. In 5–10% of cases the diagnosis is never established and the patients recover spontaneously.

Use of the so-called therapeutic test for the diagnosis of a fever is justified only when a specific disease is strongly suspected (eg, chloroquine for malaria). Hasty, empirical use of polypharmaceutical measures (eg, multiple antimicrobials, corticosteroids, antipy-

retics, analgesics) may seriously interfere with rational diagnosis and therapy and may actually be hazardous. Although mild fevers may be of psychogenic origin, this diagnosis should be made with caution and should be based upon positive psychiatric criteria after careful exclusion of the possibility of organic disease.

Clinical Classification of Causes of Fever (With Examples)

(1) Infections: Viral, rickettsial, bacterial, fungal, and parasitic infections are the commonest causes of fever. (a) Generalized infections without localizing signs (eg, septicemia). (b) Generalized infections with localizing signs (eg, pharyngitis, scarlet fever). (c) Localized infections (eg, pyelonephritis).

(2) Collagen diseases: Systemic lupus erythematosus, polyarteritis nodosa, dermatomyositis, rheumatoid arthritis, rheumatic fever.

(3) Central nervous system disease: Cerebrovascular accidents, head injuries, brain and spinal cord tumors, degenerative CNS disease (eg, multiple sclerosis), spinal cord injuries.

(4) Malignant neoplastic disease: Primary neoplasms (eg, of thyroid, lung, liver, pancreas, and genitourinary tract). Secondary neoplasms, carcinoid.

(5) Hematologic disease: Lymphomas, leukemias, multiple myeloma, pernicious anemia, hemolytic anemias, hemorrhagic disease (eg, hemophilia).

(6) Cardiovascular disease: Myocardial infarction, thromboembolic diseases, bacterial endocarditis, congestive heart failure, paroxysmal tachycardias.

(7) Gastrointestinal disease: Inflammatory bowel disease, hepatic cirrhosis (necrotic phase), liver abscess.

(8) Endocrine disease: Hyperthyroidism, pheochromocytoma.

(9) Diseases due to physical agents: Heat stroke, radiation sickness, trauma (eg, surgery).

(10) Diseases due to chemical agents: Drug reactions, anesthesia, anaphylactic reactions, serum sickness, chemical poisoning, pyrogen reactions (following intravenous fluids).

(11) Disorders of fluid balance: Dehydration, acidosis.

(12) Other miscellaneous diseases: Sarcoidosis, amyloidosis.

(13) Psychogenic fever.

(14) Factitious or "false" fever.

(15) Unknown causes.

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 solely toward depression of elevated body temperature are not indicated except for high, prolonged fevers.

Prevention of the serious "malignant hyperpyrexia" which may follow certain types of general anesthesia can best be accomplished by recognizing the hereditarily predisposed patient (history or evidence of myopathy; past personal or family history of difficult anesthesia) and by proper choice of anesthetic agent, with temperature monitoring during anesthesia.

B. Reduction of Fever by Nonspecific Means: When the body temperature is greater than 40° C (104° F), particularly if prolonged, symptomatic treatment may be required (Table 1–1). Since moderately high fevers are usually well tolerated by the body, with little evidence of direct tissue damage, aggressive symptomatic treatment should be avoided. Extreme pyrexia (hyperthermia)—temperatures in excess of 41° C (106° F)—is a medical emergency. (See Heat Stroke, p 932.)

1. Measures for removal of heat—Alcohol sponges, cold sponges, ice bags, and icewater enemas will reduce fever and provide physical comfort for patients who complain of feeling *hot.* Use of these measures should be appropriate to the degree of fever and discomfort and is to be avoided when the febrile patient feels and looks *cold.*

2. Antipyretic drugs—Aspirin or acetaminophen, 0.3–0.6 gm every 4 hours as needed, is quite effective in reducing fever due to diseases that act upon the

