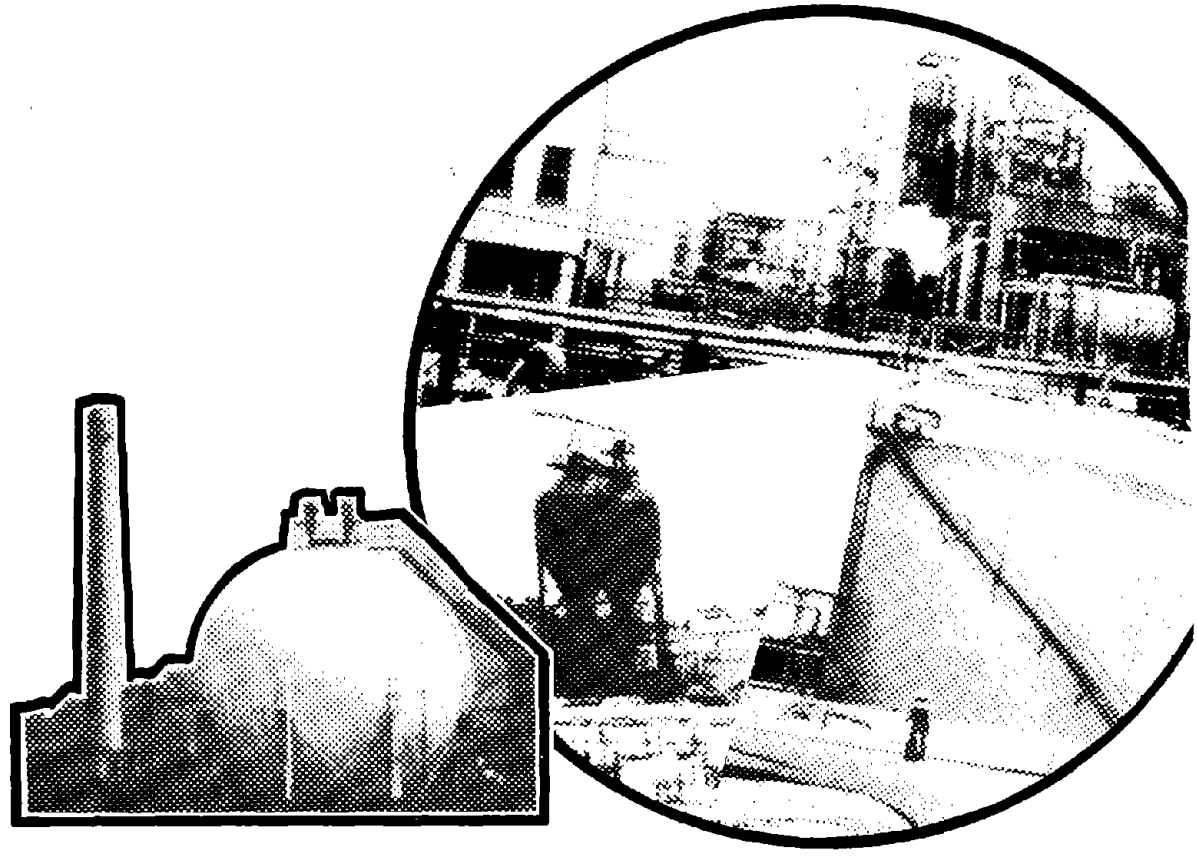
Proceedings of

NIOSH

STYRENE-BUTADIENE BRIEFING



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Proceedings of

NIOSH
STYRENE-BUTADIENE BRIEFING

Covington, Kentucky
April 30, 1976

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PREFACE

A briefing on styrene-butadiene was called by the National Institute for Occupational Safety and Health on April 30, 1976, at Covington, Kentucky, for the purpose of bringing together those persons with an interest in, and concern for, the hazards that have surfaced in the utilization of styrene-butadiene in the production of rubber. The immediate concern was raised by the report of one employer of the existence of a cluster of leukemia deaths related to a possible exposure to styrene-butadiene. The notice of the briefing was sent to all known interested parties and was publicized. The meeting was open to the public and participation from the floor was encouraged. Participants included NIOSH personnel and others to survey the state of the art and problem areas with contributions from union and employer representatives. It is hoped that this publication of the proceedings of the briefing will contribute to a continuing of the interchange of information that is necessary to a solution of the problem.

ABSTRACT

The National Institute for Occupational Safety and Health held a briefing April 30, 1976, at Covington, Kentucky, to explore with concerned persons from government, labor, management, and academic areas the implications of data so far reported on the possible linkage between exposure to styrene-butadiene and leukemia deaths, the potential problems to be anticipated, and alternatives for action. Chemicals and working conditions in two Port Neches styrene-butadiene plants were described. Reports of leukemia and related disease among styrene-butadiene workers included eight leukemia deaths in two plants in Port Neches, Texas; a six-fold excess of leukemia and lymphoma deaths in a single Akron, Ohio, plant; three deaths (one from leukemia and two from Hodgkin's disease) in a Louisville, Kentucky, plant; and two leukemia deaths and one lymphoma death among 563 styrene workers in a plant in Pennsylvania. Speakers presented suggestions for epidemiologic studies, both industry-wide and in specific plants, and discussed sampling and analytical methods, engineering controls, work practices, and standards development as they relate to controlling exposures in styrene-butadiene plants.

CONTENTS

INTRODUCTION

J. WILLIAM LLOYD

I want to thank the many persons for the work that they did to get this meeting put together on such a very short notice. The purpose of this meeting as stated in the handout you all should have is to present and to consider scientific information concerning the possibilities of a previously unrecognized hazard among styrene-butadiene workers. Specifically, we're talking about leukemia and, possibly, lymphoma.

This morning we hope to present what evidence has been accumulated in such a short time on the question, to consider that evidence, and to determine what it tells us about the possible relationship between the exposure at the plants and the leukemia experience. This afternoon we hope to have some discussion about proposed activities in NIOSH and consideration of other factors for the control of these environments.

I think it is significant that in the short time since we identified the vinyl chloride problem, we have put into effect a standard of one part per million, which is about fifty times lower than the standard at the time we first became aware of the problem. As a consequence, many people will not have to die of angiosarcoma or of other tumors in the future. Unfortunately, there were many people exposed prior to our identification of the problem. In the case of the polymerization workers, we have identified, to date around the world, 48 workmen with angiosarcoma of the liver.

The problem we're going to talk about today is in some respects different. On March 23, 1976, NIOSH was advised by the B. F. Goodrich Company that they were aware of four cases of leukemia among workers in one of their plants in Texas where they produce styrene-butadiene rubber. All of these cases have occurred since 1970; in addition, subsequent to that report, they identified another case which has moved from that plant to another B. F. Goodrich facility.

The information that we received from that plant and from an adjacent plant and a review of the information from a study being conducted at the University of North Carolina indicated to us that there was a good possibility that people working in plants making styrene-butadiene rubbers were experiencing an excess of mortality from leukemia and lymphoma.

Because we had information on only a very small part of the total population working with these materials, we sent out letters to all of the companies making these products and to the unions that are represented at those plants asking that they bring to this meeting any information that would help us decide what this means.*

The morning part of the agenda will be chaired by Dr. Joseph Wagoner and will be concerned with the epidemiological evidence. He will present the speakers and then give the members of the audience an opportunity to ask questions and present any information they can provide to this proceeding.

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*Editor's Note: NIOSH has identified 55 plants at which styrene-butadiene polymers are being manufactured or have been produced in the United States. And an estimated 10,000 workers are employed in such plants.

Styrene-butadiene (SBR), a synthetic elastomer (rubber), is the most widely used elastomer in the world. Approximately 3 billion pounds of styrene-butadiene elastomers are domestically manufactured each year. Sixty-five per cent of the SBR is consumed in automobile tires; the balance is used in a variety of rubber products. SBR is produced principally by the emulsion polymerization of styrene and butadiene in a modification of the process developed during World War II. SBR is available in the form of synthetic rubber as well as uncoagulated latex (a dispersion of SBR in water).

In addition to SBR elastomer, a number of other styrene-butadiene copolymers are commercially available. These synthetic materials include styrene-butadiene copolymer resins (frequently sold in latex form, major uses being carpet back coatings and paper coatings) and acrylonitrile-butadiene-styrene resins (which find applications in pipe fittings, automotive parts, appliance parts, and packaging materials, including margarine tubs).

CURRENT PERSPECTIVES: BACKGROUND

JOSEPH K. WAGONER

Dr. Lloyd has already filled us in on some of the background under which we approached this problem and, specifically, on the sense of urgency similar to that generated by the vinyl chloride problem. In addition I think we have learned another lesson from the vinyl chloride situation and that is that cancer knows no national boundary. And in the spirit of that, I take this opportunity to welcome investigators from the United Kingdom rubber industry, Dr. Parks and Dr. Waterhouse. Hopefully, we can look across the Atlantic for information that they have that may aid us in an early resolution of this problem.

Why are our concerns for leukemia heightened? If one looks at the material that is available from the National Cancer Institute, and particularly the study of cancer by counties, one sees a geographical clustering that causes concern. The National Cancer Institute material shows that the rate for leukemia for males per 100,000 population during the period 1950–1969 was 8.8 for the United States; 9.19 for Texas; 11.1 for Jefferson County, Texas; 10.7 for Orange County, Texas, and 13.2 for Chambers County, Texas.

The areas where some of the SBR plants are located in the Texas region, obviously, are subject to leukemia risks that are substantially above those of Texas or of the United States as a whole.

With the recognition of the importance of occupational cancer and the special emphasis on the prevention of cancer, the Congress this last year gave our institute a new carcinogen initiative. Thus, within a week and four days, subsequent to the notification by the B. F. Goodrich Company of the leukemia situation at their Port Neches Plant, we were able to mobilize a team, enter those facilities, and are at this meeting today.

I would like now to turn the presentation over to two members of my staff, Mr. Lemen, an epidemiologist, and Mr. Young, a chemical engineer, to present our current status report concerning the investigations at the SBR plants.

INVESTIGATIONS OF HEALTH HAZARDS IN STYRENE BUTADIENE RUBBER FACILITIES

RICHARD A. LEMEN
RONALD YOUNG

MR. LEMEN:
Mr. Young and I will briefly go through what we did on our site visit. On March 31st, Dr. Wagoner, Mr. Young, Dr. Lucas of our staff in Cincinnati, and I visited the B. F. Goodrich plant and the Texas–U.S. Chemical facility in Port Neches, Texas.

We went to the B. F. Goodrich plant on April 1 and to the Texas–U.S. Chemical facility on April 3. Both plants produce synthetic rubber using the styrene-butadiene process and both were originally built and operated for the U.S. Government in 1943.

The government had foreseen shortages of natural rubber and established a government corporation known as the Rubber Reserve Company in 1940. Under the aegis of this Company, the government financed the construction of 15 SBR rubber plants, 16 butadiene production facilities, and 5 styrene plants. Between 1946 and 1955, these plants were sold to various private companies that continued to utilize them.

Mr. Young will now give you a brief description of our meeting with the company and our walk-through visits of the two facilities, and then I will give a description of the cases.

MR. YOUNG
Being an industrial hygienist, I would like to give some industrial hygiene observations on the SBR facilities.

In this slide (Figure 1), you will see that the materials are manually dumped into blend tanks and used for the process. Note the series of tanks (Figures 2 and 3). The material is pumped out of these 55-gallon drums into smaller containers and then manually poured into the openings that you saw.

This is what the reactor chain looks like (Figure 4). At the end of the reactor chain there is a radiation density meter that's used to ascertain the degree of polymerization. The housekeeping in these facilities is rather poor; also there is eating in areas where toxic materials are stored and handled (Figures 5 and 6).

In this scene we have vessel entry to clean out these reactors and stripping columns with no respiratory protection being worn (Figure 7). Maintenance leaves quite a bit to be desired. Here's a case of a leaking pump — the vapors were very strong in this area.

Contrary to popular belief, chemical plants are not always closed systems and there are several areas where it's more of an open system and there are opportunities for exposures. Figures 8 through 17 illustrate this.

NIOSH plans to conduct an industrial hygiene in-depth study of these facilities to characterize the specific compounds that are present.

MR. LEMEN:

Mr. Young has given you a visual picture of what the facilities look like on the inside. Now I will briefly go through the cases. I feel that the person who can really correct me if I make any mistakes on this is Dr. Hanby, who is the physician representing both B. F. Goodrich and the Texas–U.S. Chemical facility and is here in the audience. There are five known cases of leukemia at the B. F. Goodrich facility.

The first case was a 59-year-old man who had

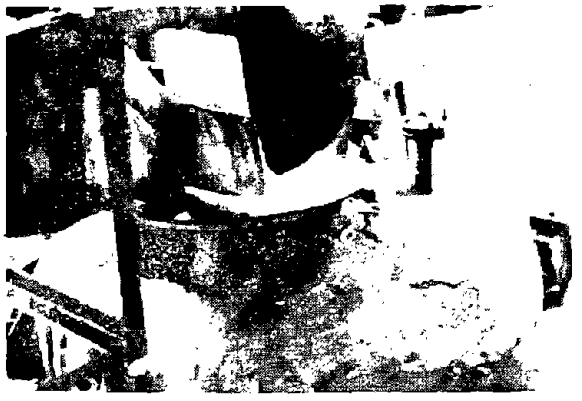

Figure 1. Pigment blend tank. As can be seen, materials are manually dumped into these mixing vessels for use in the process.

Figure 4. Reactor chain.

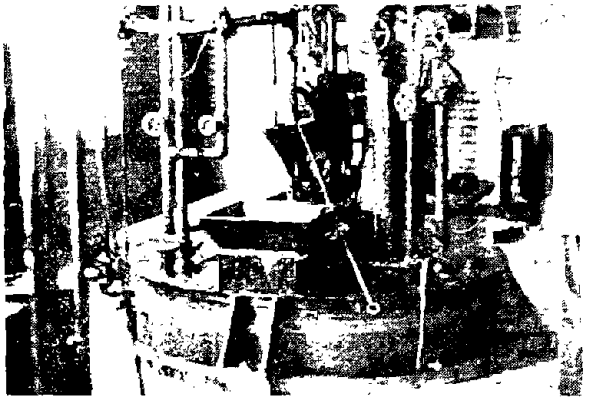

Figure 2. Antioxidant mix tank.
(Spillage of raw materials and poor housekeeping.)

Figure 5. Radiation density meter.

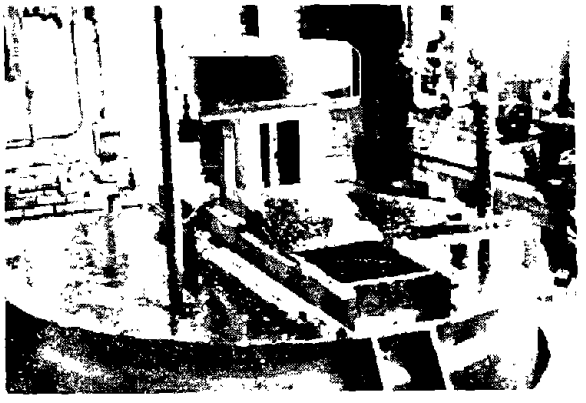

Figure 3. Feed tank.
(Spillage of raw materials and poor housekeeping.)

Figure 6. Poor housekeeping under antioxidant tanks.

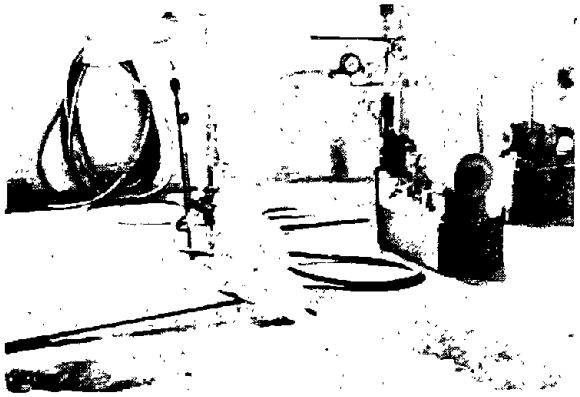

Figure 7. Poor housekeeping in pump house.

Figure 10. Operator's desk (Pigment). Eating in areas where toxic materials are stored or handled.

Figure 8. Soap mix tank.

Figure 11. Open reactor manhead.

Figure 9. Operator's desk-blend tank.

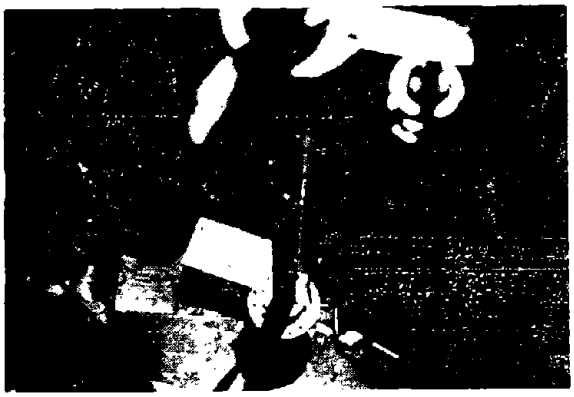

Figure 12. Inside reactor. Workers are required to enter vessels for cleaning and maintenance.

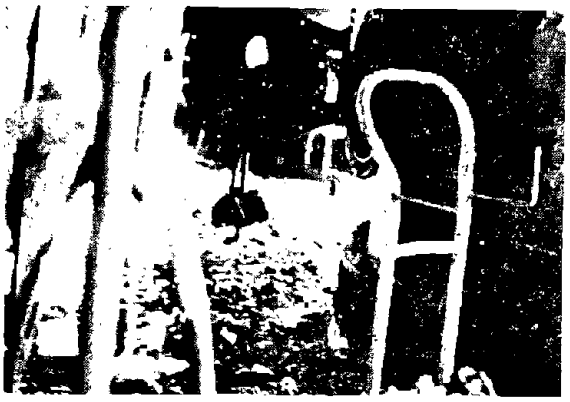

Figure 13. Cleaning a stripping column.

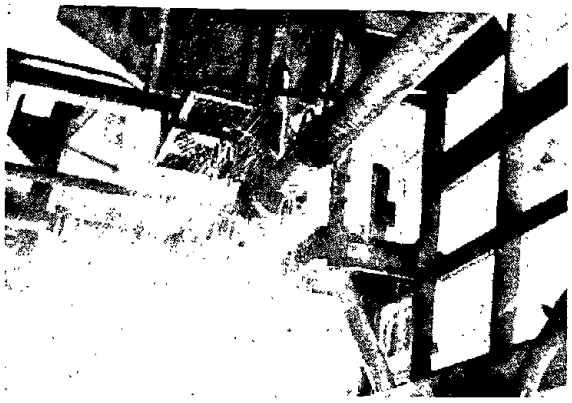

Figure 15. A leaking pipe, indicative of poor maintenance.

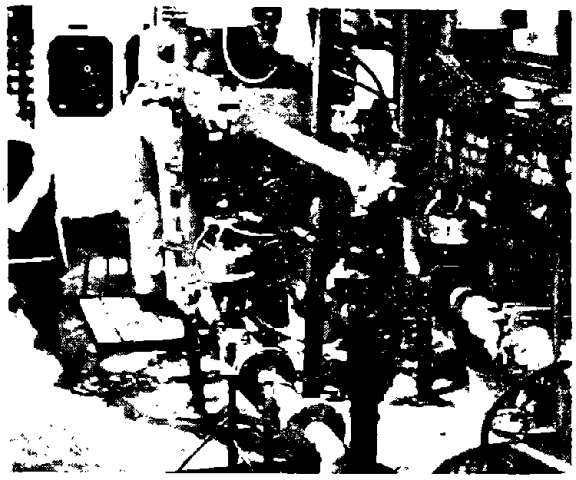

Figure 14. Reactor charge area. A pump was in repair. The material on the floor is an activator.

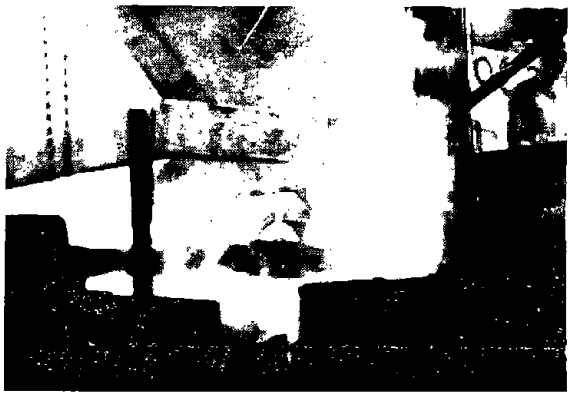

Figure 16. Poor engineering design of exhaust systems.

Figure 17. Area under coagulation tanks.

acute myelocytic leukemia and died in January 1976. He had worked as a laborer, a column cleaner, and a fork truck operator prior to his death. The second case was a retired employee who had retired in 1960 and died in September 1972 at the age of 77 of acute lymphoblastic leukemia. Prior to death, he had been treated for several years with the drug chloramphenicol, which has some bearing on the cause of aplastic anemia.

Case number three was an individual who died in 1971 of granulocytic leukemia at the age of 64. He had worked in the processing department. Case four is a man who is still alive and under treatment at the present time for acute myelocytic leukemia. He had worked at the plant as a pipe fitter.

There was a fifth case — a 46-year-old man who had worked in the facility until 1955 and transferred to another similar facility in West Virginia where he died in 1967 of acute myoblastic leukemia.

At the B. F. Goodrich plant, there was really no apparent job site association so far as we can see at the present time. The cases seemed to have occurred randomly throughout the company.

The second set of leukemia cases were from the Texas–U.S. Chemical Plant.

The first case was a 62-year-old man who died of malignant lymphoma in 1971. The second case was a 46-year-old man who died in 1976 of acute myelogenous leukemia. The third case is a case now in remission of a 44-year-old man with lymphocytic leukemia.

There are two other non-leukemia cases that were mentioned as being possibly relevant: one in the Texas–U.S. Chemical Plant in a 62-year-old man; the other in a 66-year-old man who died in 1975 of thrombocytopenia.

This fairly well summarizes the cases we have to date. It's interesting to note that seven of the eight cases have died since 1971 — this was in a workforce of approximately 2,000 people. The current workforce in both plants combined is now less than 1,000.

The cases identified by the company were from retired individuals and from currently employed individuals only; and therefore, a larger segment of those who are at risk from leukemia are still untraced as far as determining vital status and cause of death for those deceased. This is why the week after our site visit, we began to microfilm the employment histories for all employees in both the B. F. Goodrich and the Texas–U.S. Chemical Plants. This included everyone who had ever been employed in either plant from the beginning of the plant — at B. F. Goodrich Plant since 1943 and at the Texas–U.S. Chemical Plant only since 1950.

The process of microfilming will be completed at the B. F. Goodrich Plant, probably by the end of this week, and if not, by the early part of next week. The process of microfilming at the Texas–U.S. Chemical Plant will probably be completed within the next two weeks. After this process is complete, we will begin to trace all of the individuals that have ever worked in those facilities to determine vital status and obtain causes of death on those who are deceased. The mechanisms that we use to trace these individuals are rather conventional. We have a very good rapport with the State of Texas Health Department and will cycle the names of these individuals through their Vital Statistics Office and through the Texas State Motor Vehicle record department. We will also be going to the Social Security Administration to get information as to the current vital status of each of these individuals. It will probably take from 6 to 8 months to completely do the follow-up process.

Basically, this is what we know at the present time from the facilities that we have been in contact with. And, I think at this time it's best to let Dr. Wagoner finish; then Dr. Spirtas can tell us much more based on his report of the styrene-butadiene rubber industry that was published in a recent issue of the Journal of Occupational Medicine and is really the hardest data that we currently have on leukemia and hematopoietic disease among styrene-butadiene workers.

DR. BLEJER:

I am Hector Blejer. Could you go over the age,

date, cause of death, or year of death for the seven cases involved?

MR. LEMEN:
I will start with the B. F. Goodrich cases. The first case was 59 years of age; he died on 1-5-1976. His cause of death on the death certificate was gastrointestinal hemorrhage due to thrombocytopenia, due to acute myelocytic leukemia. The second case was age 77; he died on 9-9-72. He had septicemia due to acute lymphoblastic leukemia.

Case number three was 64 years of age; he died on 12-6-71 of granulocytic leukemia. Case four is alive; he was born in 1926; he has acute myelocytic leukemia. The fifth case was the case that moved in 1955 from the Port Neches facility to West Virginia. He died in 1966 at the age of 46, of acute myoblastic leukemia.

There were three cases at the Texas–U.S. Chemical facility. The first case died at age 62 on 10-31-71. He had malignant lymphoma with well differentiated lymphocytic-type with lymphocytic leukemia. Case number two died at age 46 on 1-29-76; he had acute myelogenous leukemia and lumbar pneumonia. Case number three is the one currently in remission at age 44. He has lymphocytic leukemia.

As I mentioned earlier, if any of these are incorrect, maybe Dr. Hanby might have a statement at the present time. I can give a complete work history on each of these eight men if you would like.

MORTALITY AMONG RUBBER WORKERS: RELATIONSHIP TO JOBS WITH STYRENE-BUTADIENE EXPOSURES

ROBERT SPIRTAS

DR. WAGONER:
The next presenter will be Dr. Robert Spirtas from the University of North Carolina, who will present ongoing studies at the University of North Carolina under agreements with the United Rubber Workers and the rubber companies in the United States.

DR. SPIRTAS:
The first thing I would like to say is philosophical. At the beginning of World War II, our government asked the rubber manufacturers to produce a certain material and the rubber manufacturing industry complied in the war effort — something that they felt was their patriotic duty, but something that they had no idea might later prove to be suspect of causing health problems. Similarly, the workers who went into the production of this material saw it at that time as a good job and, probably, had no idea that it might be a potential health hazard.

Now, both parties are having second thoughts and are turning to us, the scientists, for answers; and as a scientist, it's difficult to give a quick answer. Today, I'll give you some information that we have been able to gather. It doesn't point in any direction and it's not as specific as we would like it to be.

I expect that what I present may not be completely clear to members of the audience and I would invite people to interrupt me at any time during the talk to clarify any points that I'm going over. I brought along twenty copies of the paper that Dick Lemen referred to from the Journal of Occupational Medicine.[1] Rather than try to read it to you, I will have those available for any interested parties. The relevant tables in this paper are Tables 3 and 5.

In Table 3, you will note that the ratio of age-adjusted rates of exposure during 1940 to 1960 to the specific work area which we call the synthetic plant, and what I'll call the "Cohort A" in Akron, Ohio, had a relative exposure of 4.4 for those people who had spent greater than 2 years in this area and a relative exposure of 5.6 for those who spent more than 5 years in this area. (See Appendix C.)

Table 3 from the JOM article has been confused somewhat with Table 5 where we say that the relative risk of lymphatic and hematopoietic cancer among workers in the synthetic plant was 6.2. I would like to try to clarify this morning what we mean by relative risk and what we mean by relative exposure.

By relative risk we mean the probability of disease in the exposed population divided by the probability of the disease in a non-exposed population. That is, if you look at all exposed workers in the cohort — in whatever way we define exposure — and then try to determine how many of those have got the disease and use that rate as your numerator — and divide that numerator by the rate of disease in the non-exposed population, you then have what we call a measure of relative risk.

By relative exposure is meant the probability of exposure among the diseased individuals (in this case, death from neoplasms of lymphatic and hematopoietic tissue) divided by the probability of exposure among the total population.

This is explained in the March paper[1] and in another paper we have published in the Journal of the American Statistical Association.[2] If one wants to go into these confidence intervals that we have placed on the individual points, it's important to note that we use a slightly different statistical approach so that in reading Table 5 especially, in our report, be careful to note the footnotes and the asterisks as to precisely what we are saying here.

One of the other points that I would like to make is going to involve the use of slides to explain the way that we accumulate time or the way that we measure exposure. We can't go back to 1940 and take industrial hygiene analytical measurements so we use a surrogate measure of exposure: the work history. We break the work history into categories and enter this information into the computer and summarize the information based upon an arbitrary decision as to what we are trying to see, what we're trying to look for, and we do it in a way that is scientifically objective so that we treat the cases the same as we treat the controls. Because this information was already in the computer when the request came to us to gather the information from the company and the union involved (United Rubber Workers) we were able to quickly sort the information out and produce a report which was given to the company and the union. So, if I can have the first two slides, I can show you how we have created this measure of exposure and apply this to Table 3, the ratios of age-adjusted rates of exposure during 1940 to 1960 — how we did that.

Table 1. Transcribed work history.

Name:	John Doe	Social security number:	000-00-0000
Birth date:	05-18-23		
Marital status:	Married	Sex:	Male
Education:	4 years high school	Place of birth:	Cleveland, Ohio

Line number	Job	Date in	Date out
1	B	1-1-41	6-30-44
2	C	7-1-44	12-31-44
Time slice			
3	A	1-1-45	12-31-48
4	C	1-1-49	6-30-55
5	A	7-1-55	6-30-66
6	D	7-1-66	12-31-75

Slide 1 (Table 1) is a transcription of a work history, and work histories are usually messier than this in general. What we do is take every job that a worker has ever had, and these appear as line numbers. This particular worker had six different jobs; he hops back and forth from time to time during his career and spends varying lengths of time at each of these jobs.

What we then do is group these jobs into what we call occupational title groups or OTG's.[3] (See Table 2.) So, for this particular worker, we may have decided for the purpose of the given study, that job A fell into Group One, jobs B, C, and D were similar and could be categorized into Group Two and job E was something that should be categorized into Group Three. For this particular worker, then, we would have taken the various jobs and the times in those jobs and added them up; and it may have been that we felt the relevant etiologic period was after a certain date when, perhaps, some new chemical was introduced into the industry to before a certain date, given that we're looking for a certain latency period. There may have been no time spent in job E in this particular study. In addition, since we didn't want to consider any jobs held before a certain date we sliced the total time here to get 15 years of experience in Group One and 16 years of experience in Group Two.

