# 11 Local and Systemic Manifestations of Cardiovascular Disease

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A good deal of information about cardiovascular diseases can be obtained by the thorough inspection of a patient using only the unaided senses. Inspection is a frequently overlooked aspect of cardiovascular physical diagnosis. This chapter discusses the recognition of the local and systemic manifestations of cardiovascular disease under the following headings: general observations, congenital syndromes, vascular diseases, valvular heart disease, endocrine and metabolic diseases, inflammatory diseases, diseases of connective tissue and joints, pharmacological agents, musculoskeletal diseases, and tumors. Associated cardiovascular findings are placed in brackets.

## GENERAL OBSERVATIONS

The patient's height, weight, degree of alertness, skin, nails, and clothing are initially evaluated *(1)*.

### *Height*

A tall thin patient with an arm span exceeding the height, ectopia lentis, long thin fingers, hyperextensible joints, and high arched palate suggests *Marfan syndrome*. Such patients often have aortic regurgitation, dissecting aneurysm of the aorta, and mitral valve prolapse *(2)* (Fig. 1A,B).

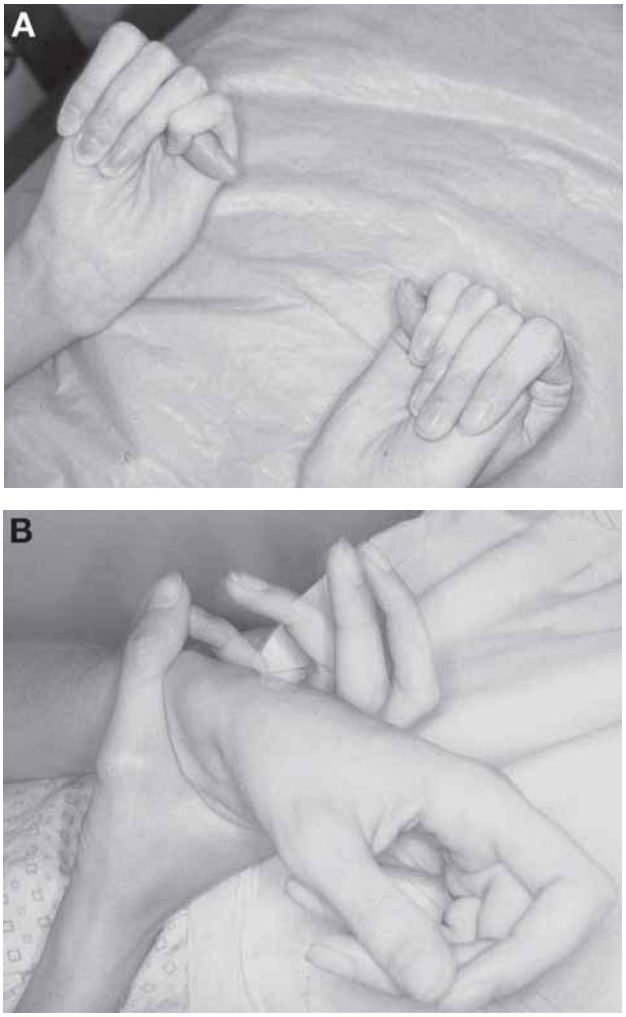



Fig. 1. **(A,B)** Twenty-seven-yr-old female with Marfan syndrome showing arachnodactyly (positive thumb and wrist signs). Her arm span = height = 73 in. She had aortic insufficiency and a dilated aortic root measuring 6 cm in diameter.

The characteristic features of *Turner syndrome* (coarctation of the aorta) are: female patients, <5 ft height with webbing of the neck, widely spaced nipples, and long fourth finger *(3)*.

### *Weight*

Obese patients have a body mass index exceeding 26 kg/m$^2$. Obesity localized to the abdomen (android or central type) has a higher incidence of hypertension and diabetes *(4)*.

A large protuberant abdomen may result from central obesity or ascites. Patients with ascites may have liver disease or less commonly right heart failure *(5)*.

Weight gain or loss can be visually assessed by noting the changing position of the belt buckle markings, how well the clothing fits or whether a wedding ring is too loose or too tight *(1)*.

### *Degree of Alertness*

Patients who fall asleep frequently during an interview may have *sleep apnea syndrome*. Such patients may or may not be obese and may have coexisting polycythemia, cor pulmonale, or systemic hypertension *(6)*.

### *Skin*

Skin color alterations and edema provide useful clues in the detection of underlying cardiovascular disease. Alterations in skin color may be a result of cyanosis, polycythemia, anemia, periodic facial flushing, jaundice, or bronzed pigmentation.

*Cyanosis* is a bluish discoloration of the skin that occurs when there is at least 5 g% of reduced hemoglobin circulating in the capillaries and venules. Cyanosis may be of central, peripheral, or mixed origin.

*Central cyanosis* is often associated with clubbing and polycythemia. It is visually detected when the arterial saturation is less than 80% and is best seen under the tongue *(7)*. Central cyanosis is seen in patients with intracardiac right-to-left shunts (e.g., tetralogy of Fallot, Eisenmenger's syndrome), Pulmonary arteriovenous (A-V) fistula, or intrapulmonary shunts (e.g., chronic obstructive lung disease, pulmonary infarction).

*Differential cyanosis* may occur in persistent ductus arteriosus with right-to left-shunting of blood. The cyanosis may be more pronounced in the legs and left arm than in the right arm and head. Coexisting coarctation of the aorta will aggravate this differential cyanosis *(8,9)*. If transposition of the great vessels coexists with a persistent ductus arteriosus with right-to-left shunting, then cyanosis is more prominent in the upper extremities and head than in the lower extremities *(9a)*.

*Peripheral cyanosis* is seen in low-output states or localized venous obstruction. Thus, it is common in congestive heart failure, Raynaud's disease, or vena caval obstruction. It may be detected in the ears, nailbeds, or the lips. Clubbing and polycythemia are absent *(9)*.

Patients with polycythemia have a ruddy complexion and brick red conjunctiva. Polycythemia is of primary or secondary origin. Secondary polycythemia is seen in patients with arterial hypoxemia because of right-to-left intracardiac shunting or secondary to intrapulmonary shunting (e.g., COPD). There is an increased incidence of myocardial infarction and thrombo-embolism in patients with primary polycythemia *(10)*. Secondary polycythemia is rarely a cause of myocardial infarction *(10a)*.

Anemia is best detected by looking for conjunctival pallor *(11)*. Nailbed and palmar crease pallor are unreliable signs of anemia *(11)*. Anemia may account for a pulmonary flow murmur, *bruit de diable*, venous hum, and high-output failure. Although the cardiac output is almost always raised when the hemoglobin is <6 g% *(12)*, high-output failure may occur at higher levels of hemoglobin concentration in the presence of underlying ventricular dysfunction.

*Periodic flushing* of the skin of the face, neck, and chest is seen in patients with *carcinoid syndrome*. Patients with carcinoid syndrome have a high incidence of tricuspid regurgitation and pulmonic stenosis *(13)*.

Jaundice may be detected as a yellowish tint of the skin, the subglossal mucosa, or sclera and is usually mild in cardiac disease. Jaundice is seen in patients with (1) hepatic congestion because of right heart failure, tricuspid regurgitation, or constrictive pericarditis or (2) hemolysis associated with prosthetic valve dysfunction.

Patients with *hemochromatosis* have iron and melanin deposits in the skin producing a diffuse slate grey or bronzed appearance especially prominent in the face, neck, and distal parts of the extremities. Diabetes and hepatic dysfunction frequently co-exist along with a restrictive or a dilated cardiomyopathy *(14)*.

Multiple *café au lait macules* larger than 1.5 cm in diameter occur in neurofibromatosis. Other skin lesions consist of neurofibromas, axillary, or inguinal freckling. These skin lesions are randomly distributed but appear most commonly over the back and chest. Neurofibromatosis (von Recklinghausen's disease) is associated with hypertension because of renal artery stenosis or pheochromocytoma *(15)*. Cardiac neurofibromas may produce outflow tract obstruction *(16)*.

Bilateral edema of the legs is seen in heart failure, venous insufficiency, venous thrombosis, lymphoedema, hypoalbuminemia, or severe anemia *(17)*. Of the causes of bilateral leg edema, only heart failure is associated with an elevated jugular venous pressure *(17)*. Unilateral leg edema is usually a result of local venous obstruction. Edema of the upper extremity is seen in superior vena cava syndrome, subclavian vein thrombosis, thoracic outlet syndrome, or lymphatic obstruction because of breast cancer *(17,18)*. Edema of the hand may be caused by all the causes mentioned for upper extremity edema as well as local causes such as infection or trauma *(19)*. The shoulder–hand syndrome as a cause of hand edema is rarely seen now.

### *Nails*

The nails are examined for clubbing, subungual hemorrhages, subungual fibromas, and any distinctive color.

Subungual hemorrhages (*splinter hemorrhages*) are seen in endocarditis and usually involve the middle portion of the nail. Subungual hemorrhages may also be seen in trauma, vasculitis, or systemic embolism *(20,21)*.

Subungual fibromas (hands, feet) are a feature of tuberous sclerosis *(22)*.

White nails (*Terry nails*) are in my opinion commonly seen in chronic hepatic congestion resulting from heart failure but may also be seen in liver cirrhosis *(23)*. *Blue–gray nails* are seen in hemochromatosis (cardiomyopathy), Wilson's disease (cardiomyopathy), and ochronosis (aortic or mitral valvular disease) *(24)*. *Black nails* are seen in Cushing's syndrome (hypertension) *(24)*.

Onycholysis (*Plummer's nails*) is seen in hyperthyroidism, but may also occur in trauma, psoriasis, or syphilis *(25)*. A red lunula is associated with heart failure, but is also seen in psoriasis and collagen diseases *(26)*.

### *Gait*

A high steppage gait is seen in muscular dystrophy (cardiomyopathy), whereas sensory ataxia and pes cavus are seen in Friedreich's ataxia (cardiomyopathy).

Tabes dorsalis, a manifestation of tertiary syphilis, is characterized by sensory ataxia, Argyll Robertson pupil, and optic atrophy (aortic regurgitation).

A festinating gait with orthostatic hypotension is seen not only in Parkinson's disease, but also in the Shy–Drager syndrome *(27)*.

## CONGENITAL SYNDROMES/DISEASES

Inspection of the head and/or hands *(8)* is often useful in detecting congenital disorders associated with underlying heart disease. In this section I will mention the Down,

Leopard, Noonan, Williams', Osler–Weber–Rendu, and Holt–Oram syndromes, as well as tuberous sclerosis and cyanotic congenital heart disease. The importance of clubbing will be discussed under the latter heading.

