DISORDERS OF BLOOD FLOW

CHAPTER 24
HYPERLIPIDEMIA

- TYPES OF LIPIDS:
  - 1) TRIGLYCERIDES: used for metabolic energy.
  - 2) PHOSPHOLIPIDS: components of cell membranes, myelin sheath, clotting factors.
  - 3) CHOLESTEROL: hormone precursor, cell membranes

- Cholesterol and triglycerides are insoluble in blood, transported attached to fat-carrying proteins = lipoproteins.
LIPOPROTEINS

5 TYPES:
1) CHYLOMICRONS
2) VLDL- very low density lipoprotein.
3) IDL- intermediate density lipoprotein.
4) LDL- low density lipoprotein.  
5) HDL- high density lipoprotein.
LIPOPROTEINS

- For everything you ever wanted to know about lipid metabolism, see:
  - http://www.acpmedicine.com/sample/ch0902s.htm
LDL – WHERE IT COMES FROM

- Synthesized in the liver. Also:

- VLDL: synthesized in the liver, contains triglycerides and cholesterol.

- VLDL → carries triglycerides to fat and muscle → triglycerides are removed for energy or storage → VLDL becomes IDL, rich in cholesterol → recycled in the liver into VLDL or converted in the blood to LDL.
LDL

- The main carrier of cholesterol.
- “Bad” cholesterol- involved in the genesis of atherosclerosis.
- Removed from the circulation by:
  
  1) Non-receptor mechanisms- scavenger cells: monocytes, macrophages.
  
  2) 70%: LDL receptor-dependent pathway.
LDL RECEPTOR-DEPENDENT PATHWAY

- 75% are located on the hepatocytes.

- LDL binds to the receptor $\rightarrow$ endocytosis $\rightarrow$ fuses w/ lysosomes $\rightarrow$ LDL enzymatically degraded $\rightarrow$ free cholesterol released into the cytoplasm.
NON-HEPATIC LDL RECEPTORS

- Adrenals, smooth muscle, endothelial cells, lymphoid cells.
- Use cholesterol for membrane production and hormone synthesis.
- When LDL level exceeds receptor availability
  → LDL removed by scavengers → uptake of LDL by macrophages in the arterial wall → accumulation of cholesterol esters → atherosclerosis.

Not clinically significant, but when LDL level exceeds receptor availability, part of it remains in the vessel wall.
HDL

- Synthesized in the liver.
- “Good cholesterol.”
- Carries cholesterol from the tissues to the liver where it is excreted.
- Also clears cholesterol from atheromatous plaques excreted by the liver.
HYPERCHELOSTEROLEMIA

- **NCEP: National Cholesterol Education Project**
- **RECOMMENDS:**
  - Fasting lipoprotein panel: Total cholesterol, LDL, HDL, Triglyceride.
  - Beginning at age 20.
  - Every 5 years, if “normal.”
  - More often if elevated or increased risk of cardiovascular disease.
HYPERCHOLESTEROLEMIA

- ELEVATED CHOLESTROL DUE TO:
  - 1) Nutrition / diet (your fettuccini Alfredo).
  - 2) Genetics (your uncle Alfredo).
  - 3) Metabolic disease (thyroid disease, diabetes).

MOST CASES ARE MULTIFACTORIAL
Combination of over-consumption, under-excretion, inadequate LDL receptor function or number, etc
“NORMAL” VALUES

- TOTAL CHOLESTEROL:

  DESIRABLE: < 200

  BORDERLINE HIGH: 200 – 239

  HIGH: ≥ 240
“NORMAL” VALUES

- **LDL:**

  OPTIMAL: < 100
  NEAR OPTIMAL / ABOVE OPTIMAL: 100 - 129
  BORDERLINE HIGH: 130 – 159
  HIGH: 160 – 189
  VERY HIGH: ≥ 190
“NORMAL” VALUES

- **HDL:**
  
  LOW: < 40

  HIGH: ≥ 60
ATHEROSCLEROSIS

- A type of arteriosclerosis.
- 40% of all deaths in the U.S.: due to M.I., stroke, peripheral vascular disease.
- The formation of “fibro fatty” lesions in the intimal lining of the arteries.
- Medium and large: aorta, its branches, coronaries.
ATHEROSCLEROSIS