Table 2. Conceptual framework of experience transformation algorithm.[4]

Line number	Job group 1	2	3
	Job A	Jobs B, C, D	Job E
1		1- 1-41	
2		7- 1-44	
Time slice			
3	1-1-45		
4		1- 1-49	
5	7-1-55		
6		7- 1-66	
End of study		12-31-75	
Totals	15.0	16.0	0.0

QUESTION:
Could you explain the word algorithm?

DR. SPIRTAS:
Algorithm is a 75-cent word that means formula. In this case, it's a computer program that grinds through all of the work history in the computer and summarizes it after we've made these arbitrary decisions as to how we want to slice up the work history and how we want to group it.

The first study that we did was a study on leukemia that appeared about a year ago in the Journal of Occupational Medicine[5] where we had certain ideas as to which jobs might be similar. For the current study of SBR workers,

Table 3. Demographic and work history data for cases of NLHT who ever worked in the synthetic plant.

Initials	Sex	Race	Birth	Death	Age	Study cause of death ICDA (8th R.)	Synthetic jobs		Solvent jobs		Job description	Hire	Termination (last work day)
							First exposure	Total exposure (yr)	First exposure	Total exposure (yr)			
GSA	F	W	06-14-91	12-03-70	79	202.2	11-18-42	6.8			Female janitor, sweeper	11-18-42	01-26-55
DAC	M	W	08-15-99	10-29-73	75	200.1	05-02-51	12.8			Repairman, painter	05-02-51	08-29-64
WLI	M	W	06-02-11	06-29-70	59	204.0			09-04-42	6.7	Cement (solvent) mixer	09-04-42	07-14-68
							03-27-50	18.1			Utility, cleanup Latex blender		
SHO	M	W	02-11-02	02-21-64	62	205.1	08-27-51	10.3			Pipefitter	08-27-51	05-19-62
HAO	M	W	11-15-00	12-09-70	70	207.9			08-10-44	9.3	Machine repairman	08-07-42	09-26-64
							01-12-59	0.1			Machine repairman		
LHR	M	W	07-18-14	08-03-69	55	201	10-16-42	26.5			Pumphouse op., compress. house attend	10-16-42	04-07-69

we wanted to break out the jobs in the synthetic plants so we created a specific occupational title group which had been lumped together with other ones in the previous study.[1] In each study we had the capability of arbitrarily grouping, as well as arbitrarily slicing on some definition of time, and getting a summary in terms of years spent in these various categories. We can take that information and feed it into our statistical computer programs and try to relate this measure of exposure to the disease or cause of death of interest.

So, fortuitously, we had just come out with this publication in March,[1] which was about the time that the interest in this subject peaked; and at the request of companies and union, we went back and actually did another study. We have several cohorts, several matched case control groups — information on various workers that have been chosen scientifically for various purposes which are in our computer. We went back to our computer and addressed this specific question of whether working in the synthetic plant was associated with death from neoplasms of lymphatic and hematopoietic tissue.

We have in Table 3 the six cases in this first cohort, cohort A, of neoplasms of lymphatic and hematopoietic tissue which I've prepared at the request of Dick Lemen of NIOSH, and I can give you that information.

We have six cases of neoplasms of lymphatic and hematopoietic tissue (I.C.D.A. code 200 to 209 in the eighth revision) who worked in the synthetic plant of cohort A. Three of those deaths were due to true leukemia, that is, I.C.D.A. codes 204 to 207. Of those three true leukemias, two had experience with solvents other than in the synthetic plant — that is, they worked with chemicals which may have or may not have contained benzene which is known to cause, or is highly suspected of causing leukemia or being associated with leukemia.

There were three non-leukemia deaths in this group; that is the lymphomas. Of those three, none had any experience in areas where solvents were used.

As to jobs of the workers with the leukemia deaths — one was a utility worker, clean-up worker, and a latex blender. That person also

was a cement mixer which involved working with solvents. Another of the leukemias was a pipefitter in the synthetic plant, but was also a machine repairman working with solvents. The third leukemia death was a machine repairman in the synthetic plant.

The three lymphomas, a 202.2, a 200.1, and a 201 — those are the diseases like lymphosarcoma and Hodgkin's disease — worked only in the synthetic plant. One was a janitor and a sweeper, one was a repairman and a painter, and one worked in the pump house operation and as a compressor house attendant. Interestingly, of the three lymphoma deaths, the latency period, which I'll define as the date from first exposure until the date of death, ranged from 22 to 28 years so that if we had to make a guess, based on just this information, it would be that the lymphomas are the cause of death which we would suspect more than the true leukemias. If it's true that it takes something like 20 to 30 years to start seeing these things, then, we may just be seeing the beginnings of something. But, we have only this limited information, so it's really too early to tell — to put any statistical confidence in the information that we have. The general principle of public health that I've been taught is that it's our duty as scientists to alert, but not alarm the public. What I would gather from this, then, is that we should be aware of what's going on, but not be alarmed today based upon this information.

We also had information on another plant in Akron.

DR. INFANTE:
I am Peter Infante with NIOSH. I have two questions: What were the cell types of the leukemias?

DR. SPIRTAS:
We have to go back to the death certificates to get that but we can get that for you.

DR. INFANTE:
I have a second question. You have in your study deaths in the 10-year period from '64 through '73. How did you determine the population for those deaths — are they deaths when people became ill while working or does this include people who had left the plant, died in the jobs during this period, or where does your mortality come from?

DR. SPIRTAS:
The paper in the Journal of Occupational Medicine,[1] the March paper, and our paper from a year ago[5] will give you all that information. We try to follow this population and define them as workers — anyone who was 40 years old or older in 1964 and who at that time either was actively employed or pensioned was included in the cohort. If he subsequently left the employment, we followed him up, and we think we have a fairly complete follow-up of that cohort.

MR. MOURE:
Dr. Spirtas, my name is Rafael Moure and I am an industrial hygienist for the Oil, Chemical, and Atomic Workers. I have this question about the leukemia deaths that you were describing. Those deaths refer to a synthetic rubber plant as defined in your OTG's, or do you refer to it in your paper in April of 1975? You mentioned one of the persons in that group was involved in cementing work or in compounding cement. What I'm worried about is how you define a synthetic rubber plant. When does the problem stop? Can you clarify that point for me, please?

DR. SPIRTAS:
I can try; I don't have the paper with me, but I think your point is a good one, Mr. Moure. Some of these men have mixed exposures and we have to try to sort all this out. If I'm correct in recalling what you're referring to, the cement house operation would have been part of the rubber tire manufacturing, separate from the synthetic plant. Does that answer your question?

MR. MOURE:
So these people that you were describing were involved in that cementing and tire building itself?

DR. SPIRTAS:
Some of them were, at some time or some point in their career. In other words, the question we tried to address was: did the deaths from neoplasms of lymphatic and hematopoietic tissue ever work in synthetic plants and we found six of those, but, of the six, two had spent some time in other suspect jobs, not in the synthetic plant, but involving solvents or cements.

DR. LILIS:
When you are talking about synthetic plants, do you exclude any solvent exposure there?

DR. SPIRTAS:
No, a synthetic plant is simply working in a department where synthetic rubber was manufactured. Now, there is a process of solvent emulsion or solvent polymerization in synthetic rubber production. To the best of our knowledge, this process was not used in this particular plant so that I don't think there would have been a great solvent exposure in this particular synthetic plant.

DR. LILIS:
Are there any hard data on exposure levels of those people?

DR. SPIRTAS:
Not in the past.

DR. LILIS:
And the present?

DR. SPIRTAS:
Yes, there probably are such data, but our industrial hygiene part of the report deals with a walk-through. I'm just giving you the epidemiology now. We came at this from three approaches, the epidemiological approach, the industrial hygiene approach, and the toxicologic approach. I'm trying to give you the epidemiological information now, and at Dr. Lloyd's request I can give you the information from the second cohort unless you want me to give these death certificates first.

DR. BLEJER:
In the occupational title classification (which obviously defined something of exposure or as you said relative exposure), where were the janitorial and maintenance and repair people classified, as no exposure, minimal, or what?

DR. SPIRTAS:
That's a judgmental decision.

DR. BLEJER:
I would like to know.

DR. SPIRTAS:
This is the most difficult part of doing this type of study — how you classify workers who may incidentally pass through a department. In other words, a trucker or a janitor or a sweeper or repairman or maintenance worker. What we did is ask our industrial hygienists to make a judgmental decision on the basis of the job description, their walk-through evaluation, their discussion with plant management, and their discussion with the workers and with representatives of the union. We get a lot of help from people like Lou Beliczky, who is a certified industrial hygienist, as to where we draw the line.

DR. BLEJER:
The reason I'm asking this is because some of these people do have severe high exposure to almost anything within the plant. I notice within the list that you very kindly handed to me that there are four of these people who were either janitors or maintenance or repair people who had long periods at their jobs — for example, 1942 through '55, '51 through '64, '42 through '64, and '42 through '69. Therefore, what I'm trying to say is, how did you classify those people as far as their occupational title with "relative exposure"? If they appeared in "having little or none," then that would not be in my opinion or in my experience correct. I'm questioning the occupational title grouping and the relative exposure for those people in particular.

DR. LLOYD:
Let me try to help clarify what Dr. Spirtas has here. In the paper that was published in the March issue of JOM,[1] they pointed out that they were seeing an excess of leukemia and lymphoma mortality in people who were described as having worked in synthetic rubber. When we became aware of the situation in Texas, they went back and looked at this information — these people were coming from a single plant. It is true that all six of these people had worked in various areas, and I think he said specifically that two of the leukemia cases were known to have, at a prior time, been exposed to high levels of solvents in other areas. Does that help at all to clarify what we're talking about? So he's not saying that they couldn't have had other kinds of exposures — it is just that they saw this cluster of persons who had worked in styrene-butadiene rubber at some time in their career.

DR. SPIRTAS:
Are you satisfied, Dr. Blejer?

DR. BLEJER:
Yes.

DR. SPIRTAS:
Let me go through some of these death certificates if that would shed any light on this issue.

These are very difficult to read. I have a malignant lymphoma of lungs, kidney and lymph nodes, lymphosarcoma which is due to macroglobulinemia, acute lymphatic leukemia, chronic myelogenous leukemia, a probable leukemia, and Hodgkin's disease. Since these have to be classified to some standard system, we have a nosologist at the National Center for Health Statistics code this into the standard code, the International Classification of Diseases category — the eighth revision of that category — and those are the numbers that I was reading to you so they may not make a lot of sense to a layman, but they are the precise definitions that compare with the national standard for mortality data. Are there any other questions?

If not, I can go on and give you the epidemiological results for the second cohort. (See Appendix D.)

These results are more equivocal and, in fact, I'll read from that report.

A cohort study comparing the mortality due to neoplasms of the lymphatic and hematopoietic tissue of workers who spent the longest portion of their work time in batch preparation, reaction, finishing, and packing operations of synthetic latex was done, compared with that of all workers in the Akron plants. That was the first part of the study.

The second was a case control study for leukemia deaths who spent some portion of their work time in what we categorized as synthetic jobs, and for leukemia deaths who spent some time in other departments thought to be similarly exposed. This information was provided to us by the corporate medical director who wanted us to look at some other departments which may have had exposure, but which we were not classifying initially as a synthetic exposure. This again relates to Dr. Blejer's question of where you draw the line, which is critical in all these studies. We made our initial judgment and tried to do a study. We then took additional information supplied to us by the company and used that to see if that information when applied both to those cases and the appropriate control group produced any other insights.

The third was a case study of non-leukemia deaths in the categorization of 200 to 209, that is other than leukemia, and having some exposure in the areas described in the second study.

Study one showed no deaths due to these neoplasms of lymphatic and hematopoietic tissues among workers with the largest portion of work time in the occupational title group (O.T.G.) synthetic.

Studies two and three showed no deaths due to neoplasms of lymphatic and hematopoietic tissue who had ever spent time in the O.T.G. synthetic. However, 4 of 37 leukemia deaths and 6 of 44 non-leukemia NLHT deaths spent time in the departments with possible similar exposures to those in the O.T.G. synthetic.

In particular, two of the leukemia deaths and one of the non-leukemia NLHT deaths had been pipe fitters working in this area. Pipe fitters can be considered maintenance workers, which again leads back to the point Dr. Blejer raised.

Of the controls for Study two, 7.4% had spent some time in departments of interest.

The point estimate of relative risk of death due to leukemia for everyone having worked in the departments of interest is 1.5. There may be some excess risk of death due to NLHT among workers in the synthetic latex production area although this added risk, if it exists, is small.

That essentially summarizes our epidemiological data. I did not read the first cohort report. I do want to give you the point estimate of relative risk in cohort A, which was 2.4. This compares with the point estimate of relative risk of 6.2 for the same cohort when we used the different control group. Thus, we have for cohort A, two estimates of relative risk: 6.2 based upon a very

large control group and 2.4 based upon a smaller matched control group. We can expect a relative risk somewhere between those two numbers.

For cohort B, we have more equivocal information — with a point estimate of relative risk of 1.5. Is that point clear?

DR. NICHOLSON:
I am William Nicholson from the Mount Sinai School of Medicine. Could I ask you a question as to the starting point of the operation, that is in the two plants.

DR. SPIRTAS:
They were both started about the same time.

DR. NICHOLSON:
No, I'm sorry. The chemical starting point is what I meant. Did they bring in the raw material as styrene, did they bring in ethyl benzene to make styrene, did they bring in benzene to make ethyl benzene to make styrene to the styrene-butadiene rubber?

DR. SPIRTAS:
This will be part of the industrial hygiene evaluation of these studies and, since that involves the chemical processing and may be sensitive information, that won't be part of my report today, but it will be part of our final report. That final report will be given to NIOSH and to the appropriate people whenever we can get it available, but I'm not capable of discussing the exact chemical processes. We will evaluate them and we will make that information available.*

DR. NICHOLSON:
Well, I think it's a most relevant issue. If the process went back far enough so that they began with benzene as raw material, you would have obviously enormous exposures there.

QUESTION:
We're not hearing the questions here in the back.

*Subsequent to the Briefing, the final reports were sent to NIOSH and are presented as Appendices C and D. These reports include industrial hygiene walkthrough surveys.

DR. NICHOLSON:
The question was in these particular plants — at what point in the chemical process do they start with raw materials? Do they start with benzene to make ethyl benzene to make styrene to polymerize styrene-butadiene rubber or do they start with styrene as a raw material? Obviously the initial raw materials would have a significant effect upon the health experience of the group and this described disease.

DR. SPIRTAS:
Your point is well taken. When we put our information together, we have to consider the studies that NIOSH is doing and somehow categorize exposure — putting together which ones are similar processes and which ones are different and this is what we are trying to do. With the two plants, we have tried to look at the difference in mortality experience and tried to see if that relates to the difference in exposure. So, we will try, after making the individual report on the individual cohorts, to make a comparison between these two populations and the two chemical processes. I can't speak for NIOSH, but I expect that we will cooperate with them in whatever way we can.

MR. YOUNG:
The Texas facility started with styrene.

DR. SPIRTAS:
Thank you.

DR. LONGLEY:
I am Mars Longley, Standard Oil of Ohio. In your efforts to connect these jobs with the disease we're talking about here, wouldn't it be a lot easier if you could just use the data that say that these people worked with styrene-butadiene and a number of common aromatic solvents, most notably benzene? Wouldn't that make the whole thing just sort of fall into place for you as far as the data are concerned? You seem to be having some problem with some of your cases being really not too firmly associated with the two chemicals that you are talking about today.

DR. SPIRTAS:
I think the issue is to try to determine whether exposure to styrene-butadiene is dangerous. The problem is that these men are exposed

to other things so our approach has been to try to find out what the man's total exposure is and to try to somehow compare it with exposure of those who worked with this chemical only and with this process and had a different mortality experience from those who had a mixed exposure. Your point is a good one — if we could somehow lump this information together, we would have larger numbers and would do more with the data. We certainly will try to look at this from every angle. What I'm presenting today are the results of our initial investigations and, as I tried to point out, we don't quite have all the answers — we put together as much as we could as quickly as we could, and that's what we've got to date.

MR. BELICZKY:

I'm Lou Beliczky, Director of Industrial Hygiene for the United Rubber Workers of the International Union. Somehow, I think that we are getting a feeling that we are trying to relate the situation that occurred in Port Neches, Texas, to that of the rubber worker facilities in Ohio or wherever else they may be. My knowledge of the facilities in Texas, both the U.S.–Texas and the B. F. Goodrich Plants, indicates their prime responsibility is to make the rubber or the latex. We have to understand the fact that the facilities that Bob Spirtas is discussing at the present time are facilities that not only may have made the SBR rubber, but use it to make a product, or may have been involved in the manufacture of P.V.C. resins. So, we don't have a pure exposure to styrene-butadiene copolymer. Dr. Spirtas is relating possibly the leukemia that he has found in the epidemiological studies and trying to associate it with workers who may have spent a portion of their time in the synthetic plant. These facilities may be contiguous. The polymer plant may have been contiguous to the rubber facility. And people change jobs. I think that with the best methods that they have available, they are trying to put together, in a multi-faceted job responsibility of twenty or thirty lifetime worker experiences, a kind of relationship in the synthetic facilities that could shed some light on the leukemias that we have found.

DR. SPIRTAS:

Thank you, Lou.

DR. WAGONER:

I think there are a couple of questions that are in order. I feel that this is a very open meeting and it's a fact finding meeting. Certainly we need all of the guidance that we can get in order to undertake the necessary studies for the basic purpose that we're here today to discuss — worker protection. We would look forward to the corporations who are involved in these studies to more critically examine and to discuss their processes so we know whether in fact we are talking about the basic processes of the styrene monomer production with its potential for benzene exposure or is there a problem unique in the process of styrene-butadiene rubber production?

Now, our investigations found that the Port Neches facilities are not styrene monomer plants. They do not produce their butadiene. These facilities are using the SBR process with no known, to our knowledge anyway, direct exposure to benzene.

One additional question I would like to ask Dr. Spirtas. There has been a recent major concern about the diagnosis one way or the other of aplastic anemia. Have you reviewed any death certificates so you could speak to the non-neoplastic hematopoietic effects on death certificates that would not appear in your table but would certainly indicate that we may be seeing either misdiagnosis or a much larger problem involving the hematopoietic system?

DR. SPIRTAS:

Yes. At the request of Dr. Lloyd and Mr. Lemen, we went back and tried to find any other blood discrasias. We looked at the ICDA Group 280 to 289 — I believe that's the group involving blood discrasias — and found one aplastic anemia who had solvent exposure — no butadiene-styrene, no synthetic exposure, but who had had the solvent exposure, which is in addition to other data on leukemia with solvent exposure. That may strengthen the association between solvents and the diseases of this type (blood discrasias and leukemias) but it doesn't help any with the current issue.

Let me make a brief statement about the industrial hygiene survey. We sent two of our industrial hygienists to Akron to walk through

both plants and they are preparing reports now which will give their evaluation, and we will make that information known to the companies and union as soon as we can.

A walk-through industrial hygiene survey of a synthetic plant was made for each plant. It appears that there is potential for exposure to volatile materials, including both butadiene and styrene, during production in a tank farm and during early stages of the process. It is recommended that these areas receive special attention in efforts to minimize exposure. This is tentative — and it's the best we could do on short notice.

On this issue, there may be other comments from other speakers today, but this is our initial evaluation. That takes care of the industrial hygiene part of it. The only thing remaining is the toxicologic part of our walk-through, and I can present that in one table (Table 4) and, also, give you one reference which is not here.

We searched the literature on styrene-butadiene rubber manufacturing and cross indexed that with literature on toxicology, and what we have done is put an asterisk by those chemicals or chemical families which we suspect as being potential carcinogens. In this table then, of the monomers used, styrene is a potential carcinogen or procarcinogen and hydroperoxide which is an initiator is a potential carcinogen. P–nitroaniline is questionable; it is a modifier and it's a questionable carcinogen. Sodium dimethyl dithiocarbamate which is used as a short-stop is another questionable carcinogen.

In addition, there is a table, and Lou has this information, a publication by Erslev and Wintrobe in 1962[5] which gives a list of chemicals which are suspected of causing blood discrasias. The list includes those that Dick Lemen referred to — chloramphenicol, arsenic, gold salts. The list in that particular publication may be of interest to some people.

What we've tried to do is go back to our data base which we've been working on for several years and try to answer specific questions. Our results are equivocal as I've said. We've given these results today as only tentative results. Thank you.

Table 4. Toxicologic information on compounds used in SBR research and production.

(NOTE: Information was obtained from available literature; only certain of these ingredients have been used in the Akron plant.)

Monomers
Styrene*
Butadiene
Initiators
Persulfates
Hydroperoxide, e.g., p-menthane-8-hydroperoxide, cumene hydroperoxide*
Azobisisobutyronitrile (AIBN)
Sodium-formaldehyde sulphoxylate (Sulphoxylate formula)
Modifiers
Aliphatic mercaptans, e.g., n-dodecylmercaptan
p-Nitroaniline (*?)
Thioethers
Chlorinated hydrocarbons
Short-stops and Antioxidants
Sodium hydrosulfide
Hydroquinone
Phenyl-β-naphthylamine#
Trialkyl phenol phosphites
2,6-Ditert-butyl-p-cresol (BHT)
Sodium dimethyl dithiocarbamate (*?)

* and *? indicate potential or procarcinogens

#Editor's note: Subsequent to this presentation, NIOSH issued a Current Intelligence Bulletin, which noted that phenyl-β-naphthylamine can be converted by the body into the known human carcinogen, β-naphthylamine.

DR. WAGONER:

I would like to make one or two statements and again reiterate my earlier statement. We are here to seek information to resolve this problem. If there is a problem, we had better know about it. If there's not, we had better know that also. I would hope that somebody would come forward and describe the processes that we are talking about. I think that is critical.

Second, I make that first statement in light of the fact that there are those who would maintain that the associations between benzene and leukemia are fortuitous and fortuitous only and there are others, such as myself, who have taken a much stronger stand. Indeed, if we are talking about solvents and benzene, then process information is as critical to a determination of their role as it is to whether there is an

inherent problem in the styrene-butadiene operations.

Now, I think Mr. Lemen has some information on the risk assessment in the populations in SBR work in Port Neches where they are not producing styrene or butadiene in the facilities that we observed.

MR. LEMEN:
I wanted to wait until after Bob Spirtas talked because these calculations, more or less, follow what he has said to a certain extent. There were approximately 2,000,000 deaths in the United States in 1975 — about 15,000 were due to leukemia. The leukemia death rate is higher for males by about four to three ratio. Approximately seven to eight per thousand deaths can normally be expected from leukemia.

The 4 definitely identified leukemia deaths, out of the total of approximately 150, were the cases known to both Goodrich and Texas management and represent at least a three-fold excess mortality. This excess remains impressive even when the cases probably due to chloramphenicol are discounted. The known morbidity instances, 2 cases out of a worker population of less than 1,000, are also far in excess of the expected approximately one new case annually per 10,000 workers or 8 per 100,000 workers.

One last note I want to make for the NIOSH survey team which applies to not only the plants in Texas but may well apply to other plants — about the risk from the other products that are being used in the facility and, specifically, from talc. We have observed the indiscriminate handling of talc, and very, very similar situations which I know exist in other rubber plants because I've been in them. Not only should we look at just one probable cause of a problem such as leukemia, but we have to keep in mind that there are other substances and chemicals that are just as dangerous and can cause disease among the workers and should be reckoned with as well.

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REVIEW OF PRESENTATIONS

J. WILLIAM LLOYD
JOSEPH K. WAGONER
RICHARD A. LEMEN
RONALD YOUNG

DR. LLOYD:
While we are waiting for Dr. Wagoner, I would like to summarize what we have done in the first part of this session.

1. The mortality experience at the B. F. Goodrich Plant at Port Neches indicated a much higher leukemia mortality than you would expect, not only on the basis of the rates for the State of Texas or for the United States, but for that county where there is an excess of leukemia.

2. At an adjacent plant, Texas–U.S. Chemical, an excess of leukemia was also observed.

3. Following that observation, NIOSH looked for other information on the question and, specifically, they wrote to the companies and asked them to come here and present whatever information they had.

4. One of the first sources of information was the University of North Carolina; in particular, their report in the March (1976) issue of the Journal of Occupational Medicine presenting their observations on a six-fold excess of leukemia and lymphoma in people working in synthetic rubber at a styrene-butadiene plant. You heard the three cases of leukemia and lymphoma described and you also were told that some of these people had exposure in their history to agents that might be suspected of being leukemogenic. Nobody has denied that they might have such an exposure — they did cluster people who worked in synthetic rubber plants.

5. Subsequent to that report the North Carolina group, reviewed their study at another styrene-butadiene plant, where they had not noticed any excess of leukemia. They noted in this review of the plant study four cases of leukemia who would have at some time worked in an area where they could have had exposure where styrene-butadiene rubber was made. The relative risk in that area was estimated to be 1.5 and that means that the rate based on some comparison was fifty per cent greater than expected with those small numbers.

6. What we have at this point is two plants in Texas where the leukemia rate is out of line, another plant in the State of Ohio where we have recorded excess amounts of leukemia and lymphomas, and another plant where the rate appears to be in excess.

7. A great deal still has to be worked out on this: We need to know what are the specific chemicals that these people are exposed to and we need much more detail on the process or the processes that are being used and that is why I have invited you people here. We hope you can tell us much more about this problem. I will now turn this back to Dr. Wagoner.

DR. WAGONER:
Before we go to the Mount Sinai group which is going to be discussing its observations in a styrene monomer facility, I would like to go back to Dick and Ron to clarify two points of view.

First, to describe some of the processes and the chemicals that are being used. Basically, one of the problems we face right now is we're not sitting in a unique position of one heavy marker disease, such as angiosarcoma of the liver. Second, we are in a facility which is predominantly of one particular chemical usage, but also uses a variety of chemicals.

Now, as part of the observations on the processes in the Port Neches facilities, I think it's noteworthy that this plant or these plants do not produce styrene, they do not produce butadiene, and the butadiene is piped into the plant and the styrene is trucked by tank cars into the facility. We have had the opportunity of looking at what is available for the butadiene facility which is adjacent to the two SBR plants and I think this might give us some further indication of where we are.

MR. LEMEN:
With Dr. Hanby's assistance, we obtained a listing of the deaths from a company that's adjacent to the B. F. Goodrich and the Texas–U.S. Chemical Plant and we have 122 deaths in which there are no leukemias observed. This is out of a facility that makes the butadiene that is piped into the other facilities.

The total number of deaths that I didn't give you before for B. F. Goodrich where we observed the 5 leukemias was 96 and at Texas–U.S. Chemical, the total was 50. I think it is relevant to note that there were no leukemia deaths or blood disease deaths from the company that makes the butadiene.

MR. YOUNG:
When we were planning the meeting, some questions arose as to whether the process should be described. Obviously, it should; but, I didn't particularly want to try to describe how to make SBR rubber to a group of producers. However, I will make a few general comments. If there are people who would like to correct me as I go along, I realize you're the experts.

As Mr. Lemen has indicated, 15 SBR plants were built by the government in the early 40's. We seem to have a leukemia problem reported in three of these facilities. It is interesting to note that one of the facilities is no longer in operation so you now have 3 out of 14 facilities reporting abnormal findings.

The plants that we visited were primarily emulsion polymerization type plants. They brought in butadiene; they brought in styrene. In various areas of the plants, their soap solutions were made up, their catalysts, their initiators, and their activators; these were charged to their reactor chain.

In the early days of the process it was a batch operation. Later on, it was converted to continuous polymerization and the stream goes from one reactor to another. You saw slides with a series of reactors. At the end of the reactor chain, when the degree of polymerization that is wanted is ascertained, they stop the reaction by an addition of a short-stop. Then, the material goes to a recovery area and the unreacted monomers are recovered.

Basically, you have a blow down tank and a flash tank for the butadiene. The butadiene is a gas and under normal temperature it would flash off. With the butadiene removed, the material goes to a stripping column where it is sparged with steam and the styrene is removed. The styrene-butadiene are recycled and go back to the process.

The material now is a latex that has been removed and the unreacted monomers. We go to latex storage — here is where you would add your antioxidants, antiozonants, oil extenders, carbon black. The mixture is coagulated, filtered, dried, and bailed.

That is a very general overview of how you make SBR rubber. There are a variety of chemicals involved, probably well over 100 chemicals. I will mention a few.

A good description I might add of styrene-butadiene rubber is given in the article by Saltman which appears in Rubber Technology, Chapter Seven. The typical formulation for cold SBR rubber is basically as follows: butadiene, styrene, tert-dodecyl mercaptan (it's interesting to note that this chemical does not appear in NIOSH's extensive book on registry of toxic chemicals), diisopropylbenzene-monohydroperoxide, p-menthane hydroperoxide, ferrous sulfate, potassium pyrophosphate, trisodium phosphate, EDTA, sodium formaldehyde sulfoxylate, and your resin acid soap and water.

Carbon black was added somewhere in the late 50's at these facilities, and also various extender oils are used.

Obviously, you have soaps — it's an emulsion polymerization process. One emulsifier, sodium condensed naphthalene sulphonic acid, appears

in the NIOSH sub-file of suspected carcinogens. Other interesting compounds are diphenylamine and carbon black.

Phenyl-β-naphthylamine aroused my suspicion initially, but further investigation indicated, apparently, this had nothing to do with β-naphthylamine so it is not listed as a suspect carcinogen at this point. (See Table 4, Editor's Note.)

