



Smoking Related Pathology

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Overview

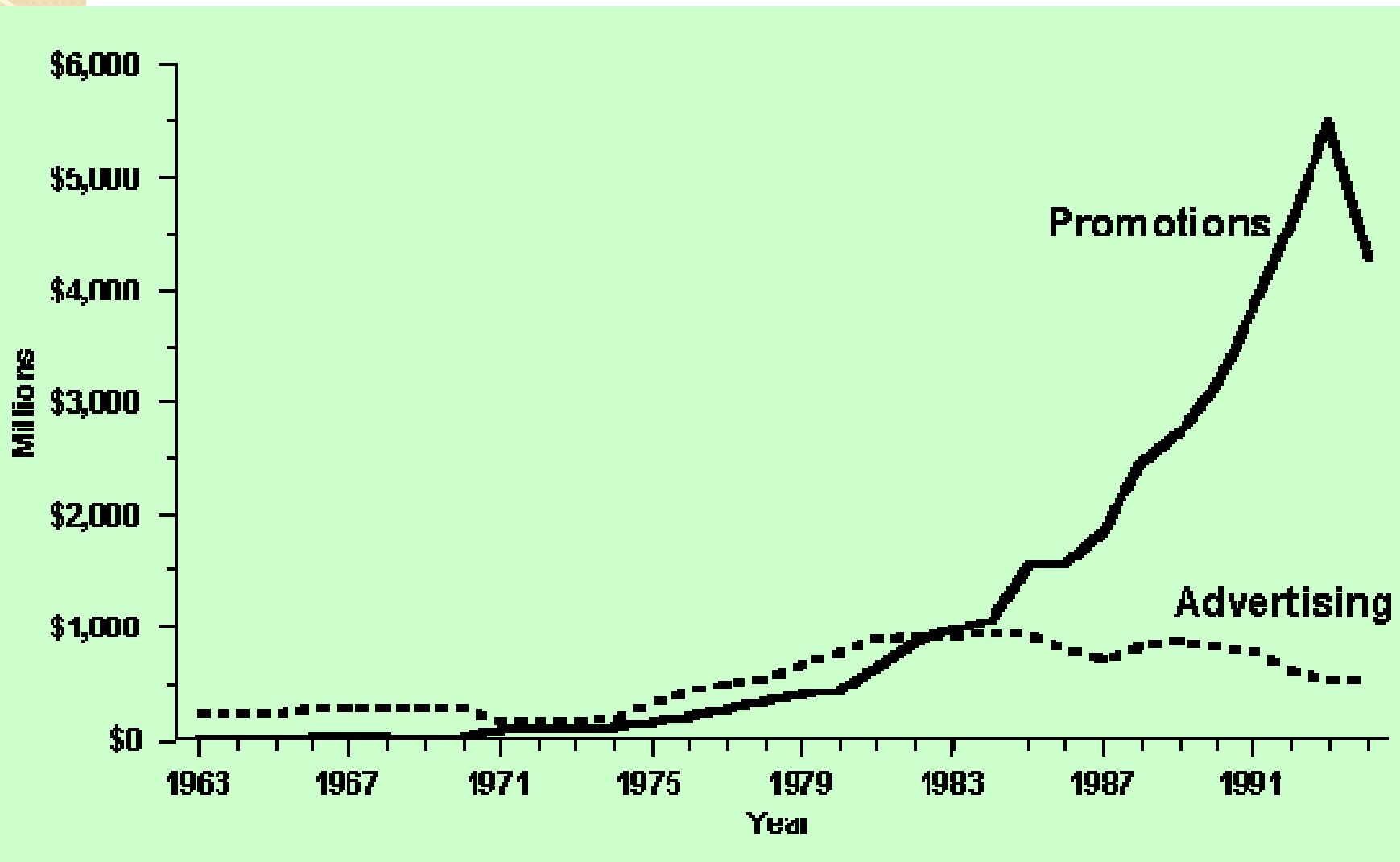
- ❑ General smoking related health conditions
- ❑ Smoking related pathology
- ❑ Smoke and its constituents
- ❑ Prevention of smoking related diseases.



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





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 particulate 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 – nitrosornicotine

