Environmental pathology

Prof.T.Kerényi 13.12. 2017

Environmental toxic agents are natural and man-made

$\Rightarrow$ environmental disease

outdoor environment (20%)----------indoor environment (80%)

occupational diseases

Long term exposures in polluted areas $\Rightarrow$ excess chronic respiratory diseases

$\Rightarrow$ reduced life expectancy

U.S. air quality standards for

- sulfur dioxide
- nitrogen dioxide
- ozon
- lead
- carbon monoxide
- suspended particles

Natural sources of nitrogen oxides: volcanoes, oceans
lightning strikes
biological decay

amounts released from natural sources in the world per year
20-90 million tonnes

from human sources world-wide
24 million tonnes

Natural sources of sulphur dioxide: release from volcanoes
forest fires
biological decay

amounts released from natural sources in the world per year
80-288 million tonnes

from human sources world-wide
around 69 million tonnes

rainwater is naturally acidic as a result of CO_2 dissolved
natural sources of **sulphur and nitrogen oxid emissions can contribute** further to the acidity of rainwater

Air pollution:
the release of chemicals and particulates into the atmosphere
Common gaseous pollutants: carbon monoxide, sulfur dioxide,
nitrogen oxides industry and motor vehicles.
chlorofluorocarbons (CFCs)
Photochemical ozone and smog are created as nitrogen oxides
and hydrocarbons react to sunlight
Particulate matter, is characterized by their micrometre size PM_{10} to $PM_{2.5}$.

Water pollution, by the discharge of wastewater
from commercial and industrial waste into surface waters
such as chlorine, and including urban runoff
agricultural runoff, which may contain
chemical fertilizers and pesticides disposal
leaching into groundwater
Plastic pollution: involves the accumulation of plastic products

Soil contamination occurs when chemicals are released
by spill or underground leakage
they are mostly hydrocarbons, heavymetals,
MTBE, herbicides, pesticides
chlorinated hydrocarbons

MTBE = Methyl *tert*-butyl ether is an organic compound
it is a gasoline additive to raise the octane number.

Cities were always the cesspools of pollution
industrial revolution gave birth to environmental pollution
recently the term **persistent organic pollutant (POP)** describes a group of chemicals such as PBDEs and PFCs among others.

PBDEs = Polybrominated diphenyl ethers used as flame retardant.
for building materials, electronics, furnishings, motor vehicles, airplanes
plastics, polyurethane foams, and textiles.

PFCs = Polyfluorocarbons and their derivatives are
useful fluoropolymers, refrigerants, solvents, and anesthetics

From the effects of external environmental factors pathological changes may result : e.g.: goiter (iodine deficiency)
mottled enamel of the teeth
(excessive amounts of fluoride)

Episodes of outdoor air pollutions ⇒ substancial number of excess deaths
France, Meuse-valley 1930; U.S.A Donora, Pennsylvania 1948
U.K. London fog of 1952 ⇒ 4000 excess deaths (smoke + fog = smog)
8000 in the next two weeks
excess acute mortality in **the very old**
the very young
chronic cardiopulmonary diseases

Smog: ozon, NO, SO_2 ⇒ bronchial hyperreactivity
alveolitis – lung fibrosis
emphysema

SO_2 : a greenhouse gas - **significant warming** of Europe, Asia, North America
a precursor to **acid rain** - it is released naturally by **volcanic activity**
the amount of SO_2, released by the industry in the U.S. 17,1 Mt
higher levels ⇒ chronic bronchitis in schoolchildren

Respiratory mortality and hospital admissions are strongly related to the previous days levels of air pollutnats

smoking is a voluntary healt risk

leads to the greatest number of problems of any drug in use

contributes to **more than 400,000 deaths each year** in the USA

Persons **in the lowest occupational levels** start to smoke earlier

and in greater numbers

The largest single preventable cause of disease, disability and mortality

it accounts for more than a third of all deaths in middle age

In the cardio-respiratory system:

