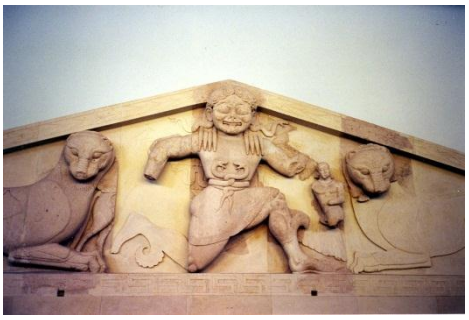
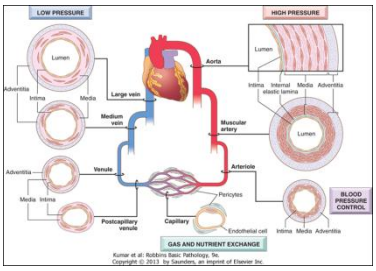
Blood Vessels
Chapter 9 Basic Robbins
Chapter 11 Big Robbins
M. E. Bauman, MD



Structure and Function of Blood Vessels

Intima (figure 9-1)

Internal elastic lamina



Media

External elastic media

Adventitia

Vasa vasorum:

Vascular Organization

Large elastic arteries→small arteries→arterioles→capillaries→postcapillary venules→veins

Pericytes

Lymphatics

Endothelial Cells

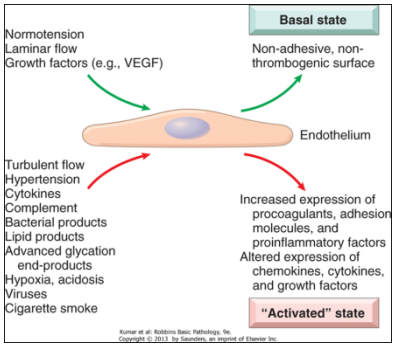
Continuous lining of entire vascular tree

Interendothelial junctions

Fenestrations

Blood-brain barrier

Endothelial activation (figure 9-2)



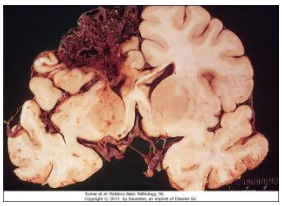
Endothelial dysfunction

Vascular Smooth Muscle Cells

Congenital Anomalies

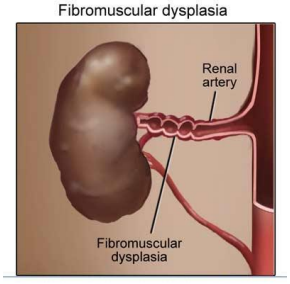
Saccular (berry) aneurysms : see aneurysm section below

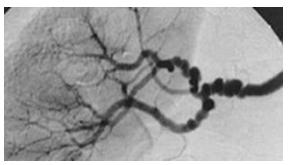
Arteriovenous fistulae (fistulas) (figure 22-11)

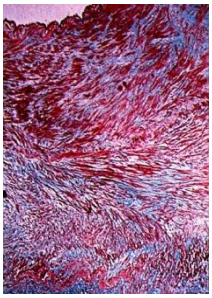


Jill Bolte Taylor: My Stroke of Insight

Fibromuscular dysplasia (Figures not in book)

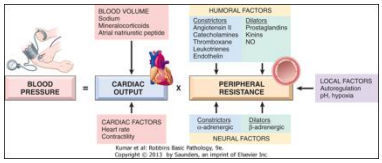






Blood Pressure Regulation

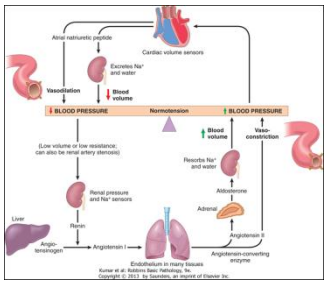
BP = Cardiac Output X Peripheral Resistance (figure 9-3)



