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CANCER MORTALITY AMONG MALE WORKERS IN THE POLISH RUBBER INDUSTRY

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Abstract. The rubber industry, acknowledged by the International Agency for Research on Cancer (IARC) to be a cancer risk technology is, because of difficulty in identifying causal factors, the subject of intensive epidemiological studies in many countries. In the presented study, cancer risk in the rubber industry was evaluated on the basis of long-term observation (1945–1985) of a cohort of 6978 male workers employed in a rubber goods factory, predominantly engaged in producing rubber footwear. The reference group was the general male population of Poland. Standardized mortality ratios (SMRs), calculated by means of the person-years method, were used in the evaluation of death risk. The observation of a whole cohort indicated an excess of cancer, in general (approx 12%), lung cancer (approx 40%) and gallbladder cancer (approx fourfold). In the subcohorts, distinguished according to peculiarities of individual production sections, cancer risk of the large intestine and larynx was significantly increased. The highest cancer risk was found in compounding, mixing, milling and vulcanizing sections. Hence, β-naphthylamine, benzidine and solvents (benzene) were used in technological processes in the past, bladder cancer and leukemia were considered as most specific for the rubber industry. In the cohort observed, the risk of death from bladder cancer was significantly increased only in those who had been employed during the years 1945–1953, namely during the period when β-naphthylamine was in use. No excess of deaths from leukemia was observed.

INTRODUCTION

The rubber industry is a typical example of working conditions which are particularly strenuous. There are two basic characteristics of this industry: the wide use of a large number of chemical substances, and the generation of compounds of chemical structures not yet fully recognised. They are present during technological processes in the form of dusts, vapours, gases and curing fumes, especially in higher temperatures.

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A significant excess of bladder cancer found in rubber workers by Case and Hosker during the 1950's (3) stirred up interest in the carcinogens occurring in this industry. The excess of bladder cancer resulted from exposure to carcinogenic aromatic amines and especially to α-naphthylamine and β-naphthylamine used at that time in rubber production. An increased risk of leukemia in workers employed in the rubber industry, found during the 1970's, was related to exposure to solvents, mainly benzene (4, 15, 22). As various epidemiological studies indicated an excess of bladder cancer and leukemia in rubber workers and its relationship with exposure to given carcinogens, they have been recognised as occupational cancers typical for this industry (12).

The cohort studies did not identify any excess of bladder cancer or leukemia in rubber workers after the industry had discontinued use of α- and β-naphthylamine, benzidine and benzene. However, in the majority of cohorts observed, a significantly higher cancer risk of different sites was found. These observations suggest that other carcinogenic agents occur in the working environment.

Processes in the rubber production involve hundrends of chemical compounds. Natural, synthetic, styrene-butadiene and chloroprene rubbers are used. Carbon black or silica (white compound) are applied as fillers and other raw materials are added which, according to recipes, enter into the composition of the rubber mix: anti-aging agents (antioxidants, p-phenyldiamine derivatives, amine and phenol compounds), vulcanization activators and accelerators, mainly I-III amines and their derivatives (potential N-nitrosamine precursors, retardants). During this stage of production, the highest concentrations of dusts, especially carbon black, are observed. During the next stage (extruding and milling of the rubber mix) which requires higher temperatures, vapours, gases and new substances (nitrosamine) are produced. During further stages (extruding, mixing and moulding of ingredients) plastifisers and softeners (oils, resins, coal and wood tars) are added. These processes take place also in higher temperatures. Sulphur and its compounds are common vulcanizing agents. During the vulcanizing process, carried on in temperatures of 100–200 C°, various compounds whose chemical composition is not fully recognised, are released. Among the compounds applied in rubber factories as additives in different periods and proved to be carcinogenic, are aromatic amines (α- and β-naphthylamine, 4-aminodiphenyl, benzidine), benzene, mineral oils, carbon black, asbestos; styrene, acrylonitrile, nitrosamines, formaldehyde and carbon tetrachloride are still suspected compounds.