cause of chronic bronchitis and emphysema of the lung

increased numbers of lung and larynx cancers

increased numbers of cases of atherosclerotic heart disease

smoker's leg

In the GI system

increases the risk for cancers of the esophagus, pancreas

and for gastritis, gastric ulceration

In the urinary system

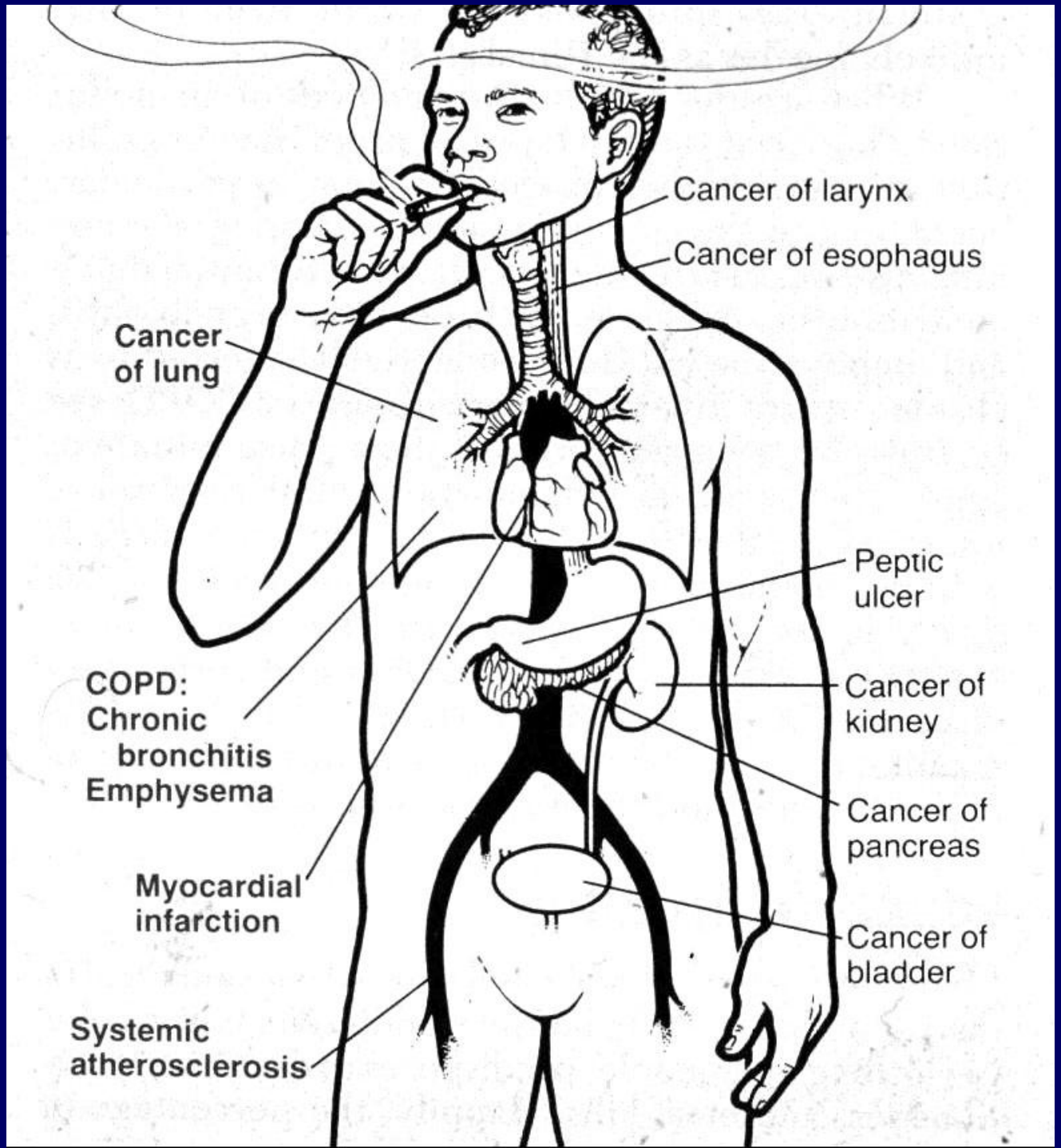
bladder, kidney cancers

Gynecological and neonatological problems

risk for cervix cancer
decreased birth weight,
premature birth
increased perinatal mortality
spontaneous abortion
in mothers who smoke more than 3 cigarettes per day
are increased fetal deaths late in gestation
50% hyaline membrane disease of the child

Other risk:

cataracts of the crystalline lens of the eye


Cancer of larynx
Cancer of esophagus
Cancer of lung
Peptic ulcer
COPD: Chronic bronchitis Emphysema
Cancer of kidney
Cancer of pancreas
Myocardial infarction
Cancer of bladder
Systemic atherosclerosis

Occupational causes of lung cancer

Agents	Occupations
Arsenic	Smelting metal ores
Asbestos	Mining and milling of asbestos. Insulation and construction workers
	Textile manufacture, *etc.*
Bischloromethyl ether	Ion exchange resin manufacture
Hexavalent chromium salts	Chrome pigment manufacture
Polycyclic aromatic hydrocarbons	Coke oven workers
	Gas retort workers
Mustard gas	Mustard gas manufacture
Nickel (probably nickel oxide or subsulphate)	Nickel refining
Radiation	Underground miners: uranium, fluorspar, haematite

Alcoholism

Definition: regular and excessive use of alcohol with concomitant social interpersonal, legal, occupational, and/or physical problems

Regular use of alcohol has resulted in a state of physiologic tolerance!

Epidemiology: Alcohol is consumed at some time by **up to 80% of the population**

approximately 20% of patients have alcoholism

Lifetime risk for alcohol dependence in Western countries

~10–15% for men and 5–8% for women

statistics are higher for alcohol abuse

Distribution: all socioeconomic strata and all racial backgrounds

Risk Factors: Genetic factors

diminished alcoholism risk in ~50% of Asian men and women

due to an inactive form of alcohol dehydrogenase, which results in

higher levels of toxic acetaldehyde following alcohol ingestion

Family history: **4-fold increased risk in children of alcoholics**

risk increased even if adopted at birth and raised without knowledge of biologic parents

Presence of other **psychiatric disorders** - vulnerable personality

Male sex

Environmental factors

Peer group pressure

Access to alcohol

Alcohol is a central nervous system (CNS) depressant that acts on receptors for γ-aminobutyric acid (GABA), the major inhibitory neurotransmitter

