Cancer Epidemiology

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What do you expect from this seminar?

What do you want to learn?

OCCURRENCE OF CANCER

OCCURRENCE OF CANCER Incidence

OCCURRENCE OF CANCER Incidence Prevalence

OCCURRENCE OF CANCER Incidence Prevalence Mortality

ASR (age-standardised rate or age-adjusted rate)

ASR is a summary measure; it is the rate that a population would have if it had a standard age structure. Standardization is necessary when comparing several populations that differ with respect to age structure, because age has a powerful influence on the risk of cancer. The most frequently used standard population is the World standard population. The calculated incidence rate is then called the World Standardised incidence Rate. It is also expressed per 100,000. The World standard population used in this application is as proposed by Segi (1960) and modified for the first volume of the series by Doll and *al.* (1996).

RISK FACTORS

Non-modifiable

RISK FACTORS

Non-modifiable Modifiable

RISK FACTORS

Non-modifiable Modifidable

PREVENTION Primary, secondary, tertiary,...

Primary prevention

• Prevent occurrence of the disease

Secondary prevention

• Early diagnose – optimally pre-cancerosis

Tertiary prevention

 To find recurrence of the disease or distant metastases

If we are not successful, we have to do our best to improve or at least keep as long as possible the quality of life of the patients.



ON THE 2ND PLACE OF THE CAUSE OF DEATH IN MOST DEVELOPED COUNTRIES

Changes in the structure of the cause of death with the age in Czech Republic. 2002



Where can you find information concerning incidence/mortality of cancer?

Cancer register HEALTH INSURANCE SYSTEM

World Health Organisation

International Agency for Research on Cancer, Lyon, France

WWW.IARC.FR





International Agency for Research on Cancer World Health Organization



Cancer Registries

Cancer Incidence in Five Continents

Vol. I to VIII

CI5 I-

D.M. Parkin, S.L. Whelan, J. Ferlay and H. Storm IARC CancerBase No. 7

International Agency for Research on Cancer World Health Organization		n on Cancer	GLOBAL CANCER OBSERVATORY	
HOME	ABOUT	DATABASES	CANCER REGISTRY RESOURCES	HELP

The Global Cancer Observatory (GCO) is an interactive web-based platform presenting global cancer statistics to inform cancer control and research.

CANCER TODAY

Provides data visualization tools that present current national estimates of the incidence, mortality, and prevalence of 36 cancer types in 185 countries, by sex and age group. Go to website.



Undergoing further development; will provide data visualization tools that document the changing rates of cancer incidence and mortality over the course of half a century, based on high-quality data from 40 countries. Go to website.

CANCER TOMORROW

A tool that predicts the future cancer incidence and mortality burden worldwide from the current estimates in 2018 up until 2040. Go to website.

CANCER CAUSES

An expanding set of visualization tools that links the cancer burden to underlying causes, quantifying the extent to which different cancers are attributable to key lifestyle and environmental risk factors worldwide. Go to website,



Year of Diagnosis

Year of Diagnosis



http://onlinelibrary.wiley.com/doi/10.3322/caac.21166/full#fig



CA: A Cancer Journal for Clinicians

Volume 63, Issue 1, pages 11-30, 17 JAN 2013 DOI: 10.3322/caac.21166 http://onlinelibrary.wiley.com/doi/10.3322/caac.21166/full#fig4

Do you know any risk factor of cancer - risk factors for nearly all cancers?

AGE GENETICS

Less developed countries (2002)



More developed countries (2002)



International Agency for Reczech Republic (2007)



International Agency for Findia (3 registries) (2007)



International Agency for China (3 registries) (2007)



International Agency for Philippines, Manila (2007)



*The Gambia (1997-1998)



CI5VIII

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Where is the highest incidence & mortality of cancers in the world?



Estimated age-standardized incidence rates (World) in 2018, all cancers, males, all ages

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Data source: GLOBOCAN 2018 Graph production: IARC (http://gco.iarc.fr/today) World Health Organization





Estimated age-standardized incidence rates (World) in 2020, all cancers, males, all ages



Estimated age-standardized incidence rates (World) in 2020, all cancers excl. non-melanoma skin cancer, males, all ages

Data source:GLOBOCAN 2020 Graph production: Global Cancer Observatory (http://gco.iarc.fr/) © International Agency for Research on Cancer 2021


Estimated age-standardized mortality rates (World) in 2018, all cancers, males, all ages

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Data source: GLOBOCAN 2018 Graph production: IARC (http://gco.iarc.fr/today) World Health Organization





Estimated age-standardized mortality rates (World) in 2020, all cancers, males, all ages



Estimated age-standardized mortality rates (World) in 2020, all cancers, males, all ages



Estimated number of prevalent cases (5-year) as a proportion in 2018, all cancers, males, all ages

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Data source: CLOBOCAN 2018 Graph production: IARC (http://gcolarc.fr/today) World Health Organization