Angiotensinogen —Renin→ Angiotensin I —ACE→ Angiotensin II

Vasodilators

Adrenal aldosterone



Atrial natriuretic peptides (figure 9-4)

Hypertensive Vascular Disease

<u>Epidemiology of Hypertension</u>
"140/90 mm Hg"

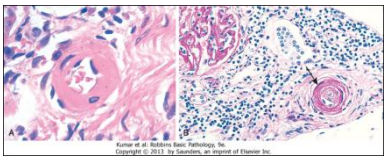
Morbidity increases with other cardiovascular risk factors

"Malignant hypertension"

"Essential hypertension"

Mechanisms

Morphology (figure 9-5)



Hyaline arteriolosclerosis

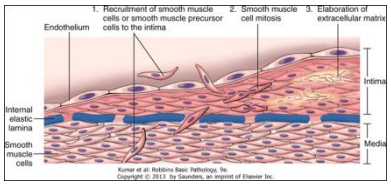
Nephrosclerosis

Hyperplastic arteriolosclerosis

Vascular Wall Response to Injury

Etiologies of vascular injury

Responses to vascular injury (figure 9-6)

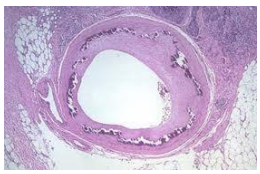


Stenosis =

Arteriosclerosis

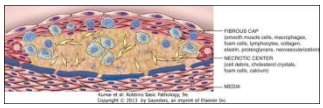
Arteriolosclerosis (see above)

Mönckeberg medial sclerosis (figure not in book)

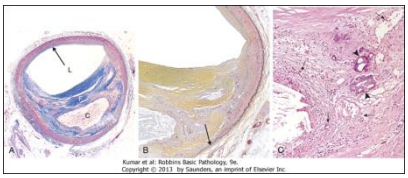


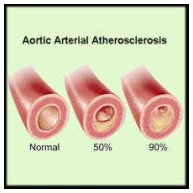
Atherosclerosis

Atherosclerosis =



Atheroma/ Atheromatous plaque (figures 9-7 and 9-13)





Epidemiology of Atherosclerosis
Framingham Heart Study

Constitutional Risk Factors

Genetics: family history is the most important independent risk factor for atherosclerosis

Age:

Gender:

Modifiable Risk Factors

Hyperlipidemia/Hypercholesterolemia

LDL

HDL

Diet

Omega-3 fatty acids

Exercise/EtOH

Statins: inhibit hydroxymethylglutaryl coenzyme A (HMG-CoA)

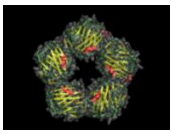
Hypertension

Cigarette smoking

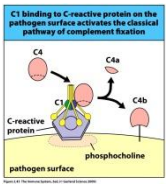
Diabetes mellitus

Additional Risk Factors

C-Reactive Protein (CRP figure from Protein Data Bank)



Wikipedia: The physiological role of CRP is to bind to phosphocholine expressed on the surface of dead or dying cells (and some types of bacteria) in order to activate the complement system. CRP binds to phosphocholine on microbes and damaged cells and enhances phagocytosis by macrophages. Thus, CRP participates in the clearance of necrotic and apoptotic cells.



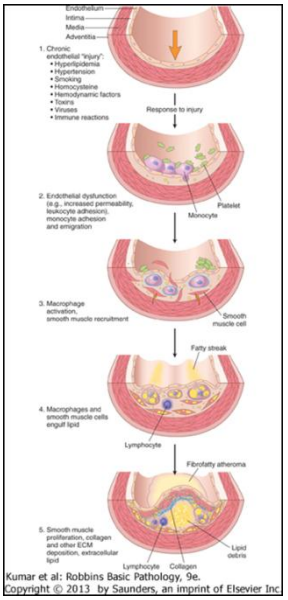
CRP serum test (< 8.0 mg/L)
hsCRP serum test (detects to 0.2 mg/L)

Hyperhomocysteinemia

Homocysteine: an amino acid homologue of cysteine (homocysteine has an additional methylene –CH2- group)

