CARDIOVASCULAR SYSTEM

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RMC
I have learned to seek my happiness by limiting my desires, rather than attempting to satisfy them.
OBJECTIVES:

To help develop an understanding of pathologic basis of vascular and heart diseases.

The learner will be able to correlate and interpret this understanding in a patient presenting with the symptoms of these diseases.
CARDIOVASCULAR SYSTEM

Lectures outline:

Total 08 lectures, interactive

1. Brief introduction & revision of anatomy and physiology of CVS
2. Diseases of blood vessels with emphasis on clinically important diseases
3. Diseases of heart commonly encountered in clinical practice
4. Students presentations (clinical scenario based)
HEART

- aorta (from the left ventricle to the body)
- pulmonary artery (from the right ventricle to the lungs)
- superior vena cava (from the head and arms into the right auricle)
- pericardium
- right auricular appendage
- right auricle
- right coronary artery
- inferior vena cava (bringing blood from the legs and trunk into the right auricle)
- left auricle
- left auricular appendage
- left coronary artery
- left ventricle
- apex of the heart
HEART – CUT SECTION

- aorta (to the body)
- pulmonary artery
- superior vena cava
- pulmonary veins
- right auricle
- tricuspid valve
- semilunar valve of the pulmonary artery
- semilunar valve of aorta
- mitral (bicuspid) valve
- septum (the wall dividing the heart into two parts)
- left ventricle
- right ventricle
- myocardium
CONDUCTION SYSTEM

- SA node
- AV node
- AV bundle (bundle of His)
- Purkinje's fibers
- Left/right bundle branches
CONDUCTION SYSTEM
CORONARY CIRCULATION
Endothelium

The thin layer of cells lining the inner surface of blood vessels and lymphatics forming an interface between circulating blood or lymph in the lumen and the rest of the vessel wall.

The cells that form the endothelium are called endothelial cells.
Endothelium

Vascular endothelial cells line the entire circulatory system, from the heart to the smallest capillaries.
Functions of Endothelium

- Barrier
- Maintenance of a non thrombogenic interface between blood and tissues
- Modulation of vascular resistance
- Hormones trafficking
- Regulation of inflammation
- Effect on growth of other cell types
- Fluid filtration
- Angiogenesis
Functions of Endothelium

- Antithrombotic
- Anti-inflammatory
- Anticoagulant
- Prothrombolytic
- Endothelium-dependent Vasodilatation
- Antihypertrophic
Endothelial Cell Activation

By:

- Cytokines
- Bacterial products
- Hemodynamic stress
- Lipid products
- Advanced glycosylation products
- Viruses
- Complement components
- Hypoxia
Activated Endothelium

- Adhesion molecules expressed
- Cytokines, chemokines, GF, MHC molecules
- VC or VD
- Procoagulant & anticoagulant moieties
- NO & endothelin production
Products of Endothelial Cells

Matrix Products
- fibronectin
- laminin
- collagen I, II, III, IV, VIII, XVIII
- proteoglycans
- proteases

Antithrombotic factors
- PGI₂
- thrombomodulin
- AT III
- tPA
- heparin sulfate

Procoagulant factors
- vWF
- TXA₂
- thromboplastin
- Factor V
- PAF
- PAI-1, PAI-2

Lipid Metabolism
- LDL-receptor
- lipoprotein lipase

Inflammatory Mediators
- IL-1, 6, 8
- LTB₄, C₄, D₄, E₄
- MCP-1, MCP-2
- MHC II
- CAM

Vasomotor factors
- relaxing
  - NO
  - PGI₂/E₂
  - EDHF
- constricting
  - ACE
  - TXA₂/F₂a
  - EDCF
  - leukotrienes
  - free radicals
  - endothelin

Growth factors
- PDGF
- EDGF
- FGF
- IGF
- TGF-b
- GM-CSF
- G-CSF
Endothelium

Endothelial Cell Dysfunction:
Cell structural alteration
  → impaired vasoreactivity
  → induction of thrombogenic surface
  → increased adhesion to inflammatory cells
Endothelial Dysfunction

- Smoking
- Hypertension
- Diabetes
- ?Unidentified systemic factor(s)
- LDL cholesterol
- Homocysteine ADMA
- Oxidative stress

Endothelial Dysfunction

- Vasoconstriction
- Increased leucocyte adhesion & infiltration
- Platelet aggregation & thrombosis
- Lipid accumulation
- Vascular smooth muscle cell proliferation
CARDIOVASCULAR SYSTEM

Diseases of Blood vessels

Diseases of Heart
Diseases of blood vessels

Congenital anomalies
Arteriosclerosis
Hypertensive vascular disease
Aneurysms & Dissections
Vasculitis
Tumors
Diseases of blood vessels

Congenital anomalies:

- Berry aneurysms
- Arterio-venous fistulas/malformations
- Fibromuscular Dysplasia
Diseases of blood vessels

ARTERIOSCLEROSIS:

Atherosclerosis
Monckeberg medial calcific sclerosis
Arteriolosclerosis
Atherosclerosis
WHAT COULD BE THE IMPACT???
Atherosclerosis

Clinical impact depends upon the BV affected

Coronaries $\rightarrow$ IHD
Cerebrals $\rightarrow$ Stroke
Limbs $\rightarrow$ Gangrene
Atherosclerosis

Fatty streaks $\rightarrow$ Aortas of children

**Risk factors** $\rightarrow$ Atheroma in adults

↓ ↓

Ischaemic Heart Disease
Atherosclerosis

RISK FACTORS:

Non Modifiable

Modifiable
Atherosclerosis

NONMODIFIABLE (constitutional):

Age:
- advancing age

Sex:
- males > females
- postmenopausal risk equal

Genetics:
- familial predisposition
Atherosclerosis

MODIFIABLE:

Hyperlipidemia:

hypercholesterolemia
LDL (bad cholesterol)
HDL (good cholesterol)

↓ by obesity & smoking
↑ by exercise
Atherosclerosis

Diet

↑ cholesterol & saturated fats → egg yolk, butter, animal fat

↓ cholesterol & polyunsaturated fats → omega 3 FA (fish oils)

Statins ↓ cholesterol

(HMG-CoA reductase inhibition)
Atherosclerosis

Hypertension:
60% increased risk of IHD
>169/95 mm Hg 5 fold ↑ risk

Smoking:
200% ↑ death rate

Diabetes Mellitus:
hypercholesterolemia
twice ↑ risk of MI
gangrene lower limbs (200% risk)
Atherosclerosis

Others:

- inflammation * (CRP)
- homocystinemia & homocystinuria
- metabolic syndrome (glucose intolerance, central obesity, HTN)
- lipoprotein a (apolipoprotein B-100 of LDL)

Factors affecting hemostasis

- lack of exercise, stressful lifestyle, type A personality, obesity
Atherosclerosis

Multiple risk factors $\rightarrow$ Multiplicative effect
“I had my plumber install new pipes. I got tired of fretting about my cholesterol!”
"Don't wish it were easier, wish you were better. Don't wish for fewer problems, wish for more skills. Don't wish for less challenges, wish for more wisdom."
Atherosclerosis

PATHOGENESIS:

“response to injury hypothesis”

A disease of intima

Chronic inflammation of arterial wall in response to injury to endothelium
Atherosclerosis

- Chronic endothelial injury $\rightarrow$ activation
- Accumulation of lipoproteins (LDL)
- Oxidation of LP
- Monocyte migration $\rightarrow$ macrophage accumulation
- Foam cells
Atherosclerosis

- Platelet adhesion
- Chemical mediator release
- Smooth muscle cells migration
- SMCs proliferation
- ECM deposition
- Lipid accumulation
Stages of atherosclerotic plaque development

Expert Reviews in Molecular Medicine ©2005 Cambridge University Press
Atherosclerosis

1. Endothelial injury:
   endothelial dysfunction → injury
   repetitive, non denuding → intimal thickening

   → Mechanical, toxins, chemical mediators, infections, immune complexes, irradiation hemodynamic disturbance
Atherosclerosis

hyperlipidemia
HTN
Toxins (cigarette, homocysteine, infectious agents)
Inflammatory cytokines (TNF)

“hemodynamic disturbance& hypercholesterolemia”
Atherosclerosis

Hemodynamic disturbances:

