1. Cardiovascular System Part 1

Cardiovascular System
Part 1

Basic Human Pathology II, 2008

Michael A. Kahn, DDS
Professor and Chairman
Department of Oral and Maxillofacial Pathology
Tufts University School of Dental Medicine

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

2. Normal Heart Anatomy

Normal Heart Anatomy

Image not available due to copyright restrictions.

Note: it is advisable to review normal pathology of the heart before viewing the rest of the presentation.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
3. The Heart

Image not available due to copyright restrictions.

4. Normal Vasculature

Image not available due to copyright restrictions.
5. Normal Vasculature

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

6. Normal Arterial and Venous Blood Flow

Source: http://www.nhlbi.nih.gov/
(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
7. Normal Muscular Artery Anatomy

Normal Muscular Artery Anatomy

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

8. Normal Vessel Anatomy

Normal Vessel Anatomy

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
9. Normal Cardiac Muscle

![Normal Cardiac Muscle](source)

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

10. Arterial Diseases/Disorders

**Arterial Diseases/Disorders**

- **Important causes of morbidity and mortality in most western societies**
- **Arteriosclerosis**
  - General term for three types of vascular disease
    > Monckeberg arteriosclerosis (medial calcific sclerosis)
    > Arteriolosclerosis
    > Atherosclerosis
  - Each has thickening and rigidity (sclerosis) of the walls of arteries
  - **Effects**
    - **Internal diameter of arterial lumen reduced so reduced amount of blood flow**
    - **Thickened and rigid arterial wall with reduction in ability to contract and relax**
    - **Loss of elasticity**

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
11. Arterial Diseases/Disorders

Arterial Diseases/Disorders

❖ Arteriolosclerosis
   – Hyaline thickening, hardening or proliferative changes of the walls of small arteries and arterioles, esp. kidneys
   – Usually wall completely effaced with destruction of thin smooth muscle layer
   – Most frequently consequence of systemic hypertension or diabetes mellitus

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

12. Arterial Disease/Disorders

Arterial Disease/Disorders

• Arteriolosclerosis variants (2)
  – Hyaline
    • Hyaline thickening of arteriolar walls
    • Kidneys – benign nephrosclerosis; associated with hypertension
  – Hyperplastic
    • Concentric, laminated, onionskin thickening of the arteriolar walls
    • May be accompanied by necrotizing arteriolitis
      – Intramural deposition of fibrinoid material; necrosis and inflammation
    • Kidneys – malignant nephrosclerosis; associated with malignant hypertension

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
13. Arterial Diseases/Disorders

Arterial Diseases/Disorders

- **Atherosclerosis (atheroma)**
  - Specific degenerative disease affecting large and medium arteries in systemic circulation
  - Most frequent cause of significant morbidity caused by vascular disease
  - Seen worldwide
    - Highest incidence in Finland, Great Britain, other northern European countries, United States, and Canada
- Begins affecting tunic intima -> tunica media -> thickening and hardening of artery wall
- Most common cause of arteriosclerosis of medium and large-sized arteries

14. Arterial Diseases/Disorders

Arterial Diseases/Disorders

- **Characteristics**
  - Atheromas are fibrous, lipid-rich plaques within the intima of high pressure arteries (large and medium, systemic; > 2mm)
    - Esp. proximal portions of the coronary arteries, larger branches of the carotid a., circle of Willis, large vessels of lower extremities (e.g., iliac, femoral), renal, and mesenteric arteries
  - **NOT** pulmonary arteries or any veins unless subjected to hypertension
15. Arterial Diseases/Disorders

Arterial Diseases/Disorders

❖ Atheromas composition

– Central core
  • Cholesterol and cholesterol esters
  • Lipid-laden macrophages (foam cells)
  • Calcium
  • Necrotic debris

– Subendothelial fibrous cap – covers core
  • Smooth muscle cells
  • Foam cells
  • Fibrin and other coagulation proteins
  • Extracellular matrix (collagen, elastin, glycosaminoglycans, and proteoglycans)

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

16. Well-developed Atheromatous Plaque

Well-developed Atheromatous Plaque

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
17. **Atheromatous Plaque**

**Atheromatous Plaque**

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

18. **Atheromatous Plaques**

**Atheromatous Plaques**

A = fibrous cap (F) and central lipid core (C) with moderately narrowed lumen (L);

B = internal and external elastic membranes destroyed and media thinned (arrow) under most advanced plaque;

C = junction of fibrous cap and core with calcification (large arrow) and neovascularization (small arrows)

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
19. Arterial Diseases/Disorders

Arterial Diseases/Disorders

- **Atheroma formation**
  - Damage to endothelium with entry of LDLs into intima
  - Lipid (LDLs) taken up by macrophages in the intima
    - A receptor-independent pathway allows excess lipid to accumulate --> visible pale bulge, the fatty streak

- **Fatty streak**
  - Focal accumulations in the intima of lipid-laden foam cells
  - May appear as early as first year of life
  - Present in the aorta of most older children

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

20. Fatty Streak

Fatty Streak

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
21. Fatty Streak – Foam cells in intima

Image not available due to copyright restrictions.