Doubtful utility for assessment of cardiovascular risk

Pathogenesis of atherogenesis: Response to injury hypothesis (Figure 9-10)



Endothelial injury

Endothelial dysfunction

VCAM-1

Macrophage activation, smooth muscle recruitment

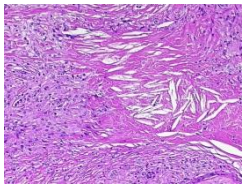
Lipid engulfment

Atheroma: Smooth muscle cells, macrophages, T cells, collagen deposition, extracellular matrix, and intracellular and extracellular lipids.

Foam cells

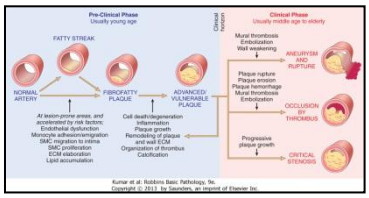
Cholesterol clefts (figure not in text)

Neovascularization



<u>Clinical Consequences of Atherosclerotic Disease</u>

Critical stenosis (Figure 9-14)



Stable angina

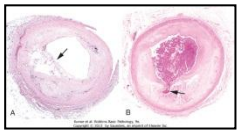
Bowel ischemia

Claudication

Ischemic encephalopathy

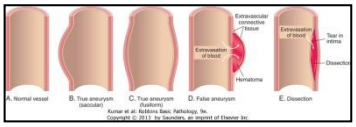
Acute plaque change (Figure 9-16)

Ulceration →

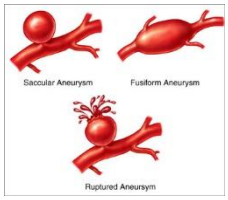


Aneurysms and Dissections

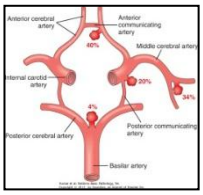
True aneurysm (Figures 9-17, 22-9 and others)



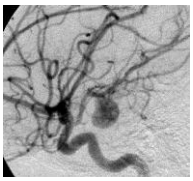
Saccular (berry)



Fusiform



Pseudoaneurysm

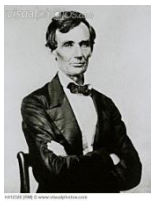


Dissection (see below)

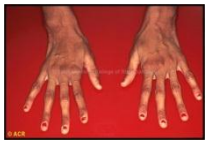
Pathogenesis

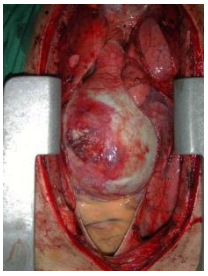
Abnormal connective tissue synthesis/ Cystic medial degeneration

Marfan syndrome

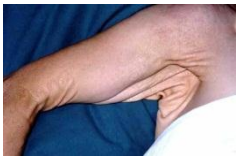


Arachnodactyly





Ehlers-Danlos syndrome



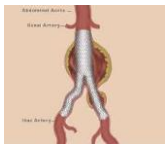
Atherosclerosis

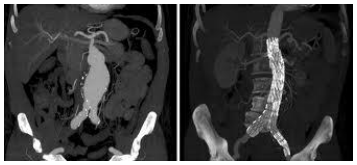
Hypertension

Mycotic aneurysm

Obliterative endarteritis

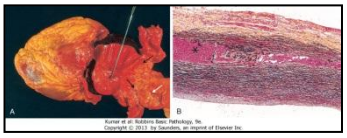
Abdominal aortic aneurysm (AAA) and thoracic aortic aneurysm