Plaques occur at ostia and points of bifurcation
Posterior wall of abdominal aorta
Atherosclerosis

2. Lipids:
   cholesterol & its esters in atheromas
   Oxidized LDL in macrophages
   Dyslipoproteinemias
   alteration in apoproteins
   lipoprotein receptors on cells
   alteration in circulating lipids (nephrotic synd, DM, alcoholism, hypothyroidism)
Atherosclerosis

Common lipoprotein abnormalities:
- increased LDL
- decreased HDL
- increased lipoprotein (a)

**EVIDENCE:**
- Cholesterol & cholesterol esters in atheromas
Atherosclerosis

- Genetic defects ⇔ hyperlipoproteinemia ⇔ AS
- MI at young age with ↑ cholesterol
- DM, hypothyroidism → ↑ cholesterol → AS
- High cholesterol diet ⇔ AS
- Severity of AS ⇔ levels of cholesterol
- Reducing cholesterol levels → risk of AS ↓
Atherosclerosis

Mechanism:
1. Chronic hyperlipidemia $\rightarrow$ EC activation or dysfunction $\rightarrow$ ↑ toxic O$_2$ radicals $\rightarrow$ ↓ NO $\rightarrow$ ↓ VD
2. Chronic hyperlipidemia $\rightarrow$ LP accumulate in intima
3. $\rightarrow$ Oxidized LDL $\rightarrow$ macrophages $\rightarrow$ foam cells
   $\rightarrow$ monocyte accumulation
   $\rightarrow$ GF, cytokine release & chemokines
   $\rightarrow$ ECs, SMCs cytotoxicity
Atherosclerosis

3. Inflammation (chronic):
   - role from initiation - complications
   - dysfunction $\rightarrow$ endothelial cell adhesion mol
   - VCAM-1 $\rightarrow$ bind monocytes & T cells
   - $\rightarrow$ adhesion & migration $\rightarrow$ macrophage accumulation in intima $\rightarrow$ foam cell formation
   - oxidized LDL activates macrophages
   - $\rightarrow$ IL-1, TNF $\rightarrow$ leucocyte adhesion & MCP-1
Atherosclerosis

Macrophages
- toxic oxygen species $\rightarrow$ oxidation of lipids
- GF $\rightarrow$ smooth muscle cell proliferation
- Recruitment of T lymphocytes
  $\rightarrow$ chronic inflammation
  $\rightarrow$ cellular & humoral
  $\rightarrow$ $\gamma$ IFN
  $\rightarrow$ activate macrophages, endothelial cells & smooth muscle cells
Atherosclerosis

**Infection:**
Causative role ???
Herpesvirus
CMV
Chlamydia Pneumonae

| all present in plaques |
Atherosclerosis

4. **Smooth muscle cells:**
SMCs migration proliferation & ECM deposition

↓

Fatty streak → fibrofatty atheromatous plaque

PDGF, TGF-a, FGF

Foam cells

ECM (collagen) deposited

SMCs apoptosis
Atherosclerosis

MORPHOLOGY:

Fatty streak:

- children aortas
- coronaries in adolescents
- multiple, flat yellow dots
- coalesce to streaks
- lipid laden foam cells
FATTY STREAK
Atherosclerosis

Atherosclerotic plaque:
- elastic & muscular arteries
- lower abdominal aorta > thoracic aorta
- ostia and branches
- symptomatic AS disease
  - MI $\rightarrow$ heart attack
  - cerebral infarction $\rightarrow$ stroke
  - peripheral vascular $\rightarrow$ gangrene
Atherosclerosis

- aorta > coronaries > popliteal > internal carotid > circle of willis
- white – white yellow
- patchy lesions
- variable size (0.3 – 1.5 cm)
- eccentric lesions
- obstruction of lumen
Mild, Moderate, Severe AS
Atherosclerosis

Components:

1. Cells:
   - SMCs
   - macrophages
   - T lymphocytes
   - other leukocytes
Atherosclerosis

2. ECM:
   - collagen
   - elastic fibers
   - proteoglycans

3. lipids:
   - intracellular
   - extracellular
Atherosclerosis

Atheroma:
- fibrous cap
- shoulder
- necrotic core
- cholesterol clefts
- neovascularization

Fibrous plaque
Fibrous plaque (on opposite wall)

Optical "empty", needle-like cholesterol crystals

Endothelium

Vascular lumen

"Fibrous cap"

Atheroma core
Atherosclerosis

Sequelae of AS:

- Atherosclerotic stenosis
- Acute Plaque change
- Thrombosis
- Vasoconstriction
Atherosclerotic Stenosis

Symptomatic atherosclerotic disease:
Depends on the
- size of artery
- plaque stability
- degree of degeneration of underlying wall

Critical stenosis $\rightarrow$ chronic occlusion
$\rightarrow$ reduced supply on increased demand

$\rightarrow$ Stable angina
Pieces of plaque can break free, travel to the brain, and block blood vessels that supply blood to the brain.
Arteries become narrowed and blood flow decreases in atherosclerosis.

Build up of fatty substances in the wall of the artery.
Acute Plaque Change

- Acute tissue infarction
Enlargement
Ulceration/erosion
Rupture/Fissuring
Haemorrhage
- Unstable angina
Atherosclerosis

Thrombosis
Embolism
Calcification
Aneurysmal dilation
Vasoconstriction
The purpose of life is to live a life of purpose.
The dead take to the grave, clutched in their hands, only what they have given away...
CARDIOVASCULAR SYSTEM

ARTEIOLOCLEROSIS:

Hyaline

homogenous pink hyaline thickening
→ narrowed lumen
chronic hemodynamic stress → endothelial damage → leakage of plasma proteins

Elderly
Hypertension (turbulence)
Microangiopathy of DM (hyperglycemia)
Benign nephrosclerosis (HTN)
Hyperplastic:

**Malignant HTN**

Onion skin

Concentric, laminated thickening

SMCs & thickened BM

Necrotizing arteriolitis (fibrinoid deposits & necrosis)
The pessimist complains about the wind. The optimist expects it to change. The leader adjusts the sails.
ANEURYSM:
Localized abnormal dilation of a blood vessel or heart.

True aneurysm
   all layers of BV or heart
False aneurysm (pseudoaneurysm)
   extravascular hematoma (pulsating)

Congenital
Acquired
AORTIC ANEURYSM
AORTIC ANEURYSM
CARDIOVASCULAR SYSTEM

Pathogenesis:

- Defect of vessel wall connective tissue
  - Marfan’s syndrome (fibrillin)
  - Loeys-Dietz syndrome (elastin, collagen I, II)
  - Ehlers-Danlos syndrome (collagen III)
  - Vitamin C deficiency (collagen cross linking)
Disturbed balance of collagen synthesis & degradation

- inflammatory infiltrates
- ↑ MMP (macrophages in AS, vasculitis)
- ↓ TIMP
CARDOVASCULAR SYSTEM

- Loss of smooth muscle cells or defective ECM
  - Ischemia of inner media
    - AS thickening of intima
    - HTN $\rightarrow$ narrow vasa vasorum
    - degenerative changes $\rightarrow$ smooth muscle cell loss
    - scarring $\rightarrow$ inadequate ECM
    - amorphous ground substance
  - “Cystic Medial Degeneration”
CARDIOVASCULAR SYSTEM

Atherosclerosis
(Abdominal aorta)

Aneurysm

Hypertension
(ascending aorta)
Other causes:

- Trauma (A-V aneurysms)
- Congenital defects (berry aneurysms)
- Infections (mycotic)
  - embolization (infective endocarditis)
  - adjacent suppurative lesion
- bacteremia
- Vasculitis
CARDIOVASCULAR SYSTEM

Types:

- Saccular
- Fusiform

Sites:

- Abdominal aorta
- Common iliac artery
- Arch of aorta
- Descending thoracic aorta
Berry aneurysm on the anterior communicating artery of the brain

Bottom view of brain and major arteries of the brain

Circle of Willis
CARDIOVASCULAR SYSTEM

ABDOMINAL AORTIC ANEURYSMS (AAA):
Atherosclerosis
> 50 yrs
> males, smokers

Genetic susceptibility → ↓ connective tissue strength
MMP ⇔ TIMP
HTN
CARDIOVASCULAR SYSTEM