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

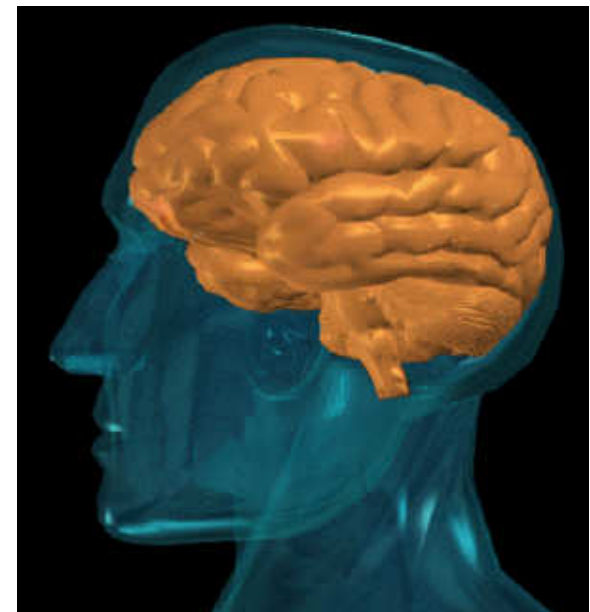
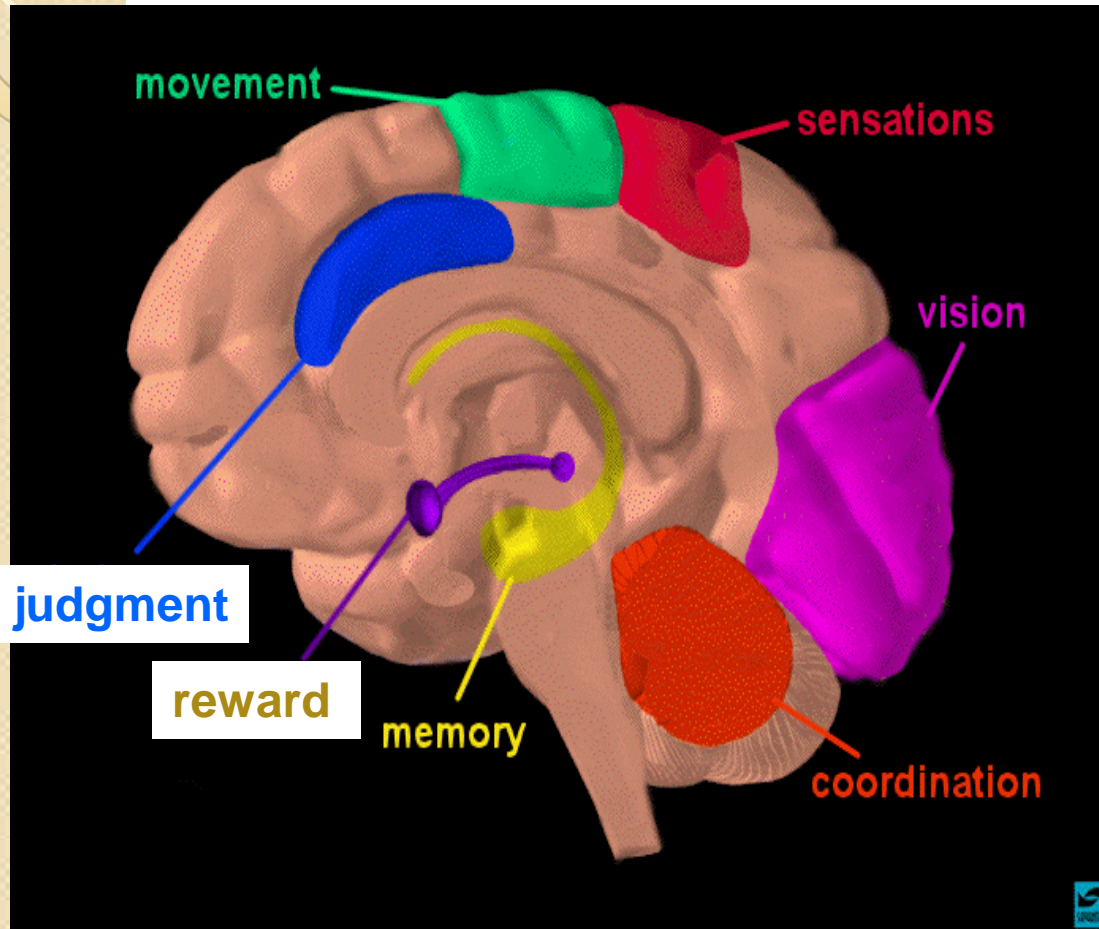
- Nicotine is an alkaloid
- Readily crosses blood brain barrier.
- Stimulates nicotinic receptors in the brain
 - Responsible for pharmacological effects:
 - Increase HR & BP
 - Increase coronary artery blood flow
 - Increased contractility and cardiac output
- Nicotine responsible for the addiction.

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

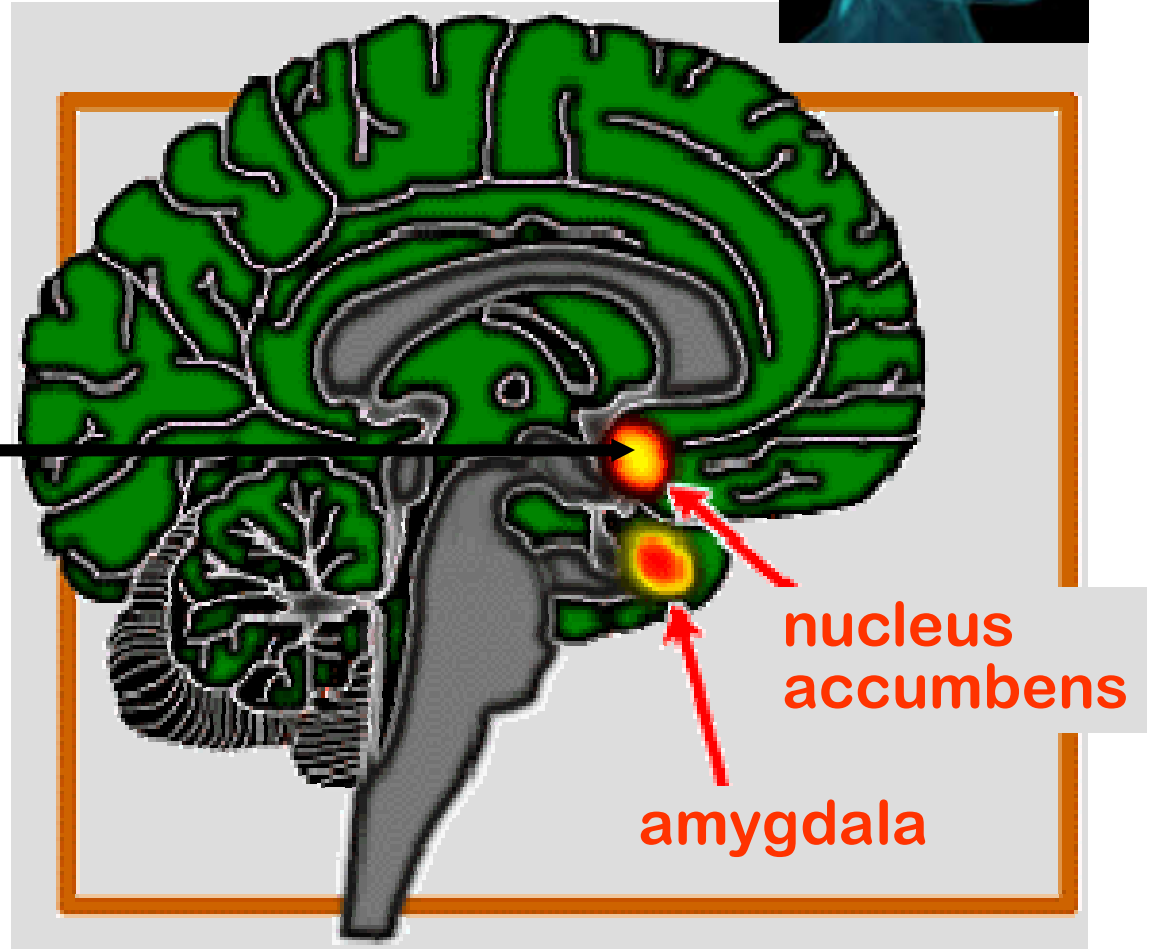
Approx. 44% of the cigarettes smoked in the United States are smoked by the mentally ill.
— Harvard Medical School study (11/2000)