Table 1–1. Pathophysiologic basis for symptomatic treatment of fever.*

Pathophysiologic Basis for Fever	Clinical Findings	Treatment
Endogenous pyrogens act on hypothalamus to induce fever (eg, infection, collagen disease, allergy)	Patient complains of feeling cold. Shivering. "Gooseflesh." Cold extremities. Minimal sweating.	Antipyretic drugs: aspirin or acetaminophen, 300–600 mg 4 times daily. Supply clothing and covers just sufficient for maximal comfort. *Avoid* measures for physical removal of heat (eg, sponging, ice bags).
Agent or illness acts on hypothalamus to induce fever (eg, CNS lesions, toxins, radiation)		
Heat production exceeds normal heat loss mechanisms (eg, malignant hyperthermia, thyroid storm)	Patient complains of feeling hot. Hot extremities. Active sweating (except in cases where there is defective heat loss mechanism).	Remove excessive clothing or covers. Eliminate excess environmental heat source. Employ measures for physical removal of heat (eg, sponging, ice bags, icewater enemas). *Avoid* antipyretic drugs.
Environmental heat load exceeds normal heat loss mechanisms (eg, exposure to industrial heat, overuse of sauna)		
Defective heat loss mechanisms cannot cope with normal heat load (eg, heat stroke, burns, sweat gland disorders)		

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hypothalamic thermoregulatory center. The drugs may occasionally obscure the clinical picture and cause undesirable side-effects such as excessive sweating, nausea and vomiting, skin eruptions, and hematologic changes (see p 9).

3. Fluid replacement—Oral or parenteral fluids must be administered in amounts sufficient to compensate for the extra fluid losses from perspiration and all other causes.

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SHOCK SYNDROME (Circulatory Shock)

"Shock" is a complex and incompletely understood acute cardiovascular syndrome which defies precise definition because of its heterologous origins. It is practical, however, to consider shock as a disturbance of circulation resulting in ineffective or critical reduction of perfusion of vital tissues and a wide range of systemic effects. The term is descriptive of a "classical" but highly variable pattern of signs and symptoms which usually includes arterial hypotension, altered sensorium, ashen pallor, clammy skin, rapid and weak pulse, air hunger, thirst, oliguria, and a tendency to steadily progress toward a refractory and so-called "irreversible" phase. Recognition of early shock may be obscured by factors such as anxiety, complicating medical problems, and surrounding circumstances. The "classical" signs of shock may appear suddenly and often represent fully developed shock.

In so-called "warm shock" such as is seen in some patients with endotoxin septic shock, the skin is dry, pink, and warm and the urine volume is adequate despite the arterial hypotension and peripheral pooling.

The 3 major pathophysiologic mechanisms involved in the production of shock are (1) hypovolemia (decreased effective blood volume), (2) cardiac insufficiency (pump failure), and (3) altered vascular resistance (vasoconstriction or vasodilatation).

Alteration of one or more of these factors may result in diminished microcirculatory flow. It is the adaptation or failure of adaptation of the microcirculation that is responsible for arteriovenous shunting, decreased urine output, fluid loss from the capillaries, sludging of red blood cells, stagnant tissue hypoxia, acidosis, hyperlacticacidemia, and cellular injury, all of which occur in the shock syndrome. Little is known regarding the actual mechanisms of the metabolic vicious cycle leading to "irreversible shock."

Debility, malnutrition, senility, temperature extremes, alcoholism, hypotensive drugs, anesthetics, autonomic disorders, diabetes, and adrenocorticoid disorders are factors which can predispose to shock.

Factors which unfavorably influence the prognosis in shock states include coma, acidosis (pH $<$ 7.30), $P_{aCO_2} > 45$ mm Hg, serum lactate $>$ 2 mmol/liter, severe sepsis, anuria, heart disease, hepatic disease, and advanced age ($>$ 70 years).

Classification

No classification of shock is completely satisfactory, but one which is based upon the predominant hemodynamic changes in the various types of shock is clinically the most useful (Table 1–2). It should be apparent that in a given patient with shock several hemodynamic mechanisms are at work simultaneously so that continuous monitoring of multiple parameters of cardiovascular function is required. For example, hypovolemia and altered peripheral resistance may be significant factors in cardiogenic shock, and pump failure may be an important feature of hypovolemic shock. Therapeutically, this implies a real hazard in focussing on only a single deranged mechanism in treating a so-called specific type of shock.

