# EPIDEMIOLOGY AND CONTROL OF CANCER

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## **CARCINOGENESIS**

### 1. Mutagenic theory

- Origin change of genetic information in a cell by
  - a chemical factor carcinogen (some 500 established in animals, about 100 in humans)
  - a physical factor radiation (ionizing, UV)
  - a biologic factor oncogenic viruses, parasites

A long multistage process follows

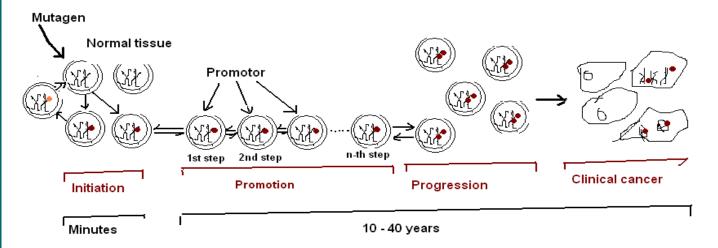
### **Stages**

- 1. Initiation the original structural change in the DNA of the attacked cell. The change is reversible, reparable.
- 2. Promotion. The transition to this stage is caused by further chemicals promoters.

The initiated cell develops differently from a normal one. In some cases (skin, liver, intestine), small and so far harmless deposits are formed (polyps, papillomata etc.) Development in single small steps, each of them is reversible.

- 3. Progression, consisting again of single steps. Development of precancerous and later cancerous tissue.
- 4. Clinical cancer fully developed, clinically discernible.

#### Scheme of carcinogenesis



## Carcinogenic process

In general: - very long process, 10 - 40 years from stage 1 to stage 4.

- reversible by intrinsic reparation processes and extrinsic factors for the most part of the time

Inhibitors of mutagenesis - antioxidants (scavengers of free radicals) and very many other components of food (flavonoids, fatty acids, hemoproteins, tannins etc.)

(Free radicals - atomic or molecular species that, by virtue of possessing unpaired electrons, are extremely reactive)

- immune defence mechanisms
- genetic interference

## 2. Epigenetic theory

Some cases of cancer are caused by other mechanisms not acting through DNA

Factors promoting cell proliferation

## NOSOLOGY

- Cancer encompasses a family of several hundreds of diseases which are distinguished in humans by site, morphology, clinical behaviour and response to therapy.
- The tumours have not only different clinical symptoms but also different risk factors

Prevention of each type of cancer must be considered separately, the causes are different

= we must consider cancers of different organs (tissues) as largely independent

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#### diseases

Cancers of three organs (lung, breast and large intestine) are of outstanding importance

they account for half the cancer deaths

## SOME ESTABLISHED CARCINOGENIC AGENTS AND CIRCUMSTANCES

#### **Physical:**

- Ionizing radiation (occup., med.) ... marrow and probably all other sites
- UV light (occup., social) ... skin, lip

#### **Inorganic:**

- Arsenic (occup.) ... skin, lung
- Asbestos (occup.) ... lung, pleura (mesothelioma), peritoneum
- Cadmium (occup) ... prostate
- Chromium (occup) ... lung
- Nickel (occup.) ... nasal sinuses, lung

#### Organic:

- Aromatic amines: benzidine, 2-naphtylamine etc. (occup.)
   ... bladder
- Alkylating agents (cytostatics), (med.) ... bladder, marrow
- Benzene (occup.) ... marrow (leukaemia)
- Estrogens (med.) ... endometrium
- Immunosuppresive drugs (med.) ... reticuloendothelial system
- Phenacetin (med.) ... kidney
- Steroids anabolic, contraceptives (med.) ... liver
- Vinyl chloride (occup.) ... liver
- Polycyclic aromatic hydrocarbons (occup., med.) ... skin, scrotum, lung

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#### **Biologic:**

- Parasites: Schistosoma haematobium (social) ... Bladder
- Virus HBV (social) ... liver, cervix uteri, skin
- HPV (social) ... cervix uteri
- HTLV (social) ... marrow, reticuloendothelial system
- (=Human T-cell Lymphotropic virus)

#### **Circumstances:**

- Tobacco smoking (soc.) ... mouth, pharynx, larynx, lung,
  - oesophagus, bladder
- Alcoholic drinks (soc.) ... mouth, pharynx, larynx, oesophagus, liver
- Obesity (soc.) ... endometrium, gallbladder
- Sexual promiscuity (soc.) ... cervix uteri
- •Furniture manufacture (occup.) ... nasal sinuses
- Leather goods manufacture (occup.) ... nasal sinuses

