

# Epidemiológia/epidemiology

(görög, „epi” = között és „demos” = nép/Greek “epi” = upon and “demos”= the people)

is the study of

- a) factors that influence health and disease occurrence in populations,
- b) the distribution and determinants of health-related states or events (including disease).

It is the scientific foundation of public health preventive medicine and of the control of diseases and other health problems.

Methods can be used to carry out epidemiological investigations:

- surveillance and descriptive studies to study distribution;
- analytical studies to study determinants.

<http://www.who.int/topics/epidemiology/en/>



1913: established by 10 medical doctors and 5 citizens,  
in New York City  
American Society for the Control of Cancer

<http://www.cancer.org/index>

# Epidemiológia

(görög, „epi” = között és „demos” = nép/Greek “epi” = upon and “demos”= the people)

Definíció:

- a betegségek előfordulását, elterjedését,
- a betegségek által okozott halálozást,
- az egészséget veszélyeztető /betegségek kialakulását befolyásoló kockázati tényezőket
- betegségek megelőzésének lehetőségeit vizsgálja.

Következtetéseit *egyedi* megfigyelések sokaságára alapozza, de csak *közösségekre* vonatkoztatja.



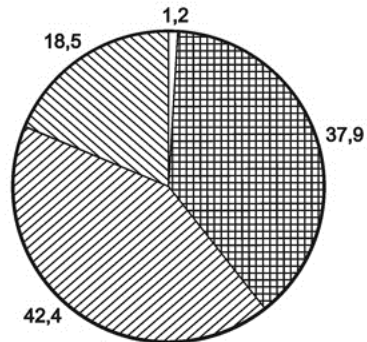
1913: 10 orvos és 5 polgár, New York City  
American Society for the Control of Cancer

<http://www.cancer.org/index>

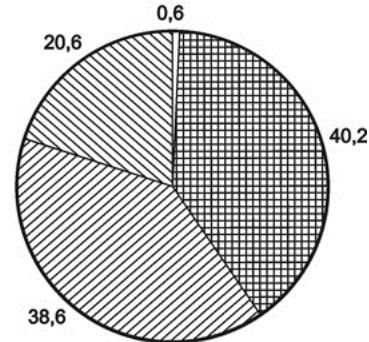
# Rosszindulatú daganatok okozta halálozások százalékos megoszlása Distribution of cancer caused mortality

Total  
Hungary, 2003

összes rosszindulatú daganat

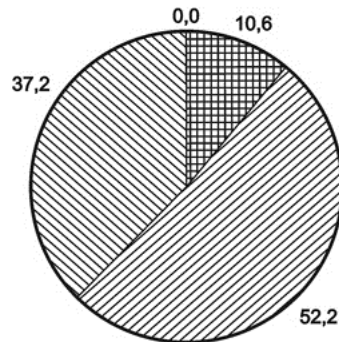


női emlőrák



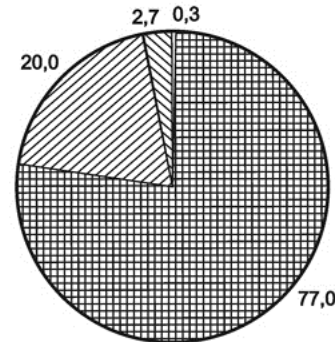
breast

prosztatatarák



prostate

ajak- szájüreg- és garatrágok



oral cavity

korcsoportok osztályköz-határai években



# Historical background

Three important observations launched the field of cancer epidemiology :

**1620, Thomas Venner**, London : "*Via Recta*" tobacco dangers "immoderate use of tobacco hurts the brain and the eye and induces trembling of the limbs and the heart."

**1713, Bernardino Ramazzini**, an Italian doctor, reported the virtual absence of cervical cancer and relatively high incidence of breast cancer in nuns : in some way related to their celibate lifestyle.

- identification and understanding the importance of hormones (changes that come with pregnancy)
- sexually-transmitted infections and cancer risk.

**1761, John Hill**, London: "*Cautions Against the Immoderate Use of Snuff.*" linking tobacco and cancer led to epidemiologic research

**1775, Percival Pott**, Saint Bartholomew's Hospital, London  
an occupational cancer in chimney sweeps, cancer of the scrotum, which was caused by soot collecting in the skin folds of the scrotum. - Carcinogenic exposures.

# Előzmények

1620, Thomas Venner, London : "*Via Recta*" a dohányzás ártalmairól  
"immoderate use of tobacco hurts the brain and the eye and induces trembling of the limbs and the heart."

1713, Bernardino Ramazzini, olasz orvos : a méhnyak tumor (cervical cancer) és az emlőrák magas emlőrák magas előfordulási aránya összefügghet az apácák életmódjával :

- A hormonok szerepe (pl. terhesség)
- Szexuálisan terjedő fertőzések

1761, John Hill , London: "*Cautions Against the Immoderate Use of Snuff.*"

- Dohányzás és tumor

1775, Percival Pott, Saint Bartholomew's Hospital , London :  
kéményseprők munkája korom (soot) és a hererák (scrotum)/bőr elváltozás.

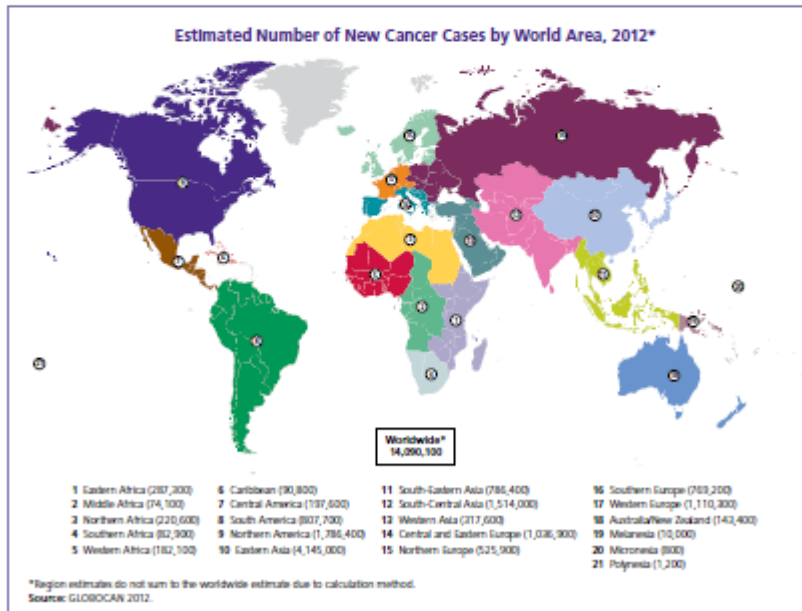
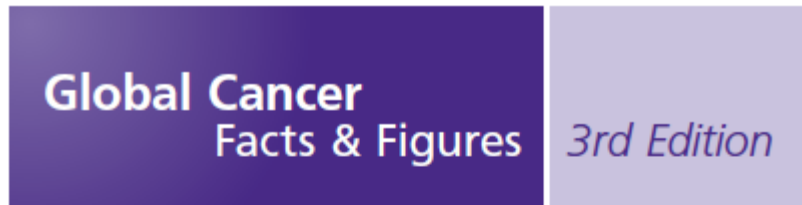
- Foglalkozás és karcinogenezis

# Előzmények/History: XX. század/century

1950s/early 1960s: smoking causes lung cancer

1952: American Cancer Society annually publishes: „Cancer Facts & Figures“

1964: *Smoking and Health*, US Surgeon General's 1964 report *Smoking and Health*.



Fő kutatási irányok/Main directions:

- Okok
- dohányzás (smoking),
  - elhízás (obesity)
  - sugárzás (e.g. UV)

- Megelőzés, védelem (prevention)
- mozgás (training)
  - táplálkozás (nutrition)

<http://www.cancer.org/index>

## Fogalmak /Definitions

***Morbiditás (morbidity):*** (incidencia, gyakoriság) egy adott népességben, időegység (pl. egy év) diagnosztizált új daganatos megbetegedések /100.000 fő. (New cases/year.)

***Mortalitás (mortality):*** a daganatos betegség okozta *halálesetek száma* időegység (pl. egy év) /100.000 fő. (Death/year.)

***Túlélés (survival):*** a diagnózis felállítása és a beteg elhalálása között eltelt idő (év); a kezelés eredményességének mérése. (Time between diagnosis and death.)

***Prevalencia (prevalence):*** egy adott népességben a „túlélők” száma; a diagnosztizált rákbetegek száma, akik kezelést kaptak és egy adott időben még életben vannak (követést, utókezelést, gondozást igényelnek).

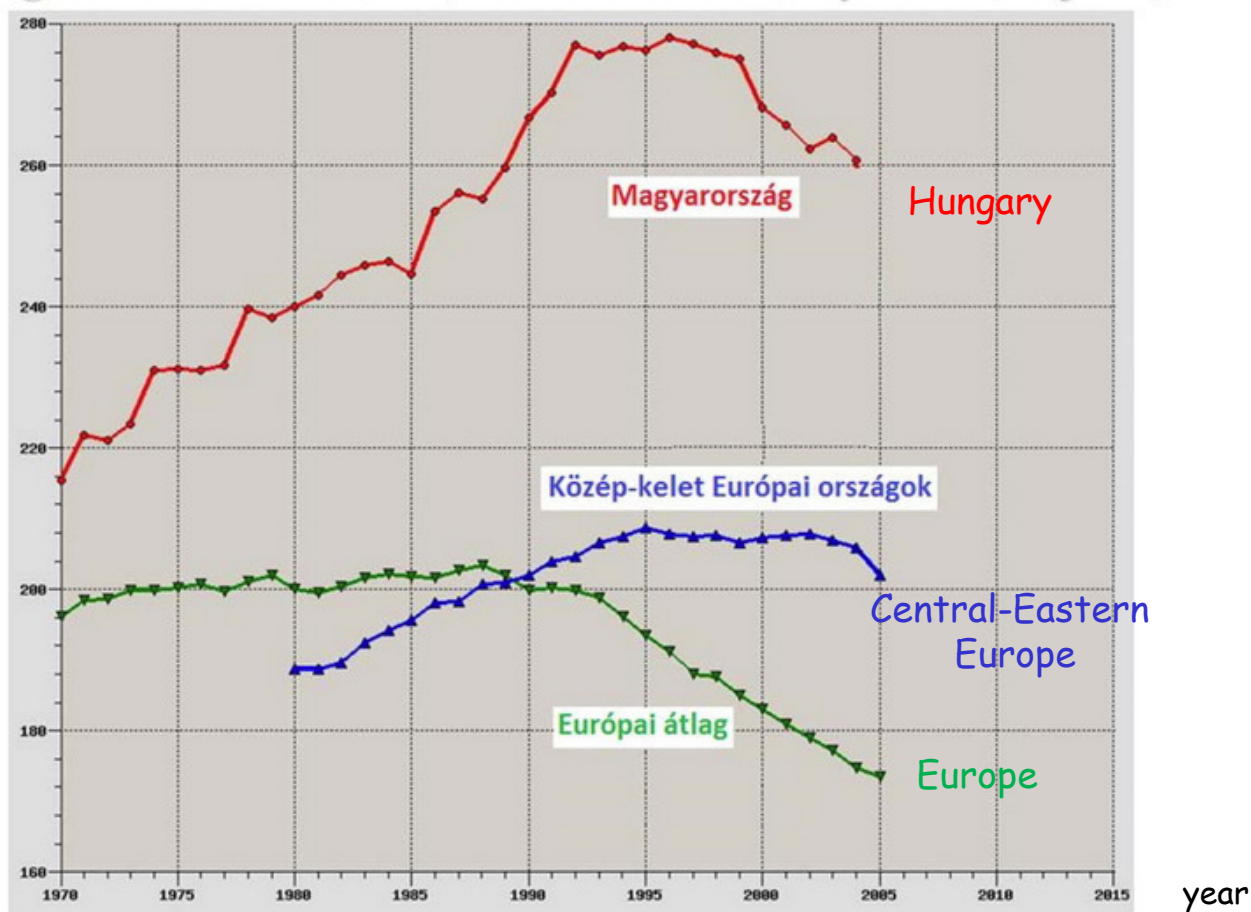
Döbrössy L.: A daganatos betegségek epidemiológiája, jegyzet. Semmelweis Egyetem és D. L.: A daganatok epidemiológiája. A daganatos betegségek helyzete és várható alakulása.