### *Down Syndrome*

Down syndrome occurs in 1 of 1000 newborns and is characterized by a vacant expression on the face, mental retardation, slanting of the palpebral fissures, Brushfield spots, small ears, macroglossia, a simian crease, and a small fifth digit *(28)* (The associated congenital heart defects are A-V canal, ventricular septal defect, and tetralogy of Fallot) *(29)*.

### *LEOPARD Syndrome*

Patients with this syndrome have *Lentigenes* (1- to 5-mm brown macules on back, thorax, and neck), *Electrocardiographic* conduction defects, *Ocular* hypertelorism, *Pulmonic* stenosis (and other cardiovascular system abnormalities such as hypertrophic cardiomyopathy), *Abnormalities of genitalia* (hyopgonadism), *Retardation* of growth, and *Deafness* of sensorineural origin *(30)* (Fig. 2). Patients with LEOPARD syndrome are predisposed to sudden death if there is coexistent hypertrophic cardiomyopathy *(31)*.

### *Noonan Syndrome*

This syndrome consists of hypertelorism, mental retardation, high arched palate, webbing of neck, a simian crease, and cryptorchidism (the associated congenital heart defect is pulmonic stenosis) *(32,33)*.

### *Tuberous Sclerosis*

This entity is inherited as an autosomal dominant trait (1:10,000) and diagnosed by detecting angiofibromata of the lower half of the face (adenoma sebaceum). There is often a history of mental retardation, seizure disorder, and multiple subungual fibromas. These patients often have a rhabdomyoma, which may occasionally obstruct the right ventricular or left ventricular outflow tract *(22)*.

### *Williams' Syndrome*

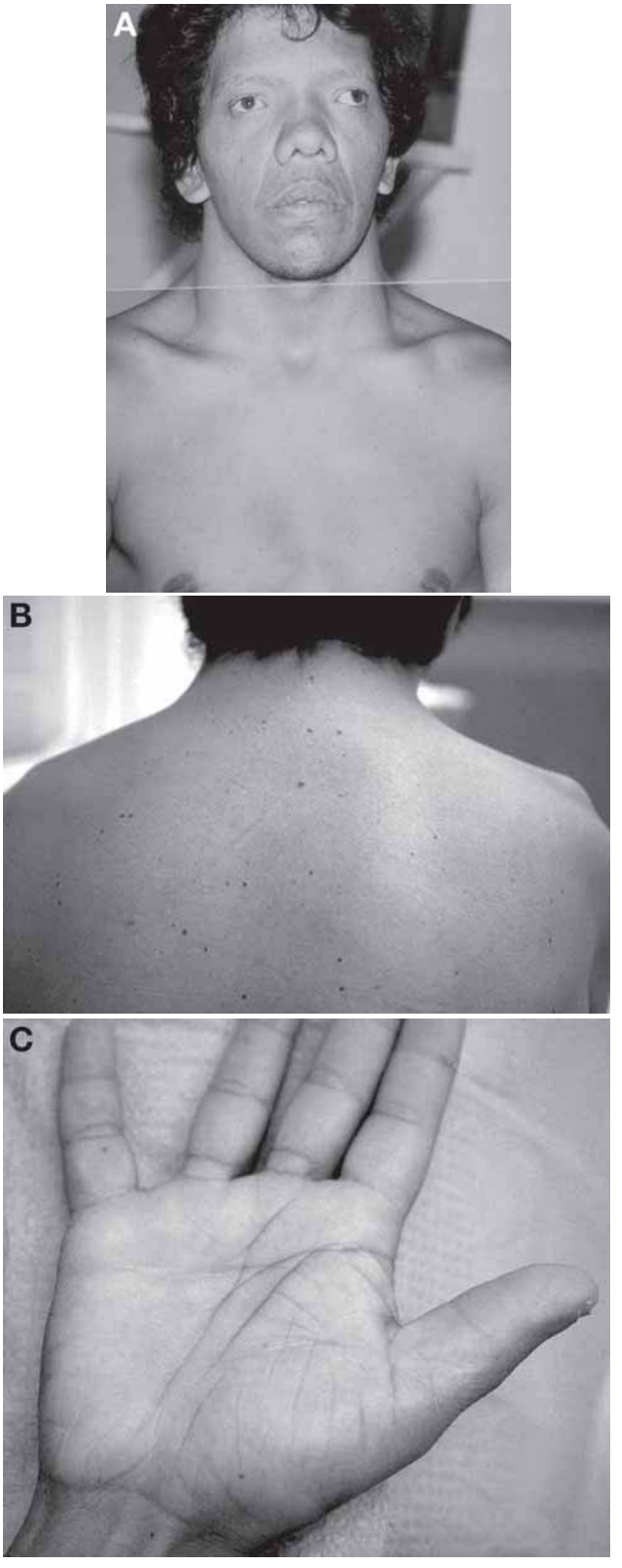
Patients with this syndrome have a large forehead, upturned nose, a long philtrum, an enlarged overhanging upper lip, deformed teeth, puffy cheeks, and a friendly disposition (an elfin-like appearance). The voice is hoarse and has a metallic tone *(34)*. The associated lesion is supravalvular aortic stenosis and patients may occasionally have pulmonary artery branch stenosis *(35)*.

### *Osler–Weber–Rendu Syndrome*

This autosomal dominant entity is characterized by capillary angiomata of the tongue and lips *(36)* (Fig. 3). Epistaxis and gastrointestinal bleeding may also occur (The associated lesion is pulmonary A-V fistula) *(37)*.

### *Holt–Oram Syndrome*

This is an autosomal dominant condition in which patients with a secundum atrial septal defect have various hand abnormalities such as a long first proximal phalanx (fingerized thumb) or a missing thumb or an extra digit *(38)*.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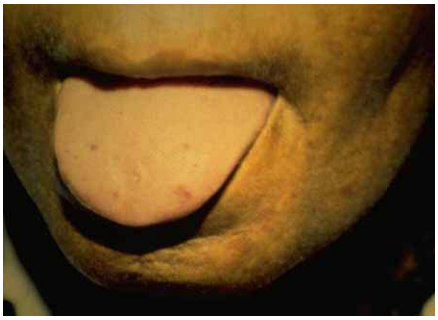

Fig. 3. (Color Plate 5, following p. 270) Osler–Weber–Rendu syndrome. This 44-yr-old female had capillary angiomata on the tongue and telangiectasia of the cheeks. There was no history of epistaxis or gastrointestinal bleeding.

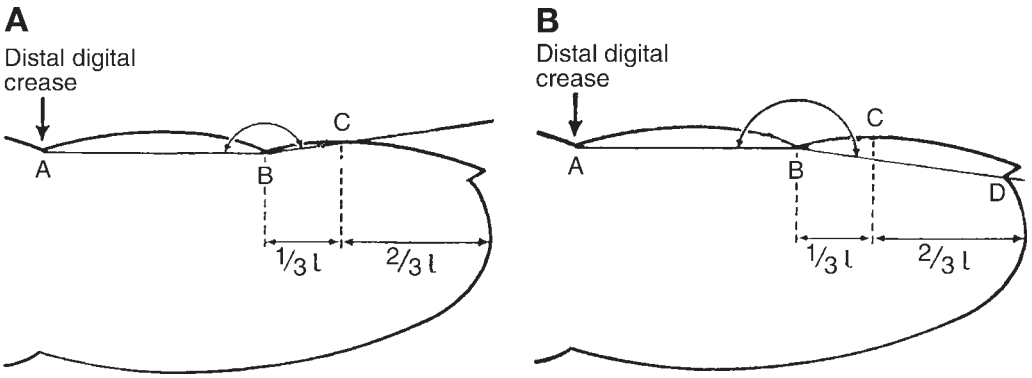


Fig. 4. **(A)** The profile nailbed angle ABC is depicted (normal = 150–170°). **(B)** The hyponychial nailbed angle ABD is seen (normal = 178–192°). (Modified from ref. *40*.)

### *Cyanotic Congenital Heart Disease*

Patients with clubbing, cyanosis, and polycythemia often have cyanotic congenital heart disease (tetralogy of Fallot, tricuspid atresia with right-to-left shunt at atrial level, or Eisenmenger's syndrome).

*Clubbing* is a very important physical finding in the detection of cardiopulmonary disease and needs some discussion as to its detection and usefulness.

The normal angle that the nail plate makes with the adjacent skin fold is 150–170° *(39)* (Fig. 4A) and the hyponychial angle (nail plate to distal nail angle) is 178–192° *(40)* (Fig. 4B). In clubbing, the nail bed angle or profile angle exceeds 180° and the hyponychial angle is increased. Normally there is a window formed between the thumbnails when they are held together and seen in profile. In clubbing, the hyponychial angle is increased and the window between the two pressed-together thumbnails is lost (*Shamroth's clubbing sign*) *(41)*.

Fig. 2. *(Opposite page)* Thirty-five-yr-old Mexican male with features of leopard and Noonan syndromes showing chest wall lentigines, webbing of the neck, hypertelorism **(A,B)**, and a variant of a simian crease **(C)**. He had mental retardation and pulmonary stenosis.

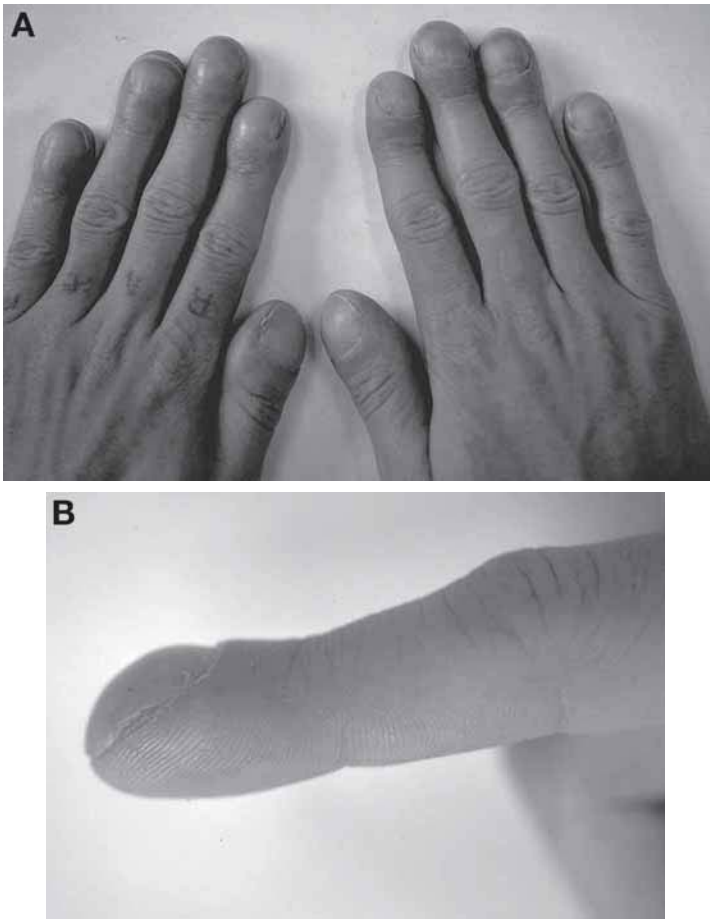


Fig. 5. Tetralogy of Fallot: A 23-yr-old man with polycythemia (hemoglobin 21 g%) and advanced clubbing (hyponychial angle 2108) and cyanosis . The hands show **(A)** subcuticular edema and **(B)** bulbous fingertips. Right ventricular pressure was 135/1; pulmonary artery pressure 13/5. There was a ventricular septal defect with a. pulmonary:systemic blood flow ratio of 0.8.

