Mortality Among Rubber Workers: Relationship to Specific Jobs

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In an earlier article, the nine year mortality experience of a population of 6678 male rubber workers, during 1964-72, was described.[1] As a group, these active or retired production workers, from a single large tire-manufacturing plant in Akron, Ohio, experienced death rates from various specific causes of death that differed noticeably from those prevailing within the national male population. In particular, excess mortality occurred from cancers of the stomach, colon, prostate, and lymphatic and hematopoietic system, as well as from diabetes mellitus, arteriosclerosis, and (in the 40-54 age-range) ischemic heart disease and stroke. The question immediately arises: are these mortality excesses related to specific jobs within the rubber industry?

The rubber-tire manufacturing industry uses a vast and ever-changing variety of organic and inorganic chemicals. Further, because of the high temperatures involved in several of the processes, there are many chemical reaction by-products produced, most of which remain unidentified. Among the chemical ingredients now or previously used are various proven or suspected carcinogens, such as beta-naphthylamine, benzene, asbestos (in talc dust), and various nitrosamines.

The primary focus of this article is the analysis of the association between excess mortality and specific jobs within this same plant. These analyses have been carried out for specific causes of death observed to be in excess in the study population, and also for two causes reported to have been in excess in earlier studies of the rubber industry (bladder cancer and lung cancer).[2 3 4] The cases studied here come from deaths in the ten year period 1964-73.

The identification of the study population, and its mortality experience, has been described in detail.[2] Thirty-eight percent of the population was aged 40-54 at 1/1/64, 30% was aged 55-64, and 32% was aged 65-84. Eighty-six percent were white males, and 14% were black males. Forty-eight percent began work in the plant at least twenty-five years before 1964, and all but 1% had worked for at least ten years by 1964.

The Figure summarizes the 1964-73 mortality experience of the total study population, presenting age-race-standardized mortality ratios (SMR). These ratios were calculated by comparison with the 1968 U.S. male population mortality. This particular comparison of a working population with the general community may introduce a conservative bias, resulting in some underestimation of the mortality attributable to occupational factors. However, this selection bias, known as the "healthy worker effect", usually applies less to cancer than to other causes of death.

The equivalent mortality analysis within a second, smaller population of 1339 male rubber workers, during 1964-73 from another tire-manufacturing plant in Akron, also identified mortality ex-

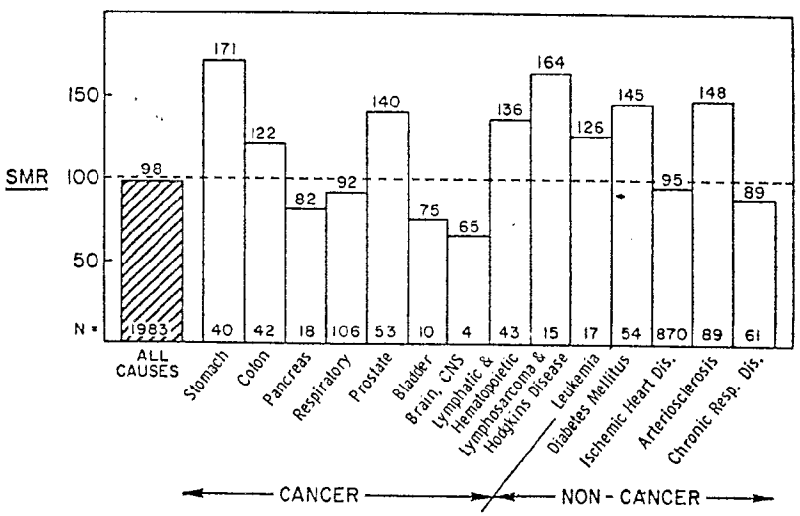


Fig 1. — Standardized Mortality Ratios[1] in population of 6,678 Male Rubber Workers, 1964-73, Ages 40-84. Expected deaths were calculated using 1968 U.S. race-age-specific death rates.

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cesses from the two cancers most elevated (figure). Within this second population, the SMR for stomach cancer was 119, and the SMR for cancers of the lymphatic and hematopoietic system was 176. Relative to the all-causes SMR of 82, excesses were again also observed from deaths due to diabetes mellitus (SMR equals 102) and arteriosclerosis (SMR equals 145).

To check whether any of these apparent cancer mortality excesses merely reflected local or regional mortality excesses, the national death rates were compared with the rates for the state of Ohio and those of Summit County (which includes Akron). The figures, available only for 1950-69, are presented in Table 1.[5] While the Summit County rates tend to have been higher than the state or national rates, these differences are not greater than could be accounted for by the estimated 20% of male Summit County deaths contributed by active, terminated and retired rubber workers during that period.

