Smoking Related Pathology

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Overview

- General smoking related health conditions
- Smoking related pathology
- Smoke and its constituents
- Prevention of smoking related diseases.
General Information

- Use of tobacco products is associated with more mortality & morbidity than any other personal conditions.
- Famous study followed smokers vs non-smokers and established epidemiological association between lung cancer and smoking.
- Smoking was popular in sixties and fashionable.
- Current evidence suggest a decline in smoking among males in developed countries but increasing among women.
- Laws introduced to stop smoking advertisement in sports.
Tobacco advertising & promotion trends

![Graph showing trends in tobacco advertising and promotions from 1963 to 1991. The graph indicates a significant increase in promotions spending, particularly from 1983 onwards.]
General Information

- Smoking companies moved to developing countries due to strict laws in developed countries.
- Smoking among teenage is very high.
- Smoking in developing countries is very high.
- Smoking is major risk factor for lung cancer.
- Smoking can also interact with environmental factors to increase risk e.g. lung cancer risk in smokers exposed to asbestos.
True story of tobacco executive-turned-whistleblower, Jeffrey Wigand
Smoke Constituents

- Main stream smoke is composed of a particulate phase & a gas phase.
- Tar is total particular phase without H2O or nicotine.
- There are 0.3-3.3 billion particles per millilitre of mainstream smoke.
- >4000 constituents.
- 43 known carcinogens.
Organ Specific Carcinogens

Lung, larynx – polycyclic aromatic hydrocarbons
Esophagus – nitrosonornicotine
Pancreas
Bladder – 4-aminobiphenyl, 2-naphthylamine
Oral cavity – polonium 210, polycyclic aromatic hydrocarbons
Carcinogens in Smoke

- In addition to chemical carcinogens, smoke contains metallic carcinogens.
- These include:
  - Arsenic
  - Nickel
  - Cadmium
  - Chromium
  - Irritants – nitrogen dioxide
  - Cilia toxins – hydrogen cyanide
- Many more
Smoke & Nicotine

- Nicotine is an alkaloid
- Readily crosses blood brain barrier.
- Stimulates nicotinic receptors in the brain
  - Responsible for pharmacological effects:
    - Increase HR & BP
    - Increase coronary artery blood flow
    - Increased contractility and cardiac output
- Nicotine responsible for the addiction.
Nicotine dependence

- Addiction/dependence
  - can’t stop when you want to
  - continue use, despite clear evidence of harm
  - clear withdrawal symptoms
    - *nicotine*: depressed mood, insomnia, irritability, difficulty concentrating

- *but* no intoxication
  - unlike cocaine, heroin, alcohol

Approx. 44% of the cigarettes smoked in the United States are smoked by the mentally ill.
— Harvard Medical School study (11/2000)
Brain regions & pathways

movement

sensations

vision

judgment

reward

memory

coordination
Nicotine action

- Accelerates release of neurotransmitter dopamine in the brain’s NA* & increases metabolism in NA
- Dopamine ~ pleasure, emotions, addiction … “reward system”

*NA = nucleus accumbens
Smoking & Associated Pathology

- Inhaled agents in smoke may act directly on the mucous membranes, swallowed in saliva or absorbed from alveolar capillaries.
- Smoking associated with increased risk of:
  - Coronary artery disease
  - Hypertension
  - Hypercholesterolemia
  - AMI
  - Platelet aggregation and lead to AMI
  - Poor pregnancy outcomes – LBW, prematurity, PROM among others.
  - Many more – pancreas, peptic ulcer, thrombosis
- Increased risk of respiratory problems including CA
## Cause of Death from Smoking (USA)

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Number of Deaths</th>
<th>Percentage of Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cancer</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trachea, lung, bronchus</td>
<td>123000</td>
<td>90</td>
</tr>
<tr>
<td>Larynx</td>
<td>3600</td>
<td>82</td>
</tr>
<tr>
<td>Lip, oral cavity, pharynx</td>
<td>5500</td>
<td>92</td>
</tr>
<tr>
<td>Bladder &amp; urinary tract</td>
<td>7600</td>
<td>80</td>
</tr>
<tr>
<td>Cervix</td>
<td>1800</td>
<td>50</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1400</td>
<td>30</td>
</tr>
<tr>
<td>Stomach</td>
<td>8000</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>1800</td>
<td>20</td>
</tr>
<tr>
<td><strong>IHD</strong></td>
<td>108200</td>
<td>27</td>
</tr>
<tr>
<td><strong>Cardiac arrest</strong></td>
<td>13700</td>
<td>37</td>
</tr>
<tr>
<td><strong>Cerebrovascular disease</strong></td>
<td>26300</td>
<td>12</td>
</tr>
<tr>
<td><strong>Chronic respiratory diseases</strong></td>
<td>62800</td>
<td>90</td>
</tr>
</tbody>
</table>