Chronic alcohol use produces physiologic and psychological dependence

Alcoholism is a complex, genetically influenced disorder

- **genes explain about 60% of the risk**
- genes affecting the intensity of the response to alcohol
- subgroups **require higher blood alcohol concentrations** to produce the effects seen at lower blood levels in other people

Social, psychological, and environmental factors also contribute to the development of alcohol-related disorders

Disorders commonly associated with alcohol dependence

- many **cancers of the head and neck, esophagus, and stomach**
- **hepatitis and cirrhosis**
- **pancreatitis**
- alcohol-induced **peripheral neuropathy** occurs in 5–15% of alcoholics

Cerebellar degeneration ~1% of alcoholics

syndrome of progressive unsteady stance and gait

often accompanied by mild nystagmus

Severe cognitive problems, alcoholic dementia syndrome

irreversible cognitive changes (possibly from diverse causes)

Psychiatric syndromes

Alcohol-induced mood disorder

Intense sadness, anxiety disorder

psychotic disorder: hallucinations and/or paranoid delusions

GI findings

inflammation of the esophagus and stomach

GI bleeding

incidence of acute pancreatitis ~25 per 1000 per year

chronic pancreatitis - almost 3-fold higher than in the general population

fatty accumulation in the liver, alcohol-induced hepatitis

cirrhosis 15–20%

Cardiovascular findings

mild to moderate hypertension

Cardiomyopathy - one-third of cases are alcohol induced

atrial or ventricular arrhythmias, especially paroxysmal tachycardia

Genitourinary system changes

- increases sexual drive and decreases erectile capacity in men
- irreversible testicular atrophy

Gynecological disorders

- amenorrhea
- decrease in ovarian size
- absence of corpora lutea with associated infertility
- spontaneous abortions

Musculoskeletal findings

- acute alcoholic myopathy
- alteration in calcium metabolism, lower bone density
- increased risk for fractures and osteonecrosis of the femoral head

Any sudden decrease in intake can produce **withdrawal symptoms**

laboratory tests for the diagnosis

- elevated γ-glutamyl transferase (>30 U)
  - and carbohydrate-deficient transferrin (>20 U/L)
  - high mean corpuscular volume
- high serum uric acid
- liver function tests abnormal

Wernicke-Korsakoff's syndrome - Wernicke's encephalopathy

Seen in <10% of alcoholics

Result of thiamine deficiency, especially in persons with transketolase deficiency

Wernicke's disease (pseudoencephalitis haemorrhagica superior) hemorrhages in the mammillary bodies - alcoholismus, beriberi, porphyria, intoxications

Imaging

brain CT or MRI

increased size of the brain ventricles and cerebral sulci are seen in ≥50% of chronic alcoholics

atrophy of the cerebellar vermis in cerebellar degeneration

Fetal alcohol syndrome, caused by heavy drinking during pregnancy

Facial changes with epicanthal eye folds, poorly formed concha, and small teeth with faulty enamel

