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Feature Articles

Development of Registration and Cancer Incidence Rates and Trends in Slovakia

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The development of cancer registration, from the introduction of obligatory notification and the establishment of National Cancer Registry of Slovakia, is described. The activity of the registry is illustrated by the list of publications which have emanated from this institution in recent years. The survey is completed by the analysis of the incidence rates of individual cancer sites in the last 5-year period (1984–1988) and by their trends in the decade 1979–1988. The positive role of the registry in the establishment of a cancer control programme and the investigation of cancer epidemiology is stressed.
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THE COMPULSORY notification of details of cancer patients and deaths introduced in Slovakia, as well as in the whole of Czechoslovakia in 1952, was considered for a long time as the satisfactory solution to cancer incidence assessment in this country. In spite of this hope, shortages and stagnation in the notification of newly diagnosed cases together with inadequate evidence, based on the simple computation of the numbers of notified diseases but not on the long-term registration of well patients, led to increasing underestimation. Morbidity/mortality ratios over 100% were obtained for the majority of individual cancer sites, indicating approximately 30% undernotification of incident cases [1]. The regularly published official cancer incidence statistics remained, therefore, highly underestimated and inexact for the 25 years following [2].

Only in the middle of the 1970s, in connection with the proclamation of the nationwide cancer control programme, did the importance of exact and reliable data on cancer incidence, as well as the failures of the existing system in their computation, become evident [2]. A population-based, pilot cancer registry covering the Eastern County of Slovakia (of about 2 million inhabitants) began its operation at the Department of Cancer Epidemiology of the Cancer Research Institute of the Slovak Academy of Sciences (SAS). In 1980 the National Cancer Registry of Slovakia, encompassing the whole population of the region (nearly 5 million) was established at the Oncological Centre in Bratislava. It consisted of two independent institutes: the Cancer Research Institute of the SAS and the National Institute of Cancer (formerly the institute of Clinical Oncology) of the Ministry of Health.

The early function and structure of the registry was positively influenced by two important events. In 1976 the International Classification of Diseases for Oncology (ICD-O) enabling the exact and uniform classification and coding of the detailed topography and morphology of neoplasms was published [3]. The collection of the data in a standardised and consequently more comparable manner was facilitated by a list of core and optional items, recommended by WHO [4]. These guidelines were later completed with the suggested priorities of each item in hospital and population-based cancer registries [5]. The more detailed notification forms introduced in this country in 1977, together with other such documents, allowed the collection of the majority of items of both categories in the registry [2].

During the first years of the existence of the registry the maximum efforts were directed toward the collection of reliable and complete cancer incidence rates. Using notification forms, death certificates, autopsy reports and other available information sources, the data base covering the decade 1968–1977 and encompassing about 140 000 cancer patients was gradually completed. All these cases were recoded using ICD-O codes for topography and morphology, and beginning with the year 1978, updated each year until the International Classification of Diseases, 9th revision (ICD-9) [6]. Progressive improvement of incidence data enabled the publication of these cases in the fifth volume of *Cancer Incidence in Five Continents* [7], (the data published in the volume IV were confined only to the territory of the Western County of Slovakia [8]). The use of ICD-O morphology codes, together with the nearly 100% histological confirmation of cancers occurring in childhood and extensive data from necropsies of children dying before the age of 15 years allowed the registry to perform detailed descriptive epidemiological studies of childhood cancer in Slovakia [9, 10] as well as the submission of data for international comparison [11]. From the beginning of its operation the work in the registry was highly computerised [12]. Recently 17 000–18 000 newly diagnosed cases have been notified yearly (18 002 in the year 1988) and the total number of cases on file in the registry had reached nearly 340 000 at the end of the year 1989.

