IN THE NAME OF GOD
Occupational Cancers

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Neoplasma

- Neoplasia: new growth

- An abnormal mass of tissue the growth of which exceeds and is uncoordinated with that of normal tissues and persist in the same excessive manner after the cessation of the stimuli which evoked the change. (Willis, 1952)
What is occupational cancer?

Occupational cancer is cancer that is caused wholly or partly by exposure to a carcinogen at work.
What is a carcinogen?

*A carcinogen is a substance, mixture or agent that can cause cancer or it increases the risk of developing cancer.

*Known carcinogens include viruses (e.g., Hepatitis B), hormones (e.g., estrogens), chemicals (e.g., benzene), naturally occurring minerals (e.g., asbestos), alcohol, and solar radiation (e.g., ultraviolet radiation).
How common is occupational cancer?

Research shows that the amount of cancer related to occupational exposure varies with the type of cancer.

The most common types of occupational cancer are lung cancer, bladder cancer and mesothelioma.
<table>
<thead>
<tr>
<th>Type of Cancer</th>
<th>Related to Occupational Exposure Estimated % (USA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>6.3-13%</td>
</tr>
<tr>
<td>Bladder</td>
<td>3-19%</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>?</td>
</tr>
<tr>
<td>Leukemia</td>
<td>0.8-2.8%</td>
</tr>
<tr>
<td>Laryngeal</td>
<td>1-20% (men)</td>
</tr>
<tr>
<td>Skin Cancer (non-melanoma)</td>
<td>1.5-6% (men)</td>
</tr>
<tr>
<td>Sinonasal and nasopharyngeal</td>
<td>31-43% (men)</td>
</tr>
<tr>
<td>Kidney</td>
<td>0-2.3%</td>
</tr>
<tr>
<td>Liver</td>
<td>0.4-1.1 (vinyl chloride only; men)</td>
</tr>
</tbody>
</table>
Scientists identify cancer-causing agents using information from:

* Studies that look at the relationship between an exposure and the risk of developing cancer in human populations
* Experiments that examine the relationship between an exposure and the risk of developing cancer in laboratory animals
* Tests that examine the ability of an agent to cause mutations (genetic changes) in cells, and
* Knowledge of chemical structures and the way in which chemicals interact with the body
*Identifying carcinogens is complicated. Fortunately, there are several organizations that evaluate the available information according to specific criteria.

*The most authoritative lists of carcinogens are published by the:

*International Agency for Research on Cancer (IARC), an agency of the World Health Organization

*American Conference of Governmental Industrial Hygienists (ACGIH), an independent US organization

*US National Toxicology Program (NTP), a US interagency program
IARC (International Agency for Research on Cancer)

**IARC classifies each agent or exposure into one of five groups according to the strength of scientific evidence for carcinogenicity, as follows:**

**Group 1 - Carcinogenic to humans**
**Group 2A - Probably carcinogenic to humans**
**Group 2B - Possibly carcinogenic to humans**
**Group 3 - Not classifiable as to its carcinogenicity to humans**
**Group 4 - Probably not carcinogenic to humans**
American Conference of Governmental Industrial Hygienists (ACGIH)

*ACGIH assigns chemicals or agents to one of the following 5 categories:
*A1 - Confirmed human carcinogen
*A2 - Suspected human carcinogen
*A3 - Confirmed animal carcinogen with unknown relevance to humans
*A4 - Not classifiable as a human carcinogen
*A5 - Not suspected as a human carcinogen
Every two years, NTP publishes a list of agents that they have evaluated and assigned to one of two categories:

- Known to be Human Carcinogens
- Reasonably Anticipated to be Human Carcinogens
Etiology of cancer

- Personal characteristics such as age, sex, and race
- Family history of cancer
- Diet and personal habits such as cigarette smoking, alcohol consumption
- The presence of certain medical conditions
- Damage in different genes
- Exposure to cancer-causing agents in the environment (workplace)

Cancer is \([\text{Gene}^n \times \text{environment}^n]\) interactions
Cancer Clusters

Cancers clusters: an unusual concentration of cancer cases in a defined area or time, among workers of a different age or sex group.


