PATHOPHYSIOLOGY of TOBACCO-RELATED DISEASE

2004 SURGEON GENERAL's REPORT: THE HEALTH CONSEQUENCES of SMOKING

ADVERSE HEALTH EFFECTS ASSOCIATED with SMOKING

- Cancer
- Cardiovascular disease
- Respiratory disease
- Reproductive complications
- Osteoporosis
- Periodontitis
- Cataract
- Postoperative complications

USDDHHS. (2004). *The Health Consequences of Smoking: A Report of the Surgeon General.*

TOBACCO and CANCER: CANCERS CAUSED by TOBACCO

- Lung
- Larynx
- Oral cavity and pharynx
- Esophagus
- Pancreas
- Bladder and kidney
- Cervix
- Stomach
- Bone marrow (acute myeloid leukemia)

USDHHS. (2004). *The Health Consequences of Smoking: A Report of the Surgeon General.*

TOBACCO and CANCER: CARCINOGENS in TOBACCO PRODUCTS

- Polycyclic aromatic hydrocarbons (PAHs)
  - Benzopyrene
  - Benzanthracene
- Tobacco-specific nitrosamines (TSNAs)
- Aromatic amines
- Formaldehyde
- Benzene
- Vinyl chloride
- Cadmium
- Radioactive polonium-210

TOBACCO and CANCER: CARCINOGENS (cont'd)

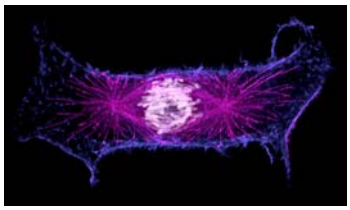
Cancer site	Likely carcinogen(s)
Lung	PAHs, nitrosamines, aldehydes, benzene, heavy metals
Larynx	PAHs
Oral cavity	Nitrosamines
Esophagus	Nitrosamines
Pancreas	Nitrosamines
Cervix	PAHs, nitrosamines
Bladder/kidney	Aromatic amines
Bone marrow (AML)	Benzene

Adapted from Hecht. (2003). *Nat Rev Cancer* 3:733–744.

TOBACCO and CANCER: MECHANISM of CARCINOGENESIS

- Compounds in tobacco function as
  - Carcinogens
    - Initiate tumor growth
  - Tumor promoters
    - Stimulate the development of established tumors
  - Co-carcinogens
    - Enhance the mutagenic potential of carcinogens; possess little or no direct carcinogenic activity
  - Irritants
    - Induce inflammation and compromise tissue integrity

TOBACCO and CANCER: CELL DIVISION



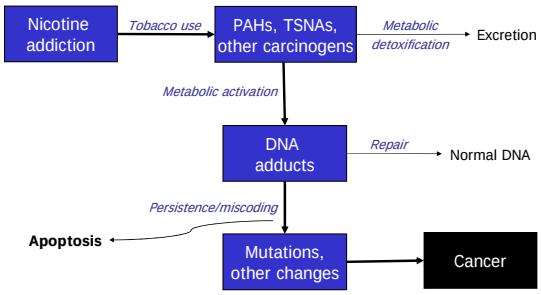
A cancer cell dividing its chromosomes (shown in white) into two new cells

Image courtesy of Dr. Paul D. Andrews / University of Dundee

TOBACCO and CANCER: MECHANISM of CARCINOGENESIS (cont'd)

- Formation of DNA adducts
  - Covalent binding product of carcinogen (or its metabolite) to DNA
  - Leads to miscoding and point mutations
  - Mutations of oncogenes or tumor suppressor genes can lead to uncontrolled cellular growth and development of cancer

TOBACCO and CANCER: MECHANISM of CARCINOGENESIS (cont'd)



Adapted with permission. Hecht. (1999). *J Natl Cancer Inst* 91:1194–1210.