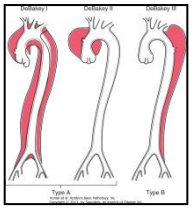




http://www.youtube.com/watch?v=qUpXJBoAoWI&feature=related

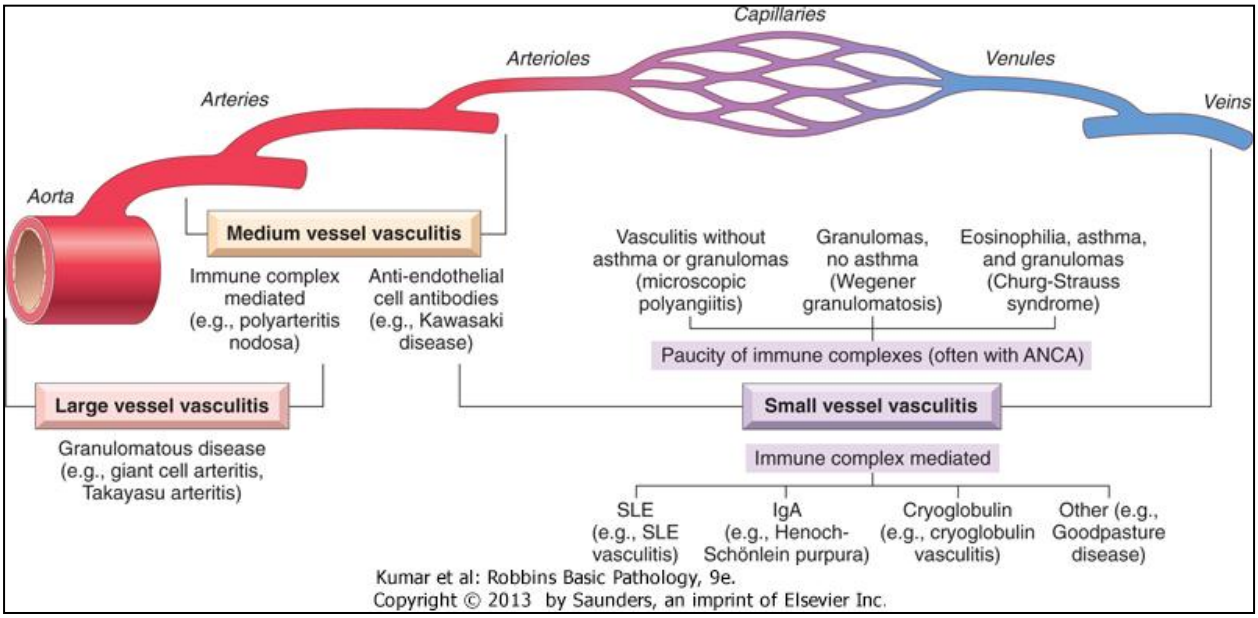
Aortic Dissection (Figure 9-20)





Vasculitis

Figure 9-22



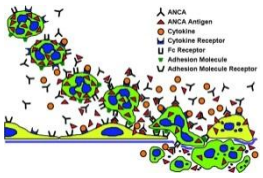
Immune-mediated *vis-a-vis* infectious vasculitis

<u>Immune-Mediated (non-infectious) Vasculitides</u>

Immune Complex-Associated Vasculitis

Drug hypersensitivity

Anti-Neutrophil Cytoplasmic Antibodies (ANCA)
(Figure from **Jennette J C et al. JASN 2006;17:1235-1242)**



Antiproteinase-3 (PR3-ANCA, c-ANCA)

Association

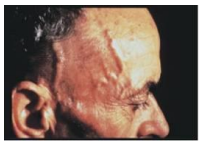
Anti-myeloperoxidase (MPO-ANCA, p-ANCA)

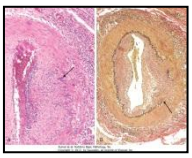
Association

Anti-Endothelial Cell Antibodies

Association

Giant Cell (Temporal) Arteritis (Figure 9-23; other figures not in text)





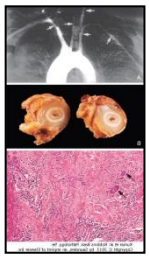
Age

Site:

Histology

Clinical features

Takayasu Arteritis (pulseless disease) (Figure 9-24)