Table 1. — Average Annual Age-Adjusted Cancer Mortality Rates (per 100,000), White Males, 1950-69: Comparison of Summit County Rates With State and National Rates.

Cancer Site	United States	State of Ohio	Summit County, Ohio (includes Akron)
All Malignant Neoplasms	174.0	178.4	185.5
Stomach	15.2	15.1	16.2
Colon	16.5	18.6	19.6
Rectum	7.7	8.3	7.9
Pancreas	9.6	8.9	10.4
Respiratory	38.0	38.1	39.0
Prostate	17.8	18.9	19.8
Bladder and other urinary organs	6.8	6.9	8.0
Brain and central nervous system	4.4	4.6	5.4
Hodgkin's disease	2.3	2.4	2.2
Lymphosarcoma, reticulosarçoma, other lymphoma	4.9	5.1	6.8
Multiple myeloma	1.8	1.7	2.0
Leukemia and aleukemia	8.8	8.9	9.3

Source: Mason, T.J., McKay, F.W. U.S. Cancer Mortality by County: 1950-69.[5]

Methods

The rubber industry working environment is very diverse in its physical and chemical exposures. Further, an individual rubber worker typically spends time in 15-20 different jobs during his working career, often embracing a number of quite different work areas within the plant. A summary description of the major work areas is presented in Table 2. Note that the first eleven categories are listed in the order they occur on the production line.

In order to take account of the complete exposure experience of the individual worker, detailed work histories were obtained from the plant personnel office. Because of the several hundred different jobs within the plant, and their changing nomenclature and numbering with time, it was necessary to develop a job classification system that would be of general utility in epidemiologic studies of both the exploratory and hypothesis-testing kind.

Objective criteria were therefore specified by the research group's industrial hygienists, for the grouping of jobs into "Occupational Titles" (OT). Each OT contains functionally similar jobs that entail working with similar materials and processes. Sixty OT's were required, to embrace all present and past jobs at this particular plant, and these OT's were therefore used in classifying the contents of the work-histories in this study. OT codes were assigned blind to all jobs listed on each work-history, without knowledge of the vital status of the study subject. A detailed discussion of this job classification appears elsewhere in this issue.

Because of the high costs and time delays involved in the collection, coding, and data-preparation of detailed work-histories, a study design was used that required work-histories for only a minority (about one quarter) of the study population. This design enabled each case group of interest (e.g. stomach cancer deaths) to be compared to a sample of the total study population for differences in work-histories. Once this initial "case-control" comparison had identified differences between the cases and the population sample, in frequency and duration of employment within specific job categories, the design then enabled an estimate to be made, in cohort analysis fashion, of the risk ratio associated with that particular job category. The rationale and theoretic statistical basis for this hybrid (ambidirectional) study design, and its risk estimates, have been discussed by Kupper et al.[6]

Potential confounding factors in this study (i.e. risk indicators of the cause of death under investigation, that are also likely to be associated with the kind of job done within the rubber industry) were sex, age and race. Sex was controlled by restriction of the study to male workers; age by age-stratification and age-adjustment procedures; and race by subsequent review of the data. This latter approach was necessary because information on race was not initially available on much of the study population, at the time of sampling. Smoking, known as a risk indicator for cancers of the lung and bladder, and for chronic cardiovascular disease, was not an obvious confounding factor, since recent cross-sectional studies in two other tire-manufacturing plants have demonstrated no strong association of smoking habits with job category. Unfortunately, satisfactory retrospective information on smoking habits was not available for study subjects in this present study.

Using the sample size formulae of Kupper et al.,[6] applied to predicted exposure frequencies and mortality effects, sampling fractions of 9%, 13%, and 14% were indicated for the three age strata in the study population (40-54, 55-64, 65-84). As both a precautionary measure against erroneous predictions of exposure frequency, and knowing that the sample would be used for multiple comparisons, the actual sampling fractions used were 20%, 25%, and 23% (representing 500 in each age stratum). Com-

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plete work-histories were subsequently obtained for 1482 (99%) of this age-stratified random sample.

In the initial case-control comparisons, the OT's were grouped, a priori, into 16 broader groups of similar jobs, known as Occupational Title Groups (OTG) (Table 2). Frequency and duration of employment within these sixteen OTG's (henceforth referred to as "exposure rates", to accord with conventional epidemiologic terminology) were then calculated for each study subject. The exposure rates in each case group were age-adjusted (by the direct method) to the age-distribution of the population sample, thereby ensuring mutual comparability of the adjusted rates in each case group.