In: *Kopper L, Jeney A: Onkológia. A géntől a betegágyig.* pp. 115-137. Medicina. Budapest (2002) alapján

# Mortality / 100 000 capita

Semmelweis Egyetem

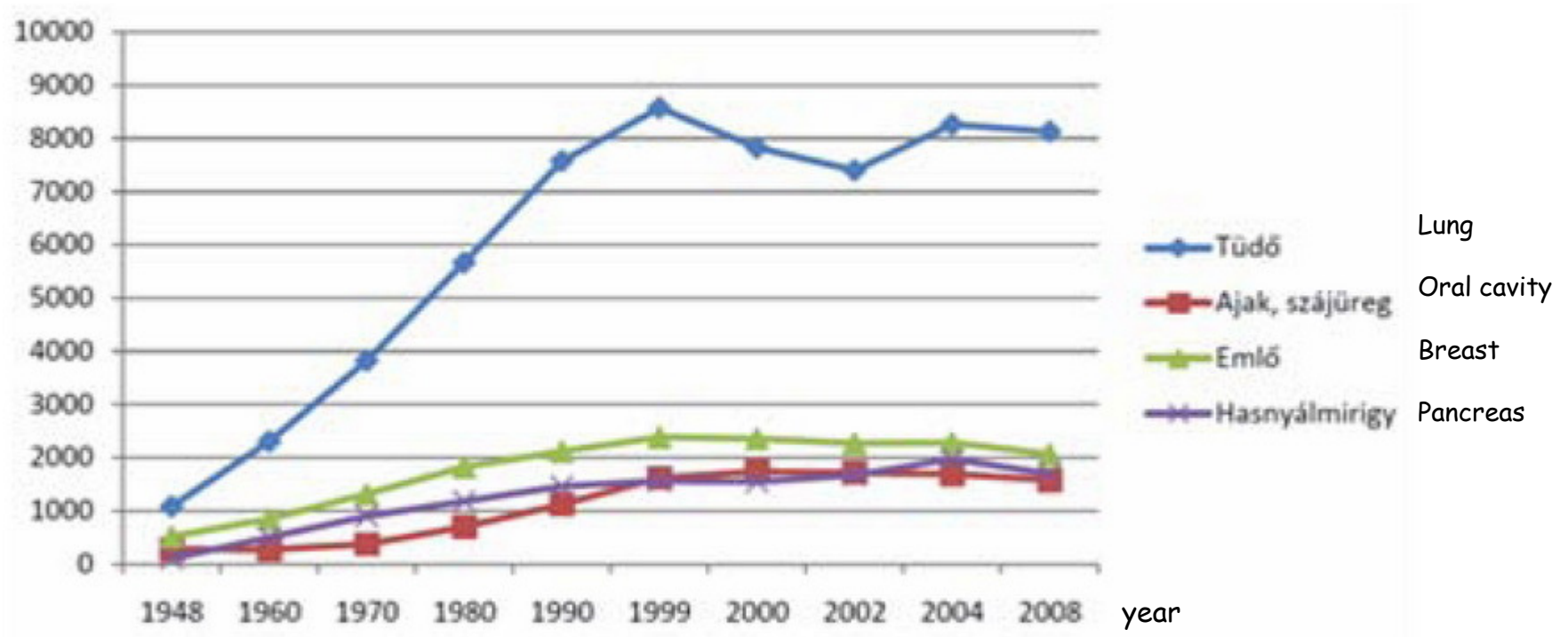
## *Daganatos halálozás (minden korosztály 100ezer főre)*



Semmelweis Egyetem



## Egyes daganatok időszora KSH 1948-2008



## Risk of lung (a,b) and of esophagus (c)

### (a) Radioactivity and smoking

	Radon level in a flat	
	50 Bq/m <sup>3</sup>	50 Bq/m <sup>3</sup>
Non-smoker	1,0	2,8
Smoker	6,8	17,3

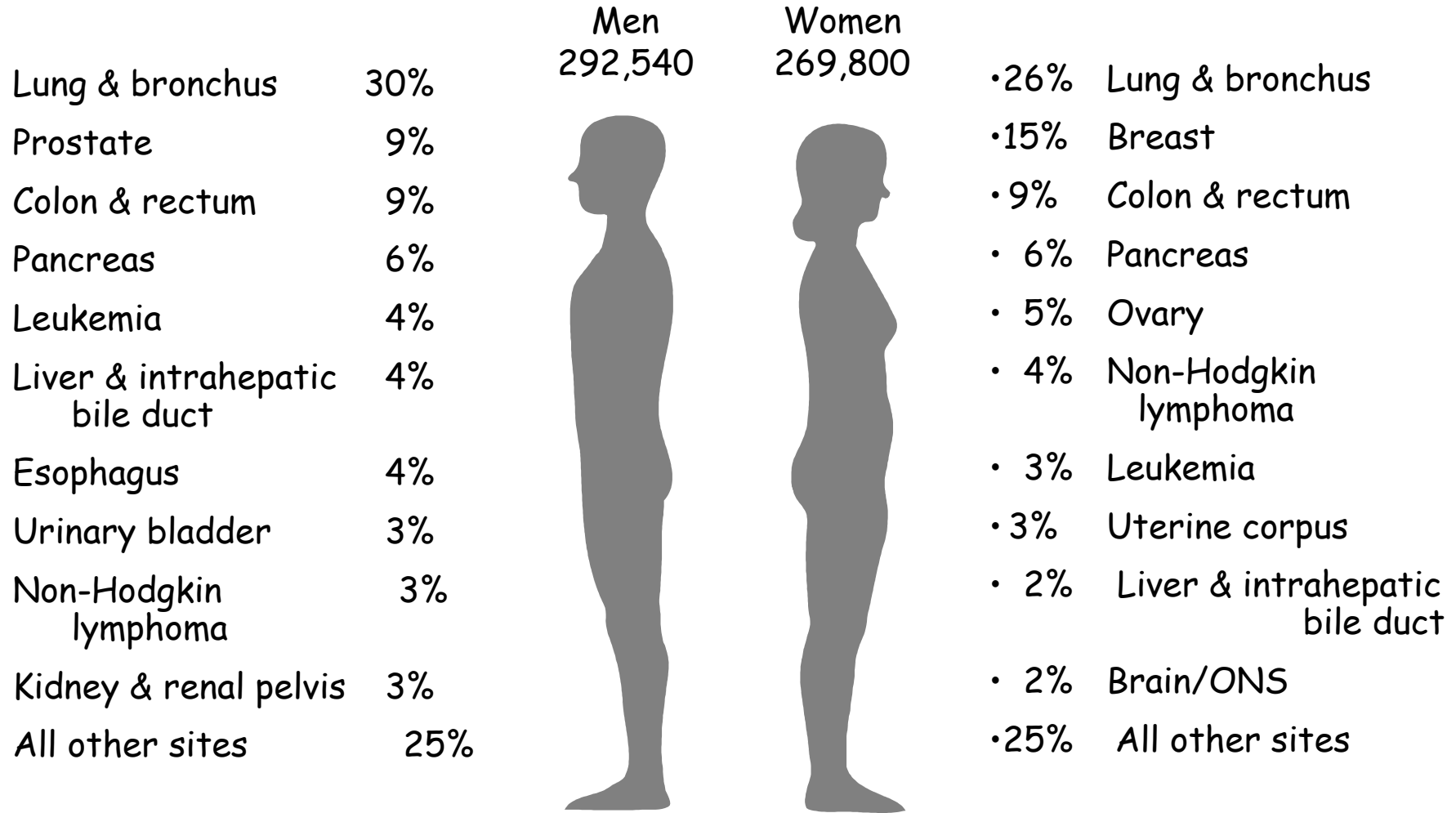
### (b) Asbestos/hydrocarbons and smoking

	Cigarette/day		
	0 - 9	10 - 19	20
Control	1,0	4,0	6,3
Hydrocarbons	1,3	7,0	9,9
Asbestos	2,8	6,8	12,4
CH + Asbestos	2,8	34,5	16,4

### (c) Alcohol and smoking

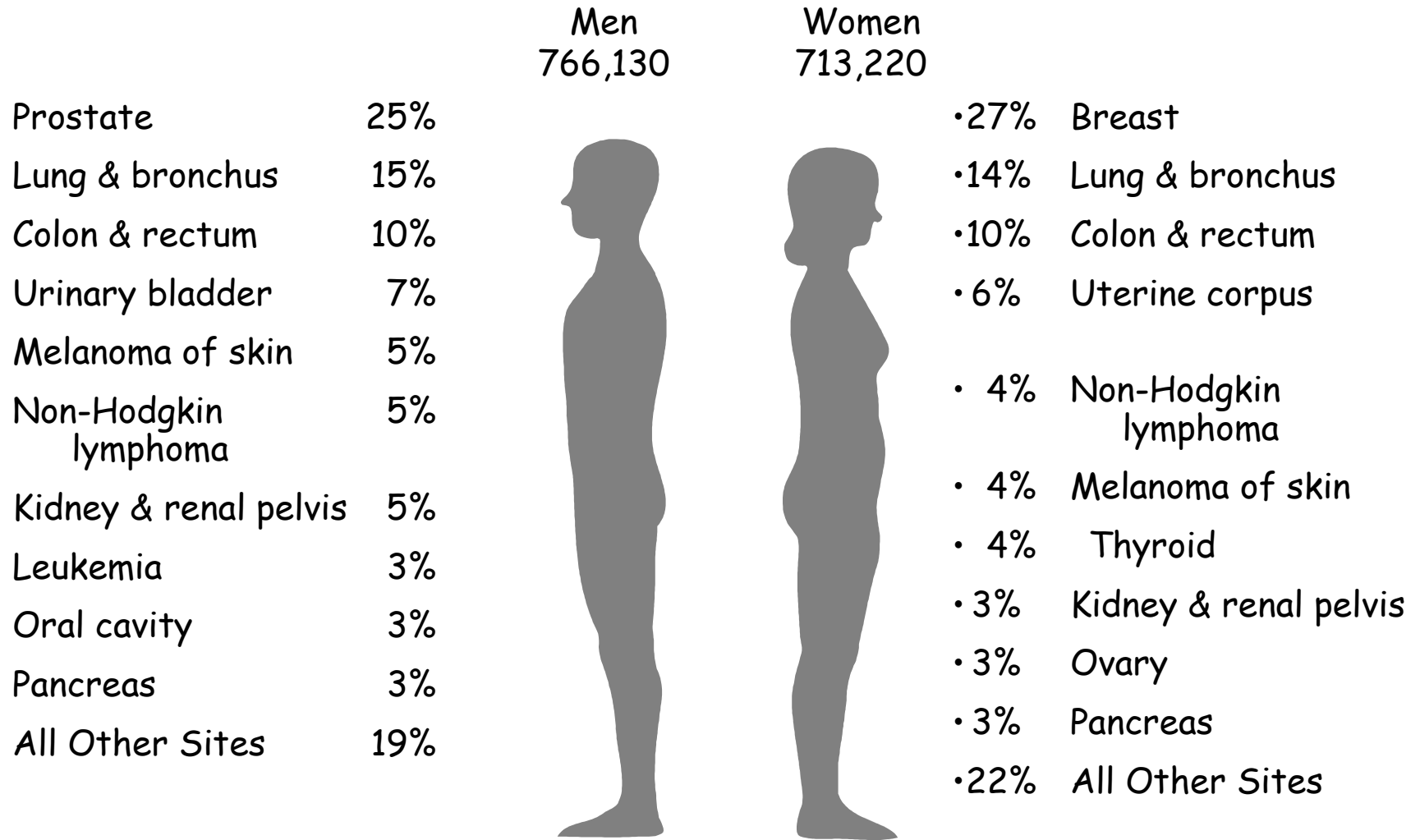
	Consumption of alcohol (g/day)		
	0 - 40	41 - 80	80
0 - 9	1,0	7,3	18,0
10 - 19	3,4	8,4	19,9
20	5,1	12,3	44,4

