Endocrine Disorders

The endocrine system consists of a group of integrated glands and cells that secrete hormones. The secretion of hormones by these glands is controlled by feedback mechanisms in which the amount of hormone circulating in blood triggers factors that control production. Diseases of this system can result from conditions in which too much or too little hormone is produced. Diseases of this system can also result from either dysfunction of the glands themselves or a problem in the mechanism that controls hormone production. Some of the endocrine gland diseases in which oral changes occur are included here.

also result from either dysfunction of the glands themselves or a problem in the mechanism that controls hormone production. Some of the endocrine gland diseases in which oral changes occur are included here.

HYPERPITUITARISM

Hyperpituitarism is excess hormone production by the anterior pituitary gland. It is caused most often by a benign tumor **(pituitary adenoma)** that produces growth hormone. If the increase in growth

hormone production occurs during development, before the closure of the long bones, **gigantism** results. **Acromegaly** results when the hypersecretion occurs in adult life.

Gigantism includes excessive growth of the overall skeleton. Affected individuals can be more than 8 feet tall and weigh several hundred pounds, and as adults they experience headaches, chronic fatigue, and muscle and joint pain.

Clinical Features and Oral Manifestations

Manifestations

Acromegaly affects both men and women and most commonly occurs in the fourth decade of life. The onset is slow and insidious. Patients experience poor vision, sensitivity to light, enlargement of the hands and feet, and an increase in rib size. The facial changes include enlargement of the maxilla and mandible, frontal bossing (an enlargement of the bones of the forehead), and enlargement of the nasal bones. An enlargement of the maxillary sinus also occurs, which causes a characteristically deep voice. The enlargement of the maxilla and mandible causes separation of teeth and malocclusion. Mucosal changes such as thickened lips and macroglossia (enlarged tongue) have also been described in patients with acromegaly **(Figure 9-1)**.



HYPERTHYROIDISM

Hyperthyroidism, also called **thyrotoxicosis**, is characterized by excessive production of thyroid hormone. It is much more common in women than in men. Hyperthyroidism has several different causes. The most common cause is Graves disease. The exact cause of Graves disease is not clear, but it appears to be due to an autoimmune disorder in which a substance that abnormally stimulates the thyroid gland is produced. Other causes of hyperthyroidism include hyperplasia of the gland, benign and malignant tumors of the thyroid, pituitary gland disease, and metastatic tumors.

metastatic tumors

Clinical Features

The clinical features of hyperthyroidism include rosy complexion, erythema of the palms, excessive sweating, fine hair, and softened nails. Exophthalmus (protrusion of the eyeballs) may be seen in hyperthyroidism. Anxiety, weakness, restlessness, and cardiac problems may be associated with the disorder.

Oral Manifestations

Hyperthyroidism in children may lead to premature exfoliation of deciduous teeth and premature erup

Oral Manifestations

Hyperthyroidism in children may lead to premature exfoliation of deciduous teeth and premature eruption of permanent teeth. In adults, osteoporosis may occur, which may affect alveolar bone. Dental caries and periodontal disease appear to develop and progress more rapidly in these patients than in other patients. Burning discomfort of the tongue has also been reported in patients with hyperthyroidism.

Treatment

Treatment of hyperthyroidism may include surgery, medications to suppress thyroid activity, or the administration of radioactive iodine.

ministration of radioactive iodine.

HYPOTHYROIDISM

Hypothyroidism is characterized by decreased output of thyroid hormone. When hypothyroidism is present during infancy and childhood, it is known as **cretinism**. In older children and adults, the condition is known as **myxedema**. Causes include developmental disturbances, autoimmune disease, iodine deficiency, drugs, and pituitary disease. In infants, facial and oral changes include thickened

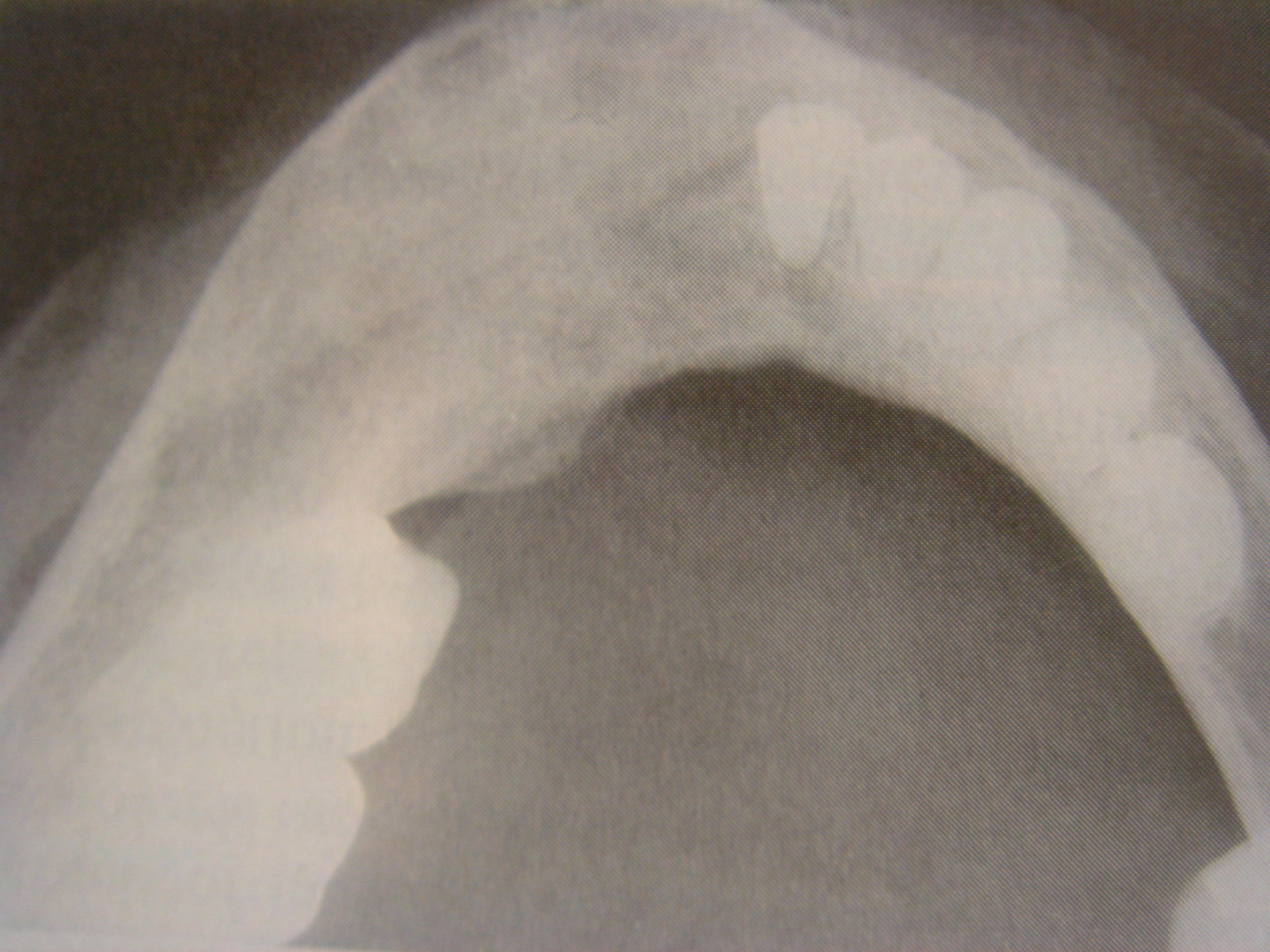
HYPERPARATHYROIDISM

Hyperparathyroidism results from excessive se-
cretion of parathyroid hormone (parathormone
[PTH]), which is secreted by the parathyroid glands
The four parathyroid glands are located near the thy-
roid gland. Parathyroid hormone plays an importan
role in calcium and phosphorus metabolism
Elevated blood levels of calcium (**hypercalcemia**)
low levels of blood phosphorus (**hypophos-
phatemia**), and abnormal bone metabolism charac-
terize hyperparathyroidism.