## **Epidemiology**

The number of new cases of cancer that occurs worldwide in 2000 has been estimated at about 10 million, including 5.3 million in men and 4.7 million in women. Among men, lung, stomach, colorectal, prostate and liver cancers are the most common malignant neoplasms, while breast, cervical, colorectal, lung and ovarian cancers are the most common neoplasms among women

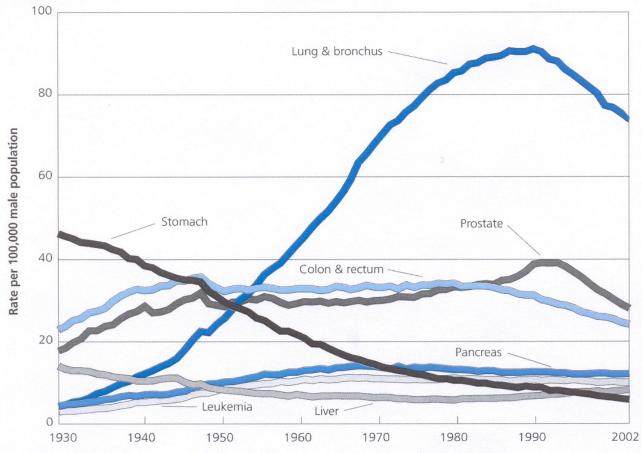
#### Some general trends can be identified:

- A decrease in stomach cancer incidence in most countries
- A plateau or decrease in the incidence of lung cancer and, to some extent, other tobaccorelated cancers among men from developed countries, and a corresponding increase among men in developing countries and women in developed countries;
- A very modest improvement in survival, in particular for highly lethal cancers.
- Cancer incidence and cancer mortality in the USA
- trends

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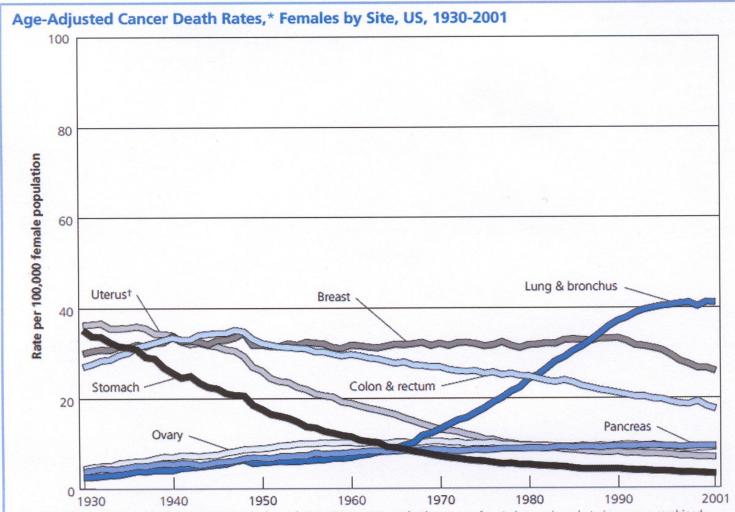


<sup>\*</sup>Per 100,000, age-adjusted to the 2000 US standard population.

**Note:** Due to changes in ICD coding, numerator information has changed over time. Rates for cancer of the liver, lung and bronchus, and colon and rectum are affected by these coding changes.

**Source:** US Mortality Public Use Data Tapes 1960 to 2002, US Mortality Volumes 1930 to 1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 2005.

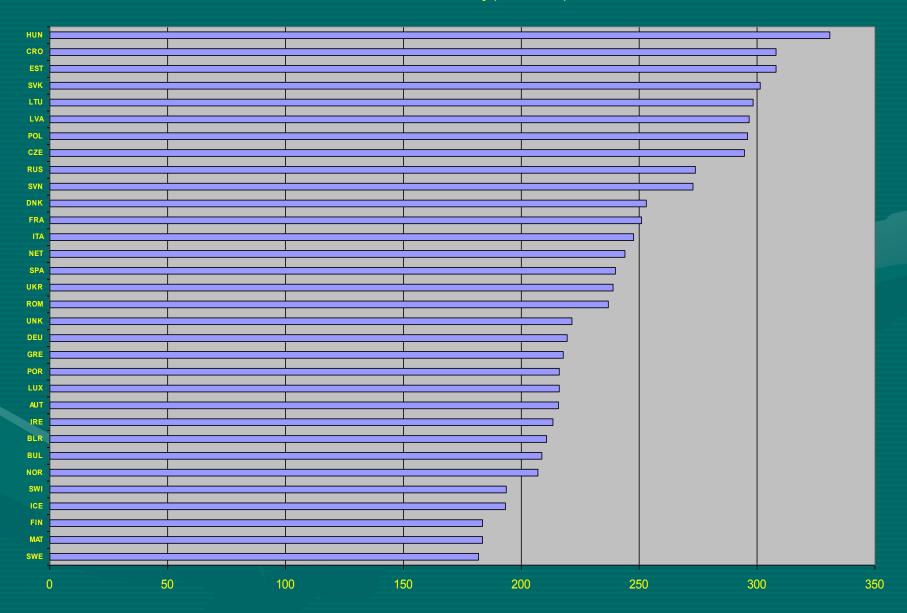
American Cancer Society, Surveillance Research, 2006