There are various other chemicals that are used as ozonants and oxidants; and there are various other defoamers and drying agents such as talcs and synthetic amorphous silicium.

I've tried to give you a little description of the process and some of the compounds present. We do have extensive lists of compounds, and they are available. We are conducting literature reviews on the substances, but you quite quickly run out of literature on several of the compounds.

CANCER EXPERIENCE AMONG WORKERS IN A CHEMICAL PLANT PRODUCING STYRENE MONOMERS*

RUTH LILIS
WILLIAM J. NICHOLSON

DR. WAGONER:
Dr. Lilis from the Mount Sinai Staff will now discuss the investigation that the School of Medicine at Mount Sinai has been undertaking with regard to a styrene facility in the United States.

I think it's noteworthy that we have now got some very limited feel for what we haven't seen in the butadiene and if we could look at the other basic monomer or material that's used in the SBR, that might give us some leads as to what we have.

DR. LILIS:
After the vinyl chloride experience that we went through and after our extensive clinical studies of workers exposed to vinyl chloride which led to the identification of several non-malignant pathological effects which we described, and some of which we thought were possibly precursors of malignant changes, we found that it was interesting to look at some other monomers widely used in the plastic industry.

One of the monomers we found to be of a high degree of interest was styrene because it is a vinyl compound (vinyl benzene) but doesn't have the chloride that vinyl chloride has.

Starting there, we made a thorough search of the literature and found that very little data were available on the long-term toxicity of this compound. There were extensive data available on acute experiments in animals showing that styrene was highly irritating for the mucous membranes and the lungs at high exposure levels. Also, there were indications, again from acute experiments, that liver and kidney toxicity may be expected. There was some indication as to central nervous system effects.

Very little data were available, as I said, on long term experiments in animals and there was a scarcity of data on human effects. Only several studies were reported in the literature on the styrene effects on exposed workers and those were usually formulated in quite vague terms.

The data emphasized the irritating effects and some of the central nervous system effects, especially in some of the reports we went through, but there was no clear picture that emerged from that literature review, and we found it was worthwhile to consider examining the working force of one styrene polymerization plant.

We tried to identify one styrene polymerization plant where the exposure would be "pure." In doing so, we chose a plant which is now engaged only in styrene polymerization to polystyrene and in some extrusion. Nevertheless, since we were going to examine workers who had had relatively long exposure in this plant, we found it worthwhile to get as much information as possible on the history of the plant and to look at what the processes had been like when the plant first started operating some thirty years ago.

Slide 1 shows the present status of the technology — the main line of technology employed in this plant. The raw material, which is ethyl benzene, is brought in; ethyl benzene is changed to styrene; and styrene is changed to polystyrene; and then there are some extrusion operations.

In the process of the transformation of the ethyl benzene to styrene, there are a number

*See Appendix E for text of preliminary report of study, which is basis for Dr. Lilis and Dr. Nicholson's presentation.

of by-products, mainly benzene and toluene, which are recirculated and then shipped out of the plant.

That makes it clear that there is some benzene exposure in this area of the plant even now. We don't know precisely what the level of that benzene exposure is, and we suspect that it fluctuates widely with certain incidents in production and leaks.

Slide 2 shows the history of the plant. As you see, when the plant started operating, production started from coke oven by-products from which benzene was derived and from benzene it went to ethyl benzene and from ethyl benzene, to styrene and then from there, to the butadiene and polystyrene.

Thereafter, there were changes after various periods of time. The butadiene process was eliminated back in the 50's; the coke-oven products were replaced by benzene directly shipped to the plant in '65, if I'm right; and later on, the last change in the plant's operation was relatively recent and was the substitution of ethyl benzene for benzene as the starting point of the whole operation. Given this history of the plant, it became obvious that all the workers who had been active before the most recent change of production would have had some benzene exposure in the past. As I mentioned before, some benzene exposure may be present even now in the early stages of the process.

We examined 494 workers employed in this plant and we tried to categorize them into two broad groups. One was high exposure and one was relatively low exposure. That was done after extensive discussion with the worker representatives and with management and a review of the whole process. We ended up with two groups, one of relatively high and one of relatively low exposure, being aware of the fact that these are rather gross dividing lines.

The total number of workers examined was 494, the median age was 40, but the age distribution (because of hiring practices) is bimodal. The majority of all those examined were men; only 9 women were part of that group. See Table 1, Appendix E.

The duration of exposure is presented in Table 2. As you can see, 42 per cent of all those examined had more than 20 years since onset, but there were 30 per cent who entered the plant after 1970 — just 6 years of exposure.

Our examination included a complete and detailed occupational history; past medical history; and a questionnaire on symptoms possibly related to exposures on the job (such as eye irritations, mucous membranes, eye, nose, ear and throat, bronchial irritation, skin irritation, and prenarcotic symptoms).

We also included the respiratory questionnaire, the MRC questionnaire for chronic bronchitis, and a complete physical examination.

A broad spectrum of laboratory investigations was used in order to detect possible adverse health effects due to styrene exposure.

Our tests included a complete blood count and platelet count; routine urinalysis, metabolites of styrene in urine like mandelic, phenylglycoxilic, and hippuric acid; styrene in blood and styrene in fat tissue; the carcinogenic embryonic antigen (CEA test) chromosome studies; sputum cytology tests; chest X-rays; pulmonary function tests, including diffusion for 60 workers; nerve conduction velocity measurements, and reaction time tests. We are here reporting only on a part of all results since not all of them have been evaluated at this point.

As expected, we have found that some of the workers had experienced prenarcotic symptoms. The overall prevalence was 13 per cent, not very high. Workers with high styrene exposure had significantly more prenarcotic symptoms than those with low exposure.

Irritation of mucous membranes with styrene exposure has been frequently reported at levels starting with 50 to 100 ppm in the working environment.

We found such symptoms reported in an overall percentage of 18 per cent of all those examined. Irritation symptoms were not found with higher frequency in those people who we thought had higher exposure and that may have to do with the fact that the so-called lower exposure was sufficient to give irritation symptoms.

One question we systematically asked was whether they had experienced acute tightness in the chest and wheezing while on the job in order to elicit if there was any bronchial irritation present due to styrene. There were 11 per cent of the workers giving positive answers to this question. Interestingly, the prevalence of this symptom was higher in those with so-called high exposure.

Looking for the prevalence of chronic bronchitis according to the MRC definition, we found that 19 per cent of the workers qualified, according to these criteria. There were 6 per cent of non-smokers, people who never had smoked, who had positive answers to the chronic bronchitis questionnaire and we have to consider the possible contribution of styrene exposure to this syndrome.

Airway obstruction (defined as forced expiratory volume per second over forced vital capacity being less than 75 per cent) was found in 35 per cent of those examined and was more frequent in the workers with the highest exposure. In 31 per cent of non-smokers, we found evidence of airway obstruction, and these workers had never smoked. As expected, more obstruction was found in the smoking population, especially in those with longer duration of exposure, but the difference in prevalence of obstructive respiratory dysfunction between smoking and non-smoking workers was much less than expected, 38 per cent versus 31.6 per cent.

The X-rays were read according to the ILO U/C International Classification of Radiographs of pneumoconiosis. Except in individuals with past exposure to asbestos, coal, or silica, no significant abnormalities were found.

Liver function was investigated using the bilirubin, alkaline phosphatase, SGPT, GGPT, and SGOT determinations. The GGPT test showed more abnormalities in the group with higher styrene exposure. The relationship was unchanged when workers who had a history of significant alcohol intake were excluded. The hematological changes investigated included hemoglobin, white blood count, and platelet count. Fourteen per cent of the workers had hemoglobins below 14 grams per cent, 2.7 per cent had white blood counts below 4,800, and 7.4 per cent had platelet counts below 180,000. No clear trend according to length or level of exposure was found so far as the hematological changes are concerned.

The results on the other tests that we performed are not yet completely evaluated and we are looking for the CEA results and the sputum cytology, especially, in order to find more answers to the question in today's discussion.

Our clinical survey up to now confirms that styrene has an irritant effect at levels now present in industry. The possibility that styrene is significant in producing airway obstruction and chronic bronchitis has to be considered.

Liver damage attributable to styrene exposure at levels prevalent in the plant we studied does not seem to be a major problem although there was some indication, especially the GGTP elevations I mentioned. More follow-up is necessary in order to bring more complete answers to this question of liver damage.

DR. NICHOLSON:

At the time that we undertook the clinical program to evaluate the effects of styrene, we also began a mortality study of workers of the same plant. Using available records, we identified 563 individuals who were employed for at least 5 years as of May 1, 1960, in the production facility that was described by Dr. Lilis. Follow-up has continued through December 1975; and 562 of the 563 have been traced and their vital status determined.

Among the 562, there were 84 deaths. Of the 84 deaths we have 83 death certificates and, at the present time, pathological specimens and hospital records are being received. The information at this time is only that which is supplied on the death certificate. When the follow-up is completed and verification of the causes of death obtained, a complete report will be submitted for publication.

Of the 83 deaths for which death certificates are available, 9 were of violent causes, suicide, or accident; and of the 74 remaining, 18 were of cancer. There were six lung-cancers (these are again death certificate diagnoses), two gastro-intestinal cancers, one abdominal cancer, three

prostatic cancers, two pancreatic cancers, one liposarcoma, one acute myeloblastic leukemia, one Hodgkin's sarcoma, and one mesothelioma.*

If we consider the last three cases, because they may be job related, the leukemia was in an individual who died in 1965 after having been employed in 1951. He was an electrician. The Hodgkin's sarcoma was in a millright, first employed in 1943, who died in 1968. The worker who died of mesothelioma was also an electrician, starting work in 1943 and dying in 1973. I mentioned the mesothelioma because it illustrates one problem of chemical plants — that there can be ubiquitous exposures to various carcinogenic materials, particularly among maintenance personnel. In this plant there were exposures to benzene, to styrene, to other hydrocarbons, and to asbestos from the insulation (which may be causally related to the mesothelioma death). In addition to the cancer deaths, there was an individual who died of a coronary, but had leukemia at the time of death. He was an insulator who first worked in 1944 and died in 1970. Additionally, there was a lung cancer in an individual who was certified as dying of a coronary.

We have additionally 21 death certificates, available from union files, of individuals who died in recent years. These individuals were not in the cohort because they did not have five years of employment as of 1960, or they were not employed on the date of the seniority list that we had at hand. Among these 21 deaths, there were an additional leukemia and an additional lymphoma. Thus, in 104 deaths for which we have certificates, there were two deaths of leukemia, one with leukemia, and two lymphomas. While the total number of deaths is small, the finding of five leukemias and lymphomas among 104 deaths is cause for concern.

One can look for possible relationships in exposures present at the plant and the observed causes of death. From its inception until 1969 (1962 — see Mr. Knauf's following comment), the plant used benzene as the raw material in the production of ethyl benzene, which in turn was used to produce styrene. Subsequent to 1962, there was still some benzene exposure from that which contaminated either the ethyl benzene, now shipped to the plant, or the styrene which was produced. It was of sufficient quantity to be recovered in a facility in which one operator would be employed per shift. The plant also produced styrene-butadiene rubber (styrene and butadiene — see Mr. Knauf's following comment) until about 1950 at which time it went primarily to styrene production and, subsequently, to polymerization of styrene. For the last ten years it has also produced a styrene-butadiene rubber latex. (One of the individuals out of our cohort who died of leukemia was employed in this facility.) However, because of the multiplicity of exposures to benzene, to styrene, and to a limited extent, to butadiene, it is not possible to make a direct causal association between a single chemical and any of the deaths observed.

At this time, it's our intent to extend the investigation of this mortality study, first to those with five years of employment both subsequent and prior to 1960, and, thereafter, if feasible, to those individuals with shorter exposure. Thank you.

DR. WAGONER:
Are there any questions?

MR. KNAUF:
Yes, my name is Bill Knauf and I'm with ARCO Polymers and the plant that was referred to was one of our plants. We did not produce styrene-butadiene rubber in the early days; we produced two main ingredients — styrene and butadiene. These materials were then shipped to the Akron area for production of the styrene-butadiene rubbers and, I believe, the benzene was not used after about 1962, not 1969.

DR. WAGONER:
Thank you.

DR. LILIS:
I would like to make one further statement as to styrene as a potential carcinogen. There has been work completed in our department on the mutagenesis of styrene oxide which is the first step in the metabolic pathway of styrene in the human body, and the oxide has been proven to be a potent mutagenic agent. That would, in

*Speaker's added note: Verification of causes of death has been completed. All but one of the cancer deaths were correct as recorded on the death certificates. In one case, however, pancreatitis was the cause of death rather than pancreatic cancer.

my view, warrant extensive experimental work on animals to find out if styrene or styrene oxide is carcinogenic in animals.

DR. WAGONER:
Do you have a question?

QUESTION:
Yes, from Standard Oil again. I want to know if you in your studies have knowledge of the levels of any of these chemical products and particularly of styrene in the plant?

DR. LILIS:
No, we had no levels as to past exposure and we only had deductions as to the levels of the present exposure given the symptoms we were able to identify in those people examined. Prenarcotic symptoms were found and are known to occur at levels of several hundred ppm's.

QUESTION:
I wonder how you are able to make a statement about levels of benzene and you're calling the levels of other chemicals ubiquitous, but there are no measurements that have been made now or in the past and this goes along with some of the others —

DR. NICHOLSON:
There has been one industrial hygiene survey by NIOSH during 1974, of exposures in the plant. They reported that levels of benzene following the spills were in excess of thirty parts per million. Similar levels occurred in other measurements taken in the facility so that this current operation —

QUESTION:
Spill of what?

DR. NICHOLSON:
Of benzene — in the benzene purification unit. As with any chemical plant, some spills will occur during its operation. These can give rise to concentrations that are above that of the current TLV. The fact is that they have occurred in recent years. The presumption would be that such spills or leaks within the system would have occurred in earlier years.

As far as general exposures go, one can, in that plant, detect the odor of styrene at various locations so we know that a completely closed system does not exist, as is the case with most chemical plants. The statement that there are general exposures to various chemicals is something that, in essence, is taken for granted.

QUESTION:
I think that's a poor assumption. I don't see with these chemicals why measurements can't be made. It's not that complicated.

DR. NICHOLSON:
They have been made during the one industrial hygiene survey that I know of by the local NIOSH group. The records of that are available through that organization. I don't know of any measurements made at this plant in earlier years, for example, in the years prior to 1962, when benzene was a major raw material used.

QUESTION:
I'm not convinced that we really know what chemicals we are dealing with.

MR. SOLOMAN:
Norman Soloman of the Ashland Chemical Company and I have two questions which I'd like to raise. One, for clarification of the flow chart of the plant history. It appeared to me that between 1962 and 1969, benzene was a starting material. Prior to '62 I thought I saw on the chart coke oven by-products being converted to benzene and then to ethyl benzene, is that correct?

DR. LILIS:
Yes.

MR. SOLOMAN:
In that case, since the studies involved workers with exposure prior to 1962, any effects could be resulting from exposure to coke oven by-products which include many chemicals besides benzene which are known carcinogens.

DR. NICHOLSON:
That possibility can exist.

MR. SOLOMAN:
And the second question I have concerns the statements about styrene oxide, stating it is a potent mutagen. Is this through in vitro or in vivo studies?

DR. LILIS:
This was done using the Ames bacterial test system.

DR. JOHNSON:
I am Maurice Johnson of the B. F. Goodrich Company. I have a question for Dr. Nicholson. On the 21 cases that did not fit your original cohort, if you redefine your original cohort so they would be included, do you have any idea how big it would get? Do you have any guesstimate at that?

DR. NICHOLSON:
I'm sorry, I don't. I could not tell you the size of the cohort if we, for example, included anyone that had ever worked for five years of employment. Roughly, my guess would be that you could add another 400 or 500. If one did so, one would have or could have a five-year cohort of about 1,000 people.

DR. JOHNSON:
Then if you possibly added another 500 people, you could take in enough to have these 21 deaths included?

DR. NICHOLSON:
Yes, but many more deaths, in addition to the 21, would also be included. The 21 happened to be deaths that were available that occurred in the last 4 or 5 years if I'm not mistaken — since the 1970 period of time. They were in essence really random deaths of which the union had knowledge.

A KENTUCKY STUDY: 1950-1975

J. BRADFORD BLOCK, M.D.

DR. WAGONER:

Dr. Bradford Block from Kentucky has undertaken a study in the Kentucky area and would like to present some material from the study.

DR. BLOCK:

First, I'd like to express my appreciation to Dr. Wagoner and Dr. Lloyd for offering this opportunity to present our data. We came into this by the back door as you'll see as I explain how we came by the data.

This all began with vinyl chloride as some of the other speakers have indicated. The union people in our area were very much concerned that perhaps there was a vinyl chloride in their plant that was unrecognized at that particular time. So with their urging, we undertook to look at six chemical plants in the Louisville area. They were representative of 63 such plants in the area in terms of mortality studies.

This did not include the B. F. Goodrich Company because they were already under rather extensive study. However, one of the six plants that was included happened to be a butadiene-styrene operation, the American Synthetic Rubber Company.

The time period covered by our studies was from 1950 to 1975. We obtained lists of names of deceased employees from the companies and from the union — individuals who died during that period of time. Death certificates were obtained on all of these individuals. These death certificates were then reviewed and compared with the doctor and hospital records to assure that the diagnosis was correct and to determine any contributory causes that did not appear on the death certificates.

This type of study has one particular problem in addition to those that are generally associated with death certificates and that is we were not able to obtain a complete list of everyone who ever worked in the plant that had died during this period. We made an effort to obtain as much information in this area as we could, and we think that we have a majority of those individuals included.

After the death certificates were reviewed and the diagnoses were confirmed, we divided our group into four major categories: 1) those that died of heart disease including myocardial infarction and acute types, but not including chronic congestive heart failure; 2) cancer in general; 3) other causes including chronic congestive heart failures; and 4) violent deaths.

In order to have some idea of the significance of our findings, we developed a control group which consisted of individuals of the same age, sex, race, social-economic background, and similar occupation who died in the same months as the individuals from the chemical plants, but who were not chemical workers. For example, a carpenter working in a chemical plant was matched with another craft person from a nonchemical plant. We did not match carpenters with physicians. The chemical workers were not compared with the general population.

The results of our studies indicated that heart disease was the number one problem in terms of chemical workers in general. This was significant at a 0.001 level using chi square. The next most significant thing we found had to do with cancer deaths. The total number of cancer deaths for the sample population and for the control were about the same. However, when we broke it down as to the site of the cancer (organ) chemical workers seem to have a higher proportionate mortality due to lung cancer. This difference was significant at the .01 level.

We also found 15 per cent of the population consisted of what we call maintenance men — I should perhaps define maintenance men before somebody asks. They were anyone who was not

directly involved in the process, such as carpenters, electricians, plumbers, and pipe fitters. The reason for this is that different companies classify maintenance men differently. Some people call them all maintenance mechanics and others have it broken down according to their craft or trade.

We took the American Synthetic Rubber Company, which was one of the six companies in the study, and looked at their data individually as a result of the NIOSH findings and the article that was published in the Journal of Occupational Medicine in March.*

We had a total of 53 individuals in this plant. Of those, 26 died of heart disease, 4 died of lung cancer, 2 died of stomach cancer, which is also mentioned in that article, 2 from esophageal cancer, and 2 from Hodgkin's disease, and I want to elaborate on those two in a minute. There were also one colon, one brain, one larynx, one melanoma, one liver, one duodenum, and one leukemia. Now, about the individuals who are of particular importance. First of all, the leukemia.

The leukemia death was in a 67-year-old black male who died in December 1972. He was a retired truck driver at the time of his death and he died of acute myolitic leukemia. Among other chemical workers in the study, there were 3 other cases of leukemia. One was in a 49-year-old white male chemical operator who died of acute monocytic leukemia. Another was in a 56-year-old white male chemist who died of acute myolitic leukemia and the other was a 64-year-old white male maintenance mechanic who died of chronic myelogenous leukemia.

One of the 2 cases of Hodgkin's disease or lymphoma that were recorded in this study of the American Synthetic Rubber Company was a 36-year-old white male who died on July 17, 1966; he was an instrument control man and I do not have the complete history of his work. The second man who died of Hodgkin's disease was a 54-year-old white male who died on March 23, 1970; he was a guard.

I think that there is a great deal that needs to be done in terms of identifying more about the work histories of these individuals and we intend to undertake that.

I have given you this information because I think that it's pertinent and because, from our past experiences with vinyl chloride, I think that every bit of data that we can get together and bring to focus on this particular problem will be helpful. I thank you for hearing what we have.

DR. WAGONER:
I would like to ask a question. When you were going through the number of deaths, there was one case of leukemia among the workers at American Synthetic, and then you listed four. Could you clear that up?

DR. BLOCK:
Yes, I thought that I also said, when I was talking, that the other three cases were of other chemical workers that were included in the study. They were not from American Synthetic, that's correct.

The processes involved in the other five plants were not at all related to the process at American Synthetic. So in terms of leukemia, as it relates to the problem that we're here to discuss today, we only have one case. That was in a retired truck driver which I found interesting, but if you read the March article, you'll find that they also found leukemia in a truck driver and couldn't explain it either so that's where that particular case came from.

MR. BELICZKY:
I would like to ask Dr. Block a question. When you first spoke about the number of deaths that

*Speaker's note:
Since our presentation on April 30, we have done an in-depth review of the deaths at the American Synthetic Rubber Company. With the aid of Local 423 and the company, we have been able to find an additional 19 deaths. One died of leukemia. We now have a total of 72 death certificates from this plant.

We still have nine names that we have been unable to trace. Some of the names on our list may represent the same individual or fictitious persons as many do not have any personnel record or record of employment with the company.

Also, since that time, we have discovered a second leukemia death. This death was not previously reported because it occurred after the cut-off date for our original study. The death was in a 45-year-old white male, truck driver who died of acute stem cell leukemia on January 28, 1976. (Letter, Dr. Block, July 7, 1976.)

you looked at, at American Synthetic's, and the group that you studied, you gave a number and I didn't quite catch that number.

DR. BLOCK:
There were 53 total deaths.

MR. BELICZKY:
From when?

DR. BLOCK:
From 1950 to July 1, 1975.

QUESTION:
How many lymphomas?

DR. BLOCK:
Two lymphomas and one leukemia. I think that I didn't give you the total breakdown: five were violent deaths (auto accidents, murder, etc.), one was pneumonia, one was a pulmonary aneurism, one was cirrhosis of the liver, one was a uremia, and the other is unknown. That should total up to 53 — 26 heart, 17 cancer, 5 other, and 5 violent.

DR. WAGONER:
Any other questions?

MR. INFANTE:
Peter Infante, NIOSH. With regard to the methodology, you said you don't have all the deaths that died, you just have the ones that you received from the company or from the unions?

DR. BLOCK:
That's correct.

MR. INFANTE:
In other words there's a question mark as to how many people had worked there for various lengths of time and how many died.

DR. BLOCK:
That's correct.

MR. INFANTE:
And the other question is that many people would have died at other hospitals outside of the Louisville area, and you would not have any information on that. Is that correct?

DR. BLOCK:
We have information only on the individuals for whom the company had records or who died and the union had the records.

MR. INFANTE:
Does it make any difference where they died?

DR. BLOCK:
No, it does not make any difference where they died. We did not limit where the people died. It could have been in Louisville or in Florida.

MR. INFANTE:
How did you pull the control for the person who died in Florida, for example?

DR. BLOCK:
Since these people primarily lived in Louisville and retired in Florida, the control was drawn from the people who lived and died in Jefferson County which is the county where Louisville is located.

MR. INFANTE:
So then you may have some problems in terms of the diagnosis?

DR. BLOCK:
In this particular case we had some people from Indiana who lived right across the river — like across the river from Cincinnati, but I don't think the situation in New Albany was much different from that in Louisville. The great majority of these people did live and die in Louisville.

Apparently, this is a type of situation or operation so that when a man goes into this thing, he stays with it. These were not people who were in and out of it for a short period of time. It's my understanding that there were draft deferments available during World War II that encouraged people to work in these places and they tended to stay on. It's not that difficult although it might be rather hazardous.

DR. WAGONER:
I have a question also relating to the ascertainment of the deaths. If they come by way of two various mechanisms — either because they are retired and are being pensioned or because they're in an acute episodic event where a person has a massive coronary, and happens to be on the job — (the company obviously is aware

of these) — then in a sense you may be overloading your proportions disproportionately with individuals who had acute coronaries while in the employment who had never reached retirement age and your distributions certainly would be biased to show an effect of over proportion of heart disease and, thereby, using the proportion of mortality and under ascertainment of the two cancer experiences.

DR. BLOCK:
Well, I think this is a very valid criticism, and I think that first of all we have to look at what we have available to us and we did not have the staff, the money, or the help to run every individual down who ever worked for the company.

I think that through the cooperation of the union and the company that we got the majority of people — I would say we got 99 per cent of them. We did look at people who were retired, not just active workers, and in our heart deaths, there were retired people included in that. I did not bring the data with me where I'm prepared to break down how the heart attacks occurred or in what group or in what age. The one thing that we did know in analyzing the data is that the heart attack rate in terms of the age at which the heart attack occurred was somewhat younger than is found in the general population. It was also younger in our chemical workers than it was in the control group.

I don't know whether I have completely answered your question or not but, as I pointed out from the very beginning, any study of this type is riddled with all kinds of problems and it's a matter of trying to get an overview of what's going on and I think that there needs to be a great deal more work done. We were trying to identify a large problem and we did not undertake this study to particularly look at American Synthetic Rubber or butadiene or any one particular chemical. We were just looking for a gross pattern and I think that all we have discovered is the tip of an iceberg and we do not know or understand all that lies beneath the water, and I would hope that that's the idea of this meeting today to try to find out just exactly what we need to study.

MR. SAMUELS:
I am Sheldon Samuels of the Industrial Union Department. Dr. Block, have you initiated any clinical studies of the workers at American Synthetic, any industrial hygiene studies? Has the Kentucky OSHA program done a walk through in the plant?

DR. BLOCK:
Since I'm not a part of the compliance effort, I do not have privilege to what compliance does. I do not know whether American Synthetic has ever been visited by the compliance people or not. If there are representatives from the company here, they might be better able to answer that.

In terms of what we have done to date, since we did not recognize styrene or butadiene as a particular problem until it was brought to our attention by others, we have not done this. We do have plans to do this. We have discussed this problem with the corporate and medical directors and with people who are involved in terms of their own internal operations. We do wish to follow up on this. As I said, this study was done primarily as a fishing expedition to find out if there were problem areas and I think that this conference today indicates that there definitely is a problem.

We do plan to follow up on this and we have had good cooperation from both union and from the company in terms of follow-up. The design of that right now is being carried out and we we have not yet done anything in terms of going back to the company. We just completed the analysis of these data about a month ago.* But that is a very good point and I do intend to follow-up.

MR. BENTLEY:
My name is George Bentley and I am an employee of the American Synthetic Rubber Corporation and I'm the union representative. As far as I know, we have never been in contact with Dr. Block as far as your investigation, and I would like to ask the gentleman a question on the clinical research.

For the past two years, we have approached

*Speaker's Note: A comprehensive industrial hygiene survey of the plant was completed in the summer of 1976 and a copy of the survey report was supplied to NIOSH and Mr. Samuels. (Letter, Dr. Block, August 24, 1976.)

the company on initiating this type of program, the surveillance of the employees at American Synthetic and we received very little cooperation on the part of the company and we are still in the process of trying to get this clinical surveillance program set up and anything that Dr. Block could do to help us initiate this program we would very much appreciate it on his part.

DR. BLOCK:
I think you have a very valid concern and, as you're well aware, the Commissioner of Labor in Kentucky is an ex-employee of your organization and he shares your concern. We intend to do whatever we can to encourage the company to look further into this particular problem.

I think the problem right now is one that all of this body are here to decide and that is just exactly how are we going to approach the problem, what kind of medical surveillance is indicated, and just exactly what are we going to do. I think that this afternoon's panel is going to talk about that.

I share your concern about this and I'm concerned about the heart diseases, the lung cancer, and the Hodgkin's disease. I think these are things that we've got to look at and the only way we're going to find out about it is through this type of thing.

Your earlier remark about not having direct contact with us is correct. We have never had direct contact with the union as such, but it's my understanding that they have contacted the Department of Labor; at least my commissioner tells me that this is the case and this is where I got the encouragement to go ahead and do this study.

MR. BENTLEY:
One thing I would like to state to you and to the gentleman who, I think, was from Standard Oil who was talking about the levels of exposure of chemicals to the employees in a synthetic rubber plant of styrene and butadiene. I can guarantee you, I've worked in about eighty per cent of the operations from start to finish, even down to cleaning the vessels, and at times I have been exposed to what I consider a 100 per cent level. This is because, in part of the operation, it's necessary that the chemicals like butadiene in one part of the recovery operation — like on a decanter vessel where you separate the water from the butadiene — it's necessary to blow the water off of the bottom of the tank and in the process of blowing off this excess water, you also get to the butadiene — it is also blown out and you directly breathe this butadiene. So, the level is very high in certain areas in dealing with the chemicals.

LABOR UNION COMMENTS

LOUIS BELICZKY
TROY CARDEN
STEVEN WODKA

DR. WAGONER:
I think it's a matter of record that we have corresponded across the board with every labor group in the United States who is deeply involved in these areas as well as every management group and we are looking forward to a very candid and open discussion of any information that is available to collectively lead us as a society towards any resolution of this problem.

MR. BELICZKY:
My name is Louis S. Beliczky and I'm Director of Industrial Hygiene for the United Rubber Workers International Union. I do want to state that among us today are our representatives from at least five of our local unions. The rubber workers here probably total about 22 or 23 people.