A useful measure of early clubbing is to determine if the ratio of the distal phalangeal depth to the interphalangeal joint depth in the index finger exceeds 1.0 (normal ratio using a micrometer is 0.9) *(42)*. This distal/interphalangeal ratio may also be visually assessed at the bedside with a "shadowgram" of the finger in profile *(43)*.

Subcuticular edema and ballotability of the nail itself are often present, but may be a late sign of clubbing *(44)*. Clubbing needs to be distinguished from nail beaking. In nail beaking the nail is curved, the hyponychial angle is preserved, and there is loss of pulp tissue *(45)*. Nail beaking is not associated with cardiac disease *(46)*.

Clubbing of the fingers is usually associated with pulmonary disease (80% of cases), with cardiac disease accounting for 10–15% of cases *(47)*. Cardiovascular associations include right-to-left shunts (e.g., tetralogy of Fallot, transposition of the great vessels), infective endocarditis (IE) *(47)* (Fig. 5), myxoma of left atrium *(48)*, and rarely an infected abdominal aortic graft *(49)*.

Unilateral finger clubbing is seen in aortic or subclavian aneurysm or, rarely persistent ductus arteriosus with right-to-left shunting and an absent aortic arch *(50)*.

*Differential clubbing*, in which clubbing is more prominent in the feet than in the hands, occurs in persistent ductus arteriosus when there is a right-to-left shunt or an infected abdominal aortic graft *(49)*.

## VASCULAR DISEASES

### *Coronary Artery Disease*

Coronary artery disease may be suspected if any of the cardiac risk factors are present (hypertension, hyperlipidemia, smoking, diabetes, obesity) or in the presence of a diagonal ear crease sign, prior mediastinal radiation, progeria, polycythemia, Tangier disease, or in a cocaine user.

#### Hypertension

Hypertension may be detected by a funduscopic examination. Hypertensive retinopathy is graded by the *Keith–Wagner–Barker criteria (51)*:

Grade 1: There is generalized narrowing of the arterioles, with the A-V ratio falling to one-third from the normal value of two-thirds.
Grade 2: There is further narrowing of the arterioles with focal areas of spasm.
Grade 3: The arteriolar walls thicken and take on a copper wire appearance. Hemorrhages and exudates appear.
Grade 4: The arterioles thicken further and appear like silver threads. There are pronounced A-V nicking, hemorrhages, and exudates, and papilledema is now seen.

#### Hyperlipidemia

Hyperlipidemia may be suspected if there is arcus corneae or xanthomas are seen. Arcus corneae is a gray-yellow band up to 1.5 mm wide that may surround the rim of the cornea. It occurs with aging, but if seen before the age of 40 in a Caucasian may be a marker of coronary artery disease *(52)*.

*Xanthomas* are seen in hyperlipidemia as follows.

##### Hypercholesterolemia

Eyelid xanthomas (*xanthelasma*) are multiple soft elevated yellow plaques that usually occur near the inner canthi bilaterally. About 50% of patients will have normal lipid levels, and the rest have elevated serum cholesterol (Fredrickson type II) *(53)*.

Tendon xanthomas are yellow papular–nodular lesions found on the dorsum of the feet, the achilles' tendon, or on the extensor tendons over the metacarpals (type II) *(54)*.

##### Hypertriglyceridemia

*Eruptive xanthomas* are discrete yellow papular lesions surrounded by a red base and are most commonly found on the buttocks, back, elbows, and knees (Fig. 6). These lesions may be mistaken for acne. The lesions appear in crops and may coalesce to form plaques. Eruptive xanthomas usually appear when the plasma triglyceride exceeds 1000 mg/dL *(55)*. *Lipemia retinalis* may be detected when the plasma triglycerides are greater than 3000 mg/dL *(56)*. A milky white serum occurs when the plasma triglycerides are greater than 600 mg/dL *(57)*. Eruptive xanthoma may thus be seen in Fredrickson Types I, III, and V.

Fig. 6. (Color Plate 6, following p. 270) Eruptive xanthoma: The skin lesions were seen over the back and chest and resemble acne. Serum triglyceride level was >2000 mg%.

**Dysbetalipoproteinemia (Type III)**

Patients with this disorder have elevated serum cholesterol and triglyceride levels and exhibit characteristic *palmar xanthoma*. Palmar xanthomas consist of yellow infiltrations of the palmar and digital creases of the hand *(58)*.

*Tuberous xanthomas* and eruptive xanthomas may also be seen in dysbetalipoproteinemia *(58)*.Tuberous xanthomas are flat or elevated yellow nodules surrounded by a red margin seen mainly on the knees or elbows.

## Smoking, Obesity and Diabetes

Patients who are smokers may exhibit tobacco-stained fingers, a tobacco odor to the clothing, or cigarette burns on their clothing. Excessive and premature wrinkling (especially "crow's feet" around the eyes) is seen in heavy smokers, but can also be seen in nonsmokers chronically exposed to sunlight *(59)*.

Central obesity with a waist measurement exceeding 35 in. in a woman and 40 in. in a man represents another easily recognizable coronary risk factor *(60)*.

Diabetes may be suspected by detecting vascular changes on funduscopic examination and the presence of small vessel disease in the feet.

## Other conditions with increased risk for Coronary Artery Disease (Myocardial Infarction)

The diagonal *ear crease sign* is said to be a marker for coronary artery disease, but its utility is controversial *(61)*. If seen in patients younger than 40 yr, I believe other coronary artery risk factors should be looked for.

Patients who have received extensive *radiation therapy to the mediastinum* may show atrophy of the paravertebral muscles of the back as well as chronic radiation dermatitis. Such patients have a higher incidence of coronary artery stenosis *(62)*.

*Progeria* is characterized by premature aging, best seen by examining the face. The skin is thin and translucent and lacks wrinkles. There is also alopecia and dwarfism. These patients usually die before the age of 15 of a myocardial infarction *(63)*.

Patients with primary polycythemia have a higher incidence of coronary artery disease *(9)*.

*Tangier disease* (hypoalphalipoproteinemia) is a very rare condition characterized by very low high-density lipoprotein cholesterol and low total cholesterol blood levels *(64)*. Cholesterol esters are deposited on the tonsils, producing a characteristic orange tiger-striped appearance. These patients have premature coronary artery disease *(65,66)* and peripheral neuropathy *(67)*.

*Cocaine use* may be suspected if there is perforation of the nasal septum *(68)*, speckled enamel loss on the buccal surfaces of the teeth *(69)*, skin popping, or venous track sites. Cocaine use is associated with myocardial ischemia or necrosis, hypertension, or endocarditis *(70)*.

*Pseudoxanthoma elasticum* (PXE) is characterized by a network of closely grouped yellow papules (plucked chicken skin appearance). The skin is lax and hangs in folds. PXE occurs in the neck, axilla, abdomen, and thighs *(71)*. There may be associated angioid streaks and retinal hemorrhages. PXE is associated with mitral valve prolapse, hypertension, peripheral vascular disease, and premature coronary artery disease *(72)*, the latter being a common cause of early death *(72)*.

Scars of a median sternotomy, radial artery, or saphenous vein-harvesting sites point to prior coronary artery bypass surgery.

### *Unilateral Internal Carotid Artery Disease*

Internal carotid artery disease may be suspected if the external carotid or unilateral arcus signs are present along with a *Hollenhorst plaque* seen on fundoscopy. Patients with internal carotid artery stenosis have an increase in blood flow in the ipsilateral external carotid artery, so that its superficial temporal artery branch is more prominent than on the nonobstructed side (*Olivarius's external carotid sign*) *(73)*. This is a useful sign, especially if combined with greater prominence of the ipsilateral brow arterial pulse *(73)*.

Unilateral arcus is very rare and suggests internal carotid artery stenosis on the nonarcus side *(74)* provided that ocular hypotony has been excluded *(75)*.

A Hollenhorst plaque is a cholesterol-laden crystal that embolizes to a retinal arteriole usually from an ipsilateral atherosclerotic internal carotid artery or less often from the aorta or cardiac valves *(75)*. These emboli are pale yellow and refractile.

### *Temporal Arteritis*

This occurs in patients over the age of 50 and is characterized by scalp tenderness in the temporal area followed occasionally by scalp necrosis. The superficial temporal artery is tender and pulseless and feels ropy. There may be lingual gangrene and jaw claudication. Polymyalgia rheumatica may coexist. Blindness may occur in #5 mo after the onset of symptoms *(75a)*.

### *Cholesterol Emboli to the Lower Extremities*

These emboli originate from an atherosclerotic descending aorta in which plaques may break off from the aorta either spontaneously, following surgical manipulation of the aorta *(76)* or angiography or associated with the use of anticoagulants *(77)* or fibrinolytic agents *(78)*. Cholesterol emboli may present as *livedo reticularis*, gangrene, or *the purple toe syndrome*. Livedo reticularis is a red pruritic macular eruption resembling the imprint of fine wire mesh on the skin of the legs and especially the feet. The foot pulses are usually present, but often diminished *(79)*. The purple toe syndrome is characterized by multiple bluish-red toes and palpable arterial pulses *(76,79)*.

### *Buerger's Disease (Thromboangiitis Obliterans)*

Buerger's disease is a nonatherosclerotic inflammatory obliterative disease characterized by thrombotic occlusion of the small and medium-sized vessels of the lower extremities and, less commonly, the upper extremities. Gangrene of one or more digits may occur. Buerger's disease has usually been regarded as occurring mostly in males less than 40 yr of age who are heavy smokers. Recent studies *(80)* show that Buerger's disease is now more common in the 40- to 60-yr age group and that the male:female ratio has dropped from 9:1 to 3:1. Thirty percent of patients have an associated superficial thrombophlebitis *(80)*.

