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Tobacco-Related CVD

Cigarette smoking

- A leading preventable risk factor for development and progression of CVDs
- Active smoking and secondhand smoke
- Mixture of several toxic chemicals
- According to WHO: nearly 5.4 million premature deaths a year attributable to tobacco smoking worldwide
- Tobacco causes endothelial dysfunction, inflammation, insulin resistance, alteration of lipid profile, hemodynamic alterations, hypercoagulable state

→ All of these act synergistically as mechanisms of atherothrombosis in tobacco users

Components of cigarette smoke

- Toxic mixture of more than 5,000 chemical compounds
- Complex aerosol consisting of vapor and particulate phases

Vapor phase: Carbonmonoxide, acetaldehyde, formaldehyde, acrolein, nitrogen oxides, carbon dioxide

Particulate phase: Nicotine and various particulate matters (collectively known as “tar”)

Compounds of cigarette smoke contributing the most to CVD

Nicotine
Carbon monoxide
Oxidant gases

Nicotine

- Ganglionic and central nervous system stimulant
- Each puff contains approx. 50 µg of nicotine
- Sympathetic neural stimulation → Cardiovascular effect
- Primarily mediates hemodynamic effects of cigarette smoking
- Increases heart rate, blood pressure (acute + throughout the day), and cardiac output
  → Increase in myocardial oxygen demand

Carbon monoxide

- In healthy persons, CO in concentrations similar to cigarette smoking does not affect blood pressure, plasma catecholamines, platelet aggregation, or serum C-reactive protein
- CO exposure in patients with CAD can cause:
  - Lower thresholds for exercise-induced ischemia
  - Ventricular dysfunction
  - Increased ventricular arrhythmias

Oxidant gases

- Free radical-mediated oxidative stress
  → Atherosclerosis
- Prime mediators of endothelial dysfunction
- Lower plasma levels of antioxidants (Vitamin C, Beta-carotene)
- Metals (e.g. aluminum, cadmium, copper, lead, mercury, nickel, zinc) catalyze oxidation of cellular proteins
  → Structural cellular damage + endothelial dysfunction
- Acrolein (reactive aldehyde produced by endogenous lipid peroxidation) adversely modifies HDL
  → Endothelial cell death + dysfunction
- Polycyclic aromatic hydrocarbons in tar accelerate atherosclerosis

Pathophysiologic mechanisms of tobacco smoke in cardiovascular disease

Key pathobiologic mechanisms:

Endoathelial dysfunction

Increased oxidative stress

Hypercoagulable state

Vascular and endothelial dysfunction

- Smoking damages vascular wall
  → Impaired prostacyclin production and enhanced platelet-vessel wall interactions
  → Reduce elastic properties of vessels
  → Stiffening and trauma to the wall
- Impairment of endothelium-dependent vasodilation of coronary arteries
- Reduced coronary flow reserve
- Risk factor for coronary vasospasm

Inflammation

- Central role in pathogenesis of atherosclerosis
- Cigarette smoking associated with chronic inflammation
- 20–25% increase in leukocyte count
- Increased level of inflammatory markers (IL-6, CRP, TNF alpha)
- Elevations of proinflammatory cytokines increase leukocyte–endothelial cell interaction
  → Leukocyte recruitment → Atherosclerosis
- Elevated fibrinogen levels

Prothrombotic state

- Higher rates of acute MI and sudden death
- Alteration of thrombotic factors, fibrinolytic factors, platelet-mediated pathways
- Elevated fibrinogen concentration + increased expression of tissue factor
- Platelets in chronic smokers have increased propensity to be stimulated and to aggregate spontaneously
- Increased platelet-dependent thrombin generation
- CO-induced hypoxemia → Higher red cell mass
  → Increased blood viscosity

Effect on lipid profile

- Higher levels of cholesterol, triglycerides, LDL
- Lower levels of HDL
- Smoking cessation improves total HDL

Smoking and Insulin-resistance / Metabolic syndrome

- Smokers are more insulin-resistant and hyperinsulinemic
- Risk factor for development of type-2 diabetes
- Smokers with diabetes:
  - Higher HbA1c levels
  - Require more insulin
  - Increased risk of microvascular and macrovascular complications of diabetes
- Enhanced insulin resistance, central obesity, dyslipidemia
  → Increased risk of metabolic syndrome
  → Endothelial dysfunction
  → Increased oxidative stress

Secondhand smoke

- Exposure to secondhand smoke (environmental tobacco smoke, passive smoking) has a similar health risk
- Increases risk of developing CAD by 25–30%

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