

OCCUPATIONAL CANCER

Occupational Cancer

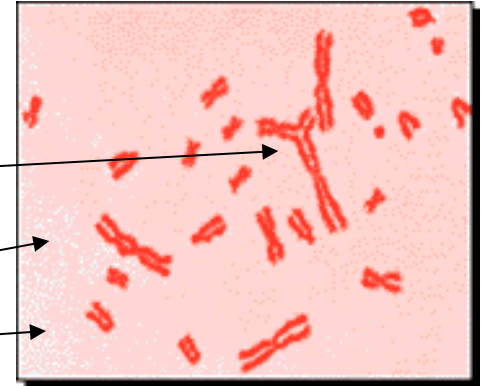
- **About 30-40 % of the population in industrialised world develops malignant disease during their lifetimes.**
- **Recently, 70 – 80 % are attributed to environmental causes:**
 - **30 % smoking**
 - **30 % food**
 - **10 % alcohol**
 - **5-10 % occupational exposure (chemicals, asbestos, radiation)**

Cancers arise from a single abnormal cell

- **Initial change** – result of a mutation in the genetic material – occurs spontaneously
- or after exposure to exogenous factors
- **Development of a tumour** depends on a variety of factors :
 - ability of the cell to **repair** the damage
 - presence of agents influencing tumour development
 - **effectiveness of the immune system**

Monitoring of the exposure to carcinogens in preventive examinations

- CHROMOSOMAL
- ABERRATIONS
exchanges,
- dicentric chromosomes
- breaks



(Normal 2% cells with aberrations)

Increased percentage is a sign of increased exposure to genotoxics!

- Chemical carcinogens: breaks of one chromatid
- Ionizing radiation: double breaks -dicentrics, rings

HUMAN CARCINOGENS ACCORDING TO IARC/WHO

(International Agency for Research on Cancer in Lyon, France – www.iarc.fr)

- **1) SUFFICIENT EVIDENCE OF CARCINOGENICITY (118 human carcinogens, by epidemiology):**
- **asbestos-arsenic- benzene-benzidine- beryllium - chromium^{VI}- radon-hard wood dust- *hepatitis B,C virus* – 2,3,7,8-TCDD – tobacco smoke- alcoholic beverages – formaldehyde - ionizing radiation – silica - diesel exhaust fumes – *Papillomavirus*, *Helicobacter pylori* – soots - use of solarium -polychlorinated biphenyles (PCBs)...**
- **2) LIMITED EVIDENCE OF CARCINOGENICITY (proven in animals and/or some groups of workers)**
- **2A – CHEMICALS PROBABLY CARCINOGENIC (75 items)**
- **acrylamide – cisplatine – perchloroethylene...**
- **2B - CHEMICALS WITH POSSIBLE CARCINOGENICITY**
- **(288 items - one species, inadequate doses, too few animals)**
- **Inadequate evidence of carcinogenicity**
- **lead- chloroform – cobalt - styrene –welding fumes – gasoline exhaust fumes – TiO₂....**

HUMAN CARCINOGENS ACCORDING TO IARC/WHO

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- **3) CHEMICALS NOT CLASSIFIABLE (503 items)**
- **coal dust- toluene- printing inks- tea- cyclamate - cholesterol – diazepam – mineral oils - chromium^{III}**
- **4) CHEMICALS PROBABLY NOT CARCINOGENIC TO HUMANS**
(only 1 chemical – kaprolactam)

IARC also studies organs involvement – this is important
for preventive examinations in workers (Table 4)

<http://monographs.iarc.fr/ENG/Classification/Table4.pdf>

SOME INDUSTRIAL PROCESSES CAUSALLY ASSOCIATED WITH HUMAN CANCER

- shoe manufacture and repair **benzene** leukaemia
- coal gasification **PAH** lung, kidney ca
- coke production **PAH** lung, kidney ca
- furniture manufacture **wood dust** - nasal cavity
- rubber industry **aromatic amines**, bladder
solvents leukaemia
- asbestos manufacture mesothelioma, lung ca
- PVC production **VCM** liver angiosarcoma