Cardiac atrial or ventricular septal defects

Aberrant palmar crease and limitation in joint movement

Microcephaly with mental retardation

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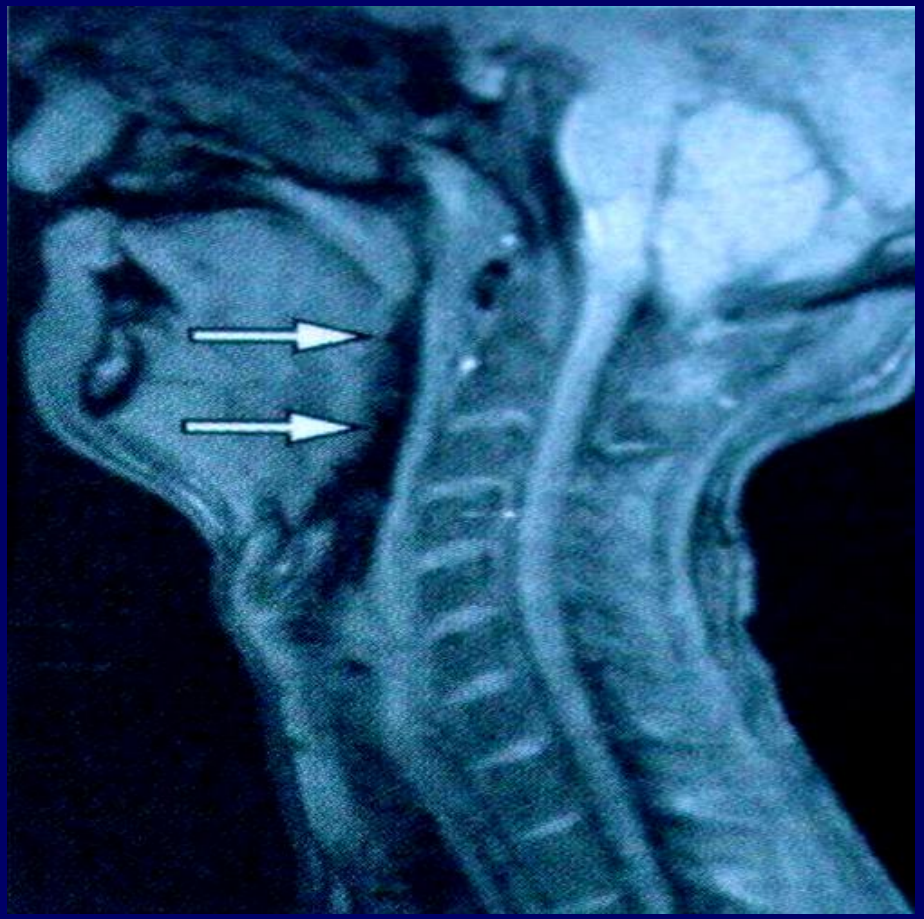
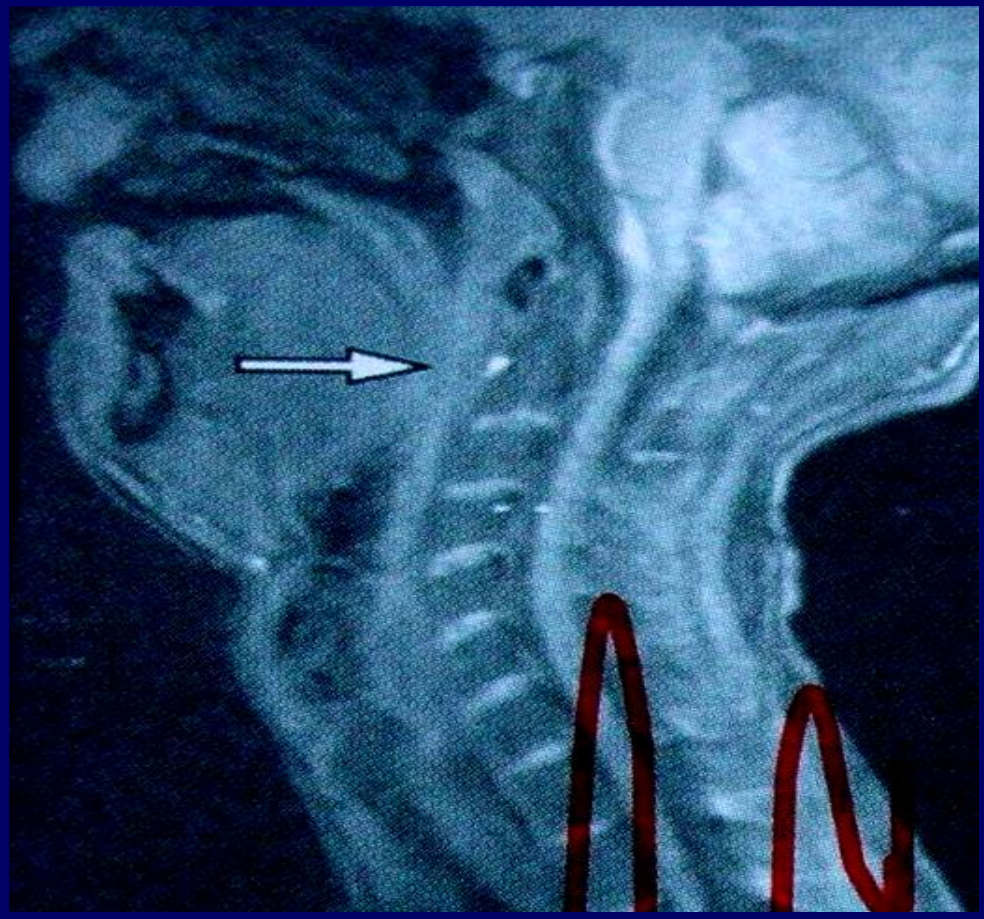
Sleep apnea