METHODS AND MATERIALS

In order to evaluate cancer mortality risk in workers exposed to harmful factors in the rubber industry, a cohort employed in one of the rubber goods factory, predominantly engaged in producing rubber footwear, was observed. The cohort consisted of 6978 male workers employed for a period of at least three months during the years 1945–1973. The entry of each worker consisted

of his dates of entering and leaving employment in the factory, section and working post, as well as kind and concentration of harmful factors indirectly estimated. In the case of death, date and cause of death were identified. Persons from the cohort were followed up until December 31, 1985. The accessibility in the cohort reached 90%. Standardized mortality ratios (SMRs) calculated by means of the person-years method on the basis of the reference population, namely the general male population of Poland, were used in the risk evaluation. The Poisson distribution was applied in order to determine the significance of the ratio. Methods, characteristics of the group under study, and general mortality were presented in a separate publication (21).

The so called "cancer latency", defined for this kind of epidemiological study as the period between entering employment with exposure to harmful factors and death from malignant neoplasm, was analysed in this study.

RESULTS

Cancer risk

In the male cohort observed during the years 1945–1985, altogether 299 deaths from neoplasms were registered. The mortality risk was significantly higher than in the general population; SMR = 112.7 (Table 1).

TABLE 1. Cancer mortality among rubber male workers employed during the years 1945–1973.

Cause of death (according to Ninth ISCDICD)	Number observed	Number expected	SMR
Neoplasms (140–208)	299	265.3	112.7*
Tangue (141)	2	0.9	218.6
Oesophagus (150)	9	7.9	114.3
Stomach (151)	57	63.9	89.2
Large intestine (153)	11	6.7	164.7
Rectum (154)	8	8.2	97.2
Liver (155)	11	12.2	89.8
Gallblader (156)	12	2.7	443.9**
Pancreas (157)	13	8.8	147.2
Larynx (161)	13	7.4	176.5
Trachea, bronchus and lung (162)	101	70.0	144.2**
Thymus, heart and mediastinum (164)	1	1.5	65.7
Bone and articular cartilage (170)	2	2.7	74.6
Melanocarcinoma (172)	1	1.3	78.8
Other malignant neoplasms of skin (173)	1	1.5	66.6
Masculine mamma (175)	1	0.2	420.9
Prostate (185)	9	9.6	93.5
Penis and other male genital organs (187)	1	0.7	149.1
Bladder (188)	10	8.4	119.0
Kidney and other urinary organs (189)	6	4.6	130.1
Eye (190)	2	0.3	630.9
Brain (191)	7	5.5	127.8
Lymphatic and haematopoietic tissue (200–208)	7	14.2	49.2

a) Table does not include as separate items 14 deaths from neoplasms of undefined sites
* $p < 0.05$
** $p < 0.01$

TABLE 2. Standardized mortality ratio due to selected cancers by duration of exposure, age at first employment and department.

Specification	Cancer					
	Total	Lung	Larynx	Large intestine	Gall-bladder	Pancreas
Age at first employment						
below 40 years	115.0 (157)	152.7** (55)	147.5 (6)	175.6 (6)	317.4 (4)	171.2 (8)
above 40 years	110.3 (142)	135.2 (46)	213.7 (7)	153.3 (5)	554.3** (8)	120.2 (5)
Departments of highest cancer risk						
directly engaged in production	117.0* (189)	150.2** (64)	155.9 (7)	270.4** (11)	304.7 (5)	111.5 (6)
mixroom, millroom and vulcanization workshop	138.8* (73)	193.2** (27)	–	226.8 (3)	556.3* (3)	171.0 (3)
lacquering, product building and automatic operation workshops	114.3 (41)	125.9 (12)	590.9* (6)	222.7 (2)	–	–

Note: in parantheses there is number of deaths observed
*$p < 0.05$
**$p < 0.01$

TABLE 3. Periods of significantly increased risk of death from cancer according to the site.