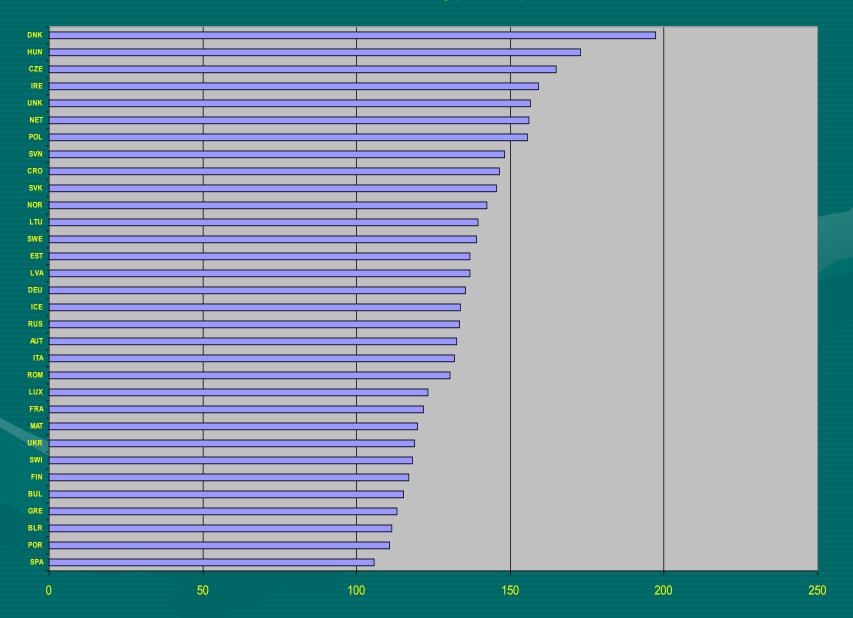
\*Per 100,000, age-adjusted to the 2000 US standard population. †Uterus cancer death rates are for uterine cervix and uterine corpus combined. **Note:** Due to changes in ICD coding, numerator information has changed over time. Rates for cancers of the lung & bronchus, colon & rectum, and ovary are affected by these coding changes.

**Source:** US Mortality Public Use Data Tapes 1960-2001, US Mortality Volumes 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 2004.

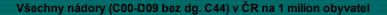
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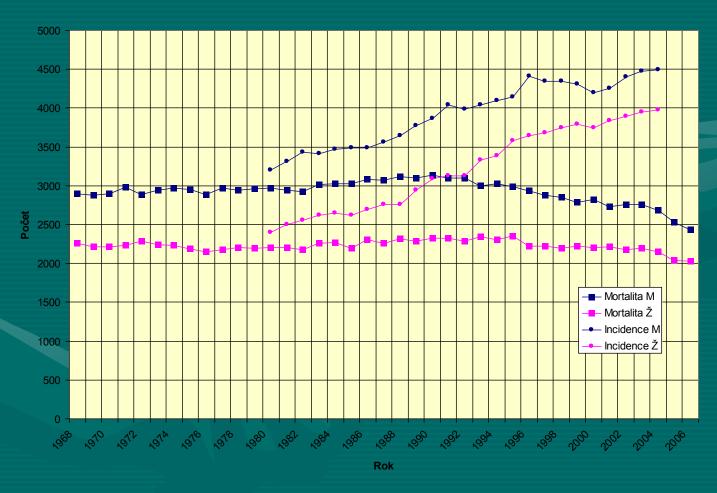


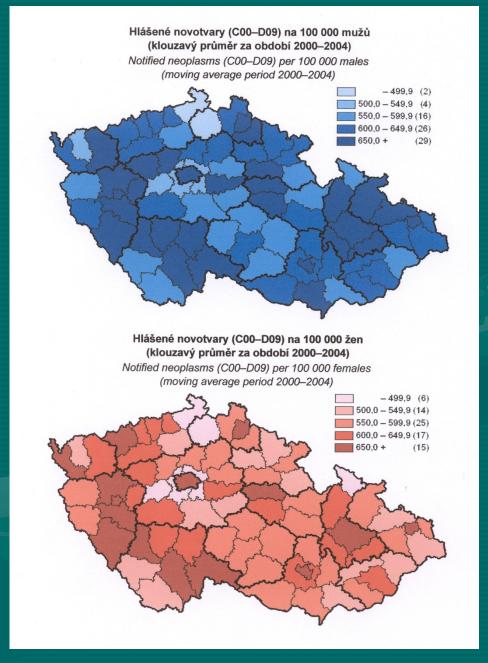
CANCER - Standardized Mortality (2004 - 2005) - FEMALES



