Risk Factors of ATH

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B. Modifiable major risk factors (potentially controllable)

1. Hyperlipidemia:
   - Is a major risk factor of ATH (hypercholesterolemia), by following evidences:
     1. LDL is associated with increased risk of ATH (LDL precipitate the cholesterol into vascular wall).
     2. HDL is protective lipid against ATH (HDL mobilize cholesterol from existing atheroma's & transport cholesterol to the liver for excretion in the bile).
   - Both exercises & moderate consumption of ethanol raise level of HDL, whereas obesity & smoking lower it.
   - Egg yolk, animal fat & butter & polyunsaturated vegetable fat decrease level of HDL, while fish oil has beneficial effects in ATH.
2. Hypertension:
   - Is a major risk factor for ATH in all ages, by following evidences:
     1. Those patients with blood pressure 170/95 mmHg have 5 folds greater risk of IHD than those with blood pressure of 140/80 mmHg, both systolic & diastolic blood pressures are important in increasing risk of ATH.
     2. Antihypertensive treatment decrease risk of ATH related diseases & IHD.
3. Cigarettes smoking:
   - Is well established risk factor in men (recently is also important risk factor in female).
   - The death rate of IHD increase by up to 200% in heavy smoker (2 or more packs of cigarettes are smoked /day for several years).

4. Diabetes Mellitus:
   - Diabetes increase risk of ATH because diabetes mellitus induce hypercholesterolemia, (increased risk of M.I, stroke & ATH induced gangrene).

C. Lesser, uncertain, unquantitated risk factors:

1. Obesity (because obesity increases risk of hypertension, diabetes mellitus, hypertriglyceridemia & decrease HDL).
2. Physical inactivity (sedentary factor).
3. Stressful life style (type A personality).
4. High carbohydrate intake.
5. Postmenopausal estrogen treatment.

6. Unsaturated fat intake.
7. Chlamydia pneumoniae.

Pathogenesis of ATH:

The most acceptable theory of pathogenesis of ATH is called **Response to injury hypothesis** which consist of following steps:
1. Chronic endothelial injury: endothelial cells dysfunction, increased vascular permeability & leucocytes adhesion.
2. Accumulation of lipoproteins mainly LDL within the wall of injured vessel.
3. Modification of lesional lipoproteins by oxidation.
4. Adhesion of monocytes (and other leucocytes) to the endothelium, followed by migration into the intima & their transformation into macrophages & foam cells.
5. Adhesion of platelets.
6. Release of factors from activated platelets, macrophages, or vascular cells that cause migration of SMC from media into the intima.
7. Proliferation of SMC into the intima & elaboration of extracellular matrix, leading to accumulation of collagen & proteoglycans.
8. Enhanced accumulation of lipids both within cells (macrophages & SMC).

Hypertensive Vascular Diseases (Hypertension):

- Sustained diastolic pressure in excess of 90 mmHg or a sustained systolic pressure in excess of 140 mmHg is considered as hypertension.

Hypertension is regarded as major risk factor of ATH & also one of the most important risk factors in both coronary heart disease & Cerebrovascular accidents (CVA)

Causes of Hypertension:

- 95% of cases of hypertension are idiopathic or essential hypertension (within these cases about 95% of cases are benign hypertension & 5% are malignant or accelerated hypertension).
- 5% of cases are secondary hypertension (within these cases about 95% are malignant hypertension & 5% are benign hypertension).

Causes of secondary hypertension:

1. Renal causes: like acute glomerulonephritis, polycystic renal disease & renal artery stenosis.

2. Endocrine causes: like
   - Cushing syndrome (increase steroid hormones), exogenous steroid intake.
   - Pheochromacytoma (adrenalin & noradrenalin secreting tumor).
   - Acromegaly (increase level of growth hormone).
   - Hypothyroidism & hyperthyroidism.
   - Pregnancy induced hypertension.
3. Cardiovascular causes.
   - Coarctation of aorta.
   - Polyarteritis nodosa.
4. Neurologic causes:
   - Increased intracerebral pressure.

Regulation of normal blood pressure:

The blood pressure level is determined by the interaction of multiple genetic, environmental & demographic factors that influence two important hemodynamic variables (cardiac output & total peripheral resistance).

1. Cardiac output is affected by blood volume, which is greatly dependent on body sodium homeostasis.

2. Total peripheral resistance is predominantly determined at the level of arterioles & depends on the effects of neural & hormonal influences (this hormonal influences control the vascular tone by a balance between vasoconstrictor factors (e.g. angiotensin II & catecholamine's) & vasodilator factors (e.g. kinins, prostaglandins & nitric acid).