# Estimated US Cancer Deaths\*



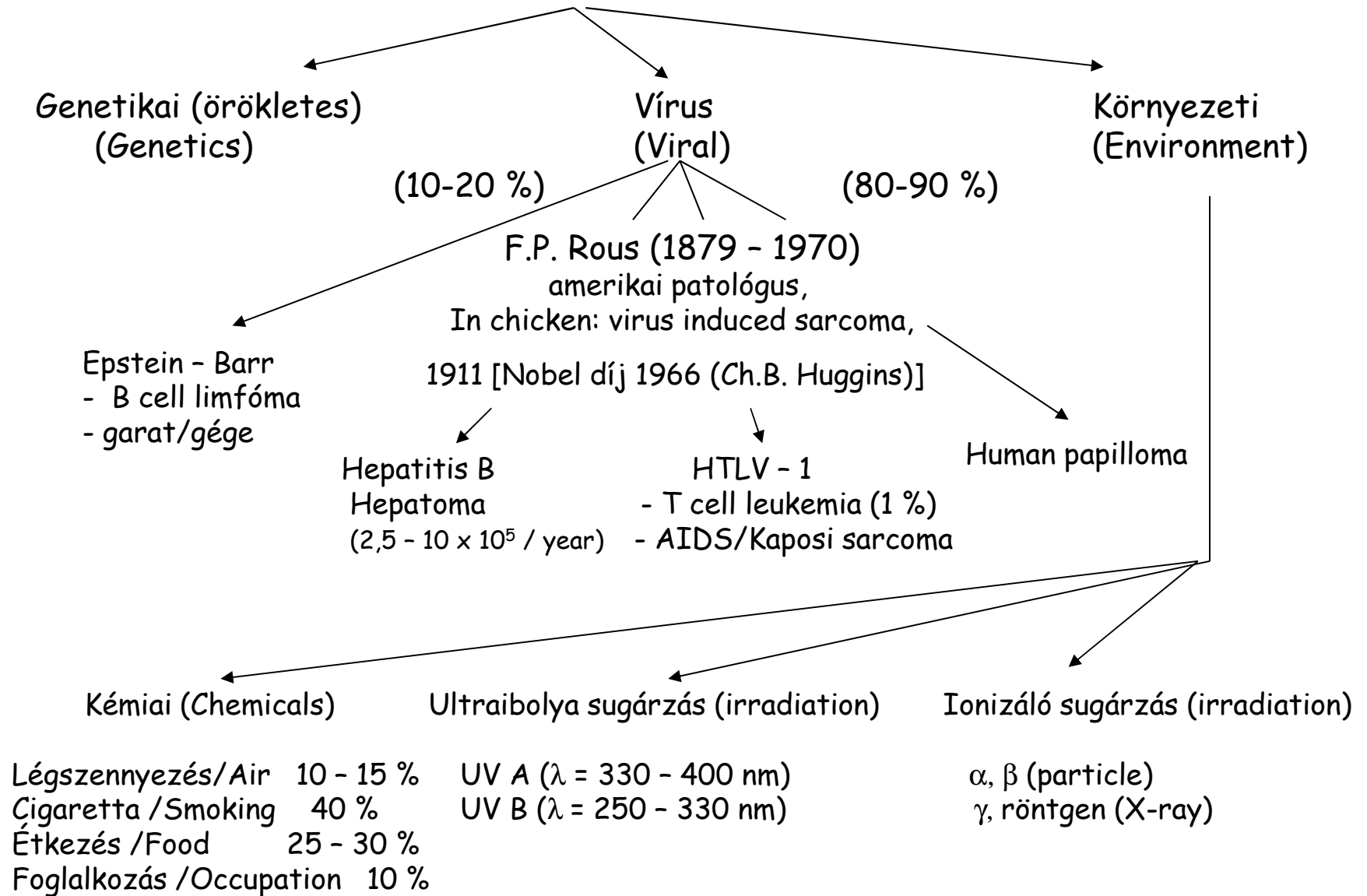
ONS=Other nervous system.  
 Source: American Cancer Society, 2009.

# Estimated US Cancer Cases\*



\*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.  
 Source: American Cancer Society, 2009.

# Tumorok keletkezésének okai/Origins

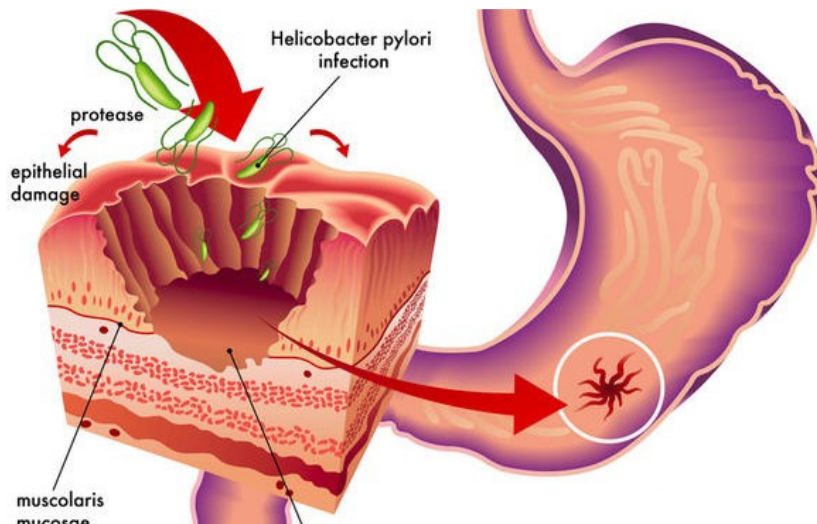


# The stomach bacterium *Helicobacter pylori* changes the activity of genes in gastric cells



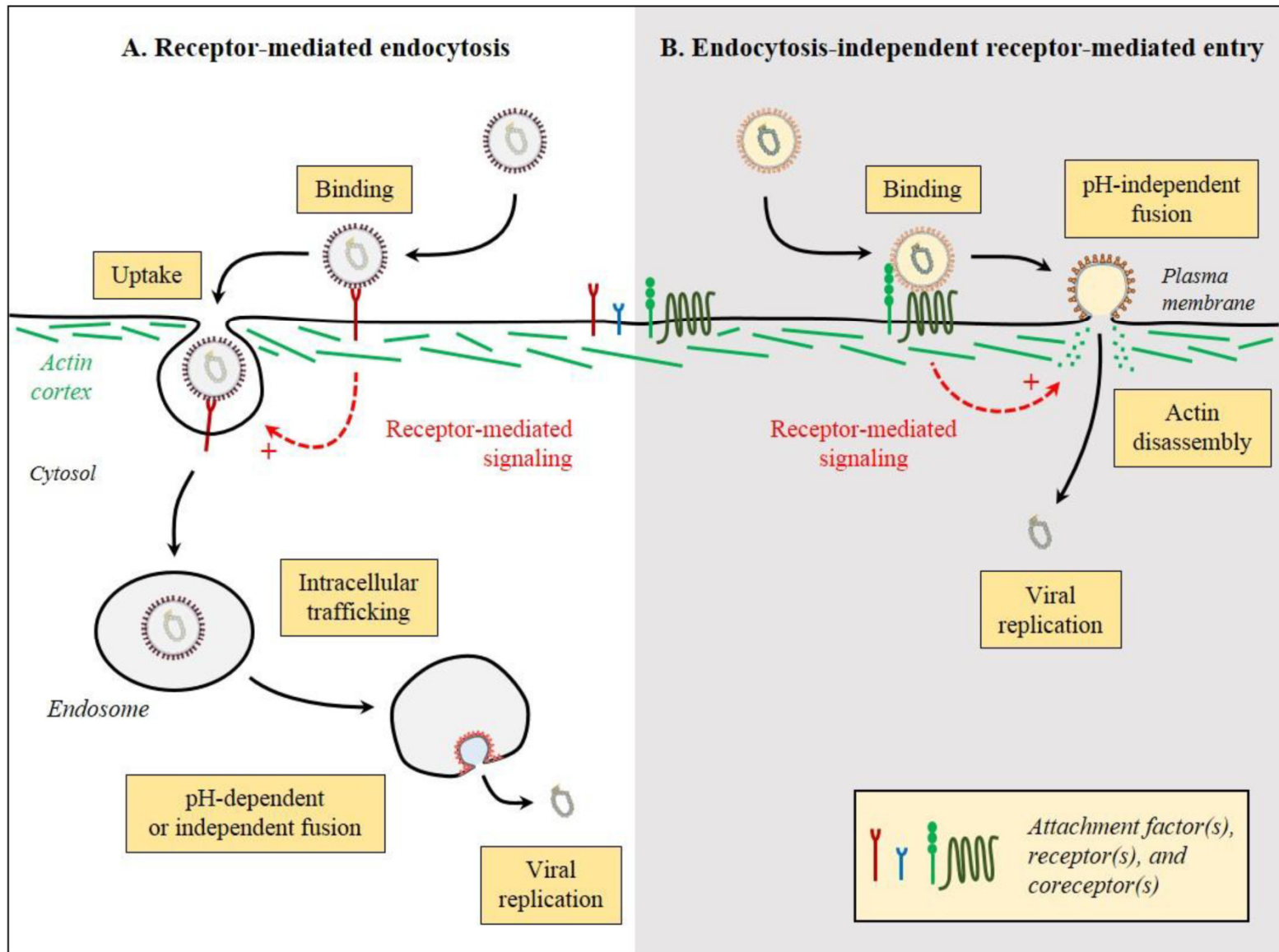
© MPI f. Infection Biology  
<https://www.mpg.de/9264796/helicobacter-pylori-fingerprint-gastric-cancer>

P. Hawtin, University of Southampton/  
Science Photo Library  
Oncology in Practice p.22, 3/1994

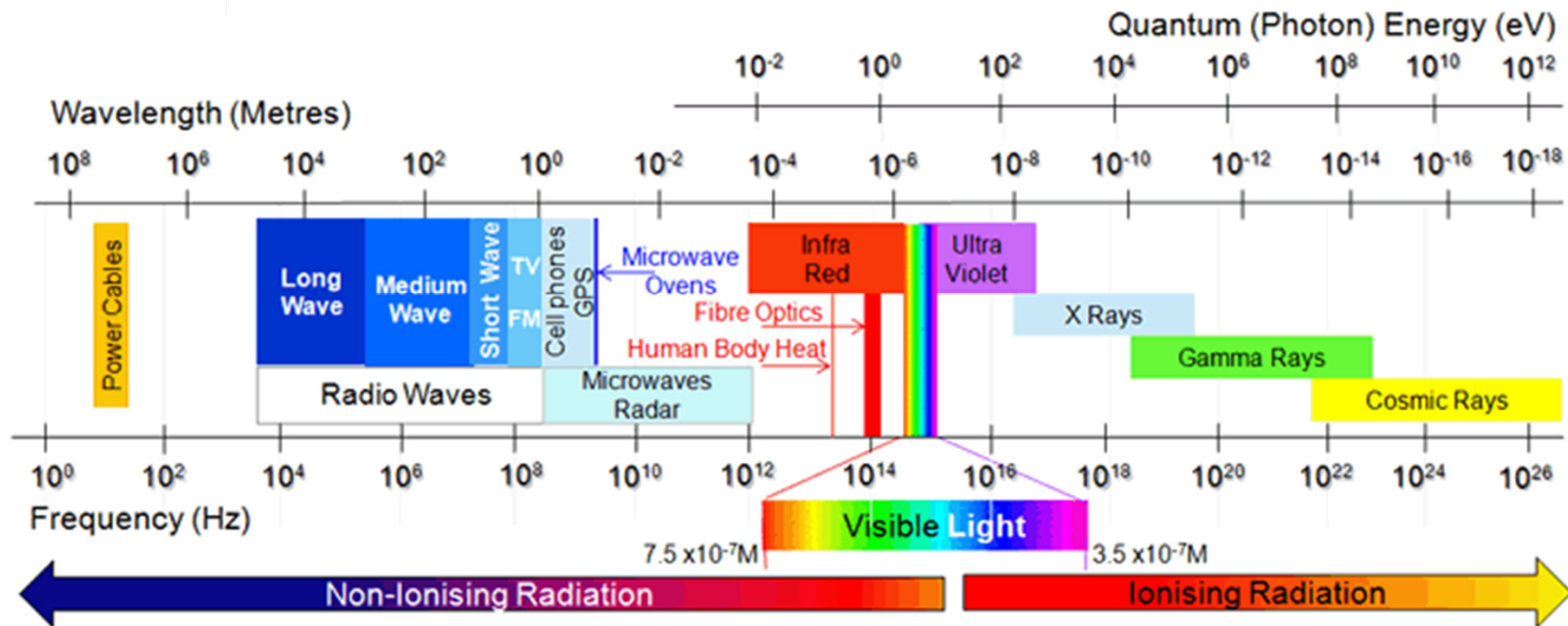
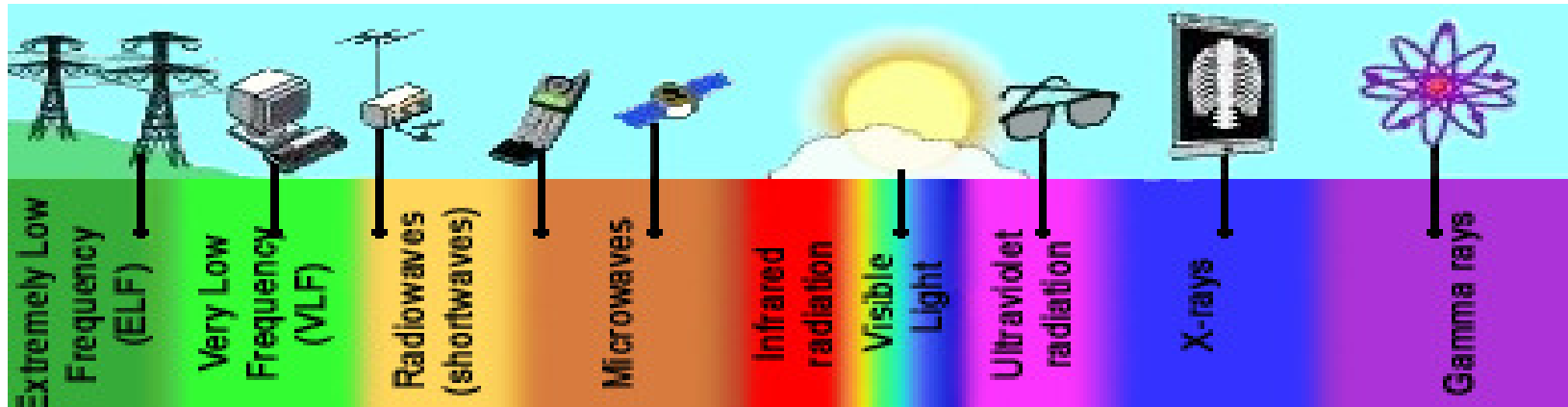