Brain regions & pathways



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)

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

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

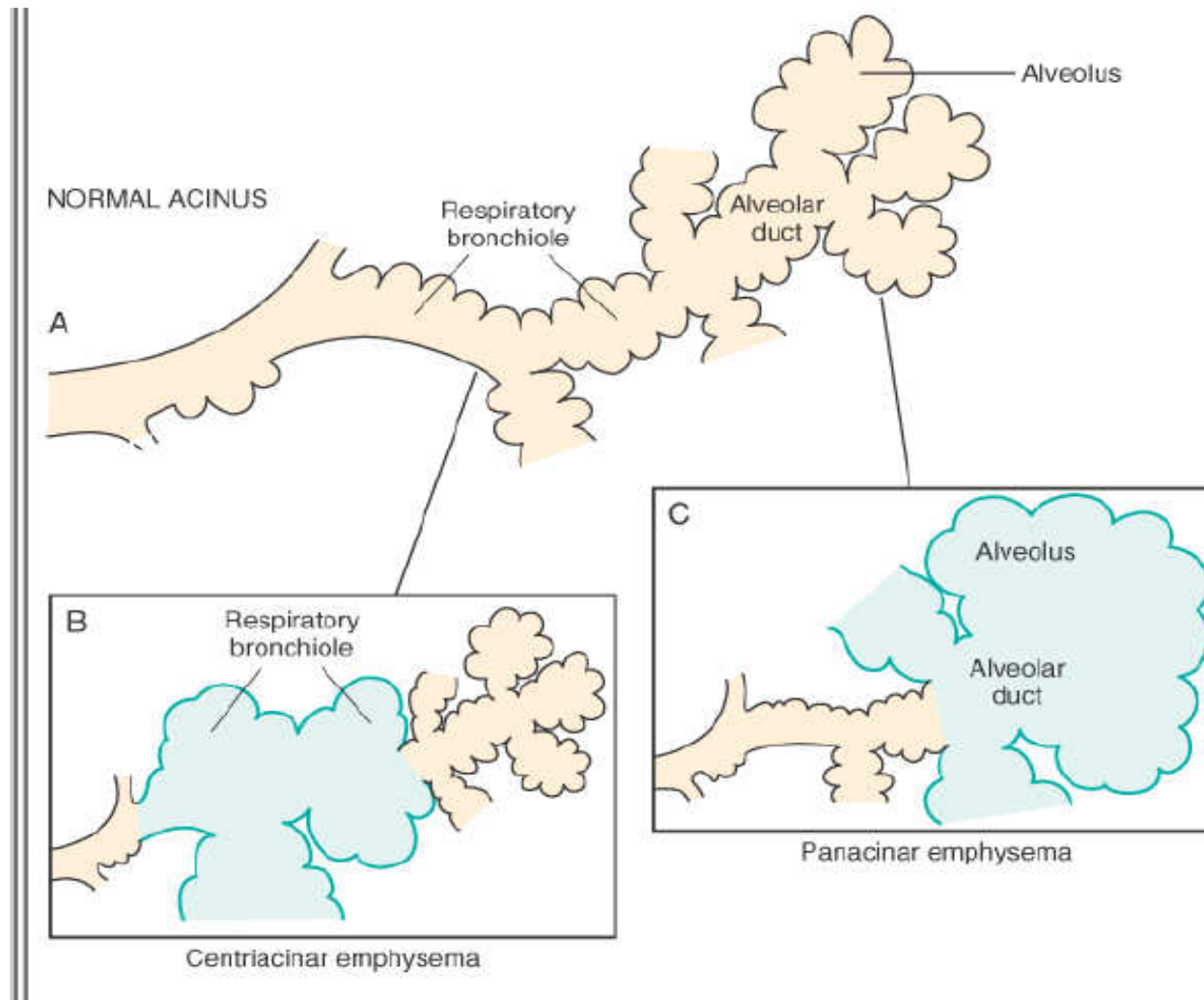
- Characterised by:
- abnormal permanent dilation of spaces distal to terminal bronchiole.
- Destruction of alveolar walls without obvious fibrosis



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, scarring or atelctasis.
- Dilated airspaces appear as cystic spaces (0.5-2.0 cm).
- Occasionally associated with large subpleural bullae or blebs.

