CANCER EPIDEMIOLOGY

Cancer is on the 2nd place of the causes of death in most especially developed countries. This "epidemic" started around the half of twenties century when first tumours caught attention of doctors and epidemiologists because of higher frequency of death due to cancer.

The paleopathological analyses of skeleton remains in central European buried places during the ceramic volute era near Stuttgart, Germany, show a total proportion of over 10% of traces indicate the presence of tumours in the available complete skeletons. The life expectancy in that time was much lower than now, so if the start point of increasing the specific type of cancer is about 55 years, in period with life expectancy of 30 years was a small probability of such tumours.

Still we have lack information concerning the risk factors of most tumours. One of the main risk factors is **age.** The frequency of most cancers is increasing with increasing age. If we would like to compare incidence of tumours in different population, we can compare either mortality/incidence in specific age groups (e.g. 35 – 64 years, *untimely death*) or we can compare **standardised data**. Mostly is used standardisation to worlds' age, which allows us to compare incidence/mortality in any population.

The most precise data concerning the incidence/prevalence/mortality of tumours are available from **cancer registers**. Unfortunately in most countries cancer register is not centralised and blanket, there are several registers in smaller regions. Anyway information from all registers is available in **IARC** (International Agency for Research on Cancer). Cancer registries are the source of information on incidence of cancer in defined populations, as well as on outcome, in terms of survival. They also provide a framework for conducting epidemiological studies into the cause of different cancers. In many parts of the world, cancer registries provide the only available information on the nature and evolution of the local cancer problem. The comparative value of the statistics, which cancer registries produce, depends upon the use of common methods, and definitions, so that international collaboration in this area has a very important role.

One of the most frequent tumours in males was **lung cancer**, especially in developed countries. It was just this tumour, which attracted the interest of epidemiologists. Already in 1938 R. Pearl calculated from medcare insurance data that the life expectation in smokers was much shorter than in non-smokers. Subsequently Ochsner and de Bakey published a paper dealing with the high proportion of smokers among lung cancer patients admitted to their

clinic. Doll and Hill first published really serious studies trying to establish the actual relation between lung cancer and smoking.

Smoking is generally considered as the most significant risk factor in lung cancer. There is a clear dose-response relationship between lung cancer risk and the number of cigarettes smoked per day, the degree of inhalation, and the age at initiation of smoking.

Passive exposure to tobacco smoke (*ETS- Environmental tobacco smoke*) is also a well-known risk factor for lung cancer. It is estimated that exposure to ETS increases risk by 15-20%. It seems that exposure to ETS increases the risk of squamous cell carcinoma more than adenocarcinoma and small-cell carcinoma.

Other factors known to increase risk of lung cancer are *occupational exposure* to **asbestos**, some **metals** (e.g. nickel, arsenic, and cadmium), **radon**, and **ionising radiation**. However, their contribution to the number of cases occurring in the population is small. *Diets* high in vegetables and fruits (especially green vegetables, cruciferous, and carrots) may provide some modest protection.

The often discussed air pollution effects are according to current experience merely of a supportive character as these effects alone are unable to induce lung cancer except for exposures of the above risk factors. The individual epidemiological studies assessing the potential origin of lung cancer vary in risk factors estimate, however, never exceed 5%.

There are several studies that confirm the role of genes in cancer epidemiology and also the lung cancer is one of those with positive association with some gene mutation. Some of these mutations are in positive correlations with protective effect of isothiocyanates; it means that there is an indirect effect of genes mutation and cancer occurrence.

Worldwide**, breast cancer** is the most frequent cancer not only in women. The highest incidence rates are observed in North America, whereas the lowest risk of breast cancer is observed in Asia and Africa. There are several factors, both endo- and exogenous, which are known to affect the risk of breast cancer in the population.

These include *lifestyle factors* (i.e. childbearing, type of diet and obesity), *hormonal status* (influencing age at menarche and menstrual cycle, and determined by endogenous hormones), *anthropometric characteristics, radiation, and genetic predisposition.*

There have been several studies showing a relationship between *reproductive factors* and the risk of breast cancer. It has been shown that risk increases with decreasing age at menarche, increasing age at first pregnancy, increasing age at menopause, and low parity.