Morphology:
- B/W bifurcation & renal arteries
- saccular/fusiform
- variable size
- thromboemboli
- occlusion of ostia
Lung
Heart
Kidney
Abdominal aortic aneurysm
CARDIOVASCULAR SYSTEM

Variants:

Inflammatory AAA
- dense periaortic fibrosis
- inflammatory cells (lymphos, plasma cells, macrophages, giant cells)

Mycotic AAA
- AS AAA + bacteremia
- Salmonella gastroentritis
CARDIOVASCULAR SYSTEM

Complications:

- Rupture
- Obstruction of adjacent BV
- Embolism
- Compression of adjacent structures
- Abdominal mass
CARDIOVASCULAR SYSTEM

SYPHILITIC ANEURYSM:

Leutic
Obliterative endarteritis
vasa vasorum
lymphocytes & plasma cells
syphilitic aortitis
CARDIOVASCULAR SYSTEM

- weakening of media
- tree barking
- aortic valve insufficiency
- cor bovinum (cow’s heart)
SYPHILITIC ANEURYSM
SYPHILITIC HEART
"Some people talk in their sleep. Lecturers talk while other people sleep."
CARDIOVASCULAR SYSTEM

AORTIC DISSECTION

“Dissection of blood between & along laminar planes of media”

1. HTN + 40-60 yrs males
2. CT defects + young age
3. Iatrogenic
4. Pregnancy
CARDIOVASCULAR SYSTEM

Pathogenesis:
HTN → medial hypertrophy of vasa vasorum
(Mechanical &/or ischemic injury)
→ degenerative changes in media
→ smooth muscle cell loss
→ Weakness of wall
→ Intimal tear → blood flow into media
MORPHOLOGY:

intimal tear
10 cm from aortic valve
transverse / oblique
sharp edges
extension
→ dissecting hematoma
Intimal tear
Aortic Dissection
Ruptures out → massive hemorrhage → pericardial, pleural, peritoneal cavity → double barreled aorta

Classification:
Type A: Proximal I II DeBakey classification
Type B: Distal III
DeBAKEY CLASSIFICATION

A

I

II

III

B
Genius ain't anything more than elegant common sense.
CARDIOVASCULAR SYSTEM

VASCULITIS:
Inflammation of vessel wall.
Symptoms related to site affected
Constitutional symptoms
   Infectious
direct invasion
   immune mechanism
Immune mediated
Isolated Forms
Affect only one organ.
Examples:
- Brain
- Eye
- Skin

Generalized Forms
Affect many organs at the same time.
Examples:
- Brain
- Eye
- Lung*
- Heart
- Kidney
- Skin

* Vasculitis can appear as either a shadow or a nodule on the lung.
CARDIOVASCULAR SYSTEM

PATHOGENETIC CLASSIFICATION:
Direct infection:
   Bacterial, Rickettsial, Spirochetal, Fungal, Viral
Immunologic:
   immune complex mediated
   ANCA mediated
   Anti-Endothelial cell antibodies
   Cell mediated
   Unknown
CARDIOVASCULAR SYSTEM

CLASSIFICATION ACCORDING TO SIZE:
Large vessel
Medium sized vessel
Small vessel
Immune Complex mediated:

like other conditions (arthus reaction, serum sickness) diseases (SLE, Polyarthritis Nodosa)
Antibody/complement detectable
immune complexes detectable (DNA-AntiDNA)
drug hypersensitivity (penicillin)
viral infections (30% PA have HBV → HBsAg-anti HBsAg)
Antineutrophil Cytoplasmic Antibodies (ANCA):  

autoantibodies (neutrophil primary granules, monocyte lysozome, endothelial cells)  
c-ANCA, p-ANCA  
  MPO-ANCA (p-ANCA)  
  PR3-ANCA (c-ANCA)  
PR3-ANCA → Wegeners Granulomatosis  
MPO-ANCA → Microscopic Polyangitis, Churg-Strauss syndrome
CARDIOVASCULAR SYSTEM

Diagnostic value
Follow up/relapse
ANCA titres ⇔ disease activity
Neutrophil activation → enzyme & ROS release
Endothelial cell-neutrophil interaction → endothelial cell damage
Surface expression of ANCA antigens ?

Mechanism of action:
TNF-alpha and other cytokines → Activation of neutrophils and endothelial cells → Migration of PR3 and MPO antigens to the cell membrane and binding to circulating ANCA → Conformational change in neutrophil adhesion molecules → Adhesion of neutrophils to endothelium (no rolling) → Release of ROS from primed neutrophils → Endothelial damage → Secretion of inflammatory cytokines by activated neutrophils → Influx of inflammatory cells
CARDIOVASCULAR SYSTEM

Anti-endothelial cell antibodies:
  Kawasaki disease

MORPHOLOGICAL TYPES:
  Granulomatous
    granuloma formation
    giant cells
  Necrotizing
    fibrinoid necrosis
    fibrous thickening of wall
<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Giant cell arteritis (Aorta &amp; large arteries)</td>
<td>temporal artery, &gt;50yrs, T cell mediated ? TNF. Intimal thickening &amp; medial granulomatous → elastic lamina fragmentation. T cells + giant cells + macrophages. Medial scarring. Ophthalmic A → blindness</td>
</tr>
<tr>
<td>Takayasu arteritis (Large arteries)</td>
<td>granulomatous, younger (&lt;50yrs), aortic arch, great BV, transmural fibrous thickening of aorta → narrow lumen. ocular disturbances, Pulseless disease. Histology same as above</td>
</tr>
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</table>
# CARDIOVASCULAR SYSTEM

<table>
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<tr>
<td><strong>Wegener Granulomatosis</strong> (small-medium BV)</td>
<td>Acute necrotizing granulomas respiratory tract, necrotizing/granulomatous vasculitis, focal necrotizing, crescentic glomerulonephritis. T cell mediated. PR3-ANCA in 95%.</td>
</tr>
<tr>
<td><strong>Churg-Strauss syndrome</strong> (small vessel)</td>
<td>Allergic granulomatosis and angiitis. Eosinophil rich necrotizing vasculitis associated with asthma, allergic rhinitis, extravascular necrotizing granulomas &amp; eosinophilia. MPO-ANCA</td>
</tr>
</tbody>
</table>
A. Normal artery

Normal blood flow

Artery wall

Artery cross-section

B. Narrowed artery (with inflammation)

Decreased blood flow

Inflammation

C. Totally occluded artery

No blood flow

Inflammation and scarring

D. Aneurysm

Abnormal blood flow

Dilation containing very thin arterial wall

Thrombus (clot)
It is wise to keep in mind that no success or failure is necessarily final."
CARDIOVASCULAR SYSTEM

TUMORS OF BLOOD VESSELS:
Vascular malformations
  Hamartomas
Reactive vascular proliferations
  Bacillary angiomatosis
Endothelial derived
Supporting cells derived
CARDIOVASCULAR SYSTEM

Benign tumors:
- Blood/lymphatic filled channels
- Transudate
- Endothelial lining without atypia

Malignant tumors:
- More solid & cellular
- Atypia ++, Mitotic figures
- No well formed vascular channels
- CD 31, vWF
CARDIOVASCULAR SYSTEM

Benign:

- Hemangioma
  - capillary
  - cavernous
- pyogenic granuloma
- Lymphangioma
  - simple
  - cavernous
CARDIOVASCULAR SYSTEM

Glomus tumor
Vascular ectasias
  nevus flamus
  spider telangiectasia
  hereditary haemorrhagic telangiectasia
Reactive vascular proliferations
  bacillary angiomatosis
CARDIOVASCULAR SYSTEM

Intermediate grade tumors:

  Kaposi sarcoma
  Hemangioendothelioma

Malignant neoplasms:

  Angiosarcoma
  Hemangiopericytoma
HEMANGIOMA:

- localized
- superficial
- head & neck
- internal (1/3rd in liver)
- angiomatosis

7% of benign childhood tumors

CARDIOVASCULAR SYSTEM
CAPILLARY HEMANGIOMA:

Gross:

- skin, sub-cutaneous tissue, mucus membranes
- liver, spleen, kidneys
- variable size
- bright red – blue
- flat/elevated
- intact epithelium
CARDIOVASCULAR SYSTEM