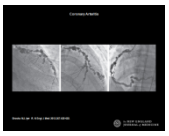


Age

Site

Histology

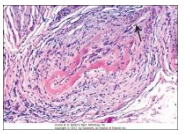
Clinical features



Polyarteritis nodosa (PAN)

Age

Site

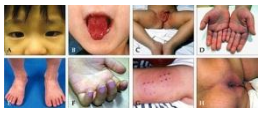


Histology

Clinical features

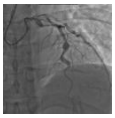
Hepatitis B infection

Kawasaki Disease (Mucocutaneous lymph node syndrome) (Figures from Wikipedia)



Age

Site

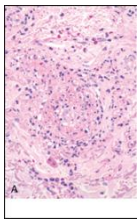


Histology

Clinical features

Microscopic Polyangiitis (Hypersensitivity/leukocytoclastic Vasculitis) (Figure 9-26A)

Site



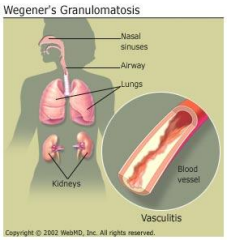
Histology

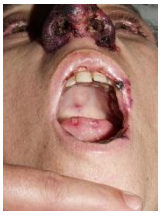
Clinical features

Wegener Granulomatosis

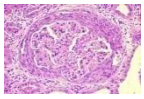
Age

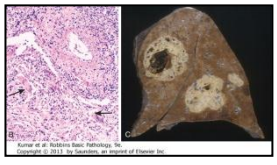
Site





Histology



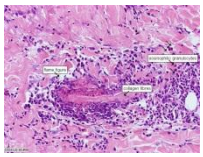


Clinical features

Churg-Strauss Syndrome (Allergic granulomatosis and angiitis)

Site

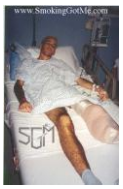
Histology



Clinical features

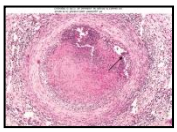
Thromboangiitis Obliterans (Buerger Disease) (Figure 9-27. Other figures not in text)

Age



Histology

Clinical features



Bauman's Synopsis of Immune-mediated Vasculitides

Anti-Neutrophil Cytoplasmic Antibodies (ANCA)

- Anti-proteinase-3 [c-ANCA] (Wegener granulomatosis)
- Anti-myeloperoxidase [p-ANCA] (Microscopic Polyangiitis and Churg-Strauss)
- Anti-endothelial (Kawasaki disease)

<u>Large vessel</u> vasculitis

- Giant Cell Temporal Arteritis: Granulomatous inflammation. Headache, blindness
- Takayasu Arteritis: Mononuclear inflammation. Pulseless disease. Aortic arch

<u>Medium size</u> vessel vasculitis

- Polyarteritis nodosa: Fibrinoid necrosis. Hepatitis B infection.
- Kawasaki Disease: Fibrinoid necrosis. Mucocutaneous lymph node syndrome. Children. Coronary artery aneurysms

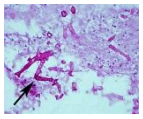
<u>Small vessel vasculitis</u>

- Microscopic Polyangiitis: Fibrinoid necrosis of small vessels and capillaries. Leukocytoclastic vasculitis. MPO-ANCA. Necrotizing glomerulonephritis, pulmonary capillaritis.
- Wegener Granulomatosis: Granulomatous inflammation. Upper and lower respiratory tracts. Glomerulonephritis. PR3-ANCA
- Churg-Strauss Syndrome: Allergic eosinophilic granulomatosis and angiitis. Asthma, rhinitis. MPO-ANCA.
- Buerger Disease: Thromboangiitis Obliterans. Medium and small vessels. Smoking.

<u>Infectious Vasculitis</u>

Angioinvasive organisms

Invasive fungal sinusitis, Aspergillus and Mucor spp.