Gastric ulcer

# Viral entry into cells



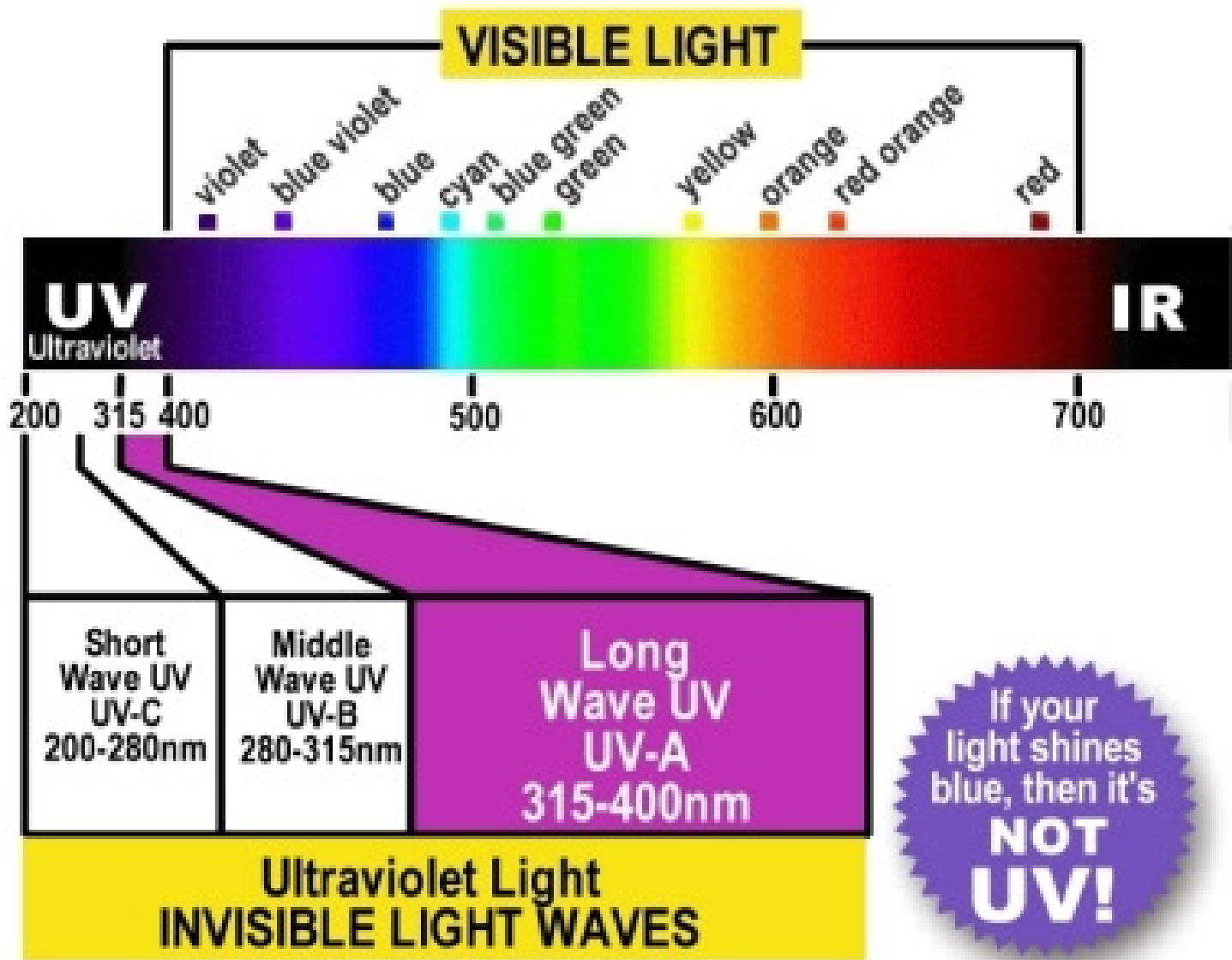
# Electromagnetic radiation spectrum



<http://www.astrosurf.com/luxorion/qs1-em-radiation.htm>

<http://www.mpoweruk.com/radio.htm>

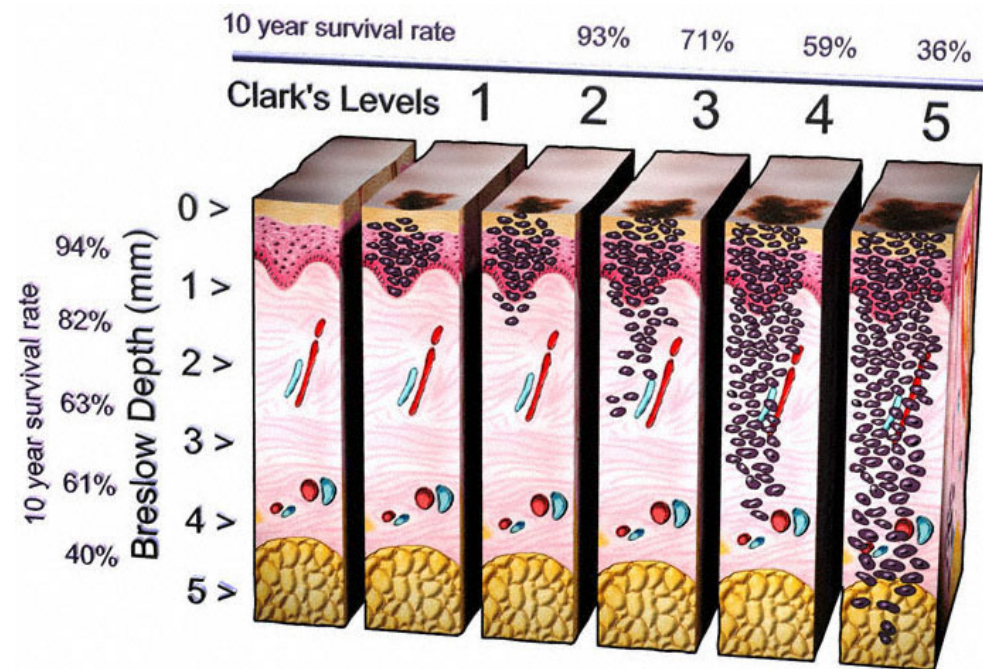




# Malignus melanoma

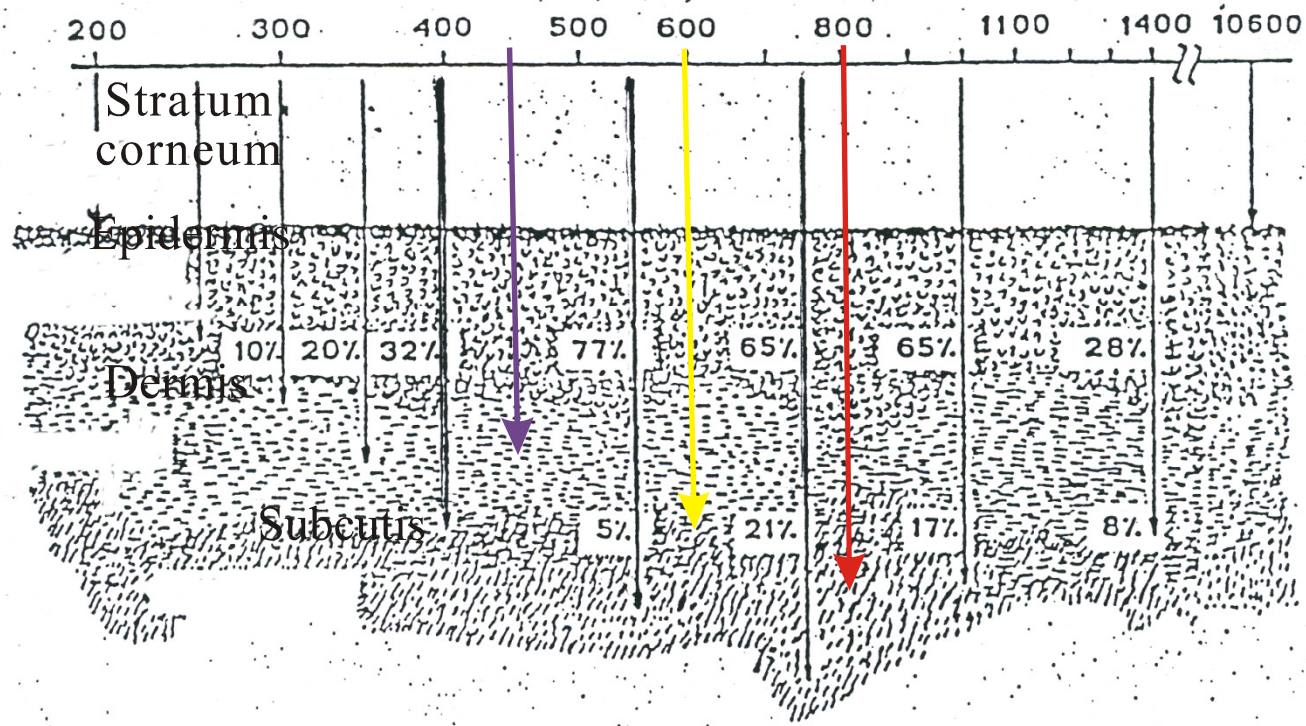


Kings College School of Medicine,  
Department of Surgery,  
Science Photo Library