### *Raynaud's Phenomenon*

Patients with *Raynaud's phenomenon* have reversible digital artery spasm precipitated by cold or emotional stress. The digits become pallid, then blue, and on rewarming or relief of the emotional stress become hyperemic. It is most commonly associated with collagen vascular disease (scleroderma or disseminated lupus erythematosus), but may also be associated with Buerger's disease, primary pulmonary hypertension, or thoracic outlet syndromes *(81)*.

Patients with scleroderma and Raynaud's phenomenon may show digital ischemia, fingertip necrosis (rat-bite lesions), and even autoamputation *(82)*.

### *Superior Vena Cava Syndrome*

Obstruction of the superior vena cava may be caused by encroachment of the superior vena cava by an intrathoracic tumor *(83)* or an aortic aneurysm *(84)* or thrombosis associated with a transvenous pacemaker *(85)*. Patients may have a ruddy complexion aggravated by recumbency, bluish-red discoloration of the upper chest and neck, edema of the head and neck and upper extremities, neck vein distention, venous stars, and collateral veins on the anterior chest wall. The extent and location of these collateral veins depend on how rapidly the obstruction occurs and whether the obstruction of the superior vena cava occurs above, at, or below the azygos vein *(83)*.

### *Subclavian Vein Thrombosis*

Subclavian vein thrombosis gives rise to a swollen arm, distended veins in the arms, and cyanosis. Because the arm may be painful to move, eliciting *Pemberton's sign* (suffusion of face with arms held above the head) *(86)* is, I believe, impractical.

### *Inferior Vena Cava Syndrome*

Obstruction of the inferior vena cava may occur because of a malignancy or an underlying thrombophlebitis or thrombosis *(87)*. Distended venous collaterals are seen on the lateral aspect of the abdominal wall. There may be bilateral leg edema. Coexistent ascites points to an inferior vena caval obstruction superior to the renal veins *(87)*.

## VALVULAR HEART DISEASE

Only the more advanced forms of valvular heart disease may be visually detected:

1. Tricuspid regurgitation: Tricuspid regurgitation may be suspected on observation if there are ear lobe pulsations, a prominent *v wave* in the jugular venous pulse, as well as hepatic pulsations.

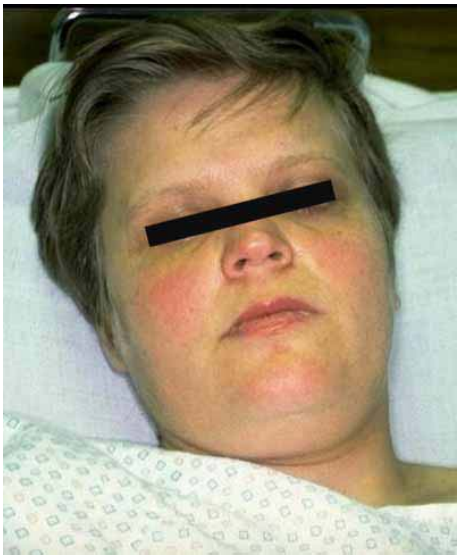

Fig. 7. (Color Plate 7, following p. 270) Mitral facies: 35-yr-old Polish female P1 G6 Ab4 showing a malar flush. She had mitral stenosis and mitral regurgitation.

2. Mitral stenosis: Caucasian patients with mitral stenosis may have venous telangiectasia of the cheeks (malar flush) because of a low-output state and an elevated pulmonary vascular resistance *(88)* (Fig. 7).
3. Aortic regurgitation: A patient may be suspected of having aortic regurgitation if he presents with dyspnea, a head that shakes with each arterial pulsation (*de Musset's sign*), and prominent arterial pulsations in the neck.

## ENDOCRINE AND METABOLIC DISEASES

A careful examination of the face will detect patients with acromegaly, thyroid disease, Cushing's disease, amyloidosis, gout, and ochronosis.

### *Acromegaly*

Acromegaly is detected by looking at the head and the hands. These patients have a lantern jaw, coarsening of the facial features (best determined by comparing old photographs), widely spaced teeth, macroglossia, and spade-shaped hands (Fig. 8) Acromegaly is associated with hypertension of the low-renin type *(89)*. There is an increased incidence of premature coronary atherosclerosis in acromegaly because of coexistent diabetes and hypertension.

### *Hyperthyroidism*

Patients with hyperthyroidism are often detected by looking at the face. There may be lid lag, exophthalmos, ophthalmoplegia, and temporal muscle wasting. Other features include palmar erythema, warm moist palms, fine tremor of the outstretched hands, proximal myopathy, pretibial myxedema, and an enlarged thyroid (Fig. 9). The patient may appear restless and show evidence of weight loss by wearing loose-fitting clothes.

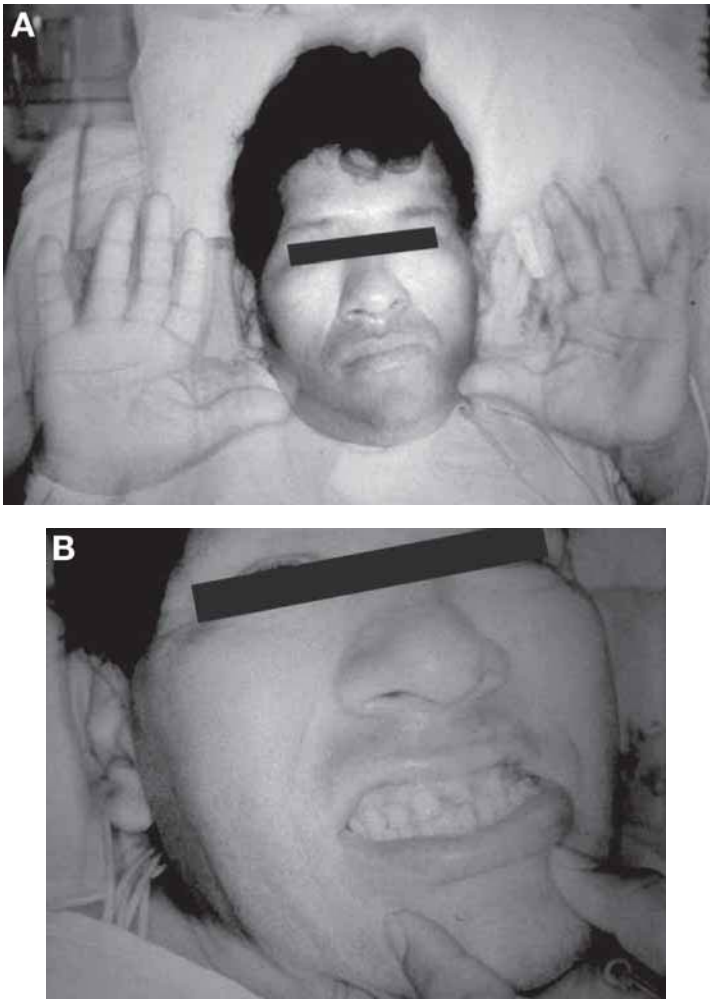


Fig. 8. Acromegaly: 40-yr-old man admitted to the hospital with an acute anterior wall myocardial infarction. He had a lantern jaw, coarse facial features, **(A)** spade-like hands, and **(B)** widely spaced teeth.

Hyperthyroidism may be associated with a high-output failure, atrial fibrillation, or a cardiomyopathy *(90)*. Some elderly patients with hyperthyroidism may not have the above eye or skin changes, but present with heart failure or atrial fibrillation (apathetic hyperthyroidism).

### *Myxedema*

Peri-orbital puffiness, brittle hair, dry skin, slowing of cerebration, low husky voice, macroglossia, and delayed relaxation of heel reflexes are the main clinical features of myxedema (Fig. 10) Thyroid-replacement therapy may lead to a striking improvement of the facies. Myxedema is associated with pericardial effusion, which rarely leads to cardiac tamponade *(91)*.

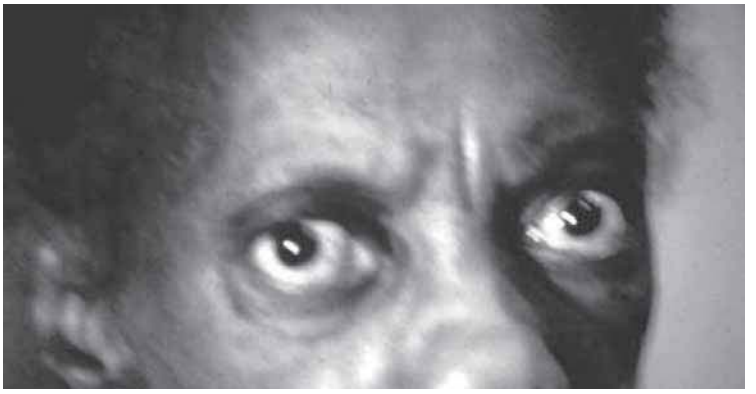

Fig. 9. Hyperthyroidism: 60-yr-old female with lid retraction, exophthalmos, and facial muscle wasting.

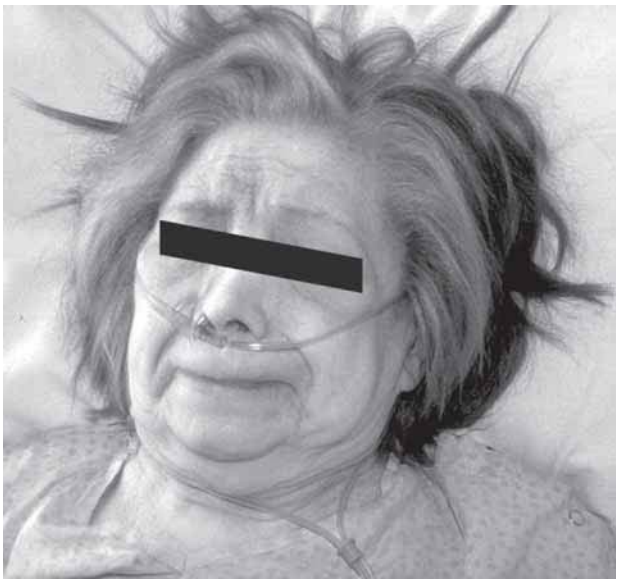

Fig. 10. Myxedema: 80-yr-old female admitted in heart failure. She had stopped taking her thyroid medicine a year before. She has a pasty face, some periorbital puffiness, dry skin, and coarse hair. Thyroid-stimulating hormone level was 100 μU/mL.