Irregular Emphysema

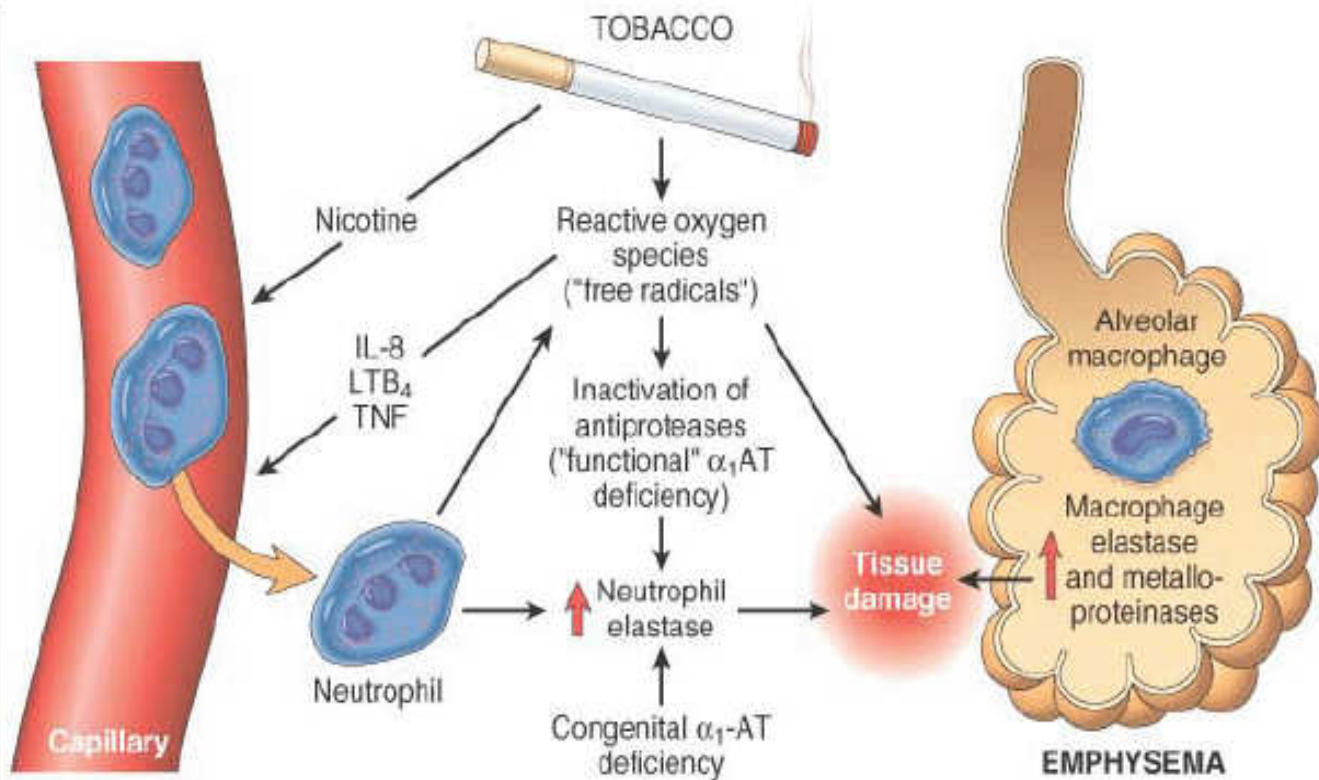
- Irregular involvement of acinus.
- Invariably associated with scarring.
- Usually complication of various inflammatory processes.
- Complications
 - Chronic bronchitis
 - Interstitial emphysema
 - Pneumothorax – from rupture of a bullae or surface blebs.



Pathogenesis

- Destruction of alveolar walls by un-opposed action of elastase and deficiency of anti-elastase action of α 1-antitrypsin.
- Smoking increases elastase level and activity.
- Smoking attracts PMNs & macrophages – sources of α 1-antitrypsin.
- There is a also a hereditary form of α 1-antitrypsin deficiency. Pi (protease inhibitor gene) on chromosome 14 affected.

Pathogenesis of Emphysema

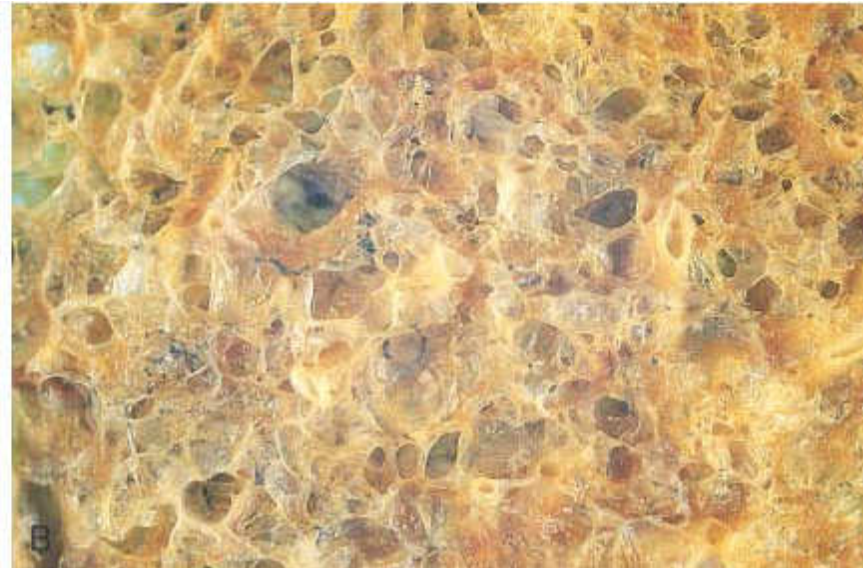


Ref: Pathological Basis of Diseases, 7th Ed.