Becker CG, Pathology of environmental & occupational disease, 1996
Smoking & Lung Pathology

- Lung pathology associated with smoking include:
  - Cancer
  - Increase incidence of acute respiratory infections
  - Acute & chronic sinusitis
  - COPD

- Exacerbates – bronchitis, asthma, pneumoconiosis
Smoking & Lung Pathology

- Greatest number of deaths due to:
  - Lung cancer
  - Ischaemic heart disease
  - Chronic Obstructive Lung Disease
Chronic Obstructive Pulmonary Disease

- COPD refers to group of conditions characterised by:
  - Dyspnoea
  - Chronic or recurrent obstruction to airflow within the lung
COPD contd..

- COPD covers
- Chronic bronchitis
- Bronchiectasis
- Asthma
- Emphysema
Emphysema

- Characterised by:
  - abnormal permanent dilation of spaces distal to terminal bronchiole.
  - Destruction of alveolar walls without obvious fibrosis
Types of Emphysema

- 4 types
- Centrilobular (centriacinar)
- Panacinar
- Paraseptal
- Irregular
Types of Emphysema

Ref: Robins Pathological Basis of Diseases, 7th Ed
Centrilobular Emphysema - Pathology

- dilation of respiratory bronchioles localised to upper part of pulmonary lobes.
- The central or proximal parts of acini are affected.
- Distal alveoli spared.
- 95% of cases and common form.
- Hence normal & emphysematous airspaces exists in this form.
- Associated inflammation present
Centrilobular Emphysema

- Large black pigments present in the walls of emphysematous air spaces.
- Predominant in smokers.
- Often in association with bronchitis.
- Pneumoconiosis morphology similar to centrilobular emphysema and may have similar pathology or synergistic risk effect.
Panacinar (panlobular) Emphysema

- Dilation of entire acinus, including alveoli, alveolar ducts, respiratory bronchioles & terminal bronchioles.
- Uniform distribution throughout the lung.
- Tend to occur more commonly in the lower zones & anterior lung margins.
- Associated with loss of elasticity & deficiency of $\alpha_1$-antitrypsin ($\alpha_1$-protease inhibitor).
Paraseptal (Distal Acinar) Emphysema

- Normal proximal acinus
- Dilation of distal part of acinus involving alveoli and alveolar ducts.
- Tends to localise adjacent to pleura and interlobar septa.
- More severe upper half of lungs.
- Occurs adjacent to areas of fibrosis, scaring or atelectasis.
- Dilated airspaces appear as cystic spaces (0.5-2.0 cm).
- Occasionally associated with large subpleural bullae or blebs.
Irregular Emphysema

- Irregular involvement of acinus.
- Invariably associated with scaring.
- Usually complication of various inflammatory processes.

Complications
- Chronic bronchitis
- Interstitial emphysema
- Pneumothorax – from rapture of a bullae or surface blebs.
Pathogenesis

- Destruction of alveolar walls by un-opposed action of elastase and deficiency of anti-elastase action of $\alpha_1$-antitrypsin.
- Smoking increases elastase level and activity.
- Smoking attracts PMNs & macrophages – sources of $\alpha_1$-antitrypsin.
- There is also a hereditary form of $\alpha_1$-antitrypsin deficiency. Pi (protease inhibitor gene) on chromosome 14 affected.
Pathogenesis of Emphysema

Ref: Pathological Basis of Diseases, 7th Ed.
Emphysema - Morphology

Centriacinar emphysema. Central areas show dilation.

Panacinar emphysema. Entire pulmonary parenchyma dilated.

Ref: Robins Pathological Basis of Diseases, 7th Ed.
Bullaous Emphysema

Numerous bullae bulging out from pleura

Ref: Internet Pathology Laboratory, University of Utah
Emphysema - Morphology

Ref: Internet Pathology Laboratory, University of Utah
Chronic Bronchitis

- Clinically defined as:
  - Productive cough for 3 consecutive months over 2 consecutive years.
- Hypersecretion of mucus (hyperplasia of mucus-secreting submucosal glands)
- Very common among habitual smokers (4-10x) Air pollution.
- When persistent for years may lead to:
  - COPD
  - Cor pulmonale
  - Cancer transformation (atypical metaplasia & dysplasia of respiratory epithelium).
Chronic Bronchitis - Pathogenesis

- 2 factors important in genesis
  - Chronic irritation by inhaled substances
  - Microbiological infections (secondary insult)

- 4-10x more common in smokers regardless of age, occupation, sex and place of dwelling.
Bronchitis - Pathogenesis