2001 Image by Med-Art ~ <http://www.med-ars.it>

## A fény behatolási mélysége a bőrbe In depth penetration of light into the skin

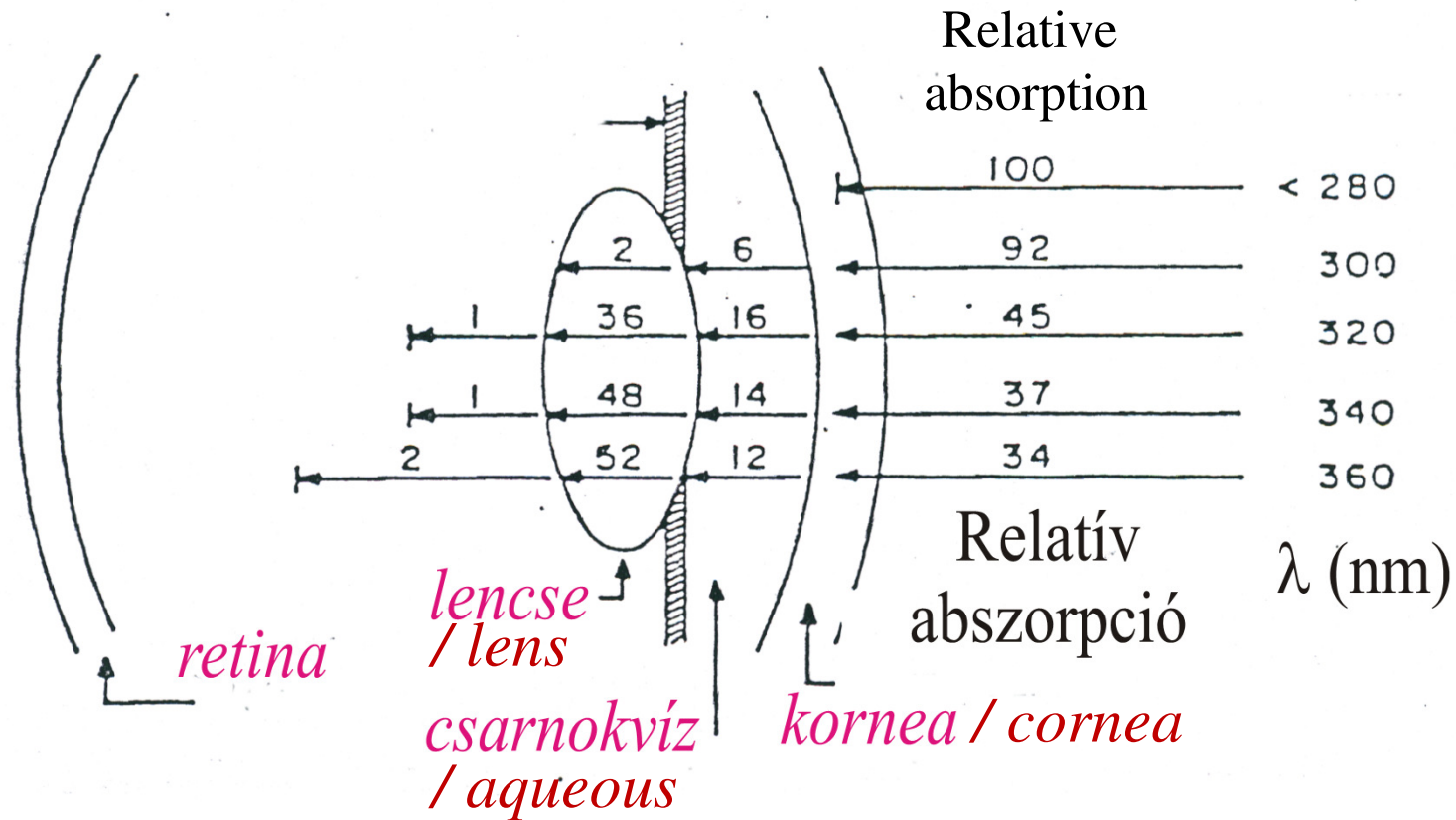


-Hullámhosszfüggő / Wavelength dependence

-A legnagyobb a vörös tartományban / Most pronounced in the range of red

# A fény behatolási mélysége a szemben

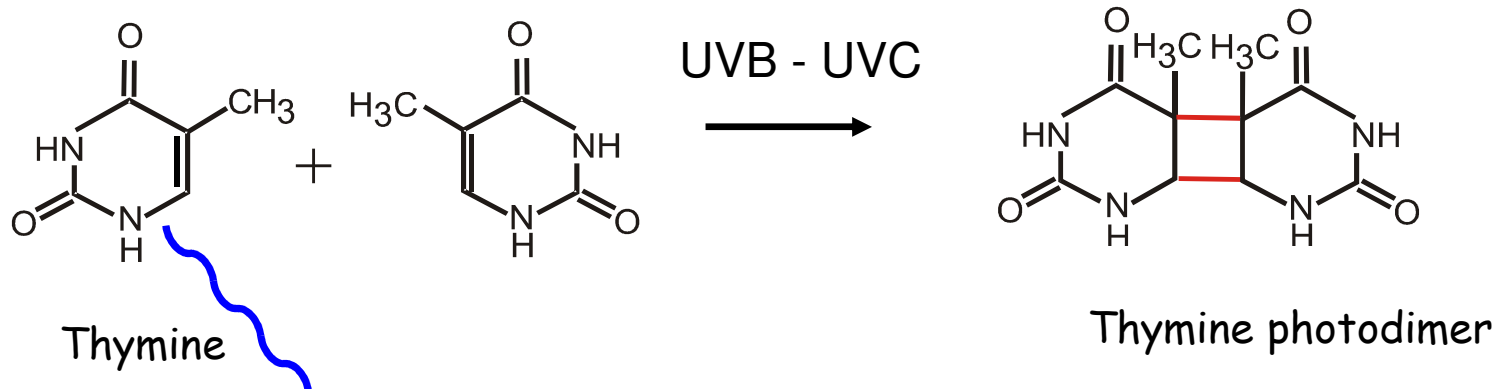
## In depth penetration of light into the eyeball



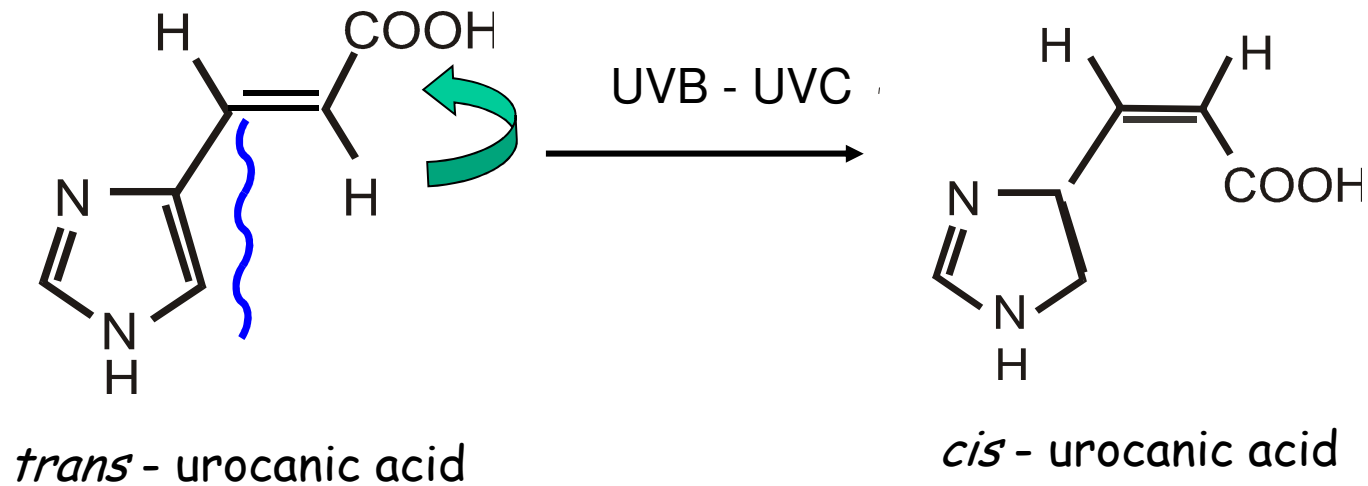
- Wavelength dependence

# Direct photochemical reaction

Cycloaddition - e.g. formation of pyrimidine dimers in the DNA



Isomerization - e.g. urocanic acid *trans* (from L-His) to *cis*



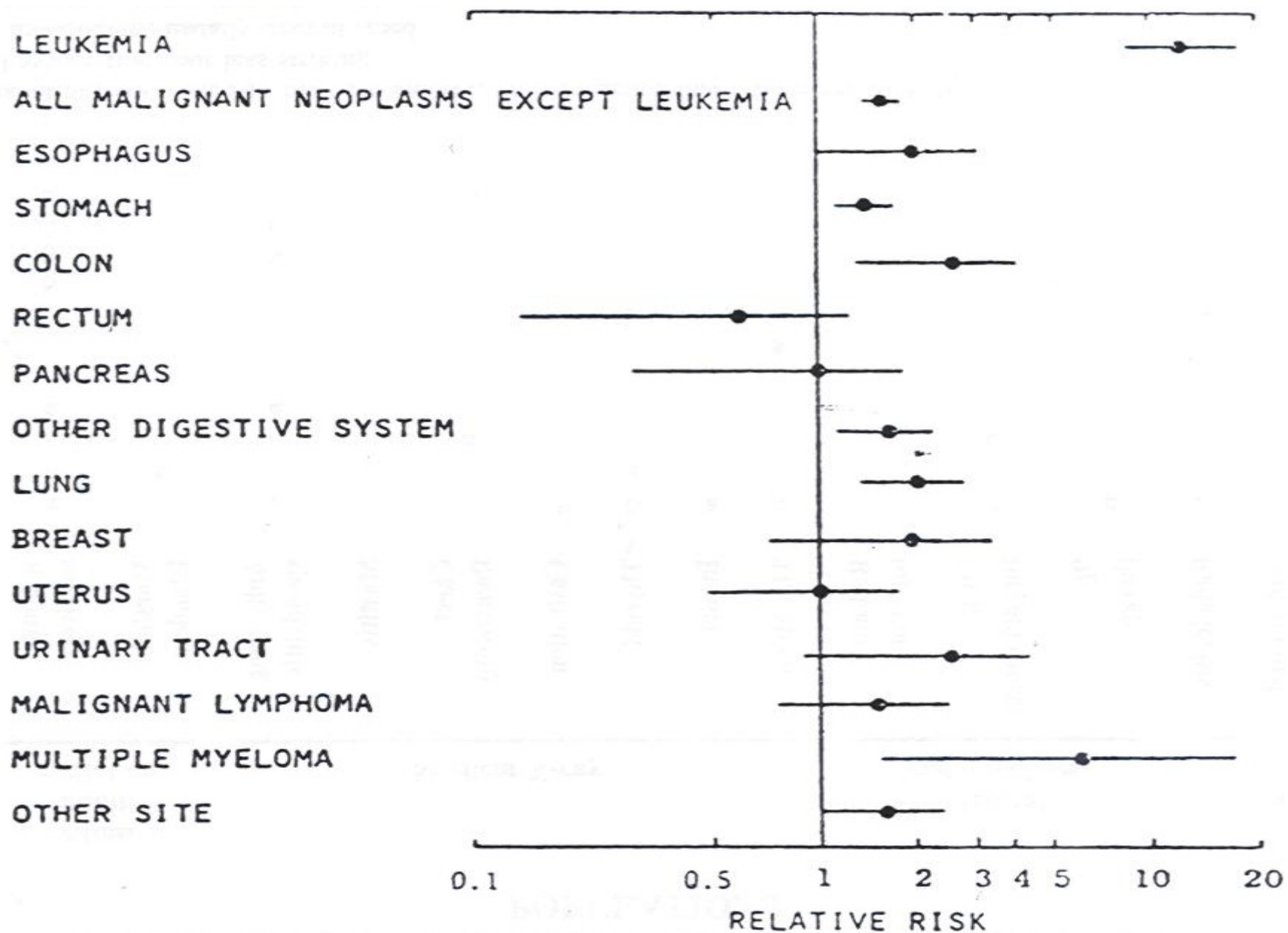


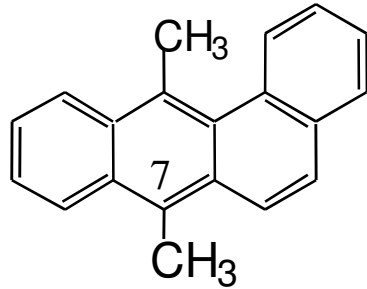
FIGURE 3. Relative risk and 90% confidence intervals for specific cancer sites, 1950 to 1978, 200 + rads vs. 0 rad. (From Kato, H. and Schull, W. J., *Radiat. Res.*, 90, 395, 1982. With permission.)