Emphysema - Morphology



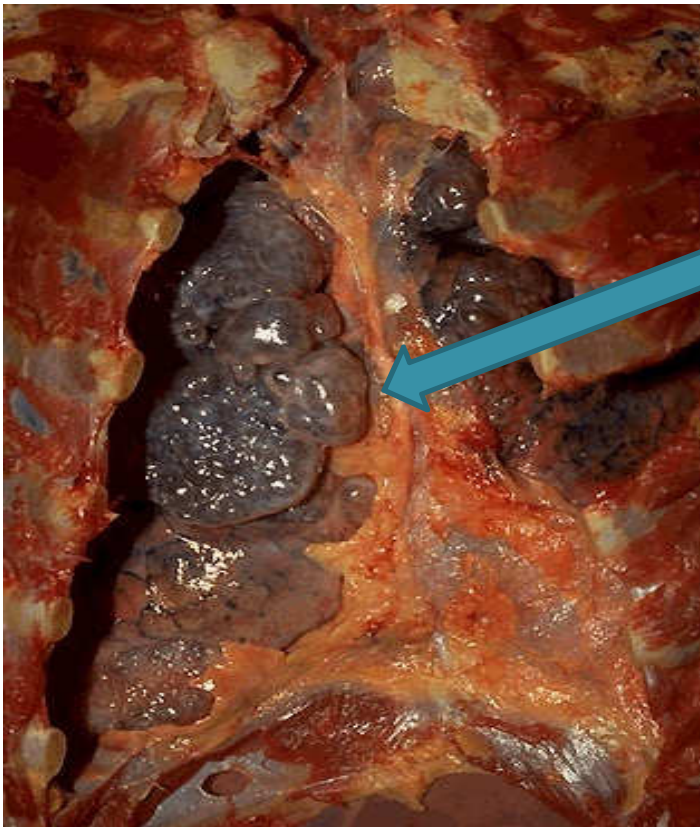
Centriacinar emphysema. Central areas show dilation.



Panacinar emphysema. Entire pulmonary parenchyma dilated

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

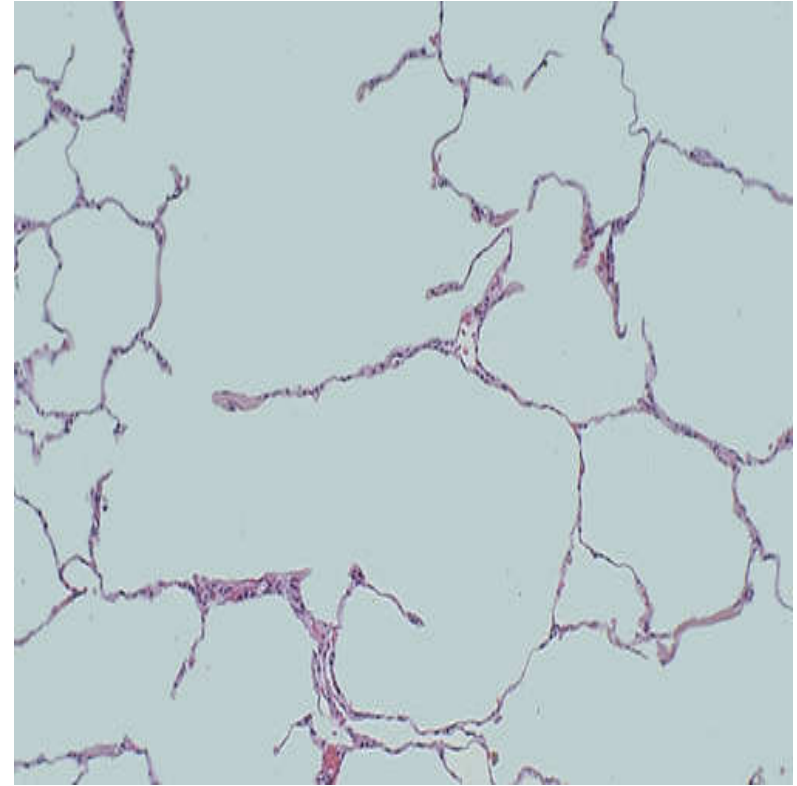
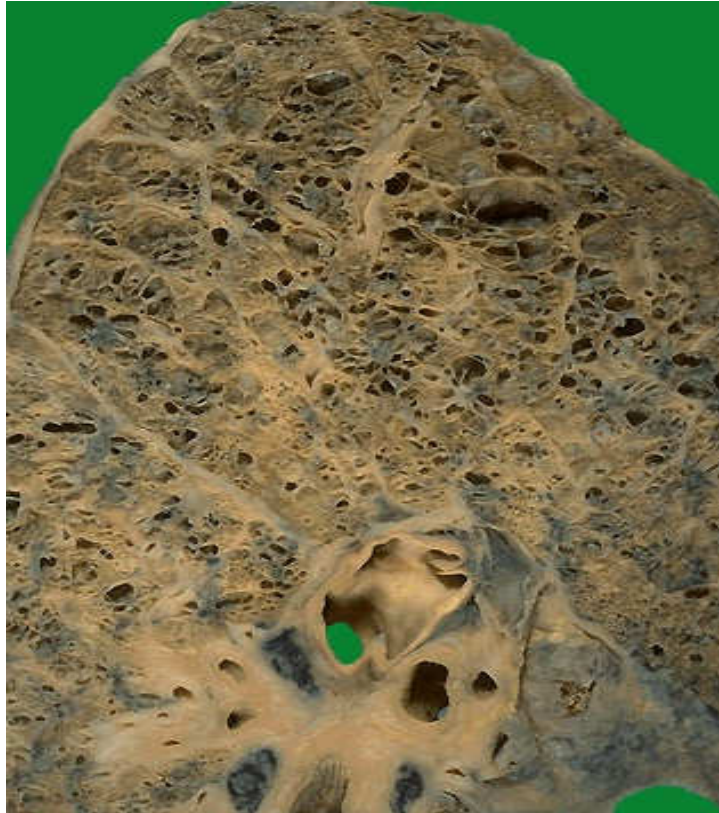
Bullaous Emphysema



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.