- Chronic irritation leads to hypersecretion of mucus in large airways (hypertrophy of submucosal glands)
- There is also increase goblet cells in small airways in chronic cases.
- There is also associated bronchiolitis (co-existing emphysema).
- Infection is secondary assault and significant in maintaining & prolonging condition.
- Smoking predisposes to respiratory tract infection: damage ciliary action, direct damage to epithelium, inhibits alveolar macrophages.
Morphology - Bronchitis

- **Macro:** hyperemia and swelling of mucus membranes
- **Micro:** enlargement of mucus secreting glands in trachea and bronchi.
- Reid index is increased (normal = 0.4).
  - *Ratio of mucus gland layer: wall thickness between epithelium & cartilage.*
Comparison of Bronchitis & Emphysema

Ref: Robins Pathological Basis of Diseases, 7th Ed.
Bronchiectasis

- Permanent abnormal bronchial dilation caused by chronic infection.
- With inflammation & necrosis of bronchial wall.

- *Chronic necrotizing infecting of bronchi & bronchioles leading to abnormal permanent bronchial dilation*
Bronchiectasis - Pathogenesis

- Bronchial obstruction – tumor, foreign bodies, mucus impaction especially in asthmatics.
- Congenital or hereditary conditions e.g. Cystic fibrosis, immotile cilia.
- Necrotising pneumonia – TB or staphylococci or mixed infections.
Morphology

- Dilation usually affects lower lobes & maybe dilated up to 4x normal size.
- If tumors or foreign body involved, maybe localised to a single segment.
- Cut section the bronchi will be followed to the pleura. Normally bronchioles will not be visible/followed 2-3cm before plura.
Bronchiectasis - Morphology

Focal areas of dilated bronchi

Dilated bronchi with necrotizing inflammation

Ref: Internet Pathology Library, University of Utah.
## Clinical Signs & Symptoms

<table>
<thead>
<tr>
<th>Disease</th>
<th>Signs &amp; Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic bronchitis</td>
<td>Cough &amp; sputum production, “blue bloater”, barrel shaped chest, muscular chest</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>Cough, purulent sputum, fever</td>
</tr>
<tr>
<td>Emphysema</td>
<td>“Ping puffer”, thin chest, dyspnoea</td>
</tr>
<tr>
<td>Asthma</td>
<td>Episodic wheezing, cough, dyspnoea</td>
</tr>
</tbody>
</table>
Lung Cancer

- Lung CA is second to breast CA (women) & prostate (men) worldwide.
- Smoking is associated with primary lung tumors.
- Various other pollutants and industrial hazards can cause lung CA.
- Types:
  - SCC – 25-40%. Usually arise from a foci of squamous metaplasia in chronic bronchitis and occurs in smokers.
  - AdenoCa – 25-40%
  - Small cell Ca – 20-25%
  - Large Cell Ca – 10-15%.
Cardiovascular System

• **Smoking** is a significant risk factor for:
  ◦ AMI
  ◦ CVA
  ◦ Hypertension

• Smoking increases risk of thrombosis.

• Smoking promotes hypercholesterolemia and artherosclerosis genesis.
GIT

- Smoking is risk factor:
- Bowel Ischaemia
- Peptic ulcer diseases
- Colonic malignancies
- Pancreatitis
- Others
Why Do People Smoke?

Survey among 2nd year Lae School of Nursing students (n=31), 1999
Why Do People Smoke?

- Pleasure & relax: 47
- Just to try it out or peer pressure: 14
- Felt sick without it: 6
- To lose weight: 29
- Other: 4

Survey among 2\textsuperscript{nd} year Lae School of Nursing students (n=31), 1999
Are teens influenced by advertising?

Period of study
1973-1993

Percent

Marlboro  Newport

advertising  teens  adults
From ASH, Australia
WARNING CIGARETTES CAUSE MOUTH DISEASES
Cigarette smoke causes oral cancer, gum diseases and tooth loss.
Health Canada

WARNING CIGARETTES LEAVE YOU BREATHLESS
Tobacco use causes crippling, often fatal lung diseases such as emphysema.
Health Canada

WARNING CIGARETTES ARE A HEARTBREAKER
Tobacco use can result in the clogging of arteries in your heart. Clogged arteries cause heart attacks and can cause death.
Health Canada

WARNING TOBACCO USE CAN MAKE YOU IMPOTENT
Cigarettes may cause sexual impotence due to decreased blood flow to the penis. This can prevent you from having an erection.
Health Canada
If you smoke, please quit!
END

Reference: Robins Pathological Basis of Diseases, 6th & 7th Ed.

Download PDF copies of seminar notes at:

www.pathologyatsmhs.wordpress.com