MOST COMMONLY AFFECTED AREAS:

- 1) ABDOMINAL AORTA, ILIAC BRANCHES.
- 2) CORONARY ARTERIES.
- 3) THORACIC AORTA.
- 4) FEMORAL, POPLITEAL ARTERIES.
- 5) INTERNAL CAROTID.
- 6) VERTEBRAL, BASILAR, MIDDLE CEREBRAL ARTERIES.
RISK FACTORS FOR ATHEROSCLEROSIS

1) AGE:
Men > 45
Women > 55, or w/ premature menopause and no E.R.T

2) FAMILY Hx OF PREMATURE CHD:
M.I. / Sudden death < 55 in father or 1st degree male relative; OR < 65 in mother or 1st degree female relative.
RISK FACTORS FOR ATHEROSCLEROSIS

3) SMOKING (CURRENT).
4) HYPERTENSION, OR ON MEDS.
5) HDL < 40.
6) DIABETES MELLITUS.
7) PRESENCE OF C-REACTIVE PROTEIN (CRP)

PROTECTIVE (“NEGATIVE RISK FACTOR”)
HDL > 60.
MECHANISM OF DEVELOPMENT

3 TYPES:

1) FATTY STREAK
2) FIBROUS ATHEROMATOUS PLAQUE
3) COMPLICATED LESION
FIBROUS ATHEROMATOUS PLAQUE

- Accumulation of intra- and extra-cellular lipids.
- Proliferation of vascular smooth muscle.
- Formation of scar.

- Results in:
  1) ↓ lumen size → ↓ flow → occlusion.
  2) Thrombus formation.
THE COMPLICATED LESION

- Has elements of the atheromatous plaque, but w/ hemorrhage, ulceration, and scar tissue debris.

- Thrombosis caused by ↓ flow and ulceration of the plaque (plaque rupture).
THE ACTUAL CAUSE

Still being investigated, but what we know is that it involves:

1) Hemodynamic factors, turbulent flow.

2) Damage to the endothelial/intimal lining of the vessel- by smoking, hypertension, immune mechanisms, free radicals, other.
HOW IT HAPPENS

↑ LDL → Monocytes attach to endothelium → migrate into sub-endothelial spaces → release free radicals → oxidize LDL.

Oxidized LDL → endothelial loss, exposure of sub-endothelial tissue → platelet adhesion, fibrin deposition.

Factors released, promoting proliferation of vascular smooth muscle, deposition of an extracellular “matrix.”
HOW IT HAPPENS

Macrophages ingest oxidized LDL → become “foam” cells → release lipids → forms the lipid core of an unstable plaque.

plaque is structurally unstable, breaks off and creates an embolus. embolism is a free floating thrombus.
CLINICAL MANIFESTATIONS

1) ACUTE ARTERIAL OCCLUSION
2) ATHEROSCLEROTIC P.V.D.
3) RAYNAUD’S
4) ANEURYSMS
5) AORTIC DISSECTION
6) STROKE
7) CARDIOVASCULAR DISEASE (CVD), AKA CORONARY ARTERY DISEASE (CAD), AKA ASCVD = ARTERIOSCLEROTIC CORONARY VASCULAR DISEASE.

Claudication: pain related to severe slowing of blood flow. Do slow walking to create blood vessels to bypass clots. This is collateral flow.
ACUTE ARTERIAL OCCLUSION

- Usually the result of an embolus or thrombus.
- Occasionally by spasm, foreign body.
- **EMBOLI:** most result from cardiac disease:
  - Myocardial ischemia
  - Atrial fib.
  - Rheumatic heart disease.
  - Prosthetic valves.
  - Occasionally fat emboli, amniotic fluid.

  abnorm heart rhythm - top 2 chambers fibrilate, not contract. Flow of blood then gets turbulent, causing tiny blood clot in the atria, embolus forms on its' own, can then go into blood stream. Patients with chronic atrial fib are on blood thinners for this reason.