In 75% of alcoholic men over age 60 relaxes muscles of the pharynx → snore

arterial oxygen saturation is reduced

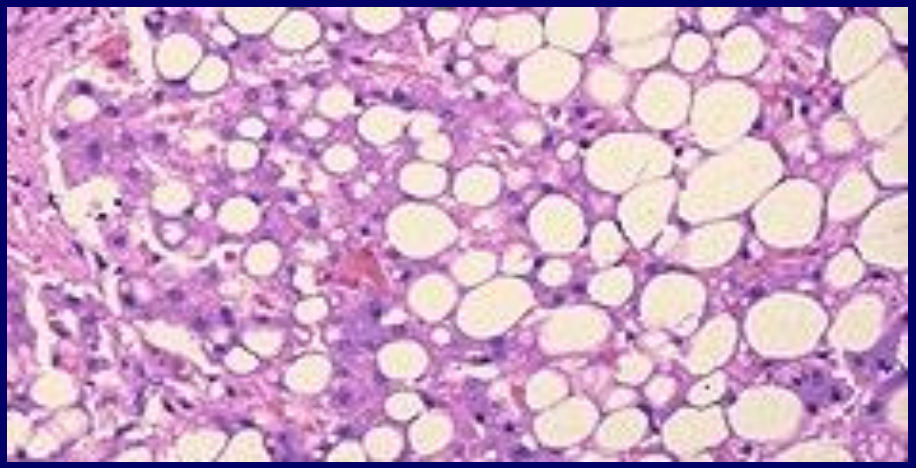




Nonalcoholic steatohepatitis - NASH

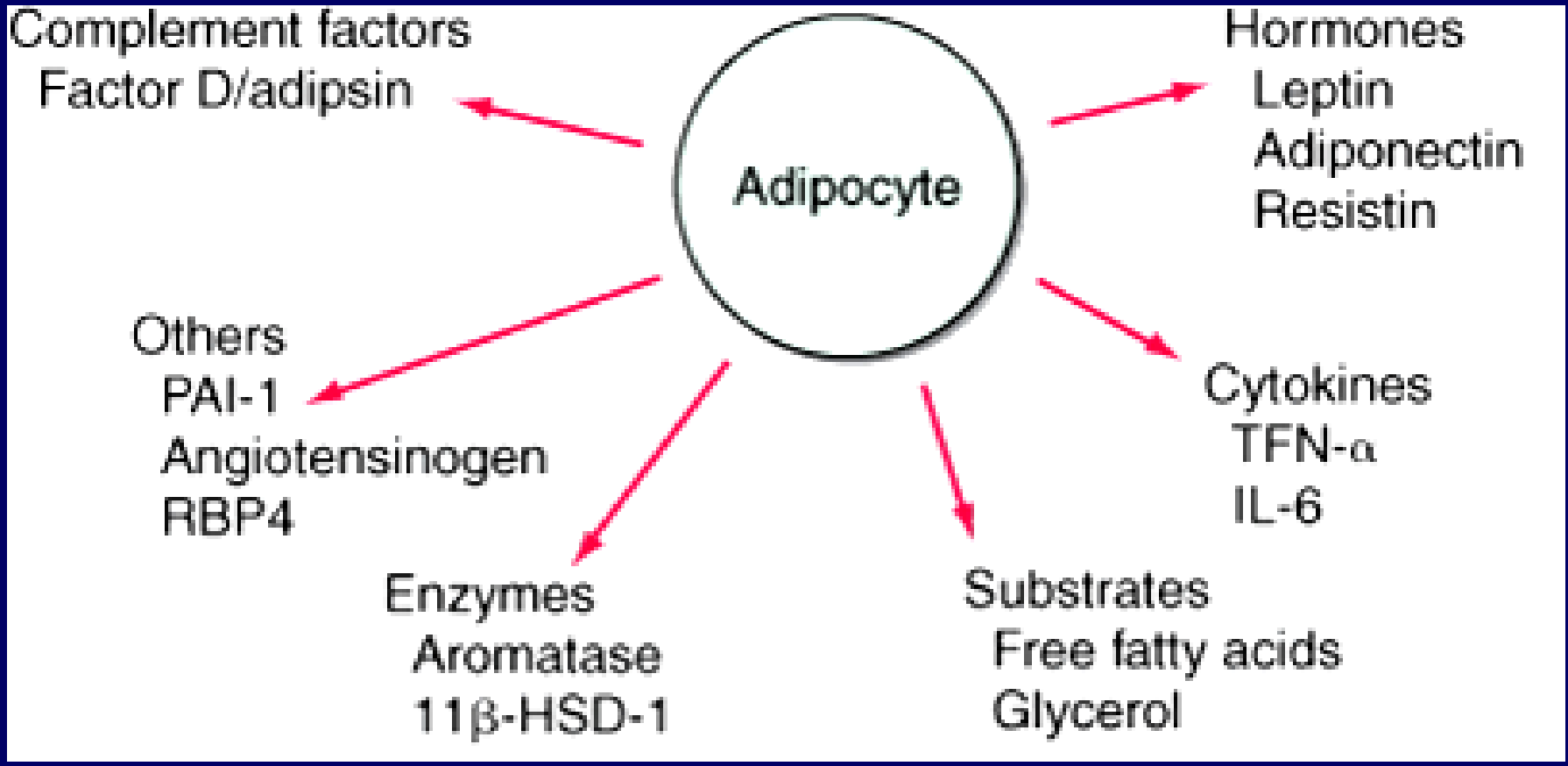
common, often “silent” liver disease - **it resembles alcoholic liver disease**

Morphology: fat in the liver, along with inflammation and damage
can be severe and can lead to cirrhosis
the liver is permanently damaged and scarred
Liver biopsy reveals NASH or simple fatty liver