22. Arterial Diseases/Disorders

- Atheroma formation – cont’d
  - Macrophages release lipid into intima
  - Cytokines released by macrophages stimulate proliferation of myofibroblast (myointimal)-like cells of the intima → secrete collagen → plaque becomes fibrotic (raised yellow lipid plaques) → pressure atrophy of the intima and elastic lamina disrupted
  - Fibrous cap forms on the plaque (hard and white fibrolipid) with free lipid and oxidized lipid in macrophages
  - Collagenization of the media → weakened wall, endothelium ulcerates → platelets aggregate, thrombosis
23. Atheromatous Plaque Formation - 1

Atheromatous Plaque Formation - 1

Image not available due to copyright restrictions.

23

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS


Atheromatous Plaque Formation - 2

Image not available due to copyright restrictions.

24

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
25. Atheromatous Plaque Formation - 3

Atheromatous Plaque Formation - 3

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

26. Atheromatous Plaque Formation - 4

Atheromatous Plaque Formation - 4

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
27. Atherosclerosis Events and Cellular Interactions

Atherosclerosis Events and Cellular Interactions

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

28. Arterial Diseases/Disorders

Arterial Diseases/Disorders

- Atheromas (plaques) may be complicated by:
  - Ulceration
  - Hemorrhage
  - Calcification
  - Thrombus formation - - -> obstruction
  - Emobilization of overlying thrombus or of the plaque material itself

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
29. Atheromatous Plaque in Segments of Aorta

Atheromatous Plaque in Segments of Aorta

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

30. Atherosclerotic Coronary Artery

Atherosclerotic Coronary Artery – rupture of plaque and an overlying occlusive thrombus

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
31. Atherosclerotic Plaque Rupture

Atherosclerotic Plaque Rupture

Image not available due to copyright restrictions.

32. Atheroma Complication - Thromboembolism

Atheroma Complication - Thromboembolism

Image not available due to copyright restrictions.
33. Morphologic Manifestations

Morphologic Manifestations

Morphologic manifestations of coronary atherosclerosis, complications, and syndromes

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

34. Arterial Diseases/Disorders

Arterial Diseases/Disorders

Consequences – atherosclerosis
- Ischemic heart disease and myocardial infarction
  - Most significant since most common cause of death within the U.S.
  - Reduction in size of lumen
  - Poor perfusion of tissues --> hypoxia --> cell death may occur
- Thrombus formation
  - Intima and endothelium lining damage predispose
- Stroke
  - From cerebral ischemia and infarction

- Ischemic bowel disease
- Peripheral vascular occlusive disease
  - May observe claudication, ischemic necrosis, gangrene
- Renal arterial ischemia
  - With secondary hypertension
- Aneurysm formation
  - Weakening of the vessel wall
  - Tunic media structure changes --> elasticity loss with dilation over years
  - Especially large arteries
    - Ex. abdominal aorta below origin of renal arteries

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
35. Complications / Consequences

Complications / Consequences

Complications/Consequences of Atherosclerotic Plaque:

A = narrowing of artery
B = thrombus on plaque
C = bleed into plaque
D = aneurysm

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

36. Atherosclerosis in the Aorta

Atherosclerosis in the Aorta

A = mild with fibrous plaque
B = severe with diffuse, complicated lesions

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
37. Atherosclerosis in the Aorta

Atherosclerosis in the Aorta

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

38. Artherosclerosis in the Aorta

Artherosclerosis in the Aorta

Images not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
Arterial Diseases/Disorders

- **RISK FACTORS — ATHEROSCLEROSIS**
  - Increased age
  - More common in men in all groups
    - Also postmenopausal women
  - Familial
  - Hypercholesterolemia
    - Serum cholesterol may be exogenous (dietary) origin or endogenous (biosynthesis)
      - Cholesterol and dietary fats associate with apolipoprotein molecules and circulate as lipoproteins

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

Arterial Diseases/Disorders

- **RISK FACTORS — ATHEROSCLEROSIS (cont’d)**
  - Hypercholesterolemia — cont’d
    - Clinical predictors of atherogenesis
      - Relative concentrations of lipoprotein fractions
        - Ratio between Total/HDL cholesterol should be < 4.0; ratio between LDL/HDL should be < 2.5
        - Serum concentrations of LDL (“bad” cholesterol) directly related to risk
        - Serum concentrations of HDL (“good” cholesterol) inversely related to risk
          - Protective effect by removing cholesterol from tissues and from atherosclerotic plaques