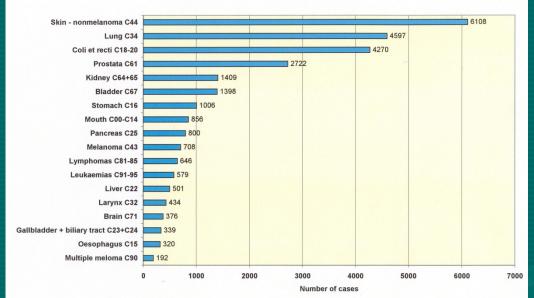
### Trends of incidence and mortality of malignant neoplasmes, ČR



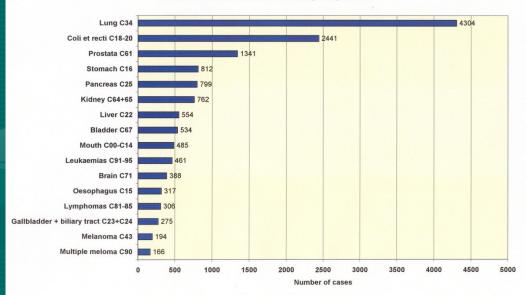


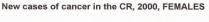


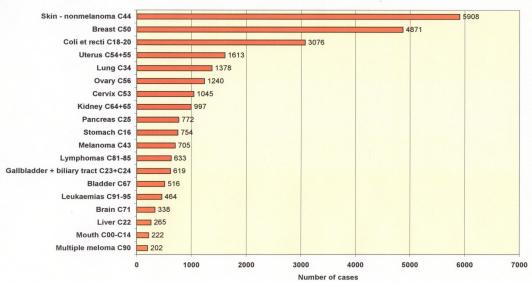
#### New cases of cancer in the CR, 2000, MALES



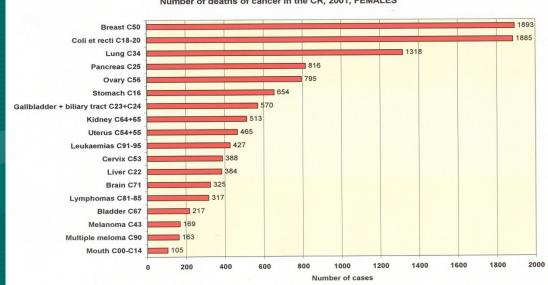












## **AVOIDABILITY**

#### Much human cancer is avoidable

#### **Evidence:**

- 1. Differences in incidence in different parts of the world
  - some cancers among people of the same age vary by at least ten and possibly by the hundredfold
- 2. Changes in incidence on migration, e.g. Japanese in USA
- 3. Changes in incidence over time
- 4. Identification of causes and successful prevention
  - giving up smoking and lung cancer
  - 2-naphtylamine and bladder cancer

Table: Contribution of major causes to human cancer burden (attributable fraction in percent) Peto 2001, HCCP (Harvard Center for Cancer Prevention) 1996. .

Cause	Peto		НССР
	Smokers	Non-smokers	
Tobacco	60	0	30
Dietary factors	4 – 12?	10-30?	30
Obesity	4	10	30
Sedentary life	0.4	1	5
Biological agents	2	5	5
Occupation	0.4	1	5
Alcohol	0.4	1	3

### **Table continued**

Cause	Peto HCC		HCCP
	Smokers	Non-smokers	
Environmental factors	0.4	1	2
UV/ionizing radiation	0.4	1	2
Reproductive factors	N/A	N/A	3
Medical factors	N/A	N/A	1
Food additives	N/A	N/A	1
Perinatal factors	N/A	N/A	5
Socio-economic factors	N/A	N/A	3
Genetic factors	N/A	N/A	5

N/A ... not available

## Estimate of the percentage of cancer deaths attributable to different controllable causes (in United Kingdom)

(Doll, R., Rev.Epidém. et Santé Publ., 2001)

CAUSE	%	CAUSE	%
Tobacco	29-31	Reproductive hormones	10-15
Alcohol	4-6	Occupation	2-3
Elm radiation	5-6	Pollution	1-4
Infection	10-20	Physical inactivity	1-2
Diet	20-50	Medicines	<1

## Tobacco

#### Far most important factor

In developed countries in 1995 smoking was responsible for 39% of all cancer deaths in men and 15% in women (estimated, Peto R. et al. 1994).