3. Kidneys play an important role in regulation of blood pressure, by the followings:

I. Through rennin- angiotensin system, kidney influence both total peripheral resistance & sodium homeostasis, by stimulate this system (Angiotensin II elevate blood pressure by increasing both peripheral resistance by stimulation of sympathetic system & blood volume) by stimulation of aldosterone secretion & increase renal tubular reabsorption of sodium.

II. Kidneys produce antihypertensive substances like prostaglandin & nitric oxide.

Morphology (pathological changes) of hypertension:

1. Hypertension accelerates ATH & induces degenerative changes in wall of large & medium size arteries.

2. Hypertension in small vessels is associated with two forms of vascular diseases:

I. Hyaline arteriolosclerosis:

- Can be seen in normotensive patients, but it is more severe in hypertensive patients. Also can be seen in diabetic patients
- Vascular lesion consists of a homogeneous, pink hyaline thickening of the walls of arterioles & narrowing of lumen.
- This hyaline thickening is due to leakage of plasma components across vascular endothelium & also due to excess extracellular matrix production by the SMC_s as response to hypertension.
- Hyaline arteriolosclerosis is diffuse process; it is typically seen in (benign nephrosclerosis).

II. Hyperplastic Arteriolosclerosis:

- Characteristic of malignant hypertension (diastolic blood pressure above 120 mm Hg).
- Vascular lesion characterized by onion-skin, concentric, laminated thickening of the walls of arterioles with progressive narrowing of lumen (this lamination under electron microscope is consist of SMC, thickened basement membrane.
- Hyperplastic lesion is accompanied by fibrinoid necrosis of the vessel walls, mainly seen in the kidney.

ANEURYSMS

An aneurysm is abnormal dilatation of a blood vessel or heart.
It is either

- ✓ True aneurysm (when aneurysm is bounded by arterial wall components or the attenuated wall of the heart).
- ✓ False aneurysm, (pseudo aneurysm) is a beach in the vascular wall leading to an extravascular space.

- ✓ Examples on true aneurysm are atherosclerotic, syphilitic & congenital vascular aneurysm.
- ✓ Examples on false aneurysm are post- myocardial rupture within a pericardium.

Causes of aneurysm:

1. ATH.
2. Cystic medial degeneration of arterial media.
3. Trauma.
4. Congenital defect (Berry aneurysm).
5. Infections (Mycotic aneurysm) or Syphilis.
6. Vasculitius.

Classification of aneurysms:
Aneurysms can classified according to macroscopic shape & size into
1. Saccular aneurysm: only involve a portion of vessel wall, spherical, size from 5 to 20 cm in diameter, often filled with thrombus.
2. Fusiform aneurysm: involving a long segment of blood vessel, a size varies up to 20 cm in diameter, e.g. aneurysm involves entire ascending & transverse portions aortic arch.

Abdominal Aortic Aneurysms (AAA):
- Site of AAA: Abdominal aorta usually below the renal arteries & above the bifurcation of the aorta.
- Shape & size: AAA is saccular or fusiform, up to 15 cm in diameter & up to 25 cm in length.
- Sex: more in the male.

Cause of AAA:
1. ATH (commonest).
2. Familial (associated with HT).
3. Marfan syndrome.

Complications of AAA:
1. Rupture into peritoneal cavity, or retroperitoneal tissue with massive, fatal hemorrhage.
2. Obstruction of a vessel, particularly iliac, renal, mesenteric, or vertebral branches that supply the spinal cord.
3. Embolization from atheroma or mural thrombus formed within the aneurysm.
4. Compression of adjacent organs (compression of a ureter or erosion of vertebrae).
5. Presentation of an abdominal mass (often palpably pulsating) that simulates a tumor.

Syphilitic (Luetic) Aneurysm:
Site:
- ✓ Thoracic aorta (in the third stage of syphilis).

Cause:
- ✓ Due to obliterative endarteritis that involve Vasa Vasorum of aorta (thoracic aortitis), which is result in weakening of media that is result in aneurismal dilatation.

Gross:
- ✓ Contraction of fibrous scars may lead to wrinkling of intervening segments of aortic intima, which is called (Tree barking).

Complications of syphilitic aneurysm:

1. Superimposed atherosclerosis of aortic root (garden ATH).

2. Aortic valve insufficiency (due to involvement of aortic valve ring), which result in massive left ventricular wall hypertrophy (about 1000 grams) this is called Cow's heart.

3. Other complications of syphilitic aneurysm:

a. Compression on mediastinal structures.
b. Compressing on the lungs & other airways (shortness of breath).
c. Compressing on the esophagus (difficulty in swallowing).
d. Compressing on the recurrent laryngeal nerve (Persistent cough).
e. Severe pain due to erosion of bones.
f. Cardiac disease (cardiac failure), due to involvement of aortic valve & narrowing of coronary artery.
g. Aneurysmal rupture.

THANKS