Vinyl chloride, angiosarcoma of the liver hydraulic cleaner from an open vinyl chloride reactor, 1974.
## Asbestos: Types

<table>
<thead>
<tr>
<th>Serpentine</th>
<th>Amphibole</th>
</tr>
</thead>
<tbody>
<tr>
<td>(93% of commercial use)</td>
<td>(7% of commercial use)</td>
</tr>
<tr>
<td>Chrysotile</td>
<td>Actinolite, Amosite, Anthophyllite, Crocidolite, Richterite, Tremolite</td>
</tr>
</tbody>
</table>

- **Serpentine**: The most common type, comprising 93% of commercial use.
- **Amphibole**: Less common, comprising 7% of commercial use.
What is Asbestos?

Because asbestos fibers are so small, once released into the air, they may stay suspended there for hours or even days.
Blue asbestos

White asbestos

Brown asbestos
Exposure setting

- Industries:
  mining, friction product, asbestos cement, textile, shipyard, construction, insulator (roofing, flooring, heat insulation), plumbers & pipefitters, steamfitter, transport, ...
  brake, roofing, flooring, heat & acoustic insulation
Epidemiology

- Linear dose-response relationship
- Some exposure threshold (malignancy and plural diseases have not)
- Mortality: 38% lung cancer
  20% asbestosis
  8% mesothelioma
- Occupational exposure standard: 0.1 fiber/ml (2/1000, 5/1000)
Asbestosis

- May or may not accompanied with pleural disease
- Additive or synergistic effect of smoking and welding
- Worsen even after exposure ceases
- Increase risk for lung cancer, mesothelioma, laryngeal cancer
Asbestos Diseases

Asbestosis
Pleural Plaques
Lung Cancer
Mesothelioma
G-I Tract
Lung cancer

* Most common problem with asbestos
* Heavily exposed workers have 5-7 times increased risk over lifetime
* About same level of risk as a pack a day cigarette smoking
* Interacts with cigarettes: 50-90 times increased risk for both combined
* Quitting smoking reduces risk
Other Cancers

**Mesothelioma**
Cancer of lining of the lungs—
Only caused by asbestos—
Smoking not a risk factor—

**G-I tract cancer**
2-3 times increased risk for heavily exposed
Asbestos

- classified Commercially
  - white asbestos (chrysotile)
  - brown asbestos (amosite)
  - blue asbestos (crocidolite)

- 90% of industrial use is chrysotile
- All types can lead to all disorders
- Pulmonary & non-pulmonary
- Malignant & non-malignant
NIOSH CARCINOGEN LIST

Potential occupational carcinogen:

1. Aniline and homologs, Asbestos
2. Chromates, Cadmium dust and fume, Coal tar pitch volatiles; coal tar products, Coke oven emissions
3. Arsenic and inorganic arsenic compounds, beryllium and beryllium compounds, cadmium compounds, nickel compounds, and crystalline forms of silica.
4. Diesel exhaust, DDT, Dimethyl Sulfate, Dinitrotoluene, Dioxane
5. Environmental Tobacco Smoke (ETS) or passive smoking, Gasoline, Uranium, insoluble compounds, Uranium, soluble compounds, PVC
6. Wood dust, Zinc chromate; class, chromium hexavalent
Classification of Carcinogens:

1. Cancer in humans: asbestos, coal, benzene, radon, 
   strong evidence of cancer in humans

2. Possibly (or probably) causative of cancer in humans: 
   crocidolite, diesel exhaust, formaldehyde, 
   polychlorinated biphenyls (PCBs)