Increased *weight* (measured by body mass index – BMI) **decreases** breast cancer risk **before** menopause, and **increases** risk **after** menopause.

Some studies show no significant relationship between breast cancer risk and consumption of *meat and dairy products*. The association with *fat consumption*, as well as with consumption *of fruits and vegetables*, is rather weak.

The role of *breast-feeding* in reducing risk has been suspected for almost a century. The association is not strong, but some minor reduction of risk possibly exists.

Alcohol consumption increases the risk of breast cancer. For each additional 10 grams of alcohol per day, the risk increases by approximately 10%.

The role of past *oral contraceptive* (OC) use in the development of breast cancer is unclear. Women with a *family history* of breast cancer are at increased risk of the disease. It was estimated, based on the 52 epidemiological studies, that having one first-degree relative with breast cancer increases risk by about 80%, two first-degree relatives increases risk approximately 3-fold, and in those with 3 or more first-degree relatives the risk is elevated 4 fold. About 10% of breast cancers in developed countries may be due to genetic predisposition. The lifetime risks of developing breast cancer for BRCA1 and BRCA2 (breast cancer susceptibility genes) mutation carriers are 80-85%.

In advanced developed countries there is another type of cancer of big concern – **colorectal cancer**. This cancer is relatively rare in most developing countries. Based on the latest epidemiological research, there is a lot of unclearness concerning the risk factors of this type of cancer. Nutrition is playing definitely important role in developing of colorectal cancer, but on both sides – as a risk and also protective factor. Probably the most important exogenous risk factor is obesity and lack of physical activity. The most important endogenous risk factor is polyposis of the colon.

Colorectal cancer is preventable through regular testing, and through the removal of polyps (adenomas) in the colon, which often grow into cancerous tumours.

Incidence of **cervical cancer** is connected with the pathogenic role of infections. For many years is strongly associated with infection by oncogenic forms of human papillomavirus (HPV). Although most women are able to clear an HPV infection, some develop persistent infections that may lead to cancer. The determinants of persistent infection are largely unknown.

Another challenge of our time are the infections and cancer. Some of these stories are well-known like HPV (Human papillomavirus), hepatitis B & C or Helicobacter pylori. But still even in these “old” stories there is a lot to do. Which type of HPV is the most important and

which other types of HPV can contribute to any other type of cancer – and which type of cancer could be connected with chronic infection of HPV?
To find new associations of cancers – hormonal, genetic or infections – is still possible for those who are interested in searching new connections between known factors or would like to explain some unclearness they meat. Epidemiological features of infection-associated cancers (but not only these types) could be unusual age distribution or social class associations, clustering or excess in people prone to infections.

Figure 7b: Mortality of cervical cancer (female) in selected countries.

In many types of tumours and in many countries we can see increasing tendency in incidence but rather stable figures of mortality during the last third of twenty century. The main role on that field played and still plays **screening**. Screening has important ethical differences from clinical practice as the health service is targeting apparently healthy people, offering to help individuals to make better informed choices about their health. However, there are risks involved and it is important that people have realistic expectations of what a screening programme can deliver.

Screening means the use of tests or examinations on asymptomatic individuals, to identify disease at early stage (before it becomes clinically apparent). It is essential, if screening is to be of any value, that this results in an improvement in outcome (lowers the risk of death, or complications of treatment). Screening is suitable in tumours with high frequency.

Figure 8: Incidence of stomach cancer (male) in selected countries.

Screening has to be:

1. Cheap
2. Available (for everybody)
3. Easy (method)
4. Method with high specificity (as high as possible)
5. Method with high sensitivity (as high as possible)
6. Able to detect early stage of tumour

Not all tumours are suitable for screening; from the rules presented above there is only limited number of tumours where we are able to apply screening. To be cheap, it is necessary to apply

screening method on tumours with high frequency in population and from the age when the frequency increasing accelerate.

