A RETROSPECTIVE ASSESSMENT OF THE EPIDEMIOLOGICAL USEFULNESS OF ARCHIVAL MATERIALS FROM 1954-1994, IN THE COLLECTION OF THE DEPARTMENT OF TUMOUR PATHOLOGY, GREATER POLAND CANCER CENTRE, POZNAN

RETROSPEKTYWNA OCENA PRZYDATNOŚCI DO CELÓW EPIDEMIOLOGICZNYCH MATERIAŁU ARCHIWALNEGO Z LAT 1954-1994 ZE ZBIORÓW ZAKŁADU PATOLOGII NOWOTWORÓW WIELKOPOLSKIEGO CENTRUM ONKOLOGII W POZNANIU

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Summary: Cancer is not an invention of the 20th century. Since Hippocrates and Avicenna up until the times of Rudolf Virchow, Karl Thiersh, Walter Schiller and Albert Compton-Broders, attempts to define and classify cancers as malignant processes have evolved many times. This continued until the great technological advances of the latter half of the 20th century, which had an enormous influence on developments in the medical field. These advances also enriched our understanding of tumours, offering increasingly precise diagnoses and more effective treatment and rehabilitation. An important aspect of the activities of oncological centres is prevention. This is broadly understood to be primary and secondary prophylaxis but also includes the work of cancer registries which gather data about neoplastic diseases, including the morbidity and mortality rates in the population. This allows us to monitor the threat of cancer and to foresee actions necessary in the fight against it.

The purpose of this work is to retrospectively assess the epidemiological usefulness of archival materials held in the Department of Tumour Pathology of the Greater Poland Cancer Centre in Poznan (Zakład Patologii Nowotworów Wielkopolskiego Centrum Onkologii), in the context of data gathered by the Greater Poland Cancer Registry (Wielkopolski Rejestr Nowotworów), in addition to epidemiological data from the years 1954-1994. A detailed analysis of the paper archive enabled the creation of interesting algorithms for cancer morbidity relative to sex and age for the most frequently noted neoplasms. It also confirmed that cancer incidence is increasing and underlines the need for further research.

Keywords: archives, medical oncology, histology

Streszczenie: Choroby nowotworowe nie są wynalazkiem XX w. Od czasów Hipokratesa, Awicenny czy wreszcie Rudolfa Virchowa, Karla Thierscha, Waltera Schillera, Alberta Compton-Brodersa próby zdefiniowania raka jako procesu złośliwego i jego klasyfikacji wielokrotnie ewoluowały. Dopiero niezwykły postęp technologiczny, jaki dokonał się w II połowie XX w., wywarł ogromny wpływ na rozwój wielu dziedzin medycyny i wzbogacił wiedze o nowotworach, dając szanse na precyzyjna diagnoze, skuteczne leczenie i rehabilitację, także w Polsce. Ważnym aspektem działalności leczniczej ośrodków onkologicznych jest również prewencja, szeroko rozumiana profilaktyka pierwotna i wtórna oraz działalność rejestrów nowotworów, które gromadzą dane o zachorowaniach na nowotwory, zgonach z powodu choroby nowotworowej, i o populacji, której ten problem dotyczy. Umożliwia to monitorowanie zagrożeń nowotworem, pozwala na planowanie różnorakich działań dotyczących walki z rakiem. Celem niniejszej pracy jest retrospektywna ocena przydatności do celów epidemiologicznych materiału archiwalnego pochodzącego z zasobów Zakładu Patologii Nowotworów Wielkopolskiego Centrum Onkologii w Poznaniu, w kontekście gromadzonych danych przez Wielkopolski Rejestr Nowotworów, jako uzupełnienie danych epidemiologicznych pochodzących z lat 1954-1994. Szczegółowa analiza archiwum papierowego umożliwiła stworzenie interesujących algorytmów zachorowalności na nowotwory wg płci, wieku i najczęstszych notowanych nowotworów. Potwierdziła też tendencję wzrostowa zachorowań na choroby nowotworowe i dała asumpt do kolejnych poszukiwań.