Hyperparathyroidism may be the result of hy-
perplasia of the parathyroid glands, a benign tumo

parathyroid tumor. The disease is found in middle-aged adults and is far more common in women than in men.

Calcium is obtained mainly from dairy products and plays an important role in the contraction of all types of muscle. Parathyroid hormone maintains normal blood levels of calcium through its effects on the kidney, gastrointestinal tract, and bone. It increases the uptake of dietary calcium from the gastrointestinal tract and is able to move calcium from bone to circulating blood when necessary. The hormone appears to be able to remove calcium from bone through the action of osteoclasts.



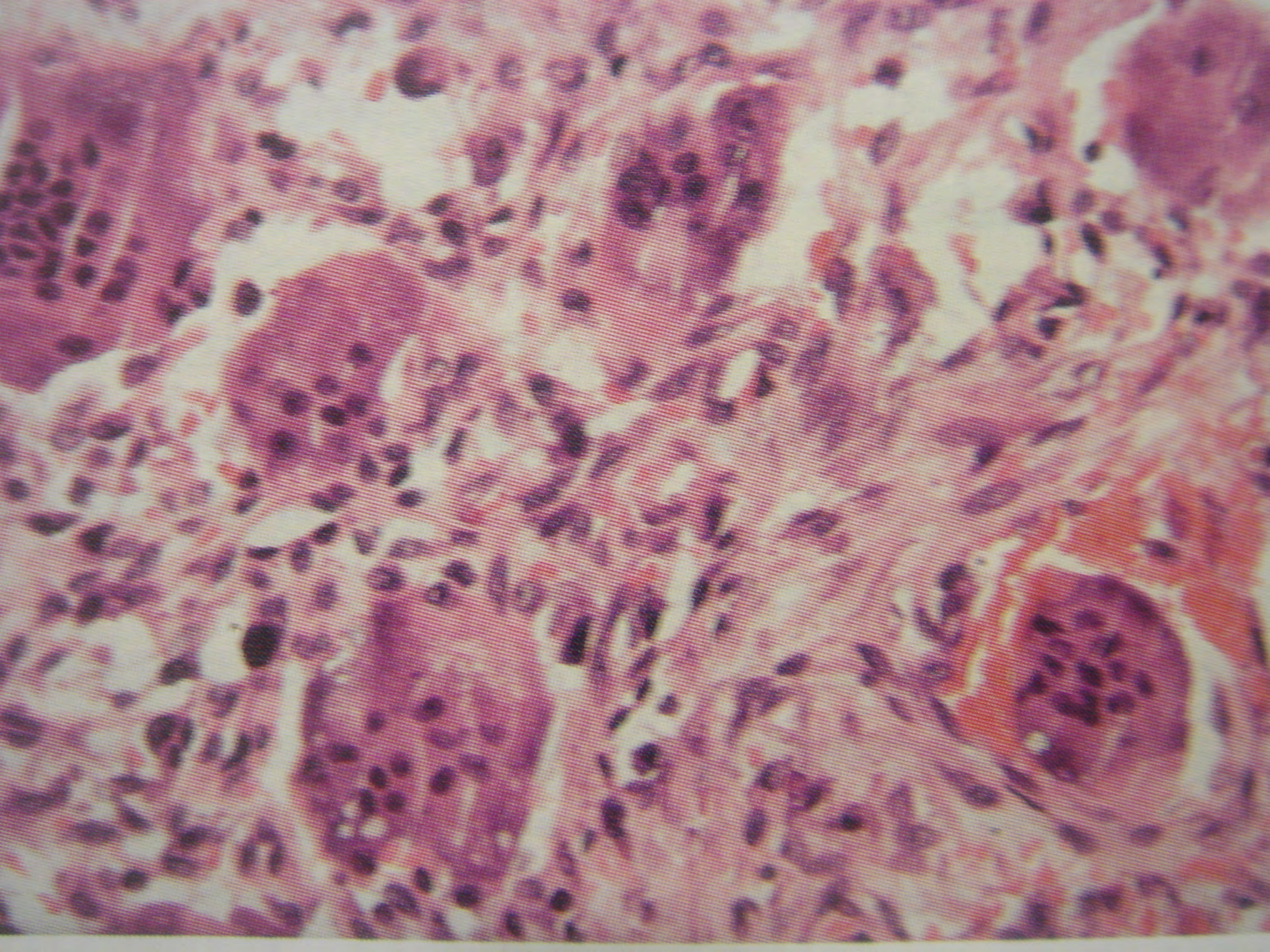
Hyperparathyroidism that results from an abnormality of the parathyroid glands is called **primary hyperparathyroidism**. **Secondary hyperparathyroidism** occurs when calcium is abnormally excreted by the kidneys and the parathyroid glands increase their production of parathyroid hormone to maintain adequate blood levels of calcium. The most common cause of secondary hyperparathyroidism is kidney failure.

Clinical Features

The clinical manifestations of hyperparathyroidism

Oral Manifestations

The oral manifestations of hyperparathyroidism include changes in the bone of the mandible and maxilla. The chief oral manifestation is the appearance of well-defined unilocular or multilocular radiolucencies (**Figure 9-2**, *A*). Microscopically these lesions appear indistinguishable from central giant cell granulomas (described in Chapter 2) (**Figure 9-2**, *B*). There have also been reports of a few cases of peripheral giant cell granulomas associated with hyperparathyroidism. Other radiographic changes that occur in hyperparathyroidism include a generalized mottled appearance of the bone and partial loss of the lamina dura. Loosening of teeth can also occur.



DIABETES MELLITUS

Diabetes mellitus is a chronic disorder of carbohydrate (glucose) metabolism and is characterized by abnormally high blood glucose levels **(hyperglycemia),** which result from a lack of the hormone insulin, defective insulin that does not work effectively to lower blood glucose levels, or increased insulin resistance because of obesity. Diabetes is appropriately considered a syndrome because it has several components, including both acute and chronic complications. This disorder of carbohydrate metabolism also leads to disorders of protein and fat metabolism. Normally, glucose signals the beta cells of the pancreas to make insulin. This hormone is then

Types of Diabetes

Insulin-dependent diabetes mellitus

Two major types of diabetes have been recognized and classified. The first type **(type 1 diabetes)** is called **insulin-dependent diabetes mellitus (IDDM)**. Autoimmunity appears to play a key role in the development of type 1 diabetes, leading to the destruction of the insulin-producing beta cells of the pancreas and, ultimately, profound insulin deficiency. Only 3% to 5% of all diabetic patients have this type of diabetes. IDDM can occur at any age, but its time of onset is usually at a peak age of 20 years. The onset is abrupt and can have the three Ps (or the complications of these signs): (1) **polydipsia** (excessive

Noninsulin-dependent diabetes mellitus

The second type **(type 2 diabetes)** is **noninsulin-dependent diabetes mellitus (NIDDM)**. Increased insulin resistance, rather than profound insulin deficiency, is characteristic of type 2 diabetes. Approximately 95% of all diabetic patients have type 2 diabetes. The onset of this type of diabetes is gradual and usually occurs in patients who are 35 to 40 years of age or older. Obesity is a common finding in many of these individuals. Obesity probably decreases the number of receptors for insulin binding in sensitive tissues, such as fat and muscle, thereby leading to the development of the diabetic state

Oral Complications

The oral complications of diabetes are most severe when blood glucose levels are not controlled. In some patients, control is difficult, even with careful monitoring of these levels and insulin injections. These patients are said to have **brittle diabetes** and may benefit from recent advances with insulin pump therapy.