Estimated age-standardized incidence rates (World) in 2018, all cancers, females, all ages

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Data source: GLOBOCAN 2018 Graph production: IARC (http://gco.iarc.fr/today) World Health Organization





Estimated age-standardized incidence rates (World) in 2020, all cancers, females, all ages



Estimated age-standardized incidence rates (World) in 2020, all cancers excl. non-melanoma skin cancer, females, all ages



Estimated age-standardized mortality rates (World) in 2018, all cancers, females, all ages

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Data source: GLOBOCAN 2018 Graph production: IARC (http://gco.iarc.fr/today) World Health Organization





Estimated age-standardized mortality rates (World) in 2020, all cancers, females, all ages

Estimated number of prevalent cases (5-year) as a proportion in 2018, all cancers, females, all ages



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Data source: CLOBOCAN 2018 Graph production: IARC (http://acolarc.fr/today) World Health Organization



Which cancers are the **most** frequent in the world?

The most frequent cancers in the world (without C44) (absolute numbers)



World: Both sexes, all ages

The most frequent cancers in the world (without C44) (ASR)



Incidence Mortality

Where is the highest incidence of lung cancer?



Estimated age-standardized incidence rates (World) in 2020, lung, males, all ages



Estimated age-standardized incidence and mortality rates (World) in 2020, lung, males, all ages



Estimated age-standardized incidence rates (World) in 2020, lung, females, all ages



Estimated age-standardized incidence and mortality rates (World) in 2020, lung, females, all ages

Where is the highest incidence of breast cancer?



Estimated age-standardized incidence rates (World) in 2020, breast, females, all ages



Estimated age-standardized incidence and mortality rates (World) in 2020, breast, females, all ages

Where is the highest incidence of cancer of colon & rectum?



Estimated age-standardized incidence rates (World) in 2020, colorectum, males, all ages



Estimated age-standardized incidence and mortality rates (World) in 2020, colorectum, males, all ages



Estimated age-standardized incidence rates (World) in 2020, colorectum, females, all ages



Estimated age-standardized incidence and mortality rates (World) in 2020, colorectum, females, all ages

Where is the highest incidence of stomach cancer?



Estimated age-standardized incidence and mortality rates (World) in 2020, stomach, males, all ages



Estimated age-standardized incidence and mortality rates (World) in 2020, stomach, females, all ages

Where is the highest incidence of prostate cancer?

Estimated age-standardised incidence rate per 100,000 Prostate, all ages



a < 36.1 **b** < 70.5 **b** < 104.9 **b** < 139.3 **b** < 173.7

GLOBOCAN 2008 (IARC) - 9.10.2013



Estimated age-standardized incidence and mortality rates (World) in 2020, prostate, males, all ages

Where is the highest incidence of melanoma?



Estimated age-standardized incidence and mortality rates (World) in 2020, melanoma of skin, males, all ages



Estimated age-standardized incidence and mortality rates (World) in 2020, melanoma of skin, females, all ages

TRENDS OF INCIDENCE C43 (UZIS)



-MUŽI -ŽENY
Trends of mortality C43, ASR-W (UZIS)



Trendy v incidenci C44, ASR-W (UZIS)



Trendy v mortalitě C44, ASR-W (UZIS)



Estimated number of new cases in 2020, Czechia, males, all ages



Data source:GLOBOCAN 2020 Graph production: Global Cancer Observatory (http://gco.iarc.fr/) © International Agency for Research on Cancer 2022



Estimated number of new cases in 2020, Czechia, females, all ages

Data source:GLOBOCAN 2020 Graph production: Global Cancer Observatory (http://gco.iarc.fr/) © International Agency for Research on Cancer 2022

International Agency for Resear

Norway: Mency for Research on Cancer

Estimated number of cancer cases, all ages (total: 13,210)



Norway: Women or Research on Cancer Estimated number of cancer cases, all ages (total: 11,390)



nter United Kingdom: Menesearch on Cancer

Estimated number of cancer cases, all ages (total: 151,827) Organization



errUnited Kingdom: Womenarch on Cancer

Estimated number of cancer cases, all ages (total: 152,408)



^{en} United States of America: Men^{on} Cancer

Estimated number of cancer cases, all ages (total: 745,187) Organization



Iter United States of America: Women ancer

Estimated number of cancer cases, all ages (total: 692,012) Organization



The Gambia: Men Research on Cancer

Estimated number of cancer cases, all ages (total: 477) Organization



nter The Gambia: Womenesearch on Cancer

Estimated number of cancer cases, all ages (total: 527) Organization



Inter India: Maleency for Research on Cancer

Estimated number of cancer cases, all ages (total: 477,482) Organization



InterIndia: Femalecy for Research on Cancer

Estimated number of cancer cases, all ages (total: 537,452) Organization



Japan: Menney for Research on Cancer

Estimated number of cancer cases, all ages (total: 361,600).