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
41. Arterial Diseases/Disorders

Arterial Diseases/Disorders

- **Risk factors – atherosclerosis (cont’d)**
  - Hypertension
    - Major risk factor for and associated with premature atherosclerosis
  - Diabetes mellitus
    - Associated with premature atherosclerosis
    - Peripheral vascular occlusive disease often leading to gangrene of the lower extremities is common
  - Cigarette smoking
  - Others – less firmly established
    - Obesity, physical inactivity, “type A” personality, hyperuricemia, hyperhomocysteinemia, methylene tetrahydrofolate reductase mutations, lipoprotein A, infection with *Chlamydia pneumoniae*, and oral contraceptive drugs

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

42. Arterial Diseases/Disorders

Arterial Diseases/Disorders

- **Pathogenesis – atherosclerosis; still uncertain!**
  - Older hypotheses
    - Lipid Insudation
      - Infiltration of the intima with LDLs - - -> oxidized to toxic, pro-inflammatory and chemotactic factors; and protein is the primary atherogenic event, accelerated by hypercholesterolemia
    - Encrustations (thrombogenic)
      - Organization of repeated mural thrombi on the intimal surface leads to build up of plaques filled with lipid derived from breakdown of platelets and leukocytes
    - Monoclonal Proliferation
      - Smooth muscle migration and proliferation within atheroma as a neoplastic growth (single cell precursors) and hyperlipidemia may incite proliferation

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
Arterial Diseases/Disorders

Pathogenesis – atherosclerosis

Current hypothesis – Reaction to injury

- Primary event is chronic, low-grade injury to or dysfunction of arterial endothelium due to hypercholesterolemia, mechanical injury, hypertension, immune mechanisms, toxins, or viruses
- Hyperlipidemia may initiate endothelial injury, promote foam cell formation, chemotactic factor for monocytes, inhibit macrophage motility, or injure smooth muscle so that...

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

Arterial Diseases/Disorders

Pathogenesis – atherosclerosis

Current hypothesis – reaction to injury (cont’d)

- Entry of monocytes and lipid into subendothelium, sometimes with platelet adhesion and aggregation at the injury site
- Release of mitogenic factors (platelet-derived growth factor) from platelets, and perhaps monocytes
- Mitogenic growth factors induce proliferation and migration of smooth muscle into the intima -> production of c.f. matrix proteins
- Monocytes and smooth muscle engulf lipid and contribute to lipid deposition into lesions
  - Monocytes convert to lipid-laden foam cells

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
45. Pathogenesis of Atherosclerosis

Pathogenesis of Atherosclerosis

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

46. Atherosclerosis Pathogenesis

Atherosclerosis Pathogenesis

Processes in the Response to Injury Hypothesis – atherosclerosis pathogenesis

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
Atherosclerosis Pathogenesis

Processes in the Response to Injury Hypothesis – atherosclerosis pathogenesis

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

Summary of Atherosclerosis Pathology, Pathogenesis, Complications, Consequences, and Natural History

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
49. **Aneurysms**

**Aneurysms**

- An abnormal focal dilatation of an artery or vein

**Causes**
- Atherosclerosis – most frequent
- Any abnormality that weakens the t. media
- Permanent or transient hypertension

**Main complication**
- Erode adjacent structures or rupture
- Predisposition to thrombosis

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

50. **Ruptured Aortic Aneurysm**

**Ruptured Aortic Aneurysm**

Source: www.cdc.gov

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
51. Aneurysm

Aneurysm

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

52. Left Ventricular Aneurysm

Left Ventricular Aneurysm

Left Ventricular Aneurysm with bulging of wall (V)

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
53. Aneurysms - Types

Aneurysms - Types

- Atherosclerotic – common
  - Especially abdominal aorta (descending)
  - Thinning and replacement of media
- Berry – common
  - Small, saccular
  - Weak bifurcation sites of cerebral arteries (esp. circle of Willis)
    - Congenital defect(s) in elastic lamina/media
    - Unrelated to atherosclerosis
    - Most frequent cause of subarachnoid hemorrhage

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

54. Berry Aneurysm

Berry Aneurysm

Images not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
55. Aneurysm – Types (cont’d)

Aneurysm – Types (cont’d)

• Cystic medial necrosis - rare
  – Aortic root
  – Degenerative changes in the media with destruction of elastic and muscular tissues

• Syphilitic (luetic) – rare
  – Manifestation of tertiary syphilis
  ❖ Ascending aorta and arch - - -> sometimes aortic valve insufficiency
  – Obliterative endarteritis of the vasa vasorum and inflammatory destruction of media with fibrous replacement
    • “tree bark” gross appearance