3. Weak causative of cancer in humans: 
   ELF, caffeine, coffee, WHO
# Chemical Carcinogenesis in humans

<table>
<thead>
<tr>
<th>Target organs</th>
<th>Agents</th>
<th>Industry</th>
<th>Tumour type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>Asbestos, Arsenic, Mustard gas, nickel, PAH (poly aromatic hydrocarbons), Tobacco smoke</td>
<td>Shipyard &amp; Insulation workers, Smelting of copper, zinc, lead, Mustard gas production w. Nickel mining, refining, plating; Coke oven workers, Aluminum reduction workers, Environment with active smoker</td>
<td>Squamous, large cell and small cc, adenocarcinoma</td>
</tr>
<tr>
<td>Pleura</td>
<td>Asbestos</td>
<td></td>
<td>Mesothelioma</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>Tobacco smoke, alcohol beverage, Nickel</td>
<td>Boot &amp; shoe productions. Furniture manufacture, Alcohol productions</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>GI</td>
<td>Smoked, salted, pickled food, Tobacco, alcohol</td>
<td>Rubber Industry</td>
<td>adenocarcinoma Squamous CC</td>
</tr>
<tr>
<td>Liver</td>
<td>Aflatoxin, vinyl chloride, tobacco, alcohol, thorium dioxide</td>
<td></td>
<td>Hepatocellular C, Hemangiosarcoma</td>
</tr>
</tbody>
</table>
# Chemical Carcinogenesis in humans

<table>
<thead>
<tr>
<th>Organ</th>
<th>Chemicals/Activities</th>
<th>Carcinoma Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>Tobacco Smoke, phenacetin</td>
<td>Renal cell Carcinoma</td>
</tr>
<tr>
<td>Bladder</td>
<td>Tobacco, phenacetin, benzidine</td>
<td>Transitional cell carcinoma</td>
</tr>
<tr>
<td>Prostate</td>
<td>Cadmium</td>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td>Skin</td>
<td>Arsenic, benzopyrene, coal, mineral oil, cyclosporin A, PUVA</td>
<td>SCC, BCC</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>Benzene, tobacco, Ethylene oxide, Anti-neoplastic agents cyclosporin A</td>
<td>Rubber workers</td>
</tr>
</tbody>
</table>
Classification of occupational cancers

The most common occupational cancers:

1. Lung Cancer & mesothelioma
2. Skin Cancer
3. Bladder Cancer
4. Leukemia
Clinical evaluation

Symptoms:

1. Central growth: cough, hemoptysis, wheeze and stridor, dyspnea from obstruction, pneumonitis

2. Peripheral growth: pain (pleural involvement), cough, dyspnea, lung abscess syndrome
Lung Carcinoma
Environmental tobacco smoke (ETS)

- ETS as a significant lung cancer risk factor accounts for 3000 lung cancer deaths/year in non-smokers (US)
- Tobacco smoking contains 500 chemicals, more than 20 are carcinogens
- Specific chemicals in tobacco is PAH, N-nitrosamine, aromatic amines, ethylene oxide
- Recent cigarette has less tar (PAH) and nicotine, tobacco –specific nitrosamine
- Lower nicotine cigarettes ➔ more smoke (↑nicotine –addiction)
Asbestos and smoking interact in a multiplicative manner.

Decrease in the risk of lung cancer when exposure to either agent is stopped.

The majority of smoking-related tumours are SCC from upper lobes of lung.

Asbestos related tumours are adenocarcinomas from lower lobes and associated with areas of fibrosis.

In contrast no increase risk of mesothelioma in asbestos workers who smoke.
Mesothelioma

- Asbestos: major risk of mesothelioma
- Latency period: 30-35 years (short –term 1-2 y)
- Clinical features:
  - Chest pain, dyspnea, weight loss, cough, fever, Pleural effusion, CXR; unilateral fluid
- Diagnosis; pleural fluid is exudative, hyaluronic acid in fluid
  - CXR, CT, biopsy (spindle cell type)
- Average survival: 12 months
- Treatment: No effective treatment, palliative care, surgery, chemotherapy, radiotherapy
Malignant Mesothelioma
Bladder Cancer

- Occupational risk e.g. aromatic amines manufacturing, rubber, leather workers, painter, truck drivers, Aluminium workers: 21-27%
- Cigarette: 47%
- Transitional cell carcinomas
- Latency period: From 4 to 45 years
Prevention