  This can cause turbulent flow also. Porcine valves work better, but don't last as long.

Most common cause of arterial occlusion.
ACUTE ARTERIAL OCCLUSION

- EMBOLI: TEND TO LODGE IN THE BIFURCATION OF MAJOR ARTERIES – AORTA / ILIAC, FEMORAL / POPLITEAL.
ACUTE ARTERIAL OCCLUSION

SIGNS / SX’S OF ARTERIAL OCCLUSION

- The Seven P’s:
- 1) Pistol shot (sudden)
- 2) Pallor
- 3) Polar (cold)
- 4) Pulselessness
- 5) Pain
- 6) Paresthesias
- 7) Paralysis.

Tissue death occurs if circulation not restored.
ATHEROSCLEROTIC PERIPHERAL VASCULAR DISEASE

Your text calls this Atherosclerotic Occlusive Disease
Atherosclerotic Peripheral Vascular Disease

- Atherosclerosis of the vessels of the LE: femoral, popliteal arteries.
- Risk factors: same as for atherosclerosis elsewhere.
- Disease is worse in diabetics.
- Primary symptom is intermittent claudication.
  Other Sx’s: thin skin, pallor, atrophic changes, decreased size of the extremity
- Signs: LE is cool, ↓ popliteal / pedal pulse.

Claudication = pain produced by walking, often in the calves. Pain is caused by inadequate flow, not complete occlusion.
ATHEROSCLEROTIC PERIPHERAL VASCULAR DISEASE

- **DIAGNOSIS:**
  - Physical exam, doppler studies, ultrasound, MRI, angiography.

- **TREATMENT:**
  - Evaluate for co-existing C.A.D. (huge), antiplatelet meds, others, surgery: ie a “fem-pop” = a femoral-popliteal bypass.
RAYNAUD’S

- Intense vasospasm of the arteries and arterioles of the fingers, occasionally toes.
- Vasospasm = excessive vasoconstriction in response to stimuli that typically cause only mild to moderate vasoconstriction.
- Ischemia → Pallor → Cyanosis → Numbness, tingling.
- After the ischemia → hyperemia → throbbing, paresthesias → normal color
RAYNAUD’S

- Comes in 2 exciting flavors:
  - 1) Raynaud’s Disease.
  - 2) Raynaud’s Phenomenon
RAYNAUD’S DISEASE

- “Primary.” Occurs w/ no demonstrable cause.
- Otherwise healthy young women.
- Precipitated by cold, emotions.
- More benign than Raynaud’s phenomenon.
- Specific cause unknown.
RAYNAUD’S PHENOMENON

- Occurs in association w/ other diseases, conditions.
- Seen w/ previous vessel injury (trauma), frostbite
- Also seen in collagen diseases (sometimes called collagen vascular disease or connective tissue disease), chronic arterial occlusive disease, some neurologic diseases.
- Often is the 1st sign of a collagen disease, such as scleroderma.
ANEURYSMS

- An abnormal dilatation of a vessel.
- More common in arteries, esp. the aorta.
- **2 TYPES:**
  - 1) **TRUE-** $\uparrow$ diameter of 50%. Bounded by a complete vessel wall.
  - 2) **FALSE:** Localized dissection or tear of the inner wall of the artery w/ an extra-vascular hematoma- bounded only by outer layers of vessel wall.
ANEURYSMS

- **BERRY**: Small, spherical dilatation, typically found at a bifurcation, such as the Circle of Willis.
- **FUSIFORM**: Involves entire circumference of the vessel; gradual, progressive dilatation; up to 20 cm; thoracic and abdominal aorta.
- **SACCULAR**: Extends over part of the circumference of the vessel.
ANEURYSMS

**CAUSES:**
- 1) Congenital.
- 2) Trauma.
- 3) Infection (syphilis).
- 4) Atherosclerosis.

Weakness in the wall allows for growth in size → ↑ tension → ↑ risk of rupture.
AORTIC ANEURYSMS

- 90% are abdominal.
- Thoracic aneurysms - tertiary syphilis.
- Usually below the level of the renal arteries, involving the bifurcation.