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

56. Cystic Medial Necrosis

Cystic Medial Necrosis

Images not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
Aneurysm – Types (cont’d)

- **Arteriovenous fistula (aneurysm) - rare**
  - Abnormal communication between an artery and a vein
  - Can be secondary to trauma or other path processes that mechanically penetrate the walls of the artery and vein
  - May result in ischemic changes (diversion of blood), aneurysm formation (increased venous pressure), or high output cardiac failure (hypervolemia)

- **Infective (mycotic) - rare**
  - Any site
  - Destruction of wall by bacteria in infected thrombus

Dissecting Aneurysm

- **Longitudinal tear in the intima (intraluminal) -**
  - tracking of blood into the arterial media -
  - splits with second arterial lumen
  - Not a true aneurysm
  - No relation to atherosclerosis

- **Most common site is aorta**
  - False channel formed between the inner 2/3 and outer 1/3 of the medial thickness
59. Proximal Aortic Dissection

Proximal Aortic Dissection

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

60. Aneurysm with Dissection of Wall

Aneurysm with Dissection of Wall

L = lumen of vessel; D = dissection

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
61. Dissecting Aneurysm

Dissecting Aneurysm

- **Predisposing factors**
  - Hypertension – 70%
  - Degenerative changes in the aortic media (medial mucoid degeneration)
    - Often associated with disorder of support tissue e.g., Marfan syndrome, Ehlers-Danlos syndromes
  - Atherosclerosis
    - Original intimal tear at the edge of atheromatous plaque (esp. distal aorta)
  - Instrumentation of an artery
    - Ex – cannulation; arterial puncture
    - Often heals spontaneously without rupture

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

62. Dissecting Aneurysm

Dissecting Aneurysm

- **Severe, tearing chest pain often radiating through to the back**
  - Clinical differential diagnosis = acute MI
- **Often associated with cystic medial necrosis**
- **Possible outcomes**
  - External rupture of thoracic aorta - - - -> massive fatal hemorrhage into thoracic cavity
  - Retrograde spread (toward heart) - - - -> rupture into pericardial cavity - - - - -> fatal hemopericardium (cardiac tamponade)
  - Internal rupture - - - -> rupture through inner media and intima - - - - -> blood back into lumen - - - -> double channeled aorta

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
63. Three Outcomes Following Aortic Dissecting Aneurysm

Three Outcomes Following Aortic Dissecting Aneurysm

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

64. Ruptured Aortic Abdominal Aneurysm

Ruptured Aortic Abdominal Aneurysm

Images not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
Hypertension

- Sustained diastolic pressure arbitrarily assigned greater than 90 mmHg
  - There is no threshold below which a person has no risk of developing pathology
- Blood pressure is a continuous variable in the population with increase in its value --> increase risk of disease
- An important and treatable cause of disease

---

Pathological consequences
- Heart
  - Left ventricular myocardium hypertrophy
  - Coronary blood flow may be insufficient --> ischemic heart disease --> left ventricular failure
- Brain
  - Rupture of intracerebral blood vessels --> massive intracerebral hemorrhage and microinfarcts of the cerebral hemispheres filled with fluid (hypertensive lacunae)
67. **Left Ventricular Myocardium Hypertrophy**

*Image not available due to copyright restrictions.*

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

68. **Hypertension**

- **Pathological consequences - cont’d**
  - Kidney
    - Arteriosclerosis \(\rightarrow\) progressive ischemia of the nephron (slowly, one at a time) \(\rightarrow\) glomeruli destruction and atrophy of tubules
    - \(\rightarrow\) slowly progressive chronic renal failure and benign hypertensive nephrosclerosis, esp. in middle-aged and elderly population
  - Aorta
    - Severe atherosclerosis
    - Abdominal aortic aneurysms
    - Dissecting aneurysms

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
Hypertension

- Primary (essential)
  - Elevation of blood pressure with age but with unknown etiology
    - 90-95% of all cases
    - Usually occurs after age 40
  - Determinants – interaction
    - Genetic (familial) predisposition
      - African lineage more common
    - Obesity
    - Increased dietary sodium intake
    - Increased stress
    - Increased alcohol consumption
    - Physical inactivity
    - Cigarette smoking

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

Hypertension

- Primary (essential)
  - Can predispose to ischemic heart disease or stroke
  - If not treated then
    - Retinal changes
    - Left ventricular hypertrophy
      - Cardiac failure
    - Benign nephrosclerosis