BENZENE

- after latency of 10- more years:
- **acute or chronic LEUKEMIAS**
- **Symptoms:** weakness, anorexia, fever, hepato-splenomegaly, lymph node enlargement, leukocytosis – immature white cells, anaemia, thrombocytopenia
- **Prevention:** lowering exposure – recommended limit
- under 3 mg/m³ - no leukaemia's observed

VINYL CHLORIDE MONOMER

Uses

Gas from which PVC is produced by polymerization

PVC, used in varied industries such as construction, packaging, consumer goods, automotive and for medical use



VINYL CHLORIDE MONOMER

ANGIOSARCOMA OF THE LIVER



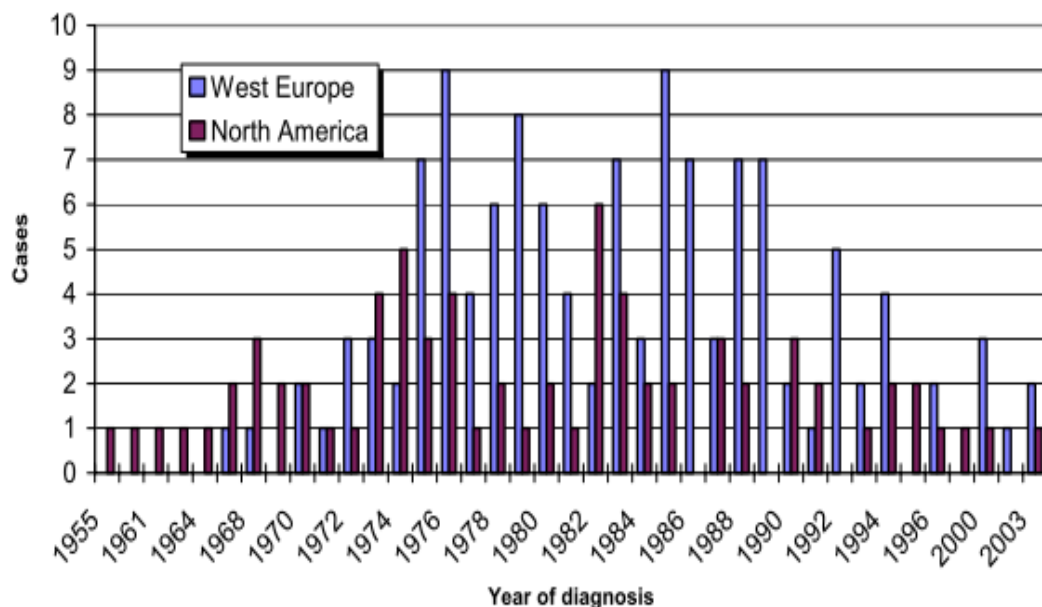
- Up to 1974 (Louisville, Kentucky) thought to be harmless
- Until 1980 10 tumours diagnosed
- Reactive metabolites – **vinyl chloride epoxide**

Symptoms : longtime non-specific

- hepatomegaly, right upper quadrant abdominal pain, weight loss, jaundice
- dg. by sonography, CT, MRI, arteriogram and liver biopsy
- **Latency period: 11 – 37 years**
- **Prognosis** : survival 6 months
- **Prevention** : lowering exposure under 1mg/m³

Angiosarcomas until 2004 in the World Register of ASL (except China and Russia)

ASL CASES FOR NORTH AMERICA AND WESTERN EUROPE



Western Europe

Country + Plant Code	Number of cases
Germany [4]	22
United Kingdom [2]	17
Germany [8]	13
France [3]	13
France [2]	9
Italy [1]	6
France [5]	6
United Kingdom [1]	5
Sweden [1]	5
Total cases	96