Signs / Sx’s:
- Abdominal, back pain. Thrombus formation, peripheral emboli. Rupture.
AORTIC DISSECTION

- Weakness of the elastic and smooth muscle layers of the aorta → hemorrhage into the vessel wall → longitudinal tearing of the wall to form a blood-filled channel.
AORTIC DISSECTION

- 2/3 involve the ascending aorta.
- 2nd most common- thoracic aorta just distal to the sub-clavian.

CAUSED BY:
- 1) Hypertension.
- 2) Degeneration of the medial layer.
- 3) Marfan’s Syndrome.
- 4) Assoc. with congenital defects, ie coarctation.
AORTIC DISSECTION

- MANIFESTATIONS:
  - Abrupt onset of pain - anterior chest, back/neck.
  - Loss of BP in the arms as the dissection progresses, disrupts flow.
  - Syncope, hemiplegia, paralysis of LE’s.
DISORDERS OF THE VENOUS CIRCULATION

CIRCULATION IN THE LOWER EXTERMINITIES

The “muscle pump”- contractions of the gastrocnemius and soleus muscles exert pressure on the veins, causing upward flow; pumps blood from the superficial circulation to the deep circulation, and from the deep circulation upward.

Downward / retrograde flow is prevented by the venous valves; see fig. 24-13.
VARICOSE VEINS

- In short, due to incompetence of the valves.
- Caused by:
  1) ↑ intra-abdominal pressure- lifting, pregnancy.
  2) Prolonged standing.
- MANIFESTATIONS:
  - Cosmetic.
  - Aching.
  - Edema.

valves get leaky over time and we’re on our feet a lot - causes venous pooling. legs swell. moving yourself around will help the blood return to the heart. if patient has this, more at risk for DVT. Pain in the calves (sometimes thighs and pelvis—vaguer pain)
CHRONIC VENOUS INSUFFICIENCY

- The physiologic consequence of DVT, valvular incompetence, or both.
- Most common cause is DVT, which causes valvular incompetence.
- Impairment of flow → tissue congestion, edema, impaired tissue nutrition → necrosis of sub-q fat, skin atrophy, breakdown of RBC’s → brownish discoloration from accumulation of hemosiderin.

Can have the necrosis without the DVT too. Fat necroses first.
CHRONIC VENOUS INSUFFICIENCY

- Secondary lymphatic congestion secondary to the pressure; sclerosis of lymphatic channels in the face of increasing need for clearance of interstitial fluid.

hardening of the lymphatic channels - refer pts to a lymphedema clinic with special massages and venous type pump machines like Shirley had on after surgery.
STASIS DERMATITIS

- Thin, shiny, bluish-brown skin; irregularly pigmented desquamative skin.
- Small tissue injury $\rightarrow$ painless ulceration $\rightarrow$ difficulty healing due to inadequate tissue nutrition = STASIS ULCER- most are just above the medial malleolus.
VENOUS THROMBOSIS

- Formation of a thrombus w/ accompanying inflammation.
- May occur in:
  1) Superficial venous circulation.
  2) Deep venous circulation. (DVT)

- DVT is a serious event as it leads to the development of P.E. = pulmonary embolus
VENOUS THROMBOSIS

- **VIRCHOW’S TRIAD:**
  - 1) Venous stasis.
  - 2) Hypercoagulability.
  - 3) Vascular trauma.

See chart 24-2.
VENOUS THROMBOSIS

- MANIFESTATIONS:
  - Pain, swelling, muscle tenderness.
  - If superficial \(\rightarrow\) palpable cord.
  - Many cases of DVT are asymptomatic.
  - Most common sites: venous sinuses in the soleus muscle, and in the posterior tibial and peroneal veins.

- HOMAN’S SIGN: pain in the calf on dorsiflexion of the foot.
VENOUS THROMBOSIS

- CAN RESULT IN:
  1) Pulmonary Embolus.
  2) Recurrent episodes of DVT.
  3) Chronic venous insufficiency, stasis, ulceration.