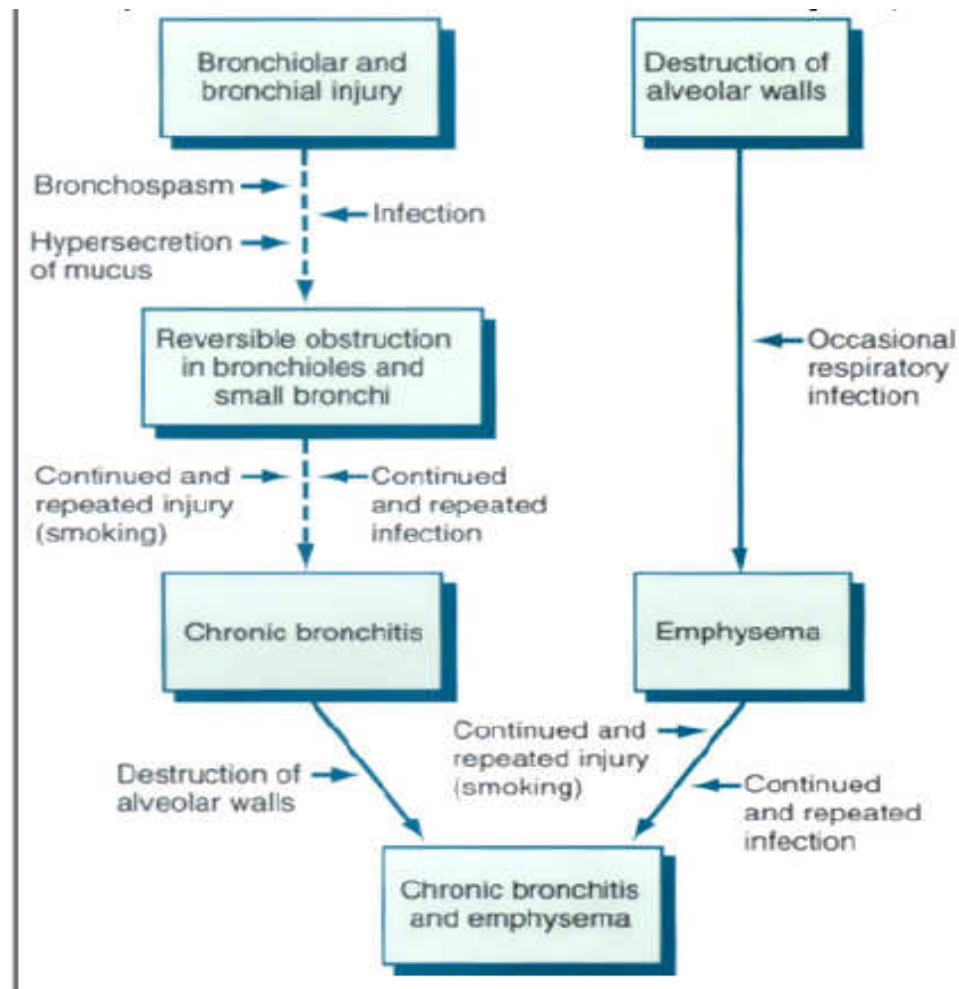
Bronchitis - Pathogenesis

- 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

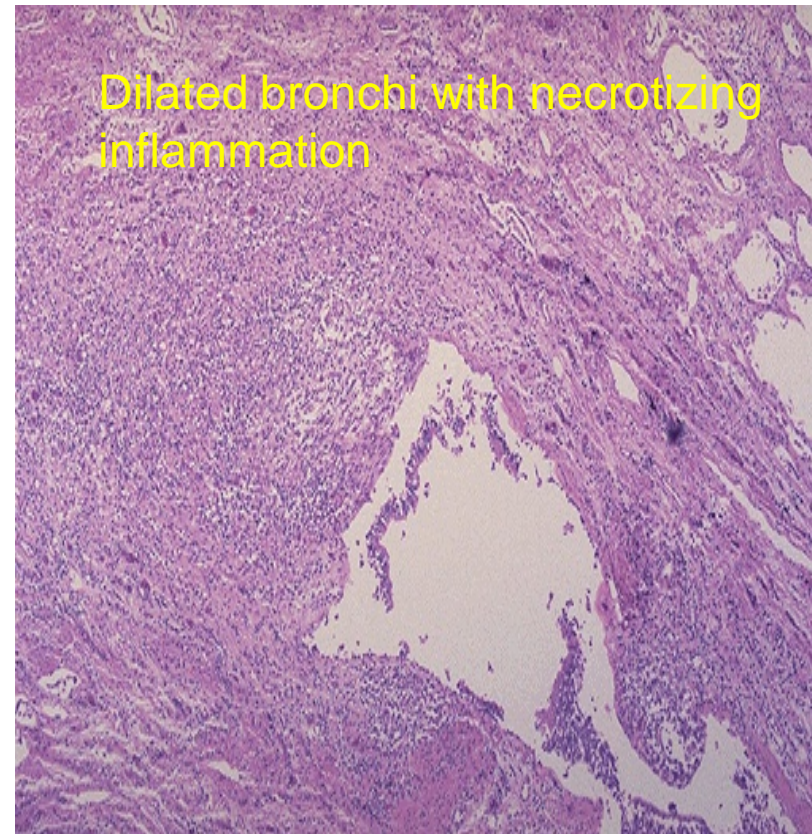
- Bronchial obstruction – tumor, foreign bodies, mucus impaction especially in asthmatics.
- Congenital or hereditary conditions e.g. Cystic fibrosis, immotile cilia.
- Necrotising pneumonia – TB or staphylococci or mixed infections.



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.
- Micro: acute & chronic inflammation. Areas of necrotizing ulceration.

Bronchiectasis - Morphology



Ref: Internet Pathology Library, University of Utah.