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
71. Hypertension

Hypertension

- Secondary ("to causes")
  - About 5-10% of all cases
  - Mechanism
    - Activation (stimulation) of the renin-angiotensin-aldosterone system
      - Juxtaglomerular cells respond to decreased vascular tone by secreting renin $\rightarrow$ angiotensin I $\rightarrow$ angiotensin II $\rightarrow$ vasoconstrictor and aldosterone secretion $\rightarrow$ sodium and water retention

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

72. Regulation of Blood Pressure

Regulation of Blood Pressure

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
73. Hypertension

Hypertension

- Secondary – cont’d
  - Etiology
    - Renal disease – most often by far
      - Disorders of the renal parenchyma
        - Postinfectious glomerulonephritis, adult polycystic disease, diabetic nephropathy
      - Unilateral renal artery stenosis
        - Caused by atherosclerosis or unilateral fibromuscular dysplasia

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

74. Hypertension

Hypertension

- Secondary – cont’d
  - Etiology
    - Endocrine disorders
      - Primary aldosteronism (Conn syndrome)
        - Assoc. with adrenocortical adenoma or bilateral adrenal hyperplasia
        - Increased serum Na⁺ and reduced serum K⁺ --> sodium and water retention
      - Diabetes mellitus
        - If complicated by diabetic glomerulosclerosis

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
75. **Hypertension**

### Secondary – cont’d
- **Etiology (cont’d)**
  - Endocrine disorders (cont’d)
    - Pheochromocytoma
      - Epinephrine-norepinephrine secreting tumor of the adrenal medulla → paroxysmal hypertension
    - Acromegaly
    - Cushing syndrome – excess cortisol
    - Hypothyroidism
    - Hyperparathyroidism

76. **Hypertension**

### Secondary (“to causes”) – cont’d
- **Etiology (cont’d)**
  - Other causes
    - Coarctation of the aorta
      - Congenital narrowing of the aorta → arms, head and neck affected
      - Increased collateral circulation → rib notching
    - Preeclampsia
      - Toxemia of pregnancy
    - Neurogenic
    - CNS disorders
      - Esp. brain tumors
    - Drugs and chemicals (poisons)
      - Steroids
      - Amphetamines

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
77. Hypertension

Hypertension

• **Clinical course**
  - Benign type
    • Stable elevation over many years
  - Malignant (accelerated) type
    • Severe elevation and worse over a short period of time

78. Hypertension

Hypertension

• **Benign type**
  - Vessel changes occur gradually in response to a persistent stable elevated blood pressure
  - Tissue ischemia and brain vessel fragility, hemorrhage
  - Small arterial change
    • Hypertrophy and thickening of the muscular media
    • Thickening of elastic lamina
    • Fibroelastic thickening of the intima
    • Reduction in lumen size
  - Arteriole change
    • Hyaline wall thickening (hyaline arteriosclerosis)
    • Increased rigidity (limited capacity to expand and constrict)
    • Reduction in lumen size
79. Benign Hypertension

Benign Hypertension

Images not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

80. Hypertension

Malignant type

- Can be complication of either essential or secondary hypertension
- Accelerated clinical course
- Sudden, marked increase in diastolic blood pressure
  - - - > acute, destructive changes and proliferative reparative responses in the small vessel walls (intimal only)
  - - - > cessation of blood flow through the small vessels
  - - - > multiple foci of tissue necrosis (e.g., renal glomeruli)
- Focal retinal hemorrhages and papilledema
- Left ventricular hypertrophy
- Left ventricular failure

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
81. Malignant Hypertension

Malignant Hypertension

Images not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

82. Malignant Hypertension

Malignant Hypertension

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
83. Hypertension

Hypertension

- Malignant type
  - Occurs in < 5% of patients with elevated blood pressure, most often young African-American males
  - Most often results in early death from congestive heart failure, CVA, or kidney failure
  - Malignant nephrosclerosis
    - Arterioles or glomerular capillaries rupture
    - -> "flea-bitten" kidney
    - Multiple pinpoint petechial hemorrhages
  - Large, swollen kidneys
  - Necrotizing arteriolitis
  - Glomerulitis with fibrinoid necrosis
  - Hyperplastic arteriolosclerosis

84. Hypertension

Hypertension

- Pulmonary arterial hypertension
  - Consequence of increased pressure in the pulmonary capillary bed due to:
    - Raised pressure in the left atrium and left ventricle
      - Inadequate emptying of the left heart chamber (left heart failure) due to:
        - Ischemic heart disease
        - Aortic valve stenosis
        - Mitral valve stenosis
    - Destruction lung capillary bed
      - Emphysema
      - Interstitial fibrosis of lungs
85. Pulmonary Hypertension