Cancer	Number of years since entering employment (period of latency)	Number of deaths	SMR
Total	20–29	109	126.4*
Digestive organs and peritoneum (150–159)	10–24	74	141.5**
Gallbladder (156)	5–	12	470.6**
Pancreas (157)	15–29	10	238.1*
Lung (162)	20–	67	178.5**

*$p < 0.05$
**$p < 0.01$

The analysis of mortality according to places of employment indicated excess of deaths from neoplasms in sections directly engaged in production by approx 17% and in mix, mill and vulcanization workshops, by approx 40% (Table 2). An increased risk was most evident in the period of 20–29 years after entering the industry (Table 3).

Lung cancer

The analysis of lung cancer mortality showed a statistically significant excess in the whole cohort of 44% and of 50% in the subcohort of workers engaged directly in production (Table 1). Among 18 production sections, lung cancer risk was doubled in mixing, mill and vulcanization workshops (SMR = 193.2). Age at entering employment with exposure to harmful factors was important for the value of lung cancer death risk: in persons entering the industry below 40 years of age, risk was significantly increased; SMR = 152.7 (Table 2).

A significant excess of the cancer mortality rate was observed in the cohort 20 years after the first exposure (Table 3).

Larynx cancer

In the cohort observed, 13 deaths from larynx cancer were registered. A considerable excess of larynx cancer was noted in workers employed in lacquering and automatic operation workshops where six deaths were registered. The larynx cancer death risk was almost six times higher in these workshops than in the reference population.

Cancer of the large intestine

All 11 cases of death from cancer of the large intestine were registered in workers directly engaged in the production. The risk of death from large intestine cancer was over 2.5 times higher in production sections than in the general population. An especially high risk was found in the workshop where rubber footwear was moulded (SMR = 802.7).

Bladder cancer

Risk of death from bladder cancer was over four times higher in the cohort than in the general population (Table 1). In mix, mill and vulcanization workshops the mortality excess was five times higher. A significantly increased risk referred to male workers who had entered the rubber industry in the age below 40 years; SMR = 554.3 (Table 2).

Cancer of the pancreas

Among 13 deaths from cancer of the pancreas, there were 9 deaths of males employed short-term. In this group, risk was over twice as high.

Increased cancer mortality was observed in the whole cohort in the period 15–29 years after entering employment with exposure (Table 3).

Cancer of the urinary bladder

In the whole cohort 10 deaths from cancer of the urinary bladder were registered including 6 deaths among workers employed in sections directly engaged in production. The risk in the whole cohort was not significantly increased (Table 1). A significant, 2.5 times excess of mortality from cancer of the urinary bladder (SMR = 276.2; 6 deaths) was observed in the subcohort employed during the years 1945–1953. The latency period was 23 years, on average, and it was, in fact, the same in the groups of workers entering employment in the industry in both younger and more advanced age (Table 3).

Leukemia

Seven deaths from leukemia were registered in the whole cohort including 6 deaths in the group directly engaged in production (SMR = 68.5). In the mill room, where the largest number of deaths was found, the risk was higher by approx 50% than in the reference population (SMR = 147.3), however, four deaths observed did not increase the risk significantly.

DISCUSSION

Table 4 displays sites of malignant neoplasms which proved to be of a higher risk in the rubber industry according to the International Agency for Research on Cancer (12), and the levels of risk found in our own studies. Two sites of cancer, namely the larynx and gallbladder attracted our attention. They are not mentioned in the IARC monography but they showed a significant excess in the cohort under study. According to the analyses of cancer risk presented, thus far, in the literature, cancer of bile duct and gallbladder is rare and its excess has not been noted. A higher risk of this cancer was found in studies carried out by Delzell et al. (5, 6). Mancuso (13) devoted much of his attention to these sites and presented very extensive deliberations based on experimental, clinical and epidemiological data. In his work he turned attention to well known similarities between chemical structures of certain experimental nitrosamine carcinogens (e.g. dimethylonitrosamines) and natural components of gall as well as substances applied or produced in the rubber production processes. A fourfold or even a sixfold, in some subcohorts, increase of risk of bile duct and gallbladder cancer gives, in view of Mancuso's deliberations (13), the ground for a hypothesis on a cause–effect relationship between exposure to nitrosamines in the rubber industry and incidence of this cancer. However, this hypothesis could be verified only on the basis of a specially oriented investigation.