Słowa kluczowe: archiwa, onkologia, histologia

INTRODUCTION

The history of the term cancer as a malignant disease goes back to ancient times. This name was used by Hippocrates of Kos, Aulus Cornelius Celsus, and by Paul of Aegina, and was broadly spread by the Persian physician and philosopher Ibn Sina, also known as Avicenna. Paul of Aegina described the observed changes as appearing in every part of the body, often with sore, hard tumours featuring radiating swollen veins. The appearance of the skin of the nipple in the advanced stages of the disease was similarly described and associated with a crab-like shape.

The invention of the light microscope and the ability to observe small objects, invisible to the naked eye, was a milestone in the development of the natural sciences and has contributed to a greater understanding of many diseases, including neoplastic disease. The first microscopes were created around 1590 and enabled observation at ten-fold magnification. A real breakthrough was made by Antoni van Leeuwenhoek, in refining and spreading their production. Around 1655, Robert Hook used adjustable lenses in a microscope so that better image quality could be obtained. However, it was not until the 19th century that enormous progress was made in many fields of medicine, including pathology.

In 1865, surgeon Karl Thiersch together with the pathologist Heinrich Wilhelm von Waldeyer-Hartz developed the modern meaning of the word cancer as a neoplastic malignant disease originating from epithelial tissue. It was a bold view, being in opposition to the that presented by the eminent scholar, great authority, and creator of contemporary pathology, Rudolf Virchow [9].

The remarkable progress that has been made in the last twenty years in many fields of science, especially concerning the development of modern technologies, has contributed to a better understanding of the essence of cancer. It allowed for the development of such fields as immunohistochemistry and molecular biology, which focus on genetic changes and enable us to make more precise diagnoses and to better assess prognostic and predictive factors. Today we know that carcinogenesis is a complex process, which is a consequence of disturbed cell biology, altered control mechanisms for cell proliferation, and the accumulation of genetic errors in subsequent generations of daughter cells caused by DNA mutation. Examples of promoting factors include: age, environmental and geographical factors (diet, lifestyle and environmental exposure) and changes to precursors resulting from chronic tissue damage or long-term inflammatory processes [6, 7].

Currently, anatomic pathology is a medical specialty using a wide range of diagnostic methods: fine needle biopsies under ultrasound and CT guidance, core needle biopsies, analysis of tissue fragments, partially and wholly resected organs, gynaecological and general cytology, and techniques based on cytochemistry, histochemistry, immunology and molecular biology. Despite huge changes in modern cancer diagnostics supported by modern imaging methods (computed tomography, Magnetic resonance (MR), positron emission tomography (PET) and others), the pathology report is still the decisive test upon which patients treatment schemes are developed. The first mention of the fight against cancer in Poland appeared in 1584, when Piotr Skarga founded the Brotherhood of Mercy of the Mother of God who looked after patients with cancer. In 1591, the first cancer hospital in Europe was opened in Warsaw. It was not until 1906 that a special committee was formed for the purpose of testing and treating cancers. The committee's tasks included educational activities and increasing access to health care, as well as the collection of epidemiological data and the creation of cancer clinics. Subsequently, committees were established in Krakow, Lodz, Poznan, Vilnius and Lviv. In 1923, the 25th anniversary of the discovery of radium, Maria Skłodowska-Curie publicly expressed the wish to establish a Radium Institute in Warsaw, modelled on the "Institut du Radium" in Paris. The Polish Committee for Fight against Cancer (PKZR) appealed to the public to collect funds for this purpose. The official opening took place on May 29th, 1932, when Maria Skłodowska-Curie handed Institute representatives the first gram of Radium offered by the American and Canadian Poles. Unfortunately, the outbreak of World War II interrupted the promising activity of the Radium Institute. Reconstruction began in 1945, and in 1946, its activity was resumed [9, 3].