In the analysis of exposure rates, certain criteria were stipulated with respect to time and duration of exposure. Firstly, cumulative exposures of less than two years to an OTG were excluded from this analysis. (In view of the chronic and complex etiology of the causes of death under investigation, this criterion might forfeit some relevant exposure data; yet preliminary analyses indicated that this criterion was desirable since it eliminates considerable "noise" from the work-history data due to the many instances of brief job tenure.) Secondly, in the analyses of cancer deaths, discussion is here restricted to exposures that occurred during the presumed etiologic period, 1940-60. Current information indicates that for environmentally-induced cancers in adults, in general, the average latency period between first exposure and disease diagnosis is in the range 10-30 years.[7] The 1940-60 stipulation means that for the "average" death in this study (occurring in 1968), the period between first exposure and death could range from 8 to 29 years. Analyses of exposures outside the 1940-60 period showed that in no instance did the strength of association of cancer with an OTG exceed those presented below.

Results and Discussion

Table 3 presents, for the seven cancer case groups, the ratios of their age-adjusted OTG-exposure rates to the rates within the population sample. These ratios provide a convenient preliminary measure of association between cancer type and OTG. Since the proportions of the population sample exposed to any one OTG are low (typically 5-15%), hence the ratios presented in Table 3 are an approximation for the more conventional odds ratio, which in turn is an approximation for the risk ratio.[8] Thus, the ratios in Table 3 provide a useful, age-adjusted approximation of the increased risk of death from a specific

Table 2. — Summary Description of Major Work Areas (Occupational Title Groups).

1. Receiving & Shipping
Receiving unloads and stores all incoming ingredients that go into making the final product, e.g. carbon black, pigments, rubber, etc. Shipping stores and loads the final product (e.g. tires) into trucks or boxcars.

2. Compounding & Mixing, Cutting & Milling; Cement Mixing
Raw ingredients (rubber, fillers, oils, pigments) are weighed and mixed together in a banbury (BB) mixer. Environmental exposure to particulates (e.g. carbon black, accelerators, antioxidants, talc) is high. Cements are solvents such as paraffin HC (e.g. hexane), aromatic hydrocarbons (e.g. toluene, xylene), chlorinated HC (e.g. CC14, trichloroethylene), ketones (e.g. methyl ethyl ketone).

3. Mill-mixing; Service to Batch Preparation
Mill mixing is a largely superseded mixing process. Service jobs are for the Compounding and Mixing Operations. Environmental exposures are similar to Compounding and Mixing.

4. Milling
Rubber mix from BB is processed further under heat and pressure, till rubber is in a soft, plastic state. This is probably the first work area where there is substantial exposure to reaction products.

5. Calender, Plystock Handling
The rubber stock from the mill is rolled out into a sheet of controlled thickness, usually covering a fabric. The calender stock (plystock) is then cut and spliced for use in building the ply of the tire. There is some exposure to reaction products and solvents.

6. Tuber (extrusion), tread cementing
Rubber stock from a mill is forced through a die forming a tread or tube. The tread is cut in appropriate lengths and cemented with solvents on the cut end so as to be tacky.

7. Tire Building, Bead Building
Beads are rubber and fabric covered wire that in a finished tire rest on the rim of the wheel. The treads, beads and plystock are used to build the tire. The major exposures is to solvents.

8. Green tire inspection, Paint & Line
The green (uncured) tire is inspected and repaired, and sprayed with solvents or lined with talc so it will not stick in the curing mold. Solvents, and in some cases, talc are the major environmental exposures.

9. Tube & Flap Building, Valves
The tube from the extruder is cut, valves attached, the inside of the tube coated with talc and then spliced together. The major environmental exposure is to talc. Valve making involves adding a rubber patch to the valve. The rubber is cured, buffed, and sprayed with solvent to make it tacky.

10. Curing
The green uncured product (tire, tube) is cured under heat and pressure. The major environmental exposure is to reaction products, and, in tube curing, to talc also.

11. Inspection, Finishing, Repair
The cured product is inspected (repaired if necessary) and made ready for shipping (finishing). Environmental exposures are mostly in repairing (solvents, rubber dust).

12. Maintenance
This job group includes mechanics, pipefitters, electricians, welders, painters, carpenters.

13. Mechanical & Special Products
A variety of products and jobs are included in this group, most of them similar to machine-shop types of exposures.

14. Reclaim Operations
Scrap vulcanized rubber products are shredded, ground up, and "devulcanized". By the application of heat and chemicals, the rubber compound is restored to its original plastic state. Exposures are to particulates and chemicals.