Pulmonary Hypertension

- Increased pulmonary flow
  - Cardiac shunts (ASD, VSD)
- Pulmonary venous congestion
  - Mitral valve disease especially stenosis
  - Chronic left ventricular failure
- Mechanical arterial occlusion
  - Multiple pulmonary thromboemboli
  - Foreign body emboli (drug addicts)
- Alveolar hypoxia causing pulmonary vasoconstriction
  - High altitude
  - Obesity
  - Chronic obstructive airways disease
- Destruction of lung capillary bed
  - Emphysema
  - Interstitial fibrosis of lungs
- Idiopathic
  - Primary pulmonary hypertension: rare disease of young women due to increased tone in pulmonary vessels, leading to progressive vascular changes and death
  - Pulmonary veno-occlusive disease: rare disease causing fibrous obliteration of pulmonary vessels – some case thought to be due to vascular thrombosis

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

86. Vasculitis

Vasculitis

- Inflammation and damage to the vessel wall
  - Capillaries, venules, arterioles, arteries and occasionally large veins
- In mild cases, transient damage with only visible change being cellular infiltration and leakage of red blood cells
- In severe cases leads to irreversible vessel wall destruction

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
87. Medium to Small Vessel Vasculitis

Medium to Small Vessel Vasculitis

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

88. Vasculitis Syndromes (Vasculitides)

Vasculitis Syndromes (Vasculitides)

- Inflammatory and often necrotizing vascular lesions that occur in almost any organ
- Usually mediated by immune mechanisms
  - Most often immune complex depositions
  - Frequent antigens in immune complexes
    - DNA
    - Hepatitis B surface antigen
    - Hepatitis C RNA

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
89. Vasculitis Syndromes (Vasculitides)

Vasculitis Syndromes (Vasculitides)

- **Main groups (3)**
  - Hypersensitivity – most common
    - Capillaries and venules affected
    - Skin rash usually
    - Ex. – drug allergy, viremia, bacteremia, Henoch-Schonlein purpura, serum sickness, cryoglobulinemia
  - Multiorgan autoimmune diseases
    - Ex. - systemic lupus erythematosus and rheumatoid arthritis
  - Systemic
    - Unknown etiology with differing patterns of vessel wall destruction
    - Ex. – polyarteritis nodosa

90. Vasculitis

**Polyarteritis nodosa**

- Necrotizing immune complex inflammation small and medium sized arteries
- Systemic disease; patchy and focal
- Marked by destruction of arterial media and internal elastic lamella \(\rightarrow\) aneurysmal nodules
- Etiology unknown
  - Probably immune complex mediated
  - Association with chronic hepatitis B infection – 30%
- Inflammatory necrosis of small and medium sized arteries’ intima \(\rightarrow\) thrombosis \(\rightarrow\) vessel occlusion \(\rightarrow\) small areas of infarction
91. Vasculitis

Vasculitis

- **Polyarteritis nodosa – cont’d**
  - Sites
    - *Especially kidneys*
      - Microinfarcts; immune complex vasculitis in the arteries and glomeruli
      - Most often causes death – renal lesions and hypertension
    - Heart (infarction)
      - Coronary arteries – ischemic heart disease
    - Alimentary tract
      - Microinfarcts; nausea, vomiting, or abdominal pain
    - Liver
    - CNS (infarction) or peripheral nerves (necrosis)
    - Musculoskeletal system
      - Myalgia, arthralgia, or arthritis
    - Skin
    - Eye

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

92. Polyarteritis Nodosa – Skin Involvement

Polyarteritis Nodosa – skin involvement

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
93. Vasculitis

Vasculitis

• Polyarteritis nodosa – cont’d
  ❖ Often associated with perinuclear antineutrophil cytoplasmic antibodies (P-ANCAs)
    – Clinical
      • Fever, weight loss, malaise, abdominal pain, headache, myalgia, and hypertension
    – Histology
      • Frequently fibrinoid necrosis of a segment of artery wall
      • Necrosis of muscle cells, destruction of elastic lamina - - -> healing - - - - > fibrous replacement

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

94. Polyarteritis Nodosa

Polyarteritis Nodosa

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
Vasculitis

**Wegener granulomatosis**
- Disease of unknown etiology characterized by necrotizing granulomatous vasculitis of the small- to medium-sized vessels of the respiratory tract, kidneys, and other organs
- Dominated by respiratory signs and symptoms esp. paranasal sinuses and lungs, and necrotizing glomerulonephritis

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

Wegener granulomatosis - cont’d
- Manifested by fibrinoid necrosis of small arteries and veins, early infiltration by neutrophils, subsequent mononuclear infiltration, and fibrosis
- Granuloma formation with giant cells is prominent
- Most cases have circulating antineutrophil cytoplasmic antibodies with a cytoplasmic staining pattern (C-ANCAs)

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
97. Wegener Granulomatosis

Wegener Granulomatosis

- Gingival changes
- Neutrophil (green) and giant cell (blue) vasculitis

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

98. Vasculitis

Vasculitis

- **Giant cell arteritides**
  - Seen in medium- to large-sized arteries
  - Characterized by granuloma formation with giant cells
  - Infiltrates of mononuclear cells, neutrophils, and eosinophils
  - Two distinct clinical syndromes
    - Temporal arteritis
    - Takayasu arteritis (pulseless disease)

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
99. Giant Cell Arteritis

Giant Cell Arteritis

Image not available due to copyright restrictions.