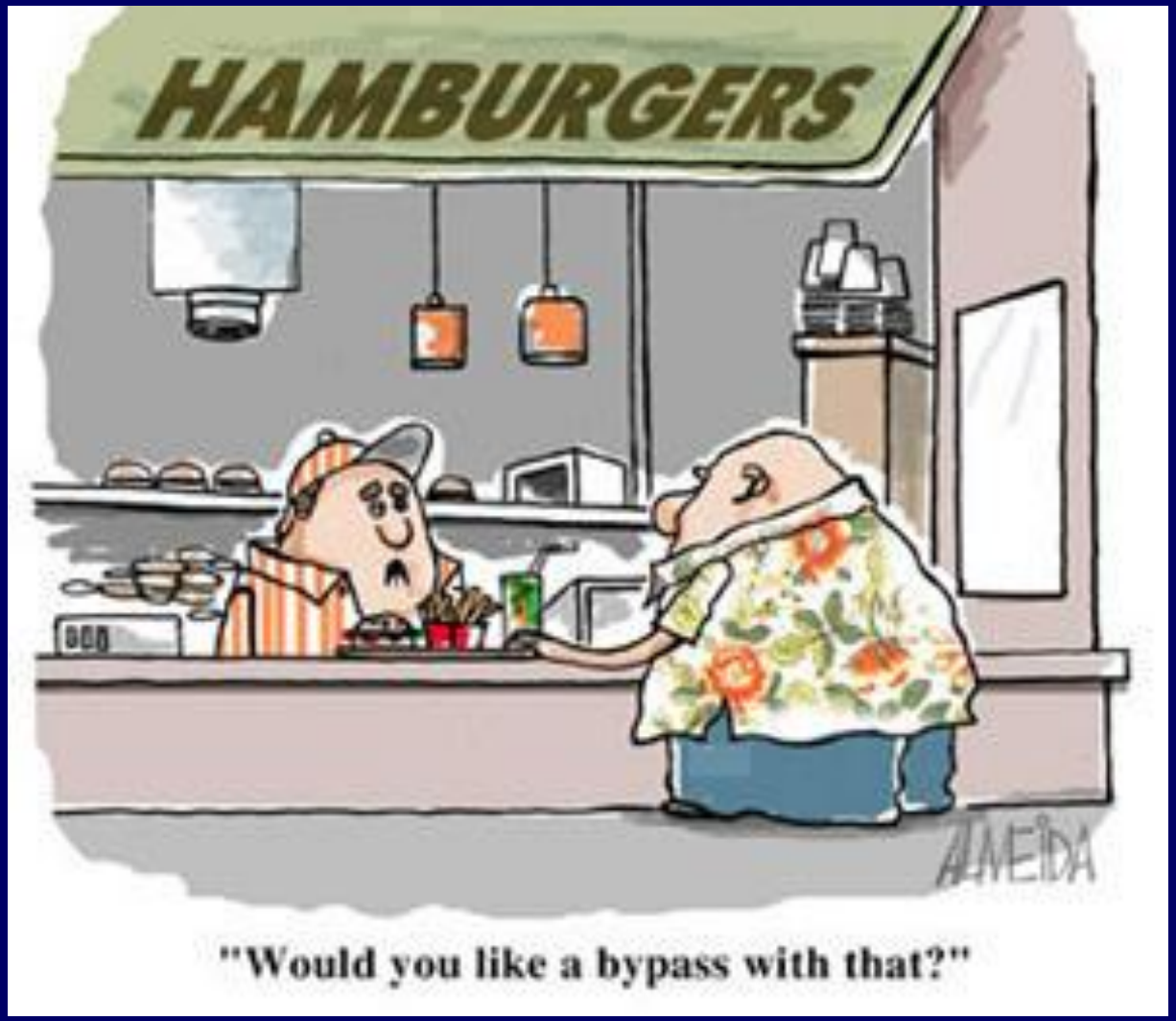
Epidemiology**: it affects 2 to 5 percent of Americans**
Non-alcoholic fatty liver are becoming more common
because of the greater number of Americans with obesity
in the past 10 years, the rate of obesity has doubled in adults
and tripled in children - NASH can occur in children

Complications: Obesity also contributes to diabetes and high blood cholesterol



Factors released by the adipocyte that can affect peripheral tissues

PAI, plasminogen activator inhibitor
TNF, tumor necrosis factor
RBP4, retinal binding protein 4.



25% overweight = 175% morbidity and mortality!!!

Nutrition and Cancer: Dietary Recommendations

1. Avoid obesity.
   Individuals who are 40% or more overweight increase their risk for certain types of cancers.
2. Reduce total fat consumption.
   A high-fat diet may be a factor in the development of particular cancers.
3. Eat more high-fiber foods: whole grain cereals, fruits, vegetables.
   Studies suggest that a high-fiber diet may help to reduce the risk of colon cancer.
4. Include foods rich in vitamins A and C daily.
   Vitamin A
   - Dark green, deep yellow vegetables and fruits: spinach, carrots, apricots

   Vitamin C
   - Oranges, grapefruit, strawberries, green and red bell peppers
5. Include cruciferous vegetables regularly
   Vegetables in the cruciferous family include cabbage, broccoli, brussels sprouts, cauliflower.
6. Minimize consumption of smoked, salt-cured, and nitrite-cured foods.
7. Keep alcohol consumption moderate.

Adapted from *Cancer Facts & Figures—1992*. Atlanta, GA: American Cancer Society; 1992:21.

Anabolic-Androgenic Steroids (AAS)

its use has increased substantially over the past two decades, mainly

for their effect of **increasing muscle mass**
increasing athletic **performance**
enhancing physical appearance

do not increase the level of skill in performance and
cardiovascular function

adverse effects to AAS use: testicular atrophy, gynecomastia
decreased testosterone production
decreased breast size
hypertension, fluid retention
increased risk for heart disease
and sudden death
decreased HDL cholesterol
increase of cardiac size
myocardial fibrosis, cardiomyopathy
tendon injuries, nosebleeds
sleep disorders
increasing risk for morbidity and mortality

major psychiatric effects: mood disorders
depression and mania
decreased sexual function

Intravenous Drug Abuse

many drugs can be injected intravenously
the drugs have the major effect of impairment of mental function
heroin can produce a nephropathy

the route of administration can have serious complications
a wide variety of infections: human immunodeficiency virus
the causative agent for AIDS
viral hepatitis
particularly hepatitis B and C
bacterial infections
are more likely to have tuberculosis

"talc granulomatosis" can occur because many injected drugs
have been adulterated with an inert substance
(such as talcum powder)
to "cut" or dilute the amount of drug