The following table taken from

Chen et al. The environment, geoepidemiology and ANCA_associated vasculitides. Autoimmunity Reviews. Vol 9, Issue 5. March 2010, Pages A293-A298.

http://dx.doi.org/10.1016/j.autrev.2009.10.008

Table 1. Classification of vasculitis according to the Chapel Hill Consensus Conference [49].

Large vessel vasculitis	
Giant cell (temporal) arteritis	Granulomatous arteritis of the aorta and its major branches, with a predilection for the extra cranial branches of the carotid artery. Often involves the temporal artery. *Usually occurs in patients older than 50 and often is associated with polymyalgia rheumatica*
Takayasu's arteritis	Granulomatous inflammation of the aorta and its major branches. *Usually occurs in patients younger than 50*
Medium sized vessel vasculitis	
Polyarteritis nodosa	Necrotizing inflammation of medium-sized or small arteries without glomerulonephritis or vasculitis in arterioles, capillaries, or venules
Kawasaki disease	Arteritis involving large, medium sized, small arteries, and associated with mucocutaneous lymph node syndrome. *Coronary arteries are often involved. Aorta and veins may be involved. Usually occurs in children*
Small vessel vasculitis	
Wegener's granulomatosis[a]	Granulomatous inflammation involving the respiratory tract, and necrotizing vasculitis affecting small to medium-sized vessels (e.g. capillaries, venules, arterioles, and arteries). *Necrotizing glomerulonephritis is common*
Churg-Strauss syndrome[a]	Eosinophil-rich and granulomatous inflammation involving the respiratory tract, necrotizing vasculitis affecting small to medium-sized vessels, and associated with asthma and eosinophilia
Microscopic polyangiitis[a]	Necrotizing vasculitis, with few or no immune deposits, affecting small vessels (i.e. capillaries, venules, or arterioles). Necrotising arteritis involving small and medium sized arteries may be present. Necrotizing glomerulonephritis is very common. Pulmonary capillaritis often occurs
Henoch-Schönlein Purpura	Vasculitis, with IgA-dominant immune deposits, affecting small vessels i.e. capillaries, venules, or arterioles). *Typically involves skin, gut, and glomeruli, and is associated arthralgia or arthritis*
Essential cryoglobulinaemic vasculitis	Vasculitis, with cryoglobulin immune deposits, affecting small vessels (i.e. capillaries, venules, or arterioles), and associated with cryoglobulins in serum. *Skin and glomeruli are often involved*
Cutaneous leucocytoclastic angiitis	Isolated cutaneous leucocytoclastic angiitis without systemic vasculitis glomerulonephritis

a
Associated with anti-neutrophil cytoplasmic antibodies.

Disorders of Blood Vessel Hyperreactivity

Raynaud Phenomenon

"Red-white-and-blue disease"

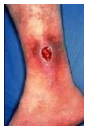
Primary and secondary Raynaud Phenomenon

Myocardial Vessel Vasospasm
Endogenous and exogenous vasoactive mediators

Veins and Lymphatics

Varicose Veins
Superficial dilated tortuous veins secondary to increased intraluminal pressures and weakened vessel wall support. (Figures not in text)

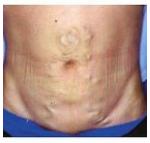
Etiologies



Stasis dermatitis/ulcerations

Esophageal varices

"Caput Medusae"



Hemorrhoids

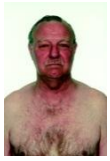
Thrombophlebitis/Phlebothrombosis
Deep leg veins

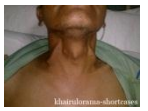
Etiologies

Deep Vein Thrombosis (DVT)

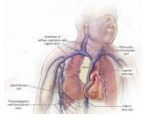
Migratory thrombophlebitis (Trousseau syndrome)

Superior and Inferior Vena Cava Syndromes (Figures not in text)
SVC





IVC



Lymphangitis/Lymphedema

Chylous ascites/chylothorax/chylopericardium

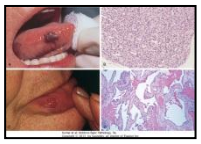
Tumors

Benign Tumors and Tumor-Like Conditions
Vascular Ectasias
Telangiectasia

Nevus flammeus (birthmark)/Port wine stain/spider telangiectasias
(Port wine figure not in text)

Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu disease)

Hemangiomas
Capillary/Juvenile/Cavernous (Figure 9-28)



Pyogenic granuloma

Lymphangiomas

Simple and cavernous lymphangioma (cystic hygroma) (Figure not in text)

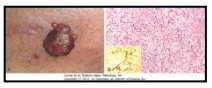
Glomus tumors (Glomangiomas)

Painful subungual tumors of specialized smooth muscle cells of glomus bodies (Arteriovenous structures of thermoregulation)

Bacillary angiomatosis

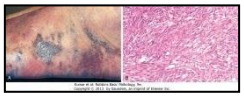
Vascular proliferation in immunocompromised hosts (Figure 9-29)

Bartonella family (gram neg bacilli)



<u>Intermediate –Grade (Borderline) Tumors</u>

Kaposi Sarcoma (Figure 9-30)



4 forms of KS

Occurs with malignancy, HIV negative and HIV positive patients

Caused by KSHV (Kaposi sarcoma herpes virus) = HHV-8 (Human herpes virus-8)

Lytic and latent infection in endothelial cells

Produces a viral homologue of cyclin D

Prevents apoptosis by inhibit p53

Patch → Plaque → Nodule stages (potential nodal and visceral involvement)

Hemagionendothelioma

Borderline vascular neoplasm

<u>Malignant Tumor</u>

Angiosarcoma

Well differentiated to anaplastic histology

Common sites: skin, breast, liver

Clinically aggressive, 30% five year survival

Hemangiopericytoma

Pericytes: myofibroblast-like cells surrounding capillaries and venules

<u>Pathology of Vascular Intervention</u>

Thrombosis following balloon angioplasty

Proliferative in-stent restenosis (drug eluting stents)

ADDED SECTION ON HYPERLIPIDEMIA/HYPERCHOLESTEROLEMIA

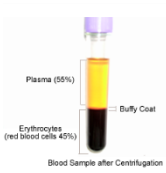
Hyperlipidemia, specifically hypercholesterolemia

Lipoprotein Class	Density (g/mL)	Origin	Apolipoproteins	Lipid
Chylomicrons	<0.95	Intestine	C-II, E	TG (85%), cholesterol (10%)
VLDL	<1.006	Liver	B-100, C-II, E	TG (55%), cholesterol (20%)
IDL	1.006–1.019	VLDL catabolism	B-100, E	TG (25%), cholesterol (35%)
LDL	1.019–1.063	IDL catabolism	B-100	TG (5%), cholesterol (60%)
HDL	1.063–1.25	Liver, intestine	A-I, E	TG (5%), cholesterol (20%)

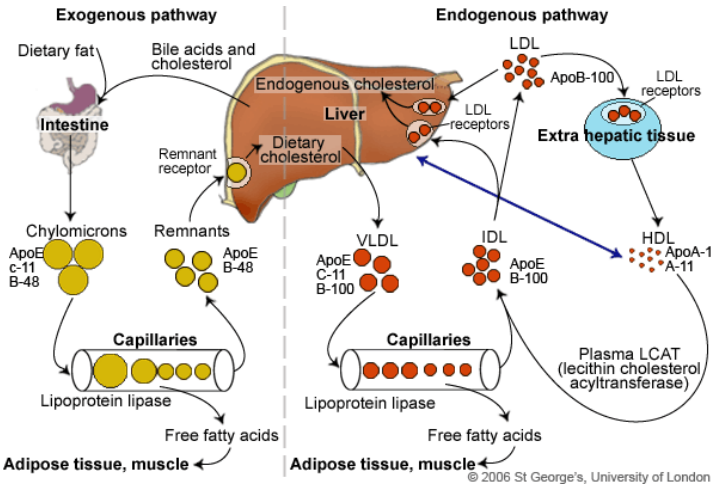
HDL, high-density lipoprotein; IDL, intermediate-density lipoprotein; LDL, low-density lipoprotein; TG, triglyceride; VLDL, very-low-density lipoprotein.