Thrombophlebitis is NOT DVT, but can lead to it. Thrombophlebitis is just inflammation in the vein leading to a thrombus there. Thrombophlebitis is a clinical presentation: pain, redness, swelling, increasing discomfort upon walking.
DISORDERS OF BLOOD PRESSURE REGULATION

CHAPTER 25
REGULATION OF BLOOD PRESSURE

- Read text re:
- Systole, diastole.
- Chemoreceptors, baroreceptors.
- Autonomic nervous system, vagus nerve, epinephrine.
HUMORAL CONTROL OF BP

- **EPINEPHRINE**: released by:
  - 1) Sympathetic nervous system.
  - 2) Adrenal medulla.

- **CAUSES**:
  - 1) \( \uparrow \) heart rate and contractility.
  - 2) Vasoconstriction in selected organ systems
    \( \rightarrow \) \( \uparrow \) peripheral vascular resistance, \( \rightarrow \) \( \uparrow \) BP.
HUMORAL CONTROL OF BP

RENIN-ANGIOTENSIN-ALDOSTERONE

- **RENIN**: enzyme made by the kidney; released in response to:
  1) ↑ sympathetic activity.
  2) ↓ in BP.
  3) ↓ extra-cellular volume.
  4) ↓ extra-cellular sodium.

- Promotes conversion of Angiotensinogen to Angiotensin I
HUMORAL CONTROL OF BP

RENIN-ANGIOTENSIN-ALDOSTERONE

- Angiotensin I ➔ Lung ➔ Angiotensin II, by angiotensin converting enzyme ("ACE").

ANGIOTENSIN II:

1) Strong vasoconstrictor.

2) Stimulates secretion of aldosterone from the adrenal cortex ➔ sodium retention ➔ water reabsorption ➔ increased intravascular volume ➔ ↑ blood pressure.
HUMORAL CONTROL OF BP

**VASOPRESSIN:**

- Aka A.D.H.
- Released by the posterior pituitary.
- Released in response to:
  - 1) ↓ blood volume.
  - 2) ↓ blood pressure.
  - 3) ↑ osmolality of blood
HUMORAL CONTROL OF BP

- **VASOPRESSIN:**
  
  Causes:
  1) Vasoconstriction.
  2) Reabsorption of water at the level of the renal tubule.

  Not likely responsible for long term control of blood pressure.
HYPERTENSION

- NIH 2003- JNC-7
- 1) Normal = 120 / 80.
- 2) Hypertension = 140 / 90.
- 3) “Pre”-hypertension = 120-129 / 80-89.
- For diabetics the goal is 130 / 80.

- STAGE I – 140-159 / 90-99
- STAGE II - > 160 / > 100
SYSTOLIC HYPERTENSION

- SYSTOLIC > 140
- ↑ RISK FOR EVENTS CAUSED BY:
  1) The actual pressure - ↑ systolic pressure puts ↑ demand on the LV, resulting in LVH, ↑ oxygen demand, and CHF.
  2) ↑ pulse pressure - ↑ stretch → vascular damage, aneurysms, intimal damage → atherosclerosis, thrombosis.
ESSENTIAL VS. SECONDARY HYPERTENSION

- **ESSENTIAL (PRIMARY) HYPERTENSION**: occurs in the absence of other diseases.

- **SECONDARY HYPERTENSION**: occurs as a result of another disease- renal disease, thyroid disease, adrenal disease, pheochromocytoma.
ESSENTIAL HYPERTENSION

- Cause not specifically known.
- But we do know Risk Factors:
  - 1) Family Hx.
  - 2) Age.
  - 4) Lifestyle factors: ↑ sodium intake, obesity, inactivity, excess alcohol consumption, ↓ potassium intake.
- Also: OCP’s, stress.
ESSENTIAL HYPERTENSION

- MANIFESTATIONS:

- Asymptomatic.
- Effects are those related to “Target Organ” damage:
  - Heart: LVH, angina, MI, CHF.
  - Brain: stroke / TIA.
  - Renal disease.
  - Peripheral vascular disease.
  - Retinopathy.
ESSENTIAL HYPERTENSION

- Significant risk factor for atherosclerosis.
- Leads to atherosclerotic cardiovascular disorders and peripheral vascular disease.

