

ORIGINAL PAPERS

CASE-REFERENT STUDY ON SKIN CANCER AND ITS RELATION TO OCCUPATIONAL EXPOSURE TO POLYCYCLIC AROMATIC HYDROCARBONS. I. STUDY DESIGN

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Abstract. The authors present the first stage of a case-referent study conducted in order to confront a hypothesis which suggests the existence of an important casual relationship between the exposure to polycyclic aromatic hydrocarbons and skin cancer. The investigated group consisted of patients suffering from skin cancer, while control groups comprised individuals from the general population and patients from hospital departments and dermatological outpatient clinics. The present paper deals with the characteristics of cases and their referents, ways of selecting examinees, a method of data collecting (history of a patient in the form of a questionnaire), the work of interviewers and the information concerning localization and histopathological forms of diagnosed skin cancers, as well as reasons for not examining all persons.

INTRODUCTION

Skin cancer is supposed to be the form of cancer most frequently found in humans. From the data of American scientists, it emerges that in 40–50% of all persons who live to be sixty-five, at least one skin cancer is diagnosed (2, 3). In spite of such a marked disease prevalence, epidemiological data concerning the conditioning of this disease process in particular populations are insufficient and inaccurate (9). The evaluation of the effect of environmental agents on the disease is rather difficult due to the usually long latency period between exposure to a presumed etiological factor and the occurrence of the disease (4, 5, 6, 11). In the case of working environment factors, manifestation of skin cancer in elderly persons who are no longer subject to direct examinations of the industrial health service, and the lack of obligation to collect

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information on occupational contact with carcinogenic agents after diagnosing a neoplastic process, both result in the fact that the majority of cases are erroneously not accounted for by the occupational etiology. For instance, in Poland between 1971 and 1983, neoplasms which according to official medical statistics were found to be occupationally-related, constituted as little as 0.15% of the total number of 23,500 cases of skin cancer in males (34 cases), while skin neoplasms resulting from exposure to chemical agents in the working environment reached 0.08% of this number (19 cases) (7, 8). Thus, only 15 out of each 10,000 cases were causally related to occupational exposure, and in only 8 cases, a presumed etiological factor was represented by chemical cancerogens. In the light of the above-mentioned facts, the necessity of estimating the actual role of occupational cancerogenic factors in the pathogenesis of skin cancer becomes clear. This estimation would determine the usefulness of elaborating and implementing effective prevention programmes. Having this in mind, a case-control epidemiological study concerning the relation between selected chemical agents and skin cancer occurrence has been started at the Institute of Occupational Medicine in Lodz within the context of the Central Programme "Cancer control".

AIM AND METHOD

This study is devoted to the problem of occupational factors which influence skin cancer incidence in the large urban population of Lodz. The principal aim of the study is to test the hypothesis which suggests that exposure to polycyclic aromatic hydrocarbons does significantly affect skin cancer incidence. Another, additional, aim of the study is to determine those occupational groups of workers whose work increases the risk of incidence of skin cancer, in order to include them in a special prophylactic programme. Information obtained in the course of the study is also expected to improve knowledge on the occurrence of the occupational exposure to polycyclic aromatic hydrocarbons in the working environment.

Due to the long latency period in skin cancer, the complex character of the disease etiology and the relatively rare occurrence of occupational exposure, a case-referent strategy was chosen for the purposes of the study (5, 10).

Taking into account the type of the exposure analysed as well as the legal regulations in Poland which forbid the employment of women to do the majority of jobs performed in exposure to polycyclic aromatic hydrocarbons, only males were included in the study.



Cases

A group of potential cases comprised men living in Lodz, in whom skin cancer was found for the first time in their lives in the period between 1.07.1983 and 30.06.1988. Since the data on skin cancer incidence are usually lowered in oncological registers, the information from the documentation of the Histology Division of the Department of Oncology, Medical Academy in Lodz where specialist examinations on all skin lesions suspected to have a neoplastic origin is carried out, were used as a source of the choice of the study population. The material thus

TABLE 1. Cases of Skin Cancer by the Year of Birth

Year of birth	n	%
1900—1904	9	2.3
1905—1909	39	10.4
1910—1914	52	13.8
1915—1919	49	13.0
1920—1924	66	17.6
1925—1929	64	17.0
1930—1934	41	10.9
1935—1939	20	5.3
1940—1944	9	2.4
1945—1949	12	3.2
1950—1954	13	3.5
1955—1959	1	0.3
1960+	1	0.3
Total	374	100.0

TABLE 2. Cases of Skin Cancer by Age at the Moment of Diagnosis of the Disease

Age (diagnosis)	n	%
20—24	1	0.3
25—29	1	0.3
30—34	8	2.1
35—39	11	2.9
40—44	12	3.2
45—49	13	3.5
50—54	32	8.6
55—59	57	15.2
60—64	70	18.7
65—69	53	14.2
70—74	56	15.0
75—79	43	11.5
80+	17	4.5
Total	374	100.0

obtained concerned 534 men with skin cancer diagnosed using histopathological examination in the period under consideration. All persons born before 1900 (i.e. 14 men) were excluded from this group; the remaining 520 men were subjected to a further examination.