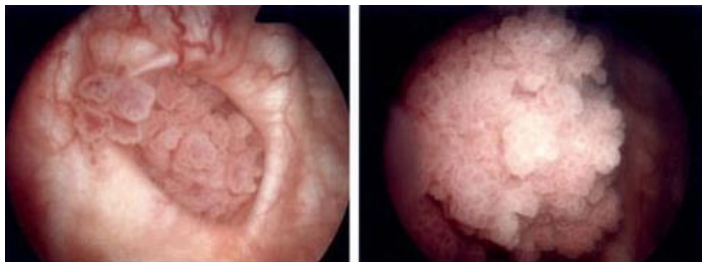
North America

Country + Plant Code	Number of cases
United States [1]	23
United States [2]	12
Canada [1]	12
United States [3]	8
Total cases	55

Eastern Europe

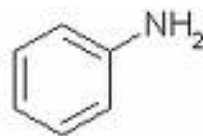
Country + Plant Code	Number of cases
Croatia [1]	14
Slovakia [1]	9
Total cases	23

Total cases	174
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AROMATIC AMINES

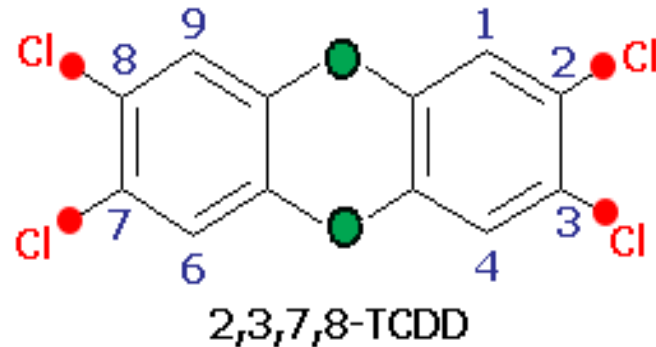
aniline-derivatives



- benzidine, 4-aminobiphenyl, 1-naftylamine
- **dyes and rubber production, textile industry**
- Carcinogenicity known since 1895
- **BLADDER CANCER**
- carcinogenic are metabolites in urine – hydroxalamines in the bladder trigone area
- **Symptoms** : hematuria, vesical irritability, nycturia
- dg. by cytologic examination, cystoscopy
- **Latency period**: 4-10 years
- **Prognosis**: 5-years survival is common
- **Prevention** : change of technology, lowering exposure

2,3,7,8-tetrachlorodibenzo-*p*-dioxin

Dioxin



Guinea-pig LD_{50} p.o. 1 $\mu\text{g/kg}$

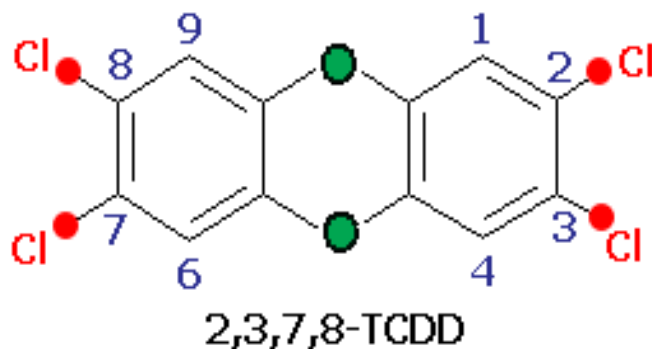
Animals die during 2-3 weeks due to „wasting syndrom“

IARC proven human carcinogen - Group 1 (all organs possibly involved – lung, kidney, thyroid,..)

Accumulation in the fat

Elimination half-life in humans about 7-10 years

2,3,7,8-tetrachlorodibenzo-*p*-dioxin TCDD



IARC Carcinogen Group 1 (lungs, kidneys, any other organ)

Guinea-pig

LD₅₀ p.o.

1 µg/kg

Animals die during 2-3 weeks due to „**wasting syndrom**“

Accumulation in the fat

Elimination half-life in humans 7-10 years

(Pelclova et al.: Adverse effects in humans exposed to TCDD.