### *Cushing's Disease*

Moon facies, buffalo hump, truncal obesity with thin limbs, and red abdominal striae are the usual features of Cushing's disease. It is associated with hypertension in 80% of cases *(92)*.

### *Amyloidosis*

Primary or hereditofamilial amyloidosis may involve the deposition of an amyloid protein consisting of light-chain immunoglobulins in the heart, skin, or tongue *(93)*. Patients with amyloidosis may have waxy yellow translucent papules and plaques on the

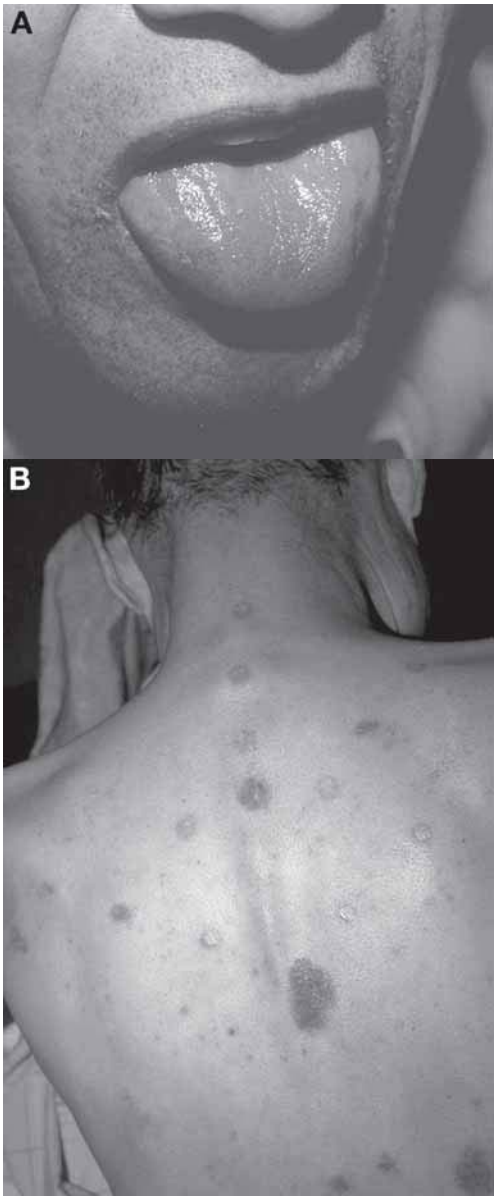


Fig. 11. Amyloidosis: 60-yr-old man with **(A)** large tongue and **(B)** brown maculopapular lesions on the back. He was admitted in heart failure because of a restrictive cardiomyopathy. Echocardiography showed biventricular hypertrophy and a sparkling appearance to the myocardium. He had biopsy-proven amyloidosis.

eyelids, naso-labial folds, and mouth *(94)*. Purpura frequently occurs in these areas after minor trauma *(94)*. The tongue may be diffusely or irregularly enlarged *(94)*. Restrictive cardiomyopathy is often seen in amyloidosis *(93,94)* (Fig. 11).

### *Hemochromatosis*

(*See* General Observations, Skin Color on p. 364.)

### *Gout*

The patient may have gouty tophi (urate deposits) on the ears or the small joints of the hand. Rarely, urate deposits may involve the heart valves or the conducting system, causing complete heart block *(95)*. Patients with gout, via its association with elevated serum uric acid levels, have a higher incidence of hypertension *(96)* and possibly coronary artery disease *(97)*.

### *Alkaptonuria (Ochronosis)*

Alkaptonuria (*Ochronosis*)is a defect in tyrosine metabolism in which homogentisic acid is deposited in the skin, joints, ear, and the mitral and aortic valves. The skin on the ears gradually darkens, and the fingernails show a blue-gray discoloration. Aortic stenosis is the most significant lesion associated with it *(98)*.

## INFLAMMATORY DISEASES

Inflammation may be caused by chemical or physical agents or infections. In this section infective endocarditis (IE), syphilis, and sarcoidosis will be discussed.

### *Infective Endocarditis*

Patients with IE may or may not have evidence of recreational drug use (e.g., skin popping, venous tracks). Systemic manifestations of IE are said to be less frequent now, but are still quite common in poorer patients, who are often late in coming to get medical attention. The fundi may show flame-shaped hemorrhages and Roth spots (microinfarct of the retina). The hand may reveal *Osler nodes* (red subcutaneous nodules 2 mm in size on the tips of the fingers, thenar or hypothenar areas that disappear after a few days) *(99)*. Splinter nailbed hemorrhages may be seen, but can also occur with local trauma, vasculitis, or systemic embolism *(20)*. *Janeway lesions* are painless red macules or nodules seen on the palms or soles of the feet *(100)* (Fig. 12). Clubbing may occur in late cases of IE *(99)*. Petechial hemorrhages are seen in the conjunctiva, palate, buccal mucosa, and extremities *(17)*.

### *Syphilis*

Patients with tertiary syphilis may have a saddle-shaped nose, optic atrophy, Argyll Robertson pupil, and evidence of aortic regurgitation.

### *Sarcoidosis*

Patients with sarcoidosis may have skin and cardiac involvement. The skin lesions that involve the face may take two forms: red papules around the eyes, nose, and mouth, which are pruritic and do not ulcerate; purple plaques that produce a bulbous nose, thickened cheeks, and thickened ears (lupus pernio) *(101)*. There may also be erythema nodosum (red nodules on the legs) *(101)*. Twenty percent of patients with sarcoidosis have cardiovascular findings at autopsy *(102,103)*. Clinical manifestations include congestive heart failure, ventricular tachycardia, complete heart block, or cor pulmonale *(102,103)*.

## DISEASES OF CONNECTIVE TISSUE AND JOINTS

In this section, inherited disorders of the connective tissue (Ehlers–Danlos syndrome, osteogenesis imperfecta, Marfan syndrome, pseudoxanthoma elasticum) and immune-

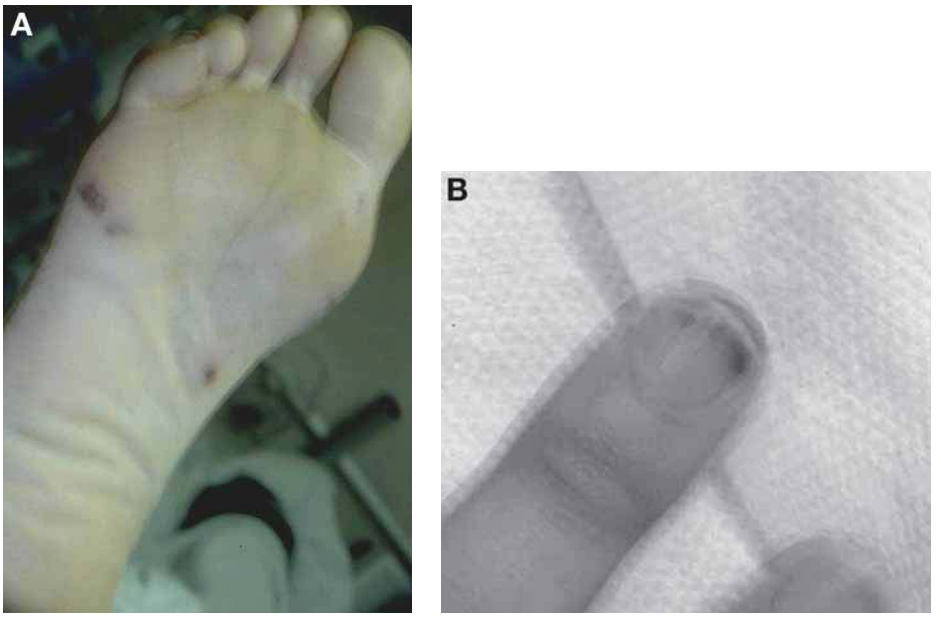


Fig. 12. Infective endocarditis: 50-yr-old drug addict admitted with fever and mitral regurgitation. She had **(A)** Janeway lesions on the soles of her feet (Color Plate 8, following p. 270) and **(B)** subungal hemorrhages. There was vegetation on the mitral valve.

mediated diseases of the connective tissue (systemic lupus erythematosus [SLE], scleroderma, polyarteritis nodosa, rheumatic fever, ankylosing spondylitis, and Reiter's syndrome) are discussed.

### *Ehlers–Danlos Syndrome*

Usually Ehlers–Danlos syndrome is characterized by excessive mobility of joints and a thin stretchable skin. However, in type 4 Ehlers–Danlos syndrome these findings are attenuated and patients have bruises and pigmented scars over the bony prominences. Patients with type 4 Ehlers-Danlos syndrome may have an aortic aneurysm and rupture as well as mitral valve prolapse *(103a)*.

### *Osteogenesis Imperfecta*

Patients with osteogenesis imperfecta have a decrease in bone mass and thus a tendency to have multiple bone fractures on minor trauma. Blue sclera and kyphoscoliosis are seen along with aortic and mitral regurgitations. (*See also* page 384 under section on "Musculoskeletal Diseases").

### *Marfan Syndrome*

(*See* General Observations, Height on p. 361.)

### *Pseudoxanthoma Elasticum*

(*See* Coronary Artery Disease, Pseudoxanthoma Elasticum on p. 371.)

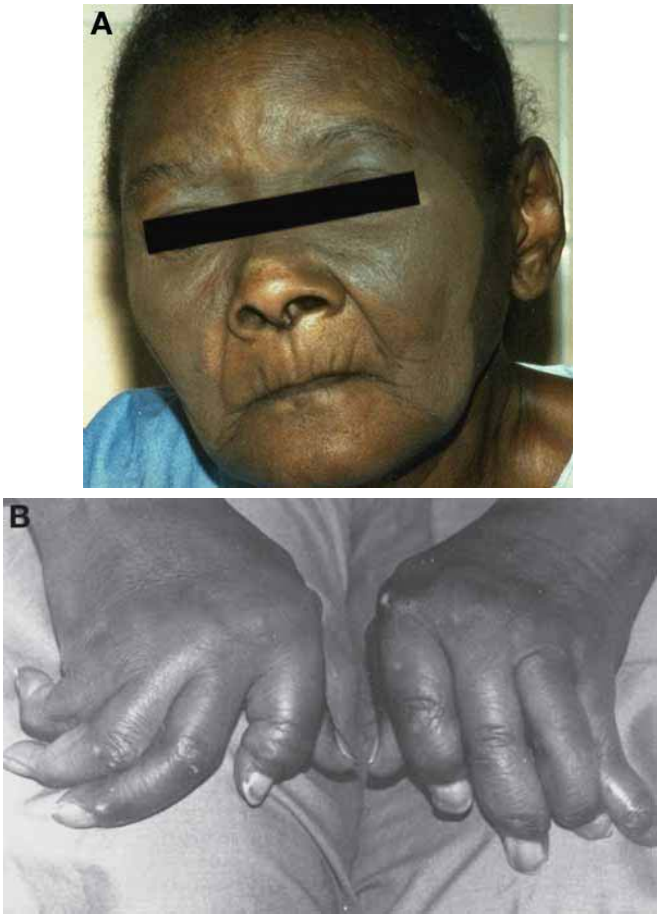


Fig. 13. (Color Plate 9, following p. 270) Mixed connective tissue diseases (lupus, rheumatoid arthritis, scleroderma). **(A)** The patient had a mask facies with puckering of skin around lips and malar depigmentation. **(B)** The patient's hand showed ulnar deviation of the metacarpophalangeal (MP) joints as well as a taut shiny skin.