TABLE 4. Cancer of increased risk in rubber workers.

Location according to IARC (12)	Risk (SMR) according to own studies [1]).
Significant excess and sufficient evidence on its relationship to exposure	
urinary bladder	276.2 *
leukemia	351.2
Significant excess and limited evidence on its relationship to exposure	
stomach	210.0 *
lung	170.6 *
Limited evidence on relationship between excess and exposure	
large intestine	299.2 **
prostate	107.0
lymphomas	102.5
Insufficient evidence on relationship between excess and exposure	
pancreas	530.6 *
oesophagus	268.0
brain	127.8
thyroid	
larynx	590.9 **
gallbladder	622.8 **

[1] The column gives the highest SMR values identified according to the feature analysed
*$p < 0.05$
**$p < 0.01$

An increased risk of larynx cancer in the rubber industry was mentioned only by Gustavsson (9) but this did not refer to workers engaged directly in production. Risk of death from larynx cancer observed in the cohort was six times higher than in the general population and it referred to male workers employed in the lacquering workshop where exposure to solvents predominated. Solvents are substances which irritate the throat and larynx and produce inflammation, atrophy and hypertrophy of mucous membranes. There is a common view that these conditions increase risk of cancer. Exposure to irritating factors in association with intensive smoking in this group (an uncontrolled factor) seem to be a probable interpretation of this fact.

An excess of malignant neoplasm of urinary bladder, typical for the rubber industry in the period when aromatic amines (α- and β-naphthylamine, bensidine) were used, was confined to workers employed in this industry during the years 1945–1953. A similar observation was made in many cohorts engaged in rubber production (7, 10, 11, 16, 17).

There is sufficient evidence that leukemias are also related to exposure in the rubber industry where solvents, mainly benzene, are used (5, 6, 7, 9, 10, 14, 16, 17). An excess of leukemias was found in some sub-groups but it was insignificant.

Malignant neoplasm of the stomach in workers exposed to harmful factors in the rubber industry was excessive in many cohorts observed (2, 6, 7, 10, 14, 16, 20) however, the evidence on the relationship between exposure and excess was limited. This resulted from divergent data on exposure and production sections where the excess was noted. Our own investigations revealed a twofold excess of stomach cancer only in the lacquering and product-building workshops where exposure to solvents was quite considerable. Sorahan (20), following the model constructed by means of the logistic regression, related excess of stomach cancer with exposure to dust.

Lung cancer belongs to the group of neoplasms which show excess in the majority of cohorts employed in the rubber industry (1, 2, 7, 8, 11, 16, 17, 18, 19, 20). The highest risk of lung cancer was noted in mixing, milling and vulcanization sections. This corresponds with observations of other authors and it is related with the most unfavourable working conditions in these sections. Risk of lung, larynx and urinary bladder neoplasms is associated with smoking but because of the retrospective character of this factor it was not analysed.

In a number of epidemiological studies, excess of large intestine cancer was observed in groups directly engaged in production (1, 6, 14, 17). In the cohort observed, a threefold excess of cancer was also found in this group of workers but in the workshop of moulded rubber footwear the excess was higher by eight times.

An increased risk of pancreas cancer in the rubber industry was found in a few studies (11). Risk increased by five times was confined to those employed in calender and spreading operation workshops, and those who had entered the industry at an age below 40 years.

Excess of cancer in rubber workers, including cancer of the oesophagus (5, 20), brain (1, 16, 17), prostate (1) and lymphomas (17) has been reported in a few studies. In the cohort observed no significant excess of cancer in these sites was found.

To sum up, it sould be stressed that the results of observations indicated a significantly increased risk of cancer of the lung, large intestine and bile duct and in some sections of the larynx and pancreas, however, identification of a causal factor in working conditions is very difficult in this industry because of the peculiarity of technological processes and retrospective character of the study.

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