## CANCERS ASSOCIATED WITH IRRADIATION OF PARTICULAR POPULATIONS

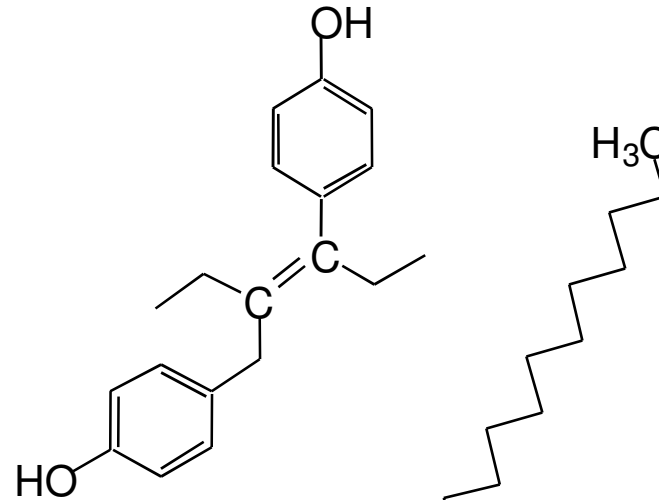
Type of cancer	Atom bomb radiation		Medical X-ray							Medical radionuclides			Occupational radiation		
	A-bomb survivors	Marshal Islanders	Ankylosing spondylitis	Mastitis	Chest fluoroscopy	Castration	Thyroid	In utero	Thoratrast	Radium injections	<sup>131</sup> I for thyroid cancer	<sup>32</sup> P therapy	Radiologists	Radium dial painters	Uranium miners
Leukemia	a		a			b	b	a	a		c	c	a		
Thyroid	a	b					a								
Breast	a			a	a										
Lung	a		a												a
Bone										a				a	
Liver									a						
Skin							b						a		
Lymphoma	b												b		
Esophagus	b		b												
Stomach	b		b												
Bladder	b														
Colon						b								c	

- <sup>a</sup> Strong association, confirmed in multiple studies, with evidence that risk increases with dose.
- <sup>b</sup> Meaningful association, but less striking.
- <sup>c</sup> Suggestive association, usually unconfirmed.

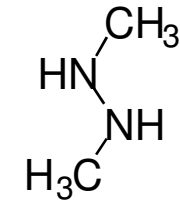
# Experimentális karcinogének/Experimental carcinogens



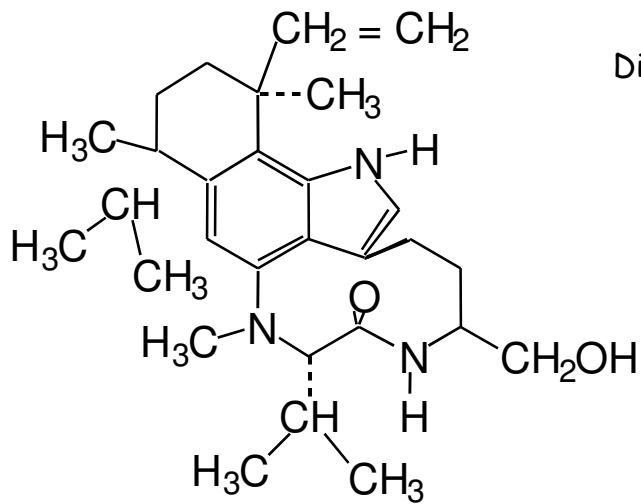
7,12-Dimethylbenz[a]anthracene (DMBA)



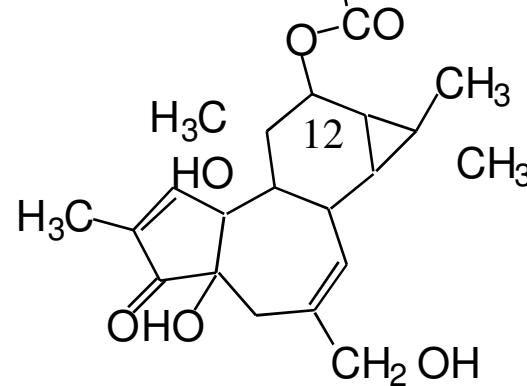
Diethylstilbestrol (DES)



1,2-Dimethylhydrazine (DMH)



Teleocidin B

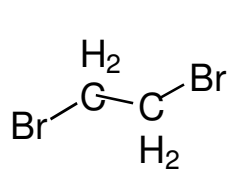


12-*O*-Tetradecanoylphorbol-13-acetate (TPA)

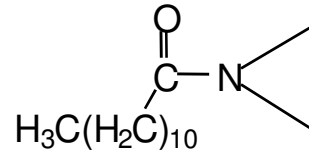


# Karcinogének/carcinogens (közvetlen hatás/direct effect)

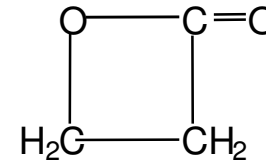
## Alkilező vegyületek/alkylating compounds



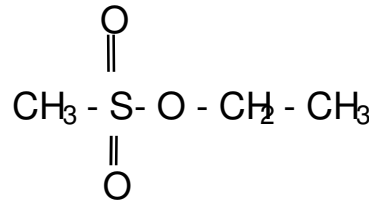
1,2-Dibromoethane,  
ethylene dibromide



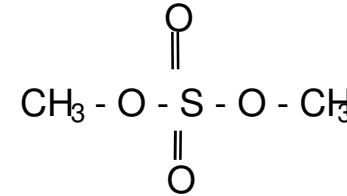
N-stearoyl ethyleneimine



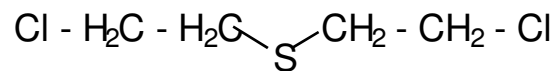
$\beta$ -Propiolactone



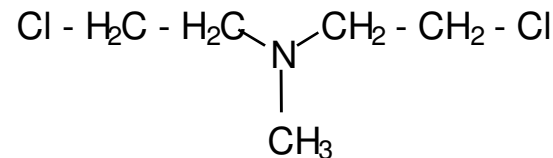
Methanesulfonic acid ethyl ester



Dimethyl sulfate



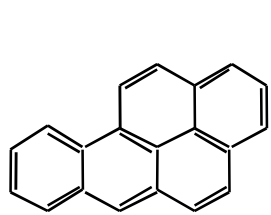
bis- $\beta$ -chloroethyl sulfide  
„Sulfur mustard“



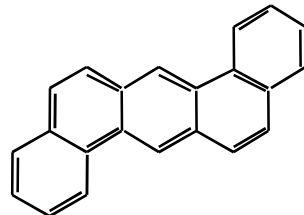
Bis (2-chloroethyl) amine  
„N-mustard“

# Karcinogének/carcinogens (közvetett hatás/indirect effect)

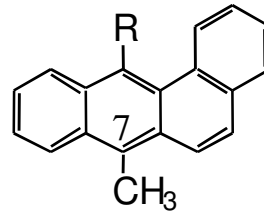
Hydrocarbons (polycyclic arenes) Sir Parcival POTT, 1775  
YAMAGIVA et al., 1915



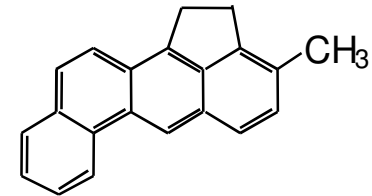
Benzo[a]pyrene



Dibenz[a,h]anthracene  
(animal)

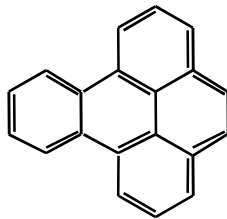


R=H, 7-metil-benz[a]antracén  
R=CH<sub>3</sub>, 7,12-dimetil-benz[a]antracén

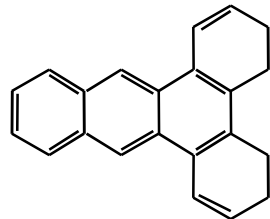


3-Methylcholanthren

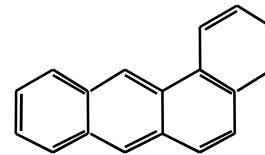
## Gyenge/nem karcinogén (weak/non-carcinogenic compounds)



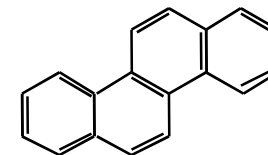
Benzo[e]pyrene



Dibenz[a,c]anthracene



Benz[a]anthracene



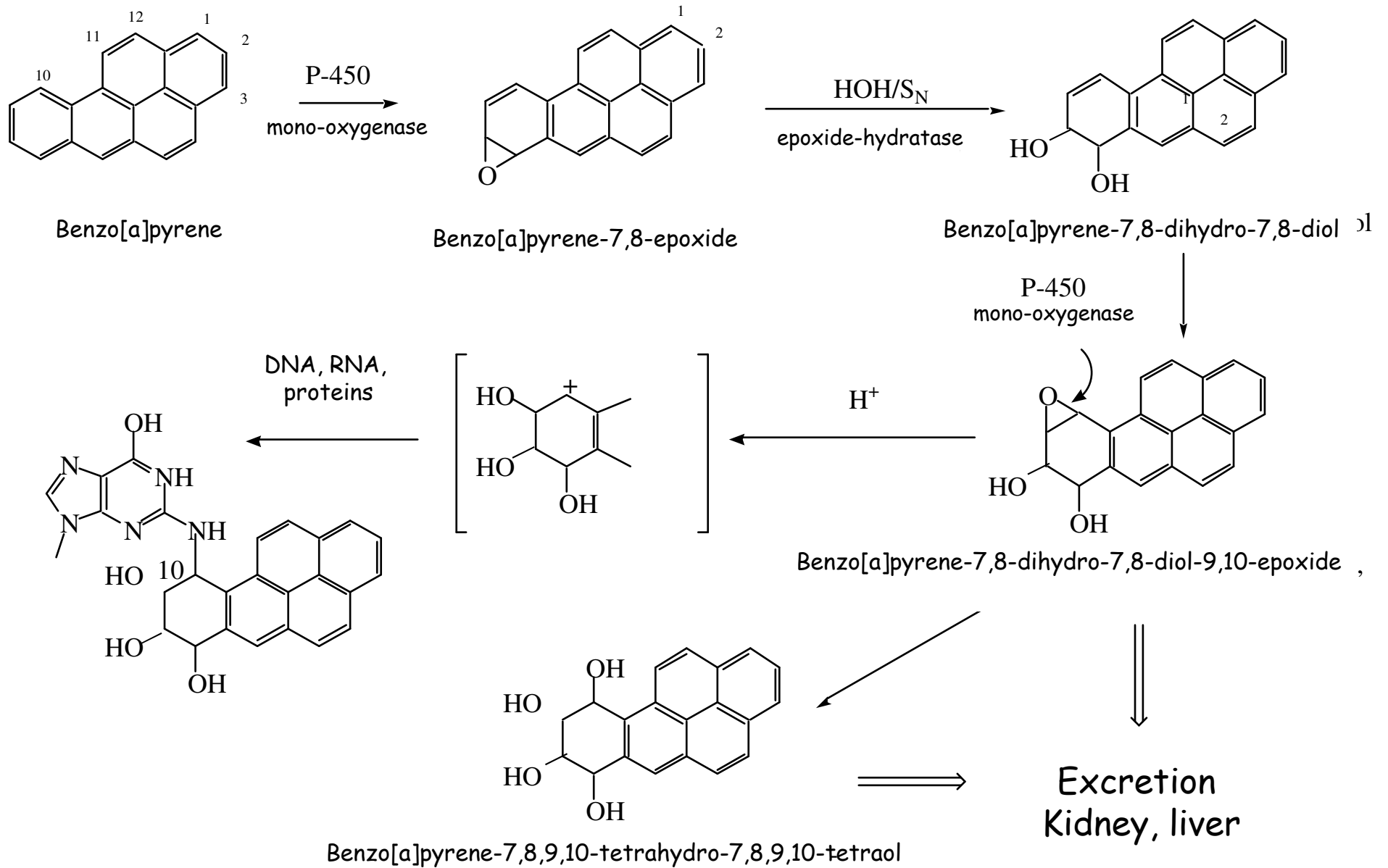
Crisen

### Forrás/source:

nem teljes oxidáció (kőszén, cigaretta, benzin)/incomplete oxidation (coal, cigarette, fuel)