## Cancers caused in part by smoking

Primary site	RR cig. smokers : non-smokers
Mouth	4:1
Pharynx	10 : 1
Oesophagus	7:1
Larynx	10 : 1
Lung	15 : 1
Pelvis of kidney	4:1
Bladder	3:1
Pancreas	2:1
Lip, nose, stomach, myeloid leukaemia, kidney, liver	1,5 : 1

Smoking of filtered cigarettes and cigarettes with reduced tar content results in a lower risk of lung and other cancers, although by no means the former products should be seen as "risk-free".

The benefit of quitting tobacco smoking in adulthood has been shown for most cancers causally associated with the habit, in any age.

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## **Alcohol**

A long way behind tobacco, causing some 3 – 12 % of cancer death in developed countries.

#### Cancers caused in part by alcohol

Primary site	RR drinkers : non-drinkers
Mouth	2:1
Pharynx	2:1
Oesophagus	3:1
Larynx	2:1
Liver	1,5 : 1
Breast	1,5 : 1

For the first four cancers of the upper aerodigestive tract, alcohol acts synergistically with smoking and most of its effect can be avoided by the avoidance of smoking.

The risks tend to increase with the amount of ethanol drunk, in the absence of any clearly defined threshold below which no effect is evident

The evidence of differences in carcinogenity among alcoholic beverages is inconclusive.

In middle-aged and old people, the benefit on cardiovascular disease is likely to offset the increased cancer risk, up to a level of approximately 20 g/day among men and 10 g/day among women

## Electromagnetic radiation

UV radiation is responsible for most melanomas and for nearly all squamous and basal cell carcinoma of the skin.

**lonizing radiation** is responsible for perhaps 5 % of all cancer deaths, mostly because of the natural radiation to which everyone is inevitably exposed.

Radon is estimated to account for some 6 % of all lung cancers (in the UK).

Radon and smoking act synergistically, most of the risk can be avoided by avoiding smoking.

Whether lower frequency radiation from radio, mobile phones, and passage of electricity can cause cancer is unclear. The risk, if any, is certainly very small.

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The available epidemiologic studies of populations exposed to ionizing radiation following military actions, accidents, occupational exposure and medical treatment represent a very comprehensive database, which has been used beyond the assessment of radiation carcinogenity, notably to elaborate models of carcinogenesis in humans and of quantitative risk assessment

Ionizing radiation causes acute lymphoblastic leukaemia, acute myeloid leukaemia, chronic myeloid leukaemia and breast, lung and thyroid cancers. Bone, rectal and brain cancers may develop following prolonged therapeutic exposure.

Levels at which people are commonly exposed to man-made radiatin in most countries carry little risk and the main exposure comes natural radiation, including indoor radon.

## Infectious agents

Parasites cause many cancer of bladder, large bowel, liver, and bile ducts in Africa and Asia.

Schistosoma heamatobium – bladder cancer (in North Africa and the Middle East)

Bacteria: *Helicobacter pylori* increases the risk of non-cardia gastric cancer, approximately sixfold.

(The incidence of adenocarcinoma of the lower oesophagus seems, in contrast, to be increased in the absence of *Helicobacter* infection.)

Other forms of bacterial infection contribute perhaps to the bladder cancer (chronic infection – local formation of nitrosamines), and to the large bowel cancer (bacteria may produce mutagens).

## Viruses cause the great majority of two of the most common cancers worldwide (liver and cervix uteri) and many of the less common cancers

#### Viral causes of cancer

Virus	Cancer
Hepatitis B	Hepatocarcinoma
Hepatitis C	Hepatocarcinoma
Human papilloma v. types 16, 18	Cervix, vulva, vagina, penis, anus
Human herpes v. type 4 (Epstein- Barr virus)	Burkitt´s lymphoma, Hodgkin´s disease, nasopharyngeal cancer
Human herpes v. type 8	Kaposi′s sarkoma
Human T-cell leukaemia type 1	Adult T-cell leukaemia/lymphoma
Human immunodeficiency virus 1	Kaposi´s sarkoma, non-Hodgk. lym.

Further virus-associated cancers are probably to be discovered.

## **Dietary factors**

Despite considerable research efforts in cancer epidemiology, the exact role of dietary factors in causing human cancer remains largely obscure.

The evidence of protective role of vegetable and, to a lesser degree, fruit intake has been evaluated as convincing for a number of important human tumours (cancer of oesophagus, stomach, colon/rectum and lung.