Histologically:
lobulated
unencapsulated
closely packed thin walled capillaries
flat endothelial lining
scanty stroma
thrombosed lumen
rupture → hemosiderin & focal scarring
CARDIOVASCULAR SYSTEM

Strawberry hemangioma (1/200 live births) newborns grows and regresses
Cavernous hemangioma:

- less common
- larger & less well circumscribed
- deep structures
- locally destructive
- no spontaneous regression
- pressure symptoms, rupture (brain)
CARDIOVASCULAR SYSTEM

Gross:

- red-blue
- spongy
- 1-2 cm

Histologically:

- sharply defined
- not encapsulated
- large cavernous vascular spaces
CARDIOVASCULAR SYSTEM

blood filled
scanty stroma
intravascular thrombosis
dystrophic calcification
Cavernous Hemangioma
CARDIOVASCULAR SYSTEM

GLOMUS TUMOR (Glomangioma):
Benign, painful
Glomus body
Distal part of digits
Small, elevated, round
Red-blue firm nodules
Branching vascular channels
Aggregates/nests of glomus cells around BV
   round, cuboidal, scanty cytoplasm
1. **Chronic/Classic/European.**
   Kaposis in 1872
   older men
   associated with altered immunity & second malignancy
   not associated with HIV
   multiple red – purple skin plaques/nodules on arms & legs
   asymptomatic & localized
   visceral involvement 10%
2. **Lymphadenopathic/African/Endemic:**
   - < 40 years seronegative individuals
   - In Bantu children of central Africa
   - lymphadenopathy
   - aggressive if visceral involvement
   - not associated with HIV
   - high mortality
KAPOSI’S SARCOMA

3. Transplant associated/immunosuppression associated:
   months-years post solid organ transplant
   aggressive
   lymph node, mucosa, viscera
   internal involvement $\rightarrow$ fatal
CARDIOVASCULAR SYSTEM

4. AIDS associated (epidemic):
   1/3\(^{rd}\) AIDS patients
   male homosexuals
   wide dissemination
   fatal
Pathogenesis of KS

HHV-8/KSHV (95%) + HIV (co factor)
Associated T cell dysfunction

KSHV $\rightarrow$ lytic/latent endothelial infection
  - Virally encoded G protein $\rightarrow$ VEGF $\rightarrow$
  - endothelial cell growth
  - inflammatory cells $\rightarrow$ cytokines $\rightarrow$ ↑ cell proliferation
  - ↓ apoptosis endothelial cells (p53 inhibition)
Morphology of KS

3 stages:

- Patches
  - pink-red-purple macules
  - single/multiple on distal lower extremities
  - dilated, irregular angulated BV
  - endothelial cell lined
  - lymphocytes, plasma cells, macrophages
CARDIOVASCULAR SYSTEM

- Plaques
  - larger, raised, violaceous
  - proximal extension
  - dermal dilated vascular channels
  - plump spindle cell lining
  - perivascular aggregates of spindle cells, red cells & hemosiderin laden macrophages
  - lymphocytes, plasma cells
Nodules

- Neoplastic
- Sheets of plump spindle cells
- Pink hyaline globules in cytoplasm
- Proliferate in dermis, subcutaneous tissue
- Slit-like spaces & small Bv + RBCs
- Hge, hemosiderin, macrophages & mononuclear cells
- Mitotic figures
- LN + visceral involvement

CARDIOVASCULAR SYSTEM
Vascular channels containing red blood cells are prominent.

Atypical cells with hyperchromatic nuclei.
Challenges are what make life interesting; overcoming them is what makes life meaningful.

Joshua J. Marine
CARDIOVASCULAR SYSTEM

DISEASES OF HEART:
Mechanisms of Cardiac dysfunction:
1. Pump failure
2. Outflow obstruction
3. Regurgitant flow
4. Shunted flow
5. Conduction defects
6. Disruption of circulation
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Genetics $\Leftrightarrow$ environment
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Heart disease:
- Congenital heart disease
- Ischemic heart disease
- Hypertensive heart disease
- Valvular heart disease
- Myocardial disease
The pessimist complains about the wind. The optimist expects it to change. The leader adjusts the sails.
Case No 1

A 55 years old obese businessman experiences acute central chest pain on waking up early in morning. He is forced to sit down due to severity of pain. He is a smoker and is on antihypertensives for the last 15 years.

What is probable diagnosis?
Contd.....

What would you do?
How will you investigate to reach a diagnosis?
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ISCHEMIC HEART DISEASE (IHD):

↓ oxygen supply
↓ nutrient supply
↓ removal of waste

90% coronary atherosclerosis ➔ CAD/CHD
Insufficient blood flow to the heart muscle from narrowing of coronary artery may cause chest pain.
4 clinical manifestations of IHD:
1. Myocardial Infarction
2. Angina Pectoris
3. Chronic IHD with heart failure
4. Sudden cardiac death

Acute Coronary Syndromes (1, 2, 4)
CARDIOVASCULAR SYSTEM

Leading cause of death

50% reduction in IHD related mortality in USA

Prevention
Early diagnosis (advanced facilities)
Therapeutic intervention (effective, safer)
CARDIOVASCULAR SYSTEM

PATHOGENESIS:

Demand $\leftrightarrow$ supply

\[
\begin{align*}
\uparrow\uparrow & \leftrightarrow \downarrow\downarrow \\
\downarrow & \\
\end{align*}
\]

ISCHEMIA
AS → obstruction → fixed / stable obstruction

→ plaque change ↓

→ vasospam ↓

→ thrombosis ↓

↓  ↓

ISCHEMIA

75% obstruction → symptomatic on ↑ demand

90% obstruction → symptomatic at rest
Atherosclerosis Timeline

- Foam cells
- Fatty streak
- Intermediate lesion
- Atheroma
- Complicated lesion/rupture
- Fibrous plaque

Endothelial dysfunction

From First Decade
- Growth mainly by lipid accumulation

From Third Decade
- Thrombosis Hematoma
- Smooth Muscle & Collagen

From Fourth Decade

Adapted from Pepine CJ. Am J Cardiol. 1998;82(suppl 10A):23S-27S.
Figure 1. Progression of atherosclerosis in the coronary arteries. Initially, the plaque deposits remain external to the lumen. As the amount of plaque increases, it begins to intrude into the lumen, decreasing the diameter of the coronary artery and causing obstruction. The resulting plaque fissure or erosion leads to angina.
CARDIOVASCULAR SYSTEM

Role of acute plaque change:

Rupture/ulceration
Erosion/fissuring  \( \rightarrow \) thrombosis
Haemorrhage

Intrinsic influences
structure & composition of plaque

Extrinsic influences
blood pressure, Plt reactivity
CARDIOVASCULAR SYSTEM

Structure of plaque
  Vulnerable plaque
    ↑ foam cells
    ↑ extracellular lipids
  thin fibrous caps
  few SMCs
  inflammatory cell clusters

Junction of fibrous cap & adjacent endothelium
Different Types of Vulnerable Plaque

A: Normal
B: Rupture-Prone
C: Ruptured / Fissured
D: Critically Stenotic
E: Eroded
F: Intra-Plaque Hemorrhage
Collagen deposition $\Leftrightarrow$ degradation metalloproteinases by macrophages

Adrenergic stimulation $\rightarrow$ systemic HTN & plt reactivity $\rightarrow$ stress on plaques

Early morning
Emotional stress
CARDIOVASCULAR SYSTEM

Role of inflammation:
All stages of AS
Macrophages & T lymphocytes
IL-1, IL-6, TNF, INF g
Metalloproteinses \(\rightarrow\) weaken plaque
Inflammation destabilizes plaque
CARDIOVASCULAR SYSTEM

Role of coronary thrombus:
Partial / total $\rightarrow$ acute coronary syndromes
Mural branch thrombus $\rightarrow$ embolize
$\rightarrow$ Microinfarcts

Role of vasoconstriction:
Potentiate plaque change
ANGINA PECTORIS:

“A symptom complex of IHD characterized by recurrent attacks of substernal/precordial chest discomfort caused by transient MC ischemia that falls short of inducing infarction.”
Angina
a type of temporary chest pain, pressure or discomfort.