It is difficult for me to begin my comments, since I get the impression that generally the tenor of the previous comments were negative and lacked positive inference with respect to the possible relationship or link of leukemia in operations where SBR rubber is produced.

For the last five or six years I have been concerned with the worker health aspects of polymer production operations. SBR in particular has been a matter of concern. I feel that the leukemias and other diseases linked with SBR production will have or have had a more far-reaching effect on members of United Rubber, Cork, Linoleum and Plastic Workers (URW) than the direct effect of vinyl chloride.

Before I begin any further comments on SBR and the reported related mortality and morbidity linked to SBR, I would like to make reference to the State of Kentucky's epidemiological study of Louisville's "Rubber Town."

Earlier this morning Dr. J. Bradford Block mentioned that he studied the 53 deaths that had occurred among workers at the American Synthetic Rubber Company of Louisville (our URW Local 423). The list of deaths from 1950 to 1974 that was provided to me by the local union president had 70 deaths occurring during that period. A more recent review of death indicates that 90 workers employed at ASRC had died of various causes. It should be obvious that there is a significant discrepancy between the data that we have and the data used by Doctor Block in his reported epidemiological survey.

Doctor Block mentioned that he had discussed his information with the local union. The nine officials of our union, present here today, had no awareness of any meeting with the State of Kentucky Health Department or Doctor Block regarding this issue.

The original list of 70 deaths at ASRC did not include the cause of death on 9 of the former workers. The original list of 70 deaths showed that 35 died of some form of heart disease. Of the 16 cancer deaths, one was a leukemia. There were also 3 violent causes of death; one death due to arthritis, and 5 accidental causes of death.

It is interesting to note that of the 9 deaths which had no listed cause of death, 3 were maintenance workers, and 2 were yardmen-cleaners. The yardmen-cleaners actually crawled into reactor vessels to chip-out and clean reactor vessels used in polymer production.

The work classification of the other nine were: 2 employed in plant protection; 2 machinists, and 1 pipefitter. The yardmen-cleaners, the machinists and the pipefitter could have had substantial and varied exposure.

The individual who was listed as dying in 1966 of leukemia was an electrician. More recently,

an April 22, 1976, letter from the ASRC indicates that Dr. Block had reported another leukemia death of a former ASRC employee who died on December 22, 1972.

Expert medical opinion expressed to me stated that the encountered leukemia deaths were considered statistically significant.

At ASRC, there have been 2 reported deaths due to leukemia — one in 1966 and one in 1972. It should be reported that in addition to producing a styrene-butadiene and butadiene copolymers, ASRC was also producing a liquid polymer used by the Thiokol Corporation in its manufacture of solid forms of rocket propellant. Benzene was used at ASRC to manufacture the liquid propellant. Based on discussion with the workers, significant exposures to this known leukemogen (carcinogen) had occurred until very recently. The potential exposure to benzene at ASRC may complicate the picture of leukemia-linked deaths or morbidity among the ASRC workers involved in SBR polymer production. I, therefore, urge Dr. Block and his associates involved in his epidemiological study to contact directly the URW Local Union or the International Union for assistance in obtaining more reliable information on work histories, since exposure levels to environmental agents were never evaluated by ASRC.

Historical development of SBR production was briefly referenced by Ron Young of NIOSH. With the advent of World War II, this country was cut-off from its supply of natural rubber. The U.S. Government contracted and supported the research development of synthetic rubbers. The six U.S. companies involved developed and produced the styrene-butadiene polymers and copolymers which still represent the majority of synthetic rubbers used today.

One can just surmise that the styrene monomer used 30 or 35 years ago was far from being the relatively pure monomer being supplied today for the manufacture of synthetic rubber.

We can realistically assume that the concentration of benzene (as an impurity in styrene monomer) was considerably higher than it is today. (Perhaps as high as 0.1 to 1% — 1,000–10,000 ppm).

Earlier this morning, Drs. Lilis and Nicholson (Mt. Sinai School of Medicine) expressed their feelings regarding styrene monomer containing benzene as an impurity. I personally feel that styrene monomer containing benzene as an impurity could be linked with the leukemias and other blood dyscrasias we have observed in Port Neches and elsewhere. We have no information regarding the degree of purity of styrene monomer used in the past. About three or four weeks ago, the Dow Chemical Company informed me that their styrene monomer contained up to 10 ppm of benzene, and also contained from 3,000 to 4,000 ppm of ethyl benzene. Information from other suppliers is not currently available. More information regarding the action of ethyl benzene on humans should be obtained.

Let's sort of set the records straight as to how we became informed of the leukemias linked to styrene monomer production in the Port Neches plants in Texas. On March 18, 1976, of this year, I was in negotiations with the B. F. Goodrich Company regarding issues that we were concerned about in areas of occupational safety and health. I left (it must have been about 11:00 o'clock or 11:15 that particular morning) and headed on to Akron and Cleveland. I found out two or three days later that one of our local presidents, who is here today, Mat Contessa, somewhere around 11:30 that day made a statement to one of the corporate negotiators in reference to the fact that he had information he had obtained from one of the OCAW (Oil, Chemical and Atomic Workers) presidents that they were concerned about the number of leukemias that they had in their plant in Texas.

Mat Contessa brought this to the attention of Harold Fast, the corporate industrial relations man, who in turn brought it to the attention of Dr. Maurice Johnson, the corporate medical director of the B. F. Goodrich Company, who in turn verified the leukemia deaths by probably talking to one of the company doctors in Port Neches.

Dr. Johnson, being a very credible individual, was concerned and went to visit NIOSH on March 22, 1976. He met with Dr. John Finklea and probably a few other NIOSH officials and reported the incident to them. I became aware of this particular situation when I was in nego-

tiations with Firestone, when I was called by the Wall Street Journal asking me what I knew about the leukemias related to styrene-butadiene production. I didn't know anything about them. That's basically how we became aware of the leukemias linked to styrene-butadiene production — the reason for this briefing.

By March 29, our union had notified all of our locals in the United States and Canada regarding the potential leukemia-styrene-butadiene problem. We also had a series of discussions with some of the corporate medical directors and their concern was obvious. We did initiate action through the University of North Carolina and Harvard to take another look at the epidemiological mortality data that they had regarding synthetic plant operations in plants where there was a relatively large data bank. The comments that Dr. Spirtas made today were related to operations where synthetic polymer was produced in Akron plants, where in addition to having exposures in styrene-butadiene production, the workers may also have been exposed to other solvents or other leukemogenic agents.

I really don't know how many related deaths there have been among rubber workers. There are 8 or 10 questionable deaths in Akron due to some form of hematopoietic damage. I'm not sure of the form of anemia or leukemia reported. I'm not quite sure whether we know what kind of leukemia we should become concerned about or whether the various leukemias that we see on death certificates may all relate to exposure to styrene-butadiene operations.

In one of our plants in Pennsylvania, an individual who worked in a synthetic plant which is no longer in operation, has been recently diagnosed as being preleukemic. I'm not quite sure what that means medically except maybe that he may have aplastic anemia.

The ASRC situation is of relatively grave concern. I have spent about two years working with our local union in trying to initiate action on the part of the company to initiate medical or clinical surveillance to evaluate the health status of the workers. Because of the information regarding leukemia associated with SBR production, we increased our effort. Hopefully, we will get assistance from some of the governmental agencies and the University of Louisville to study the health conditions in that plant. From the comments made by Dr. Block and other speakers this morning, lymphomas, lymphosarcomas, and the leukemias certainly are conditions to consider. It is obvious to me and it should also be to all of us assembled here, that there is a real worker health problem in plants where SBR and associated polymers are produced.

I think it is now very important that large and small producers (companies) of synthetic rubber, participate and cooperate with OSHA and NIOSH in obtaining more reliable information. I have a strong personal feeling that by taking a close hard look at synthetic rubber operations, we shall find much more morbidity and mortality than is currently being reported.

Multiple SBR operations and facilities peaked their production in the '40's. Some of those plants are no longer in existence — workers employed during that time (living or dead) must be part of the epidemiological mortality and morbidity investigations to be cooperatively conducted by the companies, NIOSH, and OSHA.

I urge that NIOSH, OSHA, and responsible industry also take a good hard look at other polymer operations in addition to SBR. If there is to be a NIOSH or OSHA industry-wide study, facilities where acrylonitrile-butadiene-styrene polymer is produced *must be part of the survey effort.* Some of the polymer and copolymer producers use both SBR and ABS systems.

One of the chemical plants we have organized just got out of the PVC business and is building a new ABS facility.

This morning, Dr. Spirtas seemed to imply that there may be differences in risk in operations involving liquid latex production versus operations where crumb or solid SBR is produced. This operational variation must be investigated. Perhaps we can obtain information on the type of liquid (latex) rubber that is used to produce the common foam rubber currently on the market. In addition to the so-called foam production operations, we must also evaluate worker health hazards involved in the production of the hard plastics made by SBR or ABS systems.

Let us not neglect to consider the use of the polymers to make a product.

I would appreciate NIOSH permitting one of our URW local presidents to make a few comments: Troy Carden, President of URW Local 423 of the American Synthetic Rubber Company. Mr. Carden.

MR. CARDEN:

I'm Troy Carden and I'm the President of the United Rubber Workers, Local 423 in Louisville and in the American Synthetic Rubber Corporation. We represent the production workers at the American Synthetic Rubber Corporation.

I appreciate the remarks that Dr. Block made this morning, indicating that Dr. Block, along with his team, is now ready to come in and help us run the study on the American Synthetic Rubber Corporation.

I was a little surprised, however, at the statement that Local 423 — that the unions at American Synthetic Rubber Corporation had been so cooperative with the company and the state in running his prior test because I was not aware that the test had been made until after I saw it in the paper. But, we are concerned about the health and welfare of the people at American Synthetic Rubber Corporation.

For the last 2 years or more, we have tried desperately to get this cooperation from the company in running a blood test of some kind on our people. We told them — "let's get something started" — "maybe we don't have to go through all of them, but let's find out what's causing so many heart attacks, a number of cancers in our plant."

We do know that we have two or three leukemia deaths. I was made aware of one this morning that I was not aware of, but I hope that we can now announce at the first part of the week that there will be a study made giving every employee, both management and labor in that plant, a thorough blood test. I thank you.

DR. WAGONER:

May I just respond to that by indicating that consistent with the National Institute for Occupational Safety and Health policy and consistent with the Occupational Safety and Health Act, we do acknowledge receipt of the request from the union for medical examination of those employees and we will be discussing that this afternoon as part of our ongoing program.

MR. WODKA:

My name is Steve Wodka and I'm Legislative Assistant for the Oil, Chemical, and Atomic Workers Union. I would like to say also that everyone of our local unions that has contact with styrene-butadiene or actually makes the SBR rubber is represented here today, including also one from Canada.

I think it's a shocking story that in 1976, a major health problem was uncovered because of empirical observations of the local union president of the OCAW being mentioned to a fellow union brother of United Rubber Workers prior to the negotiating session and that, in turn, got this whole episode under way.

I think it's important for everyone to realize — for those people who don't know that the people who have the information are not looking. That is one of the points I want to make today. Because, we, in every one of the facilities where the OCAW is a representative, are going to demand total disclosure of all the information that the employers have because if they're not willing to look, then we're going to have to take the responsibility ourselves and do all the looking and the checking.

We want all the mortality data, we want all your morbidity data, and we know you have it because we know that you pay the insurance premiums. We know you get these insurance records and we know you have the pension records. We know you collect death certificates, but of course, you don't do anything with the information.

We want to know all the chemicals that are used in the plant, everything including trade names. We want to know the generic names of all the chemicals used.

We want to have all the monitoring data that you have, we want to know about all the insurance carriers that come in the plant and take

samples, we want to know about your corporate industrial hygiene sample programs where you take samples and have not told our people what the levels are.

I think that another point is that we can't wait for the culprit to be found in this leukemia episode. Obviously, there are a number of chemicals that are suspect and it may take several years before the scientific and medical community can finally say that it is this chemical that's been causing all these deaths — we can't wait that long.

Our union already has at least 8 leukemias and, of those 8, 6 of our members have died. So, we can't wait any more. And already, just from the preliminary work that has been done by NIOSH, we can see that there are hazards in these operations, hazards in these plants that need to be corrected right away. For example, there are the cleaning of reaction vessels, the stripping of columns, or whatever, without proper respiratory protection.

Secondly, there is the eating of food, consuming of food, in rooms where there is also exposure to toxic materials. Now, this right now is a violation of an OSHA standard. And any prudent employer we would think, would at least follow the bare minimum requirements of the OSHA regulations and provide our people with separate lunchroom facilities where they can at least consume food in an environment free from fumes and vapors.

Third, engineering controls — anyone who knows what these facilities are like on the inside knows that there's exposure to fumes, dust, smoke — these are all things that could be engineered out by current technology.

Lastly, increased maintenance of these facilities. We know all too well how maintenance forces have been cut back year after year after year, that these plants are run until the equipment breaks down and then the repairs are made. But in the interim, the leaks have occurred, the exposure to the fumes has occurred because the equipment is broken down, and our people suffer.

Now, all these are things that the industry can do now if they want to. I want to stress this point — that we're going to be watching this industry very closely over the next couple of weeks. If we don't see a voluntary effort to clean up these plants now, let me assure you that the labor movement will seek and we will get an emergency temporary standard from OSHA in order to deal effectively with this problem.

Now, I would like at this point to call on Rafael Moure who is an industrial hygienist on our staff. He has a Ph.D. in industrial hygiene and has gone to these facilities and has performed his own study. He has a few comments.

MR. MOURE:

Thank you, Steve. I would like to clarify something first. I am in the process of finishing my dissertation for my Ph.D. in industrial hygiene and I hope at the end of the summer that I will be through.

A WALK-AROUND AT A B. F. GOODRICH PLANT

RAFAEL MOURE

I would like to report on a walk-around survey that I conducted at the B. F. Goodrich Chemical Plant, Port Neches, Texas, on March 31, 1976, following the Wall Street Journal report of the leukemia deaths at Port Neches.

One of the OCAW locals (OCAW Local 4-228) in Texas represents the people that work in this plant. This local also represents the people that work at Texas–U.S. Chemical that is a twin plant of B. F. Goodrich Chemical.

When the health and safety staff of the Oil, Chemical, and Atomic Workers found out about the leukemia deaths, we proceeded to look at the mortality statistics for cancer deaths in the specific county where these two plants are located.

We found that the highest rates for cancer of the nose, larynx, and skin in the United States from 1965-75 appear in two counties in Texas: Orange County and Jefferson County. The Port Neches SBR plants whose workers we represent are located in Jefferson County in Texas. In addition, the highest rate of leukemia in the country is also found in the Jefferson and Orange County area. (The data apply to the white male population.)

I want to reinforce the general position of OCAW on the leukemia problem by describing what I observed firsthand in the production process of SBR in the B. F. Goodrich Plant, Port Neches. From the occupational health point of view, we have to look at two aspects. One is the toxicity aspect; that is, what substances are more likely to produce toxic problems. The other is the hazard aspect; that is, if the way the substances are used will produce the toxic effects that we know.

My findings show that the toxic substances (especially carcinogens) used throughout the SBR process were used in ways conducive to high exposures to operators. I have found that the most relevant toxic substances encountered in the process are as follows:

1. ANTIOXIDANTS. I'm going to identify two of these antioxidants. One has the trade name of Stalite; it was described to us as a mixed alkylated diphenyl amine. The other has the trade name of NEPA, which again is an undeterminate mixture of alkylated diphenyl amines.

2. RADIATION SOURCES. These radiation sources, as was explained to me, are used to identify the specific gravity of the latex at the end of the process in order to determine the extent of polymerization. As I understand it, there are five units at the end of each line of the emulsion polymerization reactors. In the slides that Ron Young of NIOSH showed, you could see pictures of the radiation sources.

3. BENZENE. The styrene monomer, according to the information that I got from Lou Beliczky, might have benzene contamination as high as 10 ppm.

4. EXTENSION OILS. These oils are added after the blending process. These substances are identified by the following trade names: Sundex 790 oil, Sunthene 380 oil, Gulf 534 oil, Textract 2202 oil, and Detrex 766 oil. I understand that in the different formulations, different quantities of these oils are added to the latex after the blending process (10–20% by weight) and before the coagulation in order to modify the characteristics of the latex. Analysis of samples of these oils undertaken by Kettering Laboratory, University of Cincinnati, Medical Center gave the following results:

Extension oil	*ppm Benzo(a)pyrene in liquid*
Gulf 534	nil
Sunthene 380	100
Sundex 790	100
Detrex 766	100
Textract 2202	200

5. SHORT STOPPERS, ESPECIALLY GOODRITE 3955. Goodrite 3955 is identified as a 1:1 mixture of sodium polysulfide and a metal salt of dimethydithio-carbamate.

6. SOAPS. Additive nycol, a surfactant containing naphthalene sulfonic acid, is used in the emulsifying process preceding polymerization.

7. CARBON BLACK. Carbon black is used in the process.

8. TALC. Dick Lemen, from NIOSH, made the observation and I'm emphasizing it, that there is massive use of talcs during the bailing process of the SBR blocks. It is my understanding that talc was once used widely in the plants (10 years ago), but at this time, the information that I've got is that talc is not being used. Diatomaceous earth or filter aid or perlite dicalite is used instead (trade name of this is Bulk Aid 30).

Based on this list, I'm going to proceed to give you a description of why these toxic substances pose serious concern from the industrial hygiene point of view.

First of all, after the coagulation process, there is a rough filtration of the latex in some machines that are called "shaker screens"; this is an open process. In one of the slides of Ron Young from NIOSH, you could see a white vapor cloud rising from the "shaker screens" (average temperature is about 120°F). Exposure to items 1,3,4,5,6 in my list is a distinct possibility. In addition, lunchroom and food storage facilities are located in chemical storage areas.

Now, the workers have expressed to me their concern that their right to use these facilities might be taken away due to the leukemia problem, a right they struggled to win. I would like to make it clear that these rights should be maintained, that is lunchroom and food and storage facilities separate from the storage of chemicals and away from open processes. This is a minimal reasonable change that can be implemented in a short period of time. The cleaning of closed vessels during maintenance operations is another source of exposure. No protective respiratory equipment is used for clean-up during down time inside closed vessels.

I witnessed, for instance, the cleaning of a dryer. Hot drying of finished latex is the process following the shaker screen filtration. When the latex contains carbon black (i.e., SBR polymers for tires), the driers are covered with dried up latex and carbon black dust. During cleaning operations (done on the average once every three months), there are two or three people involved physically in scraping pieces of latex out of this dryer. Exposures to carbon black dust were quite evident. People are scraping this out of the dryers and throwing it out by hand without any respiratory protection.

In the baling part of the process, that is, after the drying part, exposure occurred to talc 10 years ago and is occurring to other silicates today. The bales of synthetic rubber are covered with talc or with the diatomaceous earth in order to avoid the sticking of the bale. There is absolutely no respiratory protection of the people doing this operation. There is no ventilation that I was aware of during this process. Another operation where exposure is apparent is the latex sampling.

Every 2 hours, a one-pint sample is extracted from the last reactor of a series to study the extent of polymerization. Twelve samples a day in five reactor lines are taken every day. Exposure to unreacted monomers, to antioxidants, and to short stoppers occurs every time a sample is taken.

I have attempted to give you a brief summary of my walkaround survey and this should reinforce the OCAW's emphasis on the imperative nature of this problem. I don't think that we can honestly tell the workers present here that are exposed to carcinogens in these plants that we're going to sit and wait to find out what is the specific causative agent of leukemia. I think that exposures to all the chemicals that have been mentioned here, most of them confirmed and suspected carcinogens, should be stopped today. And it is the responsibility of B. F. Goodrich and Texas–U. S. to take the steps necessary to avoid further exposures to workers in their facilities immediately.

DR. WAGONER:
Is there a question?

MR. SOLOMAN:
Norman Soloman again from Ashland Chemical. I would like to make a couple of comments and ask some questions. Firstly, you mentioned that in certain open operations, you considered that there may be hazardous exposure to chemicals being used. You mentioned particularly alkylated diphenyl amines, etc. Have you undertaken any analysis of those vapors to determine whether those chemicals are actually being involved and passed into the atmosphere to create a hazard?

MR. MOURE:
This is the report of my walk-around visit. I wasn't in the plant for this visit to take any air samples, but we will continue in our investigation, and we are going to study the possibilities of taking air samples in these places. I am just observing that the chemicals are widely used raw materials carelessly handled in an open process, without proper safeguards for operators. I agree with you that samples should be taken and I guess this afternoon we will be addressing ourselves to the specific samples that it will be necessary to take to evaluate exposures.

MR. SOLOMAN:
I think it is very important to note that certain chemicals are of sufficient low volatility and high molecular weight that once they may be present under the conditions of the use, they may not be involved in the atmosphere and, thereby, creating a hazard.

DR. WAGONER:
Please, could we keep the comments to a minimum at this point, because this afternoon we're going to be discussing work practices, etc. Is there any other individual in the room, labor and/or management, who has any indication of any other health related data at this point in time, at this particular stage. We will discuss the analytic, the question of work practices, etc. in the afternoon.

MR. SOLOMAN:
I would like to make one other point in reference to carbon black and the comments that this was hazardous. The animal studies that those who are familiar with carbon black must be aware of (the studies of Dr. Nou and others) are actual studies. They were done with feeding, inhalation, subcutaneous, and intraparenteral, and in no instances of such animal studies was there any evidence that carbon black produced cancer in any form.

MR. BELICZKY:
I would just like to comment for a minute. First of all, on the use of antiozonants — some of the most reactive antizonants are used in the operations that produce SBR rubber.

Whether or not they have a low vapor pressure is relatively immaterial. The material goes through the various kinds of coagulating operations and operations that involve heating and drying of the crumb and the final operations that package the material and our industry is plagued with a high incidence of skin sensitization reaction from the diphenyl amine type compound. I think one must not lose sight of the fact that when we judge a hazard, we should judge it by the way the material is introduced and used. Under no circumstances can I accept any statement relating to the use of antiozonants as being a relatively safe chemical to use.

From the standpoint of carbon black, I don't think Dr. Nou's studies were conclusive that carbon black is safe in light of the fact that under two separate studies, four carcinogens, although they were animal carcinogens, had been isolated from carbon black. I'm still quite concerned that carbon black is a hazardous material and I have the data and documentation that I would be happy to send to the individual from Ashland Oil.

STATEMENT — INDUSTRIAL UNION DEPARTMENT (AFL-CIO)

SHELDON SAMUELS

First, I would like to bring to the attention of this body, since it has not been well publicized, that on April 23rd, President Bommarito of the Rubber Workers did file a request with the Secretary of Labor for an emergency standard for benzene. That request should be joined, as Mr. Wodka has pointed out, with a request for a second emergency standard on the entire SBR process if the industry is unwilling to follow recognized industry practices established as early as 1943 and 1944.

Before demonstrating that such practices have been established, I would like to say that simply because we have not isolated all of the discrete agents, that's not a reason not to have a standard. A process standard may be appropriate, and it's obvious to me that medical surveillance, maintenance, engineering controls, housekeeping, work practices, sanitation and other measures ought to be taken now. They perhaps should have been taken when the data published by the University of North Carolina were made available to the companies last year, many months before they were actually published.

The two references which I want to enter in the record are R. H. Wilson, *Health Hazards Encountered in the Manufacture of Synthetic Rubber*, published in JAMA in 1944, listing seven procedures to protect workers. I would hope that since the procedures have been recognized by the industry since at least that time, that they would do now what they did not do a quarter century ago.

The second reference is Mallet, *Industrial Hygiene and Synthetic Rubber Manufacture* published in Industrial Medicine in 1943. This presents a specific recommendation for the protection of workers in reactors.

There are five unions represented here today. The Rubber Workers; the Oil, Chemical, and Atomic Workers; the International Chemical Workers; the Pipe Fitters; and the Allied Industrial Workers. They all urge expedited governmental action. Thank you.

DR. LLOYD:

With that, I would like to take my prerogative as the general chairman to have the last word of the morning and then we will break for lunch. I think we all recognize what has been presented this morning. Generally:

1. We're looking at small numbers; we're looking at a limited study design; and there is some question about the specificity of both the exposure and the disease response.

2. We have two plants in the State of Texas, two in the State of Ohio, one in the State of Pennsylvania, and one in the State of Kentucky where we are seeing an excess of leukemia and lymphoma in plants where they have been producing styrene-butadiene rubber.

I think we should be very concerned about that and when we come back after lunch, we're going to talk about what we might want to do. I would like to try to reconvene at 1:30 p.m.

REPORT FROM THE B. F. GOODRICH COMPANY

E. W. HARRINGTON

DR. LLOYD:

We would like to pick up where we left off this morning. Our first speaker is one of the industry representatives, Mr. Harrington, from the B. F. Goodrich Company.

MR. HARRINGTON:

Good afternoon, my name is E. W. Harrington and I'm the Director of Manufacturing for Synthetic Rubber for the B. F. Goodrich Chemical Company. For the last 2 months I have been responsible for the Port Neches Synthetic Rubber Plant about which you have heard so much this morning. I find that the company, myself, and plant management are in general agreement with many of the things that you have heard this morning. We have a new attitude. We are not going to use the fact that we don't know that an organic chemical is a carcinogen as an excuse not to reduce employee exposures.

The account that you heard from Mr. Beliczky about how we were alerted to this problem at Port Neches is absolutely correct. We wish to thank Mr. Contessa and the president of the local OCAW unit for alerting us. I wasn't at the plant at the time and, if I had been, I'm not sure that I would have been alerted. After all, two of these people had been gone from the plant for 11 years; one was age 76; and the other two of the five were brand new cases. So, we were alerted in a month and that's not bad by the old standards, but maybe not good by the standards that we would aspire to now.

When we were alerted, as you know, we notified NIOSH and invited them to assist us. We also notified our employees and the unions at the plant, and we issued a news release.

To date, at least up to this morning — we have found no reference implicating any of the materials that we use in the plant with leukemia, although toxicity studies have been carried out on a number of them, including styrene and butadiene. The point is that at this point and stage we still have no solid clue as to whether these leukemia cases are work oriented or whether any materials used at the plant or other similar SBR plants could be linked with this disease. We definitely agree, however, that it warrants the investigation going on.

We had already taken a number of steps before March 18th. We had monitored the atmospheres in the plant, by personal monitoring of the type that has been specified by OSHA for PVC plants. We haven't done it as much as we would have liked to have done it with the knowledge that we now have, but the results that we did get are as follows: the highest personal monitor reading we have found for butadiene averaged from 20 to 30 ppm. We monitored where we thought the exposures were the highest.

For styrene, our highest readings by personal monitors were from one to 15 parts per million. These were over six-hour periods for the most part, as I understand it. For butadiene, the present OSHA standard is 1,000 and for styrene it is 100 ppm.

We have strictly enforced vessel entry procedures. No person is permitted to enter a vessel without a permit from the plant safety department and until all rigid safety precautions, including ventilation, have been carried out and the atmosphere in the vessel has been checked.

We have recently established a policy since March 18th that all persons entering any of these vessels shall wear air-fed respirators. This process is being implemented as rapidly as we can acquire the approved respiratory equipment, and we expect it to be in effect in early May.

We have also offered blood tests to all employees at the plant. Between 400 to 500 employees, so

far as I understand it, have taken these. As soon as the results have been completed and analyzed, we will make the results known to NIOSH, to the unions at the plant, to the individuals on a private basis, and we will publish the results. We expect to be able to do this in the near future. In addition, over the years, many of our direct workers have had the opportunity to be given physical examinations, when they requested it, by the plant physician.

While we do not know what chemical, if any, may be linked to leukemia at this plant, and we have no reason to believe worker exposures have been excessive, as a matter of prudence, we are now implementing still more sophisticated and more frequent monitoring procedures to determine the extent of any exposures.

We are going to put in a procedure that monitors the butadiene, styrene, and benzene simultaneously, and samples will be analyzed at the plant laboratory instead of at Akron as has been done in the past.

The SBR process is mostly, as you've heard, a continuous rather than a batch process. Vessel entry is much less frequent than in other chemical operations such as PVC, for example.

SBR polymerizers or reactors need to be inspected and cleaned only at intervals of six months to a year. Blend tanks are cleaned about twice a year. Stripping columns are cleaned about once in three months.

The SBR process is efficient compared to many polymerization processes. The unreacted monomer is recovered and reused. The process is closed until after the monomers are removed and recovered in the stripping column process and then the mixture goes into open blend tanks for coagulation and drying after most of the butadiene-styrene have been removed. This accounts for the low readings that we have found in our monitoring of work atmosphere. This is not to say, like in any plant, that we don't occasionally have leaks and spills. We are obviously going to have to tighten up on those and make them less frequent.

The principal raw materials, as you've heard, are styrene and butadiene, neither of which is produced at this plant. Since styrene is made from benzene, of course, you've heard speculation that styrene may be a suspected cause of leukemia and that the benzene in the styrene may also be the suspected cause. We analyze the styrene when we get it in our own plant and, although the manufacturers say it's nil to 10 ppm, we find 0.01 per cent or 100 ppm by our chromatograph analyses. We believe this is a result of styrene being shipped to us in barges that are used alternatively for benzene, but we don't use benzene in our process nor have we monitored for it so far. But as I have said, we intend to simultaneously monitor it when we're monitoring for styrene and butadiene.

You have heard a number of other materials are used in the production of SBR. These include the soaps, extender oils, carbon black, and antioxidants. All of these must be investigated.

There is another chemical that we don't buy, but it's formed in every operation using butadiene and that is butadiene dimer. This is formed continuously as butadiene is stored no matter what you do. This is vinyl cyclohexene and it is present in our plant and is in our recycled styrene. Probably, there would be traces in the finished rubber.