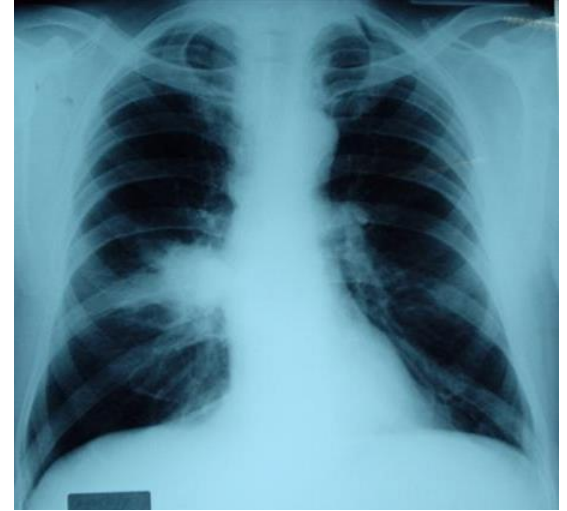
Rev Environ Health 2006)



Patient V.Y.

FURTHER CARCINOGENS:

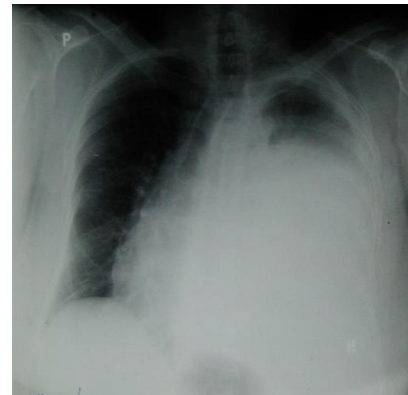
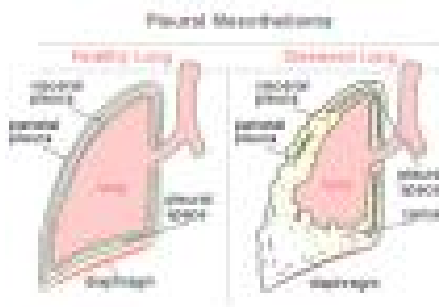
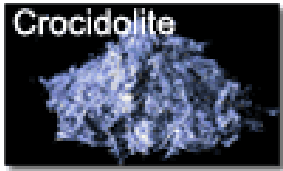
- **CADMIUM:**
- PROSTATE AND **LUNG** CANCER



- **ARSENIC:**
- SKIN AND **LUNG** CANCER



Asbestos



Mesothelioma, lung cancer, larynx, ovary

POLYCYCLIC AROMATIC HYDROCARBONS - PAH

1775 London surgeon Sir Percivall Pott
chimney sweeps - cancer of the skin of scrotum
and lung cancer

(IARC group 1)

PAH in the pitch

soots

benzo(a)pyrene

IARC 2B benzo(a)anthracene, 2A dibenzo(a,h)anthracene

latency (basalioma, spinalioma) 20-50 years

latency in lung cancer 10-13 years

B. PHYSICAL FACTORS

1. IONIZING RADIATION

RADON : LUNG CANCER

most common
occup. cancer,
in uranium miners



X-RAYS : LEUKEMIA, skin cancer

2. ULTRAVIOLET RADIATION : SKIN CANCER

OCCUPATIONAL CANCER IS UNDERDIAGNOSED!!!

- CLINICAL PRESENTATIONS
- and HISTOLOGY
- ARE NOT DIFFERENT FROM NON-OCCUPATIONAL CANCERS
- only two „signal“ tumours – mesothelioma and angiosarcoma of the liver
- LONG LATENCY PERIOD
- *(Pelclová et al.: Occupational cancer in the Czech Republic – The tip of the iceberg? Eur J Oncol 2011)*
- Follow-up of workers is needed

Avoid food with soots