100. Vasculitis

Vasculitis

- **Temporal arteritis (giant cell arteritis)**
  - Systemic disease, mainly involves head and neck, and the most frequently occurring form of vasculitis
  - Usually affects branches of the carotid artery, particularly temporal artery
    - Particularly affects temporal region
    - Sudden blindness due to ophthalmic artery
  - Elderly - > 50 years old; > women
  - Lab sign/diagnosis
    - Very high ESR/biopsy
101. Vasculitis

Vasculitis

- Temporal arteritis (giant cell arteritis)
  - Other symptoms ill-defined
    - Malaise, headache, claudication of the jaw, tenderness, absent pulse, palpable nodules along the course of the involved artery
    - Visual impairment, polymyalgia rheumatica
  - Histology
    - Vessel wall thickened, infiltrated by inflammatory cells (T lymphocytes, histiocytes, giant cells); disrupted elastic lamina
    - Often associated polymyalgia arthritis
    - Complication by thrombosis is common

102. Temporal Arteritis

Temporal Arteritis

Images not available due to copyright restrictions.
103. Temporal Arteritis

**Temporal Arteritis**

Giant cells (arrow) within a granuloma (circle) of granulomatous inflammation

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

104. Vasculitis

**Vasculitis**

- **Buerger’s disease (thromboangiitis obliterans)**
  - Acute inflammatory occlusion of small to medium sized arteries of the upper and lower limbs extending to adjacent veins and nerves
  - Related to heavy cigarette smoking
    - > young men esp. Jewish populations
  - Histology
    - Segmental inflammatory infiltration of the walls of arteries and veins with secondary thrombosis
    - Neutrophils and granulomas
    - Patients succumb to peripheral vascular insufficiency

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
105. Buerger’s Disease (Thromboangiitis Obliterans)

Buerger’s Disease
(Thromboangiitis Obliterans)

Image not available due to copyright restrictions.

106. Vasculitis Syndromes

<table>
<thead>
<tr>
<th>Vasculitis syndromes</th>
<th>Vasculitis</th>
<th>Clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersensitivity angiitis</td>
<td>Neutrophilic, fibrinoid necrosis</td>
<td>Skin, kidney</td>
</tr>
<tr>
<td>Polyarteritis nodosa</td>
<td>Neutrophilic, fibrinoid necrosis</td>
<td>Multiorgan</td>
</tr>
<tr>
<td>Wegener’s granulomatosis</td>
<td>Neutrophilic and giant cell</td>
<td>Nasal, lung and renal involvement</td>
</tr>
<tr>
<td>Churg-Strauss syndrome</td>
<td>Histiocytic and eosinophils</td>
<td>Lung, kidney, heart, skin</td>
</tr>
<tr>
<td>Kawasaki arteritis</td>
<td>Lymphocytic; endothelial necrosis</td>
<td>Skin, heart, mouth, eyes</td>
</tr>
<tr>
<td>Takayasu’s disease</td>
<td>Histiocytic; giant cell</td>
<td>Aorta and arch branches</td>
</tr>
<tr>
<td>Buerger’s disease</td>
<td>Neutrophil; granulomatous</td>
<td>Leg arteries and veins; gangrene</td>
</tr>
<tr>
<td>Connective tissue disease, eg. SLE</td>
<td>Lymphocytic</td>
<td>Skin, muscle, brain</td>
</tr>
<tr>
<td>Erythema nodosum</td>
<td>Venulitis and panniculitis</td>
<td>Deep tender lumps in legs</td>
</tr>
<tr>
<td>Pyoderma gangrenosum</td>
<td>Vasculitis and skin ulcers</td>
<td>Necrotizing ulcers of skin and subcutis</td>
</tr>
</tbody>
</table>

© 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
107. Structural Abnormalities of Veins

Structural Abnormalities of Veins

- Dilatation and congestion with blood
- Veins in pelvis and lower limbs can be aggravated by any pelvic or abdominal condition, pressure on the veins, prevention of adequate venous return
  - Pregnancy, obesity, thrombophlebitis, prolonged standing