From that point of view in most developed countries is screening used to find early stage of colorectal cancer (*faecal occult blood testing FOBT)* and breast cancer (mammography), in some countries (e.g. Scandinavian) also cervical cancer by regular sampling cytology (PAP-smears).

Figure 9: Incidence of stomach cancer (female) in selected countries.

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Although we have lack of information concerning the risk factors of cancers and although it seems that the most important risk factors should be endogenous factors (e.g. genetic factors) and our life style, every year is published a list of agents, suspected being carcinogenic, divided in four groups according to the latest knowledge of its dangerousness (carcinogenicity), where any substance ever tested for carcinogenicity can be find.

Groups of substances:

Group 1: The agent (mixture) is carcinogenic to humans. The exposure circumstances entail exposures that are carcinogenic to humans.

This category is used when there is sufficient evidence of carcinogenicity in humans. Exceptionally, an agent (mixture) may be placed in this category when evidence of carcinogenicity in humans is less than sufficient but there is sufficient evidence of carcinogenicity in experimental animals and strong evidence in exposed humans that he agent (mixture) acts through a relevant mechanism of carcinogenicity.

Figure 10: Incidence of liver cancer (male) in selected countries.

Group 2: This category includes agents, mixtures and exposure circumstances for which, at one extreme, the degree of evidence of carcinogenicity in humans is almost sufficient, as well as those for which, at the other extreme, there are no human data but for which there is evidence of carcinogenicity in experimental animals.

Figure 11: Incidence of liver cancer (female) in selected countries.

Agents, mixtures and exposure circumstances are assigned to either group 2A (probably carcinogenic to humans) or group 2B (possibly carcinogenic to humans) on the basis of epidemiological and experimental evidence of carcinogenicity and other relevant data.

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

This category is used when there is limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals. In some cases, an agent (mixture) may be classified in this category when there is inadequate evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals and strong evidence that the carcinogenesis is mediated by a mechanism that also operates in humans. Exceptionally, an agent, mixture or exposure circumstance may be classified in this category solely on the basis of limited evidence of carcinogenicity in humans.

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

This category is used for agents, mixtures and exposure circumstances for which there is limited evidence of carcinogenicity in humans and less than sufficient evidence of carcinogenicity in experimental animals. It may also be used when there is inadequate evidence of carcinogenicity in humans but there is sufficient evidence of carcinogenicity in experimental animals. In some instances, an agent, mixture or exposure circumstance for which there is inadequate evidence of carcinogenicity in humans but limited evidence of carcinogenicity in experimental animals together with supporting evidence from other relevant data may be placed in this group.

Group 3: The agent (mixture or exposure circumstance) is not classifiable as to its carcinogenicity to humans.

This category is used most commonly for agents, mixtures and exposure circumstances for which the evidence of carcinogenicity is inadequate in humans and inadequate or limited in experimental animals.

Exceptionally, agents (mixtures) for which the evidence of carcinogenicity is inadequate in humans but sufficient in experimental animals may be placed in this category when there is strong evidence that the mechanism of carcinogenicity in experimental animals does not operate in humans.

Agents, mixtures and exposure circumstances that do not fall into any other group are also placed in this category.

Group 4: The agent (mixture) is probably not carcinogenic to humans.

This category is used for agents or mixtures for which there is evidence suggesting lack of carcinogenicity in humans and in experimental animals. In some instances, agents or mixtures for which there is inadequate evidence of carcinogenicity in humans but evidence suggesting lack of carcinogenicity in experimental animals, consistently and strongly by a broad range of other relevant data, may be classified in this group.

There is a lot of unknown, a lot of uncertainty in the field of cancer epidemiology, risk factors and chance to prevent new cases, new deaths. Some cancers are avoidable (non-smoking society), some are preventable (vaccination against hepatitis B), and some infections that are known as a risk factor for cancer are treatable (H. pylori, liver flukes, schistostomiasis). In these days the best chance for many people are screening methods and research, which should find the main risk factors and a chance how to avoid them or to treat them.