Besides assessment of reliable and complete incidence rates, great attention was also paid to the development of cancer mortality rates in the registry, using the 4-digit codes of the ICD-9, and as well as to the proper distinction between people dying from and with cancer. Our experience and approach to the computation of the cancer mortality rates in the registry has

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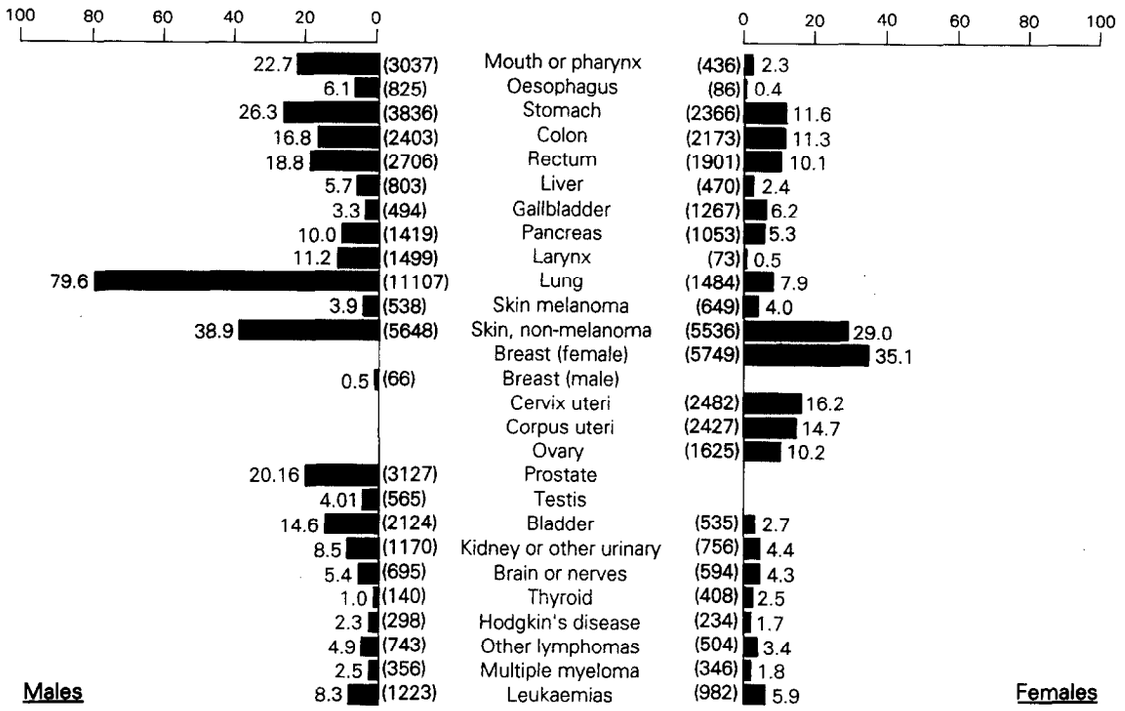

Fig. 1. Age-standardised incidence rates from major cancer sites in Slovakia, Czechoslovakia, 1984–1988. No. of registered cases is given in parentheses.

been published elsewhere [13]. In international comparisons of cancer incidence rates only mortality rates computed in the registry were used as indices of reliability [7, 8]. Moreover, information on the number of live-born children, present in every death certificate in this country until recently, was used for the study of relations between parity and cancer risk [14]. Annual reports from the registry containing detailed data on cancer incidence for the whole region, as well as for individual counties and districts, were published regularly, but data from the registry were accepted as the only source of official cancer incidence statistics for the whole region only in the year 1983.

Finally, the *Atlas of Cancer Incidence and Mortality* in Slovakia, covering the decade 1975–1984, was published in 1989. This gave the standardised rates of both mentioned indicators for major cancers in 38 districts and the evaluation of their age-adjusted rates in the years 1968–1984, as well as of the age-specific rates at the beginning and the end of the period studied [15].

In this comunication the actual incidence rates, based on incident cases, notified in the period 1984–1988 are presented together with their trends for the period 1979–1988. It is necessary to add that the cases obtained from death certificates only contributed to less than 10% of all cases (the definition of these cases in our registry is more severe; also the cases known from the death certificate and completed with other information, but without the exact date of incidence, are further considered as "death certificate only"). Histological confirmation was recently close to 80% overall.

The incident cases of individual cancer sites or their groups, diagnosed and notified to the registry in Slovakia during the recent 5 years 1984–1988 are given in Fig. 1. The data are presented in absolute numbers (as whole number cases occurring in the period) and in mean annual incidence rates, age-adjusted, using the standard world population as a reference. The use of the standard population leads to the diminishment of the crude rates but besides these and other limitations of age-standardisation the direct comparison of rates from Slovakia with those from other countries can be accurately done.