### *Systemic Lupus Erythematosus SLE*

The diagnosis of SLE may often be made by inspection of the face and the hands. In Caucasians, 10–61% (average 45%) of patients with SLE will have a characteristic malar butterfly skin lesion consisting of a red confluent maculopapular eruption with fine scaling involving the nose and cheeks *(104)*. However, in black patients with SLE there is depigmentation in the malar area. (Fig. 13) The dorsum of the hands may show red plaques or confluent red papules that spare the skin creases of the joints *(105)*. Because vasculitis is a feature of SLE, leg ulcers or livedo reticularis may be seen. Raynaud's phenomenon occurs in 27% of SLE cases *(104)*.

SLE is associated with clinically evident pericarditis in 25% of cases, hypertension in 16%, cardiomyopathy in 10%, symptomatic coronary arteriosclerosis in 10%, pulmonary hypertension in 5%, and ,rarely, aortic or mitral regurgitation or complete A-V block *(106–108)*.

### *Scleroderma*

Patients with scleroderma may initially develop Raynaud's phenomenon and then skin changes involving the face and hands. Facial edema occurs followed by the development of smooth, shiny taut skin, resulting in a loss of facial wrinkling, puckering of the skin around the mouth, and difficulty in opening the mouth wide.

The dorsum of the hands may also show skin tightening and the development of flexion contractures of the inter-phalangeal (I-P) joints (claw hand). Focal areas of skin necrosis may be seen on the fingertips (rat-bite necrosis) *(82)*. Loss of one or more of the distal phalanges may ensue. *Telangiectasia* is frequently seen in the skin of the face and the limbs *(109)*. Patients with scleroderma commonly have pulmonary hypertension, symptomatic pericarditis in 15% of cases *(110)*, and depressed left ventricular function in less than 5% of cases *(111)*.

### *Dermatomyositis*

Patients with dermatomyositis develop a dusky heliotrope eruption in the periorbital areas and may have facial fold erythema *(112)*. Violaceous papules are seen over the knuckles (*Gottron's papules*), which are virtually pathognomonic of dermatomyositis *(113)*. Raynaud's phenomenon and proximal muscle weakness also occur.

Patients with dermatomyositis may develop myocarditis leading to congestive heart failure. Pericarditis and heart block rarely occur *(114)*.

### *Polyarteritis Nodosa*

Polyarteritis nodosa is a necrotizing arteritis involving the small and medium-sized arteries of the body. Visual findings are somewhat limited because skin lesions are seen in only 15% of cases *(115)*. There may be subcutaneous red nodules following the course of a leg artery, which may ulcerate and become necrotic. Livedo reticularis may be seen over the thighs. There is often hypertension and congestive heart failure, and although coronary arteritis occurs in 50% of cases, myocardial infarction is uncommon *(116)*.

### *Rheumatic Fever*

Rheumatic fever remains quite common in developing countries. Boyd described rheumatic fever as a disease that licks the joints and bites the heart. The visible manifestations of rheumatic fever are *erythema marginatum*, subcutaneous nodules, and Jaccoud's syndrome. Erythema marginatum is a pink circular eruption with a pale center and raised red margins usually seen on the trunk, limbs, or axillae. It often precedes carditis and joint involvement. Erythema marginatum may occur in 10–25% of cases of rheumatic fever *(117)*. Subcutaneous nodules are uncommon. They occur around the elbow, knuckles, and spinous processes and usually signify cardiac involvement *(118)*. *Jaccoud's syndrome* is a rare rheumatoid-arthritis-like deformity of the hand following one or more attacks of rheumatic fever *(119)*. Patients with rheumatic fever may develop a pancarditis in the acute stage consisting of (1) valvulitis (mitral regurgitation or occasionally aortic regurgitation), (2) myocarditis and ,rarely, heart block, and (3) pericarditis. Subsequently, mitral stenosis occurs in the established case of rheumatic heart disease.

### *Ankylosing Spondylitis*

Patients with ankylosing spondylitis have limited mobility of the spine (Schober test) *(120)*, which eventually becomes rigid (*bamboo spine*). The mobility of the sacroiliac joint is reduced and chest expansion limited. Aortic regurgitation is seen in 3–10% of cases of longstanding ankylosing spondylitis *(120)*. Complete heart block is very rarely seen *(120)*.

### *Reiter's Syndrome*

The diagnosis of Reiter's syndrome (conjunctivitis, arthritis and urethritis) may also be considered in the presence of keratoderma blenorrhagica, the latter occurring in 60% of cases of Reiter's syndrome *(121)*. Keratoderma blenorrhagica occurs on the soles of the feet or the palms of the hand, mostly in Caucasian males. The skin lesions consist of red macules that become hyperkeratotic waxy papules with a central zone of yellow surrounded by a red halo. The papules coalesce to form plaques with subsequent crusting. Aortic regurgitation may occur in 60% of cases of Reiter's syndrome *(121)*. Complete heart block occurs rarely *(121)*.

## PHARMACOLOGICAL AGENTS

### *Nifedipine*

The side effects of nifedipine include postural hypotension, pedal edema, and gum hyperplasia. Pedal edema may occur with higher doses (>60 mg/d) in 5–10% of cases *(122)*. Gum hyperplasia may occur in 38% of patients who have been on nifedipine for 3 mo or more *(123)*. Patients with poor dental hygiene are more liable to have gum hyperplasia. Dilantin and cyclosporine are other drugs that may give rise to gum hyperplasia *(124)*.

### *Angiotensin-Converting Enzyme Inhibitors*

These drugs produce rapid swelling of the face, tongue, and larynx (angioedema) in 0.2% of cases. It is more common in black patients and may be fatal *(125,126)*.

### *Anticoagulants (Heparin, Coumadin)*

Heparin-induced skin necrosis may be seen in the arms and is attributed to hypersensitivity angiitis *(127)*. Bleeding into the skin or mucous linings is readily detected if the heparin dose is excessive or in the rare instance of heparin-induced thrombocytopenia *(128)* (Fig. 14).

Coumadin may also rarely (0.01%) produce extensive purpuric areas of skin necrosis involving the breasts, thighs, and extremities *(129)*. It is common in middle-aged obese females *(129)*.

Anticoagulants may also give rise to retroperitoneal bleeding and can be detected by seeing bruising of the flanks (*Grey Turner's sign*) (Fig. 15) or around the umbilicus (*Cullen's sign*) *(130)* (Fig. 16). Swelling of the tongue as a result of bleeding may also be seen if a patient is overanticoagulated.

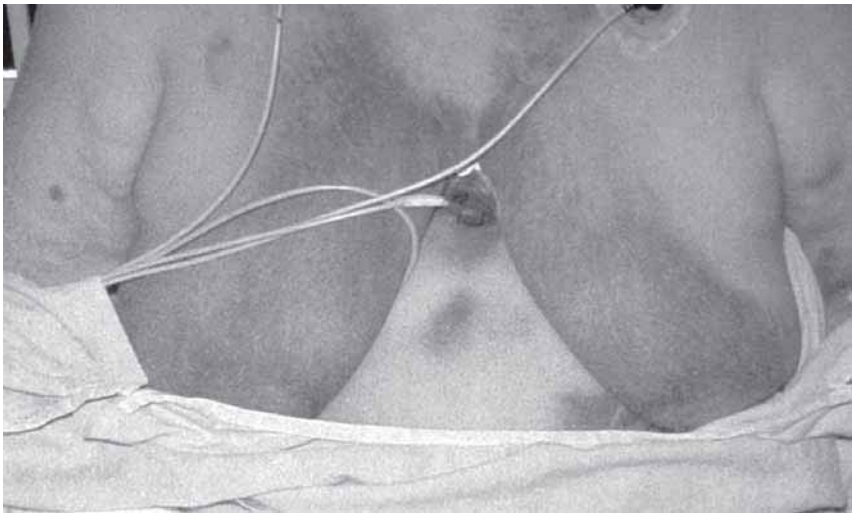

Fig. 14. Heparin-induced thrombocytopenia: 80-yr-old female who developed an extensive area of ecchymosis over the anterior chest wall and severe thrombocytopenia. Four days previously she had received (direct current) DC shock for ventricular tachycardia as well as heparin for an acute myocardial infarction. She had received heparin for a deep vein thrombosis in the past without any ill effects.

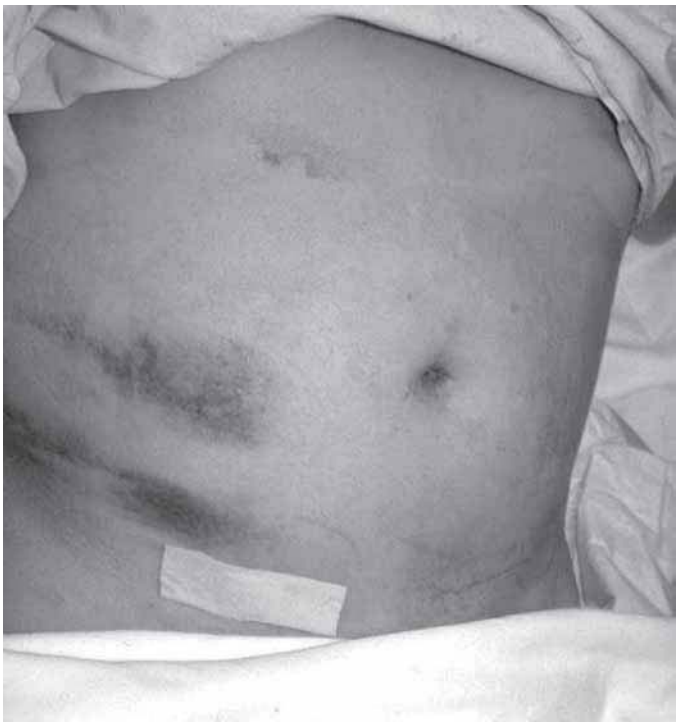

Fig. 15. Grey Turner's sign: 60-yr-old female with retroperitoneal bleeding following the use of heparin. Extensive ecchymoses seen in the right flank.