Narrowed artery
Ischemia
Heart muscle is not receiving enough oxygen due to a narrowed coronary artery.
Possible areas of radiating pain: neck, jaw, upper abdomen, shoulders and arms.
CARDIOVASCULAR SYSTEM

TYPES:

Stable / typical
Unstable / crescendo
Prinzmetal / variant
CARDIOVASCULAR SYSTEM

STABLE ANGINA:
Chronic stenosing atherosclerosis $\rightarrow$ ↓ coronary perfusion
$\uparrow$ demand $\rightarrow$ MC ischemia
Triggered by exercise, stress
Relieved by rest, nitroglycerine
CARDIOVASCULAR SYSTEM

UNSTABLE ANGINA:
Progressively ↑ing frequency
At rest
Prolonged duration
Disruption of stable atheroma → thrombosis
Embolization, vasospasm
Preinfarction angina
Plaque with fibrous cap

Cap ruptures

Blood clot forms around the rupture, blocking the artery
CARDIOVASCULAR SYSTEM

PRINZMETAL ANGINA:
Uncommon
Episodic
At rest
Coronary vasospasm
Responds to vasodilators
CARDIOVASCULAR SYSTEM

MYOCARDIAL INFARCTION:

“Heart attack”

Death of cardiac muscle due to ischemia.

Transmural infarction

Subendocardial infarction
CARDIOVASCULAR SYSTEM

Incidence & risk factors:
Any age
Risk factors of AS

Pathogenesis:
Coronary artery occlusion
Acute plaque change $\rightarrow$ thrombosis $\rightarrow$ VC $\rightarrow$
$\uparrow$ size of thrombus $\rightarrow$ complete occlusion
10% MI not associated with AS plaque change.

- Vasospasm
- Emboli (paradoxical emboli)
- Unexplained (vasculitis, SCD, amyloid, shock, dissection)
CARDIOVASCULAR SYSTEM

Myocardial response:

“Area at risk”

severity & duration of ischemia

Biochemical

Functional

Morphological
# CARDIOVASCULAR SYSTEM

<table>
<thead>
<tr>
<th>FEATURE</th>
<th>TIME</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATP depletion</td>
<td>Seconds</td>
</tr>
<tr>
<td>Loss of contractility</td>
<td>60 secs</td>
</tr>
<tr>
<td>ATP reduced to 50%</td>
<td>10 min</td>
</tr>
<tr>
<td>10%</td>
<td>40 min</td>
</tr>
<tr>
<td>Irreversible cell injury</td>
<td>20 – 40 min</td>
</tr>
<tr>
<td>Microvascular injury</td>
<td>&gt; 1 hr</td>
</tr>
</tbody>
</table>
Early identification
Reperfusion

30 min reversible injury
MC ischemia $\rightarrow$ subendocardial zone
Wavefront progression $\rightarrow$ transmural
Necrosis within 6 hrs
Grossly visible after 12 hrs
## CARDIOVASCULAR SYSTEM

<table>
<thead>
<tr>
<th>TRANSMURAL</th>
<th>SUBENDOCARDIAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full thickness of MC</td>
<td>Inner 1/3rd or half</td>
</tr>
<tr>
<td>AS $\rightarrow$ plaque change $\rightarrow$ thrombosis</td>
<td>As $\rightarrow$ plaque change $\rightarrow$ thrombosis $\rightarrow$ recanalized</td>
</tr>
<tr>
<td>Limited to area of supply</td>
<td>Hypotension / shock on chronic stenosing AS</td>
</tr>
<tr>
<td></td>
<td>Can extend beyond</td>
</tr>
</tbody>
</table>
CARDIOVASCULAR SYSTEM

Factors influencing MI:

1. Site, size, rate of development of AS
2. Size of vascular bed
3. Duration
4. Myocardial demands
5. Collateral circulation
6. Coronary artery spasm
7. BP, HR, cardiac rhythm
Take a 10-30 minute walk every day and while you walk, smile.
CARDIOVASCULAR SYSTEM

Morphology:
Left ventricle > right ventricle
Rim of subendocardium preserved
Myocytolysis (vacuolar degeneration)

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Percentage</th>
<th>Affected Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td>40 – 50%</td>
<td>Ant wall left vent, apex, ant septum</td>
</tr>
<tr>
<td>RCA</td>
<td>30 – 40%</td>
<td>Inf-post wall lt vent, post septum, post right right vent</td>
</tr>
<tr>
<td>LCA</td>
<td>15 – 20%</td>
<td>Lat wall left vent</td>
</tr>
</tbody>
</table>
## CARDIOVASCULAR SYSTEM

<table>
<thead>
<tr>
<th>TIME</th>
<th>GROSS</th>
<th>MICROSCOPIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – ½ hr</td>
<td>-----</td>
<td>myofibril relaxation, swelling of mitochondria</td>
</tr>
<tr>
<td>½ - 4 hr</td>
<td>-----</td>
<td>Wavy fibers</td>
</tr>
<tr>
<td>4 – 12 h</td>
<td>Occ dark mottling</td>
<td>Coag necrosis, edema, hge</td>
</tr>
<tr>
<td>12-24 h</td>
<td>Dark mottling</td>
<td>Necrosis, pyknosis, myocyte eosinophilia, contraction bands, neutrophils</td>
</tr>
</tbody>
</table>
1 day MI showing contraction band
<table>
<thead>
<tr>
<th></th>
<th>1 - 3 days</th>
<th>3 – 7 days</th>
<th>7 – 10 days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mottling + yellow centre</td>
<td>Red border, yellow tan center</td>
<td>Max yellow soft center, red borders</td>
</tr>
<tr>
<td></td>
<td>Loss of nuclei &amp; striations, PMNs ++</td>
<td>Disintegration, phagocytosis</td>
<td>Phagocytosis ++, granulation tissue at margins</td>
</tr>
<tr>
<td>10-14 days</td>
<td>Red-gray depressed</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Granulation tissue ++, collagen +</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 – 8 wks</td>
<td>Grey white scar</td>
<td>↑ collagen, ↓ cellularity</td>
<td></td>
</tr>
<tr>
<td>&gt; 2 month</td>
<td>Complete scar</td>
<td></td>
<td>Dense collagenous scar</td>
</tr>
</tbody>
</table>
1-2 days
Myocyte necrosis (absence of nuclei)

Leucocytes

Red blood cells
3-4 day
1-2 wks
CARDIOVASCULAR SYSTEM

Reperfusion injury:
Restoration of coronary flow $\rightarrow$ reperfusion
Ischemia $\rightarrow$ variable effects on MC
Reperfusion $\rightarrow$ salvage
  $\rightarrow$ damage
  $\rightarrow$ mechanism
  $\rightarrow$ manifestations
Reperfusion injury

**Mechanism:**
- Microvascular injury
- Inflammation (WBC activation)
- Reactive O2 radicals (damage CM, DNA, cellular proteins)
- Reduced NO
- Mitochondrial dysfunction
- Myocyte hypercontracture
- Platelet aggregation
- Complement activation
- ROS $\rightarrow$ redox signalling $\rightarrow$ apoptosis
Reperfusion injury

Manifestations:

- Arrythmias
- Microvascular dysfunction
- Myocardial stunning
- Myocyte death
Myocardial stunning

Reversible reduction of function of heart contraction after reperfusion not accounted for by tissue damage or reduced blood flow.

Persistence of biochemical & functional changes in reperfused MC

During phase of reversible ischemia
Cardiac biomarkers

- CPK (MM, MB, BB)
- AST
- LDH
- Troponins
- CRP
- Homocysteine levels
- BNP
Cardiac enzyme changes with MI

- Lactate dehydrogenase
- Troponin
- Creatine Kinase

Enzyme level increase above normal

- Onset of chest pain

Time (days)
Complication of MI

1. Contractile dysfunction → cardiogenic shock
2. Arrhythmias
3. MC rupture → cardiac rupture syndrome
4. Pericarditis
5. Right ventricular infarction
6. Extension
7. Mural thrombosis
8. Ventricular aneurysm
9. Papillary muscle dysfunction
10. Progressive late heart failure
ST Segment Elevation

- 1 mm above baseline (limb)
- 2 mm above baseline (chest)
- 0.08 sec to right of J point

Look for in two or more leads facing same area
Post Myocardial Infarction

- Hyperacute phase
- Fully evolved phase
- Resolution phase
- Stabilized chronic phase
BE GENTLE WITH THE EARTH
CARDIOVASCULAR SYSTEM

RHEUMATIC FEVER & HEART DISEASE

“A multisystem inflammatory disease having an acute onset with underlying immune pathogenesis occurring few weeks after streptococcal pharyngitis.”