Normal cholesterol metabolism

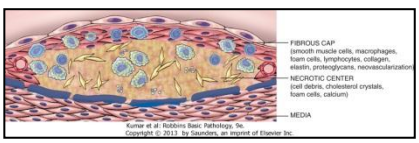
Exogenous (dietary)

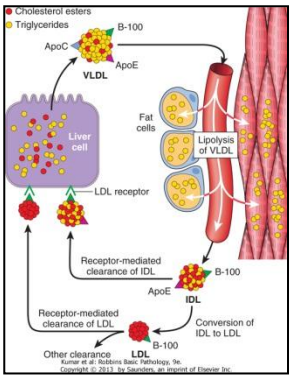


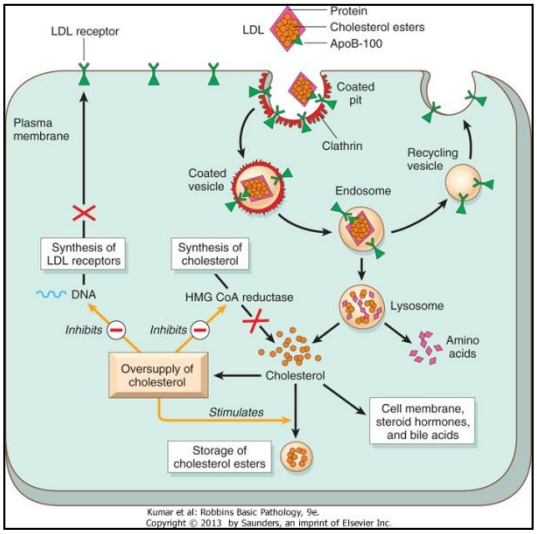
Endogenous



LDL receptor pathway and scavenger receptor/macrophage/other clearance pathway (Figures 6-2, 9-7)







Free intrahepatocellular cholesterol (Figure 6-3)

1.

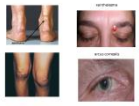
2.

3.

Familial Hypercholesterolemia: mutations of LDL receptor associated protein

Heterozygous

Homozygous

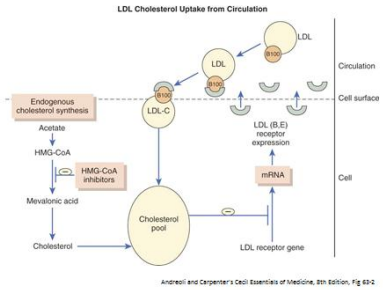


Xanthoma
xanthelasma
arcus cornealis

http://www.fhjourneys.com/healthcare.aspx

Rx:

Pharmacology



Drug Class	LDL	HDL	Triglycerides	Side Effects
HMG-CoA inhibitors	↓ 20%-60%	↑ 5%-10%	↓ 10%-30%	Liver toxicity, myositis, rhabdomyolysis, enhanced warfarin effect
Cholesterol absorption inhibitors	↓ 17%	No effect	No effect	Abnormal liver enzymes in combination with an HMG-CoA inhibitor, potential increase in cancer risk and cancer death
Bile acid sequestrants	↓ 15%-30%	Slight increase	No effect	Nausea, bloating, cramping, abnormal liver function, interference with the absorption of other drugs such as warfarin and thyroxine
Fibric acids	↓ 5%-20%	↑ 15%-35%	↓ 35%-50%	Nausea, cramping, myalgias, liver toxicity, enhanced warfarin effect
Nicotinic acid	↓ 10%-25%	↑ 15%-35%	↓ 25%-30%	Hepatotoxicity, hyperuricemia, hyperglycemia, flushing, pruritus, nausea, vomiting, diarrhea

↓, Decreased; ↑, increased; HMG-CoA, 3-hydroxy-3-methylglutaryl-coenzyme A.