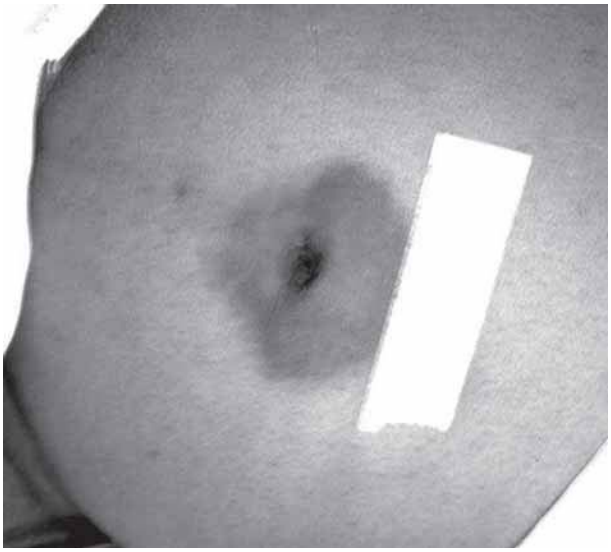

Fig. 16. Cullen's sign. This patient came into the hospital with retroperitoneal bleeding because of coumadin overdose. Ecchymosis is seen around the umbilicus. Prothrombin time was 110 s.

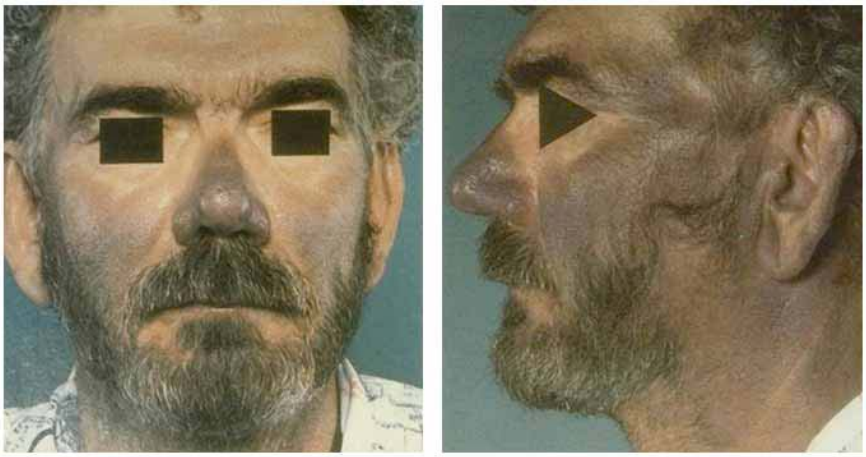

Fig. 17. (Color Plate 10, following p. 270) Amiodarone skin toxicity. There is a blue-gray dermal melanosis of the face, which partially improved 18 mo after amiodarone was stopped. (From ref. *132*.)

### *Amiodarone*

Patients on long-term high-dose amiodarone (600 mg/d for 2 yr) may develop a blue-gray dermal melanosis of the face, especially of the areas exposed to the sun *(131)*. It may take several months for the skin discoloration to resolve after stopping the drug because of its long half-life *(132,133)* (Fig. 17). A lupus-like syndrome has also been reported with amiodarone *(134)*. Hyperthyroidism, hypothyroidism, liver dysfunction, and pulmonary fibrosis are other side effects of amiodarone *(131)*.

### *Procaine Amide*

A lupus-like syndrome may occur with the use of procaine amide, but the butterfly rash is rarely seen *(135)*. Pericarditis may also occasionally be seen *(136)*.

### *Hydralazine*

This drug may also produce a lupus-like syndrome and rarely a pericarditis *(136)*. A malar butterfly rash is more often seen than in procaine-amide-induced lupus *(136)*.

### *Alpha-Methyldopa*

This drug may produce a lupus-like syndrome but without the malar butterfly rash *(135)*.

### *Digitalis, Spironolactone, Estrogens*

Gynecomastia is seen occasionally with these drugs.

### *Recreational Drugs*

Venous tracks or skin-popping sites (Fig. 18A,B) are some of the suggestive findings in a drug abuser. Additional findings in a cocaine abuser are described elsewhere *(68)*, including its association with coronary artery disease and hypertension *(70)*. Venous tracks may be seen in drug users who repeatedly inject heroin intravenously. They are usually found in the forearm or less commonly the neck. Heroin addicts are at risk for IE.

Skin-popping sites are rounded scars, 1–3 cm in diameter, seen on the legs and arms of drug abusers who inject heroin or cocaine subcutaneously. Extensive cellulitis and scarring on the thighs occur with deep and repeated subcutaneous drug injections (Fig. 18C).

## MUSCULOSKELETAL DISEASES

### *Muscular Dystrophies*

Myotonic dystrophy is the most common of the muscular dystrophies. This autosomal dominant disease shows characteristic facial features (a thin narrow face with drooping eyelids, frontal baldness) and muscle weakness of the neck, hands, and extremities. The patient has a high steppage gait and difficulty in grasp relaxation (*myotonia*). Fifty percent of such patients have a cardiomyopathy *(137)* and occasionally complete heart block *(138)*.

*Duchenne dystrophy* is a sex-linked recessive entity seen in boys characterized by proximal muscle weakness, waddling gait, and pseudohypertrophy of the calf muscles. Cardiomyopathy or atrial arrhythmias are often present *(138)*.

The Kearns–Sayre syndrome is characterized by ophthalmoplegia, short stature, and retinitis pigmentosa and is associated with complete heart block and cardiomyopathy *(34)*.

### *Friedreich's Ataxia*

Patients with Friedreich's ataxia are characterized by pes cavus, nystagmus, and sensory ataxia. Cardiomyopathy is seen in more than 50% of cases *(138)*.

### *Osteogenesis Imperfecta*

In this autosomal dominant entity, patients have multiple bone fractures, bowing of the long bones, kyphoscoliosis, pectus excavatum, and blue sclera (from loss of scleral collagen). Aortic or mitral regurgitation may be found in patients with osteogenesis imperfecta *(139,140)*.

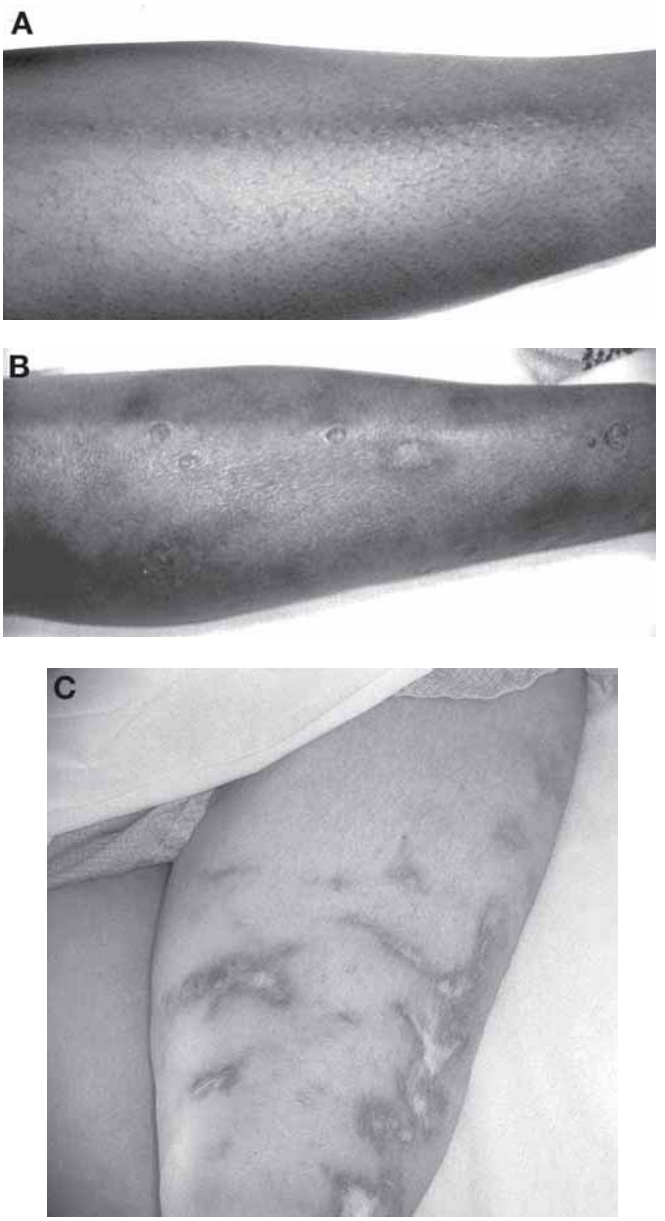


Fig. 18. Signs of drug addiction: **(A)** venous tracks in arm; **(B)** skin-popping sites in leg; **(C)** extensive cellulitis and scarring of thigh because of extensive subcutaneous injections of heroin.

### *Thoracic Cage Deformities*

Thoracic cage deformities may provide a clue to the presence of underlying cardiovascular diseases. A patient with the *straight-back syndrome* (transverse diameter: anteroposterior ratio of >3 and loss of normal kyphosis) may have an innocent pulmonary flow murmur, which may be confused with pulmonic stenosis or an atrial septal defect *(141)*.

A shield chest is a broad chest with widely spaced nipples and an increased angle between manubrium and the body of the sternum. It is seen in *Turner syndrome* (coarctation of aorta) *(3)* and LEOPARD syndrome (pulmonic stenosis) *(30)*.

*Pectus carinatum* (pigeon chest) is associated with Marfan syndrome (aortic regurgitation, dissecting aneurysm) *(2)*.

*Pectus excavatum* is seen in Marfan syndrome *(2)*, Noonan syndrome (pulmonary stenosis) *(32)*, homocysteinuria (coronary artery disease), Ehlers–Danlos syndrome (aortic dissection, spontaneous aortic rupture, and mitral valve prolapse) *(34)*, gargoylism (mitral valve disease, ischemic heart disease, cardiomyopathy) *(34)*, and osteogenesis imperfecta (aortic and mitral regurgitation) *(139)*.

A bamboo spine is seen in ankylosing spondylitis (aortic regurgitation) *(120)*.