Lung effects of selected common toxic chemical agents

Agents	Selected exposures	Effects
acid fumes H_2SO_4, HNO_3	manufacture of fertilizers, dyes explosives, rubber products	mucous membrane irritation, chemical pneumonitis
ammonia	refrigeration, petroleum refining, manufacture of plastics	mucous membrane irritation, chemical pneumonitis
cyanides	electroplating, manufacture of mirrors, photo supplies	respiratory arrest pulmonary edema death
formaldehyde	manufacture of resins, leathers, rubber, woods, emission from urethane foam insulation	same as acid fumes cancer in animals
isocyanates	production of polyurethane foams, plastics, adhesivnes	dyspnea, pulmonary edema
sulfur dioxide	manufacture of bleaches, food processing, burning of fossil fuels, wood pulp industry	mucous membrane irritant, epistaxis, chronic bronchitis

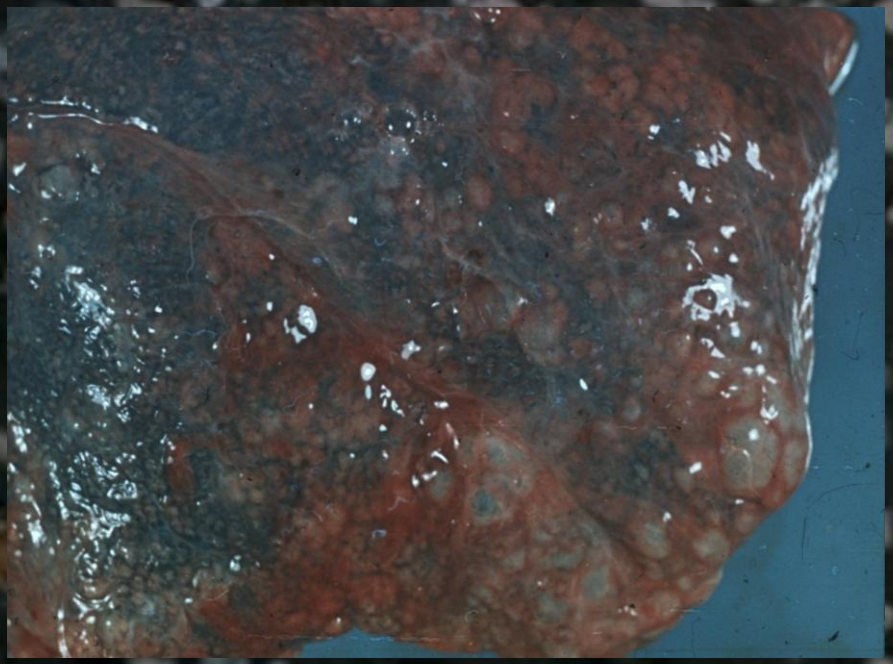
Predisposition to other diseases: asthmatic bronchitis, tuberculosis, cancer

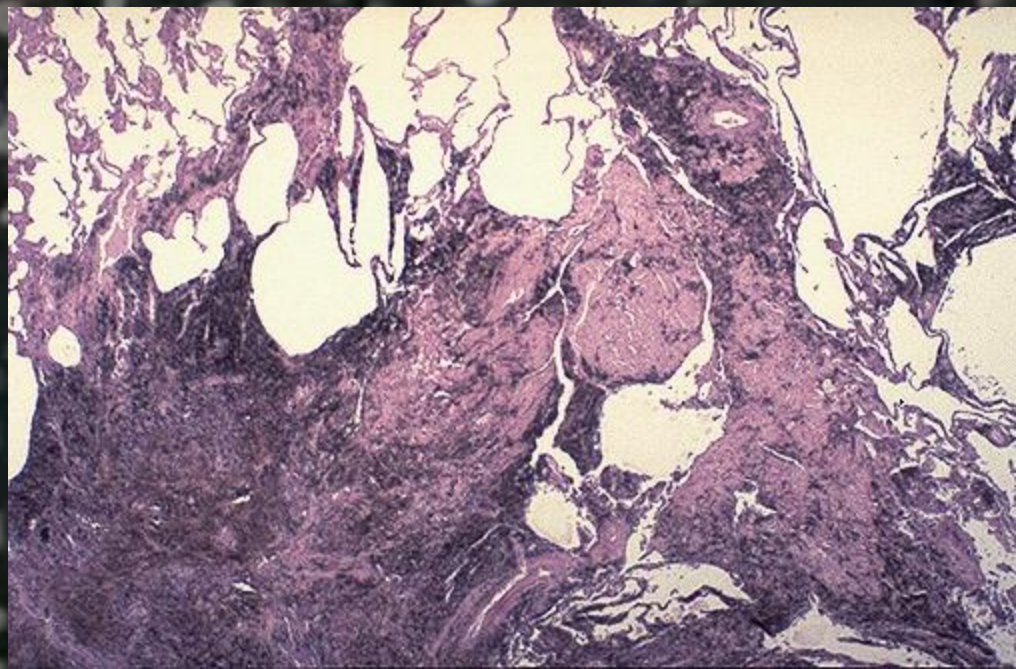
over the past twenty years, traffic-generated dust emissions have become recognised as a significant source of atmospheric particulate pollution

air pollutnats in urban atmosphere:

combustion-derived particles – anthracotic pigment
particles formed from and tire debris
paved road dust: asphalt, concrete, SiO_2

anthracotic pigment (soot) ordinarily is not fibrogenic, but in massive amounts a fibrogenic response can be elicited "black lung disease„





coal dust $\Rightarrow$ coal worker's pneumoconiosis

enormous social, economic, medical significance
- 50% of anthracite miners
- 12% of all miners

claim for damage 1.000.000 Euro pro person

prevalence is lower in bituminous coal mines (Western U.S.)