We feel that the most important part of this investigation will be the epidemiological studies. It is our belief, shared generally by scientific and medical experts, that NIOSH and the Center for Disease Control are the best agencies in the world to carry out this study. A complete epidemiological study of the SBR industry may give us the best help in unraveling this puzzle. We are certainly ready and willing to cooperate with the study.

I would certainly recommend that NIOSH study all of the remaining SBR plants and not just the ones we've heard of today. I would like to point out that SBR plants are generally in an area where there is a heavy concentration of petroleum refineries. I don't know whether that has a relationship, but it is a coincidence.

If we don't solve this problem now and find out which, if any, chemicals, including butadiene-styrene and any of these other mentioned

chemicals, are the cause, we could discover in 5, 10, or 15 years from now that the problem still exists.

We certainly hope that the investigations proceed in an atmosphere where there are no adversary positions. After all, labor, management, and government health bodies all have common interests in this investigation.

Just a few remarks about what I've heard this morning. In response to respiratory protection, I've already stated that we have instituted a policy on air line respirators that will be in effect in May. On the exposure to talc dust, I would like to point out our corporate industrial hygiene department has criticized this as well and we intend to do something about it.

We have given a complete list of chemicals used in the plants to the union involved. We have a letter from the local union requesting a lot of additional information and we are now accumulating that information and we intend to give it to the union just as asked. We are going to continue to increase our monitoring as I described and that information will be available to all the workers in the plant and to the unions and to the government health bodies who should have it.

Radiation sources are there in the plant. I'm certainly going to ask the plant to check, but it's my understanding that those are under the control of the safety precautions as specified by the Atomic Energy Commission. I believe we are complying with those precautions in protecting our employees from radiation from those devices which are low level radiation devices.

The lunchroom situation that was mentioned will be corrected. We have had engineering studies under way for a number of months on this.

I heard about the possible problem which is a little new to me this morning on the possible exposure to sampling reactors. Our production manager from the plant is here; he heard that; and I'm sure he'll investigate that quite promptly. We have had problems in other plants and we solved them and we can solve them in this plant.

I would like to thank you. Do you have any questions?

QUESTION:
I'm sorry, I didn't get your name, I came in late.

MR. HARRINGTON:
My name is Harrington and I'm the Director of Manufacturing for B. F. Goodrich.

MR. DEMERY:
My name is Bill Demery and I'm with the U. S. Department of Labor, OSHA, and I am now at the Dallas Regional Office. I just would like to clear up one minor technical thing. I think you mentioned that you were finding a tenth of a per cent of benzene in the monomer?

MR. HARRINGTON:
One hundredth of one per cent which is 100 ppm of benzene in our incoming styrene. The manufacturer says when it is shipped out, it isn't more than ten. I don't know what it was in the distant past, in the early 40's, when these plants started up. I don't think anyone had analytical equipment that sensitive at that time.

MR. SAMUELS:
My name is Samuels. Do you have plants abroad?

MR. HARRINGTON:
We're building a plant in one country, but I don't think that we have any in operation now.

MR. SAMUELS:
But in the plant you're building and in other rubber industry plants in other countries, would you recommend that these countries institute the same measures at the same time?

MR. HARRINGTON:
I think it would be only prudent.

MR. SAMUELS:
Would it be appropriate for the chairman to perhaps have an affirmatory statement from the representatives of the British Rubber Industry who are here. We're rather disturbed by the fact that for asbestos and vinyl chloride, for example, our British brothers are not given the same stringent protection.

MR. HARRINGTON:
Anything else?

DR. LLOYD:
I have a brief announcement. There are additional handouts available at the registration desk, including a supplement to the bibliography. Would anyone who hasn't registered yet, please register.

Are there any other people who would like to offer any other comments on the health effects or the epidemiological studies of the leukemia experience of workers in SBR?

SURVEILLANCE TECHNIQUES OF INTEREST

JOSEPH K. WAGONER

DR. LLOYD:

Dr. Wagoner will make a transition from what we were talking about this morning to what we shall be talking about this afternoon. He'll be followed by Mr. Baier who will chair the afternoon session.

DR. WAGONER:

Thank you. We're basically going to lay out, in an open spirit, what we feel, as a governmental agency, is the course of action for research into the problems of carcinogenic risks in the styrene-butadiene rubber (SBR) industry. I wish to commend the exemplary endorsement of the B. F. Goodrich Chemical Company for an industry-wide study of the SBR industry. I also look forward to a similar expression of support from all of the other industry and labor representatives in attendance today.

As you well know, and as we certainly openly admit, our current surveillance mechanisms are either limited or nonexistent. The truth is, however, if there is a will there is a way. I'm going to present a method whereby we can get a rapid resolution to the extent of the problem, the magnitude of the problem, and the variety of biological responses, whether carcinogenic or noncarcinogenic, involved in employment in the SBR industry. On the basis of what we have heard this morning, I would also encourage the utilization of this method for an investigation of the styrene industry.

Data recently published by Hoover and Fraumeni of the National Cancer Institute clearly demonstrate that counties in the United States having a high density of chemical industries have elevated risks of cancer relative to the total population of the United States. Specifically as seen in the table below the risk of cancer of the lung, of the bladder, and of the liver and gallbladder are significantly higher among chemical-industry counties.

Average annual age-adjusted mortality rates among white males for all malignancies and for cancer of four specific sites in the total U.S. and in 139 chemical-industry counties (1950-1969).

Area	Sites			
	Total	Lung	Bladder	Liver and gallbladder
Chemical-industry counties	179.81	41.79	7.19	5.62
Total U.S.	174.04†	37.93†	6.78†	5.16†

†Difference between rates significant at $P<0.05$.

Even more germane to the study method that I wish to propose are data seen in this table.

Average annual age-adjusted cancer mortality rates among white males in Hamilton County, Ohio, and those in counties not having large chemical industries but cities >250,000 population (1950-1969).

Counties containing large metropolitan areas	Sites		
	Lung	Bladder	Liver and gallbladder
Hamilton County, Ohio	47.2	8.8	6.9
Other counties	45.1	8.0	5.8

Within the 139 counties in the United States classified as chemical industry counties, is Hamilton County, Ohio, a county just across the river from this meeting site. That county, containing Cincinnati, a city of greater than 250,000 population, is the only county having high rates of cancer for all three sites, i.e., lung, bladder, and liver and gallbladder when compared with other nonchemical industry counties having cities of greater than 250,000 population. These data strongly indicate that the increased risk of cancer in Hamilton County, Ohio, cannot be associated only with the ills of urbanization or urban pollution.

Is it possible to identify in more detail specific etiological (industrial) agents contributing to the excess of cancer in Hamilton County, Ohio?

Yes! Dr. Mancuso using two different study approaches demonstrated that benzidine, a substance formerly produced by Cincinnati Chemical Company, was contributing to the excess of bladder cancer in Hamilton County, Ohio. As shown in this table, using Social Security Administration quarterly employment statements as a data source, Dr. Mancuso has demonstrated that workers exposed to benzidine in Cincinnati were dying of bladder cancer at a rate fifteen times higher than other residents of Ohio (6 obs. vs. 0.41 exp.).

Cancer mortality among males employed at a Cincinnati, Ohio, chemical company in 1937 and traced through 1956.

Data source	Cause of death	White		Nonwhite		Total		
		Obs	Exp	Obs	Exp	Obs	Exp	SMR
Social Security Administration records	Total cancer	14	10.30	4	4.30	18	14.60	123
	Bladder cancer	4	0.30	2	0.11	6	0.41	1463
Company personnel records	Total cancer	11	8.38	3	3.01	14	11.39	123
	Bladder cancer	4	0.25	2	0.08	6	0.33	1818

Using company employment records from that same plant as a data source, Dr. Mancuso also was able to demonstrate that workers exposed to benzidine were at an increased risk of bladder cancer (6 obs. vs. 0.33 exp.).

This latter procedure is extremely time-consuming and requires microfilm teams going through personnel records systems, a process often considered to be disruptive to industry. What I am now proposing at much less cost to our limited manpower, at much less cost to our monetary resources, and at much less impact to you in industry, is a method using the Social Security Administration to investigate potential occupational health problems.

Now, lest one consider this above example to be merely a chance occurrence, I should like to present a second example. Dr. Mancuso in 1967, again using quarterly employment statements from the Social Security Administration, has demonstrated an increased risk of total cancer and of respiratory tract cancer among both male and female employees of one major asbestos manufacturing complex utilizing predominantly chrysotile asbestos in textile friction and packing products. See table below. Studies by NIOSH of this same asbestos manufacturing complex, using company personnel records, has demonstrated an increased risk of total cancer and of respiratory tract cancer of the same order of magnitude among both male and female employees.

Thus, there are now two examples which demonstrate the utility and the validity of the Social Security Administration system as a rapid means for resolving "our" problem with the SBR industry; and I emphasize "our" because we (government, labor, and management) are all members of this society in which we live and work.

Mortality patterns among individuals employed at a Pennsylvania asbestos manufacturing plant.

Data source	Cause of death	Males		Females		Total		
		Obs	Exp	Obs	Exp	Obs	Exp	SMR
Social Security Administration records	All causes	166	130.35	20	14.67	186	145.02	128
	Total cancer	44	18.91	10	4.36	54	23.27	232
	Respiratory cancer	16	5.91	4	0.19	20	6.10	328
Company personnel records	All causes	594	480.25	61	46.59	655	526.84	124
	Total cancer	95	88.08	22	7.74	117	95.82	122
	Respiratory cancer	39	18.21	7	0.63	46	18.84	244

You will recall that I mentioned earlier that the three counties contiguous to Port Neches, i.e., Jefferson, Orange, and Chambers, have leukemia rates significantly higher than those for Texas as a state and than those for the United States as a whole. I again bring this up to draw the analogy with Hamilton County, Ohio, and the benzidine plant.

I submit that we as a governmental agency feel the necessity and the urgency to use the Social Security Administration system for a resolution of the leukemia problem in the SBR industry. Certainly, the time required to resolve our problem of leukemia in the SBR industry would be significantly reduced using this study approach.

I also solicit your open endorsement, industry by industry, to cooperate with us in this study approach as was so exemplarily put forth earlier this morning by B. F. Goodrich Company.

EPIDEMIOLOGIC STUDIES

RICHARD A. LEMEN

Essentially what we want to do in the remaining time we have this afternoon is to outline for you some of the mechanisms and what we plan on doing as far as an industry-wide study for the styrene-butadiene rubber industry.

As I indicated this morning, we are microfilming the records of the two plants, B. F. Goodrich and Texas–U.S. Chemical, in Port Neches and we have almost completed the microfilming of these records. We want to do an indepth study of these facilities. The reason that we want to do this instead of going to the Social Security Administration as Dr. Wagoner indicated, is that we can get a very detailed occupational history through the company records that we are microfilming from each facility to see if there is any specific area of the plant where there may be a clustering or an association with the leukemia or, for that matter, any other excess deaths that we may encounter.

The second thing that we are planning on doing is an industrial hygiene survey of both the B. F. Goodrich Plant and the Texas–U.S. Chemical Plant. We will be doing this probably the latter part of May. This indepth industrial hygiene survey is to ascertain the exact chemicals and the concentrations that have been found in the past and are currently being found in the plant.

The mechanism that we will use for our mortality study is to microfilm the records, bring them back to NIOSH to set up a master file, and then to use various follow-up techniques to complete the data. As I mentioned to you this morning we will use the State of Texas Vital Statistics Office and their Motor Vehicle Office for follow-up. The Social Security Administration certainly will be used as will the Post Office. Followup by these multifaceted techniques for a study of this nature is going to take about six to eight months. Whereas with the Social Security System, using the mechanism that Dr. Wagoner just showed you, it could be done in a much shorter amount of time; however, we would not get the indepth occupational history that we will get from the study of these two facilities in Texas.

Lastly, we have received a request to go to the American Synthetic Rubber Company in Kentucky to do medical screening tests; as a result of what we have heard today and as a result of what we have seen with vinyl chloride, we are going to be planning on doing not only a blood screening test program, but a much broader type screening and possibly even looking at the chromosome anomalies that could exist in a situation like this. So, this is basically in two minutes as Dr. Lloyd asked me to make it, what we are planning on doing and if there are any questions, we can entertain those for just a minute or so at the present time.

QUESTION:
I would like to ask a procedural question. Would some of you define what you mean by the styrene-butadiene industry, what your confines are of that?

MR. LEMEN:
The styrene-butadiene rubber industry is what we are looking at. Is that an answer to your question?

QUESTION:
The manufacturing of this material or —

MR. LEMEN:
Yes. To my knowledge. Maybe Mr. Baier can clarify that further, but that is what we are planning on at the present time. That's where we're concentrating our efforts. Will you comment on that, Dr. Wagoner?

DR. WAGONER:
Yes, as I indicated earlier, based on the Mount Sinai data, I think it would be an irresponsible act on the part of the U.S. Government as well

as industry not to undertake an investigation of the styrene facilities.

QUESTION:
How about butadiene?

DR. WAGONER:
I would welcome your endorsement of that also. I might put the question back — what do you people and industry feel is the posture as to what studies are needed to be undertaken?

MR. ZACK:
Matthew Zack from the Center for Disease Control. With respect to the proposal to use the Social Security records, I'm wondering whether the Social Security Administration will give out those records any more after the Privacy Act of 1974. It has been very difficult to get any information from the Social Security System. Both those studies that were shown on the board were done before 1974.

DR. LLOYD:
Let me clarify what it is that Dr. Wagoner was talking about.

Ordinarily, the Social Security Administration will not give out any information on specific companies. It is forbidden under the recent legislation, just as they will not give out any information on live individuals. With the consent of the individual firm in writing, they will provide such information, and what Dr. Wagoner has suggested is that the individual companies involved here would be asked to give such consent so that he could go to the Social Security Administration and they could identify the firm by their coded number and thus, provide us with information on which individuals who had been employed at those plants had died so we might recover the death certificates.

Dr. Wagoner says he's asking for the endorsement of that by the companies here today. Is there anybody who would like to respond for the companies? I now call for response by the corporations and unions to this overall NIOSH study proposal. Could I even get a comment as to what you people think of this study proposal?

MR. CONTESSA:
Mr. Chairman, I'm Matt Contessa from the URW Local Number 5. I would like to suggest that studies be taken in the benzene area also.

DR. LLOYD:
This is a question that was mentioned earlier and I think we would have a much more difficult problem there because of the widespread use of benzene in many plants. It would be very difficult to identify the plants.

MR. SAMUELS:
You asked for a response from us and, of course, we support Dr. Wagoner's suggestion with perhaps the additional element that the Social Security Administration also administers a disability program and, perhaps, this would give us some morbidity data, but we certainly endorse what you are doing, Joe, and I might say that it was not the legislative intent of the Privacy Act to deprive the government and other legitimate investigators of this kind of epidemiological data.

DR. LLOYD:
Thank you. All right, now I think that should conclude what we originally intended for this morning's session. This afternoon's session, which will begin now, on recommended intervention will be chaired by the Deputy Director. Before Mr. Baier, one point from Mr. Lemen.

MR. LEMEN:
In response to the question about doing a benzene study, I would just like to indicate that we do have two plants under study right now. We are looking at the benzene very vigorously and, if you have some more questions, why I'd be glad to talk to you after the meeting is over and tell you exactly what we are doing.

MR. CONTESSA:
Thank you. And another comment — I forgot to say that as far as the membership of Local 5, we completely and fully endorse any studies, any studies that are to be held and, again, I say that you could have the cooperation of our local — whatever we could make available to you that would help.

DR. LLOYD:
Thank you. Now for some comments on recommended intervention, chaired by our Deputy Director, Mr. Ed Baier.

RECOMMENDED INTERVENTION — BACKGROUND

EDWARD J. BAIER

This is a bridge session, between this morning when we were concerned with trying to characterize and identify, and this afternoon when we will try to consider what we are going to do about it.

Historically, if we look back at what has been called good industrial hygiene practice or good occupational health practice, we find that when we reached a certain measurable quantity of some air contaminant in the work place, we used that to trigger off some sort of control.

I think that the current concept, in engineering technology at least is to design the hazards out of the operation initially. We are concerned that any corrections to existing facilities might get to be quite an expensive proposition and, in fact, really not do the job that we are in business for.

I would like to read to you seven precautions for manufacturers of synthetic rubber.

One, a complete pre-employment physical examination should be given all workmen.

Two, all operating personnel should be examined every three months.

Three, all operating personnel should be impressed with the toxic hazards of the various compounds and taught to handle them properly.

Four, a closed type of operation should be mandatory and continuous inspection of all the equipment for possible leaks should be enforced.

Five, a set of safety rules regarding the use of protective equipment, gloves, goggles, masks, should be posted at the danger spot.

Six, both personal and group safety equipment should be supplied as needed.

Finally, *seven,* adequate ventilation, both local and general, should be maintained at all times.

I'm sure this is familiar to many of you because this was published by R. H. Wilson in the Journal of the American Medical Association in 1944. So after all this time, we have reached a point where we in NIOSH in terms of intervention against hazards are going back really roughly thirty years.

I would like to clarify a point of concern. A couple of years ago, Dr. Maurice Johnson and Dr. Irving Tabershaw came to visit us at NIOSH in Rockville and they had a new problem. It turned out to be the vinyl chloride problem. Not too many weeks ago, I talked with Dr. Johnson on the phone again and it almost sounded like a repeat of our couple-of-years-ago dissertation. Roughly, the same numbers of people, the same types of data, and that type of thing.

I don't honestly believe that this morning, we have been able to really pinpoint what the hazards are — but, I think it's worthwhile that we dig into the situation. I think what Dick Lemen pointed out as an approach is one approach. When we first got involved with the vinyl chloride situation, we met in Ohio, and we discussed this same thing. We wanted cooperation then and, certainly, we need that just as much now and maybe more so because at least then we had some kind of an index, we had identified a contaminant, vinyl chloride, and we were very sure in our minds that that was the direction to go.

Here, we have a whole spectrum of different kinds of air contaminants and different kinds of hazards, if you will. And so, with that, we've got to characterize not only the workmen, but we must characterize that environment and so, to talk first on how do you characterize an environment in terms of sampling and analytical methodology, we have Dr. Alexander Teass.

SAMPLING AND ANALYTICAL METHODS

ALEXANDER W. TEASS

Thank you, Mr. Baier. First, let me address the survey of what the worker is actually exposed to. There are sophisticated techniques available for doing an overall examination of personal and environmental samples. These usually apply gas chromatography, mass spectrometry, liquid chromatography, and spectrophotometry in appropriate combination. A fair amount of information concerning the identity of the contaminants to which the worker is actually exposed can be obtained. Comprehensive studies of samples generally take time and are relatively costly, but it seems that to a limited extent such studies are desirable.

Procedures for monitoring worker exposure to the monomers styrene and butadiene are already in use. In essence, the styrene and butadiene are trapped when a measured volume of air is pulled through a bed of charcoal in a glass tube. The tubes are capped and the samples sent to the laboratory. There the charcoal is treated with carbon disulfide to remove the adsorbed materials, and the resulting solutions are analyzed by gas chromatography. These procedures for styrene and butadiene have been studied and validated under the NIOSH-OSHA Standards Completion Program for use around the levels of the OSHA standards — 2200 milligrams per cubic meter for butadiene and 425 milligrams per cubic meter for styrene. At lower levels, below 0.5 times the OSHA standard, the performance of these methods in terms of precision and accuracy is unknown.

A possible problem I can see with the methods for styrene and butadiene is that in taking samples at styrene-butadiene rubber plants other contaminants will be collected along with the styrene and butadiene. Some of these contaminants may be polymerization initiators. Thus, there is some question concerning the stability of actual field samples of styrene or butadiene. We have looked very seriously at styrene-on-charcoal samples, and with our laboratory samples we found no problem with stability. But our laboratory samples were pure styrene; there were no co-contaminants. To my knowledge the stability of butadiene on charcoal has not been investigated.

The list that I saw of all the substances used at the styrene-butadiene plants contained 67 chemicals. I'm not prepared to discuss the sampling and analytical procedures for each and every one, but I should say that with 67 substances or mixtures the problem becomes pretty complex.

I trust that industrial hygienists and analytical chemists closely associated with the industry will have more information than I do on monitoring the atmospheres of these plants. I would invite them to get with us so we may share information.

ENGINEERING AND ADMINISTRATIVE CONTROLS

ROBERT T. HUGHES

MR. BAIER:
In the statement I read earlier, I spoke of adequate ventilation, a very vague term that back in '44, I guess, had a meaning. In '76, it has many meanings and Bob Hughes will now speak to that.

MR. HUGHES:
Thank you, Ed. If Ed thinks I'm going to give a definition of adequate ventilation, I'm not. I welcome any such definition that anybody can give me. I think that therein lies a part of the problem. If you look at the literature on the control technology with respect to any given substance, you will find that this is basically what would be said: you should control with adequate methods or use adequate ventilation. This isn't what we need.

I want to give a definition of control technology. As applied to the industrial workplace, control technology consists of engineering control, work practices, and personal protective equipment.

With respect to engineering controls, there are several types in the hierarchy — with some considerably better than others. Engineering control can be designed into the process or the process machinery initially or it can be obtained by making changes after the installation of the process machinery. This type of control can either completely eliminate the emission or substantially reduce it. It can prevent emissions into the workplace. Of course, if you can keep the emissions out of the workplace, you have gone about 99 per cent or better toward controlling exposure.

Another method would be the modification of operational process machinery or processes. This can do the same thing to some degree, but it's obvious that it may be very difficult for many processes and probably nearly impossible in a majority of places if the process is already in operation.

Process modification could be used. Process modification could be the substitution of a less toxic material for one that's more toxic, or it could be a change in temperature for volatile materials to prevent excess volatilization. Of course, this depends very much on the process itself, and it has to be compatible with the end product. One of the most common type of control would be what I define as an add on or retrofit. This would be a control added to the process or the machinery after it was in place. Here, our friend adequate ventilation comes into play as ventilation systems and specifically local exhaust ventilation systems are the most commonly used.

If there is a process that is emitting a substance, the only practical control may be to run enough air across it to capture the material and, hopefully, get rid of it. The serious problem with this type of control is that the material or the substance has already escaped from the process itself into the workplace. Intercepting emissions and removing them depends greatly on the design and on the continued maintenance and operation of the system.

Very briefly, I mentioned work practices. Engineering controls basically should be used to keep the emissions from getting into the workplace; either contain them within the process or capture them after emission. The work practices used may or may not eliminate emissions in a workplace.

My definition of work practice includes scheduled maintenance — the maintenance of the process or the maintenance of the control system and the engineering controls. Another area of work practice would be using specific job procedures which separate the worker from the emission. Finally, there would be personal protective equipment such as respirators and protective clothing. I won't say anything more about those latter two because Mr. Todd will be

speaking after me and will go into more detail on those items — what they are and what we are doing about them.

In the application of engineering controls to the problem at hand, it was evident from Ron Young's slides that there are some of those processes that could use some controls. It's very hard to tell about the closed portion of the system — whether it's working properly or not because it's hard to see visually. I think there were many areas where the materials were being mixed and there was an absence of any kind of ventilation so any emissions or materials that would result from the processes could get into the workplace.

The shaker screen is usually an open area and the material, being agitated, can escape. If the material does escape, it surely isn't going to be captured without some kind of control equipment. Engineering controls in general should be used in all cases where toxic emissions can occur at levels which exceed defined harmful levels.

The question arises as to controls where the levels are not known. If there is a TLV or defined standard for that material, there should be a control in place and operating suitably that would control emissions to that level. The problem occurs if there isn't a known level. As has been related here, we are not sure what the problem may be with SBR. It may be one of these substances for which there is a level, or it may be a combination, or it could be a substance that isn't adequately defined. That is a question that's very difficult to answer, and it becomes more difficult as Alex was just saying when there could be 65 substances or combinations of substances.

I would like to now define very briefly in the NIOSH program what our future efforts will be in the area of control technology and, hopefully, relate this to the problem at hand.

We are now undertaking a program of control technology assessment. We will select industries and assess the state of the art of the control technology in that industry. We will assess and document the control technology that is available and how it works. This will also tell us whether there are processes or operations where the existing control technology is not adequate or indeed in many cases where it doesn't exist.

This program will cover engineering controls, work practices, personal protective equipment, and a fourth item not discussed so far, the methods of monitoring the processes or the operations in order to provide adequate warning in the case of a process or control system failure so that there would not be harmful exposure to the workforce.

This study will be primarily oriented toward engineering controls. We will try to identify those controls that are effective and determine the degree of effectiveness. Work practices will be observed. We will note whether personal protective equipment is used or not.

We are planning several assessments. One will cover the plastics and resins industry and, specifically, the polymerization processes. The SBR rubber industry would be covered by this. I would like to refer to Mr. Harrington's remark that he is interested and willing to cooperate with us. We do need the cooperation of industry in this. We would like to have a plant or plants which are representative of the industry, the processes, the operations, and, hopefully, the control technology so our contractor can assess all of these.

A study like this just can't be done unless we have the cooperation of industry. That is basically it. Does anybody have any questions?

MR. BELICZKY:
In the comments that you made regarding what you're going to look at in the plastics industry, you referred to specifically SBR. The styrene-butadiene rubber. In my earlier comments I indicated that perhaps if you don't do it on an industry-wide basis, please take a look at the acrylonitrile-butadiene-styrene and polymers, too, and just plain simple butadiene polymers so that you have an indication of what the total picture is and just don't limit it to SBR.

MR. HUGHES:
Maybe I misled you. It wasn't the intention of our effort to limit it to SBR. We have

not yet specifically defined those areas that we are going to look at. This is a part of the process and the effort is to define the industries where we can optimize the use of our resources. I merely mentioned that the problem with SBR has come to light since we initiated this, and this would be one of the areas that we do intend to look at — we intend to look at others too.

WORK PRACTICES

WILLIAM TODD

MR. BAIER:
Bob referred several times to work practices. To give you some overview of work practices, we have William Todd:

MR. TODD:
Thank you, Ed. I'm employed in the Protective Equipment Section of the Control Technology Research Branch; what I will have to say will deal generally with work practices, but my viewpoint is from that of personal protective equipment.

I reiterate that the NIOSH role is to perform research. We provide input into the development of criteria documents. We also provide technical information for the solution of occupational safety and health problems.

The OSHA Act states a priority in the use of control methods. First priority is given to engineering controls, which Bob Hughes has just addressed himself to. His section deals with the cause and how to engineer the cause out of the process or how to control the hazardous material or materials in the process.

Second in priority is sub-part G of the OSHA regulations which refers to administrative controls, that is, not allowing the workers to be exposed to harmful levels beyond the recommended exposure limits. For example, scheduling worker time in high toxic level areas so as to limit his exposure.

Third priority is the use of personal protective equipment.

So, the user would resort to personal protective equipment only if he cannot solve the problem by the first and second method that is by engineering controls or by administrative controls.

I would like to note that the success of personal protective equipment depends upon the cooperation of the worker; something that we in NIOSH recognize as a factor in measuring the effectiveness of personal protective equipment. The workers must use the equipment or it does them no good. This we also recognize as a management problem so this approach to protecting the worker loops back into administrative controls. Management must then take adequate measures to see that personal protective equipment is used and that proper procedures are followed.

What I have to say deals with what our Protective Equipment Section is doing or plans to do in the area of personal protective equipment research.

We have two projects which relate to problems in the rubber workers industry. Adsorption capacity studies are planned both in-house and by contract. These projects are proposed at this time for chemical compounds used in the rubber industry which are known to be harmful and volatile enough to cause concentrations in work areas above the TLV.

Respirator adsorbent cartridges used against chemical vapors are currently certified by a test method using carbon tetrachloride as the assault substance. This testing is done at the NIOSH Testing Certification Laboratory in Morgantown, West Virginia. It has been demonstrated that there is a wide range of capacity that a cartridge adsorbent such as charcoal has for different chemical vapors. This was manifested in work done on vinyl chloride when it was found that the typical activated carbon charged in a canister adsorbed only about one-tenth of the vinyl chloride that could be expected based upon the carbon tetrachloride certification test. This meant that most cartridges would not provide adequate service life to protect the worker.

We realize now that the only way we can be certain that a respirator adsorbent will provide adequate capacity is to test that adsorbent

against the particular chemical species. This is what we are intending to do, not only in the case of chemicals used in the rubber industry (this is a project which is proposed at this time), but also in other industries.

It will take a long time to do this but it's the only way to determine exactly what the adsorbent capacity is.

In another study, a contract is being let to develop performance criteria for protective clothing. Special attention is being given to several carcinogenic substances and, also, to the mechanism by which carcinogenic liquids pass through the protective clothing barrier. We must be able to define and measure how these materials will pass through or permeate through the protective clothing barrier and contact the wearers' skin.

In addition to the two projects I just mentioned, the Protective Equipment Section is responsible for input to criteria documents related to personal protective equipment. The following is a format recommended for review of criteria documents which is comparable to the criteria document format currently used for respirators. For example, with protective clothing — the items considered as input for criteria documents are conditions and work situations under which specific types of protective clothing must be worn; employer-employee responsibilities; required standard operating procedures; identification requirements for types of protective clothing; maintenance and storage requirements; training employees in proper procedures; eye and face protection requirements; need for full body impervious suits; emergency procedures; and a wearing time limitation for working conditions and substance exposures.

The Protective Equipment Section also has input to criteria documents for respiratory protection. We review criteria documents for specific working conditions and substance exposures under which respirators must be worn; employer-employees responsibilities; respiratory protection program requirements such as training, maintenance and program management. In addition to these items just mentioned, our research group will review the use of approved respirators, emergencies, and time of wearing limitations.

In developing recommended standards or performance criteria for a substance, NIOSH considers the basis for the recommendation of the use of personal protective equipment. The rationale for the selection and the use of personal protective equipment would include:

First, a decision logic similar to that used in the standards completion program for the selection of respirators and protective clothing.