A. Hypovolemic Shock (Oligemic, Hemorrhagic, Traumatic, Burn, 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.

Table 1–2. Classification of shock.

I. Hypovolemic shock (decreased effective blood volume)
A. Exogenous (external) loss of fluid
1. Whole blood (eg, hemorrhage)
2. Plasma (eg, burns)
3. Fluid and electrolytes (eg, vomiting, diarrhea)
B. Endogenous (internal) loss of fluid
1. Exudative (eg, peritonitis)
2. Traumatic (eg, hematoma)
II. Cardiogenic shock (pump failure)
A. Intrinsic myocardial disorders (eg, decreased myocardial contractility)
1. Focal damage (eg, myocardial infarction)
2. Generalized disorder (eg, dysrhythmia, myocarditis)
B. Extrinsic disorders
1. Cardiac tamponade (eg, pericardial disease)
2. Obstruction of major blood channels (eg, pulmonary embolism)
III. Vascular (vasomotor, distributive, low-resistance) shock (altered vascular resistance and capacity)
A. Increased venous capacitance (pooling) (eg, bacterial endotoxin)
B. Decreased arteriolar resistance (eg, fright, pain, vasodilative drugs)

Compensatory vasoconstriction temporarily reduces the size of the vascular bed and may temporarily maintain the blood pressure, but if fluid is not replaced immediately hypotension occurs, peripheral resistance increases, capillary and venous beds collapse, and the tissues become progressively more hypoxic. 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 (eg, 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 (eg, peritonitis), (6) loss of plasma due to nephrotic syndrome, or (7) loss of fluid and electrolytes (eg, vomiting, diarrhea, endocrine disturbances).

B. Cardiogenic Shock: Shock due to inability of the left ventricle to perform effectively as a pump in maintaining an adequate cardiac output occurs most frequently following myocardial infarction, but it also occurs in serious cardiac arrhythmias, pulmonary embolism, cardiac tamponade, terminal congestive failure, or as a complication of other forms of severe shock. Shock associated with myocardial infarction or other serious cardiac disease carries a very high mortality rate (75–80%) despite therapy.

Clinical findings are of limited value in predicting the course or prognosis of cardiogenic shock. Major myocardial infarction as determined by ECG, enzyme studies, and sophisticated indices of cardiovascular function may provide reasonably reliable evidence of impending shock.

C. Vascular Shock (Vasomotor, Distributive, Low-Resistance Shock): In this type of shock the available circulating volume of blood may be unaltered, but the blood volume is inadequate because the capacity of the vascular system is expanded. The increased vascular capacity may result from widespread dilatation of arteries and arterioles, arteriovenous shunting, or from venous pooling. The venous pressure is often normal.

The most common form of vascular or low-resistance shock is that due to gram-negative bacillemia, so-called septic shock. The toxemia of overwhelming infection is characterized by an initial short period of vasoconstriction followed by vasodilatation, with venous pooling of blood in the microcirculation. There is often a direct toxic action on the heart and adrenals. The mortality rate is high (40–80%). Septic shock is most commonly caused by infection due to gram-negative organisms (*Escherichia coli,* klebsiella, proteus, pseudomonas, meningococci). Gram-negative anaerobes (eg, bacteroides) are increasingly recognized as a cause of septic shock. Septic shock occurs more often in the very young and the very old, in diabetes, hematologic malignancies, diseases of the genitourinary, hepatobiliary, and intestinal tracts, in meningitis or pneumonia, and with corticosteroid, immunosuppressive, or radiation therapy. Immediate precipitating factors may be urinary, biliary, or gynecologic manipulations. Septic shock may be obscured by ineffective antibiotic therapy.

Septic shock should always be suspected when a febrile patient has chills associated with hypotension. Early, the skin may be warm and the pulse full. Hyperventilation may occur and result in respiratory alkalosis. The sensorium and urinary output are often initially normal. The classical signs of shock become manifest later. The symptoms and signs of the inciting infection are not invariably present. (See Chapter 23.)