- Early detection: Urine cytology, 70% sensitivity and 95% specificity (asymptomatic individuals)
- Cytoscopy (symptomatic)
- DNA flow cytometry, image analysis to detect nuclear aneuploidy, IHC for p53
- Hematuria screening by urinalysis or dipstick
- Tests of genetic factors: Tumor suppressor gene combination of cystoscopy and cytology
- Survival: depends on grade & stage
- Localized disease = 95%, distant disease = 0
Screening program

1. Low exposure group: Cytologic examination & Hematuria testing at 6 months intervals for the first 2 years

2. High risk population: cystoscopy (if cytology/ hematuria +)
Ionizing radiation and cancer

- Skin cancer: the first cancers detected in x-ray workers
- Radiation-induced leukemias among radiologists and radioisotope workers
Radiation-Exposed Populations

- Atomic Bomb (Japanese survivors)
- Occupational exposures
  - Radiologists
  - Underground miners
  - Radium dial painter
  - Nuclear workers
  - Radiation technologists
- Medical exposure
  - Patients under radiotherapy (Cervical cancer, Breast cancer, ankylosing spondylitis, Hodgkin’s disease, Childhood cancer)
Skin cancer

- In 1775: Development of skin cancer (SCC of scrotum), associated with chemical exposure
  - Arsenic: SCC, BCC
  - coal tar: SSC
  - vinyl chloride
  - Smoking of tobacco: SCC
  - Sun light (UV): Non-melanoma skin cancer (NMSC)
Arsenic and skin cancer

1) Occurrence of arsenical hyperkeratosis, hyperpigmentation which occurs in lower doses of skin cancer.

2) Occurrence of multiple skin cancer in areas not exposed to the sun.

3) Skin cancer at young age.
Sunlight (UV) and skin cancer

- Skin cancer incidence is rising (1/3 of cancers in USA, most common cancer in men in Iran)
- Non melanoma Skin Cancer (BCC 80%, SCC 20%)
- Mortality is low (54000 cases last year, 7000 death)
- In regions with high solar radiation
- Exposure to sunlight for occupation (outdoor workers; farmers, sailors)
- Exposure areas: head, neck, face and arms
Risk Factors

- Fair skin, blue eye, blond hair
- Skin sensibility to sun
- Older age
- Immunosupression
- History of sunburns
- Cumulative exposure to UV radiation
Basal Cell Carcinoma
Squamous Cell Carcinoma
Malignant Melanoma
Prevention of occupational skin cancer

- Protective clothing (hat, sunglasses)
- Sunscreen ➔ 78% reduction
- Zinc oxide
- Ionizing radiation by use of gloves, lead container
- Engineering controls: constructed, shield over work area to limit exposure
Occupational medicine physician duty

1. Review all factors related to cancer risk in the environment.
2. Estimate the level and duration of exposure (employment) to carcinogenic agents.
3. Latency period: The latency period for each carcinogen is different.
4. History of smoking or exposure to secondhand smoke.

passive smoking
Medical Monitoring

معاينه افراد در معرض مواد سرطانزا شامل:

1. پایش بیولوژیکی میزان مواد شیمیایی یا متابولیت های انهدار باند (اداره، هوای بازدمی، خون، مو و عرق)

2. پایش اثر بیولوژیکی: اندازه گیری اثرات بیوشیمی

3. مراقبت های سلامتی: معاینه فیزیکی، sputum cytology (arsenic, coke ), CT
Prevention of Occupational Cancers

1. آزمایش سرطانزای مواد شیمیایی قبل از عرضه به بازار
2. حذف یا به حداقل رساندن مواجهه با مواد سرطانزا
3. آموزش افراد برای حفاظت از خود و اشنایی با خطرات احتمالی
4. غربالگری افراد با ریسک بالا (سیگاری ها)
5. غربالگری زن‌نیکی
6. مانیتور کردن محل کارجهت شناسایی عوامل سرطانزا موجود در محیط
7. توصیه به رژیم غذایی صحیح و استفاده از میوه و سبزیجات، ترک سیگار
Thanks for your attention