age. All cases were hystologically confermed. The overall crude rate was 14,89 and the age-stanardized incidence rate (world standard) was 14,61 per 100 000. The incidence rates varied by ICCC group and age group. Age - standardized incidence rate for Leukemia was 3,87, for thyroid cancer -2,66, for CNS group was 2,59. In the structure of childhood cancer the leading places belong to the Leukemia - 23,71%, Thyroid cancer - 22,61%, CNS tumors - 17,69%, Lymphomas - 13,37%, Soft-tissue sarcomas group - 5,29%, renal tumors - 4,98%, Bone tumors - 3,04%.

The highest incidence rate of childhood cancer we observed in Gomel region (20,17).

904 POSTER

Geographical clustering of adenocarcinoma of the lung and possible determinants

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The annual mortality rates of lung cancer in Japan in 1999 were 49.8 per 100,000 for men and 13.4 for women, which had been increasing for the last few decades. Among the causes of death from cancer, lung cancer is currently the highest for men and the third for women. The discrepancy between mortality and incidence rates of lung cancer are still small in Japan. We analyzed most recent data of mortality and incidence from lung cancer.

In our prefecture, cancer registry started in 1992. Using the incidence data, we analyzed geographical distribution of cancers. As the result, we detected geographical clustering of lung cancer. The standardized incidence ratios (SIRs) of lung cancer for both genders in areas along two main rivers running through the prefecture were significantly higher than those in the rest of the prefecture (the standard population).

On the other hand, when we analyzed mortality data, the standardized mortality ratios (SMRs) of lung cancer were also significantly higher in the same areas along the rivers for both men and women. In addition, the SMR of adenocarcinoma of the lung for males in areas along one of the two rivers was significantly high. For females, the SMR of adenocarcinoma was significantly high in areas near the outlet of the same river.

What are then the determinants of the observed geographical clustering of lung cancer, particularly adenocarcinoma?

Genetic background of the population in the prefecture is homogenous. No geographical difference has been reported in social status and life styles in the prefecture. Tobacco smoking has been recognized to be as the strongest risk factor of all. In the prefecture we examined, smoking rates are very similar from area to area. Adenocarcinoma, of which mortality showed geographical clustering, is known to relate to smoking least of all the histological types of lung cancer. We hence suspect that environmental determinants specific to the areas of interest are the most plausible candidates.

We previously reported geographical distribution of heavy metals in the prefecture and its relation to mortality of some types of cancer. In the case of lung cancer, we also suspect the roles of heavy metals, because there are old mines along the river. In addition to metals, we have to take into consideration chemicals that possess endocrine disrupting effects, especially dioxins. Lung cancer is listed as one of adverse health effects of dioxins on humans. We have recently measured concentration of dioxins in sediment in the areas dating back to circa 1960. It was revealed that pollution by dioxins began in early 1950s and that the peak of concentration lasted during 1970 -1990. This fact satisfies temporal sequence of the relationship between lung cancer and exposure to dioxins. The source of dioxins was mostly agricultural agents for rice production as the results of principle component analyses of isomers. Rice-producing districts mostly belong to the areas along the rivers. However, it is known that dioxins play a role in carcinogenicity as not initiators but promoters. We have to thus consider determinants of adenocarcinoma of the lung in light of combination of initiators and promoters. Further studies are needed for clarifying the determinants of clustering of lung cancer, particularly adenocarcinoma.

905 POSTER

Cohort analysis of colorectal cancer mortality in the Republic of Serbia, during the period 1971-1996

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In Serbia, the colorectal cancer mortality in 1971 ranged 5th in females, and 4th in males; it became the second leading malignancy in 1982 in females (after breast cancer), and in 1992 in males (after lung cancer).

The objective of this descriptive-epidemiological study was to investigate the colorectal cancer mortality in Serbian population, particularly the effect of cohort variations on death rates in defined age groups, during the period 1971-1996.

In the study period (1971-1996), a share of all digestive tumours in the cancer mortality has decreased, from 42.0% to 32.3%. However, the mortality risk of colorectal cancer and its share in cancer mortality have increased.

The average colorectal cancer age-adjusted death rates (1971-1996) were 11.2 per 100.000 men (95%CI: 10.1-12.3), and 8.3 per 100.000women (95%CI: 7.7-8.9). The secular linear mortality trends showed significant increase both in males (y=11.2+0.2x; p=0.000), and females (y=8.3+0.1x; p=0.000).

The highest rise in age-specific death rates, according to the linear mortality trends, was observed in males over 65 years (7.8% annually), and females between 60 and 69 years (5.9% annually).