Increased colonization of the oral mucosa by *Candida albicans* and an increased prevalence of oral candidiasis have been reported in patients with diabetes mellitus, as has mucormycosis, a rare fungal infection that affects the palate and maxillary sinuses.

Xerostomia (dry mouth) is usually associated with uncontrolled diabetes mellitus. Dehydration of the oral tissues can result, increasing the risk of the development of oral candidiasis and dental caries. Altered subgingival flora have been described in diabetes and may be the result of immunologic or salivary changes.

Patients with diabetes mellitus have an accentuated response to plaque. The gingiva can be hyperplastic and erythematous, and acute and fulminating gingival abscesses can occur. Excessive periodontal bone loss, tooth mobility, and early tooth loss can also be associated with diabetes mellitus (**Figure 9-3**). Slow wound healing and increased susceptibil-



ADDISON DISEASE

Addison disease, also known as **primary adrenal cortical insufficiency**, is characterized by an insufficient production of adrenal steroids. A malignant tumor or tuberculosis may be responsible for destruction of the adrenal gland. However, in most cases, the cause of the destruction of the adrenal cortex is unknown. In these patients the condition may be an autoimmune disease.

As a result of the decreased production of adrenal steroids, the pituitary gland increases its

production of adrenocorticotropic hormone (ACTH), which would normally increase the production of adrenal steroids. This hormone is similar to melanin-stimulating hormone and causes stimulation of melanocytes. Brown pigmentation (bronzing) of the skin occurs, and melanotic macules can develop on the oral mucosa. Treatment of Addison disease involves steroid administration (replacement therapy).

volves steroid administration (replacement therapy).

Blood Disorders

The **complete blood count (CBC)** is important in the diagnosis of blood disorders. The CBC is a series of tests that examines the red blood cells, white blood cells, and platelets. It provides information about the number of each type of cell, the ratio of types of cells, and the appearance of the cells. The information included in a CBC and normal values are included in **Table 9-1**.

DISORDERS OF RED BLOOD CELLS AND HEMOGLOBIN

Anemia

Anemia is defined as a reduction in the oxygen-carrying capacity of the blood that in most cases is related to a decrease in the number of circulating red blood cells. There are many different types and causes of anemia.

Nutritional anemias occur when a substance necessary for the normal development of red blood cells is in scant supply in the bone marrow. The most common deficiencies are of iron, folic acid, or vitamin B_{12}.

anemia and include skin and mucosal pallor, angula
cheilitis, erythema and atrophy of the oral mucos
and loss of filiform and fungiform papillae on th
dorsum of the tongue. Circumvallate papillae and fo
liate papillae are not affected.

Iron-Deficiency Anemia

Iron-deficiency anemia occurs when an insufficien
amount of iron is supplied to the bone marrow fo

red blood cell development. This type of anemia can occur as a result of a deficiency of iron intake, blood loss from heavy menstrual bleeding or chronic gastrointestinal bleeding, poor iron absorption, or an increased requirement for iron, as in pregnancy or infancy.

The Plummer-Vinson syndrome can develop as a result of long-standing iron-deficiency anemia. This syndrome includes dysphagia (difficulty swallowing), atrophy of the upper alimentary tract, and a predisposition to the development of oral cancer.

Clinical features and oral manifestations

Iron-deficiency anemia is most often asymptomatic.



Pernicious Anemia

Pernicious anemia is caused by a deficiency of intrinsic factor, a substance secreted by the parietal cells of the stomach. Intrinsic factor is necessary for the absorption of vitamin B_{12}. Normally, vitamin B_{12} is transported across the intestinal mucosa by intrinsic factor. An autoimmune mechanism is the most likely cause of pernicious anemia. Antibodies to components of gastric mucosa have been identified in patients with pernicious anemia. Other causes of pernicious anemia include surgical removal of the stomach (gastrectomy), gastric cancer, or gastritis. Vitamin B_{12} is needed for DNA synthesis; when it is lacking, the de-

A





Thus as in pernicious anemia, the red blood cells are immature, abnormally large, and nucleated (megaloblasts). Treatment involves dietary supplements.

Thalassemia

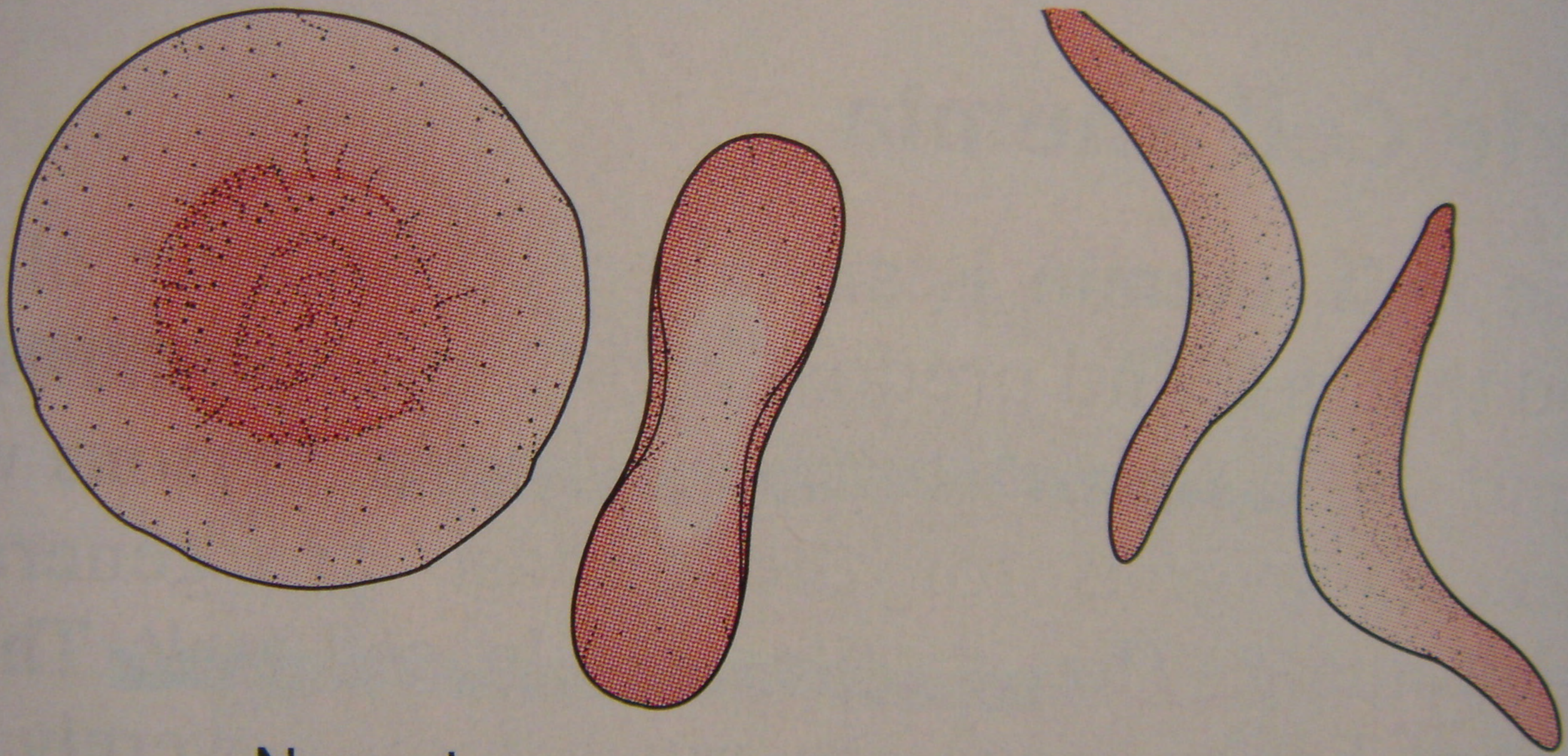
Thalassemia, also called **Mediterranean** or **Cooley anemia**, is the name of a group of inherited disorders of hemoglobin synthesis. It has an autosomal dominant inheritance pattern; therefore no predilection for either sex is seen. The heterozygous form (see Chapter 6), in which only one gene at a locus is involved, is called **thalassemia minor**