For the remaining dietary factors, few evaluations of convincing or probable associations have been made (namely high intake of total and saturated fat, and of micronutrients such as carotenoids, vitamin E and selenium. IARC: there is evidence suggesting lack of cancer-preventive activity for preformed vitamin A and for  $\beta$ -carotene when used in high doses.

The extent to which even such major components as **meat**, **fat**, and **fibre** contribute to risk is still unclear.

Nor could the IARC find any human evidence of a harmful effect of cooking.

Five relationships have, however, been established sufficiently clearly to justify intervention:

- liver cancer and aflatoxin (produced by the mould Aspergillus flavus)
- nasopharyngeal cancer with a peculiar type of decomposed salted fish (China)
- gastric cancer with salted and salt preserved foods
- > overconsumption > obesity with cancers of endometrium, gallbladder, and breast and for some cancers in the large bowel,

The investigation of dietary carcinogens presents major challenges because of the difficulties to assess precisely the relevant carcinogenic (or preventive) factors.

## Overweight and obesity

Overweight, defined as BMI over 25 kg/m<sup>2</sup>, increases the risk of colon, breast (post-menopausal), endometrial and kidney cancer and of adenocarcinoma of the oesophagus. The risk of these cancers is linearly related to severity of overweight and obesity

The magnitude of the excess risk is not very high (for most cancers the relative risk ranges between 1.1 and 1.5 for overweight and between 1.3 and 2 for obesity).

## Physical activity

Regular sustained workplace or recreational physical activity (e.g., at least 30 minutes/day) decrease risk of colon and breast cancer; a protective effect is also likely for endometrial and prostate cancer. The magnitude of risk reduction for colon and breast cancer is in the order of 40%.

## Reproductive hormones

Later menarche and multiple pregnancies followed by prolonged lactation result in greatly reduced risk of cancers of the breast, endometrium, and ovary (carcinogenic influence of oestrogen is reduced).

Endometrial cancer is caused by cumulative exposure to oestrogens in the absence of progesteron

Breast cancer is also related to cumulative exposure to oestrogens, an effect enhanced by progesterone

Ovarian cancer is related to ovulation, which is direct result of more complex hormonal changes

Prostate cancer is most likely related to cumulative exposure to testosterone, perhaps in combination with oestrogen

Current and recent (up to 10 years) use of oral contraceptives entails a small increase in breast cancer risk, but no excess risk is apparent 10 or more years after cessation of use. Long-term use of oral contraceptives is associated with an increased risk of liver cancer, while the risk of endomertrial and ovarian cancer is decreased following oral contraceptive use.

Post-menopausal hormonal therapy increases the risk of breast and endometrial cancer. In the case of breast cancer, the effect is stronger for combined estrogen-progesteron combinations than for other types of hormonal therapy.

Tamoxifen is widely used for treatment of breast cancer: beyond its therapeutic effects, it decreases the risk of contralateral breast cancer but it increases the risk of endometrial cancer

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## **Medical Procedures and Drugs**

In addition to post-menopausal hormonal therapy, oral contraceptives and tamoxifen, other drugs may cause cancer

Many cancer chemotherapy drugs are active on the DNA, in order to block the replication of cancer cells. This, however, might result in damage to normal cells, including cancer transformation.

The main neoplasm associated with chemotherapy treatment is leukaemia, although the risk of solid tumours is also increased.

A second group of carcinogenic drugs includes immunosuppressive agents, which have been studied in particular in transplanted patients. Non-Hodgkin neoplasm may be caused by these drugs.

Phenacetin-containing analgesics increase the risk of cancer of renal pelvis

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There is strong evidence from observational studies that aspirin reduces the risk of colorectal cancer, an effect probably shared by other non-steroidal and anti-inflammatory drugs.

No precise estimates are available for the global contribution of drug use to human cancer. It is unlikely, however, that drugs represent more than 1% in developed countries. Furthermore, the benefit of such therapies are usually much greater than the potential cancer risk.

Several chronic inflammatory conditions represent a risk factor for cancer: the epidemiological evidence is particularly strong in the case of colorectal cancer following inflammatory bowel disease and of lymphoma following chronic infectious diseases such as tuberculosis, malaria and herpes zoster.

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### **Genetic factors**

The notion that genetic susceptibility plays an important role in human cancer is well-established

A familial aggregation has been shown for most types of cancers. This is notably the case for cancers of the breast, colon, prostate and lung

The relative risk is in order of 2 to 4, and is higher for cases diagnosed at young age.

Some of aggregation can be explained by shared risk factors among family members

## **Sreening for cancer**

Oral cancer: inspection aimed at identifying pre-neoplastic lesions

Colorectal cancer, recommendation for individuals aged 50 and over: either annual faecal occult blood testing or flexible sigmoidoscopy every five years.