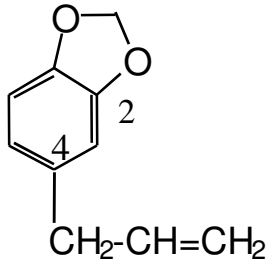


# Mutation induced by aromatic hydrocarbons

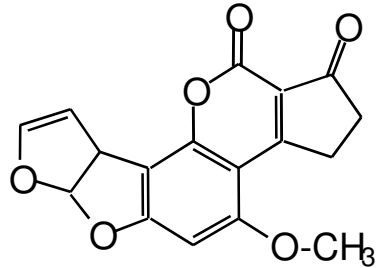


# Karcinogének/carcinogens (közvetett hatás/indirect effect)

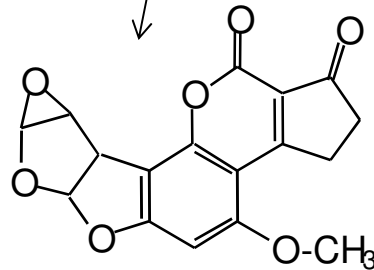
## Gyűrűs éterek/cyclic ethers



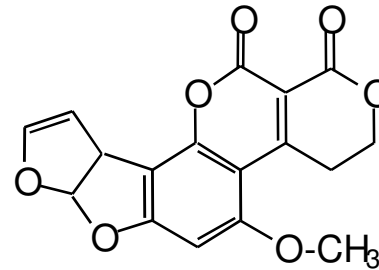
5-(Prop-2-en-1-yl)-2H-1,3-benzodioxole  
(safrole)



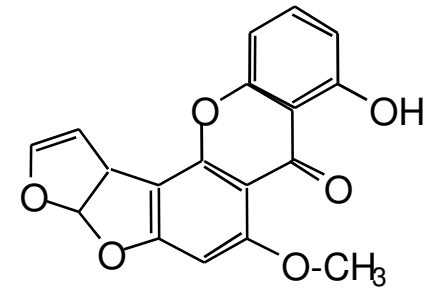
aflatoxin B1,  
Aspergillus flavus  
[20 ppb, FDA]



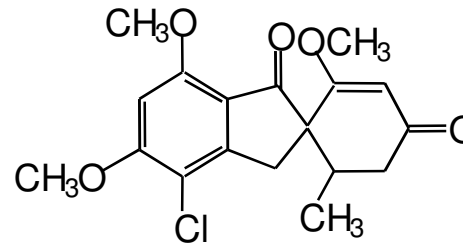
2, 3-Epoxyaflatoxin B1



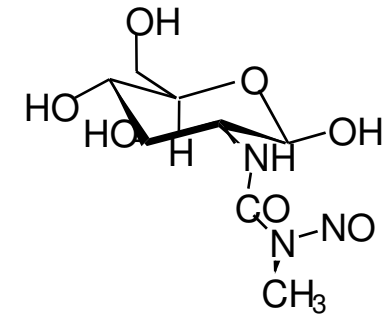
aflatoxin G1



sterigmatocitin



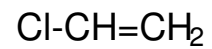
griseofulvin



streptozotocin

# Karcinogének/carcinogens (közvetett hatás/indirect effect)

Egyéb vegyületek/other compounds

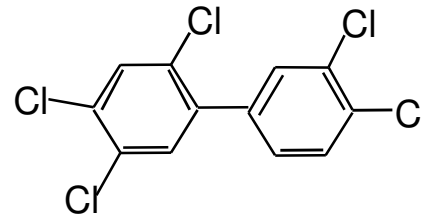


Vinyl chloride

As, Be, Cr, Cd, Ni  
salts

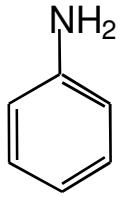
Asbestos

Co/Cr alloy

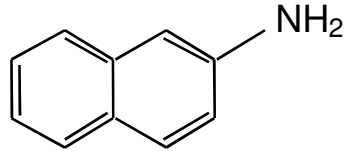


Polychlorinated biphenyl  
(PCB)

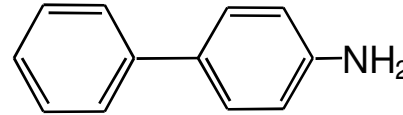
# Karcinogének/carcinogens (közvetett hatás/indirect effect)



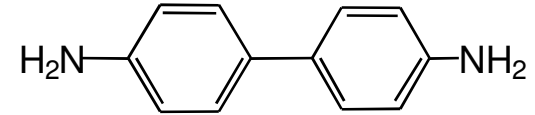
aniline  
(hólyagrák,  
Bladder cancer)



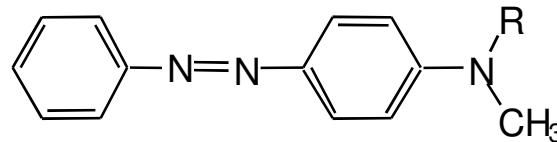
$\beta$ -naphthylamine  
(but  $\alpha$ -naphthylamine not)



4-aminobiphenyl

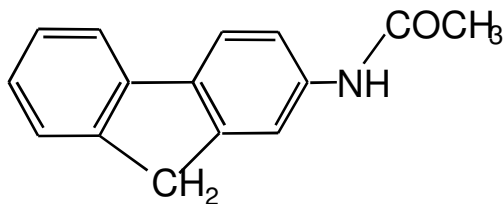


benzidine

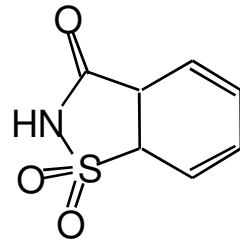


R = CH<sub>3</sub> 4-dimethylamino-azo-benzol [butter]  
R = H 4-methylamino-azo-benzol

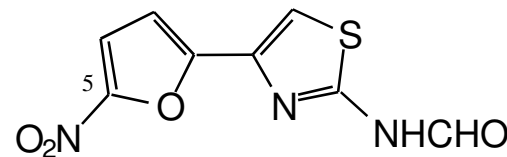
## Aromatic amides



2-acetylaminofluorene

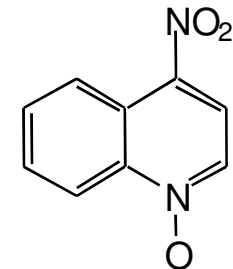
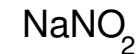


Saccharine (1977)



N-[4-(5-nitro-2-furyl)-2-thiazolil] formamide

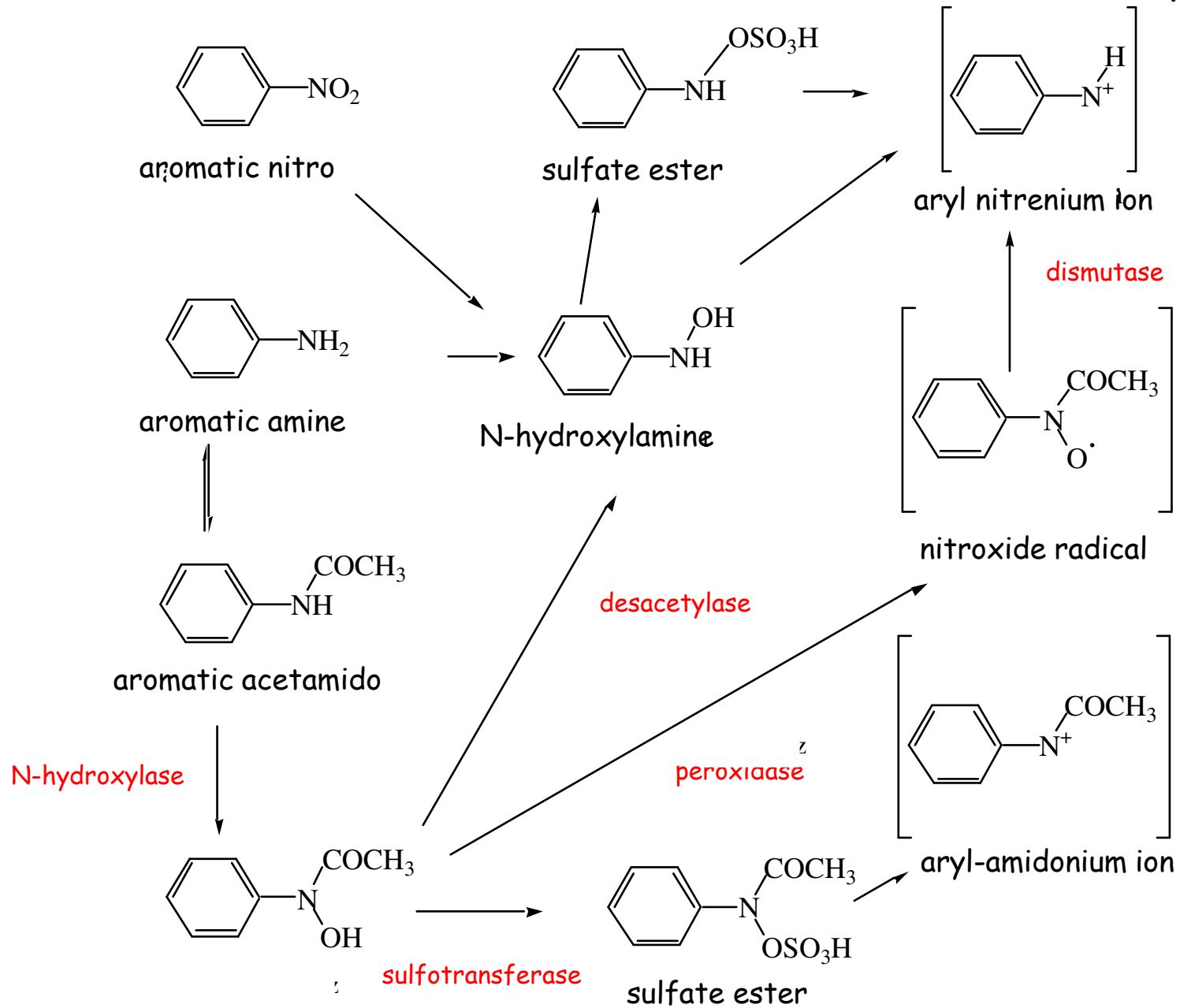
## Nitro compounds



4-nitrokinolin-1-oxide

Source: pigment industry, food additives

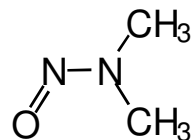
# Mechanism of action of aromatic amino/amido/nitro compounds



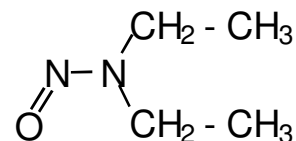


# Agents for incorporation of NO function

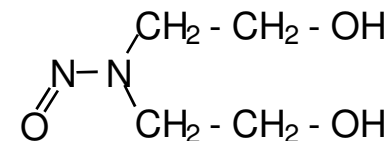
(studied cc. 300 compounds, 1994 > 90 % carcinogenic)



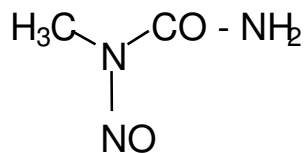
N-nitroso-dimethylamine  
(1956, beer, herbicide)



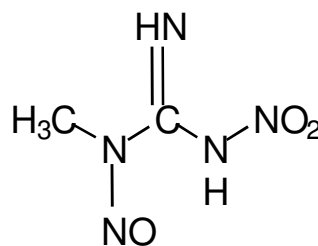
N-nitroso-diethylamine  
(whisky)



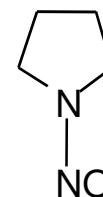
N-nitroso-dietanolamine  
(shampoo, hairdresser)



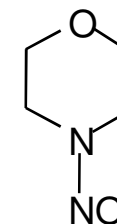
N-methyl-N-nitrosourea (MNU)  
(in the intestine)