Clinical features and oral manifestations

The severe form of the disease begins early in life. The child has a yellowish skin pallor, fever, malaise, and weakness. An enlarged liver and spleen are common. The characteristic facies includes prominent cheekbones, depression of the bridge of the nose, an unusual prominence of the premaxilla, and protrusion or flaring of the maxillary anterior teeth. Intraoral radiographs show a peculiar trabecular pattern of the maxilla and mandible. There is a prominence of some trabeculae and a blurring and disappearance of others, resulting in a "salt and pepper" effect. Thinning of the lamina dura and circular radiolucencies in the alveolar bone have also been described.

Sickle Cell Anemia

Sickle cell anemia is an inherited disorder of the blood that is found predominantly in black individuals and those of Mediterranean origin. Persons who are heterozygous for the disease are generally asymptomatic. This is called **sickle cell trait.** Those that are homozygous are much more severely affected. The disease occurs before age 30 years and is more common in women than in men. Sickle cell anemia occurs as a result of an abnormal type of hemoglobin in red blood cells. Because of this abnormal hemoglobin, the cells develop a sickle shape in the presence of decreased oxygen; hence, the name



gure 9-7 Sickled red blood cells compared with norm
d blood cells.

sickle cell anemia is largely symptomatic and supportive and involves the administration of oxygen and intravenous and oral fluids. Sickle cell anemia can result in profound changes of the heart, such as enlargement, and lead to cardiac failure.

Celiac Sprue

Celiac sprue is a chronic disorder associated with a sensitivity to dietary gluten, a protein found in wheat and wheat products. When gluten is ingested, injury to the intestinal mucosa results. Malabsorption of other nutrients, such as vitamin B_{12} and folic acid, occurs be-

Aplastic Anemia

In **aplastic anemia**, patients experience a dramatic decrease in all the circulating blood cells **(pancytopenia)** because of a severe depression of bone marrow activity. All the blood cells are produced in the marrow **(Figure 9-8)**. The cause of **primary aplastic anemia** is unknown. In **secondary aplastic anemia** the bone marrow failure is a result of a drug or chemical agent. Chemotherapy, radioactive isotopes, radium, or radiant energy have been associated with the development of aplastic anemia. Primary aplastic anemia occurs most frequently in young adults.

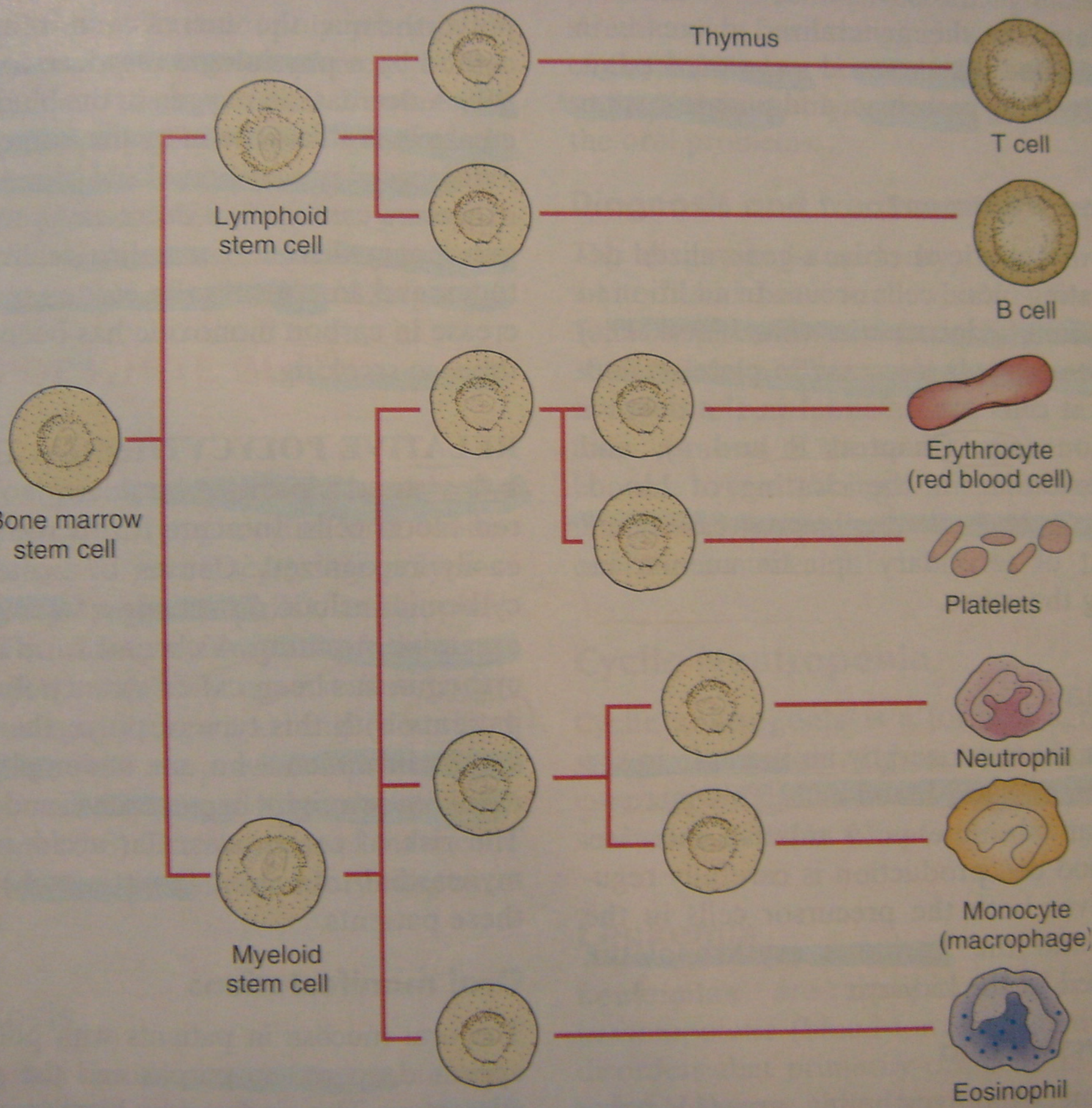


Figure 9-8 Blood cells are derived from stem cells in the bone marrow.

Polycythemia

Polycythemia is characterized by an increase in the number of circulating red blood cells. This increase can be either an absolute or a relative increase. Normal red blood cell production is carefully regulated and involves both the precursor cells in the bone marrow and the hormone erythropoietin, which is produced by the kidney.

Types of polycythemia

The three forms of polycythemia are (1) polycythemia vera (primary polycythemia), (2) secondary polycythemia, and (3) relative polycythemia.