In the cohort analysis of age-specific rates in males, younger birth cohorts were compared with older ones. The increasing colorectal cancer mortality risk has been observed for the ages over 40, with statistical significance in the age groups over 45. In the age between 45 and 59, and over 60, the youngest birth cohorts were at 2 and 2.5-fold higher cancer mortality risk than birth cohorts of the oldest generations. In the cohort analysis of age-specific rates in females, changes in the age under 50 were not so expressive. In all age groups over 50, women of younger generations were at 2-fold higher cancer mortality risk than the oldest ones. According to the present mortality trends, the further increase in colorectal cancer death rates, especially in the ages over 40, should be expected in future generations. Consistent increase in mortality risk in all younger birth cohorts of older ages, as well as in successive five-year age groups of the observed generations, could reflect the continuos increase in colorectal cancer incidence attributed to predominantly environmental exposures.

906 POSTER

Human papillomavirus and cervical cancer in Taiwan: an overlooked area of IARC

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Purpose: The overwhelming etiological role of HPV in pre-invasive and invasive cervical neoplasia has lead a way to the complete, primary prevention of cervical cancer. Before a preventive and therapeutic strategy targeting HPV can be realized, a comprehensive understanding of the prevalence and natural history of different HPV genotypes in a geographically specific way is of fundamental importance.

Methods: This report summarized three nationwide, cross-section studies of general population and patients with abnormal Pap smear, one hospital-based study of cervical cancer and one multi-center longitudinal follow-up studies of LSIL in Taiwan. The prevalence, genotypes and viral load of HPV were studied by Hybrid Capture II, degenerative PCR/reverse blot (Strip test) and/or PCR-RFLP, and quantitative PCR.

Results: The following results were observed: (1) The prevalence of HPV was 13% in general population with a higher prevalence as well as viral load in the old age. (2) The prevalence of HPV infection in patients with LSIL, HSIL and invasive cervical cancer was 82%, 91% and 100%, respectively. (3) Remission of HPV in LSIL cases typically took place within one year of follow up. (4) The natural history of LSIL related significantly with both the presence and load of HPV in cervical swabs on enrollment. (5) HPV 52 is the most prevalent HPV type in general population and women with mild abnormal Pap smear, followed by HPV 16 and HPV 58. (6) In patients with invasive cervical cancer, HPV 16 is the most prevalent type, followed by HPV 58, whereas HPV 52 is rarely found in this patient group.

Conclusion: Female population in Taiwan conferred a different epidemiological characteristic of HPV infection than Western countries. Further studies are undergoing to elucidate the consequences and underline causes of the higher prevalence of HPV infection in old women in Taiwan, the molecular characteristics of infection of the oriental-specific HPV type 52, as well as the cancer predictive value of initial HPV viral load in cervical swab. The present non-quantitative detection of high risk HPVs in a group is insufficient, more efficient tests of HPV genotyping and viral load are needed clinically. For the future vaccination of Chinese population, a different panel of coverage, i.e., HPV-16, -58, -18, -33, should be developed.

907 POSTER

From bedside to register, and back again – How can epidemiological studies using register-data influence clinical practice?

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Epidemiological studies provide powerful tools in the assessments of occurrence and cause of disease. Internal validity (how likely is the observed association to reflect reality) is a fundamental issue in epidemiological studies. Hence, a poorly performed epidemiological study may be as misleading as an experimental study with leaky test tubes. In contrast, a well-designed study performed in an appropriate context may be both highly informative and cost-effective. This "appropriate context" includes socio-economically and ethnically homogenous populations, high-quality census-data and the use of personal identifiers, a health-care system with transparent and population-based referral-patterns, a public acceptance to registration in various registers, and the existence of longitudinal data on morbidity and mortality. Many of those prerequisites are found in the Scandinavian countries. Using the clinically well-recognised problem of cancer in inflammatory bowel disease as an example, I will try to illustrate more precisely how epidemiological studies not only may contribute to our understanding of disease processes but also bridge the gap between basic science and clinical management.

Epidemiological studies of patients with ulcerative colitis or Crohn's disease have demonstrated increased risks of colorectal cancer. The same studies have also indicated that longstanding, extensive, and untreated, respectively, disease all act to further increase the cancer risk, which in absolute terms may reach as high as 35%. Since survival from inflammatory bowel disease per se nowadays is excellent, the increased occurrence of colorectal cancer has become more and more of a clinical problem, as it makes up one of the major threats to health among these patients. Accordingly, patients with inflammatory bowel disease undergo regular endoscopic surveillance, which in itself is not without risks and costs. Finding those patients among whom the yield of such surveillance efforts would be the highest is therefore clinically relevant.