N-methyl,N'-nitro,N-nitroso-  
guanidin



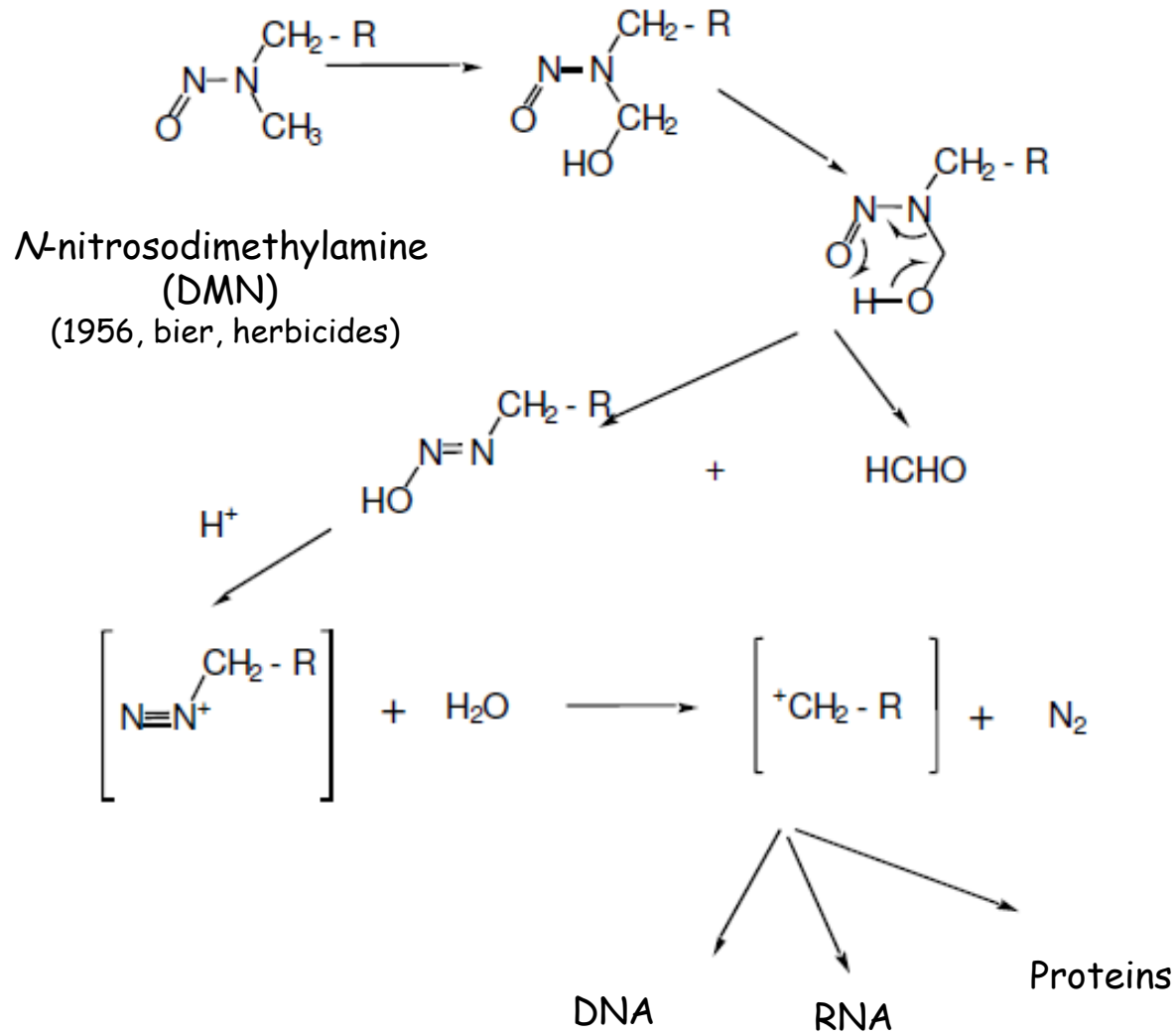
N-nitroso-pyrrolidine  
(smoked ham)



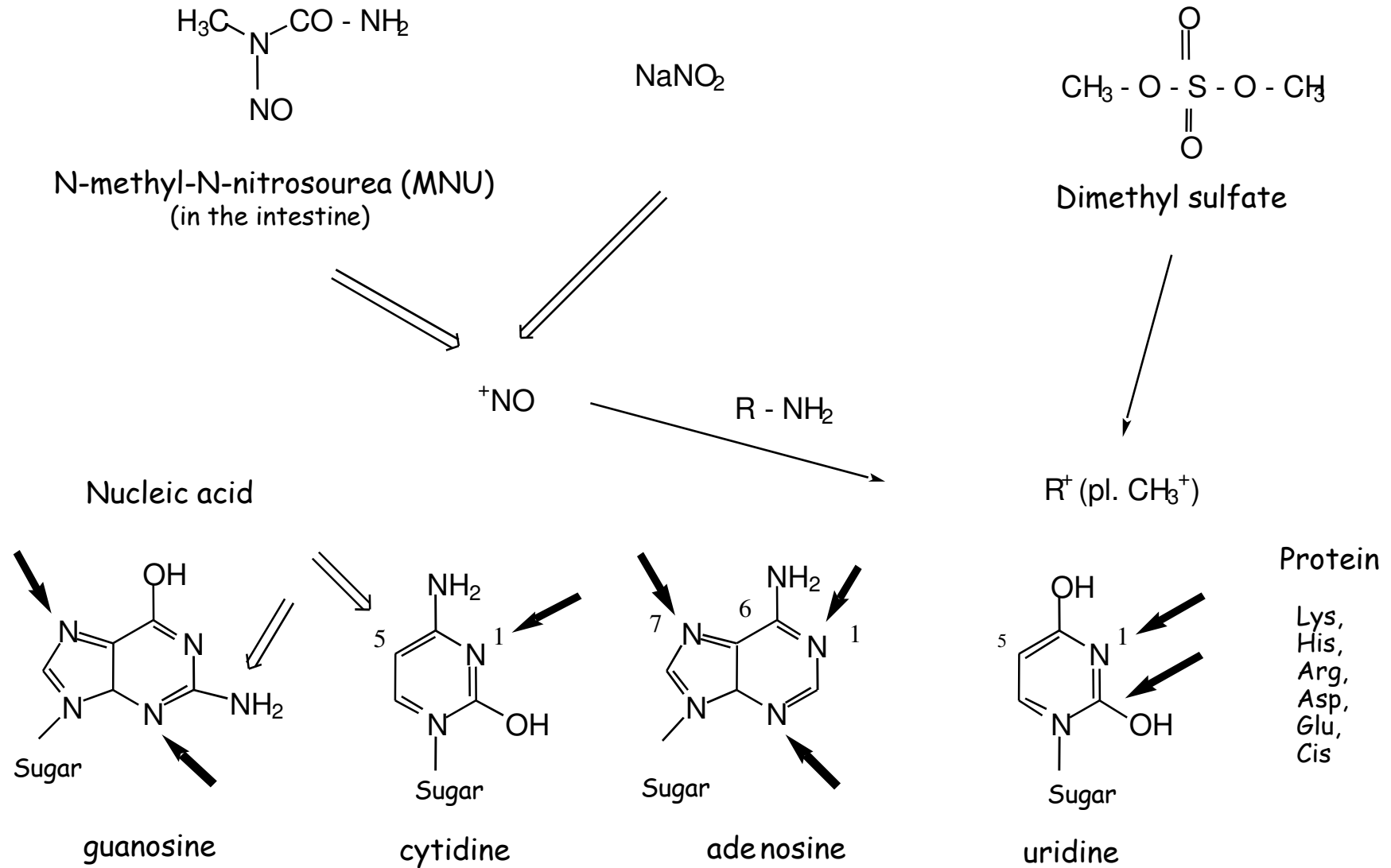
N-nitroso-morpholine

Source: tanning, upholstery, rubber industry

# Metabolic activation of dialkyl N-nitrosoamin



# Incorporation of the NO/alkyl group



## European code against cancer

Certain cancers may be avoided

- Do not smoke. Smokers, stop as quickly as possible and do not smoke in the presence of others.
- Moderate your consumption of alcoholic drinks – beers, wines, and spirits.
- Avoid excessive exposure to the sun.
- Follow health and safety instructions, especially at work when producing, handling, or using any substances that may cause cancer.
- Frequently eat fresh fruit and vegetables and cereals with high fibre content
- Avoid becoming overweight, and limit your intake of fatty food.

More cancers will be cured  
if detected early

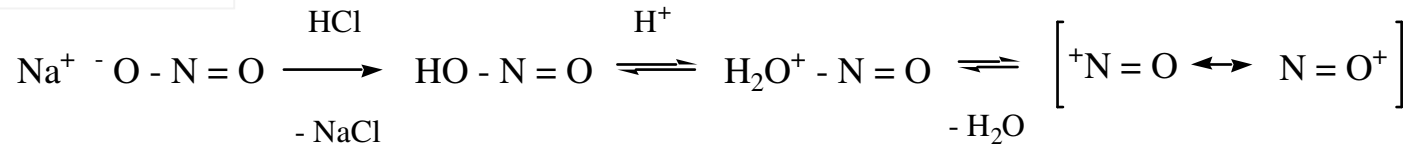
- See a doctor if you notice a lump, a change in amole, or abnormal bleeding.
- See a doctor if you have persistent problems, such as a persistent cough, persistent hoarseness, a change in bowel habits, or an unexplained weight loss.

For women

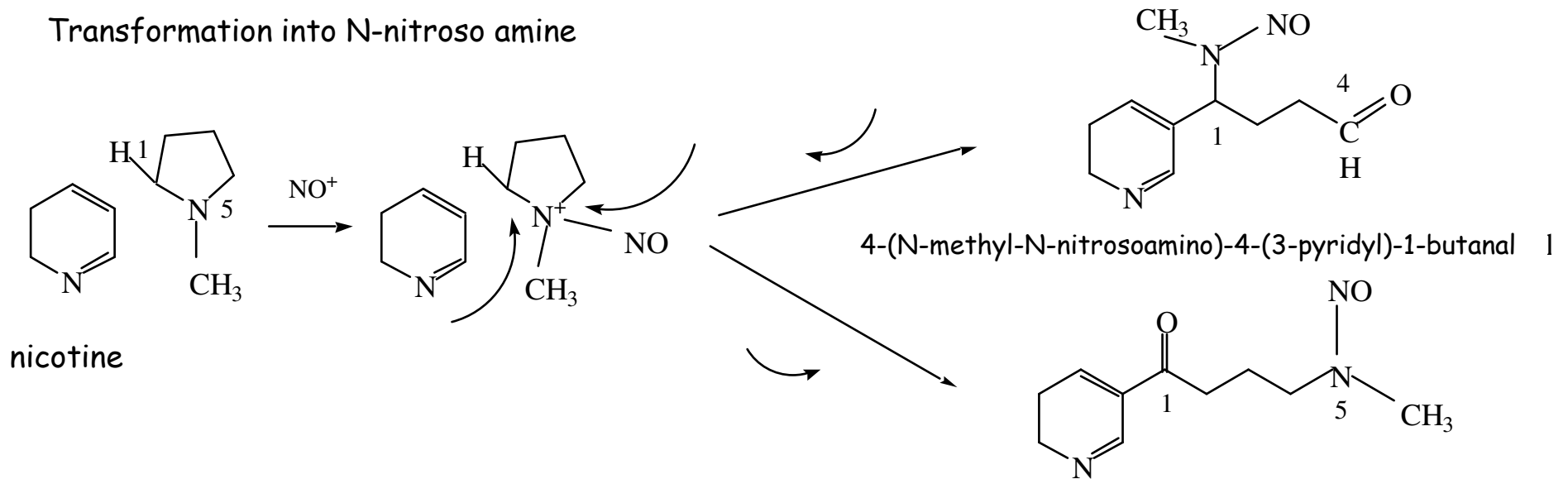
- Have a cervical smear regularly.
- Check your breast regularly, and if possible undergo mammography at regular at regular intervals above the age 50.

# Interpretation of carcinogenicity of nicotine

## Formation of NO function



## Transformation into N-nitroso amine



## Reaction of N-nitroso amine with nucleophiles