Acute Rheumatic carditis \(\rightarrow\) Rheumatic heart disease
CARDIOVASCULAR SYSTEM

Children (5-15 yrs)
10 days – 6 weeks
Arthritis & carditis
Relapsing course
Chronic Rheumatic Carditis
CARDIOVASCULAR SYSTEM

PATHOGENESIS:

Group A Streptococcal throat infection

↓

Antibodies M component streptococci

↓

Cross react glycoprotein antigens

Heart, joints, skin, brain
Rheumatic Fever (RF)

- β-Hemolytic strep is associated with 2 Types of Antigens:
  - Streptolysin O: Strongly antigenic
  - Streptolysin S: Weekly antigenic
- Streptolysin O triggers an Antigen-Antibody reaction
- A positive Anti Streptolysin O Titer (ASLO) occurs
- Thus a positive ASLO titer confirms that a β-hemolytic strep infection has occurred in the recent past
- Throat culture is always negative with RF
Major events triggering rheumatic heart disease lesions

**Expert Reviews in Molecular Medicine © 2005 Cambridge University Press**
CARDIOVASCULAR SYSTEM

RF characterized by:
Migratory polyarthritis
Carditis
Subcutaneous nodules
Erythema marginatum
Sydenham chorea
Live with the 3 E's ... Energy, Enthusiasm, Empathy, and the 3 F's ... Faith, Family, Friends.
RF: Jones Criteria

- RF affects specific areas/tissues in the body
- Major & Minor Jones Criteria specify the areas involved
- The Criteria were recognized & described by Dr. Jones

Major Jones Criteria:
- Arthritis
- Carditis
- Rheumatic Chorea
- Erythema Marginatum
- Erythema Nodosum
RF: Minor Jones Criteria and Diagnosis

Minor Jones Criteria:

- Fever
- Pain in the Right Upper Abdominal Quadrant (RUQ)
- Elevated Erythrocyte Sedimentation Rate (ESR)
- Increased C-reactive protein
- Elevated ASLO titer
- EKG changes

A Diagnosis of RF is made when the Patient has:

- Two Major Criteria OR One Major and Two Minor Criteria
MORPHOLOGY:
Acute RF → Focal inflammatory lesions →
Aschoff bodies
- swollen eosinophilic collagen
- T lymphocytes, plasma cells
- macrophages → Anitschkow cells
  - abundant cytoplasm
  - central round/oval nucleus
  - central slender chromatin → caterpillar cells
Aschoff giant cells

CARDIOVASCULAR SYSTEM
Pancarditis

- Bread & Butter Pericarditis
- Myocarditis → Perivascular Aschoff nodules
- Verrucae/vegetations on valves
- Fibrinoid necrosis
- MacCallum Plaques (left atrium)
CARDIOVASCULAR SYSTEM

Chronic Rheumatic Heart Disease:
Organization of acute inflammation
Leaflet thickening
Commissural fusion
Thickened, short & fused cordae tendinae
Progressive fibrosis
Buttonhole deformity
Fish mouth appearance
CARDIOVASCULAR SYSTEM

Mitral stenosis:

99% cases due to RHD

RHD $\rightarrow$ 65% - 70 % alone

with aortic valve 25%

Atrial dilation $\rightarrow$ mural thrombosis

Pulmonary vascular changes
Infective Endocarditis

Infection of the endocardium which may include one or more heart valves, the mural endocardium, or a septal defect.

Vegetations
  thrombotic debris & microorganisms
Infective Endocarditis

Intracardiac effects:
- severe valvular insufficiency → intractable
- congestive heart failure
- myocardial abscesses.

If left untreated, IE is generally fatal.
Clinical classification:
- Acute
- Subacute
# Infective Endocarditis

<table>
<thead>
<tr>
<th>ACUTE IE</th>
<th>SUBACUTE IE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy valves</td>
<td>Diseased/prosthesis</td>
</tr>
<tr>
<td>Highly virulent organisms</td>
<td>Low virulence</td>
</tr>
<tr>
<td>Acute &amp; severe</td>
<td>Insidious</td>
</tr>
<tr>
<td>50% mortality</td>
<td>Recovery common</td>
</tr>
<tr>
<td>Destructive necrotizing</td>
<td>Less destructive</td>
</tr>
</tbody>
</table>
Infective Endocarditis

PATHOGENESIS:
Valvular diseases (RHD, prolapse, congenital defects, degenerative calcific stenosis)
Immune compromised states
Aetiology:
  - Strep viridans (50-60%) → defective valves
  - Staph Aureus (10-20%) → healthy valves
    I/V drug abusers
HACEK group
Staph epidermidis $\rightarrow$ prosthetic valve IE
gram –ive bacilli
fungi
culture negative

Nonbacterial thrombotic endocarditis may result from stress, renal failure, malnutrition, systemic lupus erythematosus, or neoplasia.
Infected Endocarditis

MORPHOLOGY:
Bulky, Friable, Destructive vegetations
Single/multiple
Fibrin & inflammatory cells
Aortic & mitral valves
Ring abscess
Infective Endocarditis

Fungal Endocarditis
  larger vegetations
Systemic emboli → Septic infarcts
SIE → granulation tissue at base

LIBMAN-SACKS ENDOCARDITIS:
  Endocarditis of SLE
Infected Endocarditis

Dukes Diagnostic Criteria for IE (1994):

Pathologic:
  + cultures (vegetation, embolus, abscess)
  vegetation histology
  intracardiac abscess

Clinical:

Major:
  + blood culture of IE organisms
  Echocardiographic findings, valvular defects
Infected Endocarditis

Minor:

- Predisposing heart lesion, I/V drug abuser
- Fever $> 38^0C$
- Evidence of embolism (arterial, pulmonary infarcts, conjunctival heemorrhage)
- Immunologic phenomena (GN, Osslers nodes)
- Positive cultures
- Echocardiographic (removed in modified Dukes criteria 2000)
Definite diagnosis if:

- One of pathological criteria
- One of these combinations of clinical criteria
  - 2 major clinical criteria
  - 1 major and 3 minor criteria
  - 5 minor criteria

Infective Endocarditis
Infective Endocarditis

Possible diagnosis if one of the following combinations of clinical criteria are met:

- 1 major and 1 minor criteria
- 3 minor criteria are fulfilled
MYOCARDITIS:
Infections:
- Viruses (coxsackie, ECHO, influenza, HIV)
- Chlamydia
- Rickettsiae
- Bacteria
- Fungi
- Protozoa
- Helminths
CARDIOVASCULAR SYSTEM

Immune mediated
  post viral
  post streptococcal (RF)
SLE
Drugs
Transplant rejection
Unknown
  sarcoidosis
  giant cell myeloma
CARDIOVASCULAR SYSTEM

Morphology:
Hypertrophy, dilated, flabby
Diffuse/patchy
Mottled
Mural thrombi
Interstitial inflammatory infiltrate (mononuclear)
Focal necrosis
CARDIOVASCULAR SYSTEM

Hypersensitivity Mc ➔ perivascular lymphocytes
Macrophages, eosinophils
Giant cell myocarditis ➔ giant cells, lympho, eos
plasma cells, macrophages
CARDIOVASCULAR SYSTEM

PERICARDITIS:
Acute
  Serous
  Fibrinous
  Purulent
  Haemorrhagic
  Caseous
CARDIOVASCULAR SYSTEM

Chronic:
  Adhesive mediatinopericarditis
  Constrictive pericarditis

CAUSES:
Infectious (viruses, bacteria, TB, fungi)
Immunologic (RF, SLE, scleroderma, post MI, (dresslers syndrome) drugs
Miscellaneous (MI, uremia, cardiac surgery, neoplasia, trauma, radiation)
CARDIOMYOPATHIES

Intrinsic disease of myocardium:
   Primary
   Secondary
Myocarditis
Immunologic
Systemic metabolic
Muscular dystrophies
Genetic abnormalities
CARDIOMYOPATHIES