Second, the documentation of pertinent toxicological information which was used in the selection of personal protective equipment. Information on such factors as wearer acceptance, warning properties, chemical properties and the concentrations dangerous to life and health would be reviewed. The rationale for using such information would also be provided.

Third, the documentation of the limitations of various types of personal protective equipment. For example; heat stress, adsorbent capacity for individual materials; permeation of chemicals through the protective clothing and the durability of the protective clothing.

Fourth and last, references to pertinent information sources.

STANDARDS DEVELOPMENT

HOWARD L. McMARTIN

MR. BAIER:
During the day so far, I think you've gotten a feel for what NIOSH is in business for. It's basically research, as Bill pointed out, but its output is in terms of what is the toxicology of the material, what epidemiologic information we have, how does an individual sample the air at the worksite, what does the chemist do when the chemist receives the sample of that air, be it absorbed on something or whatever, what must a physician know and what kinds of medical tests should he perform to determine if anyone has been overexposed, how do you inform the people who are exposed as to what the hazard is, and what steps and means can you use to avoid that hazard. You put that all together, and we call it a criteria document. To discuss the criteria documentation process and standards development, we have Dr. Howard McMartin with us.

DR. McMARTIN:
After listening to all of the comments and discussions that went on about styrene-butadiene rubber, as a combination or singularly as styrene, discussed by Dr. Lilis this morning, or as butadiene which was discussed by others, we're sort of put on the spot in the standards development program. We can look at these two products singularly or as a combination as we have been thinking about lately or we might even consider looking at the problems of the rubber industry and the effect that styrene-butadiene has on it.

After we get the information from the work to be done in epidemiology, we may want to change our direction in looking at styrene. I would like to be sure that the recommended standard we send to OSHA is not just a number, but that it includes recommendations which will provide a suitable environment in which man can work for his full work day — whether it be 8 or 10 hours — for a full work lifetime.

We would also include recommendations and requirements for medical surveillance, work practices including protective equipment, analytical and sampling methodology and types of emergency care and equipment, depending on the nature of the substance or the type of the process or the possibilities of injury which are needed.

As far as styrene is concerned, it's presently on our criteria document schedule to be completed by May 1977. It may be put back, depending on whether or not we feel that the information forthcoming from the epidemiological studies may be pertinent. We expect that information to be available in about six months.

Styrene was put ahead in our priority list because we received information that Dr. Maltoni in Italy had been doing some work in carcinogenesis with this material. We wrote to him in February of last year but we haven't yet received any answer from him about the work that he was doing.

Butadiene is at the lower end of our priority list and from the present information that we have, I'm not sure when it will be considered. What we do with it will depend on what we find out in the next three to four months.

When we develop medical surveillance and make recommendations for it, we try to be practical asking for those tests which will be informative and leading. We likewise assume that a practicing physician can do a complete physical examination which will include routine urinalysis and complete blood count. A complete blood count would provide an early indicator that there may be something wrong or that there is no problem.

From the discussion it appears that there are possibilities of liver damage, and I'm concerned about the type of indicator tests that we should perform in liver function. This is a problem that we'll have to look into, and, certainly, we

wouldn't suggest that a series of tests be done so that you will find one that might be a valuable indicator of possible liver damage. We will at least try to find the types of tests that would give you an indication that things are going all right or that we have some problems facing us. Additional diagnostic liver function tests would be a matter of professional judgment on the part of the examining physician. I don't think I have anything more to say unless there are some questions.

DR. MOORE:
I am Roscoe Moore. Concerning the chronic data on styrene, NCI has completed a study of styrene; however, they have not analyzed the data. They are putting butadiene on test in animals.

CONCLUSION

MR. BAIER:
One of the pleas that I want to make again is that we cannot tell you the whole story — you know as much and definitely more in many instances about what we need to know. We must exchange information. Let's not wait until we have developed a criteria document, transferred it to the Labor Department, and then go into public hearings before anyone steps forth and volunteers information.

We need that information from you as you accumulate it. Our information as we accumulate it, we will be happy to share with you. I will turn the session over to the general chairman.

DR. LLOYD:
Is there anybody else with any further questions, suggestions, or complaints? We did not have the input that we expected from the number of people who are in attendance, but we do thank all of you who came and especially those of you who participated with presentations, questions, and comments. Thank you.

APPENDIX A.

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APPENDIX B.

SELECTED BIBLIOGRAPHY — STYRENE-BUTADIENE

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APPENDIX C.

TOXICOLOGIC, INDUSTRIAL HYGIENE AND EPIDEMIOLOGIC CONSIDERATIONS IN THE POSSIBLE ASSOCIATION BETWEEN SBR MANUFACTURING AND NEOPLASMS OF LYMPHATIC AND HEMATOPOIETIC TISSUES

Report Prepared For
The Joint URW-Firestone Occupational Health Committee

by

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Summary

A case-control study has been performed for deaths from neoplasms of lymphatic and hematopoietic tissues (NLHT; ICDA codes 200-209, 8th Revision) among persons whose work histories show some time of employment in synthetic rubber manufacturing from the Firestone-Akron 1964 cohort. Although the numbers involved are too small to make statements of statistical confidence levels, two findings are noteworthy.

(1) The relative risk estimate using the case-control design is 2.4. Although it is much lower than the relative risk factor of 6.2 yielded by the hybrid design study (Report F.8), this result does strengthen the hypothesis that experience in the synthetic plant may be associated with neoplasms of the lymphatic and hematopoietic tissues (NLHT).

(2) For the NHLT cases, two out of the three leukemia cases with SBR experience also had solvent exposure, while none of the three non-leukemia cases (ICDA codes 200-203) did. This would imply that the risk of SBR exposure, if any, is greater for the group of lymphomas rather than true leukemias. (This same inference can be deduced from Table 3 in report F.8.)

A walk-through industrial hygiene survey of the synthetic plant was made. It appears that the potential for exposure to volatile materials, including both butadiene and styrene, is greatest for reactor operators and tanks cleaners, with, perhaps, potential for intermittent exposures for persons such as maintenance workers and quality control sample takers in tank farm operations. It is recommended that these areas receive special attention in efforts to minimize exposure.

Toxicologic review of materials involved in the SBR process (and other synthetic rubber processes) revealed some agents which are suspect carcinogens. These are identified in the listing at the beginning of the section Toxicology Review.

I. EPIDEMIOLOGICAL REANALYSIS

Introduction

In order to probe more deeply into the alleged association of styrene-butadiene rubber (SBR) manufacturing and death from neoplasms of lymphatic and hematopoietic tissues (NLHT, ICDA codes 200-209, 8th revision), the work history file was reanalyzed for workers in Firestone-Akron. The approach used in this reanalysis involved a case-control study design involving 60 cases and 180 individually matched controls as discussed in report F.2. The previous approach involved a hybrid study design utilizing the same 60 cases and approximately 1500 randomly chosen controls as discussed in Report F.8. For purposes of the present report, these two approaches will be refered to as case-control design and hybrid design, respectively.

It should be noted that the case groups for these two study designs are identical, thus introducing an element of overlapping into the two study designs. Thus, similarity of results would not be surprising.

Methodology and Results

Taking all 60 cases and 180 matched controls who worked in Akron, the work histories were re-examined to determine how many of these workers had ever worked in styrene-butadiene production (OT = SYNT). The results showed that 6 out of the 60 cases had ever spent time in SYNT and that 8 out of the 180 controls had done likewise.

Using the traditional Cornfield estimate of Relative Risk yields RR = 2.4, i.e., the workers in SYNT were approximately 2.4 times as likely to have died of NLHT as other workers. The estimate from Report F.8, based on a considerably larger number of study subjects, was RR = 6.2.

The differences in these results may be largely due to the fluctuation one would expect in dealing with small numbers. However, the fact that both estimates are clearly greater than 1.0 is consistent with the hypothesis that working in synthetic rubber production may be associated with NLHT.

In order to probe more deeply into the possible specific exposures which may have been involved, each of the 14 work histories (6 cases and 8 controls) was reanalyzed. Tables 1 and 2 give summaries of this demographic and work history data. In addition to further breaking down the specific exposures in the synthetic plant, Tables 1 and 2 contain OHSG's estimate of solvent exposure from tire production OT's. Table 3 compares the relative strength of the exposures for cases and controls using an objective classification scheme devised by the industrial hygienists, without knowledge of study subjects' status (i.e. case or control). The criteria for making these classifications are explained in Section II: Environmental Assessment (see specifically Table 2 of that section). The results of Table 3 suggest a relatively higher exposure for cases who worked in synthetic manufacturing compared with controls.

An examination of the individual work histories of the six NLHT cases showed that two out of the three leukemia cases (ICDA codes 204-207) had also worked in jobs classified as solvent exposures by OHSC industrial hygienists. However, none of the three non-leukemia cases (ICDA codes 200-203) had any known experience with solvents. Although the interpretation of possible multiple exposures is difficult to assess, these results are consistent with the specific hypothesis that SBR exposure is associated with the lymphomas.

An additional analysis was carried out by examining cause of death for all members of the population sample used in F.8 (approximately 103) who had ever worked in SYNT. The results were inconclusive.

Table 1
DEMOGRAPHIC AND WORK HISTORY DATA FOR CASES OF NLHT WHO EVER WORKED IN THE SYNTHETIC PLANT.

Initials	Sex	Race	Birth	Death	Age	Study Cause Of Death ICDA (8th R.)	Synthetic Jobs First Exposure	Synthetic Jobs Total Exposure (yrs.)	Solvent Jobs First Exposure	Solvent Jobs Total Exposure (yrs.)	Job Description	Hire	Termination (last day work)
GSA	F	W	06-14-91	12-03-70	79	202.2	11-18-42	6.8			Female janitor, Sweeper	11-18-42	01-26-55
DAC	M	W	08-15-99	10-29-73	75	200.1	05-02-51	12.8			Repairman, Painter	05-02-51	08-29-64
WLI	M	W	06-02-11	06-29-70	59	204.0			09-04-42	6.7	Cement (solvent) mixer	09-04-42	07-14-68
							03-27-50	18.1			Utility, Cleanup		
											Latex blender		
SHO	M	W	02-11-02	02-21-64	62	205.1	08-27-51	10.3			Pipefitter	08-27-51	05-19-62
HAO	M	W	11-15-00	12-09-70	70	207.9			08-10-44	9.3	Machine repairman	08-07-42	09-26-64
							01-12-59	0.1			Machine repairman		
LHR	M	W	07-18-14	08-03-69	55	201	10-16-42	26.5			Pumphouse op., Compress. house attend	10-16-42	04-07-69

Table 2
DEMOGRAPHIC AND WORK HISTORY DATA FOR CONTROLS* WHO EVER WORKED IN THE SYNTHETIC PLANT.

Initials	Sex	Race	Birth	Death	Age	Underlying Cause Of Death ICDA (8th R.)	Synthetic Jobs First Exposure	Synthetic Jobs Total Exposure (yrs)	Solvent Jobs First Exposure (yrs)	Solvent Jobs Total Exposure	Job Description	Hire	Termination (last day work
HRC	M	W	10-26-24	05-24-72	47	412.1	01-29-51	16.0			Latex area, Coagulator op., Trucker	07-09-43	02-22-72
									01-08-44	7.9	Utility, Tube trucker		
RED	M	W	12-19-99	03-08-64	64	600	05-11-43	19.2			Solution Mixer, Reactor op.	11-30-27	02-22-64
									11-30-27	17.1	Tire Builder		
JEE	M	W	05-02-14	12-28-68	54	410.0	06-06-55	13.5			Trucker, Switchman	06-16-36	12-27-68
									04-27-48	1.2	Scrap reduction Man		
EPG	M	W	11-21-97	05-01-68	70	412.3	01-29-51	1.0			Utility, Tank Cleaner, Centrifuge op.	10-02-42	11-30-62
									01-09-52	3.2	Inspector		
CG	M	W	01-17-93	06-07-67	74	410.9	06-29-45	6.7			Utility, Baler op., Centriduge op.	05-02-29	11-30-55
									05-02-29	1.2	Handle WSW, Conveyer		
FPM	M	W	06-21-00	08-23-72	72	410.9	09-11-50	12.7			Repairman	10-13-45	02-29-64
									10-13-45	1.0	Millwright		
GSR	M	W	12-23-11	09-26-70	58	412.3	09-09-42	9.9			Reactor help., Sol. Makeup, Util., Coag. op.	09-09-42	01-31-70
									04-07-55	8.2	Gum insert op., Ser. pool		
EW	M	B	07-17-01	06-20-65	63	540.0	06-23-42	22.8			Sol. Makeup, sd.mix	01-21-25	06-11-65

*See McMichael, et. al., JOM 17:4 234-239, 1975, for contraints on control group.

Table 3

RELATIVE EXPOSURE CLASSIFICATION FOR CASES AND CONTROLS
WHO WORKED IN SYNT

Exposure to SYNT°	Cases	Controls
High	4	1
Medium-High	0	1
Medium	1	1
Low-Medium	0	3
Low*	1	2

° See Table 2 of Section II: Environmental Assessment.

* Note: This case was difficult to classify with available data.

Source: Industrial Hygiene Evaluation (Blind) of Work Histories.

II. ENVIRONMENTAL ASSESSMENT

Introduction

The Firestone Tire and Rubber Company Synthetic Plant at Akron, Ohio was visited on April 7, 1976 for the purpose of familiarizing the OHSG with the various processes, procedures, materials and equipment in use at the complex; to determine the presence and extent of any areas with potential exposures for plant personnel; to select possible locations for future detailed study and evaluation; and, equally important, to obtain detailed historical information on synthetic plant operations -- past and present. The types of historical information sought included:

1) A detailed history of plant production covering products manufactured, production rates and expansions and reductions in equipment and manufactured goods.
2) Manning charts complete for past years.
3) Flow diagrams for latex and rubber production coupled with general product recipes -- raw materials lists for major groups of latexes and rubbers.
4) Procedures for reactor cleaning.
5) Data from environmental monitoring of synthetic plant operations.

Much of the aforementioned information was requested from the company and is being funnelled through appropriate channels. At writing of this report, much of this information is still being assembled. The following report is based on data from previous information requests, informal discussions with plant personnel and observations made during the survey of the synthetic facility. Participants in this survey included the following individuals:

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Mr. C. E. Vanderslice, Technical Manager

Mr. V. A. Pulk, Safety Engineer

Mr. P. H. Johnson, Research and Pilot Plant

URW International

Ms. C. Bell, Industrial Hygienist

OHSG - University of North Carolina

Dr. M. D. Van Ert, Industrial Hygienist

Mr. T. M. Williams, Industrial Hygienist

Preliminary contact arrangements for the Akron visit were made through Dr. L. H. Ballou, Corporate Medical Director, Mr. G. L. Wilson, Corporate Industrial Hygienist and Mr. L. Beliczky, Industrial Hygienist, URW International.

HISTORICAL REVIEW OF AKRON SYNTHETIC PLANT[1]

The present Akron Synthetic Plant complex consists of two areas and/or functions. The first area, Polymer and Latex Production, was built by Firestone for the Government on 13 acres of land in the early part of World War II. Firestone operated this producing unit for the Government until purchasing it in April, 1955.

The first production unit (1-S) was completed in June, 1942. This unit had a design capacity of 15,000 long tons of dry synthetic rubber per year. Another unit (2-S) of equal capacity and similar design was subsequently constructed, and put in operation on January 21, 1943. Since the original construction, there have been additions and improvements

[1]Provided by Firestone Tire and Rubber Company.

(see listing below) to facilitate production and shipment of a variety of dry rubber and latex types. Plant personnel has varied between 462 to present enrollment 333.

The second area, presently used for Synthetic Rubber Research and Development, Technical Service and Sales, was originally the Government Evaluation Laboratories and Pilot Plant. Constructed for the Government on 5.8 acres of adjacent land east of the production unit in 1943, it served as a referee laboratory for all Government Synthetic Rubber functions and as a development group for new synthetic polymer until 1956. It was purchased from the Government by Firestone in 1957. A 3600 square foot Compound Building was added to this area in 1971.

The major Synthetic Production Plant expansions are as follows:

Increased Cold Latex Polymerization & Recovery Facilities	June 1, 1956
Add Vinyl Pyridine Latex & Nitrile Rubber Capacity	September, 1961
Expand Carboxylated Latex Capacity	November 1, 1966
Cold Latex Plant Debottlenecking	December, 1969
Expand Carboxylated Latex Capacity	March, 1971

As previously noted, more detailed historical information has been requested and, hopefully, will provide additional insights into pre-1956 synthetic plant operations. The following section covering observations and discussions made during the plant survey will detail current plant operations, thereby providing additional insights into materials, products and the level of operations of the Akron complex. Normal operations are conducted on a three shift basis: 6 AM - 2 PM, 2 PM - 10 PM and 10 PM - 6 AM.

Environmental Survey

The Akron Synthetic Plant is currently involved in the manufacture of a variety of latexes and dry rubbers as noted below. The approximate dates for introduction into synthetic operations are also listed.

Product Type	Date Introduced at Plant	Currently Produced
Cold SBR Latex	1955	Yes
Hot SBR Latex[2]	1945	Yes
Vinyl Pyridine Latex	1961	Yes
ABS Dry Rubber (Acrylonitrile-butadiene-styrene)	1972-1973	Yes
NBR Dry Rubber	1961	Yes
Carboxylated Rubber	1964-1966 (expansion period)	Yes

Synthetic products noted above are manufactured from combinations of a limited number of basic raw materials such as butadiene, styrene, vinyl pyridine and acrylonitrile. Both latex and dry rubber products are derived from batches of polymers manufactured from these ingredients. Latex forms are conveniently stored in large tanks and dispensed into drums or tank cars upon demand. However, certain products are not marketed in their latex state. Rather, they are converted into dry rubber products via additional processing which includes coagulation, drying and bagging, for example.

As with certain other synthetic operations, the manufacturing process begins once raw materials are received. The tank farm operation -- where materials are stored upon receipt -- serves as an appropriate place to begin discussion of the synthetic operation at Akron.

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[2]Dry SBR rubber terminated sometime between 1972 and 1973.

Tank Farm Operation - Department 082

Large volumes of pure monomers including 1-3 butadiene, styrene and acrylonitrile are unloaded from tank cars under pressure to appropriate storage vessels on the tank farm.[3] Butadiene vapors are heated to pressure liquid butadiene from tank cars to storage tanks. The area also serves as storage for recycled monomers -- acrylonitrile, styrene, butadiene-styrene and butadiene-acrylonitrile -- which results from varying rates of conversion during the reaction (polymerization) process for latex formation. Vinyl pyridine is stored underground near the middle of the plant. Generally speaking, the system has been closed since installations in 1961. Yet, the potential of exposure to these agents exists for the tank farm attendents on each shift who have as one of their responsibilities coupling pipes from tank cars to storage tanks. As part of quality control, acrylonitrile and styrene are collected by operators in 1 liter amounts from ports on the tops of these tanks. While collecting the liter samples, the operator wears gloves and eye protection. This particular operation was viewed during the site visit; some styrene odor was detected during styrene collection.

In contrast to styrene sampling, butadiene gas collection is completed by "lab" personnel (salaried) employing "gas bombs". The procedure was not observed during the plant visit. Overall, odors on the catawalk above the tanks in the tank farm were noticeable from time to time; but probably far below recommended standards for at least styrene (TLV = 100, Odor Threshold = 0.15 ppm), and 1,3-butadiene (TLV = 1000 ppm, Odor Threshold = 1.3 ppm).

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[3] Usually styrene and acrylonitrile arrive by truck, whereas butadeine and others arrive in tank cars. There are exceptions.

Firemen equipped with Exploi-meters and indicator tubes also work this area of the plant looking for leaks. Under critical conditions -- major leaks -- these men are provided Scott Air Packs. However, at first contact with or discovery of such a leak, a brief, acute exposure to the escaping agent may occur.

Pump house operations, involving transfer of monomers to the reactor areas, are under the jurisdiction of the tank farm attendent. Odors were obvious when one first entered the building, but difficult to differentiate. Periodically, pipes in the pump house are cleaned and may account for brief pulse exposures to monomer vapors. Continuous monitoring is performed only during these cleaning procedures. Windows provide natural ventilation; exhaust fans mounted near the floor on the east wall provide air turnover and removal of contaminant vapors.

At this stage of the process, butadiene is advanced to caustic (NaOH) decanters to remove tertiary butyl catecol (TBC) an inhibitor which prevents peroxides from forming in the 1,3-butadiene.

Reactor Operations - Department 085

Polymerization of monomers takes place in any of five reactor areas of the Akron synthetic facility as noted in Table 4 below:

Table 4. Major Reactor Areas At The Firestone Synthetic Plant At Akron.

Area
2-S Reactor Area
3-S Reactor Area
1-S Reactor Area
1-S Extension Area
4-S Reactor Area

Products manufactured in these areas vary from time to time and include SBR latex, ABS rubber, NBR rubber and carboxylated latacies. In addition to product mix changes in a given area, process changes, that is, continuous versus batch, certainly affect where specific materials are produced within the plant.

2-S - 3-S Reactor Areas

Due to the close proximity of reactor areas 2-S and 3-S, both have a common control center, the 2-S control room located in near the 2-S reactors.[4] The reactors in each group are located in the open with a limited overhead covering. Therefore, emissions from the areas would expectedly disperse quite rapidly to the atmosphere. In addition, reactors are equipped with special "rupture discs" which are designed to alleviate excess reactor pressure by diverting pressurized vapors "blow outs" to an isolated combustion tower. Nonetheless, vapor odors were obvious in the 2-S:3-S control room and in the immediate vicinity of certain reactors. Strippers (recovery units) for the 2-S and 3-S reactor areas are located immediately behind the individual reactor banks. Strippers, too, are open to natural ventilation. Strippers in the 3-S area are an exception, being completely enclosed. Three floor mounted exhaust fans (18") are provided to remove vapors. Overall, reactor operator responsibilities involve duties in the 2-S and 3-S reactor areas as well as duties in the 2-S control room and stripper areas.

A solution make-up room was noted just off the 2-S reactor control room. Reportedly, defoaming agents were stored here and added to individual strippers to prevent foaming during "steaming" -- forcing steam into (recovery) stripper units to recover and condense butadiene and styrene for return to the tank farm. Other agents observed in the make-up room were: versene (Na_4 EDTA) for iron removal from water, sodium nitrite, agents for electrolyte solutions (e.g., K_2SO_4) and the

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[4]The numbers of reactors in operation in each area are available from internal documents but have been excluded for reasons of confidentiality.

short-stop compound hydroquinone (p-dihydroxybenzene). The short-stop agent is blended in a closed system provided with exhaust ventilation inside the hatch. A scale was provided for weighing dry materials with ceiling exhaust ventilation. Odors in the room were quite noticeable. However, from the standpoint of housekeeping, the solution make-up was well maintained.

1-S, 1-S Extension and 4-S Reactor Areas

The 1-S, 1-S extension and 4-S reactor areas are all located in the same general region of the synthetic complex and are programmed through the 1-S control room. Two separate groups of reactors comprise the 1-S area, each group complimented by a pair of recovery units. Odors were evident near certain reactors in each group. High styrene polymers were formulated in the second group of 1-S reactors. Reportedly, such reactors not only require frequent cleaning but are difficult to clean. In this regard, it is interesting to note that toluene and styrene are employed (when required) in reactor cleaning procedures. "Chipping" of material from reactor surfaces may also be required. Indicator tube tests are made prior to and during these cleaning procedures.

Since 1974, high pressure water guns have been used to aid in reactor cleaning. Prior to that date, (for approximately 9 years) ineffective low pressure guns were employed requiring hand scraping. Men (factory service personnel) enter reactors to clean them; they have the option of wearing respirators during cleaning, but usually do not.

Pennstop 1866 (diethyl hydroxylamine) and sodium nitrite were noted in the area and were employed in applications similar to those already discussed for the 2S-3S reactor area.

The 1-S extension and 4-S reactor units are continuous chain type reactors. Reactors in the 1-S extension section are complimented by a pair of recovery units, whereas reactors in the 4-S group twice the size of other SBR reactors, are complimented by concentrators and columns. All reactors in the aforementioned groups (1-S, 1-S extension and 4-S) are under roof, but are not enclosed by walls.

3-S Latex Loading and Blending - Department 083

Once stripped of excess monomer, latexes are stored for subsequent loading into drums or tank cars (SBR latex generally) for customer shipments or for transfer to drying operations (NBR and ABS rubbers).

Prior to loading, tank cars are cleaned and flushed. Cars are then loaded from the top. Some odors were detected at this stage, possibly due to residual styrene in the SBR latex; at this stage essentially all the styrene and butadiene have been removed by reduced pressure and steam distillation.

Operators in department 083 are also involved in 3-S latex blending, soap solution preparation and 1-S latex building operations. Four to five people per shift are involved with such tasks.

Solution Make-Up Area - Department 083 (Continued)

Soap, electroylte (K_2SO_4) and other solutions necessary for the production of SBR and related products are formulated in the solution make-up area. Two men per shift are usually stationed in this area but may split their duties among other department 083 areas described in

previous sections of this report. The solution make-up area is quite large and open and is exhaust ventilated by two large four-foot fans located on a wall opposite a bank of windows. Ammonia, employed as a coolant for reactors, is present in the refrigeration compressors in the area. Some ammonia gas was evident in the room air, but concentrations were significantly lower than that prescribed by the Threshold Limit Values. Otherwise, the room was noticeably well maintained and relatively odor free. Another compound, "Polyamine H", was noted in the area and bore the warning "absorption through skin may be harmful." Conditions of handling were not observed during the walk-through survey of the soap preparation area. Although, we have learned subsequently that safe handling procedures are in existence and posted that employees handling this material wear face shields, impervious aprons, and long sleeved rubber gloves. Considering the nature of operations in this area, maintenance is satisfactory.

Drier Area - Department 087

Drier room operations are currently limited to the drying of NBR and ABS polymers. SBR driers have been gradually dismantled since 1946-1947 with termination of dry SBR production sometime in 1973. After several coagulation and dewatering stages followed by screening and shredding steps, NBR and ABS latexes are converted to their dry forms. NBR, a soft "popcorn" type product, is pressed into 75 pound bales, some of which are bagged. In certain instances, it may also be pulverized into a "crumb" type material, powdered with talc (in an enclosed system with a dust collector) to prevent sticking, and then boxed. Particulate exposure appeared minimal due to the large particle size of this material.

Dry ABS rubber is processed in a similar fashion to NBR; however, the finished product is hard or more plastic in nature.

With regard to personnel, the drying room is manned by a coagulator operator, two utility men responsible for antioxidant addition at the storage tank or coagulation unit stage, a bagger (baler) operator and a weigher-checker operator. Next to the reactor area, odors in the drying room, particularly on the catwalk, were probably the strongest of any area visited. In addition, the catwalk area was relatively "hot" owing to the presence of steam from drying and related operations. Exhaust ventilation was provided above open latex receiving tanks to alleviate residual styrene exposure at this stage.

Environmental Control Facility - Department 082

Water from tank car cleaning, latex-dewatering and other plant discharge operations is treated at the Company's effluent control center prior to discharge to the community wastewater treatment system. Wastewater entering the center is aerated forming a froth containing waste latex or rubber. When the BOD and residual solids have been reduced to a acceptable, level the water is discharged to the city's sewage treatment facility. Even after treatment at the effluent control center, a low level of styrene remains in the discharged water. For maintenance personnel, here, low level exposure to probably styrene and possibly acrylonitrile may occur. This is an automated system and operator presence is minimal.

Summary

The foregoing review of synthetic operations at Firestone Synthetic Plant at Akron indicate the potential for a variety of gas and vapor exposures at the complex, the potential for exposure probably being greater in the past.

For reasons previously cited, tank farm and maintenance personnel could well have intermittent exposure to raw materials including 1,3-butadine, styrene, and acrylonitrile. Firemen, too, by the nature of their job, that is, leak detection, probably fall into this category. Acute exposures resulting from spills, leaks in coupling and piping and other situations may occur in the general area of the tank farm.

The reactor-recovery area could well present itself as an area with the potential for exposure of personnel (reactor operators, tank cleaners and salaried quality control personnel) to the aforementioned monomers. Reactor cleaning procedures, although following strict protocol, may enhance the possibility for exposure. Factory service personnel thus fall into the category with potential for exposure to monomer.

The volatility of 1,3-butadiene and its elimination prior to latex handling steps, suggest that only styrene and acrylonitrile pose as exposure agents in subsequent stages of synthetic products manufacture. Latex loading, blending and tank cleaning might fall into this exposure category. Since SBR latex is the major, if not the only product distributed in the latex form, styrene probably predominates as the major exposure agent during latex blending and loading. Exposure to acrylonitrile could also occur during respective blending and loading operations.

Drier room personnel, such as the coagulator operator, have an opportunity for vapor insults from NBR and ABS agents including acrylonitrile materials. Yet, in retrospect, styrene could well have been one of the major vapor insults before dry SBR was discontinued.

Utility men, baggers (balers) and weigher-checkers, too, could have had a similar exposure experience although possibly somewhat less, since they are involved in operations somewhat remote from latex handling. Particulate exposures for baggers and weigher-checkers were minimal.

Individuals assigned to the primary solution make-up area do not have the opportunity for exposure to the major monomers employed in the manufacture of synthetic products. Rather, their exposure experience is confined to a different group of chemicals -- electrolytes, chelating agents and other dry materials -- many of which are dissolved in water. Certain of these agents, such as hydroquinones, nitrosophenyl hydroxyamines (NPH) and "Polyamine H" present their own individual problems of toxicity.