We hypothesised that, apart from duration, extent, and treatment, a familial occurrence of colorectal cancer could in itself be a risk factor for colorectal cancer, just as is the case in the general population. In a retrospective cohort-study with register-based follow-up, we tested this hypothesis. Patients with inflammatory bowel disease were identified in three already existing cohorts and in the Swedish inpatient register. In total, some 20,000 patients were identified. Using the personal identifiers and the Swedish generation register, we were able to identify 114,000 first-degree relatives of these patients. We then linked patients and relatives to the Swedish cancer register and to death- and census-registers to obtain information on cancer occurrence among all individuals, as well as information on follow-up. The results confirmed the grossly increased (relative) risk of colorectal cancer among young patients with inflammatory bowel disease. With respect to our hypothesis, the results also suggested that, just as among healthy individuals, a family history of colorectal cancer was in itself associated with a doubled or so risk of colorectal cancer. Thus, our study not only provided new insight into the pathogenesis of colitis-cancer but also indicated that information on family history be a simple but important information in the care of patients with inflammatory bowel disease. Thanks to the epidemiolgical study design, no patient contact had to be established, no blood had to be drawn, and the total cost to obtain the results was moderate.

908 POSTER

Outline of proposed topic of lecture: The epidemiology of adenocarcinoma of the esophagus

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Increasing incidence: While the incidence of squamous cell carcinoma of the esophagus is stable, that of adenocarcinoma of the esophagus and gastric cardia has increased dramatically in several Western countries. The increase in incidence is more rapid than that any other cancer in the United States[1].

Poor prognosis: Esophageal cancer is one of the most lethal forms of cancer. New therapies and improved diagnostic measures might explain the improved relative survival identified in Sweden during the recent decade, but the overall 5-year survival does not exceed 15%[2].

Risk factors: In view of the increasing incidence and the poor prognosis, it is important to identify, risk factors that might make primary prevention possible. The major risk factors for esophageal squamous cell carcinoma, tobacco smoking and alcohol use, have been known since several decades, but some strong risk factors for adenocarcinoma of the esophagus has only recently been identified. Gastroesophageal reflux is strongly associated with the risk of esophageal adenocarcinoma according to Swedish case-control and cohort data[3, 4]. Increasing frequency, severity, and duration of reflux increases the risk dose-dependently. Medications that can relax the lower esophageal sphincter may induce gastroesophageal reflux[5]. The continuous use of such medications seems to increase the risk of esophageal adenocarcinoma. There is a strong and dose-dependent relation between increasing body mass index (BMI) and risk of esophageal adenocarcinoma through the entire range of BMI values[6], which is independent of reflux. The efforts needed to identify high risk persons are considerable though[7]. The risk of esophageal adenocarcinoma is not importantly associated with smoking, snuff dipping, or alcohol use[8]. Some dietary factors seem to influence the risk of esophageal adenocarcinoma. High intake of antioxidants[9] and wheat fiber[10], reduces the risk of esophageal adenocarcinoma. But the consumption of hot beverages do not seem to be associated with esophageal adenocarcinoma[11]. Recent results indicate that infection with Helicobacter pylori strongly decreased risk of adenocarcinoma of the esophagus[12].

Potential explanations for the increasing incidence of esophageal adenocarcinoma: If gastroesophageal reflux is the main reason for the increasing incidence of the adenocarcinomas, the incidence of reflux disease should have risen as well, but data are lacking on the incidence. If this incidence is rising, this increase in turn must be caused by some other environmental or hereditary factor. Such potential environmental factors are the use of medications that relax the lower esophageal sphincter (LES). Some groups of LES-inhibiting drugs were widely introduced before the start of the epidemic of esophageal adenocarcinoma, but such use can still only explain a minor part of the increasing incidence of esophageal adenocarcinoma. It would be tempting to attribute the increase in the incidence of esophageal adenocarcinoma to the increase in average BMI observed in Western populations. However, the apparently sudden deflection of the incidence curve for esophageal adenocarcinoma, the rapidity of the increase, and the marked, 6–8 fold, male predominance, are observations not entirely consistent with this interpretation[1]. In conclusion, gastroesophageal reflux, the use of medications that might cause such reflux, and obesity might be key factors to explain the increasing incidence of adenocarcinoma of the esophagus and gastric cardia, but several inconsistencies need to be resolved before this suspicion can be established.