POLYCYTHEMIA VERA (PRIMARY POLYCYTHEMIA). In polycythemia vera, a neoplastic proliferation of bone marrow stem cells results in an abnormally high number of circulating red blood cells. The production of red blood cells is uncontrolled. The cause of this disorder is unknown. It is somewhat more common in men than in women, and the age of onset is usually between 40 and 60 years. It is generally seen in white individuals and is extremely rare in black individuals. The symptoms of polycythemia vera include headache, dizziness, and itching of the skin (pruritus). The increase in red blood cells leads to impaired blood flow, vascular stasis, and poor circulation. The formation of thrombi can cause a disruption of the blood supply to the brain, heart, or peripheral vessels. A decrease in platelets (thrombocytopenia) can occur because of the disruption of the

SECONDARY POLYCYTHEMIA. In secondary polycythemia, the increase in red blood cells is caused by a physiologic response to decreased oxygen. A decrease in oxygen in the blood triggers an increase in erythropoietin by the kidneys, which results in increased production of red blood cells. A number of factors can cause a decrease in oxygen, including pulmonary disease, heart disease, living at high altitudes, and an elevation in carbon monoxide. The increase in carbon monoxide has been associated with tobacco smoking.

tobacco smoking.

RELATIVE POLYCYTHEMIA. This is caused by a decreased plasma volume and not an increase in red blood cells. In acute forms the cause is usually easily recognized. Causes of acute relative polycythemia include diuretic use, vomiting, diarrhea, or excessive sweating. A chronic form of relative polycythemia has been called stress polycythemia. Most patients with this type of polycythemia are middle-aged white men who are under physiologic stress, mildly overweight, hypertensive, and heavy smokers. The risk of cerebrovascular accidents (stroke) and myocardial infarction (heart attack) is increased in these patients.



DISORDERS OF WHITE BLOOD CELLS

Three groups of white blood cells are found in the circulation: granulocytes, lymphocytes, and monocytes. The three types of granulocytes are polymorphonuclear leukocytes (neutrophils), eosinophils, and basophils. The primary function of the neutrophils is to defend the body against foreign invaders, such as bacteria, viruses, and fungi (described in Chapter 4). These cells are produced primarily in the bone marrow and are released into the circulating blood (see Figure 9-8). The response of these cells to infection is known as the **inflammatory response** (see Chapter 2).

Agranulocytosis

In **agranulocytosis** a significant reduction in circulating neutrophils occurs, which has serious consequences. An abnormally low white blood cell count is called **leukopenia.** Any of the white blood cells can be involved, but leukopenia most commonly involves the neutrophils. A reduction in the number of circulating neutrophils is called **neutropenia;** it can be seen in a variety of circumstances and is usually temporary and of little significance.

Agranulocytosis can result from either a problem in the development of neutrophils or a problem in accelerated destruction of neutrophils. Primary and secondary forms of agranulocytosis have been de-

contraindicated.

Cyclic Neutropenia

Cyclic neutropenia is a form of agranulocytosis. A severe depression of granulocytes (neutrophils) occurs at periodic intervals. Cyclic neutropenia is described in detail in Chapter 6.

Leukemia

Leukemias are malignant neoplasms of the hematopoietic (blood-forming) stem cells. They are disorders that primarily originate in the bone marrow. However, the most dramatic feature of

Table 9-2 Classification of Leukemias

Acute Leukemias	Chronic Leukemias
Acute lymphoblastic leukemia (lymphocytes)	Chronic lymphocytic leukemia
Acute nonlymphoblastic leukemia (granulocytes, monocytes, erythrocytes)	Chronic granulocytic (myeloid) leukemia

in chronic forms of leukemia.

Acute leukemias

Acute leukemias are characterized by the presence of very immature cells (blast cells) and by a rapidly fatal course if not treated. Acute leukemias can involve immature lymphocytes (**acute lymphoblastic leukemia**) or immature granulocytes (**acute myeloblastic leukemia**). Acute lymphoblastic leukemia primarily affects children and young adults and has a good prognosis. Acute myeloblastic leukemia involves adolescents and young adults (age range, 15 to 39 years), and the prognosis is not as good. The onset of acute leukemia is sudden and dramatic.



Chronic leukemias

In addition, several different types of chronic leukemias exist. They are all characterized by a slow onset, and they all primarily affect adults. The disease can be present for months before a diagnosis is made, and occasionally the diagnosis is made during a routine physical examination based on laboratory testing. One of the forms of chronic leukemia, **chronic myeloid leukemia**, is associated with a distinctive chromosomal abnormality, the Philadelphia chromosome. Another form of chronic leukemia, **chronic lymphocytic leukemia**, is the most common form and accounts for about one quarter of the total cases of leukemia. It may be asymptomatic for a long time. About half the patients with this type of leukemia have abnormal

BLEEDING DISORDERS

Hemostasis

Patients with bleeding disorders can have one of a number of different defects.

Hemostasis (the cessation of bleeding) is a complex process that involves a number of events **(Figure 9-11)**. When a blood vessel is damaged, marked constriction of the vessel (vasoconstriction) occurs in an attempt to stop the flow of blood. Platelets (thrombocytes) that are produced by the bone marrow and are circulating in blood adhere to the damaged surface and aggregate to form a tem-

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Table 9-3 Factors Involved in Coagulation*

Factor	Name
I	Fibrinogen
II	Prothrombin
III	Tissue factor
IV	Calcium ions
V	Proaccelerin
VII	Proconvertin
VIII	Antihemophilic factor
IX	Plasma thromboplastin
X	Stuart factor
XI	Plasma thromboplastin antecedent
XII	Hageman factor
XIII	Fibrin-stabilizing factor