15. Synthetic Plant
This is essentially a chemical plant making elastomers that approximate one or more of the properties of natural rubber. SBR (Styrenebutadiene) is the most important synthetic rubber. Others include neoprene, nitrile; ethylene-propylene-diene, etc. Exposures are to the gases or liquids that are the ingredients for the particular synthetic rubber being made.

16. Janitoring, Trucking, Power Plant, etc.
This is a miscellaneous group with a variety of different jobs and exposures.

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Table 3. — Ratios of age-adjusted* rates of exposure, during 1940-60, to specific work areas: Cancer case groups compared to study population sample.

Study Group	Population Sample†		Stomach‡		Colorectal		Respiratory		Prostate		Bladder		Lymphatic & Hematopoietic		Lymphatic Leukemia	
ICDA (8th Revision) Code	—		151		153-4		160-63		185		188		200-9		204	
Number of Cases	1482		41		63		119		52		13		51		14	
Duration of Exposure (Years)	>2	>5	>2	>5	>2	>5	>2	>5	>2	>5	>2	>5	>2	>5	>2	>5
Occupational Title Group																
1. Receiving & shipping	6%	5%	1.3	1.6	.5	.6	1.9	1.8	.6	.7	2.8	1.0	1.4	1.7	1.2	0.0
2. Compounding & mixing; cement mixing	9%	7%	1.4	1.9	.9	1.2	1.1	1.4	1.2	1.5	1.7	1.2	1.8	1.4	2.5	2.3
3. Mill-mixing; other batch preparation	4%	2%	1.0	2.0	.2	.4	1.4	2.1	.9	.4	0.0	0.0	1.8	0.0	0.0	0.0
4. Milling (refine, feed)	8%	6%	1.4	1.2	1.0	1.2	1.3	1.2	.5	.6	1.8	2.3	.8	1.0	.9	1.1
5. Calender, plystock handling	12%	8%	.9	.4	1.1	.6	.9	1.2	1.6	2.1	.8	0.0	.8	.6	1.9	1.8
6. Tubing (extrusion), tread cementing	6%	5%	2.7	2.2	2.1	2.1	1.2	1.3	1.1	.6	0.0	0.0	1.3	1.0	2.3	3.0
7. Tirebuilding, bead building	19%	16%	.9	.8	.8	.9	.6	.6	.6	.7	.3	.3	1.0	1.1	.4	.4
8. Green tire inspection, paint, line	3%	1%	2.7	0.0	0.0	0.0	.4	.5	.5	.7	0.0	0.0	.5	0.0	0.0	0.0
9. Tube and flap building, valves	3%	2%	2.9	1.7	0.0	0.0	1.1	1.1	.4	.5	0.0	0.0	.5	.8	0.0	0.0
10. Curing	15%	12%	1.3	1.4	.7	.7	.3	.6	.3	.3	.7	.8	1.0	1.1	0.0	0.0
11. Inspection, finishing, repair	9%	6%	1.8	1.7	1.2	1.4	.9	.7	1.0	1.2	1.0	1.3	1.4	1.9	3.1	3.2
12. Maintenance	11%	8%	1.1	.7	2.1	1.7	.9	.8	.2	.1	.8	0.0	.9	1.0	0.0	0.0
13. Mechanical & special products	26%	17%	.8	.5	1.3	1.1	.8	.7	.8	.7	0.7	1.0	.5	.3	.5	0.0
14. Reclaim operations	5%	4%	.3	.4	.7	.9	1.9	2.2	.5	.5	2.2	2.8	0.0	0.0	0.0	0.0
15. Synthetic plant	3%	2%	1.7	2.1	0.0	0.0	0.0	0.0	.3	.4	0.0	0.0	4.4	5.6	2.9	3.7
16. Janitoring, trucking, power plant, test driving	15%	11%	1.2	1.1	.8	.9	1.2	1.1	3.8	2.8	.3	.4	1.3	1.3	2.3	2.6

*The rate (proportion) of prior exposure to a specific OTG, for each case group, was age-adjusted directly to the age-distribution of the population sample.

†Column figures for the population sample are rates of exposure (rounded off). For example, 6% of the population sample had spent at least two years in the Receiving and Shipping OTG

‡Column figures for case groups are ratios of exposure rates (i.e. case group proportion: population sample proportion). Thus for OTG 1, 8% of stomach cancer cases had spent two years there, versus 6% of the population sample, giving a ratio of 1.3.

cause among workers with prior exposure to a particular OTG, compared to the other workers. (Comparison of Tables 3 and 5 illustrates this relationship, empirically.)