Breast cancer: mammography, the effectiveness in women older than 50 years has been demonstrated. The benefit of other screening approaches, such as physical examination and self-examination, is not known.

Invasive cervical cancer: Cytological examination of exfoliated cervical cells (the Papanicolao smear test). The benefit is in the order of a two- to four-fold decreased incidence.

Prostate cancer: Screening has been proposed, based on digital rectal examination and measurement of prostate-specific antigen (PSA). There is no evidence from controlled trials that either procedure decreases the mortality from prostate cancer. Despite this lack of evidence, these procedures, in particular the prostate-specific antigen testing, have gained popularity in many countries.

Lung cancer: despite a large body of research since 1970s, no effective screening method has yet been identified.

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#### RISK FACTORS OF INDIVIDUAL CANCER TYPES

#### Lung

Smoking cigarettes – attributed 80 – 90 % of cases

after giving up –the risk decreases to the level of non-smokers during 15 years the risk depends on the onset of smoking:

starting before 15 ... the risk in 60 is 2 to 3 times higher then with onset after 20 passive smoking: the risk of the wife of a smoker (20 cigarettes/day) is doubled

#### Air pollution in towns

- relatively weak influence, some 2 to 5 % of cases

#### Radon in the indoor air

- the risk is doubled in exposed houses

Radon is a naturally occurring radioactive gas that forms from the breakdown of uranium in soil and rocks. It cannot be seen, tasted, or smelled.

#### **Professionally:**

ionizing radiation, Ni, salts of Cr, asbestos (mesothelioma)

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#### Large intestine

#### Diet:

dietary fibre (Burkitt, 1970) dietary fat, especially saturated alcohol (beer?)

#### **lonizing radiation**

- established for therapeutic irradiation of ca cervicis and ca testis

Intrinsic risk factors: polyposis, colitis ulcerosa

Protective role: calcium, vitamin C

#### **Secondary prevention:**

rectoscopic screening, occult bleeding screening, removing of polyps

#### **Stomach**

Helicobacter pylori infection seems to be a major cause of stomach cancer, especially cancers in the lower (distal) part of the stomach.

#### **Nitrosamines**

- synthesized in the stomach : nitrites + secondary amines

(In Japan) dried, salted and smoked fish, pickled vegetables

#### Protective factors:

inhibitors of the nitrosamines synthesis - vitamin C and E, plant polyphenols = enough of fresh vegetables and fruits in the diet (refrigerators)

#### **Epidemiological note:**

meridian gradient from high incidence in Japan to lower incidence in USA

Unplanned control of Helicobacter infection via widespread antibiotic use and improved living conditions is likely to be an important component of the decline in stomach cancer incidence, which occurred in many countries during recent decades

#### **Breast**

#### Reproductive behaviour: the risk

- is highest in childless women and decreases with the number of children
- decreases with the earlier age of first delivery
- is higher in women with early menarche and late menopause
  - = connection with hormonal influences

Connection with lifestyle: - the incidence high in USA and Europe, very low in Asia - higher in the towns than in the country

**Nutrition: overeating? saturated fats?** 

lonizing radiation: higher incidence in Hiroshima and Nagasaki

Primary prevention? not known

#### Secondary prevention!

- -systematic self-checking (change of form of breast in comparison with the other side, changed look of the skin and of the nipple, spots with retracted skin
- screening: mammography

Breast cancer in men: rare (100x less than in women), worse prognosis, often late diagnosis.

#### **Endometrium**

#### Hormonal influences

higher exposure to estrogens (therapy of osteoporosis, older types of oral contraception)

#### Obesity

in the fat tissue are enzymes transforming suprarenal hormones to estron

#### Cervix uteri

**Sexual behaviour** - the risk increases with promiscuity

**Cause: Human Papillomavirus (HPV)** 

- transmitted by sexual intercourse
- presence of chemical factors also necessary (smoking?)