Eventually, a complete anamnesis in the form of a questionnaire was performed with 374 persons, which, assuming unchanged study conditions, i.e. Type I error $\alpha = 0.10$ and Type II error $\beta = 0.80$ and exposure frequency in the control group $p_4 = 0.03^{**}$ and two referents

*) Type I error is made when the experimenter rejects the null hypothesis and it is true.

Type II error is made when the experimenter accepts the null hypothesis and the alternative is true.

**) p_4 — data obtained from the Sanitary-Epidemiological Station in Lodz.

per one case, will render it possible to accept a relative risk $R > 1.97$ as the significant one in the final analysis of results.

The highest percentage (18.7%) constituted persons in whom skin cancer was diagnosed at 60—64 years of age, while skin cancer diagnosed before 60 years of age was observed in 36.1% of all the subjects (Tables 1 and 2).

Fifty percent of patients had an elementary or primary technical education; ca 21%, secondary education, university education and in-

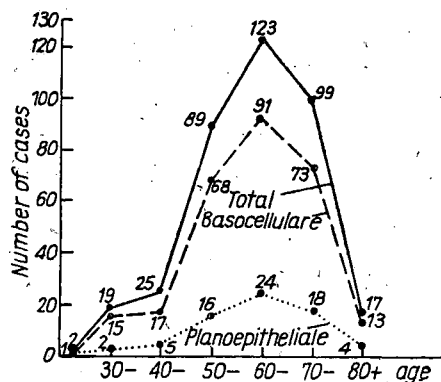


Fig. 1. Examined "cases" of skin cancer by age at the moment of diagnosing the disease and by histological form — absolute numbers.

complete university education, and 29% of persons had finished technical or grammar schools.

The data analysis which focused upon the histopathological form of skin cancer made possible the selection of basal cell carcinomas, carcinomas planoepitheliale, Bowen's disease and Arning's carcinoid from the material obtained. In the majority of persons examined, basal cell carcinoma was found (278 cases, i.e. 74.3%) and in other patients carcinoma planoepitheliale (70 cases, i.e. 18.7%), Bowen's disease and Arning's carcinoid (13 cases each, i.e. 7.0%) were diagnosed (Fig. 1).

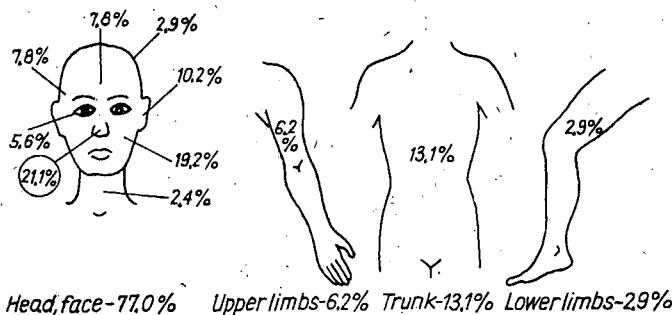


Fig. 2. Location of skin cancer in the examined group of "cases".

TABLE 3. Skin Cancer in the Examined Group of Cases by Location and Histopathological Form (Absolute Numbers and %)

Location	Total		Basal cell carcinoma		Carcinoma planoeptitheliale		Bowen's disease		Arning's carcinoid	
	n	%	n	%	n	%	n	%	n	%
Head	11	2.9	9	3.2	2	2.9	—	—	—	—
Forehead	29	7.8	26	9.3	2	2.9	1	7.7	—	—
Eye region	19	5.1	18	6.5	1	1.4	—	—	—	—
Eyelid	21	5.6	18	6.5	3	4.3	—	—	—	—
Temple	29	7.8	22	7.9	7	10.0	—	—	—	—
Nose	79	21.1	66	23.7	11	15.7	2	15.4	—	—
Cheek	51	13.6	38	13.7	10	14.3	2	15.4	1	7.7
Ear	38	10.2	22	7.9	13	18.6	2	15.4	1	7.7
Chin	2	0.5	2	0.7	—	—	—	—	—	—
Neck	9	2.4	8	2.9	1	1.4	—	—	—	—
Trunk	49	13.1	37	13.3	3	4.3	1	7.7	8	61.5
Upper extremities	23	6.2	5	1.8	11	15.7	4	30.8	3	23.1
Lower extremities	11	2.9	7	2.6	4	5.7	—	—	—	—
Other	3	0.8	—	—	2	2.8	1	7.6	—	—
Total	374	100.0	278	100.0	70	100.0	13	100.0	13	100.0
%		100.0		74.3		18.7		3.5		3.5