Kyphoscoliosis occurs in Friedreich's ataxia (cardiomyopathy) *(138)*, gargoylism *(34)*, neurofibromatosis (hypertension, outflow tract obstruction) *(15)*, and osteogenesis imperfecta *(139)*.

A barrel-shaped chest (transverse/antero-posterior (AP) diameter ratio of 1) is an unreliable sign of chronic obstructive lung disease, because it can also be found in the elderly patients without chronic obstructive lung disease *(142)*.

### *Paget's Disease of Bone*

Patients with *Paget's disease* may have a progressive increase in hat size (because of a thickening skull), a decline in height (because of kyphoscoliosis) as well as saber shins *(143)*. Aortic stenosis *(144)* and left ventricular systolic dysfunction *(145)* occur in moderately severe Paget's disease of bone, whereas high-output failure occurs in patients with more extensive osseous involvement *(145)*.

## TUMORS

Atrial myxomas may be considered in the differential diagnosis of clubbing *(48)*. The LAMB syndrome (Lentigines, Atrial myxoma, Mucocutaneous myxomas, Blue nevi) comprises 7% of all atrial myxomas and consists of lentiginous macules of the face or "freckling," atrial myxoma, mucocutaneous myxomas of the breast and skin, and blue nevi *(146,147)*. Rhabdomyomas are seen in tuberous sclerosis in 66% of cases *(22)*. Neurofibromas of the heart are seen in neurofibromatosis (von Recklinghausen's disease) *(16)*.

## SYNOPSIS

### *Step 1: Detection of the Physical Signs*

**General Observations**

Is the patient excessively tall or short? Body build should be noted. Is the patient alert or somnolent? Are there any abnormalities in the gait? Note the clothing for evidence of weight change or tobacco use.

**Head**

Are there any facial features to suggest a collagen or endocrine disorder such as butterfly eruption or exophthalmos, respectively? A mask-like face may suggest

parkinsonism, scleroderma, or myotonia dystrophica, whereas a vacant expression suggests Down syndrome.

Are the eyes widely spaced apart (hypertelorism)? Do the conjunctiva appear pale or brick red? Are there any xanthelasma, waxy eyelid plaques, or drooping eyelids? Is the sclera discolored (e.g., blue or yellow)? Is there an Argyll Robertson pupil or subluxation of the lens? Is there an arcus corneae (unilateral or bilateral)? Fundi should be checked for hypertension, diabetes, dyslipidemias, or embolic changes because of carotid artery disease or IE.

Is there unilateral temporal artery prominence to suggest ipsilateral carotid disease or temporal arteritis? Skin findings such as malar flush, angiofibromata, slate gray pigmentation because of amiodarone, lupus pernio, facial edema, or premature aging should be noted.

The mouth should be inspected for dental hygiene or enamel erosions, gum hyperplasia, widely spaced teeth, macroglossia, tongue angiomata, or sublingual cyanosis. Are there any tonsillar lesions to suggest Tangier disease? Are there any petechiae on the hard palate? Is the nose saddle-shaped? Do the ears show evidence of gout, alkaptonuria, or a diagonal crease sign?

**Neck**

Is there any webbing of the neck? Is the thyroid enlarged? Are there any surgical scars to suggest carotid or thyroid operations? Is there unilateral or bilateral jugular venous distention? Plucked chicken skin appearance of the neck?

**Chest**

Are there any deformities of the thoracic cage such as kyphoscoliosis, straight-back syndrome, pectus excavatum, shield chest, or bamboo spine? Are there any surgical scars (thoracotomy, pacemaker, intravenous access site, or vascular surgery)? Are the ribs or sternum still intact? Are there any venous collaterals on the chest wall to suggest Superior Vena Cava (SVC) syndrome? Is there gynecomastia?

**Upper Extremity**

The hand should be examined for:

1. Size and shape: acromegaly (spade-like), Marfan syndrome (arachnodactyly), rheumatoid arthritis with an ulnar drift, Ehlers–Danlos syndrome with hyperextensible joints, Holt–Oram syndrome with *fingerized thumb*. Absent digits or deformed digits are also noted. Is there clubbing?
2. Edema: superior vena cava syndrome, thoracic outlet syndrome.
3. Neuromuscular disease: myotonia dystrophica, fine tremor of hyperthyroidism.
4. Color change: nicotine staining, cyanosis of nail beds, Raynaud's phenomenon, Osler's nodes, Janeway lesions, tissue necrosis associated with vasculitis.
5. Nail abnormalities: splinter hemorrhages, Terry nails, red lunula, onycholysis, subungual fibromas.
6. Palmar changes: palmar erythema, simian crease, and yellow palmar creases.
7. Temperature change: warm hands (e.g., hyperthyroidism) or cold hands (e.g., vasculitis, arterial occlusion).

Any xanthomas (elbows, hands). Any surgical scars (brachial artery cutdown, radial artery harvesting site for coronary artery bypass graft)? Any venous tracks from intravenous drug abuse?

**Abdomen**

Is there ascites or central obesity? Is the liver enlarged, tender, or pulsating? Are there prominent venous collaterals because of inferior vena cava (IVC) obstruction? Any signs of red abdominal striae of Cushing's disease; flank or periumbilical ecchymoses?

**Back**

Deformities such as kyphoscoliosis or bamboo spine are noted. The skin lesions of neurofibromatosis or eruptive xanthoma are often seen here. Is any radiation dermatitis associated with paravertebral muscle atrophy noted?

**Lower Extremities**

Skin lesions of erythema marginatum (thighs), erythema nodosum (legs), keratoderma blenorrhagica, or Janeway lesions (soles of feet) are noted. Are skin-popping sites (legs, thighs) seen?

Is there leg swelling (unilateral or bilateral)? Does the swelling pit, or is it firm? Note evidence of pseudohypertrophy of calf muscles and saber shins. Xanthomas of the nodular or tendinous type should be noted. Check for evidence of vascular insufficiency and gangrene of toes.

### *Step 2: Correlation of Physical Signs With a Cardiovascular Entity*

**Congenital Heart Disease**

It is known that certain syndromes are associated with specific congenital cardiac conditions. Thus diagnosis of some of these syndromes from general physical signs would immediately suggest the appropriate specific associated congenital cardiac defect. Syndromes and associated defects are indicated in the following list.

- Holt–Oram syndrome (atrial septal defect)
- Down syndrome (A-V communis, ventricular septal defect, tetralogy of Fallot)
- Turner syndrome (coarctation of the aorta)
- Central cyanosis, polycythemia, and clubbing, pointing to a right-to-left shunt

**Vascular Disease**

Hypertension, hyperlipidemia, smoking, diabetes, and obesity are detectable as coronary artery disease risk factors. Ischemic heart disease may also be suspected in the presence of an ear crease sign, evidence of mediastinal radiation, progeria, polycythemia, PXE, Tangier disease, acromegaly, and in a cocaine addict. Sleep apnea, polyarteritis nodosa, von Recklinghausen's disease, Cushing's syndrome, acromegaly, and gout are associated with hypertension.

Arcus corneae, xanthoma, and lipemia retinalis suggest hyperlipidemia. Hyperlipidemia is seen in acromegaly and myxedema. Olivarius's sign, unilateral arcus corneae, and a Hollenhorst plaque occur in internal carotid artery disease.

Marfan and Ehlers–Danlos syndromes are associated with aortic aneurysms/rupture. Sleep apnea, sarcoidosis, scleroderma, and tricuspid regurgitation are associated with pulmonary hypertension. The Shy–Drager syndrome gives rise to postural hypotension.

Limb ischemia/necrosis may be because of atherosclerosis, cholesterol embolism, Buerger's disease, diabetes, Raynaud's phenomenon, or a collagen disease.

Facial edema, neck vein distention, prominent venous collateral circulation on the chest wall, and venous stars are seen in the superior vena cava syndrome, whereas prominent abdominal venous collateral circulation, leg edema, and possibly ascites point to the inferior vena cava syndrome.

Patients with the Osler–Weber–Rendu syndrome may have pulmonary A-V fistula.

**Infective Endocarditis**

The physical signs are *Roth spots*, retinal hemorrhages, subungual hemorrhages, petechiae involving the conjunctiva or palate, *Osler's nodes*, and *Janeway lesions*. Valvular heart disease may also be present.

**Valvular Heart Disease**

Some syndromes and conditions are specifically associated with certain valvular dysfunctions. Thus detection of these on general physical signs would immediately point the appropriate associated valvular lesion that needs to be considered. They are listed as follows.

- Carcinoid syndrome, pulmonary hypertension (tricuspid regurgitation)
- Carcinoid, LEOPARD, and Noonan syndromes (pulmonic stenosis)
- Osteogenesis imperfecta, PXE, and Marfan syndrome, infective endocarditis (mitral regurgitation)
- PXE, Ehlers–Danlos syndrome, and Marfan syndrome (mitral valve prolapse)
- Marfan, Reiter's, ankylosing spondylitis, tertiary syphilis, infective endocarditis, and osteogenesis imperfecta (aortic regurgitation).
- Ochronosis and Paget disease of bone (aortic stenosis)
- LEOPARD syndrome (hypertrophic cardiomyopathy)
- Williams' syndrome (supravalvular aortic stenosis)

**Heart Failure**

Patients with heart failure may have peripheral cyanosis, edema, neck vein distention, leukonychia, and mild jaundice (hypertension, coronary artery disease, valvular heart disease, myocarditis, cardiomyopathy, or pericardial disease may be the underlying cause). High-output failure is seen in Paget's disease of bone and hyperthyroidism.

**Myocardial and Pericardial Disease**

Myocardial and or pericardial disease will be the cardiac lesion to be considered when physical signs suggest some of the following disorders: hemochromatosis, muscular dystrophy, Friedreich's ataxia, hyperthyroidism, amyloidosis (cardiomyopathy), rheumatic fever, Reiter's syndrome (myocarditis), scleroderma, dermatomyositis, sarcoidosis (pericarditis), and myxedema (pericardial effusion and possibly tamponade).

**Heart Block**

Increased risk of development of delays and blocks in the electrical conduction of the heart may be suggested when general physical signs lead to the detection of

the following disorders: sarcoidosis, gout, rheumatic fever, Reiter's syndrome, SLE, and ankylosing spondylitis.

**Cardiac Tumors**

The presence of cardiac tumors such as atrial myxoma or rhabdomyoma may have to be considered when systemic examination reveals signs of the following: neurofibromatosis (neurofibromas of the heart), tuberous sclerosis (rhabdomyoma), and the *LAMB syndrome* (atrial myxoma).

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