According to the recent comparison of the incidence rates of major cancer sites in Europe [16], based on the rates from the years 1978–1982 [7] only some sites, including stomach, rectum, gallbladder, mouth or pharynx, pancreas and lungs, and uterus and breast in women, as well as leukaemias tend to be in the upper part of the range of variation between European cancer registration areas. The incidence rates of the majority of cancer sites could be placed in the middle of the range, but correspond to the rates found in the developed countries of Western Europe togther with the all-sites incidence rates. A similar pattern was found when the cancer incidence rates in several countries of the world were compared [17]. On the other hand, the incidence rates of cancer of the prostate and testis, and of the oesophagus and urinary bladder in females, could be evaluated as relatively low worldwide [7].

The incidence trends shown in Table 1 and demonstrated in the percent changes between 1984–1988 and 1973–1983 indicate for the great majority of sites an increase. The most important increase was shown for colon cancer, particularly in males, and for cancer of the testis. Strong increases were shown in skin cancers, both melanoma and non-melanoma, and cancer of the bladder, kidney and thyroid in males as well as for the majority of smoking-related cancers. A stronger decrease was seen for cancer of the stomach in both sexes and mouth or pharynx cancer in females. Stabilisation of rates or a small decrease was shown for Hodgkin's disease in males and gallbladder and thyroid cancers in females. The substantial decrease in liver cancer incidence in females could be attributed to our constant efforts to delineate correctly the primary liver cancers. For this site the mortality constantly exceeds the incidence [13].

Table 1. Percentage rate of change of age-standardised (world) incidence rates from selected cancers or groups of cancers for males and females. Slovakia, Czechoslovakia, 1979–1988

Site	ICD-9	Change (%) (1984–1988/1979–1983) Males	Females
Mouth or pharynx	140–9	+ 24.42	− 5.37
Oesophagus	150	+ 36.26	–
Stomach	151	− 15.37	− 16.10
Colon	153	+ 35.18	+ 18.93
Rectum	154	+ 19.16	+ 16.57
Intestine, total	152–4	+ 24.49	+ 17.20
Liver	155	+ 11.18	− 9.43
Gallbladder	156	+ 13.22	0.00
Pancreas	157	+ 20.43	+ 17.00
Larnyx	161	+ 6.84	+ 24.32
Trachea, bronchus, lung	162	+ 10.52	+ 14.91
Skin melanoma	172	+ 25.48	+ 15.27
Skin non-melanoma	173	+ 18.23	+ 14.60
Breast			
Female	174	–	+ 12.08
Male	175	+ 8.70	–
Cervix uteri	180	–	+ 8.64
Corpus uteri	182	–	+ 10.82
Ovary	183	–	+ 11.33
Prostate	185	+ 19.29	–
Testis	186	+ 36.86	–
Bladder	188	+ 20.16	+ 24.42
Kidney and other	189	+ 23.26	+ 30.29
urinary	191–2	+ 7.40	+ 13.03
Brain and nerve	193	+ 22.22	0.00
Thyroid	201	− 5.83	+ 4.40
Hodgkin's disease	200+202	+ 1.03	+ 24.28
Other lymphomas	203	+ 24.14	+ 18.30
Multiple myeloma	204–8	− 0.60	+ 8.86
Leukaemias			
Total, all sites	140–208	+ 12.36	+ 7.02
Total except skin non-melanoma	Total–173	+ 3.81	+ 7.52

Still of importance and interest are the relatively high rates of stomach cancer, in relation to their long-term dominant positions in the past. This site is replaced in prominence in the western part of Slovakia with colon and rectum cancer, while in some areas of eastern Slovakia the very high incidence and mortality rates of stomach cancer persist [15, 18]. Moreover, there is a tendency to stabilisation or even a small increase in incidence and mortality rates for stomach cancer in recent few years. A similar development, together with the successive predomination of the upper subsites of the stomach, was also observed in other countries [19]. The relatively high rates of gallbladder cancer, connected with the similar or even higher ones in the neighbouring countries of Central Europe, was closely analysed in our previous reports [20, 21], as well as the increasing incidence rates of malignant skin melanoma by subsites [22]. Of special interest are the increasing incidence rates of uterine cervix cancer since 1976, after their long-term fall in the previous period [23]. The relatively high and continuously increasing overall cancer incidence rates are also influenced by the extensive registration of non-melanoma skin cancers, including basaliomas. The overall standardised cancer incidence rates per 100 000 reached 356.8 in males and 220.0 in females in 1988.