Japan: Women for Research on Cancer

Estimated number of cancer cases, all ages (total: 253,907).



Risk factors

Non – avoidable

Avoidable

Risk factors

Non – avoidable • Age

Avoidable

Age-specific curves (CIVIII)

Czech Republic (2007) Male



Age-specific curves (CIVIII)

Czech Republic (2007) Female



International Agency for Research on Cancer (IARC) - 29.9.2015

Risk factors

Non – avoidable ? • Age • Genetics

Avoidable







Families with mutations in the *BRCA1* gene have a genetic susceptibility to breast and ovarian cancers.



The many cancers seen in Li–Fraumeni syndrome affect a wide spectrum of tissues.

This analysis of 91 families with inherited mutations in the *p53* gene shows the wide range of cancers with a predominance in children and young adults that characterizes the Li–Fraumeni familial cancer syndrome.

Familial adenomatous polyposis (APC)

COLORECTAL CANCER

ALSO NON-CANCER DISEASES, DESMOID TUMOURS, ODONTOMS, TUMOURS OF SMALL INTESTINE

IN 100% CASES TUMOUR OCCURS

AUTOSOMAL DOMINANT HEREDITY

Lynch syndrom I, II

Heredital nonpolypose colorectal cancer Autosomal dominant heredity Colorectal cancer, gynecological cancers, stomach, pancreatic and kidney cancers

Lynch syndrom I, II

Carrier has the longlofe risk of cancer

Colorectal	70 – 90%
Ovary	12%
Endometrium	50%
Stomach	15 – 20%
Pancreas	5%

- worse treatment results
- often are multiple
- grow quickly
- are more aggressive
- occur in younger age

Hereditary cancers

Family history !!

- Two or more cancers in one family line
- -Cancer occurence in person younger than 35 years
- Hereditary cancer in the family history

....recommendation to oncogenetic department

Risk factors

Non – avoidable ? • Age

•Genetics

Avoidable



Cause % of Tobacco Chronic infections Nutrition Any other individual cause

% of all cancers 15-30 10-25 30 ause <5



Tobacco

Cause

Chronic infections Nutrition Any other individual cause

% of all cancers



Tobacco-induced cancers

Cigarette smoking Lung Larynx Oesophagus Oral cavity Pharynx Pancreas Bladder Kidney Cigar or pipe Lip smoking Oral cavity Lung Tobacco chewing Oral cavity Tobacco and alcohol Oral cavity Oesophagus Pharynx Larynx

Another risk factors for lung cancer?
Carcinogenic agents with sufficient evidence in humans

Aluminum production

Arsenic and inorganic arsenic compounds

Asbestos (all forms)

Beryllium and beryllium compounds

Bis(chloromethyl)ether; chloromethyl methyl ether (technical grade)

Cadmium and cadmium compounds

- Chromium(VI) compounds
- Coal, indoor emissions from household combustion
- **Coal gasification**
- Coal-tar pitch
- Coke production
- Engine exhaust, diesel
- Hematite mining (underground)

Iron and steel founding

Lung cancer & asbestos

Nonsmoker nonexposed to asbestos	RR 1
Smoker nonexposed to asbestos	RR 9
Nonsmoker exposed to asbestos	RR 5
Smoker exposed to asbestos	RR 50 – 90

• RR= relativ risk;

Health effects

Asbestosis (long-term high exposure, latency cca 20 – 30 years)

Hyalinosis of pleura (relatively low exposure)

Mesothelioma of pleura or peritoneum (latency cca 30 - 50 years even after short exposure; aggressive cancer with survival about 4 - 18 months)

Lung cancer (in connection with asbestosis or hyalinosis)



Carcinogenic agents with sufficient evidence in humans

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Bis(chloromethyl)ether; chloromethyl methyl ether (technical grade)

Cadmium and cadmium compounds

- Chromium(VI) compounds
- Coal, indoor emissions from household combustion

Coal gasification

Coal-tar pitch

Coke production

Engine exhaust, diesel

Hematite mining (underground)

Iron and steel founding

Carcinogenic agents with sufficient evidence in humans

MOPP (vincristine-prednisone-nitrogen mustardprocarbazine mixture)

- Nickel compounds
- Outdoor air pollution
- Outdoor air pollution

Painting

Particulate matter in outdoor air pollution

Plutonium

- Radon-222 and its decay products
- Rubber production industry
- Silica dust, crystalline

Soot

- Sulfur mustard
- Tobacco smoke, secondhand
- Tobacco smoking
- X-radiation, gamma-radiation

Agents with limited evidence in humans

- Acid mists, strong inorganic
- Art glass, glass containers and pressed ware (manufacture of) Biomass fuel (primarily wood), indoor emissions- household
- Bitumens, occupational exposure to oxidized bitumens and their emissions during roofing
- Bitumens, occupational exposure to hard bitumens and their emissions during mastic asphalt work
- Carbon electrode manufacture
- alpha-Chlorinated toluenes and benzoyl chloride
- Cobalt metal with tungsten carbide
- Creosotes
- Frying, emissions from high-temperature
- Insecticides, non-arsenical (occupational exposures in spraying and application)
- Printing processes
- 2,3,7,8-Tetrachlorodibenzo-para-dioxin
- Welding fumes