TOBACCO and CANCER: SUMMARY

- Tobacco products cause a variety of cancers
- Carcinogens present in tobacco are responsible for these cancers
- Carcinogenesis likely involves a multistep process:
  - Formation of DNA adducts
  - Permanent cellular mutations
  - Unregulated cellular growth

SMOKING and CARDIOVASCULAR DISEASE

- Coronary heart disease
  - Angina pectoris, ischemic heart disease, myocardial infarction
- Cerebrovascular disease
  - Stroke, transient ischemic attacks
- Abdominal aortic aneurysm
- Peripheral arterial disease

SMOKING and CARDIOVASCULAR DISEASE: POSTULATED MECHANISMS

- Smoking-induced atherogenesis and thrombosis
  - Endothelial injury/dysfunction
  - Thrombosis
  - Inflammation
  - Lipids/lipid metabolism

SMOKING and CARDIOVASCULAR DISEASE: POSTULATED MECHANISMS (cont'd)

- Adverse effects on cardiovascular function
  - Increased oxygen demand
  - Decreased oxygen delivery

SMOKING and RESPIRATORY DISEASE

- Acute respiratory diseases
  - Upper respiratory tract
    - Rhinitis, laryngitis, pharyngitis, sinusitis
  - Lower respiratory tract
    - Bronchitis, pneumonia
- Chronic respiratory diseases
  - Reduced lung function in infants
  - Respiratory symptoms in children & adults
    - Cough, phlegm, wheezing, dyspnea
  - Poor asthma control
  - Chronic obstructive pulmonary disease

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

- Characterized by airflow limitation (not fully reversible)
- Progressive airflow limitation associated with abnormal inflammatory response of the lungs to noxious particles or gases
- Characteristic symptoms (cough, sputum production, dyspnea)
- Prevalence increasing worldwide

The single most important risk factor for COPD is **tobacco smoking.**

SMOKING and COPD: POSTULATED MECHANISMS

Tobacco smoke induces inflammation and damage to pulmonary tissue through

- Release of inflammatory cells and mediators
- Imbalance between proteases and antiproteases
- Oxidative stress

SMOKING and REPRODUCTIVE HEALTH

- Reduced fertility in women
- Pregnancy and pregnancy outcomes
  - Placenta previa
  - Placental abruption
  - Preterm premature rupture of membranes
  - Preterm delivery
  - Low infant birth weight
- Infant mortality
  - Sudden infant death syndrome (SIDS)

SMOKING and OSTEOPOROSIS

Smoking causes

- Low bone density
  - Postmenopausal women
- Hip fractures
  - Observed in women and men

SMOKING and OSTEOPOROSIS: POSTULATED MECHANISMS

- Direct toxic effect on osteoblasts
- Increased bone resorption
  - Smokers have decreased parathyroid, vitamin D levels
  - Reduced calcium absorption
- Early menopause
- Decreased weight-bearing forces:
  - Lower body weight
  - Less physical activity
- Vascular insufficiency

SMOKING and DENTAL DISEASE

Smoking causes periodontitis.

Possible mechanisms:

- Alterations in oral microbial flora
- Compromised oral immune function
- Impaired tissue regeneration and repair

Image courtesy of Dr. Sol Silverman / University of California San Francisco

SMOKING and OCULAR DISEASE

Smoking causes cataract.

Possible mechanisms:

- Oxidation and precipitation of lens proteins
- Tobacco smoke may alter plasma concentrations of nutrients/antioxidants essential for lens transparency

SMOKING and POSTOPERATIVE COMPLICATIONS

- Surgical wound complications
  - Delayed healing
  - Wound dehiscence
  - Infection
  - Scarring
- Respiratory complications
  - Pneumonia
  - Respiratory failure

PATHOPHYSIOLOGY of TOBACCO-RELATED DISEASE: SUMMARY

- Tobacco use harms nearly every organ of the body and is associated with a variety of adverse health outcomes resulting in significant morbidity and mortality.
- Mechanisms for disease have not been definitively established, but constituents of tobacco and smoke disrupt many normal cellular processes.
- Tobacco cessation efforts are essential to arrest or prevent disease progression.