Clinical Signs & Symptoms

Disease	Signs & Symptoms
Chronic bronchitis	Cough & sputum production, “blue bloater”, barrel shaped chest, muscular chest
Bronchiectasis	Cough, purulent sputum, fever
Emphysema	“Ping puffer”, thin chest, dyspnoea
Asthma	Episodic wheezing, cough, dyspnoea



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 atherosclerosis genesis.



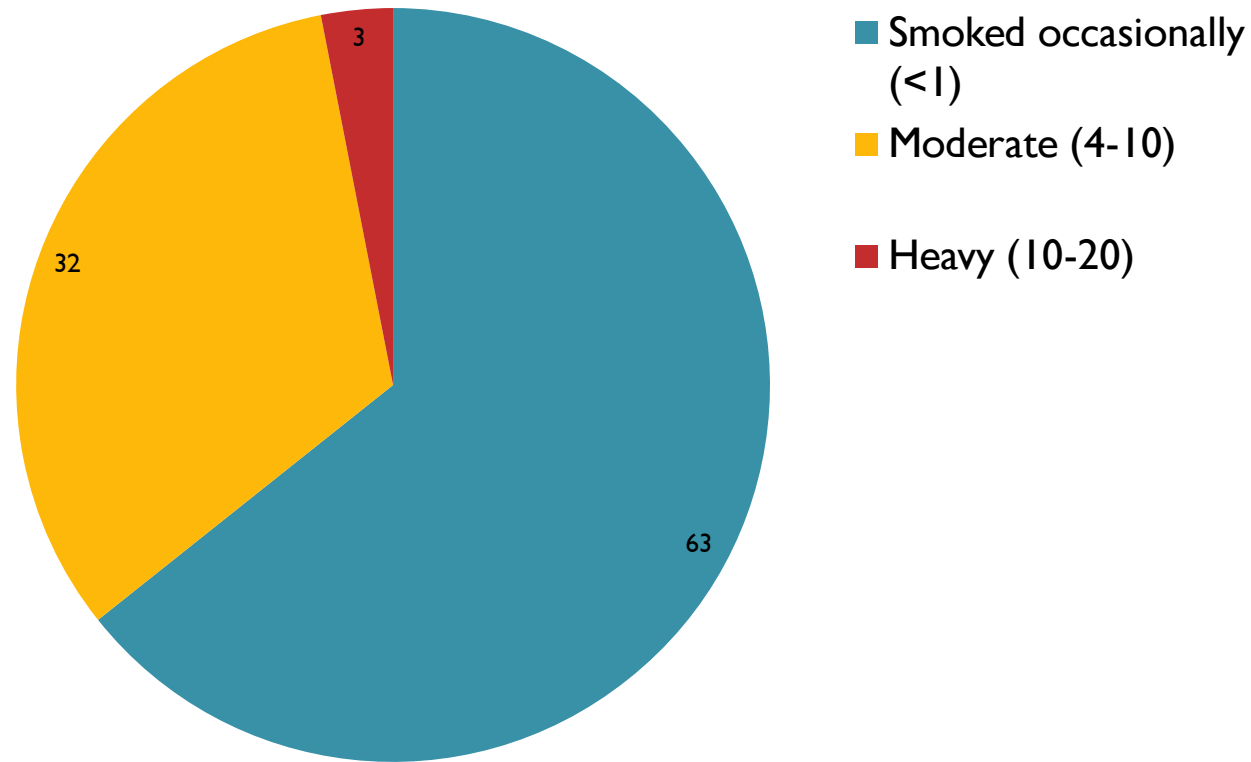
GIT

- Smoking is risk factor:
- Bowel Ischaemia
- Peptic ulcer diseases
- Colonic malignancies
- Pancreatitis
- Others