CANCER OCCURRENCE, ETIOLOGY AND MECHANISMS

2A2



Fig. 6. Relative risk of lung cancer in man-made mineral fibre production workers by time since first exposure. Results of Poisson regression analysis, adjusted for country, age, calendar period, duration of employment and technical phase. — all workers; … rockwood/slagwool; — glasswool



Cause % of Tobacco Chronic infections Nutrition Any other individual cause

% of all cancers 15-30 10-25 30 ause <5



Cause Tobacco

Chronic infectious

Nutrition

Any other individual cause

% of all cancers 15-30 10 - 25 30

< 5



Cancer	Infectious agent %	ectious agent % Caused by infectio	
Stomach	Helicobacter pylori	40	
Liver	Hepatitis B and C viruses, liver flul	kes 80	
Cervical	Human papillomavirus	99	
Anal	Human papillomavirus	80	
Vulva & penis	Human papillomavirus	30	
Oropharynx	Human papillomavirus	30	
Lymphomas	Epstein–Barr virus	10	

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Estimated age-standardised incidence rate per 100,000 Liver: both sexes, all ages

Cancer patterns vary worldwide.

Liver cancer

Cancer of the liver is most frequent in western and central Africa and in Asian countries, particularly China. This is due to the high prevalence of chronic hepatitis B virus infection and exposure to a food-borne carcinogen, aflatoxin B₁.



- 27.2.2013

Hepatitis B virus (HBV) and aflatoxins act together to cause liver cancer in Africa and south-east Asia.



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Estimated age-standardised incidence rate per 100,000 Cervix uteri, all ages



a < 11.6 **b** < 22.8 **b** < 33.9 **b** < 45.1 **b** < 56.3

GLOBOCAN 2008 (IARC) - 27.2.2013

Estimated age-standardised mortality rate per 100,000 Cervix uteri, all ages



GLOBOCAN 2008 (IARC) - 27.2.2013

Background: HPV Types in Cases of Cervix Cancer

Different Regions of the World



PAPILLOMAVIRUS CAUSE INFECTIONS IN YOUNG WOMEN AND CAUSE DEATH IN ADULS



Prevention?

VACCINATION!

Anti-tumour vaccines?

-AGAINST PAPILOMAVIRUSIS -AGAINST HEPATITIS B



Liver and colorectal cancers incidence rates in 2000 (annual cases per 100 000 population).

Colorectal cancer

Cancer of the colorectum is most frequent in North America, in Europe and in Australia. This disease is associated with a western-style diet, typically low in fibre and fresh fruit and vegetables, and high in saturated fat.

Strength of the association between some foods and the risk of developing certain types of cancer



OBESITY hot spots

In 2014, 13% of the world's adult population were obese: 11% of men and 15% of women.





Generalmente cosa c'è nella sua INSALATA MISTA? (risponda con una X ad ogni domanda)

11 🕨 P	POMODORI	sempre o quasi	frequentemente	moi o roromente
12	CAROTE			
13 🕨 1	NSALATA (foglie)			
14 🕨 P	PEPERONI			C
15 🕨 👌	ALTRO	<u> </u>		

A questionnaire is used to assess dietary habits and serving size in Italian centres of the EPIC study.







Vegetable intake and relative risk of cancer



Screening

Screening:

CHEAP AVAILABLE EASY

Screening:

CHEAP AVAILABLE EASY HIGH SPECIFICITY HIGH SENSITIVITY
Screening:

CHEAP AVAILABLE EASY HIGH SPECIFICI

HIGH SENSITIVITY

HIGH SPECIFICITY HIGH SENSITIVITY ABLE TO DETECT EARLY STAGE OF TUMOUR

AVAILABLE EASY

AVAILABLE

CHEAP

Screening:

Screening is suitable for tumours:

WITH HIGH FREQUENCY & IN WHICH WE ARE ABLE TO PROLONG THE GOOD QUALITY LIFE OF THE PATIENTS

Which tumours you suppose to be suitable for screening?

Screening in Czech Republic

Breast cancer screening – from 45 every second year mammography

Colorectal screening – from 50 either ocult blood test every year or preventive colonoscopy once in ten years

Cervical screening – from 15 every year regular check at the gynekology with pap-smears

Lung cancer screening – from 60 to 74, heavy smokers and ex-smokers (20 cig. per day for 20 years or equivalent)



Onkologiccal paradox

How to find risk factors?

Which type of studies can be used?