It is beyond the scope of this article to analyse more thoroughly the observed cancer incidence rates and trends, or their relations to possible risk factors or to the efficacy of the cancer control programme. This registry is one of the few in Eastern Europe covering an adequately large and well-defined population, and collecting highly reliable data in a standardised and comparable manner over a relatively long time. These data are partially applicable to other countries of this area, showing similar patterns and trends of cancer incidence now or in the near future, at least for the basal orientation of cancer control programmes [24].

In conclusion, we stress the use of data from this registry for the study of cancer epidemiology as well as its role in our participation in actual and future international projects [25, 26]. This role of the registry is particularly important in the countries of Eastern Europe, where the study of the epidemiology of non-infectious diseases (including cancer) was long neglected and still lags behind that of other developed countries.

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Follicular Dendritic Cells in Non-Hodgkin Lymphomas: Localisation, Characterisation and Pathophysiological Aspects

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INTRODUCTION

IN LYMPHOID TISSUE, lymphocytes and additional cells of the mononuclear phagocytic system and the dendritic cell family can be identified. Follicular dendritic cells (FDC) are restricted to the B-cell regions of secondary lymphoid tissue, i.e. lymph-nodes, spleen and tonsils. Their long cytoplasmic extensions form a dense framework throughout the follicles [1]. FDC trap and retain immune complexes on the surface of their processes for long periods [2]. During the secondary immune response, these antigen-antibody complexes are internalised by B-lymphocytes. Subsequently, they undergo rapid proliferation resulting in the expansion of the virgin-B and memory-B-cell pool and an increased level of immunoglobulins in the serum [3, 4].

FDC are also present in non-Hodgkin lymphomas (NHL) derived from follicular centre cells [1]. As they do in the non-malignant tissue, here FDC form a network which contains accumulating neoplastic B cells. This intimate association appears to be pathognomonic for germinal centre cell-derived neoplasias [5]. Occasionally FDC may be identified in non-follicular centre cell-derived NHL when a pseudonodular growth pattern is observed [6, 7]. In these cases the neoplastic lymphocytes seem to have their normal counterparts in the follicle mantle zone [6].

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In this review we will focus on the neoplasias with FDC involvement. The antigenic phenotype of FDC in normal conditions and neoplastic disorders will be summarised. *In situ*, cell borders between FDC and adjacent lymphocytes are difficult to distinguish by light microscopy. Therefore, accurate analysis of FDC surface antigenic profile has been performed by several scientists subsequent to the preparation of single cell suspensions enriched in FDC [8–12].

In vitro studies with FDC isolated from murine lymph-nodes or human tonsils indicate their importance as an accessory cell in the secondary immune response. Additionally to the presentation of antigen, a major role of FDC appears to be the stimulation of germinal centre B-lymphocytes [13]. Until now, only a very limited number of data are available on *in vitro* experiments with FDC isolated from lymphoma tissues. In the second part of this summary we will unfold the interactions between FDC, germinal centre B-lymphocytes and lymphoma cells, respectively. Finally, FDC resistance to irradiation and chemotherapeutic drugs will be considered.

FDC IN NORMAL LYMPHOID TISSUE

The detection of FDC by conventional light microscopy or histochemical techniques is difficult. The production of monoclonal antibodies (Mab) selective for FDC has enabled scientists to study the distribution pattern of FDC in lymphatic tissue [5, 14, 15]. FDC have been identified in primary follicles and germinal centres of secondary lymphoid tissue. Their branching cytoplasmic extensions form a dense, sharply demarcated dendritic web. In addition, FDC have been observed in the mantle zone that surrounds the germinal centre. In these sites their fusiform processes are more loosely arranged [1, 16].