Heart disease resulting from a primary abnormality in the myocardium

- Dilated cardiomyopathy (DCM)
- Hypertrophic cardiomyopathy (HCM)
- Restrictive cardiomyopathy (RCM)
CARDIOMYOPATHIES

Conditions associated with CM:

- Infections
- Toxins
- Metabolic
- Neuromuscular disease
- Storage disorders
- Infiltrative
- Immunological
- Genetic
DILATED CARDIOMYOPATHY

Congestive CM
Progressive cardiac dilation & Hypertrophy
Hypocontracting heart
Contractile dysfunction (systolic)

Pathogenesis:
  Genetic (20-50%)
  Myocarditis
  Alcohol & toxins (alcoholic CM)
  Childbirth (peripartum CM)
  Hemochromatosis, sarcoidosis
  Idiopathic
DILATED CARDIOMYOPATHY

Secondary:

  IHD
  Valvular heart disease
  Hypertensive heart disease
  Congestive heart disease
DILATED CARDIOMYOPATHY

Morphology:
Dilated, heavy, flabby heart
Mural thrombosis
Valvular defects
Hypertrophied cells with large nuclei
Interstitial & endocardial fibrosis
HYPERTROPHIC CARDIOMYOPATHY

Myocardial hypertrophy
Poor compliance
Diastolic dysfunction
Intermittent outflow obstruction
Genetic mutations (100%)
Hypercontracting heart
HYPERTROPHIC CARDIOMYOPATHY

Morphology:
Thickened septum
Banana like ventricular cavity
Endocardial thickening/mural plaque
(subaortic region)
⇒ Outflow obstruction
Extensive myocyte hypertrophy
myofiber disarray
Interstitial fibrosis
RESTRICTIVE CARDIOMYOPATHY

- Decreased compliance
- Diastolic dysfunction
- Idiopathic
- Radiation fibrosis, amyloidosis, sarcoidosis, metastatic tumors, inborn errors metabolism
- Firm myocardium
- Atrial dilation
- Interstitial fibrosis
RESTRICTIVE CARDIOMYOPATHY

D/D:

Endomyocardial fibrosis
Loeffler endomyocarditis
Endocardial fibroelastosis
<table>
<thead>
<tr>
<th></th>
<th>DCM</th>
<th>HCM</th>
<th>RCM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commonest 90%</td>
<td></td>
<td></td>
<td>Least common</td>
</tr>
<tr>
<td>Systolic</td>
<td></td>
<td>Diastolic dysfunction</td>
<td>Diastolic dysfunction</td>
</tr>
<tr>
<td>dysfunction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dilated heart</td>
<td></td>
<td>obstructive CM</td>
<td>Compliance ↓</td>
</tr>
<tr>
<td>Hypertrophied</td>
<td></td>
<td>Hypertrophy ++</td>
<td>Normal</td>
</tr>
<tr>
<td>Hypocontracting</td>
<td></td>
<td>hypercontracting</td>
<td>Normal</td>
</tr>
<tr>
<td>Heavy, large,</td>
<td></td>
<td>Banana-like cavity left</td>
<td>-----</td>
</tr>
<tr>
<td>flabby</td>
<td></td>
<td>vent</td>
<td></td>
</tr>
<tr>
<td>Thin walls</td>
<td></td>
<td>Thick septum++</td>
<td>&quot;&quot;&quot;&quot;&quot;&quot;</td>
</tr>
</tbody>
</table>

CARDIOVASCULAR SYSTEM
# CARDIOVASCULAR SYSTEM

<table>
<thead>
<tr>
<th>Dilated</th>
<th>No dilation</th>
<th>-----</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombosis</td>
<td>Mural palque</td>
<td>-----</td>
</tr>
<tr>
<td>Hypertrophied cells/attenuated</td>
<td>Hypertrophy ++</td>
<td>-----</td>
</tr>
<tr>
<td></td>
<td>Myofiberdisarray</td>
<td></td>
</tr>
<tr>
<td>fibrosis</td>
<td>Fibrosis</td>
<td>Patchy/diffuse fibrosis +</td>
</tr>
</tbody>
</table>
Types of Cardiomyopathy

There are three main types of cardiomyopathy—dilated, hypertrophic, and restrictive. In dilated cardiomyopathy, the ventricles enlarge. In hypertrophic cardiomyopathy, the walls of the ventricles thicken and become stiff. In restrictive cardiomyopathy, the walls of the ventricles become stiff, but not necessarily thickened.
CARDIOMYOPATHIES

DCM
Genetic (30-40%)
↓ Non genetic
↓
Force generation ↓
DCM phenotype
↓
heart failure, sudden death, atrial fibrillation, stroke

HCM
100% genetic
↓
↓
force generation ↓
HCM phenotype
↓
CARDIOVASCULAR SYSTEM

TUMORS OF HEART:
Primary (rare)
Secondary/metastatic (5% dying patients)
Benign:
  - Myxoma
  - Fibroma
  - Lipoma
  - Papillary fibroelastoma
  - Rhabdomyomas
Malignant:
  - Angiosarcoma & other SAs
CARDIOVASCULAR SYSTEM

MYXOMA:
Commonest primary tumor
90% in atria → Atrial Myxoma
Left : right = 4 : 1
Single
Near fossa ovalis
<1 – 10 cm
Sessile / pedunculated → wrecking ball effect
→ embolize
CARDIOVASCULAR SYSTEM

Hard – soft gelatinous
Stellate cells (lepidic cells)
Endothelial cells
SMCs
Undifferentiated cells
Mucopolysaccharide ground substance ++
Endothelial covering
HEART FAILURE (Congestive heart failure):
Systolic dysfunction $\rightarrow$ forward failure ($\downarrow$ CO)
Diastolic dysfunction $\rightarrow$ backward failure
(venous damming)

Pressure overload
   HTN, Aortic stenosis
Volume overload
   regurgitant valves, myocardial infarction
$\rightarrow$ Myocardial hypertrophy
Compensatory Mechanisms During Heart Failure

Cardiac
- Frank-Starling mechanism
- Ventricular dilation or hypertrophy
- Tachycardia

Autonomic Nerves
- Increased sympathetic adrenergic activity
- Reduced vagal activity to heart

Hormones
- Renin-angiotensin-aldosterone system
- Vasopressin (antidiuretic hormone)
- Circulating catecholamines
- Natriuretic peptides
Causes of Heart Failure

- Myocardial infarction
- Coronary artery disease
- Valve disease
- Idiopathic cardiomyopathy
- Viral or bacterial cardiomyopathy
- Myocarditis
- Pericarditis
- Arrhythmias
- Chronic hypertension
- Thyroid disease
- Pregnancy
- Septic shock
Cardiac and Vascular Changes Accompanying Heart Failure

**Cardiac**
- Decreased stroke volume and cardiac output
- Increased end-diastolic pressure
- Ventricular dilation or hypertrophy
- Impaired filling (diastolic dysfunction)
- Reduced ejection fraction (systolic dysfunction)

**Vascular**
- Increased systemic vascular resistance
- Decreased arterial pressure
- Impaired organ perfusion
- Decreased venous compliance
- Increased venous pressure
- Increased blood volume
CARDIOVASCULAR SYSTEM

CARDIAC HYPERTROPHY:
Pressure overload hypertrophy
   HTN, aortic stenosis
concentric hypertrophy
thickened left vent wall $\rightarrow \downarrow$ chamber
sarcomere assembly parallel
cross sectional area of myocyte $\uparrow$ not length
Volume overload hypertrophy:
large MI, regurgitant valves
ventricular dilation
wall thickness ⇔ chamber diameter
sarcomere deposition vertical
↑ length and weight
Hypertension     Valvular disease     MI

Pressure overload     Pressure &/ Volume overload     Dysfunction & vol overload

↑ cardiac work

↓

↑ wall stress

hypertrophy &/ dilation

↓

cardiac dysfunction
Diastole (filling)

Normal: The ventricles fill normally with blood.

Systolic Dysfunction: The enlarged ventricles fill with blood.

Diastolic Dysfunction: The stiff ventricles fill with less blood than normal.

Systole (pumping)

Normal: The ventricles pump out about 60% of the blood.