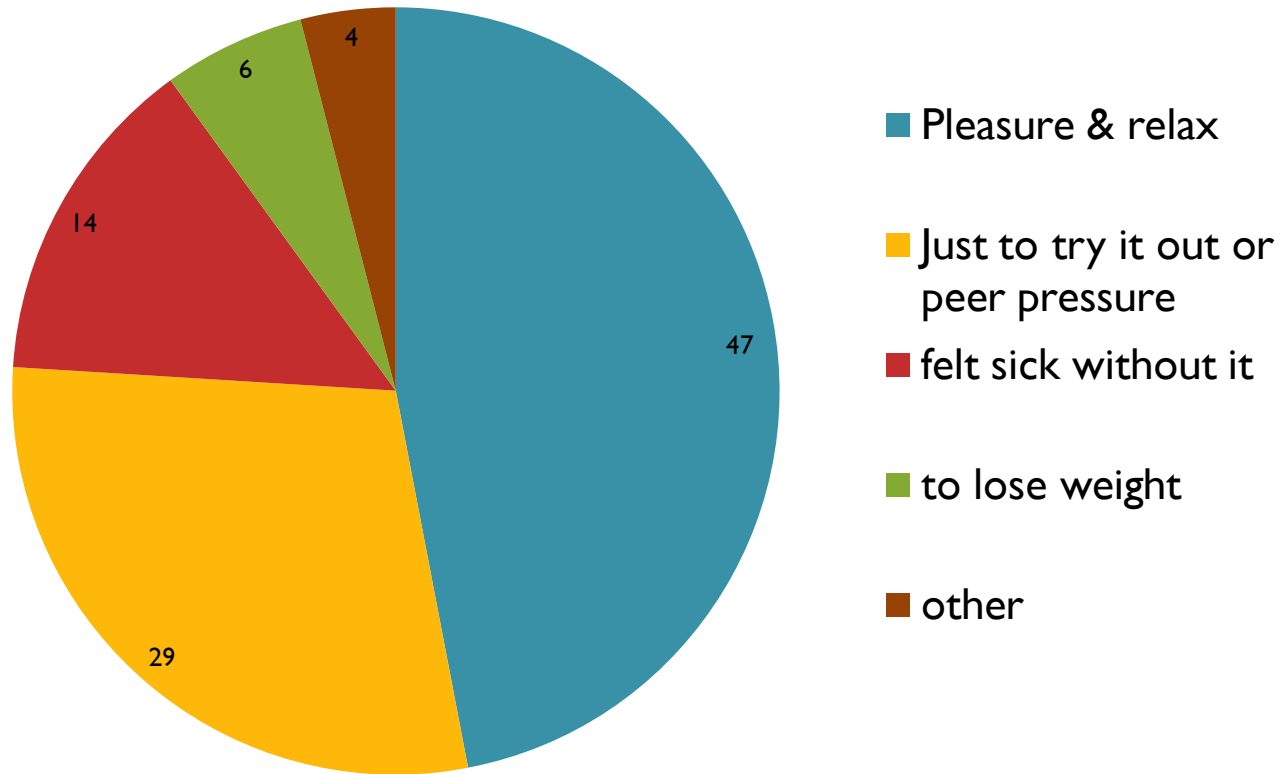
PREVENTION

Why Do People Smoke?



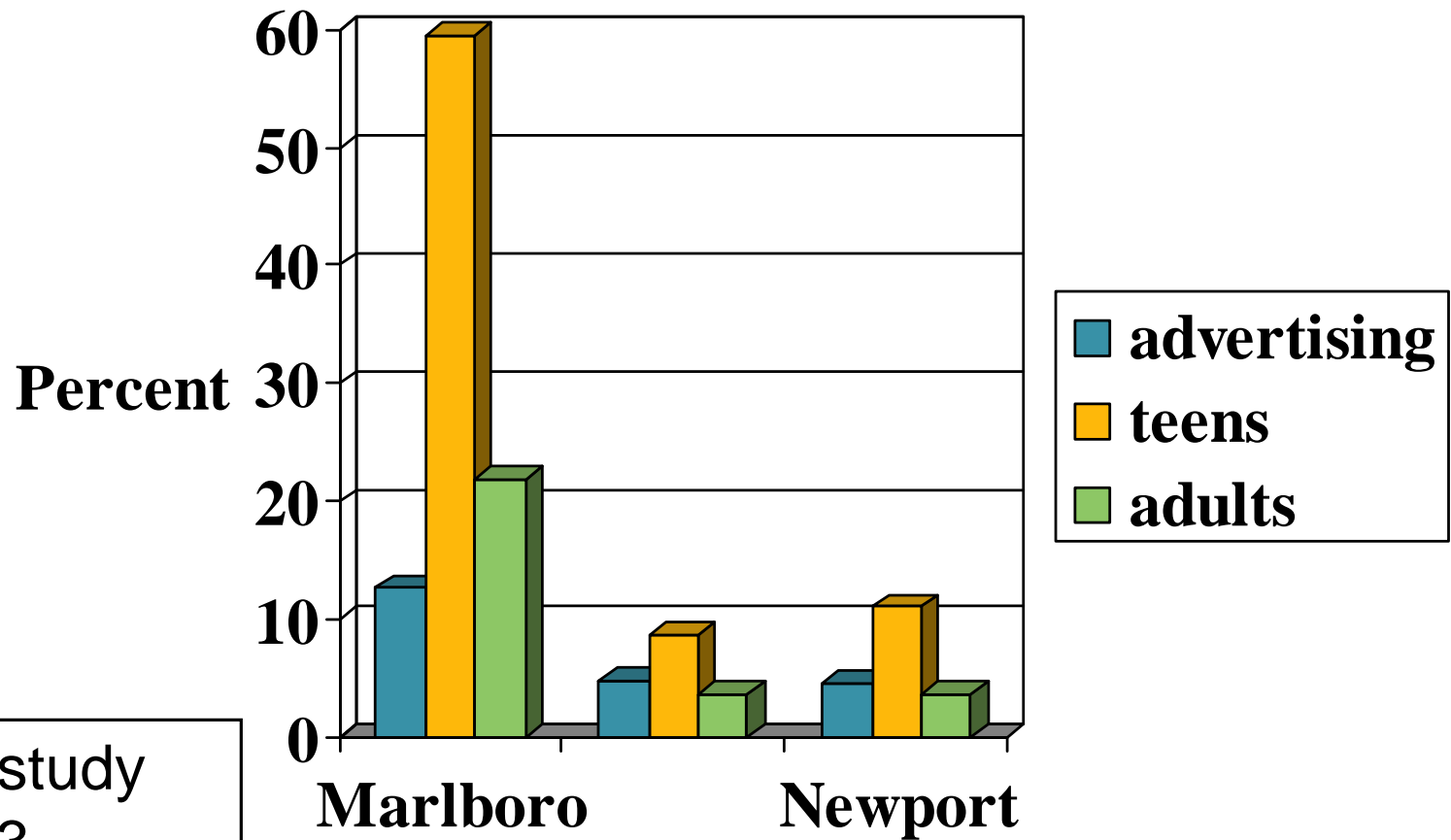
Survey among 2nd year Lae School of Nursing students (n=31), 1999

Why Do People Smoke?



Survey among 2nd year Lae School of Nursing students (n=31), 1999

Are teens influenced by advertising?



Period of study
1973-1993

From
ASH, Australia



SMOKING REDUCES YOUR ABILITY TO GET AN ERECTION



Action on Smoking
and Health



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

MACDONALD



EXPORT 'A'

25 Cigarettes • Full Flavour

Qualité classique, un goût unique
 Smooth Flavour, Classic Quality



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

damaged heart muscle - result of
 clogged artery



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

Qualité classique, un goût unique
 Smooth Flavour, Classic Quality

MACDONALD



EXPORT 'A'

25 Cigarettes • Full Flavour

If you smoke, please quit!





END

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

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www.pathologyatsmhs.wordpress.com