Neurogenic or psychogenic factors, eg, spinal cord injury, pain, trauma, fright, or vasodilator drugs may also cause vascular shock. 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. In the absence of spinal cord injury or other complicating factors, the patient usually revives promptly in the recumbent position or following the administration of simple forms of treatment (eg, spirits of ammonia, physical stimuli), but observation is necessary to prevent recurrence and possible progression.

Vascular shock may also be due to anaphylaxis, histamine response, ganglionic blockade, and hypnotic drug intoxication.

Treatment

It is of vital importance to determine the specific cause or causes, contributing factors (eg, age, prior physical status, complications), severity, and duration of shock. Prompt, calculated, and decisive action is essential. Prevention or early recognition of shock and of contributing medical factors is simpler and considerably more effective than the treatment of established shock. Observe and record vital signs (pulse, temperature, respiration, and blood pressure), color and texture of skin, and level of consciousness.

A. General Measures:

1. Position—Place the patient with the head and torso in the horizontal or slightly elevated position with moderate (30 degree) elevation of the legs. Avoid the so-called shock position. Simple elevation of the legs is considered to be more desirable since it is less apt to interfere with cerebral blood flow, although this too should be avoided if dyspnea is present.

2. Oxygen—Clear the airway of obstructions and secretions and, if necessary, insert an oropharyngeal or endotracheal airway. Start oxygen by mask or nasal catheter as soon as possible. Frequent monitoring of blood gases is of the greatest importance. If arterial P_{O_2} (Pa_{O_2}) is below 60 mm Hg or if dyspnea or cyanosis is present, increased oxygen is usually required.

Mechanical respirators may be required to maintain adequate oxygen exchange. If Pa_{O_2} fails to show a prompt rise, suspect pulmonary shunting or so-called "shock lung" (see p 142).

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

4. Analgesics—Control severe pain promptly by the use of appropriate first aid measures and analgesic drugs. Give morphine sulfate, 8–15 mg subcut, for pain. Since subcutaneous absorption is poor in patients in shock, morphine sulfate, 10–15 mg slowly IV, may be used for severe pain. ***Caution:*** Do not give morphine to unconscious patients, to patients who have head injuries, or to those with respiratory depression.

5. Laboratory studies—Determine blood hemoglobin, hematocrit, and red cell count immediately for baseline and follow-up values. Obtain blood for typing and cross-matching. Laboratory studies for rapid serial determination of serum electrolytes, pH, Pa_{O_2}, and Pa_{CO_2} may be invaluable. Present methods of blood volume determination are of limited value in monitoring the treatment of shock.

6. Urine flow—In the patient without preexisting renal disease, urine output is a reliable indication of vital organ perfusion and is perhaps the best single criterion of shock. Insert an indwelling catheter to monitor urine flow (which should be kept above 50 ml/hour). Urine flow less than 20 ml/hour indicates inadequate renal circulation which, if not corrected, can cause renal tubular necrosis.

7. Central venous pressure or pulmonary artery wedge pressure—Monitor central venous pressure (CVP) or pulmonary artery wedge pressure (PAW) continuously in all shock patients. CVP determination is relatively simple and may be useful when serial measurements are made and are correlated with simultaneous clinical and laboratory observations. CVP is not as reliable as determinations of the pulmonary artery wedge pressure (by the more sophisticated Swan-Ganz catheter technic), which better reflects left ventricular function.

In simple CVP determination, a catheter is inserted percutaneously (or by cutdown) through the antecubital or external jugular vein near or into the right atrium and is connected to a manometer. Normal values range from 5–8 cm water. A low CVP in the presence of intense peripheral vasospasm (pale, clammy skin) suggests a low blood volume and need for fluid replacement, whereas a high CVP (about 15 cm water) suggests fluid overload or insufficient cardiac output. The CVP, however, may be normal in left ventricular failure and also in neurogenic shock. CVP changes in response to cautious administration of small amounts of intravenous fluids may increase the value of CVP as an indicator of blood volume and cardiac efficiency.