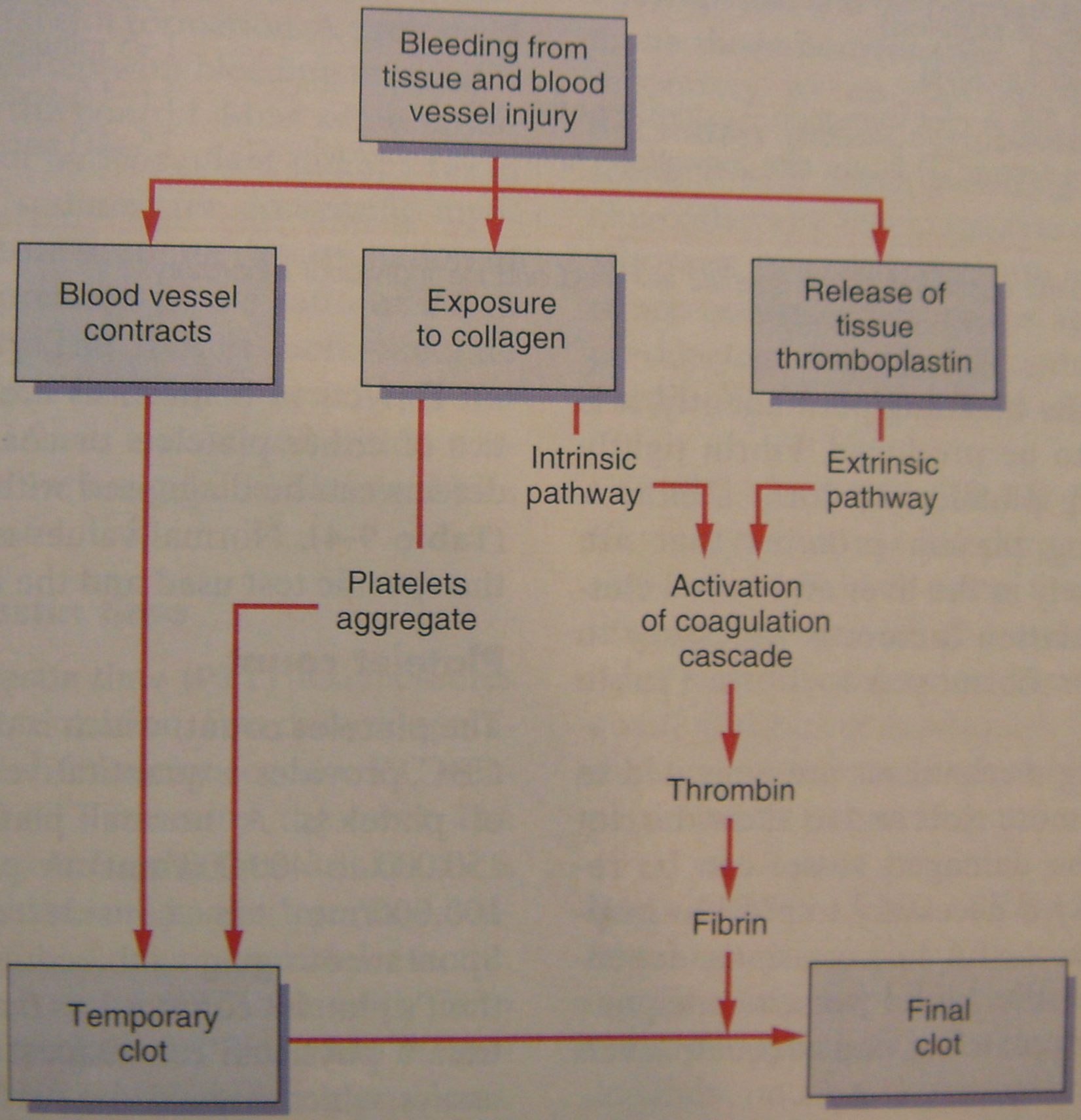


Figure 9-11 Hemostasis.

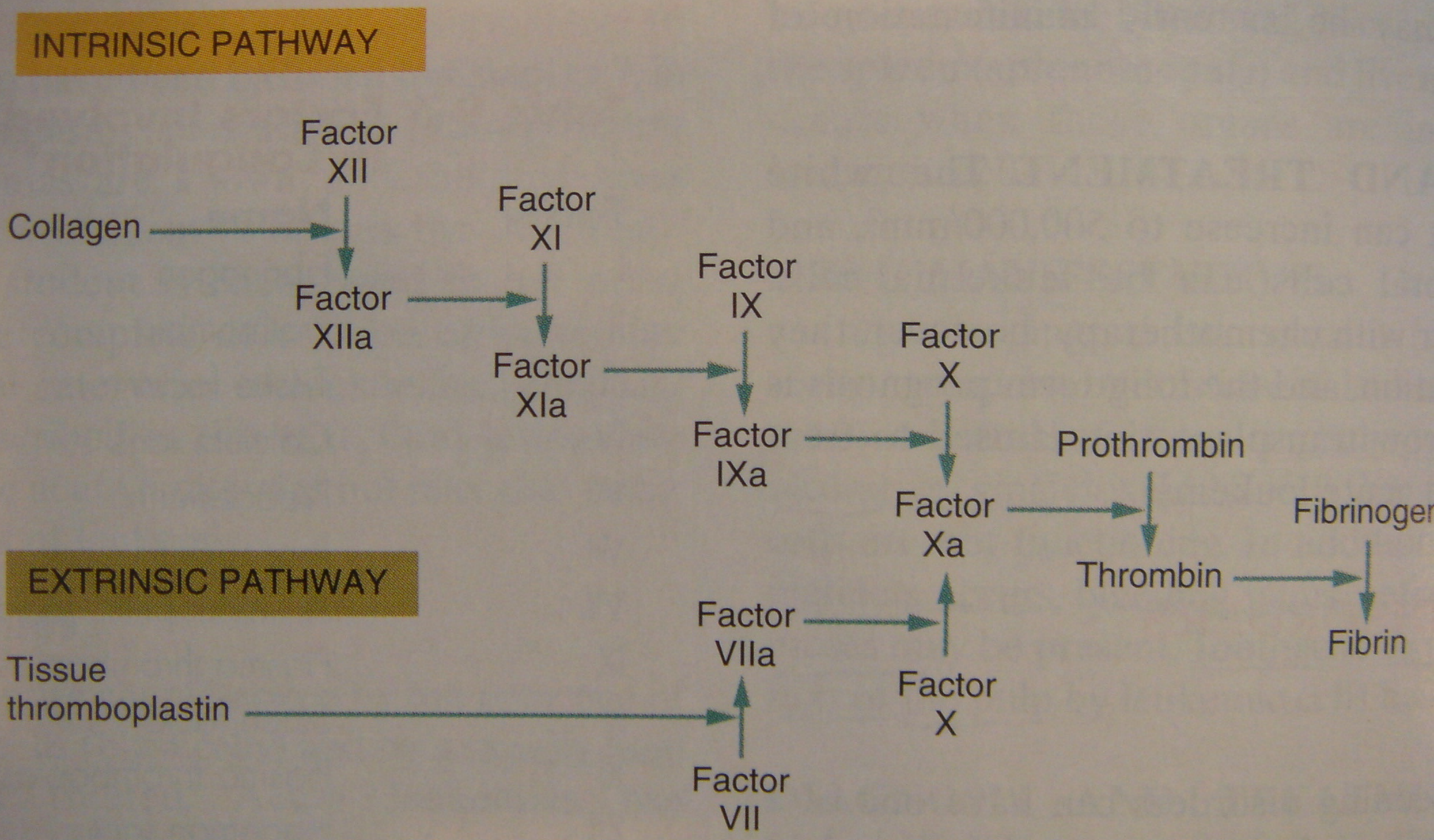


Figure 9-12 Coagulation cascade. Coagulation factors remain inactive until needed. As ea coagulation factor becomes activated (a), it is responsible for the activation of another fac until all have been activated and the final clot is formed. The two pathways by which this c cade is activated are the intrinsic and extrinsic pathways.

Factor
VII

Figure 9-12 Coagulation cascade. Coagulation factors remain inactive until needed. As each coagulation factor becomes activated (a), it is responsible for the activation of another factor until all have been activated and the final clot is formed. The two pathways by which this cascade is activated are the intrinsic and extrinsic pathways.

Table 9-4 Laboratory Tests for Hemostasis

Test	Normal Values
Platelet count (number of platelets)	150,000–400,000/mm³
Bleeding time (platelet function)	1–6 minutes*
Prothrombin time (PT) (fibrin clot formation—extrinsic pathway)	11–16 seconds*
Partial thromboplastin time (PTT) (fibrin clot formation—intrinsic pathway)	25–40 seconds*

**Normal values may differ according to the specific test used and the individual laboratory.*

porary clot. To stop the bleeding permanently, it is necessary for fibrin to be produced. Fibrin tightly binds the aggregating platelets to form a clot. A cascade of circulating plasma proteins that are made almost exclusively in the liver and called **clotting factors** or **coagulation factors** is necessary to convert the precursor fibrinogen to fibrin (**Table 9-3**; **Figure 9-12**).

Defects in hemostasis are caused by abnormalities of either platelets or coagulation factors. These defects can be diagnosed with a few laboratory tests (**Table 9-4**). Normal values may differ according to the specific test used and the individual laboratory.

Platelet count

Purpura

Purpura is a reddish-blue or purplish discoloration of the skin or mucosa that results from spontaneous extravasation of blood. It can be caused by a defect or deficiency in blood platelets or an increase in capillary fragility. A significant oral clinical finding is the oozing of blood at the gingival margins in several sites without the presence of gingivitis or inflammation. Petechiae, ecchymoses, and hemorrhagic blisters can also be present.