Systolic Dysfunction: The ventricles pump out less than 40 to 50% of the blood.

Diastolic Dysfunction: The ventricles pump out about 60% of the blood, but the amount may be lower than normal.
A tight balance between adaptation and deleterious alterations

- ↓ capillary-to-myocyte ratio \( \rightarrow \) ↓ O2 & nutrients
- ↑ fibrous tissue
- molecular changes (shift to fetal expression)
- synthesis of abnormal proteins.

Sustained cardiac hypertrophy \( \rightarrow \) decompensation

\( \rightarrow \) Heart failure
Molecular & cellular changes that initially mediate enhanced function later contributes to heart failure.

- abnormal myocardial metabolism
- altered Ca handling
- apoptosis of myocytes
- reprogramming of gene expression
Left sided heart failure:

Causes:
- IHD
- HTN
- Aortic, mitral valvular disease
- non ischemic MC disease
CARDIOVASCULAR SYSTEM

Morphology:

Evidence of cause
enlarged size
↑ left vent wall thickness
ventricular dilation
secondary effects on atria
myocyte hypertrophy & interstitial fibrosis
Extracardiac effects:

1. Pulmonary congestion & edema
   - heavy, wet lungs
   - perivascular & interstitial edema
   → Kerly’s B lines
   - widening of alveolar septa
   - edema in alveolar spaces
   - heart failure cells
Blood overfills ventricle because of damaged heart muscle.

Blood overflows back into lungs causing pulmonary complications.
CARDIOVASCULAR SYSTEM

dyspnea
orthopnea
paroxysmal nocturnal dyspnea

2. Kidneys
   ↓ renal perfusion
   pre renal azotemia
3. Brain

  hypoxic encephalopathy

Right sided heart failure:

Causes

  left sided heart failure
  chronic severe pulmonary HTN
  cor pulmonale

  parenchymal lung disease
  primary pulmonary HTN
  recurrent pulmonary thromboembolism
CARDIOVASCULAR SYSTEM

Morphology
right atrial & ventricular hypertrophy, dilation
engorgement of systemic & portal venous
systems

1. Liver & portal system:
   congestive hepatomegaly (nutmeg liver)
centrilobular necrosis
cardiac sclerosis / cardiac cirrhosis
congestive splenomegaly
CARDIOVASCULAR SYSTEM

2. Kidneys:
   severely affected
   pronounced azotemia

3. Brain:
   venous congestion & hypoxia

4. Pleural & pericardial effusions

5. Ascites

5. Subcutaneous tissues:
   edema (pedal)
   anasarca
"Smooth seas do not make a skillful sailor."
CARDIOVASCULAR SYSTEM

HYPERTENSIVE HEART DISEASE (HHD)
An adaptive response
Systemic HTN $\rightarrow$ left HHD
Pulmonary HTN $\rightarrow$ right HHD

Systemic HHD:
1. Left ventricular hypertrophy
2. Evidence of HTN
Pressure overload = afterload $\rightarrow$ concentric
Hypertrophy
$\uparrow$ weight
Defective diastolic filling
Left atrial dilation
$\uparrow$ transverse diameter of myocyte
Variation in cell size
Interstitial fibrosis
Heart Disease in Hypertension
Pulmonary HHD:
COR PULMONALE
Right vent hypertrophy & dilation
Acute/chronic
Massive pulmonary embolism → acute PHHD
Prolonged pulmonary overload → chronic PHHD
CARDIOVASCULAR SYSTEM

Acute:

Ventricle dilated ++
NO HYPERTROPHY
Ovoid shaped vent cavity

Chronic:

hypertrophy
CARDIOVASCULAR SYSTEM

CONGENITAL HEART DISEASE:
Ventricular septal defects
Atrial septal defects
Pulmonary stenosis
Patent ductus arteriosus
Coarctation of aorta
AV septal defects
Transposition of great arteries
Truncus arteriosus
Tricuspid atresia
CARDIOVASCULAR SYSTEM

TETROLOGY OF FALLOT:

1. VSD
2. Sub-pulmonary stenosis
3. Overriding aorta over pulmonary stenosis
4. Right ventricular hypertrophy
CARDIOVASCULAR SYSTEM

HYPERTENSIVE VASCULAR DISEASE:
HTN carries potential risk of
  cardiac hypertrophy → heart failure
  coronary artery disease → IHD
  CVA
Genetic
Environmental factors
CARDIOVASCULAR SYSTEM

CAUSES:
Essential HTN
Secondary HTN:
  Renal
    AGN
    CRD
    polycystic disease
    renal artery stenosis
    renal vasculitis
  Renin producing tumors
CARDIOVASCULAR SYSTEM

Endocrine:
- Adrenocortical hyperfunction
- exogenous hormones
- pheochromocytoma
- acromegaly
- hypothyroidism
- hyperthyroidism
- pregnancy induced
CARDIOVASCULAR SYSTEM

Cardiovascular:

- coarctation aorta
- polyarthritis nodosa
- ↑ intravascular volume
- ↑ CO
- rigidity of aorta
CARDIOVASCULAR SYSTEM

Neurologic:

psychogenic

↑ intracranial pressure

sleep apnea

acute stress
CARDIOVASCULAR SYSTEM

PATHOGENESIS:

\[ BP = CO \times PR \]
Blood Volume & Pressure Controls
Renal Salt Excretion

- Increased blood volume (ECV) or pressure
  - Stimulation of baroreceptors (low, high, renal) & macula densa
  - Increased RBF & GFR, filtered salt load & peritubular capillary pressure
  - Increased [NaCl] at macula densa
  - Reduced renin release
  - Reduced Na⁺-reabsorption
  - Increased urine flow and salt excretion
- Reduced sympathetic & renal vascular resistance
- Reduced blood volume (ECV) or pressure
  - Reduced stimul of baroreceptors (low, high, renal) & macula densa
  - Reduced RBF & GFR, filtered salt load & peritubular capillary pressure
- Reduced blood volume (ECV) or pressure
  - Reduced [NaCl] at macula densa

Angiotensinogen → Renin → Angiotensin I

Angiotensin I → ACE → Angiotensin II

Angiotensin II → ACTH → Aldosterone

Aldosterone → Increased Na⁺-reabsorption

ADH → Reduced urine flow and salt excretion

Maintains effective circulating blood volume
Hypercholesterolaemia

ANS
- BR dysfunction
- ↑ SNS

ENDOTHELIUM
- ↓ NO
- ↑ ET-1
- ↑ AT1

RAS
- ↑ Expression of AT1
- ↑ RAS
- ↑ Na⁺ retention and volume expansion

RENAL
- ↑ Expression of AT1 and ET-1
- ↑ Blood pressure

CELL MEMBRANE
- ↑ Cholesterol / Phospholipid ratio
- ↓ Unsaturated fatty acyl groups
- ↓ Membrane fluidity
- ↑ [Ca²⁺] in VSMC
- ↑ Myogenic tone

Key: ANS = autonomic nervous system; RAS = renin-angiotensin system; BR = baroreceptor; NO = nitric oxide; ET-1 = endothelin 1; AT1 = angiotensin II type 1 receptor; VSMC = vascular smooth muscle cell; SNS = sympathetic nervous system; Na⁺ = sodium; Ca²⁺ = calcium

Source: Br J Cardiol © 2004 Sherbourne Gibbs, Ltd.
The pessimist complains about the wind. The optimist expects it to change. The leader adjusts the sails.
Case No: 1

A 50 years old businessman, hypertensive and obese, experiences severe chest pain on learning about his huge financial loss. He is rushed to the hospital where his ECG was done and some blood tests were taken.

1. What is the likely cause for his condition?
2. Discuss the pathogenesis of underlying pathology
3. What blood tests would be useful in this patient?
4. If the treatment was delayed in this patient then what morphological changes do you expect to find in his heart at 24 hours, 01 week and 02 weeks?
Case No: 2

20 years old girl is brought with ankle joint pain & shortness of breath. There is past H/O sore throat. On examination she is pale with weak heart sounds and tachycardia. ESR is 85 mm at end of first hour.

1. How will you proceed to reach a diagnosis?
2. What is the pathogenesis of this condition?
3. What are the complication associated with it?
CARDIOVASCULAR SYSTEM

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