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Summary of Data Reported and Evaluation

[The rubber industry](#)

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THE RUBBER INDUSTRY

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5. Summary of Data Reported and Evaluation

5.1 Summary

Because of the diversity and changeability of exposures within the rubber industry, the multiple exposures experienced by many workers within the industry, and the lack of historical industrial hygiene data, most epidemiological studies of cancer in rubber workers have not been exposure-specific or have used job categories as a substitute for exposure categories. In some studies no attempt was made to subdivide factory populations.

The difficulty of identifying etiological factors in cancer causation is compounded by the need to estimate exposures that occurred several decades ago in relation to cancer occurring currently, and by frequent incongruities between the boundaries of process-defined jobs and the actual exposure to agents of interest. A further difficulty arises from the frequent lack of information about non-occupational risk factors for cancer, such as smoking and diet, which may vary among occupational subgroups of rubber workers. Such internal differences are less likely to exist, however, than are differences between populations of rubber workers and comparison populations.

When cancer excesses have been related with some consistency to specific jobs within the rubber industry, the available industrial hygiene data on the agent to which cases were probably exposed, together with evidence of any toxicological effects of those agents, assist in evaluating the etiological plausibility of the epidemiological finding.

Cancer of the urinary bladder, clearly excessive in British rubber workers employed before 1950, particularly those in jobs likely to entail exposure to aromatic amines, seems not be increased in employees who entered since that date. No clear evidence exists for a comparable bladder cancer excess in US rubber workers. Although based on small numbers, there is some evidence that an excess of bladder cancer was present in rubber workers in other countries where such studies were carried out. While the withdrawal in 1949 of certain antioxidants containing 2-naphthylamine from the UK rubber industry seems likely to have accounted substantially for the subsequent decline in bladder cancer there, a more general awareness of the carcinogenic potential of some aromatic amines, and general improvements in industrial hygiene practices, may also have contributed.

Among US rubber workers, excess malignancies of the lymphatic and haematopoietic systems, particularly lymphatic leukaemia, have been associated with jobs entailing exposure to solvents. Benzene, considered to be a human carcinogen, was once used as a solvent within the rubber industry and may still be present as a contaminant of other organic solvents.

Stomach cancer, consistently elevated in studies of US and British rubber workers, appears to be associated with jobs early in the production line, including compounding and mixing, milling and extrusion.

Lung cancer is positively related to a variety of jobs within the rubber industry. Attribution to specific factors in the workers' environment cannot be made.

Mortality from prostatic cancer was found to be moderately elevated in several studies, and some association was found with compounding and mixing jobs. In general, the etiology of prostatic cancer is not understood. The only occupational risk factor suggested to date is cadmium; compounds of cadmium are occasionally included in a rubber batch.

The lack of consistent associations between specific jobs and cancer of the large intestine does not permit a causal relationship to be inferred.

Isolated or small excesses of some other cancers (e.g., thyroid, oesophagus, brain, skin and pancreas) do not yet justify the drawing of etiological inferences. However, some toxicological and epidemiological information suggests possible mechanisms for the causation of cancers at certain sites. The strong association of skin cancer with tyre building, in the one incident study done to date, raises the possibility that skin carcinogenesis occurs *via* contact with mineral extender oils in the uncured rubber. Experimental evidence in animals that ethylenethiourea is carcinogenic for the thyroid should be noted. So also should suggestions, from epidemiological studies, of excesses of cancers of the brain and pancreas in workers in the petrochemical industry.

Many materials that occur in the work atmosphere in rubber factories are experimental mutagens or carcinogens; these include mineral oils, carbon black (extracts), curing fumes, some monomers, solvents, nitroso compounds and aromatic amines, thiurams and dithiocarbamate compounds, ethylenethiourea, di(2-ethylhexyl) phthalate, di(2-ethylhexyl) adipate and hydrogen peroxide. However, experimental toxicological information on chemicals that are used or formed is restricted to a small fraction of all chemicals used: most compounds have not been investigated for their possible mutagenic or carcinogenic effects. Studies with exposure indicators, such as mutagenic activity in urine, thioether excretion and sister chromatid exchange, point to the possibility that rubber workers are exposed to mutagens.

The combination of chemical exposures that occurs in the rubber industry is probably more relevant to the cancer pattern observed than are single compounds or groups of compounds. The variety of exposures increases the likelihood that there are interactive effects between two or more such agents, and, in turn, that there is interaction with non-occupational factors.

5.2 Evaluation

The Working Group examined the combined evidence from epidemiological data about the extent and distribution of cancer within the rubber industry and from relevant industrial hygiene and toxicological information to evaluate the carcinogenic risks within the rubber industry. The evaluation has been made in terms of the three degrees of evidence prescribed for this *Monograph* series - sufficient, limited, inadequate.

Primary consideration was given to the quality of the epidemiological research, and to the strength and consistency of the reported cancer associations within the industry. In further evaluating the likelihood of an occupational causation for these cancer excesses, judgements were made about the types of exposures experienced by groups of workers, and the evidence that such exposures have carcinogenic effects.

The Working Group thus made the following assessment: (Listing does not imply that cancer hazard is universal in all rubber factories in all countries, nor that the degree of evidence applies to all situations.)

Strength of evidence	Type of cancer	Presumed agent or job category
<i>Sufficient</i> for excess occurrence in rubber workers and for causal association with occupational exposures	Bladder Leukaemia	Aromatic amines Solvents
<i>Sufficient</i> for excess occurrence in rubber workers; and <i>limited</i> for causal association with occupational exposures	Stomach Lung	Compounding, mixing and milling Various

<i>Limited</i> for excess occurrence in rubber workers and for causal association with occupational exposures	Skin	Tyre building
<i>Limited</i> for excess occurrence in rubber workers; and <i>inadequate</i> for causal association with occupational exposures	Colon Prostate Lymphoma	
<i>Inadequate</i> for excess occurrence in rubber workers and for causal association with occupational exposures	Brain Thyroid Pancreas Oesophagus	

For definition of the italicized terms, see [Preamble Evaluation](#).

Subsequent evaluation: [Suppl. 7 \(1987\)](#)

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