PAW determinations are considerably more reliable than the CVP for assessing adequacy of restoration of fluid volume and should, therefore, be used whenever possible. A mean pressure of 12 mm Hg is considered to be the upper limit of normal. An elevated PAW ($>$ 14 mm Hg) serves as a warning of impending pulmonary edema and of the hazard of fluid overload.

8. Volume replacement—*Replace and maintain adequate blood volume.* Initial or emergency needs may be determined by the history, general appearance, vital signs and other physical findings, hemoglobin, and hematocrit, although these are not reliable guides for volume replacement. Under ordinary clinical conditions, determination of effective blood volume may be difficult and is subject to considerable variation. There is no simple technic or rule by which to accurately judge the fluid requirements. An estimate of total fluid losses is an essential first step. Continuous CVP or PAW monitoring may be useful as a guide to safe fluid replacement. Response to therapy—particularly the effect of carefully administered, gradually increasing amounts of intravenous fluids on the CVP or PAW—is a valuable index. Selection of the replacement fluid which is most appropriate for the individual case is based upon consideration of what type of fluid has been lost (whole blood, plasma, water and electrolytes), the availability of the various solutions, laboratory facilities, and, to a lesser extent, expense. Whole blood is usually the most effective replacement fluid in case of gross hemorrhage if the hematocrit is $<$ 35%, but other readily available parenteral fluids should be given immediately pending preliminary laboratory work and the procurement of whole blood. Frozen, thawed, and washed red cells in salt solution have been used with favorable results in patients with hemorrhagic shock. If the CVP or PAW is low, the hematocrit is $>$ 35%, and there is no clinical evidence to suggest otherwise, replace blood volume with saline, serum albumin, plasma, or plasma expanders.

a. Crystalloid solutions—Give immediately 500–2000 ml of sodium chloride injection (physiologic saline), lactated Ringer's injection, or Ringer's bicarbonate (Ringer's injection with sodium bicarbonate added), rapidly intravenously, under CVP or PAW monitoring, while making preparations for plasma expanders, plasma, serum albumin, or whole blood. The latter exert a more sustained increase in blood volume through their colloidal osmotic pressure effects than do crystalloid solutions, although the electrolyte solutions are remarkably effective when given in adequate doses. There is little evidence that judicious saline resuscitation induces pulmonary edema in patients in early shock who have normal cardiac and renal function. When large volumes of crystalloids are given, however, patients should be examined frequently for evidence of pulmonary edema.

b. Whole blood—(See above.) Whole blood, used appropriately, may 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. For **advanced shock**, especially with the suspicion of associated occult blood loss, administer 500 ml whole blood imme-

diately and repeat with 500 ml every half hour up to a total of 2 liters or more, depending upon the presence of continued hemorrhage, clinical course, and hematocrit and CVP or PAW findings.

c. **Plasma or serum albumin**—Various plasma preparations (such as lyophilized or reconstituted plasma) or serum albumin may be employed. Plasma is usually readily procurable for emergencies, 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. The incidence of hepatitis following the use of plasma, especially of pooled commercial plasma, is a significant deterrent to its routine use in shock. Albumin is usually administered as either 5% normal serum albumin or plasma protein fraction, but in the case of long-standing shock the albumin content of the 5% solution is insufficient.

d. **Dextrans**—Dextrans are fairly effective plasma expanders or "substitutes" in the emergency treatment of shock, but they cannot replace treatment with whole blood (or its derivatives) when the latter is necessary. The dextrans have high molecular weights, high oncotic pressures, and the necessary viscosity, but they have not proved to be as useful as plasma and their use, furthermore, is not without hazard. They have the advantages of ready availability, of compatibility with other preparations used in intravenous solutions, and of not causing infectious hepatitis.