During the survey of the plant, several minor solution make-up areas were noted, specifically those adjacent to reactor areas (see sections on Reactor Areas 2-S and 1-S). Reportedly, reactor operators periodically man these stations. As a result, their exposures are not limited to monomers in the reactor area, but to certain other dry compounds formulated in these specialized areas.

Personnel in the effluent control center are limited in exposure, for the most part, to residual styrene in waste latex. Exposure to styrene vapor, which reportedly varies, is probably quite low and well below recommended standards (TLVs).

Recapitulating, then, tank farm attendants and maintenance personnel (repairmen) having duties in the tank farm area should be considered as the group with the highest potential for monomer exposure; such exposures is probably somewhat intermittent. Reactor operators and cleaners could be described as having the second highest potential risk for monomer insult. In this regard, fourteen mortality cases with work histories

in various areas of the synthetic plant were categorized on the basis of potential for high (H) medium (M) and low (L) exposure (Table 5). Six of the fourteen individuals had died of NLHT and the remainder had different causes of death. However, classification of risk or exposure was completed with no prior knowledge of the cause of death. It is interesting that out of the six NLHT cases, four were classed as "H" for potentially high exposure, with one case classed "M" for medium risk. The latter case involved an individual who also spent six years in cement preparation (non-synthetic plant operation) -- an area of high solvent exposure. High solvent exposure has been previously associated with apparent risk of leukemia (see article referenced in footnote of Table 2). The sixth case of NLHT was not classified with respect to exposure due to lack of information on where the individual worked within the synthetic plant. A non-NLHT case was also classed "H" due to his work experience in maintenance. Certainly, not all maintenance personnel have duties in the tank farm or reactor areas of the plant. However, by the very nature of their job, certain maintenance personnel, particularly pipefitters, could be dispatched to such areas with a high potential for monomer exposure.

From the information in Table 5, it appears that the greatest risk of exposure may stem from operations at the "front end" of the process, that is, the tank farm area where monomers are received, stored and checked by quality control and tank farm personnel. Maintenance personnel are also involved in these area for reasons previously cited. It's worth noting, here, that both butadiene and styrene (and other agents mentioned earlier) are potential exposure agents at this and the reactor stages of the operation, whereas later in the process butadiene has been eliminated and only styrene persists as a residual contaminant in

formulated latexes. It follows, then, that on a qualitative basis exposures to butadeine deserve careful scrutiny. Our qualitative assessment suggests that NLHT cases have not been noted among persons who worked in areas where styrene in lower concentrations is the major exposure agent. On the other hand, any adverse health effects may be related to, or depend on, the magnitude of exposure to either butadiene or styrene at the "front end" of the synthetic process. Although a causal relationship between any particular condition of work and the occurrence of lymphomas or leukemias has not been demonstrated, an interim recommendation on industrial hygiene practice is offered.

Iterim Recommendation: Work practices and equipment should be reviewed throughout the synthetic plant with the view to minimizing exposures to volatile agents including both butadiene and styrene. Particular attention should be given to (1) tank farm operations to eliminate exposures during transfer, maintenance, and sampling operations; (2) reactor operations, particularly to reactor opening and cleaning; and (3) detection and correction of leaks in process piping, pumps, vessels, and other process equipment with special precaution to prevent exposure of personnel during all maintenance and repair operation.

Table 5. Classification of Individual Work Histories With Respect to Risk or Potential Exposure to Synthetic Plant Monomers.

Mortality Cases	Risk or Potential Exposure Level (L, M, H)[1]	Job(s) Held in Synthetic Plant	Time Period at Job(s)	Duration of Job(s)
NLHT Cases				
LHR	H	Pump House Operator & Related Positions	1942-69	27
DAC	H	Repairman (Maintenance)	1952-63	11
HAO	H	Repairman (Maintenance)	1959	1
SHO	H	Pipefitter (Maintenance)	1951-60	9
WLI	M[2]	a. Utility and Service	1950-54	4
		b. Latex Blending	1955-60	5
				9
GSA	?[3]	Janitor-Sweeper	1942-49	7
Control Cases (No NLHT)				
JEE	L	Trucker	1955-68	13
RED	L-M	a. Solution Make-Up	1943	1/2
		b. Reactor Operator	1943-44,'49	1 1/2
		c. Latex Processor	1963-64	1
				3
HEC	M	a. Utility & Service, Latex Coagulator & Latex Helper	1951	1
		b. Trucker	1958-65,'71	8
				9
EW	M	a. Janitor	1942-43	1
		b. Utility & Service	1943-45	2
		c. Solution-Make-Up	1945-60	15
				18
CG	L-M	Utility & Service, Bailer and Centrifuge Op.	1945-49	4
FRY	H	Repairman (Maintenance)	1950-63	13
GSR	L-M	a. Reactor Helper	1942	1/2
		b. Solution-Make-Up	1942-49	6 1/2
				7
EPG	L	a. Utility & Service, Coagulator Operator	1950	1
		b. Utility, Tank Cleaner and Centrifuge Operator	1951	1
				2

[1]Based on work area and job and not duration of exposure within that area or job.

[2]Individual worked six years (1942-48) in cement mixing (non-synthetic plant operation) with potentially high solvent exposure-related to development of leukemia.

[3]Not enough information to detemine the area where this individual spent the majority of his time.

III. TOXICOLOGY LITERATURE REVIEW - SYNTHETIC RUBBER

Introduction

From the available literature some of the ingredients used in SBR research and production are listed below. Only certain of these ingredients have been used in the Akron plant. Potential carcinogens or procarcinogens are indicated by asterisk - *. A summary of toxicologic information on each compound follows:

Monomers

*Styrene

Butadiene

Initiators

Persulfates

*Hydroperoxide, e.g., p-menthane-8-hydroperoxide, cumene hydroperoxide.

Azobisisobutyronitrile (AIBN)

Sodium-formaldehyde sulphoxylate (Sulphoxylate formula)

Modifiers

Aliphatic mercaptans, e.g., n-dodecylmercaptan

(*?) p-nitroaniline

Thioethers

Chlorinated hydrocarbons

Short-stops and Antioxidants

Sodium hydrosulfide

Hydroquinone

Phenyl-B-naphthylamine

Trialkyl phenol phosphites

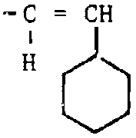
2,6-ditert-butyl-p-cresol (BHT)

(*?) Sodium dimethyl dithiocarbamate

Butadiene-Styrene Copolymers (SBR)

Production of the synthetic rubber is based on the emulsion of the purified monomers in water. An initiator is added to start the reaction, and a modifier is used to limit molecular weight and prevent cross-linking. When 60-72% of the monomers are converted to polymers, the reaction is interrupted by adding a short-stop agent. Unreacted monomer is removed and recycled, the latex is coagulated continuously with salt solutions, H_2SO_4, acetic acid, or glue. The crumbled coagulum is washed, dried, and pressed into bales. The toxicity of the compounds used, with particular reference to cancer, is summarized.

Monomers:

Styrene: (C_8H_8)  phenylethylene, vinyl benzene.

Styrene is readily absorbable into the bloodstream by all routes, although skin and lung are most important for industrial exposure. Because of its high lipid solubility, there may be extensive sequestation of styrene in fat.

Figure 1 summarizes the metabolism of styrene.

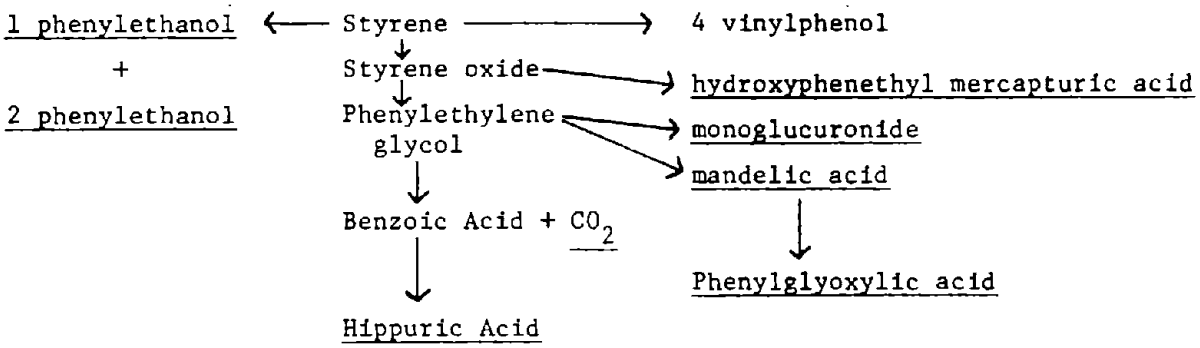


Figure 1. Metabolism of Styrene. Underlined metabolites are those excreted in urine or expired air (from 1).

The excreted metabolites of styrene metabolism are all considerably less toxic than styrene itself - at least for acute effects. [As it is with toluene, hippuric acid in the urine may provide an index of exposure to styrene (assumming no food intake of certain fruits and vegetables)]. Acute symptoms of styrene intoxication are irritation of the skin, eyes, and respiratory tract and depression of the central nervous system. Repeated 7 to 8 hour exposures to about 1300 ppm styrene resulted in no changes in blood cells in rats, rabbits and monkeys.[2] The acute toxicity of styrene oxide, however, is about 4 times that of styrene.[1,3] Epoxides have been shown to be hepatotoxins and carcinogens and exhibit radiomimetic properties such as growth-inhibitory, mutagenic, and cytotoxic activity, probably because they are alkylating agents.[1,5] Peroxides may catalyze the depolymerization of DNA and RNA in a fashion similar to ionizing radiation. Organic peroxide may also lead to the formation of epoxides, which are established carcinogens[11]. Of particular interest, styrene oxide (an epixode) was reported to produce malignant lymphomas in mice (by inhalation?) and to have carcinogenic activity when painted on the skin of mice.[4,5,6]

Butadiene: (CH_2 = CH-CH=CH_2)divinyl, biethylene.

This unsaturated aliphatic hydrocarbon forms organic peroxides on standing. At high concentrations it is an anesthetic. It is now considered to be not very toxic, and has only slight irritative effects. The TLV is 1,000 ppm.

Initiators (Activators)

Some commonly employed initiators include:

a) Ammonium and potassium persulfate ($(NH_4)_2$ S_2O_8, $K_2S_2O_8$) initiate polymerization (effective at $\geq$30°C). About 0.3 parts by weight was used in a typical recipe for GR-S rubber around 1942. These compounds are moderately toxic and strong irritants and oxidizing agents.

b) Organic hydroperoxide (e.g., p-menthanehydroperoxide)/iron sulfate/alkali pyrophosphate.

Peroxy compounds have been suggested as potential carcinogenic air pollutants and components of cigarette smoke[4,5,11]. At least one organic hydroperoxide has been shown to have carcinogenic activity when painted on mouse skin (5), and 620 mg/kg p-menthane-8-hydroperoxide was carcinogenic (malignant lymphomas and pulmonary adenomas) when inhaled by mice (11). 0.10 to 0.15 parts by weight of this compound is typically used in the production of cold rubber.

c) Hydroperoxide and polyamine with only slight traces of iron (peroxamine formula). 0.1 part by weight of Polyamine H (alkylene polyamine) is a typical component for cold rubber produced beginning about 1948. The peroxamine process is a redox polymerization process for SBR cold rubber, using the hydroperoxide as an oxidizing agent and a polyethylene polyamine as the reducing agent in the presence of traces of iron. No carcinogenic effects of aliphatic amines have been described (7).

d) Benzoyl peroxide [$(C_6H_5CO)_2\ O_2$]. The TLV for benzoyl peroxide is 5 mg/m^3, based on the prevention of irritation. Sensitization occurs upon skin contact (8). The lowest published toxic dose for mice is 25 gm/kg on skin contact for 42 weeks. Some neoplastic effects were observed (6).

e) Cumene hydroperoxide ($C_6H_5C\ (CH_3)_2\ OOH$). This liquid is highly toxic by inhalation and skin absorption and has been shown to have mutagenic properties (11). In the mouse, inhalation of 304 mg/kg resulted in malignant lymphomas and subcutaneous sarcomas (6,11). Cumene hydroperoxide was inactive on mouse skin, and had weakly active carcinogenic activity by subcutaneous injection (12).

f) Diisopropyl benzoyl hydroperoxide is available as a 52% solution in a nonvolatile solvent and is probably toxic. Of fifty mice exposed to 50μM, 10 died, 2 of malignant lymphomas and 3 of pulmonary adenomas (11).

g) Azobisisobutyronitrile (AIBN) [$(CH_3)_2$ C(CN) NNC (CN) $(CH_3)_2$] is a white powder that may be toxic by ingestion. No reports of neoplastic effects have been found.

h) Sodium-formaldehyde/sulphoxylate-ferrous sulphate complexes based on ethylene diamine tetra-acetic acid as the activating system (sulphoxylate formula) is used in emulsion polymerization of SBR cold rubber. Sodium formaldehyde sulfoxylate (SFS) has the formula HC HO · HSO_2 Na · $2H_2O$ and is a white solid that is probably toxic. No reports of neoplastic effects have been found. EDTA, $(HOOCCH_2)_2$ NCH_2 CH_2N $(CH_2COOH)_2$, is an organic chelating agent of low toxicity. No reports of neoplastic effects have been found.

Modifiers (Regulators)

These substances are added to regulate the average molecular weight and make possible the formation of shorter, more linear chain structures. This makes the rubber much easier to process and reduces the formation of undesirable insoluable polymers. Aliphatic mercatans such as n-dodecyl mercaptan (DDM) is the most common regulator, comprising 0.5 parts by weight in a standard recipe for GR-S (also used in NBR). DDM ($C_{12}H_{25}SH$), also known as lauryl mercaptan, is a toxic and irritant liquid that may form many isomers. Other regulators listed in the literature are sodium linoleate, p-nitroaniline, thioethers, chlorinated hydrocarbons, and di-isopropyl xanthogen disulfide. Nitroaniline has a TLV of 1 ppm and is a powerful methemoglobin former with finally a hemolytic effect. It is considered more toxic than aniline. No neoplastic effects are reported for these compounds. Our literature sources do not identify the specific thioethers and chlorinated hydrocarbons are used as modifiers.

Short-stop and Antioxidants

When the conversion of monomers to polymers is at 60-72%, the reaction in interrupted, as too high a conversion gives rise to insoluble materials that are difficult to process. In hot polymers, sodium hydrosulfide ($NaSH \cdot 2H_2O$) or sodium bisulfide is used. It may liberate H_2S; no neoplastic effects have been reported.

Hydroquinone [$C_6H_4(OH)_2$, para-dihydroxybenzene] is used in batch polymerization. The TLV of hydroquinone is 2 mg/m^3 based on levels which appear to cause no systemic effects. More toxic than phenol, subacute poisoning causes hemolytic icterus, anemia, leukocytosis, reticulocytosis, increased cell fragility, and hypoglycemia. A number of toxicity studies[6] on a variety of species suggest it is moderately toxic; one study where hydroquinone (800 mg/kg) was painted on mouse skin resulted in one tumor in 22 animals. The authors considered this to be not significant. Hydroquinone has been suggested as affecting mitosis, exerting a radiomimetic effect. This is disputed, however (13). There are no reports of cancer in exposed human populations[8]. In very low concentrations hydroquinone is relatively safe, and has been proposed as a food antioxidant (9).

Phenols as a group, however, have been reported to be toxic to mitosis, but had no effect on body weight or leukocyte count in rabbits given 0.05 g/kg daily (subcutaneous) of hydroquinone. 0.04 gm/kg daily of hydroquinone fed to cats resulted in anemia, hemolytic jaundice, leucopenia and slight reticulocytosis; 0.03 gm/kg administered subcutaneously to rabbits resulted in anemia and luecopenia. Hydroquinone is one of the metabolites of benzene metabolism. Nomiyama (10) has suggested that the hemopoietic disturbance in chronic benzene poisoning is the formation of catechol (ortho-dihydroxybenzene), via benzeneglycol and not formation of hydroquinone.

Phenyl B-napthylamine (PNB) which acts as a stabilizer and antioxidant, is used in continuous polymerization (1.25 parts by weight). It is of low toxicity. It has been suggested as a possible bladder carcinogen.

For light colored SBR, trialkyl phenol phosphites and 2:6-ditert-butyl-p-cresol (BHT) are used. BHT is a food antioxidant with low toxicity.

Water soluble sodium dimethyldithiocarbamate [$(CH_3)_2$ NCS_2Na)] is used for redox systems. It is moderately toxic with no reported neoplastic effects. The zinc salt of dimethyl dithiocarbamates (=ziram) is a rubber accelerator and has been shown to have neoplastic effects when 1500 mg/kg is fed to mice, and carcinogenic effects in rats when 13 gm/kg is fed for 95 weeks and 60 mg/kg implanted in rats (6).

Possible or Suspect Leukemogenic Agents

Isoprene, cyclopentadiene, hexane and benzene may be used in making emulsion polymers, latex, dry rubber or solution rubber; of these only benzene is reported to have carcinogenic properties.

Any agent capable of producing aplasia of the bone marrow should be considered as potentially leukemogenic. At present, benzene seems to be the only chemical agent to have produced occupational leukemia.[14-24]

Benzene was discovered in coal tar in 1845. Since the 1890's, coal tar derivatives have become very numerous. In industry, benzene has been used in two major ways: (1) in large quantities in closed mechanical systems (distillation of coal and coal tar, blending of motor fuels, chemical industry), and (2) as a solvent or diluent (rubber industry, boot and shoe industry, artificial leather manufacture, photograve color-printing, paint and varnish manufacture, airplane, linoleum and celluloid industries, artificial manure and glue manufacture, and extraction of certain alkaloids in the pharmaceutical industry).

Beginning in 1897, a number of deaths have occurred from the use of benzene as a rubber solvent. Chronic benzene poisoning in a British rubber factory resulted in 3 reported deaths from aplastic anemia and led to the substitution of xylene for benzene as a rubber solvent in 1918. Despite the reported toxicity of benzene, its use as a solvent increased after WWI in most industrial countries. The chief industries involved were rubber tire building, manufacture of spread rubber goods, use of rubber cements in fastening rubber heels and soles, artificial leather manufacture, dry cleaning industry, sealing of food cans with a benzene-rubber cement, and in the painting trade. In Milan, Italy, Vigliani and Saita[17] report that in 1962-3, there was a sharp rise in cases of occupationally related cases of benzene poisoning; slightly less than half the deaths were from acute leukemia, slightly more than half from aplastic anemia. In 1922, the growing menace of benzene poisoning was pointed out. In 1926, the U. S. National Safety Council ordered the improvement of rubber factory ventilation, instituted medical supervision of workers and the use of xylene as a safe substitute for benzene. This occurred 8 years after the same changes had been made in Great Britain. Around 1928, toluene was substituted for benzene in dry cleaning, thinners for quick-drying paints, and solvent for cellulose lacquers. Rubber latex was substituted for benzene in rubber cements used in the canning and boot and shoe industries. Many rubber factories returned to the use of petroleum naptha as a solvent for spread rubber goods and rubber cements.[36]

The first published cases of benzene leukemia were in 1928 and 1932. Typically, these were of prolonged exposure to benzene vapors for many years, with ultimate development of fatigue, anemia, leukocytosis, immature cells in peripheral blood, and death.

Documented cases of benzene leukemia are largely (acute?) myeloblastic leukemia, most cases being leucopenia with moderate or no splenomegely and extensive infiltration by undifferentiated cells in the bone marrow. The leukemia occurs more frequently in subjects with anemia, with the bone marrow changing from a hypoplastic to a leukemia pattern. In well documented cases of benzene leukemia in factories where aplastic anemia was also observed, the cases were all acute, the exposure was heavy and long, and the latent period long (up to 12 years).

Benzene poisoning is paradoxical in its symptomatology - being influenced by individual susceptibility, length and amount of exposure. In industry there is no explanation as to why some get leukemia, and others working alongside do not. The biological response varies from hypo- to hyperplasia of bone marrow. Chromosome aberrations, leucopenia, anemia, thrombocytopenia are the most common blood abnormalities. Studies have been reported which indicate that leucopenia is the main persisting symptoms upon removal from exposure; others indicate that thrombocytes and RBC remain low while leucocytes return to normal. Examination of 125 benzene poisoned individuals 10 years after exposure has shown that neither the severity of exposure nor the hematological changes significantly affects prognosis of those surviving the acute poisoning when compared to 86 non-benzene exposed controls. One of the 9 deaths occurring during this period was due to leukemia which occurred 7 years after initial exposure to benzene.[16]

No other aromatic hydrocarbon used industrially has yet been implicated as a leukemogenic agent. It has been suggested that the effects of benzene on the hemopoietic tissue may be due to benzene metabolites, the hydrocarbon molecule itself, or both. The metabolites seem most likely. Other alkyl benzenes (toluene, xylenes, ethylbenzene, etc.) do not appear to have

the effect of benzene on blood-forming tissue, and as a group are transformed in vivo to carboxylic acids and alcohols. The principal benzene metabolites however, are phenols which are protoplasmic poisons. The oxidation of phenols produces quinones which are potent mitotic inhibitors and might be responsible for the effect on blood-forming tissues.

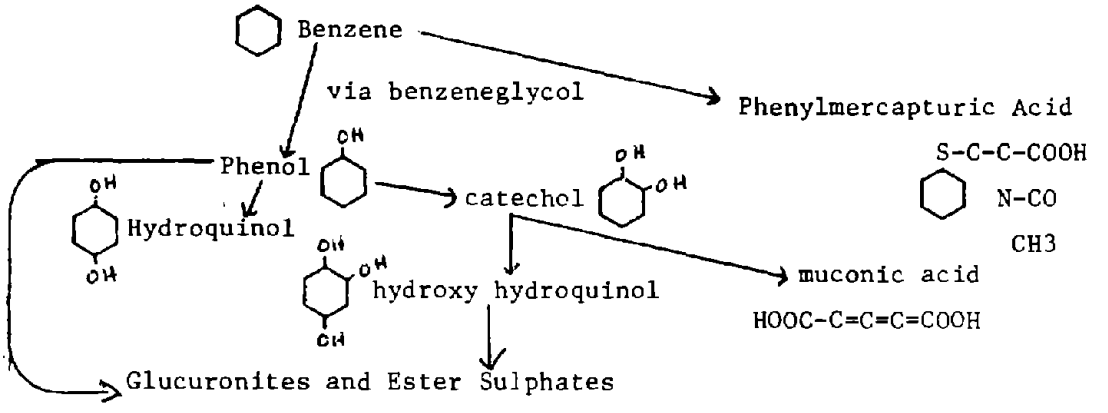


Figure 1. Metabolism of Benzene (from 34).

Nomiyama, from experiments in rats, concludes that the hemopoietic disturbances in chronic benzene poisoning is the formation of catechol via benzeneglycol.[10]

Ionizing radiation has also been implicated as a leukemogenic agent.[24,29,30,33] For leukemia there is some evidence that there is no threshold, and a linear dose-response relation may exist at lower dose levels. Acute and chronic myelogenous leukemia are usually considered the most frequent malignancies resulting from radiation exposures, although this may be due to the short latent period (<1 to 15+ years, with modal incubation time of approximately 5 years). Perhaps 5-10% of leukemia cases are caused by ionizing radiation. It has been estimated that the chance of leukemia after 1 rad of whole-body ionizing radiation is of the order of $1\text{-}2 \times 10^{-6}$/person-year. The great majority of these cases are of the myeloid type. Thus, ionizing radiation is unlikely to

account for the increased incidence of largely chronic lymphatic leukemia in older age groups.

Any bone marrow depressants or substances damaging chromosomes are possible leukemogenic agents. Other agents suggested as potential leukemogens include the following:

(a) arsenicals and sulfonamides

(b) chloramphenicol[28,35] - This broad spectrum antibiotic has become a commonly sited cause of acquired aplastic anemia. Leukemia is commonly characterized by variable degrees of bone-marrow hypoplasia. Although not usually reported, there are examples of the leukemia developing after aplastic anemia (from benzene, radiation, phenylbutazone, hypoplastic phase of paroxysmal nocturnal hemoglobmuria, and hereditary hypoplastic syndromes). Chromosomal changes have been observed in several cases of acute leukemia, similar to those following benzene and radiation exposure and in certain hereditary conditions. These may be similar to the chromosomal vacuolizations seen after chloramphenicol administration. Development of leukemia could also result from growth disturbance of the bone marrow, occurring either sequentially or together. This hypothesis suggests leukemia and aplastic anemia are different expressions of the same fundamental disturbance. Chloramphenicol is capable of destroying bone marrow - which could, for example, result in a new self-perpetuating cell line (clone), which if affecting leukocytes, could be leukemia. Three cases of acute myeloblastic leukemia that developed from chloramphenicol induced aplastic anemia have been described.

(c) hexachlorcyclohexane - This is an insecticide (Lindane) with the chemical formual $C_6H_6Cl_6$. Its effect on haemopoiesis has been reported to be similar to benzene, with one reported case of pancytopenia, and one fatal case of aplastic anemia, and failure of blood formation after

acute poisoning. Two cases of acute paramyeloblastic leukemia have been reported in blood cousins exposed to hexachlorcyclohexane 8 months prior to the onset of the disease.[27]

(d) phenylbutazone (PBZ) - This is an anti-inflammatory drug often used in the treatment of arthritis and spondylitis. Toxic side effects include those to the haemopoietic system (leucopenia, agranulocytosis, thrombocytopenia), with reported cases of aplastic anemia, depressed erythropoiesis and megaloblastosis. Complications from the blood-forming system are less common but more serious than other toxic effects.[25,26] In a retrospective study of 50 patients with acute leukemia, three patients had a history of PBZ ingestion (6% incidence), with a latent period of 15, 27 and 12 months (72, 27 and unknown grams of PBZ).[26] Since 1958, established cases of leukemia associated with PBZ administration have been reported (8 myeloblastic, 3 lymphoblastic, 1 myelomonomcytic, 2 "blast cell" leukemia, 5 chronic myelocytic leukemia). Ten of the cases had no radiotherapy. The latent period between PBZ treatment and diagnosis of leukemia varied from 4 weeks to 6 1/2 years.[26]

(e) viruses - Fowl and rodents are subject to viral leukemias. So far, it has not been shown to exist in man, although there is suggestive evidence of "microepidemics" posing the possibility of the infectious transmission of leukemia.[33]

(f) heredity - There are at least 100 instances of familial leukemia, being more common in mongoloids or feeble minded. In a New Zealand study approximately 7% of leukemia incidence could be attributed to inheritance.

(g) other agents - Chemical carcinogens such as benzypyrene, dibenzanthrocene, 9,10-dimethyl-1,2-benzanthracene and methylcholanthrene

have been shown to cause the appearance of lymphcytic leukemia in certain genetically susceptible strains of mice. Estrogens has also been established as a leukogenic agent in some mice.

Brief Summary of Agents and Some Health Effects - Other Synthetic Rubbers

NBR or Nitrile Rubber

Nitrile rubber began to be produced in this country in 1940. A nitrile rubber is a copolymer of a diene and an unsaturated nitrile, and exhibits a high degree of resistance to attack by oils, the more resistant grades having more acrylonitrile. High acrylonitrile rubber is used in oil well parts, fuel tank liners, fuel hose, gaskets, packing oil seals, and hydraulic equipment. Medium acrylonitrile rubber is used in general-purpose-oil-resistant applications, shoe soles, kitchen mats, sink topping, and printing rolls. Low acrylonitrile rubber is used in gaskets, grommets, O-rings, adhesives. The only diene used commercially in NBR is butadiene. The most common nitrile is acrylonitrile. Small amounts of styrene, methyl methacrylate, ethyl acrylate or vinylidene chloride can be used. Nitrile rubber are produced by essentially the same emulsion polymeriztion techniques used for SBR, i.e., polymerization, coagulation, washing, drying.

The components of nitrile rubber are listed below:

Monomers

Butadiene

Acrylonitrile

Initiators

Persulfate (hot process)

Cumene hydroperoxide/dextrose/sequestering agent redox system (cold process)

Peroxides (benzoyl peroxide, hydrogen peroxide)

Emulsifiers

Soaps of fatty acids (sodium salts of oleic, myristic or palmitic acid)

Anionic detergents (alkyl benzene sulfonates, dialkyl naphthalene sulfonates, higher alkyl sulfonates)

Cationic detergents (hydrochloride of diethyl amino oleomide, dodecylamine hydrochloride, lauryl pyridinium chloride).

Modifiers

Xanthogen disulfides

Higher mercaptans

Aliphatic mercaptans, e.g., dodecylamine, lauryl mercaptan (contains proportions of n-tetra decyl, and n-hexa decyl mercaptans and dodecyl mercaptan)

Short-stop

Hydroquinone

Antioxidants

Phenyl-B-naphthylamine

Alkyldiphenylamines

Hindered alkylphenols or other phenol derivatives

ABS Rubber

ABS (acrylonitrile, butadiene, styrene) is a nitrile terpolymer rubber latex (Nitrex) or a solid ABS terpolymer. Latices of acrylonitrile/butadiene/styrene terpolymers contain 10-30% styrene, 28-33% acrylonitrile. They have low water absorption and are used in impregnation, saturating agent for paper and cellulose, softener for resin latices.

ABS resin is a thermoplastic polymer blend that is used in automobile body parts and fittings, telephones, heels, luggage, packaging, refrigerator door linings, plastic pipe, building panels, shower stalls, boats and radiation grills.

Specialty Latices

1) Styrene/Butadiene/Vinyl Pyridine Terpolymer Rubber Latex. This latex is made by emulsion polymerization of butadiene, styrene and 2,3- or 4 vinylpyridine (CH_2 =CHC_5H_4N) and is used either alone or mixed with a styrene-butadiene latex for dipping tire cord, giving a stronger and more fatigue-resistant rubber/textile bond, and is especially useful for nylon and polyester cords. It is also used for belts requiring good rubber/textile adhesion.