In subsequent years, oncology care was further developed and improved. Important aspects of the fight with cancer were education, epidemiology, prophylaxis in the broad sense, and psychophysical rehabilitation as well as palliative and terminal care. New concepts arose concerning the organisation of cancer centres making comprehensive use of all available methods for organization and treatment: prophylaxis, diagnosis and rehabilitation. The inertia of successive governments, economic collapse, the lack of funds for scientific research and the implementation of modern diagnostic methods and treatment, as well issues with the modernization of the existing, gradually degraded infrastructure, resulted in a slowing in the development of oncological treatment [7, 3].

In 2002, the National Program for Combating Neoplastic Diseases was created in Poland. The main goals of this long term plan were to limit tumour incidence and attain standard rates for the detection and treatment of cancer, as well as developing primary prophylaxis and expanding national screening programs, increasing the availability of early detection methods, and improving the quality of diagnosis and therapy. It also aims to standardise radiotherapy and improve access to combined treatment, rehabilitation, palliative care, and information concerning the early detection and treatment of cancers [9, 8].

High cancer morbidity and mortality in Poland is a huge health and socioeconomic problem. Preventative steps including the promotion of a healthy and active lifestyle, and the dissemination of knowledge regarding risk factors are key factors in reducing the risk of cancer [11]. This being the case, epidemiology is extremely important, in particular the activity of the Cancer Registry, whose purpose is to collect data on all cases of malignant neoplasms in the region, in particular the demographic structure of disease, including the number of deaths and the proportion of the population covered by treatment. Also, monitoring the occurrence of cancer allows the Registry to foresee various needs in the fight against cancer, allowing for the determination of, for example, future staffing and equipment requirements. They are a valuable source of information in both on-going and prospective studies [3, 11, 5].

In 1920s and 1930s, cancer patients from the Greater Poland region were treated in the clinics of the Faculty of Medicine at the Poznan University. The first irradiation was carried out at the Radiology Clinic under the supervision of Professor Karol Mayer. It was, however, not possible to create a regional Radium Institute, and the outbreak of the war thwarted plans to create one.

The Greater Poland Cancer Centre (Wielkopolskie Centrum Onkologii) was established in March 1952 at the initiative of Czeslaw Wojnerowicz and Stefan Skowronski, in the building of the former Social Insurance Hospital. From its first years of activity, the hospital introduced interdisciplinary oncology, combining surgery with radiotherapy and histopathology. Rebuilt and modernised many times, the Centre today is an important spot on Poland's oncological map [10].

The Department of Tumour Pathology was established in 1953 as one of the main departments of the Regional Oncology Centre. The founder of the laboratory was Dr. Lucjan Przybora, a highly regarded clinical pathologist. Currently, the Department consists of histopathology, immunohistochemistry, cervical cytology, cytopathology, molecular biology and flow cytometry laboratories. The team consists of specialist pathologists, pathology residents, biologists, medical analysts, nurses, and a group of technicians. The purpose of the Department is to determine histological and cytological diagnoses. The analysis of histological and cytological materials by means of morphology, immunohistochemistry, molecular biology and flow cytometry makes it possible to precisely identify a cancer, which in turn influences the selection of appropriate treatment [10].

AIMS AND METHODS

The Department of Tumour Pathology of the Greater Poland Cancer Centre has been in continuous operation since 1953. During the whole period the Department has gathered extensive archival material, comprising of tissue and cytological specimens embedded in paraffin blocks, histological slides stained by standard methods (such as haematoxylin-eosin), and paper archives. The growing archive presented a serious problem for the Department and the lack of space in the hospital made it necessary to seek alternative storage locations. Numerous removals, inadequate storage conditions, and the activity of microorganisms have wreaked havoc on the archived material, some of which has been lost forever. Nearly 80 percent of the resources have been preserved, however.