Two minimum exposure durations (2 and 5 years, during 1940-60) were used to detect underlying dose-response relationships. However, using these particular exposure criteria, the evidence for a general relationship of this kind is only modest — of those case-OTG combinations with at least one ratio greater than 2.0, 12 out of 20 show a higher ratio with the longer exposure duration.

For stomach cancer, there is an association with prior exposure to jobs in the first four OTG's — receiving and shipping, compounding and mixing, mill-mixing, and milling. As indicated in Table 2, these OTG's entail exposure to the dusts of dry ingredients (including organic and inorganic pigments, carbon black, and talc dust), and, in mill-mixing and milling, to the fumes and vapors produced by heating the newly-compounded rubber batch. Stomach cancer was also strongly associated with extrusion and tread cementing, as was also colorectal cancer. A moderate association existed with building tubes and flaps (talc dust exposure), curing (fumes), and inspection and repair (rubber dust and solvents). A strong association with history of employment in the synthetic plant was also observed, although the numbers exposed were small (2-3% of the population sample had worked there).

A stomach cancer mortality excess in rubber workers has been reported in other plant populations in the U.S., suggesting that there is indeed a real work-related hazard involved.[9,10] Two other studies have reported, respectively, an association with rubber "processing" (compounding, mixing, milling and calendering), and with compounding, milling, calendering, and tube and tire building.[10,11] The inhalation, and subsequent ingestion, of particulate matter is one possible mechanism of stomach cancer hazard contact in these work areas.

Colorectal cancers showed fewer associations with OTG's than did stomach cancer. Strong associations existed with extrusion and tread cementing, and, to a slightly lesser degree, with maintenance jobs. A moderate association with inspection and repair jobs was also observed. Weaker associations (for exposures greater than five years) with compounding-and-mixing and milling resemble those reported by Monson and Nakano.[10]

Lung cancer mortality showed a moderate association with each of the first six OTG's. These associations

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Table 4. — Ratios of age-adjusted* rates of exposure to specific work areas: non-cancer case groups compared to study population sample.

Study Group	Population Sample†			Ischemic Heart Disease‡ (aged 40-54)§			Diabetes Mellitus		
ICDA Code	—			410-413			440		
Number of Cases	1482			58			44		
Duration (Years)	> 2	> 2	> 5	> 2	> 2	> 5	> 2	> 2	> 5
Calendar Period	Ever	1940-60	1940-60	Ever	1940-60	1940-60	Ever	1940-60	1940-60
Occupational Title Group									
1. Receiving & shipping	9%	6%	5%	1.3	1.4	1.5	.6	1.0	1.2
2. Compounding & mixing cement mixing	11%	9%	7%	.6	.7	1.0	1.7	.8	.8
3. Mill-mixing other batch preparation	6%	4%	2%	.4	.3	.9	0.0	0.0	0.0
4. Milling (refine, feed)	10%	8%	6%	1.2	1.6	1.4	.8	.7	.9
5. Calender, plystock handling	16%	12%	8%	.8	1.1	.3	1.3	.6	.7
6. Tubing (extrusion), tread cementing	9%	6%	5%	1.6	2.9	3.1	1.2	.2	0.0
7. Tirebuilding, bead building	21%	19%	16%	.8	.9	.8	1.0	.6	.5
8. Green tire inspection, paint, line	6%	3%	1%	.8	.6	0.0	0.0	0.0	0.0
9 Tube and flap building, valves	4%	3%	2%	3.4	3.4	0.0	0.0	0.0	0.0
10. Curing	19%	15%	12%	1.2	1.2	1.0	.8	.8	1.0
11. Inspection, finishing, repair	14%	9%	6%	1.3	0.0	1.4	1.5	2.1	2.5
12 Maintenance	13%	11%	8%	1.2	1.4	1.7	.4	.4	.2
13. Mechanical & special products	29%	26%	17%	1.1	1.1	.9	1.3	1.4	1.4
14. Reclaim operations	6%	5%	4%	1.0	.9	1.0	.3	.4	6
15. Synthetic Plant	4%	3%	2%	2.5	3.0	2.9	0.0	0.0	0.0
16 Janitoring, trucking, power plant, test driving	22%	15%	11%	.6	.6	.4	2.2	3.0	3.5

*The rate (proportion) of prior exposure to a specific OTG, for each case group, was age adjusted directly to the age-distribution of the population sample.

‡Column figures for the population sample are rates of exposure (rounded off).