Clinical dextran of high molecular weight (70,000) is an effective colloid because of its prolonged action, but it may interfere with blood coagulation. **Dextran 40**, a low molecular weight dextran, is available as a 10% solution in either isotonic saline or 5% dextrose in water for intravenous use. It decreases blood viscosity and possibly improves the microcirculation. Rapid initial infusion of approximately 100–150 ml within the first hour is followed by slow maintenance for a total of 10–15 ml/kg/24 hours (preferably less than 1 liter/day).

Use dextrans cautiously in patients with cardiac disease, renal insufficiency, or marked dehydration to avoid pulmonary edema, congestive heart failure, or renal shutdown. Side-effects may be fatal. Observe for possible anaphylactoid reactions. Prolongations of bleeding time have been reported. Use with caution in patients with thrombocytopenia. Obtain blood for typing and cross-matching before dextran therapy since dextran may interfere with these tests.

9. Vasoactive drugs—Because of their remarkable ability to raise the blood pressure, several of the adrenergic drugs (sympathomimetic amines) have been used extensively, on a largely empiric basis, for the treatment of all types of shock. It is now known that simple blood pressure elevation produced by the vasopressor drugs has little beneficial effect on the underlying disturbances, and there is good evidence that in many instances that effect may be detrimental. Their routine use in all cases of shock is to be deplored.

Although the pharmacologic effects of the various adrenergic drugs cannot always be clearly explained and although their action in different disease states is not always predictable, certain of the known pharmacologic effects of available agents can be selectively utilized in the adjunctive therapy of shock (Table 1–3.) The selection of the proper agent will obviously depend upon the carefully determined particular pathophysiologic derangement in any given patient. *The adrenergic drugs should not be considered to be a primary form of therapy in shock.* Immediate restoration of blood volume, correction of hypoxia, fluid and electrolyte disturbances, and search for treatable causes deserve first consideration. Continuous monitoring of vital signs, sensorium, central venous pressure or pulmonary wedge pressure, and urinary output is essential to determine if, when, how much, and for how long the adrenergic drugs are to be used.

The purely alpha-adrenergic stimulating drugs have little or no value in the treatment of shock. The mixed alpha- and beta-adrenergic agents are used most frequently, depending upon the need for adequate tissue perfusion pressure. Currently, dopamine is enjoying widespread use because of a uniquely favorable effect on renal and splanchnic blood flow, but its ultimate relative value in the treatment of shock remains to be determined. Epinephrine, of course, has a favored place among the adrenergic drugs because of its great value in the treatment of anaphylaxis, but its use is not recommended in other forms of shock. The beta-adrenergic stimulating agent isoproterenol has some value as a potent vasodilator and inotropic agent, but it is particularly apt to cause serious dysrhythmias. The alpha- and beta-adrenergic blocking agents have been largely limited to investigational use for the treatment of shock.

The principal vasoactive drugs used for shock are the following:

(1) Levarterenol bitartrate (norepinephrine) is a mixed alpha- and beta-mimetic agent, a powerful vasopressor, and a potent inotropic drug. Give 4–8 mg (4–8 ml of 0.2% solution) in 1 liter of dextrose in water IV. Avoid extravasation (may cause tissue necrosis and gangrene). With concentrations greater than 8 mg/liter, an inlying polyethylene catheter is required.

(2) Metaraminol bitartrate is both an alpha- and a beta-mimetic agent with cardiotonic as well as vasopressor effects. Give 2–10 mg IM, or 0.5–5 mg cautiously IV, or 15–100 mg by slow infusion in 250–500 ml of 5% dextrose solution IV.

(3) Isoproterenol, a beta-adrenergic stimulator, increases cardiac output by its action on the myocardial contraction mechanism and produces peripheral vasodilatation. Give 1–2 mg in 500 ml 5% dextrose in water IV. Because of its inotropic effect, an increased incidence of cardiac arrhythmias precludes its use if the cardiac rate is greater than 120/minute.

(4) Dopamine hydrochloride (Intropin) is an endogenous catecholamine which has an added advantage over other adrenergic drugs because it has a beneficial effect on renal blood flow and also increases cardiac output and blood pressure. Dopamine hydrochloride, 200 mg in 500 ml sodium chloride injection USP (400