Thrombocytopenic purpura

Thrombocytopenic purpura is a bleeding disorder

Thrombocytopenic purpura

Thrombocytopenic purpura is a bleeding disorder that results from a severe reduction in circulating platelets. The normal platelet level is 150,000 to 400,000/mm^3 of blood. Spontaneous bleeding occurs when platelet levels fall to less than 20,000/mm^3. When the cause is unknown, the condition is called **idiopathic thrombocytopenic purpura.** An autoimmune type of process has been identified for thrombocytopenia, and therefore it is sometimes called **immune thrombocytopenia.** The condition can also be secondary to an existing disease or condition. **Secondary thrombocytopenic purpura** is often associated with drugs, including those used for cancer chemotherapy. The idiopathic or primary form is usually seen in young patients, with the greatest incidence occurring before the age of 10 years. No age predilection for the secondary type and no sex predilection for either type is seen.

Nonthrombocytopenic purpura

Nonthrombocytopenic purpuras are bleeding disorders that can result from either a defect in the capillary walls or disorders of platelet function. Vascular wall alterations occur in vitamin C deficiency and infections and can also result from chemicals and allergy. Many factors can cause disorders of platelet function, including drugs, allergy, and autoimmune disease. By far the most common reason for a prolonged bleeding time is the ingestion of drugs that affect platelet function. Ingestion of small doses of aspirin (0.3 to 1.5 g) produces an impairment of platelet function for 7 to 10 days. The nonsteroidal antiinflammatory drugs (e.g., ibuprofen, naproxen, indomethacin) can also adversely affect platelet function. Patients with kidney failure and those with leukemia can have impaired platelet function. **von**

leukemia can have impaired platelet function. **von Willebrand disease** is an autosomal dominantly inherited disorder of platelet function. Both men and women may be affected with this disorder.

ORAL MANIFESTATIONS. The oral manifestations in nonthrombocytopenic purpura are the same as those that occur in thrombocytopenic purpura and include spontaneous gingival bleeding, petechiae, ecchymoses, and hemorrhagic blisters.

DIAGNOSIS AND TREATMENT. The platelet count is normal in nonthrombocytopenic purpura. The bleeding time is prolonged. Treatment includes systemic corticosteroids, splenectomy, and permanent or temporary discontinuation of the causative agent.

Hemophilia

Hemophilia is a disorder of blood coagulation that results in severely prolonged clotting time. The problem results from a deficiency of one of the plasma proteins involved in the coagulation cascade that is necessary for the conversion of fibrinogen to fibrin (see Figure 9-12).

Types of hemophilia

The two most common types of hemophilia are type A and type B. These types of hemophilia are inherited as X-linked diseases and are therefore transmit-

ted through an unaffected carrier daughter to a son. The carrier mother may have a mildly prolonged coagulation time. (Inheritance patterns including sex-linked inheritance, are described in Chapter 6.)

Type A hemophilia is the classic and most common type and is caused by a deficiency of the clotting factor called plasma thromboplastinogen or Factor VIII. This deficiency is characterized by severe hemorrhage after even mild to moderate injury or surgery. Type B, or Christmas disease, is less common. The clotting defect is in **plasma thromboplastin** or **Factor IX**.

Oral manifestations

The oral manifestations of hem-

Immunodeficiency

Immunity is described in Chapter 3. Immunodeficiency can involve the different parts of the immune system either alone or together. Immunodeficiency can involve the cell-mediated (T cell) response or the humoral (B cell or antibody) response. Deficiencies in phagocytosis can also be considered deficiencies in immunity. Immunodeficiency diseases are divided into primary and secondary immunodeficiencies. Primary immunodeficiencies are those of genetic origin, and secondary immunodeficiencies result from some other underlying disorder. The signs and symptoms that occur in a person with immunodeficiency de-

PRIMARY IMMUNODEFICIENCIES

Primary immunodeficiencies are immunodeficiencies of genetic origin and can involve B cells, T cells, or both. These primary immunodeficiencies have provided much information about the functions of the different immunologic responses and are extremely rare.

Three examples are included here. The first is **Bruton disease**, also called **X-linked congenital agammaglobulinemia** (lack of immunoglobulins), which is a disorder in which B cells do not mature. Plasma cells are deficient throughout the body; T cells are normal. Autoimmune diseases are common

cells are normal. Autoimmune diseases are common in these patients.

The second example is **DiGeorge syndrome**, which is also called **thymic hypoplasia**. It is a disorder in which the thymus is deficient or lacking, and therefore T lymphocytes do not mature. Infants and children with this syndrome are extremely susceptible to fungal, viral, and those bacterial infections that require T- and B-cell cooperation. B lymphocytes and immunoglobulins are not affected.

The third example is **severe combined immunodeficiency**. Most infants with this type of immunodeficiency die within the first year of life and are vulnerable to all forms of viral, fungal, and bacterial infections.

odeficiency. Most infants with this type of immunodeficiency die within the first year of life and are vulnerable to all forms of viral, fungal, and bacterial infections.

SECONDARY IMMUNODEFICIENCIES

Secondary immunodeficiencies are those that occur as a result of an underlying disorder. They are much more common than the primary immunodeficiency disorders. Disorders that can have accompanying immunodeficiency include malnutrition, which can lead

Table 9-5 Examples of Drugs That Can C

Name	Use
Azathioprine	Prevention of rejection Treatment of rheumatoi
Cyclosporine	Prevention of rejection
Cyclophosphamide	Cancer chemotherapy
Methotrexate	Cancer chemotherapy
Prednisone	Treatment of autoimmun vulgaris, Behçet's syn

f Drugs That Can Cause Immunosup

Use

Prevention of rejection of renal transplants
Treatment of rheumatoid arthritis
Prevention of rejection of renal transplants
Cancer chemotherapy
Cancer chemotherapy
Treatment of autoimmune diseases (such as rheum
vulgaris, Behçet's syndrome, lupus erythematosu