The aim of this study was to retrospectively assess of the epidemiological usefulness of the archival materials (papers) from 1954-1994 in the context of data collected by the Greater Poland Cancer Registry.

The subject of the analysis is the archived papers of the Department, which were collated into book form and comprise of pages of basic patient data including the patient's name, age, clinical data, and specimen type, as well as the histopathological result and date of issue. Thirteen thousand nine hundred and fifty such data-sets from 1954, 1964, 1974, 1984 and 1994 were reviewed. On the basis of the collected information, a summary of the most important information was prepared. This data includes sex, age, the most frequently occurring cancers. The results will become the basis for comparative algorithms and material for further research. All data is expressed in absolute terms, based on detailed calculations.

RESULTS

YEAR 1954

The year 1954 was the first full year of operation of the Histopathology Laboratory, hence it was the first period analysed. A small turnout of patients may result from the limited number of hospital beds (30), a lack of public health awareness, the prevailing belief that cancer "should not be disturbed", especially among the older generation, as well as ineffective primary prevention. Women represent 70.4% of cases (648), men 29.1% (276), and children under 18, 0.5% (5) (fig. 1).



FIGURE 1. Statistical data on materials diagnosed in the Department of Tumour Pathology Year 1954 Registered patients: 2492 Positive results: 920

The average age for female patients was 51.5 years, and 54.3 years for men. However, the average age of patients diagnosed with breast cancer (2.6% of all positive tests) was 48.8 years, based on sixty six cases of breast cancer. In the remaining three cases, the patient's age was not given or was illegible. Most likely, younger people were more likely to be referred to the doctor, or were more aware of the dangers, while patients in the advanced stages of disease and terminally ill patients were not diagnosed any further. The high proportion of gynaecological material (13.7%) results from with the gynaecological profile of the hospital in its initial period of activity. The remaining 73.3% of cases are mainly skin cancers (nose, ears and lips), as well as isolated cases of cancers around the anus, long bones and bone marrow cancers (fig. 2).



FIGURE 2. Most common tumour sites, material diagnosed in the Department of Tumour Pathology Year 1954

Cervix:	126
Breast:	69
Thyroid:	41
Skin (Melanoma):	9
Other:	675

YEAR 1964

In the next decade, there was a slight increase in the overall number of cases. In comparison to 1954, the difference amounts to only 296 cases, of which positive results were reported in 132 cases. Women constitute 73.4% (772) of patients, men 25.6% (269), and children under 18 years, 1% (11) (fig. 3). The average age

for women was 54 years and 59 years for men. Among women with malignant breast cancer (29.5% of positive results), the average age was 52.4. The number of women with breast cancer increased significantly, more than five times, and amounted to 11.1% of all cases. The prevalence of women (73.4%) still persisted



FIGURE 3. Statistical data on materials diagnosed in the Department of Tumour Pathology Year 1964 Registered patients: 2788 Positive results: 1052

among all patients admitted. Of the remaining diagnoses 43.4% are skin cancers (mostly from the nose, ears and lips), cancers of the final segment of the large intestine, and discreet cases of bone tumours, especially the long bones, and bone marrow diseases. Skin tumours, especially those located around the upper and lower lip, may be a consequence of tobacco smoking (fig. 4).



FIGURE 4. Most common tumour sites, material diagnosed in the Department of Tumour Pathology Year 1964

Cervix:	263
Breast:	311
Thyroid:	11
Skin (Melanoma):	11
Other:	596

YEAR 1974

The year 1974 brought no major surprises. Once again, there was a slight increase in total cases, up by 9.9% in comparison to 1964. At 71% (699), women still represented the majority of cases, while 27.6% (272) were men and children under 18 years just 1.4% (13) (fig. 5). The average age for women was 55 years, and for men 58.3 years. For women diagnosed with breast cancer, the average age was 53.4 years. Breast cancer accounted for 32% of positive results and 11.4% of all registered examinations, indicating a slight upward trend in the incidence of breast cancer. A large percentage of skin cancers, being the aftermath of tobacco abuse, were still recognized, while gastrointestinal cancers were rarely diagnosed.