OBSERVATIONAL / descriptive / correlation (ecological) studies Analytical Case – control study Cohort study Retrospective Prospective

How to get information (e.g.concerning the diet), if we need information:

- 10 – 20 YEARS OLD - BEFORE DISEASE OCCURRENCE

- INFORMATION CONCERNING THE QUALITY AND AMOUNT OF FOOD (ESP. IN MEN)

- ACCURACY OF ALL INFORMATION

Interventional studies

CONTROLLED TRIALS DOUBLE-BLINDED /TRIPLE-BLINDED

CARET Study (Beta-Carotene and Retinol EfficacyTrial)

USA

14 254 SMOKERS/FORMER SMOKERS, MEN AND WOMEN

4 060 MEN EXPOSED TO ASBESTOS + SMOKERS

PLANED 1988 - 2003

FINISHED 1996

HIGHER MORTALITY ON LUNG CANCER AND ALSO TOTAL MORTALITY IN SUPPLEMENTED GROUP ATBC Study (Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study)

FINLAND

- 29 133 MALE SMOKERS IN 4 GROUPS
- AFHA-TOKOFEROL + BETA-CAROTENE
- DOUBLE BLINDED TRIAL
- 5 TO 8 YEARS, MEDIAN 6,1 YEAR

IN BOTH SUPPLEMENTED GROUPS WAS HIGHER MORTALITY NOT ONLY FROM CANCER

HOPE-TOO STUDY

7000 diabetics + cardiovascular diseased people
Double-blinded, placebo controlled study
7 years daily vitamin E supplementation
In supplemented group increased risk of cardiac failure of 13%

Didn't decrease incidence of cancer

Cochrane Collaboration Expert Group

Vitamin supplementation, synthetic antioxids, could lead to premature death.

"Beta caroten, vitamin A & E supplementation probably increase death rate." SELECT Study (Selenium and Vitamin E Cancer Prevention Trial)

- Fred Hutchinson Cancer Research Center, Seattle, Washington.
- Over 35 000 males
- Randomized placebo controlled, double-blinded trial
- 400 iu vitamin E & 200 μg of selenium/day
- 2001 2013, stopped 2008

SELECT Study (Selenium and Vitamin E Cancer Prevention Trial)cont.

Conclusions: suplementation by selenium & vitamin E could increase risk of prostate cancer in males

- The worst result was found in men with adequate nutrition
- The risk of prostate cancer in this group increased by 91%

Is this one of possible explanation of prostate cancer increase in well-developer countries?

SELECT Study (Selenium and Vitamin E Cancer Prevention Trial) cont.

In supplemented group with vit.E incidence of prostate cancer was about 17% higher

In those with normal level of selenium at the beginning of the study, selenium supplementation increased twice risk of highly aggressive prostate cancer

In those, who could profit from selenium supplementation because of low level at the beginning of the study, supplementation by vitamin E again increased twice risk of highly aggressive prostate cancer Women's Health Study HARVARD SCHOOL OF MEDICINE

1992 - 2004

39 876 FEMALES OLDER 45 YEARS

ASPIRIN, VITAMIN E AND BETA-CAROTENE

SUPPLEMENTATION BY BETA-CAROTENE WAS FINISHED

Because of results of ATBC and CARET studies No significant difference in incidence of cancer or cardiovascular dis. or total mortality Prospective Study of Fruit and Vegetable Consumption and Risk of Lung Cancer Among Men and Women

71 910 FEMALES FROM NURSES' HEALTH STUDY

37 725 MALES FROM HEALTH PROFESSIONALS' FOLLOW-UP STUDY

HIGHER CONSUMPTION OF FRUIT & VEGETABLE HAS SMALL, NOT STATISTICALLY SIGNIFICANT, DECREASE OF CHRONIC DIS., MORE CARDIOVASCULAR THAN CANCER Fruit and Vegetable Intake and Risk of Major Chronic Disease

71 910 FEMALES FROM NURSES' HEALTH STUDY

37 725 MALES FROM HEALTH PROFESSIONALS' FOLLOW-UP STUDY

ONLY LUNG CANCER

PROTECTIVE EFFECT IN NON-SMOKERS, MALES & FEMALES

SMALL PROTECTIVE EFFECT IN FEMALES (ALL)

NO EFFECT IN MALE SMOKERS

Indoor health risk factors (according to Joint Research Center)

Inorganic chemical compounds

- •Combustion particles
- •CO
- •Radon
- •NO₂

Biological factors

• Dampness, moulds, mites

Organic chemical compounds

- Benzene
- Formaldehyde
- (S)VOCs
- ETS



Late effects of xenobotics

Teratogen Mutagen Carcinogen



IS THE FORMATION OF CONGENITAL MALFORMATIONS (MISLEADINGLY CALLED BIRTH DEFECTS).

Teratogene



Effect of Contergan [thalidomid]

Mutagen is a physical or chemical agent that changes the genetic information (usually DNA) of an organism and thus increases the frequency of mutations above the natural background level. As many mutations cause cancer, mutagens are typically also carcinogens.