**Primary prevention:** changing sexual behaviour

Secondary prevention: screening

#### **Ovary**

The risk increases with the frequency of ovulation

Protective influence of oral contraception

#### **Prostate**

Disease of old men

Large differences amongst countries (30 times)
e.g. high incidence in Scandinavia
low in south-east Asia

Risk factors are not well understood connection with testosterone production and with hyperplasia prostatae

Mouth (lips, tongue), pharynx, larynx, oesophagus

**Smoking** (also cigars and pipes)

**Alcohol** 

#### **Pancreas**

**Smoking** – only known risk factor

#### Liver (primary hepatoma)

**Virus HBV** 

**Aflatoxins** 

#### Gall bladder

More frequent in women

**Cholelithiasis** 

**Infections** 

**Inflammations** 

#### **Kidney**

**Smoking cigarettes** 

attributed 40 – 70 % of cases Also cigars

Misuse of analgesics

Different chemicals in the professional environment

#### Bladder

**Smoking cigarettes** 

-attributed 40 – 50 % of cases

Benzedine, 4-aminobiphenyle, 2-naphtylamine

1895 – study of higher incidence of bladder cancer
in the production of aniline dyes

**Analgesics with Phenacetin** 

Cytostatics, e.g. cyclophosphamide

In Africa: Bilharziosis (caused by Schistosoma haematobium)

#### Skin

**UV radiation** (wave length 280 – 320 nm)

Higher risk: - sudden exposure of untanned skin to sunlight

- in children and young people (initiation)
- in people with low production of pigment (albinos)

#### Polycyclic aromatic hydrocarbons (PAU)

-professional contact with soot, tar, asphalt

History: as early as in 1775 P. Pott described the scrotum cancer of chimney-sweeps

# Warning signs of cancer Questions for patients to check as a component of secondary prevention

**West Virginia University** 

#### Breast cancer:

- I have a lump or thick place in or near my breast.
- I have a lump or thick place under my arm.
- The size of my breast has changed.
- The shape of my breast has changed.
- I have a sore nipple.
- Stuff leaks out of my nipple.
- My nipple has sunk into my breast.
- I have noticed a change in the way my breast looks or feels.

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#### Cervical cancer

- > I have bleeding between my periods.
- I have longer or heavier periods than I used to.
- I have bleeding after I have sex.
- > I have bleeding when I douche.
- ➤ I have started bleeding from the vagina <u>after</u> going through the change of life.
- > I have more discharge or mucus from my vagina than usual.

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#### Colon cancer

- My bowel movements look black.
- I move my bowels movements more or less often than usual.
- I often have gas pains, cramps or bloating.
- > I have diarrhoea or constipation.
- ➤ I feel like my bowel does not empty all the way when I have a bowel movement.
- The shape of my bowel movement is thinner than usual.
- I feel more tired than usual.
- > I throw up for no reason.
- > I have seen blood in my bowel movements or on my toilet paper.
- I have lost weight for no reason.

#### Lung cancer

- > I have a cough that will not go away.
- ➤ My chest hurts all the time.
- > I am short of breath.
- > I am wheezing.
- > I am hoarse.
- > I cough up blood.
- > I keep getting pneumonia or bronchitis.
- > I have lost my appetite.
- > I have lost weight for no reason.
- > I feel more tired than usual.
- My face or neck is swollen.

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#### Prostate cancer

- > I need to urinate more often, especially at night.
- > I have trouble starting to urinate.
- > I have trouble holding my urine.
- > Sometimes I cannot urinate.
- > I feel pain or burning when I urinate.
- > I have seen blood in my urine or semen.
- > I have trouble getting an erection.
- > It hurts when I ejaculate.
- ➤ I often feel pain in my lower back, hips, or upper thights.

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## European Code Against Cancer and scientific justification: third version (2003)

Many aspects of general health can be improved, and certain cancers avoided, if you adopt a healthier lifestyle

- 1. Do not smoke; if you smoke, stop doing so. If you fail to stop, do not smoke in the presence of non-smokers
- 2. Avoid obesity
- 3. Undertake some brisk, physical activity every day
- 4. Increase your daily intake and variety of vegetables and fruits: eat at least five servings daily. Limit your intake of foods containing tals from animal sources

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- 5. If you drink alcohol, whether beer, wine or spirits, moderate your consumption to two drinks per day if you are a man and one drink per day if you are a woman
- 6. Care must be taken to avoid excessive sun exposure. It is specifically important to protect children and adolescents. For individuals who have a tendency to burn in the sun active protective measures must be taken throughout life

7. Apply strictly regulations aimed at preventing any exposure to known cancercausing substances. Follow all health and safety instructions on substances which may cause cancer. Follow advice of national radiation protection offices

#### There are public health programmes that could prevent cancers developing or increase the probability that a cancer may be cured

- 1. Women from 25 years of age should participate in cervical screening. This should be within programmes with quality control procedures in compliance with European Guidelines for Quality Assurance in Cervical Screening
- 2. Women from 50 years of age should participate in breast screening. This should be within programmes with quality control procedures in compliance with European Union Guidelines for Quality Assurance in Mammography Screening
- 3. Men and women from 50 years of age should participate in colorectal screening. This should be within programmes with built-in quality assurance procedures
- 4. Participate in vaccination programmes against Hepatitis B Virus infection

Thank you for your attention



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