- Varicose veins
  - Persistent, distended and tortuous superficial veins in the lower limbs
  - Incompetence of the valves allow engorgement with blood due to gravity
  - Predisposed by increased venous pressure

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

108. Varicose Veins

Varicose Veins

Images not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
109. Structural Abnormalities of Veins

Structural Abnormalities of Veins

- **Hemorrhoids**
  - Greatly distended veins in the anal canal and anorectal junction
  - Prolapsed mucosa-covered masses which often protrude through the anal orifice
  - Bleeding - may follow trauma
  - Pain - from gross protrusion and anal sphincter spasm

- **Esophageal varices**
  - Distended venous channels that develop in portal hypertension secondary to cirrhosis of the liver

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

110. Esophageal Varix

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
111. Venous Disorder

Venous Disorder

- **Venous thrombosis (phlebothrombosis)**
  - Arises most often in deep veins of the lower extremities
  - Predisposed by venous circulatory state or partially obstructed venous return such as occurs with cardiac failure, pregnancy, prolonged bed rest or varicose veins
  - May give rise to embolism with resultant pulmonary infarction
    - Hemorrhagic, subpleural, and wedge-shaped
  - Often associated with inflammation (aka thrombophlebitis)

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS

112. Venous Thrombosis

Venous Thrombosis

Images not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
113. Benign Tumors and Malformation of Vessels

Benign Tumors and Malformation of Vessels

- Most not true neoplasms but malformations / hamartomas
- **Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome)**
  - Autosomal dominant; localized dilation and convolution of venules and capillaries of the skin and mucous membranes
  - Often complicated by epistaxis or GI bleeding
- **Spider telangiectasia**
  - Dilated small vessel surrounded by radiating fine channels
  - Associated with hyperestrinism as seen in chronic liver disease or pregnancy

114. Hereditary Hemorrhagic Telangiectasia

Hereditary Hemorrhagic Telangiectasia

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
115. Benign Tumors and Malformation of Vessels

Benign Tumors and Malformation of Vessels

- **Hemangioma (angioma)**
  - Developmental malformation derived from a larger blood vessel composed of masses of channels filled with blood
  - Most common tumor of infancy and is responsible for port-wine stain birthmarks

- **Lymphangioma**
  - Often a component of hamartomatous malformations in the subcutaneous tissue of the neck and upper trunk in young people
  - Cystic hygroma – variant of lymphangioma
    - Predominant, enormously dilated lymphatic vessels in the neck or axilla in young persons (esp. neonatal)

116. Hemangioma

Hemangioma

Source: Tufts School of Dental Medicine

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
117. Hemangioma

Hemangioma

Images not available due to copyright restrictions.

118. Benign Tumors and Malformation of Vessels

Benign Tumors and Malformation of Vessels

- Hemangioma – cont’d
  - Capillary type
    - Tangle of closely packed, small, capillary-like channels
    - Skin, subcutaneous tissue, lips, liver, spleen, or kidneys
  - Cavernous type
    - Large, cavernous vascular spaces in the skin and mucosal surfaces and internal organs (e.g., liver, pancreas, spleen, and brain)
Malignant Vascular Tumors

- **Kaposi's sarcoma**
  - Derived from endothelial cells or multipotential mesenchymal cells?
  - Strong and possible causative association with HSV8
  - 3 stages
    - Patch – flat, bruise-like, purple
    - Plaque – slightly raised, firm, purple
    - Nodular – dome-shaped, firm, purple

Malignant Vascular Tumors

- **Kaposi's sarcoma four patterns of disease**
  - Endemic (African)
    - Highly malignant in children, more indolent in adults; based in lymph nodes
  - Classic
    - Rare; lower limbs of elderly males of Ashkenazic Jewish or Mediterranean origin
    - Low-grade within skin with blood and lymph mets
  - Therapeutic immunosuppression
    - Low-grade within skin
  - Epidemic
    - Component of AIDS, esp. homosexual males
    - May be related to coinfection with KS herpes virus
    - Highly malignant skin tumor with spread to lymph nodes and visceral organs
121. Kaposi’s Sarcoma

Kaposi’s Sarcoma

Images not available due to copyright restrictions.

122. Functional Vascular Disorders

Functional Vascular Disorders

- **Raynaud disease**
  - Recurrent vasospasm of small arteries and arterioles with resultant pallor or cyanosis
  - Most often in the fingers and toes
- **Raynaud phenomenon**
  - Clinically similar to R. disease but always secondary to an underlying disorder (e.g., lupus erythematosus, progressive systemic sclerosis [scleroderma])

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS
Raynaud Disease

Image not available due to copyright restrictions.

(c) 2007, Michael A. Kahn, DDS/Lynn W. Solomon, DDS