Not all mutations are caused by mutagens: So-called spontaneous mutations occur due to errors in DNA replication, repair and recombination of DNA sequences.



Carcinogens

may increase the risk of getting cancer by altering cellular metabolism or damaging DNA directly in cells, which interferes with biological processes, and induces the uncontrolled, malignant division ultimately leading to the formation of tumours.

Carcinogens cont.

Usually DNA damage, if too severe to repair, leads to programmed cell death, but if the programmed cell death pathway is damaged, then the cell cannot prevent itself from becoming a cancer cell.

Carcinogen vs mutagen

- Mutagens or genotoxic agents cause mutations in germ cells
- Mutations are transferable to new/next generation
- Carcinogen cause mutations in somatic cells

Classifications



<u>Group 1:</u> The agent (mixture) is carcinogenic to humans. The exposure circumstance entails exposures that are carcinogenic to humans.

Group 2A: The agent (mixture) is probably carcinogenic to humans. The exposure circumstance entails exposures that are probably carcinogenic to humans.

Group 2B: The agent (mixture) is possibly carcinogenic to humans. The exposure circumstance entails exposures that are possibly carcinogenic to humans.

<u>Group 3</u>: The agent (mixture, or exposure circumstance) is not classifiable as to carcinogenicity in humans.

Overall Evaluations of Carcinogenicity to Humans

Group 1: Carcinogenic to humans

AS EVALUATED IN IARC MONOGRAPHS VOL. 1-120

THIS LIST CONTAINS ALL AGENTS, MIXTURES AND EXPOSURES EVALUATED AS BEING IN GROUP 1 TO DATE.

WHERE APPROPRIATE, CHEMICAL ABSTRACT NUMBERS ARE GIVEN [IN SQUARE BRACKETS]. FOR DETAILS OF THE EVALUATION, THE RELEVANT MONOGRAPH SHOULD BE CONSULTED (VOLUME NUMBER GIVEN IN ROUND BRACKETS, FOLLOWED BY YEAR OF PUBLICATION OF LATEST EVALUATION).

IARC Monographs of Carcinogenic Hazards to Humans and Handbooks of Cancer Prevention



Group 1: Carcinogenic to humans (120)

Acetaldehyde associated with consumption of alcoholic beverages (Vol. 100E, 2012) Acid mists, inorg. acids (Vol.54, 100F, 2012) Aflatoxins (Vol.56, 82, 100F, 2012) Alcoholic beverages (Vol. 44,96,100E, 2012) Aluminium production (Vol. 34, sup. 7, 99, 100F, 2012) 4-Aminobiphenyl (Vol. 1, Suppl. 7, 99, 100F, 2012) Areca nut (Vol.85, 100E, 2012) Aristolochic acid, plants containing Aristolochic acid (Vol. 82, Vol. 100A; 2012) (NB: Overall evaluation upgraded from 2A to 1 based on mechanistic and other relevant

data)





Group 1: Carcinogenic to humans (120) Arsenic and inorganic arsenic compounds (Vol. 23, Suppl. 7;1987; 100C, 2012)

Asbestos all forms, including actinolite, amosite, anthophyllite, chrysotile, crocidolite, tremolite) (Vol. 14, Suppl. 7; 1987; 100C, 2012) Auramine production [anilin dye] (Sup. 7, Vol. 99, 100F 2012) Azathioprine [Imuran] (Vol. 26, Suppl. 7; 1987; 100A 2012) Benzene (Vol. 29, Suppl. 7; 1987; 100F 2012) Benzidine (Vol. 29, Suppl. 7; 1987; 99, 100F 2012) Benzidine, dyes metabolised to (Vol.99, 100F 2012) (NB: Overall evaluation upgraded from 2A to 1 based on mechanistic and other relevant data) Beryllium and its compounds (Vol. 58; 1993; 100C, 2012)
Benzo[a]pyrene (Vol. 32, Suppl. 7, Vol. 92; 100F, 2012) (NB: Overall evaluation upgraded from 2B to 1 based on mechanistic and other relevant data) Betel quid with tobacco (Vol.85, 100E, 2012) Betel quid without tobacco (Vol.85, 100E, 2012) Bis(chloromethyl)ether; chloromethyl methyl ether (technical-grade) (Vol. 4, Suppl. 7; 100F, 2012) Busulfan (Vol. 4, Suppl. 7; 1987; 100 A 2012) 1,3-Butadiene (Vol. 97,100F 2012) Cadmium & cadmium comp. (Vol. 58, 100C 2012) Chlorambucil (Vol. 26, Suppl. 7, 1987; 100A 2012)

Chlornaphazine (Vol.4, Suppl. 7, 1987; 100A 2012)

- Group 1: Carcinogenic to humans (120)
- Chromium [VI] compounds (Vol. 49, 100C, 2012)
- Clonorchis sinensis infections with (Vol. 61, 100B, 2012)
- Coal (indoor emissions, household combustion of) (Vol.95, 100E, 2012)
- Coal gasification (Vol. 92, 100F, 2012)
- Coal-tar distillation (Vol. 92, 100F 2012)
- Coal-tar pitch (Vol. 35, Sup. 7, 100F 2012)
- Coke production (Vol. 92, 100F, 2012)
- Ciclosporin (Vol. 50, 1990; 100A 2012)
- Cyclophosphamide (Vol. 26, Suppl. 7, 100A, 2012) Diethylstilboestrol (Vol. 21, Suppl. 7, 100A, 2012)
- 1,2-Dichloropropane (Vol. 110, in prep.)