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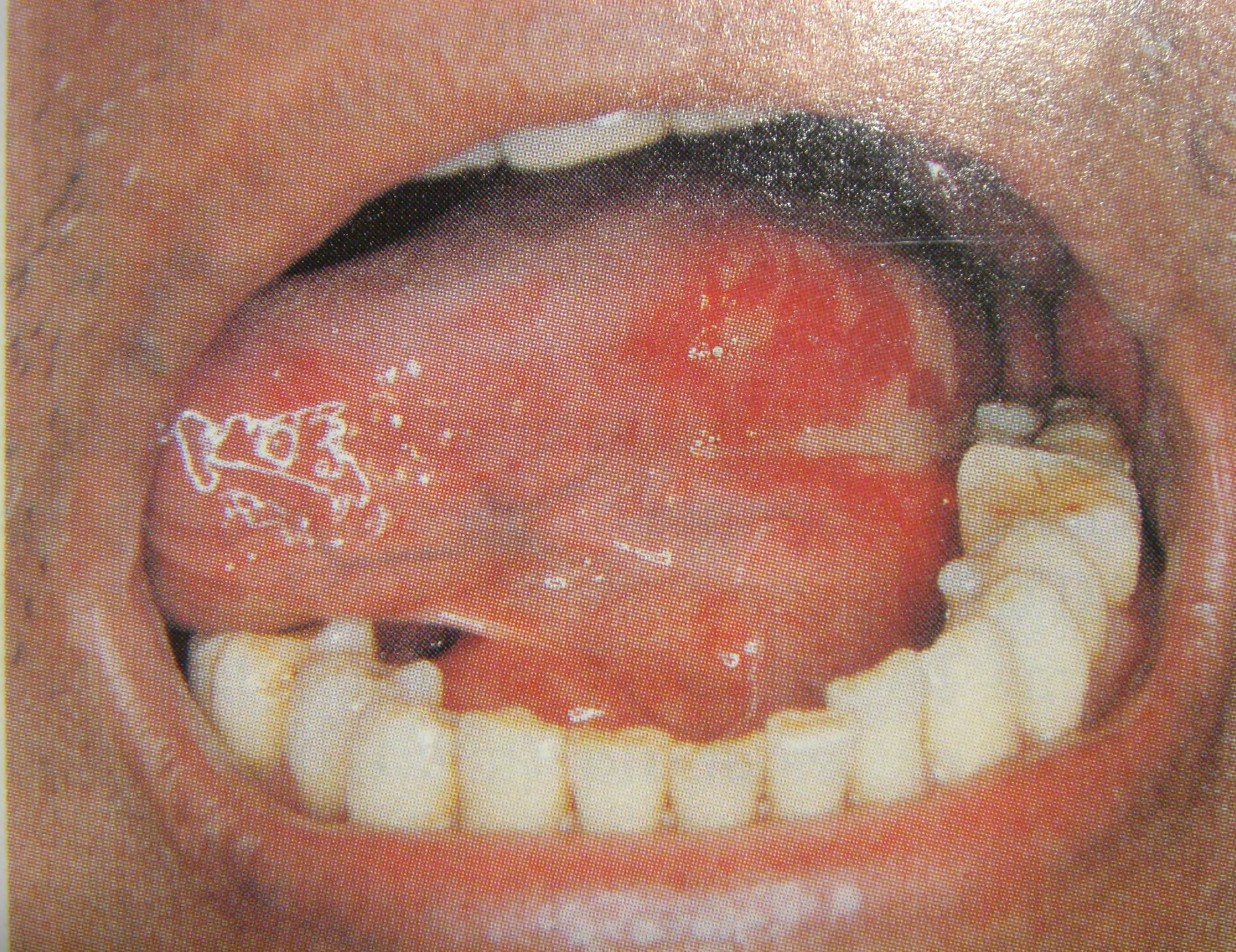
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Oral Manifestations of Therapy for Oral Cancer

Oral cancer can be treated by surgery, radiation therapy, or chemotherapy, or any combination of the three. Radiation therapy and chemotherapy can result in the development of several different oral manifestations.

RADIATION THERAPY

During radiation therapy the patient often experiences mucositis (**Figure 9-13**, *A–C*), which begins about the second week of therapy and subsides a few weeks after its completion. The mucositis is painful and appears as erythematous and ulcerated mucosa. Difficulty in eating, pain on swallowing, and loss of taste can occur as a result of the mucositis. If the



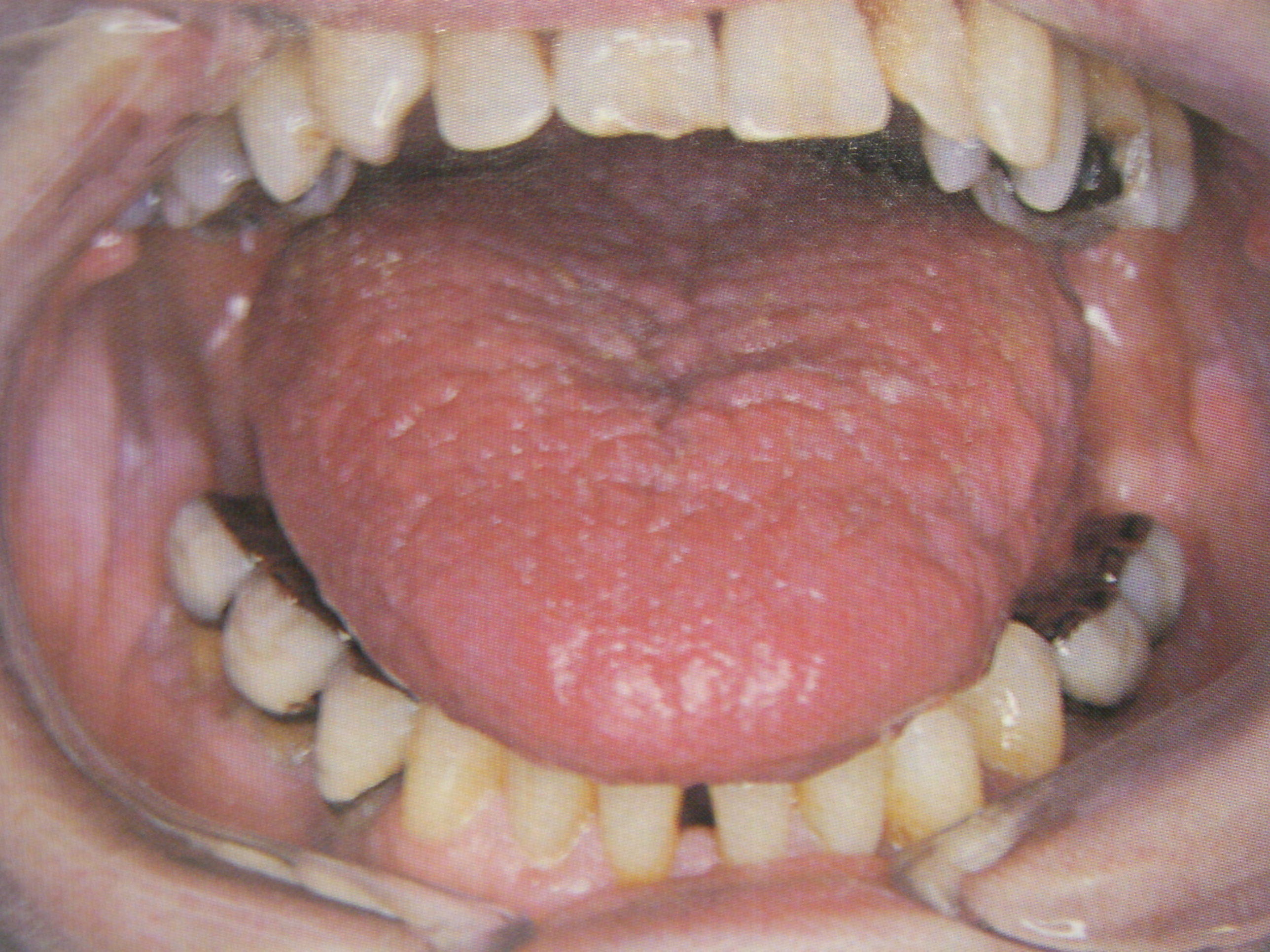






CHEMOTHERAPY

The complications of cancer chemotherapy are predictable and differ for the various types of chemotherapy used. Mucositis and oral ulceration are frequent complications because drugs used for cancer chemotherapy affect rapidly dividing cells and therefore affect the basal cells of the epithelium. The epithelium becomes atrophic and ulcerated with minor irritation. Cells of the bone marrow are also affected, and therefore a decrease in all blood cells (red blood cells, white blood cells, and platelets) can result. The patient can experience anemia because of a decrease in red blood cells, is at increased risk for





Effects of Drugs on the Oral Cavity

Many drugs can cause changes in the oral tissues. Xerostomia can be caused by drugs used to control blood pressure. Antianxiety medications, antipsychotic medications, and antihistamines can also cause xerostomia **(Figure 9-15)**. Drugs such as prednisone that suppress the immune system can increase the risk of candidiasis and other oral infections **(Figure 9-16)**. Antibiotics can also increase the risk of candidiasis. Tetracycline taken when teeth are forming can cause tooth discoloration **(Figure 9-17)**. Phenytoin (Dilantin) and nifedipine (Procardia) can