- DIAGNOSIS: average of 2 or more readings at 2 or more visits; no caffeine, nicotine prior to readings.
- End organ damage is reduced with antihypertensive therapy.
SECONDARY HYPERTENSION

- 5-10% of cases.
- Also called “reversible” or “correctable” causes of hypertension. **CAUSES:**
  1) Renal artery stenosis.
  2) Coarctation of the aorta.
  3) Drugs- amphetamines, cocaine.
  4) Obstructive sleep apnea.
  5) Renal disease.
  6) Adrenal disease, pheochromocytoma.
SECONDARY HYPERTENSION

RENAL DISEASE
- Most common cause of secondary hypertension
- Seen in:
  1) Chronic pyelonephritis.
  2) Renal failure.
  3) Acute glomerulonephritis.
  4) Polycystic kidney disease.
  5) Urinary tract obstruction.
SECONDARY HYPERTENSION

RENOVASCULAR DISEASE

- Renal artery stenosis.
- Fibromuscular dysplasia.
- Atherosclerosis involving the renal arteries.
- Activates the renin-angiotensin system
SECONDARY HYPERTENSION

**ADRENAL DISEASE**

- Excess production of mineralocorticoid (aldosterone) and glucocorticoid (cortisol) causes increased BP.
- Both facilitate reabsorption of sodium and water.
- Hyperaldosteronism- Conn’s Syndrome- excess aldosterone.
- Cushing’s Disease / Syndrome- excess cortisol.
SECONDARY HYPERTENSION

PHEOCHROMOCYTOMA

- An epinephrine and norepinephrine-producing tumor of the adrenal medulla.
- **Episodic** increase in BP → hypertensive crisis.
- **Episodic** headache, sweating, palpitations, tremor.
- Dx: assessment of urine for epinephrine metabolites – VMA = vanilmandelic acid
SECONDARY HYPERTENSION

LICORICE

- Extract of *Glycyrrhiza glabra*.
- Causes sodium retention, water reabsorption, increased vascular volume.
MALIGNANT HYPERTENSION

- Sudden onset, diastolics > 120.
- May occur in the young, blacks.
- Also in patients w/ renal & collagen diseases.
- Life-threatening.
- Hypertensive encephalopathy: ↓ perfusion as cerebral vasospasm occurs → cerebral edema → headache, restlessness, confusion, stupor, convulsions, coma.
- If prolonged → arterial damage → thrombosis
BP CHANGES IN PREGNANCY

- Pregnancy is normally associated w/:
  - 1) ↓ BP during 1\textsuperscript{st} and 2\textsuperscript{nd} trimester.
  - 2) ↑ cardiac output.
  - 3) ↓ peripheral vascular resistance.
  - 4) ↑ renin-angiotensin-aldosterone, also estrogen and progesterone- all may alter vascular reactivity.
BP CHANGES IN PREGNANCY

1) CHRONIC HYPERTENSION: HTN prior to the 20th week of pregnancy.

2) PRE-ECLAMPSIA / P.I.H.: HTN after the 20th week, w/ proteinuria.

3) PRE-ECLAMPSIA SUPERIMPOSED ON CHRONIC HTN.

4) GESTATIONAL HYPERTENSION: HTN w/out evidence of pre-eclampsia, returns to normal by 12 weeks post-partum.
ORTHOSTATIC HYPOTENSION

- An abnormal drop in BP upon arising.
- Upon standing, 500-700 cc shifted to the lower body $\rightarrow$ ↓ in central blood volume, ↓ arterial pressure $\rightarrow$ baroreceptors kick in $\rightarrow$ vasoconstriction $\rightarrow$ return on BP to normal.
- DEFINITION: fall of $\geq$ 20 systolic, 10 diastolic.
- Presence of symptoms helps firm up the Dx.
- Pulse also rises, usually $\geq$ 30 bpm.
ORTHOSTATIC HYPOTENSION

- **CAUSES:**
- 1) ↓ BLOOD VOLUME.
- 2) MEDICATION. Diuretics, BP meds.
- 3) BED REST.
- 4) DISORDERS OF THE AUTONOMIC NERVOUS SYSTEM