Engine exhaust, diesel (Vol. 46, 105, 2013) Epstein-Barr Virus (Vol. 70, 1997; 100B, 2012) Erionite (Vol. 42, Suppl. 7, 1987; 100C, 2012) Estrogen therapy postmenopausal (Vol. 72, Vol. 100A; 2012) Estrogen-progestogen menopausal terapy (combined) (Vol. 72, Vol. 91, Vol. 100A; 2012) Estrogen-progestogen oral contraceptives (combined) (Vol. 72, Vol. 91, Vol. 100A; 2012) (NB: There is also convincing evidence in humans that these agents confer a protective effect against cancer in the endometrium and ovary) Ethanol in alcoholic beverages (Vol. 96; 100 E 2012) Ethylene oxide (Vol. 60, Vol. 97,2008; 100F 2012) (NB: Overall evaluation upgraded from 2A to 1 based on mechanistic and other relevant data)

Etoposide (léčba nádorů varlat a ca plic malobuněčného) (Vol. 76, Vol. 100A; 2012) (NB: Overall evaluation upgraded from 2A to 1 based on mechanistic and other relevant data) Etoposide in combination with cisplatin and bleomycin (Vol. 76; 100A, 2012) Fissions products including strontium 90 (Vol. 100D, 2012) Formaldehyde (Vol. 88, 2006; 100F 2012) Hematite mining(undeground) (Vol. 1, Suppl. 7, 100D, 2012) Helicobacter pylori (infections with) (Vol.61, 100B in prep.) Hepatitis B virus(chronic infection with) (Vol. 59, 100B, 2012) Hepatitis C virus(chronic infection with) (Vol.59, 100B, 2012) Human immunodeficiency virus typ 1 (infection with) (Vol. 67,1996; 100B, 2012)

Group 1: Carcinogenic to humans (120) *Human papillomavirus* typ 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 (Vol. 64, Vol. 90, 100B, 2012) (NB: The HPV types that have been classified as *carcinogenic to humans* can differ by an order of magnitude in risk for cervical cancer) Human T-cell lymphotropic virus typ | (Vol. 67, 100B, 2012) lonizing radiation (all types) (Vol. 100D, 2012) Iron and steel founding (occupational exposure during) (Vol. 34, sup.7, 100F, 2012) Isopropyl alcohol manufacture using strong acid (Sup.7, 100F, 2012) Kaposi sarcoma herpes virus (Vol. 70, 100B 2012)

- Leather dust (Vol. 100C, 2012)
- Lindane (hexachlorocyclohexanes) (Vol.113, in prep.)
- Magenta production (Vol. 57, 99, 100F, 2012)
- Melphalan (Alkeran) (Vol. 9, Suppl. 7,100A, 2012)
- Methoxsalen (8-Methoxypsoralen) + UVA (Vol. 24, Suppl. 7, Vol. 100A; 2012)
- Methyl-CCNU (Sup.7, Vol. 100A, 2012)
- 4,4-Methylenebis(2-chloroaniline) (MOCA) (Vol. 57, Vol. 99; 2012)
- Mineral oils, untreated or mildly treated (Vol.33, sup.7; 100F, 2012)
- MOPP (Mustargen Oncovin Procarbazine Prednisone) and other comb. chemoterapy including alkylated agents *(Suppl. 7; Vol. 100A; 2012*)

2-Naphthylamine (Vol. 4, Suppl.7, 99, 100F, 2012) Neutron radiation (Vol. 75, 2000; 100D 2012) (NB: Overall evaluation upgraded to group 1 with supporting evidence from other relevant data) Nickel compounds (Vol. 49, 1990; 100C 2012) N'-Nitrosonornicotine (NNN) & 4-(N-Nitrosomethylamino-1-(3-pyridyl)-1-butanone (NNK) (Vol. 89, 2007; 100E 2012) (NB: Overall evaluation upgraded to group 1 based on mechanistic and other relevant data) **Opisthorchis Viverrini** (motolice jaterní) (Vol. 61,100B,2012) Outdoor air pollution (Vol. 109, 2016) Outdoor air pollution, particulate matter in (Vol. 109, 2016)

Painter (occupational exposure as a) (Vol. 47,98, Vol. 100A; 2011)

Particulate matter in outdoor air pollution (see

Outdoor air pollution, particulate matter in)

Pentachlorophenol (Polychlorophenols) (Vol. 117; in prep.)