FIGURE 5. Statistical data on materials diagnosed in the Department of Tumour Pathology Year 1974 Registered patients: 2799 Positive results: 984

This latter result may have been due to the initially latent course of the disease and to the lack of modern diagnostic methods. Diseases of the hematopoietic apparatus, kidneys, liver and bones represented just a fraction of cases (fig. 6).



FIGURE 6. Most common tumour sites, material diagnosed in the Department of Tumour Pathology Year 1974

Cervix:	52
Breast:	320
Thyroid:	18
Skin (Melanoma):	19
Other:	575

<u>YEAR 1984</u>

In 1984, a significant increase in cancer incidence became visible, up by 51% in comparison to the year 1974. There was also a noticeable drop in the proportion of women in the overall number of positive cases, this figure having fallen to 62.8% (819) from 71% in 1974. This result is naturally to the disadvantage of men who now represented 36.1% (475). Cancers in children remained at a similar level, around 1.1% (11). (fig. 7). The average age for women was 52.4 years, for men 57.4 years, for women with breast cancer, this value was 51.8 years. Breast neoplasms accounted for 26.7% of all malignant diagnoses and 6.3% of all registered cases. The share of other tumour locations remained within single-digit values: 0.5% thyroid gland, 4.3% gynaecological material, 0.9% gastrointestinal tract, 0.5% marrow,

3.4% melanoma of the skin. The drop in the number of gynaecological cases diagnosed and treated in the hospital was almost certainly associated with the establishment of a specialized gynaecology centre in Poznan (fig. 8).



FIGURE 7. Statistical data on materials diagnosed in the Department of Tumour Pathology Year 1984 Registered patients: 5477 Positive results: 1305



FIGURE 8. Most common tumour sites, material diagnosed in the Department of Tumour Pathology Year 1984

56
348
7
45
849

YEAR 1994

Much of the archival data in the form of paper archives was missing for this year and was probably destroyed during one of the numerous removals. The lack of a coherent computer program means that the only information available concerns the number of tests accepted for the laboratory. This, however, made it possible to estimate the overall incidence, in terms of morbidity, in the Greater Poland Cancer Centre. The LIMS system in use at the time, HMS, made it impossible to obtain reliable data. Reports returned various results, leaving the user with very little confidence in their credibility. Only in the case of breast cancer was it possible to find the necessary material, in the form of archival surveys, and on this basis determine the number and ages of the patients.

In 1994, 19,143 cases were accessioned to the Department of Tumour Pathology, of which 394 were cases of breast cancer. The average age of patients diagnosed with breast cancer was 50.1 years.

COMMENT AND CONCLUSION

In the analysed period, from 1954 until the end of 1994, and over the following two decades, a steady increase in the recorded incidence of malignant neoplasms is evident (920 cases in 1954, 1305 in 1984). The total number of diagnostic tests accepted has increased by more than twenty fold (2492 studies in 1954, 41434 studies in 2014), which confirms the general upward trend in the incidence of cancer (fig. 9).

The gathered material may be of interest not only with regards to the activity of the Department of Tumour Pathology, but also to the work of the Greater Poland Cancer Registry. It illustrates the development dynamics of various groups of tumours four decades. It is also a register of all the positive results from the analysed period. It is therefore a valuable database and may be of great help in further, more detailed and specific studies. It should also be noted that the Depart-



FIGURE 9. Diagnostic cases tested in the Department of Tumour Pathology, 1954-2014

ment also has an extensive archive of paraffin embedded tissue samples which are of enormous value as research material. The use of data from the paper archive, as well as the histological material, may inspire a great many comparative studies.

Bearing in mind the enormous value of this archive, every effort should be made to ensure that the accumulated material within it is made use of in upcoming scientific studies that will allow for better statistical estimates concerning cancer development.

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