†Column figures for case groups are ratios of exposure rates (i.e. case group proportion: population sample proportion). Thus for OTG 1, 12% of ischemic heart disease cases had spent two years there, versus 9% of the population sample, giving a ratio of 1.3.

§Ratios are calculated for IHD deaths at age 40-54 only, where the significant mortality excess occurred.

tended to be stronger for the five-year minimum-duration exposure. This observation is consistent with the notion of a lung cancer hazard from prolonged exposure to dusts, fumes, and vapors. However, there was a negative association with exposure to the curing process — an unexpected finding, in view of recent reports of a lung cancer mortality excess among curing workers, both in the U.S. and Britain.[4 10 11] Nor was there any association with tire-building, as found by Mancuso.[11] There was, however, a strong association with the reclaim operation, entailing some exposures similar to those in the compounding, mixing, and milling OTG's.

A separate case-control study of lung cancer deaths within three other plants belonging to the same company has revealed an association of exposure to curing with lung cancer.[9] Twenty-five percent of 61 lung cancer cases had worked in curing, compared to 15% of their pair-matched (age, race, sex) controls. Further, the exposed cases had experienced more than twice the duration of employment in curing than that of the exposed controls.

Cancer of the prostate gland showed few positive associations, being strongly associated with the calendering and the janitoring-trucking OTG's, and moderately associated with compounding and mixing. This latter association is of interest since cadmium compounds are used as vulcanization (curing) accelerators. Cadmium has previously been found to be associated with prostate cancer.[12] The significance of the excess prostate cancer mortality is underscored by the finding that mortality from prostate cancer has been found to be elevated in three of four major U.S. rubber worker cohorts recently studied.[9]

Cancer of the bladder has long been recognized as a problem within the rubber industry.[3 13] The early cause was probably an organic antioxidant added to the rubber mix, beta-naphthylamine, although subsequent concern has focussed on alpha-naphthylamine, benzidine, and four-aminobiphenyl (xenylamine). Bladder cancer, in Table 3, is associated with three of the first four OTG's, where the possibility of contact with carcinogenic raw-ingredient chemicals and the vapors of reaction products is high. It is also of interest that associations with the receiving-shipping-and-warehouse group of jobs have previously been twice reported elsewhere.[10 14] A strong association also existed between bladder cancer and employment in the reclaim OTG. It should be noted, however, that the number of

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bladder cancer cases studied was only thirteen.

Cancers of the lymphatic and hematopoietic system were associated with five OTG's — receiving and shipping, compounding and mixing, inspection, finishing and repair, synthetic plant, and janitoring-and-trucking. Lymphatic leukemia, a subset of this group of cancers, was associated with four of these same five OTG's (minus receiving and shipping), and also with two others — calendering, and extrusion and tread cementing. A case-control study of lymphatic leukemia deaths, based predominantly on the fourteen cases analyzed here, has been reported earlier.[15] The main finding of that study was a strong association of lymphatic leukemia with a history of exposure to organic solvents (including benzene) within the rubber industry. The particular solvent-exposure jobs cited in that study included cement-mixing, calendering, tread-cementing, tire-building, and finishing and repair. These probably account for some of the associations observed in this present study.

Table 3 shows that lymphatic leukemia was also very strongly associated with working in the synthetic plant, and the ratios indicate that the remaining cancers in this group were even more strongly associated with this OTG. Although the other types of leukemia were found not to be associated with this OTG, there was a strong association of the lymphoma group (comprising predominantly lymphosarcoma and Hodgkin's disease) with this type of exposure. The association of lymphatic leukemia with the janitoring-trucking OTG is not readily explainable; however (and this could apply to prostate cancer also), workers with cancers that are not rapidly fatal, if remaining actively employed while in apparent disease remission or stabilization, could well have been transferred into this OTG for medical reasons.

Table 4 presents similar information for two non-cancer causes of death — ischemic heart disease, and diabetes mellitus. Since these chronic diseases are not regarded as having a formal "latency" period, a third category of exposure has been added to those used in Table 3 (viz. at least two years exposure at any time).

Deaths from ischemic heart disease, in the age-range 40-54, were associated particularly with a history of working in the extrusion and tread-cementing OTG, and in the synthetic plant. Moderate associations were observed with receiving and shipping, milling, and maintenance jobs. Since the deaths studied here were restricted to those in younger workers, it seems unlikely that any of these associations could be accounted for by selective transfer (self- or company-initiated) of men with chronic cardiovascular limitations. Deaths from diabetes mellitus were strongly associated with working in the inspection and repair OTG and the janitoring-trucking OTG. The latter association could result from selective transfer of less fit individuals. Although moderate dose-response trends exist, in Table 4, for these associations for ischemic heart disease and for diabetes mellitus, yet no ready explanations are apparent.