- 3,4,5,3',4'–Pentachlorobiphenyl (PCB 126)(*Vol.* 100F; 2012)
- 2,3,4,7,8–Pentachlorodibenzofuran (*Vol. 100F; 2012*) Phenacetin (*Vol. 24, Suppl. 7, Vol. 100A; 2011*) (NB: Overall

evaluation upgraded from 2A to 1 with supporting evidence from other relevant data)

Phenacetin, analgesic mixtures containing (*Vol. 100A; 2011*) Phosphorus-32, as phosphate (*Vol. 78; 2001*) Plutonium-239 and its decay products (may contain plutonium-240 and other isotopes), as aerosols (*Vol.78; 2001*)

- Polychlorinated biphenyls (Vol. 18, supp.7, 107, in prep.) Polychlorinated biphenyls, dioxin-like, with a
- Toxicity Equivalency Factor (TEF) according to WHO (PCBs 77, 81, 105, 114, 118, 123, 126, 156, 157, 167, 169, 189) (NB: Overall evaluation upgraded to Group 1 with strong supporting evidence from other relevant data) (Vol. 107, 2016)
- Processed Meet (Vol. 114, in prep.)
- Radioiodines, including iodine-131 (Vol. 78, 100D, 2012) Radionuclides, a-particle-emitting, internally
- deposited *(Vol. 78; 2001)* (NB: Specific radionuclides for which there is *sufficient* evidence for carcinogenicity to humans are also listed individually as Group 1 agents)

Group 1: Carcinogenic to humans (120) Radionuclides, b-particle-emitting, internally

deposited (Vol. 78; 2001) (NB: Specific radionuclides for which there is *sufficient* evidence for carcinogenicity to humans are also listed individually as Group 1 agents)

Radium-224 and its decay products (Vol. 78; 2001) Radium-226 and its decay products (Vol. 78; 2001) Radium-228 and its decay products (Vol. 78; 2001) Radon-222 and its decay products (Vol. 78; 2001) Rubber manufacturing industry (Vol. 28, Sup, 7, 100F, 2012) Salted fish, Chinese- style (Vol. 56, 100E; in prep.)

Schistosoma haematobium (infection with) (Vol. 61; 1994)

Shale oils (Sup. 7, 100E, 2012)

Silica dust, crystalline (inhaled in the form of quartzor

cristobalite from occup.sources) (Vol. 68; 1997)

Solar radiation (Vol. 55, 100D; 2012)

- Soot (as found in occupational exposure of chimney sweeps) (Sup. 7, 100F, 2012)
- Sulfur mustard (Sup. 7, 100F, 2012)

Tamoxifen (Vol. 66; 1996) (NB: There is also conclusive evidence that this agent (tamoxifen) reduces the risk of contralateral breast cancer)

2,3,7,8 - TCDD (Tetrachlorodibenzo-*para-*dioxin) (Vol.69; 1997, 100F, 2012)

Viktor Juščenko



July 2004 December 2004

Group 1: Carcinogenic to humans (120) Thiotepa (Vol. 50; 1990) Thorium-232 and its decay products, administered intravenously as a colloidal dispersion of thorium-232 dioxide (Vol. 78; 2001) **Tobacco, smokeless** (89,100E, 2012) Tobacco smoke, second hand (83, 100E, 2012) **Tobacco smoking** (83, 100E, 2012) ortho-Toluidine (Vol. 77,99,100F, 2012) Treosulfan (Vol. 26, sup.7, 100A; 2011) Trichlorethylene (Vol. 63, 106, in prep.) Ultraviolet radiation (wavelengths 100 – 400nm encompassing UVA,UVB, UVC) (100D, 2012)

Group 1: Carcinogenic to humans (120) Ultraviolet –emitting tanning devices (100D, 2012)

Vinyl chloride (100F, 2012) Welding fumes (118, in prep.) Wood dust (100C, 2012)

X- and Gamma -Radiation (100D, 2012)

Group 2A: Probably carcinogenic to humans (81)

- Biomass fuel (primarily wood), indoor emissions from household combustion of (Vol.95, 2010)
- Chloramphenicol (Vol.50, 1990)
- Frying, emissions from high-temperature (Vol.95, 2010) Human papillomavirus type 68 (Vol.100B, 2012)
- Hairdresser or barber (occupational exposure as a)
- (Vol.57, 99 , 2010)
- Lead compounds, inorganic (Vol.87, 2006) Malaria (Plasmodium falciparum) (Vol.104, 2013) Shiftwork that involves circadian disruption (Vol.98, 2010)
- Red meat (Vol. 114, in prep.)
- Very hot beverages at above 65°C (drinking) (Vol. 116, in prep.)

Group 2B: Possibly carcinogenic to humans (299)

Group 3: Not classifiable as to carcinogenicity to humans (502)