Disease lesions were most frequently localized on the face and hirsute skin of the head; this localization was found in 74.6% of all cases in the population studied; skin cancer was also localized on the trunk (13.1% of cases); on the upper extremities (6.2%) and on the lower extremities (2.9%) (Table 3, Fig. 2).

In order to obtain full characteristics of „cases” in the study, information was collected on the progress of the disease in particular patients, simultaneously with gathering data concerning histopathological traits of the diagnosed skin cancers. This information was obtained from 279 „cases”, i.e. from 74.6% of all subjects; among whom 189 persons (66.3%) noticed the symptoms of the disease on their bodies ca. one year before undergoing a specialist examination, while 90 persons, i.e. 33.7% asked for medical advice as early as several weeks after the first changes occurred on their skin.

Referents

In the study, two groups of referents were formed. The first comprised men from the general population living in the area from which patients with skin cancer came, and the other group consisted of pa-

tients from hospital departments and dermatological outpatient clinics of the same area who were being treated in the period analysed for dermatoses other than skin cancer.

Bearing in mind the fact that skin cancer is a disease characteristic of elderly persons, and that natural skin aging conducs to the inducement of this disease, age was accepted in the study as a very important trait causally related to the pathology analysed (1). Thus, referents were selected using the matched pairs method by the year of birth ± 2 years. In this way, the comparability of cases and referents in respect of the main risk factor of the disease became possible. Such a study unit consisted of two persons from each referent groups and 1 case of skin cancer, i.e. 1860 persons in total.

Data collection

In the study, the method used in order to collect data was an inquiry in the form of a questionnaire. The specially prepared questionnaire consisted of questions covering the history of occupation of a given examinee, including detailed information on every single job he had performed and every work-post, along with a description of activities, as well as an inquiry concerning occupational contact with any of several materials or agents listed on a special card which are considered to be a source of polycyclic aromatic hydrocarbons. An especially important task for the person interviewing the subjects was the gathering of data on the names and addresses of plants in which a given examinee was employed and on the duration of work (from-till) in each plant, in order to make later verification of the data possible. Other questions focused upon the estimation of extraoccupational factors inducing skin cancer, such as: exposure to solar and ultraviolet light and ionizing radiation, past diseases, immunosuppression therapy and genetic predispositions (determined by such phenotypes as colour of eyes, hair and skin). The survey was carried out in subject's homes by specially trained interviewers who, throughout the whole period of study, knew neither the aim of the undertaking, nor the status of particular persons in the structure of the population examined.

Prior to commencing the study, letters were sent to all persons classified as cases and referents. The letter, signed by the Director of the Institute of Occupational Medicine, was to motivate and encourage the potential examinees to participate in the study and also announced the visit of interviewers. The letters were mailed ten days before the planned beginning of the inquiry. The ten day period was meant to be a sounding period of the situation, so that an estimation of the actual



attainment of the population studied and the attitude of the examinees towards this sort of study could be obtained. In the case of persons from either of the referents groups, each return of letters by post resulted in the selection of a different name from the reserve lists after the reasons for the inaccessibility of a given addressee had been analysed. On the other hand, it was impossible to do the same with cases, since the number of persons classified as „cases” was strictly limited. Therefore, the interviewers had not been informed about the return of letters from subjects in order not to „lose” any of them too soon.

The interviewers' task was to reach every person chosen by the organizers. Should any situation occur which would not permit the interview of a given examinee, the information was to be provided by relations (wife, husband, children, brothers or sisters). Data on deceased persons were gained from relations using an abridged questionnaire. These data, however, were not included in the final analysis of the study.

Eventually, a complete inquiry was performed among 374 cases (72%) and 1496 referents. It was not possible to gather sufficient information from 146 patients suffering from skin cancer. The reasons were: deaths (60 persons), refusal to be interviewed (24 persons), incorrect address (35 persons) and the absence of an examinee at the permanent address resulting, most frequently, from a permanent departure.

Performing the questionnaire interview closed the stage which comprised the designing and organizing phases and the actual inquiry. In the case-referent study, these elements play an extremely important role as they determine the estimation of results obtained.

In order to close the whole of the study, it is necessary to continue work on the verification of data on exposure and to elaborate results, which will be the subject matter of following publications.

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