Since mortality rates within the U.S. male population, for many diseases, differ between whites and nonwhites, and since there have been differences in the types of jobs done by whites and nonwhites within the rubber industry, accordingly there is a possibility that some of the abovementioned associations are partially spurious. To determine the extent of confounding by race, Tables 3 and 4 (exposure duration greater than five years, during 1940-60) were recalculated for whites only. Fewer than 10% of the exposure ratios underwent any significant change when restricted to white males. Further, the majority of these 15 changes were in cells containing small numbers, pertaining to the

Table 5. — Age-standardized risk ratios (relative risk) for death from selected causes, among workers with at least five years exposure to a specific work area, during 1940-60, relative to all other workers.

Cause of Death	Occupational Title Group (& Number Code)	Risk Ratio: Point Estimate*	Risk Ratio: 99.9% Confidence Interval†
Stomach Cancer	Compounding, mixing, cement mixing (2)	2.0	1.6-2.9
	Mill-mixing (3)	2.0	1.3-4.0
	Extrusion, tread cementing (6)	2.3	1.7-3.6
	Synthetic plant (15)	2.2	1.4-4.3
Colorectal Cancer	Extrusion, tread cementing (6)	2.2	1.6-3.4
	Maintenance (12)	1.8	1.4-2.5
Respiratory Cancer	Receiving and shipping (1)	1.9	1.4-2.9
	Compounding, mixing, cement mixing (2)	1.4	1.1-2.0
	Mill-mixing (3)	2.1	1.4-4.3
	Extrusion, tread cementing (6)	1.4	1.0-2.1
	Reclaim (14)	2.3	1.6-3.9
Prostate Cancer	Compounding, mixing, cement mixing (2)	1.6	1.2-2.3
	Calendering (5)	2.4	1.9-3.3
	Janitoring, trucking, etc. (16)	3.5	2.8-4.6
Bladder Cancer	Compounding, mixing, cement mixing (2)	1.3	0.8-3.8
	Milling (4)	9.6	1.6-4.0
	Reclaim (14)	2.5	1.8-4.1
Lymphatic & Hematopoietic Cancer	Receiving & shipping (1)	1.8	1.3-2.7
	Compounding, mixing, cement mixing (2)	1.4	1.1-2.0
	Inspection, finishing, repair (11)	2.0	1.5-2.9
	Synthetic plant (15)	6.2	4.1-12.5
Lymphatic Leukemia	Compounding, mixing, cement mixing (2)	1.3	1.0-1.8
	Extrusion, tread cementing (6)	3.2	2.4-5.0
	Inspection, finishing, repair (11)	3.7	2.8-5.3
	Synthetic plant (15)	3.9	2.6-8.0
	Janitoring, trucking, etc. (16)	2.2	1.8-2.9
Ischemic Heart Disease	Receiving & shipping (1)	1.5	.9-3.9
	Milling (4)	1.4	.9-3.4
	Extrusion, tread cementing (6)	3.3	1.8-14.9
	Maintenance (12)	1.8	1.2-3.6
	Synthetic plant (15)	3.0	1.7-12.5
Diabetes Mellitus	Inspection, finishing, repair (11)	2.8	2.1-4.0
	Mechanical products (13)	1.5	1.3-1.9
	Janitoring, trucking, etc. (16)	4.3	3.4-5.6

*These risk ratio point estimates are conservative, since the "unexposed" comparison group includes workers exposed to other high-risk OTG's (for that same cause of death).

†The 99.9% confidence intervals are relatively small since the risk estimates apply only to this particular study population.[6]

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minority of OTG's with low exposure rates in the population sample and/or to the less frequent causes of death (e.g. bladder). Of the other six changes, two examples will illustrate possible race confounding.

In many of the sixteen OTG's, there are greater than twofold differences in the proportions of whites and blacks who worked there for at least five years. In particular, 3% of whites and 27% of blacks in the study population sample had worked in the compounding and mixing OTG. For lung cancer, the exposure ratio (in Table 3) for this OTG was 1.4, while it was 0.8 for whites only. For prostate cancer, these figures were 1.5 and 0.9, respectively. Both sets of figures indicate that, for blacks within this OTG, the ratios must be higher, and that the two ratios in Table 3 (1.4 and 1.5) are clearly influenced by the racial composition of the workforce in that work area.