Caplan's syndrome = rheumatoid arthritis with an immunopathologic mechanism

sources of tire dust: vehicles
tire-derived fuel
barrier reefs
rubber as an asphalt additive

local effects of rubber dust are problems of
occupational health
public health

employment in the rubber industry ⇒
high incidence of tumors
bladder cancer
leukemia
stomach cancer
pancreas cancer
lung cancer
rectal cancer

Inhalation of dusts e.g.

asbestos ⇒ asbestosis – lung fibrosis

the most frequent inorganic dust-related pulmonary disease

exposure not limited to persons who directly handle with the material (e.g. housewife)

silica ⇒ silicosis

free silica (SiO_2) or crystalline quartz

exposures: mining, stone cutting, abrasive industries

acute silicosis fatal in 2 years

chronic silicosis after 15 to 20 years of exposure

progressive massive fibrosis

risk of silicotuberculosis

cotton dust ⇒ byssinosis

over 800.000 are occupationally exposed in the U.S.

disease in 25% of the exposed worker

bronchitis, bronchiectasia, alveolitis

INORGANIC DUSTS IN PNEUMOCONIOSIS

Pattern of response	Dusts
Retention	
Nodular	Iron
	Tin
	Barium
	Coal
Fibrosis	
Nodular	Silica
Diffuse	Asbestos
	Cobalt
Massive	Coal
	Silica
Caplan's nodules	Coal
	Silica

Opiates began their popular use in the 1800's
derivation of morphine in 1806
the invention of the hypodermic needle in 1848

Morphine was the leading pain-killing drug of the time
it was often rubbed or dusted into the wound during the Civil war

Heroin, first synthesized in by British chemist C. Adler Wright, in 1874
it has the capacity to create very high tolerance thresholds in the body
a tolerance 3 and 4 times the lethal dose limit for the normal population

most **street heroin** is "cut" with other drugs or with substances such as
sugar, starch, powdered milk, or quinine, strychnine, fentanyl

heroin abusers do not know the actual strength of the drug
they are at risk of overdose or death

withdrawal is painful and frightening visible signs of
dilated pupils, panic, chills, muscle cramps, nausea and profuse sweating

short term effects: euphoric feeling, taking 5 to 8 minutes
death within hours

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long term effects: infection of the endocardium and valves
abscesses, cellulites, and liver disease, various types of pneumonia from heroin's depressing effects on respiration

additives: clogging the blood vessels in liver, kidneys, or brain
infections, transmission of HIV
other diseases from sharing needles or other injection equipment

Cocaine

the major acute effects result from the increased circulating catecholamine

- vasoconstriction
- acute hemorrhages and infarction in the brain
- ischemic changes in the heart
  - contraction band necrosis of the myocardium
    - possible sudden death

cocaine with ethanol use can compound the myocardial damage

cocaine can affect the fetuses

- abnormalities of placental function
- low birth weight babies
- increased risk for placental abruption
- spontaneous abortion

Methamphetamine

a stimulant drug with inotropic effects upon the cardiovascular system

is metabolized to amphetamine, which is also a stimulant

there are ischemic changes to the myocardial fibers

myocardial effects are made worse by concomitant ethanol use

Ecstasy - (XTC)

methylene-dioxy derivatives of amphetamine and methamphetamine
"designer drugs" that generically are termed "ecstasy"

include 3,4-methylenedioxy-methamphetamine (MDMA), also known as "Adam"
3,4-methylenedioxy-ethylamphetamine (MDEA), also known as "Eve"
N-methyl-1-(3,4-methylenedioxyphenyl)-2-butanamine (MBDB), also known as "Methyl-J" or "Eden„
MDMA and similar compounds are "entactogens" that act upon dopaminergic and serotonergic pathways in the brain to give users a felling of euphoria, energy, and a desire to socialize

adverse effects: hyperthermia and neuropsychiatric effects
liver toxicity

long term use may be accompanied by memory deficits

a "designer drug" is a compound that is chemically altered from the form of a controlled substance in order to produce special effects and to bypass legal regulations

Gamma-hydroxybutyrate (GHB)

introduced into the U.S. in 1990 as a purported **stimulant to muscle growth**

during sleep

a metabolite of the neurotransmitter gamma aminobutyric acid (GABA)

also functions as a neurotransmitter by affecting the dopaminergic system

potentiate the effects of endogenous or exogenous opiates

soon banned because of problems with overdose and adverse reactions

effects of GHB can be potentiated by alcohol and by benzodiazepines

ingestion of GHB results in immediate drowsiness and dizziness

feeling of a "high„

a multitude of adverse effects that can occur within 15 minutes to an hour:
headache, nausea, vomiting, hallucinations, loss of peripheral

vision, nystagmus, hypoventilation, seizures, and short-term coma

withdrawl from GHB can have an onset in 12 hours and last up to 12 days