Nevertheless, for true confounding to occur, it is necessary that the "background" disease frequency (discounting any occupational exposure effect upon the disease) should "naturally" differ between white and black rubber workers. Whether this difference exists is difficult to determine. Lilienfeld et al. report that, among U.S. males, 1959-61, the mortality ratio, for nonwhites compared to whites, is 0.98 for lung cancer, and 1.69 for prostate cancer.[16] However, these ratios are not controlled for race differences in socioeconomic class and occupation, and therefore may themselves be confounded by these two factors. Thus, whereas these two ratios from the general population suggest a likelihood of race confounding in the association of prostate cancer and the compounding and mixing OTG, and no such likelihood for lung cancer, yet within this particular occupational class of persons this likelihood of confounding could be quite different.

The other four major changes between ratios in Table 3, and for whites only, each indicated an increased risk for whites. The exposure ratios increased from 1.4 to 2.7 for lymphatic and hematopoietic cancers in compounding and mixing, from 0.9 to 1.4 and 1.2 to 2.0 for colorectal cancer and prostate cancer, respectively, in inspection, finishing, and repair, and from 0.9 to 1.5 for colorectal cancer in the maintenance OTG. However, for lymphatic and hematopoietic cancers and colorectal cancers, the mortality ratios for nonwhites compared to whites in the U.S. male population are 0.9 and 0.8, respectively, suggesting little likelihood of confounding.[16]

Overall, the problem of race confounding appears to be minimal within these data. However, additional race-specific mortality data are being collected at other similar plants, and it will then be possible to determine whether the several abovementioned differences in race-specific death rates associated with particular work areas are consistent across plants.

Table 5 presents risk ratios (relative risks) for combinations of cause of death and OTG, selected from Tables 3 and 4. Selection was based on the magnitude of the exposure ratio and its consistency across exposure duration-time categories. Point estimates and confidence intervals were calculated using the formulae discussed in Kupper et al.[6] Further, since multiple intervals were calculated, the confidence level for each interval was set at 99.9% (i.e. a one-in-thousand probability of the true parameter value lying outside the calculated interval), thus ensuring an overall α level (based on all 34 calculated intervals) of about 0.04.

With this level of statistical confidence, Table 5 indicates that, in all except five instances, the true value of the risk ratio within this particular population of rubber workers exceeds 1.0. That is, in each remaining instance, there was apparently a real increase in risk of death from the indicated cause following five or more years working exposure, during 1940-60, to the listed job category.

Summary

This study has examined the ten-year mortality in a single-plant population of 6678 male rubber workers, in terms of the association of specific causes of death with a history of having worked in certain categories of jobs within the rubber industry. The work-histories of individual study subjects were analyzed, in detail, for all workers dying of selected causes of death. Comparison was made with the work-histories of a 22% age-stratified random sample of the total population.

Age-adjusted exposure ratios (Tables 3 and 4) were calculated for all nine case groups in all 16 work areas, using differing exposure criteria (i.e. duration and calendar period). These ratios provide an approximation of the increased mortality risk associated with particular work areas. The risk ratios (with their associated confidence intervals), in Table 5, provide more rigorous estimates of these instances of increased mortality risk.

For each cause of death studied, there were statistically significant associations with several work areas. For the cancers, the strongest associations tended to be with work areas at the front end of the production line (especially compounding and mixing), where the likelihood of contact with dusts, chemical ingredients, and vapors containing the early reaction byproducts, is high. The reclaim operation and the synthetic plant were each associated with several cancers (respiratory and bladder, and stomach and lymphato-hematopoietic cancers, respectively). The lymphatic leukemias were associated with solvent-exposure areas, especially inspection, finishing, and repair.

Ischemic heart disease deaths, at ages 40-54, were strongly associated with having worked in extrusion and tread cementing, and in the synthetic plant. Deaths from diabetes mellitus were strongly associated with the janitoring-trucking category, and with jobs in the inspection, finishing and repair area.

These observed associations, calculated after controlling for the variables sex and age, were apparently not due to confounding by smoking and race differences between work areas. The role of selective transfer of sick individuals (into, say janitoring or trucking) warrants further investigation. However, this mechanism is unlikely to be involved in the great majority of the observed associations. Another possible source of spurious inferences of increased risk would be correlation, within work-histories, between two job categories, one of which actually involved increased risk, while the other did not. Such associations could occur if certain job sequence trends existed within this working population. (Preliminary analyses indicate that this likelihood is not great; however, further analysis is planned.)

Detailed study of specific environmental agents, historically and cross-sectionally, is currently underway, in an attempt to identify the work-environment agents responsible for the associations reported here.

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