2) Carboxylated nitrile latex - This latex is made by including 0.5 - 10% methacrylic acid in the acrylonitrile/butadiene monomer mixture copolymerization occurring in emulsion as for nitrile rubber.

The compounds used in NBR, ABS and specialty latices that are not discussed under SBR rubber, but appear to have potential significance for health are discussed below.

Monomers

Acrylonitrile: H_2C:CHCN (propenenitrile, vinyl cyanide).

This is a clear, colorless, volatile liquid with a vapor density of 1.9 and a vapor pressure of 110-115 mmHg at 25°C. It is readily absorbed through the skin and by inhalation. Acrylonitrile is moderately toxic. It is not agreed whether the toxicity of acrylonitrile is due to cyanide formation, or to acrylonitrile itself. If it acts like cyanide in acute poisoning, cellular respiration is stopped by blocking oxidative enzymes. In chronic poisoning the CN^- ion is gradually released, converted to SCN^- and excreted as the thiocyanate ion. There is some question whether chronic cyanide poisoning occurs at all. The TLV of acrylonitrile is 20 ppm, based on animal exposure data, and by analogy with the 10 ppm TLV of hydrogen cyanide. There are no reported carcinogenic effects.[7,8]

Vinyl pyridine: ($C_5H_2NCH:CH_2$) is a colorless volatile liquid with an unpleasant, pungent odor that in commercial material contains a polymerization inhibitor. It is absorbed by the GI tract, skin and respiratory tract with resultant weakness ataxia, vasodilation, respiratory distress, and convulsions. The compound is moderately toxic; no carcinogenic effects have been reported.[7]

Methacrylic Acid ($CH_2 =C(CH_3)COOH$) is an unstable colorless liquid that will polymerize readily to give water soluble polymers. Its effects are similar to acrylic acid, which is a severe skin, eye and respiratory irritant in concentrated solutions or as a liquid. No cumulative toxic reactions are known, as acrylic acid is probably a normal metabolite. The LD_{50} for intraperitoneal injection in mice is 49 mg/kg. The oral and skin LD_{50} for acrylic acid suggest it is only slightly toxic (although Chemical Dictionary indicates it is highly toxic). It is a strong acid and should be treated accordingly.[7,35]

Emulsifiers

1) Soaps of fatty acids -

-Oleic acid ($CH_3(CH_2)_7CH =CH(CH_2)_7COOH$)

This is the most abundant of the natural fatty acids. There are no known hazards in its use in industry.

-Myristic acid ($CH_3(CH_2)_{12}COOH$) - No known hazard in industrial use. No sign of carcinogenic activity.[7]

-Palmitic acid ($CH_3(CH_2)_{14}COOH$)

One of the major saturated natural fatty acids. No known hazards. It is not carcinogenic.[7]

2) Ionic Detergents

-Alkyl benzene sulfonates - These are branched chain sulfonate types of synthetic detergents, usually a dodecyl benzene. They are known

as "hard" detergents because of their resistance to breakdown by microorganisms. The most widely used synthetic detergent is sodium dodecylbenzene sulfonate, also called alkyl aryl sulfonate ($C_{12}H_{25}C_6H_4SO_3Na$). This compound is only slightly toxic by I.V. or oral administration.[35] The linear alkyl sulfonates may also be used.

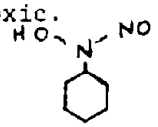
-Lauryl pyridinium chloride is a cationic detergent ($C_5H_5NCIC_{12}H_{25}$) of unknown toxicity.

Modifiers

Mercaptans are a groups of organic compounds resembling alcohols but having the oxygen of the OH group replaced by S, as ethyl mercaptan (C_2H_5SH). They have a particularly strong, skunk-like odor, are strong irritants, and highly toxic by inhalation.

Stopping Agent

EDTA may be used as a stopping agent. This is a commonly used chelating agent and is practically nontoxic.

Nitroso-phenyl hydroxylamine (NPH)  is moderately toxic in oral administration to rats. It is added at the recovery stage in making NBR rubber to prevent "popcorn" formation.

Antioxidants

1) diethylhydroxylamine [$(C_2H_5)_2$ NOH)]. This liquid antioxidant is slightly toxic on oral administration. Also used as a stopping agent.

2) Di-tert-butyl-methyl-phenol could be either 4,6-di-tert-butyl-meta-cresol (DBMC) or 2,6-di-tert-butyl-para-cresol (BHT), both with the chemical formula $[C(CH_3)_3]_2$ $CH_3C_6H_2OH$. Both are of low toxicity. BHT is used as a food antioxidant.

3) Phenol  . The TLV is 5 ppm, sufficient to prevent systemic poisoning if skin absorption is avoided. Phenol is readily absorbed through the skin, gut and lung. After absorption, most of the

phenol is oxidized and conjugated with sulfuric, glucuronic and other acids, and excreted as the conjugated and free phenol. The toxic effects of phenol are related to the amounts of "free" phenol in the blood. Phenol is moderately toxic. Ingestion may cause nausea, vomiting, circulatory collapse, tachypnea, paralysis, convulsions, coma, necrosis of mucus membranes and respiratory failure. Chronic phenol poisoning is rarely reported. Because of its low volatility, phenol does not frequently constitute a serious respiratory hazard in industry. There is no specific evidence of human cancer attributable to phenol or related compounds. However, painting phenol (5 and 10%) on mouse skin induced both papillomas and carcinomas.[6-9]

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APPENDIX D.

A STUDY OF POSSIBLE ASSOCIATIONS BETWEEN EXPOSURE TO SBR PROCESSES AND MORTALITY FROM LEUKEMIA AND RELATED DISEASES BASED ON TOXICOLOGIC, INDUSTRIAL HYGIENE AND EPIDEMIOLOGIC CONSIDERATIONS (FOR WORKERS IN THE 1951 AND 1964 COHORTS AND DEATHS 1964-1973)

Report Prepared For
The Joint URW-Goodyear Occupational
Health Committee

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A STUDY OF POSSIBLE ASSOCIATIONS BETWEEN EXPOSURE TO SBR PROCESSES AND MORTALITY FROM LEUKEMIA AND RELATED DISEASES BASED ON TOXICOLOGIC, INDUSTRIAL HYGIENE AND EPIDEMIOLOGIC CONSIDERATIONS (FOR WORKERS IN THE 1951 AND 1964 COHORTS AND DEATHS 1964-1973)

Summary

The results of three epidemiologic studies are included here. These studies are as follows:

(1) A cohort study comparing the mortality due to neoplasms of the lymphatic and hematopoietic tissue (NLHT) of workers who spent the longest portion of their work time in batch preparation, reaction, finishing and packaging of synthetic latex (OTG Synthetic) against that of all workers in the Akron plants.

(2) A case-control study for leukemia deaths who spent some portion of their work time in OTG Synthetic, and for leukemia deaths who spent some time in other departments thought to have some involvement in synthetic latex production.

(3) A case study of non-leukemia NLHT deaths having some exposure in the areas described in 2, above.

The study described in 1 showed no NLHT deaths among workers with the largest portion of work time in OTG Synthetic. Studies 2 and 3 showed no deaths due to NLHT had ever spent time in OTG Synthetic. However, 4 of 37 leukemia deaths (10.8%) and 6 of 44 (13.6%) non-leukemia NLHT deaths had spent time in the departments with possible similar exposures to those in OTG Synthetic. In particular, 2 of the leukemia deaths and 1 of the non-leukemia NLHT deaths had been pipefitters working in this area. Seven and four-tenths percent of controls for study 2 had spent some time in the departments of interest.

The point estimate of relative risk of death due to leukemia from having ever worked in the departments of interest is 1.5.

One of the departments thought to have exposures similar to those in OTG Synthetic was found to be of a different nature prior to 1972. Since all experience in that department considered here was prior to 1972, studies described in (2) and (3) were repeated omitting this one department. It was found that 8.1% of leukemia deaths, 4.5% of non-leukemia NLHT deaths, and 5.4% of controls for study (2) had spent some time in these departments. The point estimate of relative risk of death due to leukemia from having ever worked in this group of departments is 1.6.

It appears that there may be some excess risk of death due to NLHT among workers in the synthetic latex production area, although this added risk, if it exists, is small.

It was found that 9.1% of non-leukemia NLHT deaths had, in 1961 or earlier, worked in Department 348, identified above as being a non-synthetic operation prior to 1972. In comparison, fewer than 3% of the leukemia study cases and controls ever worked in that department. This indicates a need for further study of mortality among those who worked in Department 348 and similar operations.

A walk-through industrial hygiene survey of the synthetic plant was made. It appears that the potential for exposure to volatile materials including both butadine and styrene, is greatest in the tank farm and during early stages of the process. It is recommended that these areas receive special attention in efforts to minimize exposure.

Toxicologic review of materials involved in the SBR process (and other synthetic rubber processes) reveal some agents which are suspect

carcinogens. These are identified in the listing at the beginning of Section III, Toxicology Review.

I. EPIDEMIOLOGICAL ANALYSIS

The main purpose of the investigation presented in this report was to explore the possible associations between exposures in production of Styrene-Butadiene Rubber (SBR) and deaths from leukemia or related diseases.

Our first response was to examine the mortality of members of the 1964 cohort who had as their Most Representative Occupational Title Group (MROTG) "Synthetic Latex Manufacturing", which includes workers directly associated with batch preparation, reaction, finishing and packaging of synthetic latex. MROTG is assigned to each worker by first finding the department in which the worker spent the greatest portion of work time, assigning an occupational title (OT) to that department, then grouping these OT's.

Approximately 1% of the members of the 1964 cohort, both in terms of person-years experience and actual numbers of workers, had as their MROTG the Synthetic operation.

For white males, the all causes Standardized Mortality Ratios (SMRs) for the MROTG Synthetic workers were 123 for age group 40-64, 65 for age group 65-84. For the entire cohort, these SMRs were 92 and 95, respectively. In the calculation of expected numbers and the SMRs, the U.S. 1968 white male population was used as the standard.

To study mortality by work area, SMR's were computed separately for each of 28 MROTG's, using the whole cohort as the standard. That is, in each of the 28 cases, those 1964 cohort members who had their greatest portion of work time in the OTG of interest were considered as the population at risk (PAR), and the entire cohort (white males) was used as the standard.

For workers with MROTC Synthetic, a significant excess of deaths was observed due to malignant neoplasms of the respiratory system (ICD codes 160-163), specifically malignant neoplasms of the trachea, bronchus, and lung (ICD code 162), with three deaths observed and less than one expected based on the experience of the entire cohort. For no other disease group was there observed either a significant excess or deficit of deaths for workers with this primary OTG.

In particular, for those white male workers with OTG Synthetic, no deaths due to neoplasms of the lymphatic and hematopoietic tissue (ICD codes 200-209) were observed. For this OTG, less than one death due to this cause was expected based on the experience of the entire cohort.

From the larger 1951 cohort consisting of 31,759 workers, which includes anyone who worked any length of time as an hourly employee during the period January 1, 1951 through December 31, 1971, we found that 1 out of 147 known cases of death due to neoplasms of the lymphatic and hematopoietic tissue had as the MROTG Synthetic. This individual died of acute myelocytic leukemia. So, among cases, 1 of 147, or 0.7%, had as the MROTG Synthetic. Among workers in the 1951 cohort with at least 10 years total service, 0.7% had as the MROTG Synthetic. Very roughly, this implies that the number of deaths due to neoplasms of the lymphatic and hematopoietic tissue in this cohort having MROTG Synthetic is about what would be expected based on the experience of the entire cohort.

An on-going case-control study (based on the 1964 cohort) of leukemia deaths being carried out by Ms. Pamela Wolf was used to find further information. The study includes 37 leukemia (ICD codes 204-207) deaths and 4 matched controls for each death, or case. Among the

37 cases, none had worked any time in OTG Synthetic. Three of the 148 controls had spent work time in this OTG.

At this point in the study, the company medical director informed us of six departments whose workers might have had work associated with the synthetic operation. These departments are 313, 345, 346, 347, 348, and 441. In each case, all departments, regardless of fourth-place letter, (e.g., 313A, 313B, etc.) were included. Some workers in these departments were included in the OTG Synthetic Latex Manufacturing. Other workers in these departments held jobs such as pipefitter, cement house, etc., which were not included in OTG Synthetic. Further, prior to 1961, departments 348A, 348B, and 348C were involved in the manufacturing of bullet seal fuel cells and pliocels. Thus, exposures prior to 1961 in these departments should be regarded differently than exposures after 1961. In fact, it was not until 1972 that departments with number 348 were instituted as part of the synthetic segment of the plant. Hence, no worker in departments numbered 348 under study for this report was actually involved in the synthetic process. However, as requested, all experience in these departments was included in our analysis.

Upon re-examination of the work histories for all cases and controls, including Departments 348 A, B, anc C in the analysis, four of the 37 leukemia cases were found to have spent time in one or more of these departments, with two cases having at least 5 years time in the departments of interest. Certain information on these cases, including year in and year out of the industry, year of first exposure, department, duration of exposure, age at death, year of death, sex, race and cause of death, are found in Table 1. The average duration of work in the departments of interest for the four cases was 6.3 years.

Eleven of the 148 controls had spent time in one or more of these departments, with 7 controls having at least 5 years time in the departments of interest. Average duration of exposure in these departments for the eleven controls was 10.3 years.

The point estimate of relative risk of death from leukemia (ICD codes 204-207) for having worked in these departments, including Departments 348A, B, and C, for any length of time is 1.5. However, considering exposures of at least 5 years, the relative risk for having worked at least 5 years in these departments is 1.2.

Since it has been found that department 348 had no involvement in the synthetic process during the time period covered here, we decided to analyze the 37 leukemia cases considering exposures in departments 313, 345, 346, 347, and 441, which may have had involvement in the synthetic process. Three of 37 cases had spent time in these departments, with one case having at least five years time in the departments of interest. Table 1A contains, for these three cases, information like that in Table 1. The average duration of work in the departments of interest for the three cases was 6.7 years.

Eight of the 148 controls had spent time in one or more of these departments, with seven controls having had at least five years time in the departments of interest. Average duration of exposure in these departments for the eight controls was 13.9 years.

The point estimate of relative risk of death from leukemia (ICD codes 204-207) for having worked in departments 313, 345, 346, 347, and/or 441 for any length of time is 1.6. Considering exposures of at least five years, the relative risk for having worked at least five years in these departments is 0.5.

There has also been some question raised as to the possibility of a relationship between worker exposures in production of SBR and neoplasms of the lymphatic and hematopoietic system other than leukemia. No deaths due to such causes were found among workers in the 1964 cohort with MROTG Synthetic. Further, in studying the work histories of the 44 known deaths due to this group of causes among members of the 1964 cohort, none of these workers were found to have spent any time in the synthetic OT.

However, six of the 44 deaths due to this cause group did have experience in one of the departments 313, 345, 346, 347, 348, or 441. Information similar to that in Table 1 is found in Table 2 for these workers. A specific set of controls for workers with this cause of death group has not been selected. Some comparison can be made, however. Table 3 shows a comparison of the percentage of cases and controls in the leukemia study who had experience in the departments of interest, along with the percentage of cases of non-leukemia neoplasms of the lymphatic and hematopoietic tissue who spent time in these departments. Also given for each of the three groups of workers in these departments is the average duration in these departments. Information in Table 3 does not produce any clear cut conclusions. While a higher percentage of workers in the case groups spent time in these departments, the average duration in the departments was less for cases than for controls.

We also analyzed these data for experience in departments 313, 345, 346, 347, and 441 (omitting 348 from the above list) because of the fact that departments numbered 348 were not involved in the synthetic process prior to 1972. Two of the 44 deaths due to this cause group did have experience in one of the departments of interest, 313, 345, 346, 347,

and 441. Table 2A contains information like that in Table 2 for these two cases.

Table 3A gives information like that of Table 3, but for departments 313, 345, 346, 347, and 441. Among persons who died of neoplasms of the lymphatic and hematopoietic tissue other than leukemia, a smaller percentage had work experience in the departments listed than did either the cases or controls for the leukemia study. In contrast with the information in Table 3, that in Table 3A tends to incidate that having worked in departments 313, 345, 346, 347, or 441 may not cause any additional risk of death due to non-leukemia neoplasms of the lymphatic and hematopoietic tissue.

However, considering work experience in departments numbered 348, about 9.1% of cases of NLHT other than leukemia spent some time in these departments, while fewer than 3% of leukemia cases or controls spent time in those departments. This indicates a need for further study of mortality among persons who worked in Department 348 prior to 1972 and persons who worked in similar operations.

No worker known to have died in the period 1964-1973 due to neoplasms of the lymphatic and hematopoietic tissue spent any time in a job identified by OHSG as having the OTG Synthetic. However, some workers who died of neoplasms of the lymphatic and hematopoietic tissue did spend time in departments identified by the company as possibly having involvement in the synthetic operation. From the data available, there may be a very slightly increased risk of dying due to neoplasms of the lymphatic and hematopoietic tissues from having worked in these departments. The magnitude of this risk is not large, however.

Perhaps of concern for the future is the fact that from 1958 through 1973, benzene was used in the synthetic operations in department 346. None of the workers having died due to neoplasms of the lymphatic and hematopoietic tissues during the period 1964-1973 ever worked in this department. However, given that the latency period for such disease may be long, perhaps in the order of seven or more years (see page 31 of this report), workers who spent time in department 346 during the period 1958-1973 should be followed carefully.

Table 1

Year into and out of Industry, Year of First Exposure, Department, Duration of Exposure, Age at Death, Year of Death, Sex, Race and Cause of Death for Four Leukemia Cases Having Exposure in One or More of These Departments: 313, 345, 346, 347, 348, and 441.

Case	Year in	Year out	Year of First Exposure	Dept.	Duration of Exposure	Age at Death	Year of Death	Sex**	Race**	Cause of Death*
A	1945	1960	1953	348A	5 yr., 4 mo.	69	1964	M	W	Acute Monomyelocytic Leukemia
B	1928	1972	1958 1961	441A 313	3 yr., 2 mo. 12 yr., 8 mo.	66	1973	M	W	Chronic Lymphatic Leukemia
C	1944	1961	1958	441A	3 yr., 7 mo.	65	1964	M	W	Acute Myeloblastic Leukemia
D	1925	1965	1942	345	0 yr., 7 mo.	68	1972	M	W	Chronic Leukemia

* In all instances, this is underlying cause.

** M=Male, W=White.

Table 1A

Year into and out of Industry, Year of First Exposure, Department, Duration of Exposure, Age at Death, Year of Death, Sex, Race and Cause of Death for Three Leukemia Cases Having Exposure in One or More of These Departments: 313, 345, 346, 347, and 441.

Case	Year in	Year out	Year of First Exposure	Dept.	Duration of Exposure	Age at Death	Year of Death	Sex**	Race**	Cause of Death*
B	1928	1972	1958 1961	441A 313	3 yr., 2 mo. 12 yr., 8 mo.	66	1973	M	W	Chronic Lymphatic Leukemia
C	1944	1961	1958	441A	3 yr., 7 mo.	65	1964	M	W	Acute Myeloblastic Leukemia
D	1925	1965	1942	345	0 yr., 7 mo.	68	1972	M	W	Chronic Leukemia

* In all instances, this is underlying cause.

** M=Male, W=White.

Table 2

Year into and out of Industry, Year of First Exposure, Department, Duration of Exposure, Age at Death, Year of Death, Sex, Race, and Cause of Death for Six Deaths Due to Neoplasms of the Lymphatic and Hematopoietic Tissue Other than Leukemia Having Exposure in One or More of these Departments: 313, 345, 346, 347, 348, and 441.

Case	Year in	Year out	Year of First Exposure	Dept.	Duration of Exposure	Age at Death	Year of Death	Sex**	Race**	Cause of Death*
E	1944	1965	1953	348A	5 yr., 8 mo.	71	1972	M	W	Hodgkins Disease
F	1946	1970	1946	313	14 yr., 3 mo.	58	1971	M	W	Recticulum Cell Sarcoma with Metastases
G	1950	1971	1966	345A	0 yr., 2 mo.	45	1972	M	W	Lymphosarcoma
H	1942	1964	1953	348A	5 yr., 11 mo.	57	1965	F	W	Lymphoblastoma (disseminated)
I	1940	1966	1954	348A	4 yr., 9 mo.	64	1973	F	W	Lymphosarcoma
J	1942	1970	1954	348A	0 yr., 3 mo.	46	1971	F	W	Hodgkins Disease

* Underlying cause.

** M = Male, F = Female, W = White

Table 2A

Year into and out of Industry, Year of First Exposure, Department, Duration of Exposure, Age at Death, Year of Death, Sex, Race, and Cause of Death for Two Deaths Due to Neoplasms of the Lymphatic and Hematopoietic Tissue Other than Leukemia Having Exposure in One or More of these Departments: 313, 345, 346, 347, and 441.

Case	Year in	Year out	Year of First Exposure	Dept.	Duration of Exposure	Age at Death	Year of Death	Sex**	Race**	Cause of Death*
F	1946	1970	1946	313	14 yr., 3 mo.	58	1971	M	W	Recticulum Cell Sarcoma with Metastases
G	1950	1971	1966	345A	0 yr., 2 mo.	45	1972	M	W	Lymphosarcoma

* Underlying cause.

** M = Male, W = White

Table 3
Percentage and Average Duration for Persons Who Had Work Experience in Department 313, 345, 346, 347, 348, or 441 for Three Groups of Workers.

	Percentage Who Spent Any Time In Department(s) Of Interest	Average Duration In Departments	Percentage Who Spent At Least 5 Years In Department(s) Of Interest
Controls For Leukemia Study	7.4% (11/148)	10.3 yr.	4.7% (7/148)
Leukemia Cases	10.8% (4/37)	6.3 yr.	5.4% (2/37)
Cases of Neoplasms of Lymphatic and Hematopoietic Tissue Other Than Leukemia	13.6% (6/44)	5.2 yr.	6.8% (3/44)

Table 3A
Percentage and Average Duration for Persons Who Had Work Experience in Department 313, 345, 346, 347, or 441 for Three Groups of Workers.

	Percentage Who Spent Any Time In Department(s) Of Interest	Average Duration In Departments	Percentage Who Spent At Least 5 Years In Department(s) Of Interest
Controls For Leukemia Study	5.4% (8/148)	13.9 yr.	4.7% (7/148)
Leukemia Cases	8.1% (3/37)	6.7 yr.	2.7% (1/37)
Cases of Neoplasms of Lymphatic and Hematopoietic Tissue Other Than Leukemia	4.5% (2/44)	7.2 yr.	2.3% (1/44)

II. ENVIRONMENTAL ASSESSMENT

Introduction

A preliminary survey of the Goodyear Synthetic Plants (Synthetic Latex Plant, Synthetic Pilot Plant, Chemigum Plant and Solution Polymer Semi-Works Plant) at Akron, Ohio was conducted on April 8, 1976. The purpose of this preliminary survey was to obtain historical and current information on various processes, procedures, materials and equipment used by the plant. Much of this information was requested from the Company and is be ng forwarded through appropriate channels. This report is based on data from previous information requests, informal discussions with plant personnel and observations made during the survey of the synthetic facilities. The survey was conducted to subjectively evaluate environmental conditions within the work areas of the plants.

Historical Background

The U. S. Government, through the Reconstruction Finance Corporation, established the Rubber Reserve Company on June 28, 1940 to accumulate a stockpile of natural rubber and to start a synthetic rubber program. In May, 1941, the President approved the construction of several GR-S (Government Rubber-Styrene) plants in which one was operated by Goodyear Tire and Rubber Company at Akron, Ohio. The first production of GR-S (SBR) in the Government plant operated by Goodyear occurred in May, 1942. Production of GR-S which was in dry form as a final product continued until August 1947 at which time the plant was closed. During these five years of production the basic formulation and procedures of the process were unchanged. The technical Committee of Rubber Reserve Company which coordinated this program obtained agreement that the plant should produce GR-S, a copolymer made from a charge ratio of 75 percent

butadiene and 25 percent styrene. This Goodyear operated plant had an annual capacity of approximately 10,000 long tons at the beginning of its operation, 1942, to a maximum capacity of 30,000 long tons in 1945. Expansion of the process and increased man hours occurred during this time. Maximum total employees numbered approximately 250 during these peak production years in the 1940's. Prior to 1947 engineers learned to operate the polymerization system continuously, whereby monomers and other ingredients were changed to the first of a series of reactors and the latex removed from the last. Use of this principle greatly increased the capacity of the original copolymer plant, primarily because the entire capacity of the reactor was made available. A batch process utilized only 85-90 percent of the volume of a reactor initially, and an additional shrinkage in volume occurred as polymerization progressed.

Observation of the housing facilities which still exist for the GR-S production between 1942 and 1947 indicated potentially well ventilated areas. The reaction vessels and dryer units were housed in areas with high ceilings and large windows on the side that could be opened. Degasing tanks and stripping columns were located inside and outside the building as were the holding tanks for the monomers.

In January 1951, the plant reopened producing GR-S dry, now referred to as SBR dry, in much the same way and with virtually the same equipment as previously used. The SBR dry production required more employees (both production and maintenance) than is required for a similar latex production plant. This process slowly converted to SBR latex by 1952; this production has continued until the present time. The main difference in the SBR dry and the SBR latex involves the final steps of operation - concentration. There have been a few modifications of the continuous latex operation between 1952 and the present time, but basically the process has remained the same. The few modifications that have occurred

appear not to have been of a kind which would change worker exposure.

Synthetic Latex Plant

Butadiene and styrene are the chief raw materials required in the manufacture of SBR latex. Butadiene is obtained from its manufacture in high purity (98 percent or higher) by a final fractionation process. The monomer is stabilized against polymerization during storage by the addition of an inhibitor, p-tertiary-butyl catechol, in small amounts (25-50 ppm). Butadiene has a TLV of 1000 ppm and an odor threshold of less than 2 ppm. Styrene has a purity of 99 + percent, and is usually inhibited from polymerization during storage with a small amount (10 ppm) of p-tertiary-butyl catechol. Styrene has a TLV of 100 ppm and an odor threshold of less than 0.5 ppm. Other raw materials required in smaller amounts are fatty and rosin acid soaps, mercaptan modifiers, catalysts, shortstopping agents, coagulating agents and antioxidants.

Butadiene and styrene are delivered to the plant by either tank cars, or tank trucks. These monomers are then piped to their individual storage tanks within the tank farm for storage until used in the polymerization process. Butadiene is stored in tanks in underground concrete vats and covered with water. If butadiene gas leaks occur they are easy to detect because of bubbles in the water. There are three such storage areas within the tank farms and each area contains five 22,000 gallon tanks. Heavy duty constructed sides have been placed around each of the three butadiene storage areas. These sides support the lights and sprinkle system, but the primary reason for creating the underwater storage tanks and heavy duty constructed sides relates to an airplane accident in the forties which was a near miss of the butadiene storage tanks. In the walk-through survey around the tank farm, there was a slight odor occasionally - perhaps styrene, which is stored in above ground tanks and/or butadiene. One employee per shift is involved with

various operations within the tank farm, taking samples for quality control, emptying tank cars and overseeing the general operation.

The pump house and control equipment supplies the monomers to the reaction tanks and is located near the tank farm. One employee per shift controls these facilities. Many of the pumps and controls are located outside or in partially enclosed structures. Only a slight odor was detected in these areas during the survey.

Reactors can either be continuous or a batch type depending on the demand for the SBR latex. The continuously operated reactors allow monomers and other ingredients to be charged to the first of a series of reactors and the latex removed from the last. The batch type allows the complete process to take place in one tank then the latex is flushed out. There are three enclosed areas which contain the reactors; one area has ten 3,750 gallon reactors, another has eighteen 3,000 gallon reactors, and a third has sixteen 3,000 gallon reactors. Soap solution is mixed in these reactors with the monomers to be emulsified. The solution make-up room primarily uses water as a base for soap and chemical solutions. Other chemicals stored in this room are sodium hydroxide, acids and electrolytes. No solvent odor was detected here in the course of the walk-through survey. Central areas within each of the reaction tank areas also contained chemical make-up tanks for charging with the emulsions. Lauryl mercaptan, a modifier which regulates the molecular weight of the polymers, potassium persulfate an initiator of polymerization and various other chemicals, are mixed with water and added at various times to the reactor through piping systems. As the reaction begins, cooling water is circulated in the jacket or pipes within the reactor. A conversion of 70-75 percent of monomers to polymers is normally achieved in 12-15 hours reaction time. At this point, addition by a closed pipe system of an aqueous solution, the shortstopping agent, stops further polymerization.

Instrumentation and controls for the various reactors are centralized. Throughout the control and reactor area there was a slight solvent smell occasionally. Ventilation in the three reactor areas was provided by open windows as well as floor level exhaust systems. A rupture disc located on each of the reactors is a precaution in case there is an excessive build up of pressure within the vessel. If rupture does occur, the charge is piped away from the main plant and burned at a centrally located tower. Periodic purging of this system with nitrogen removes residual monomers and other chemicals away from the main plant. This system has been utilized since the plant operation began.

Procedures for cleaning the various reactors are relatively consistent; periodic cleaning may vary 90-100 days. The cleaning procedure after removal of SBR latex involves the evacuation of the tank followed by flushing with water and ventilating after the man-way is opened. High pressure water guns are used from outside the tank to break the accumulated coagulum from the tank walls and from the cooling pipes. Before workers may enter a reactor to break loose coagulum with water guns from the lower portion of the tank, test are made to determine the oxygen content within the work area. While in the tank, workers wear rubber suits and face shields to protect them from flying debris as well as the water spray. There was little or no solvent smell detected during this operation. Plant personnel indicated major precautions have been taken in the past as well as at present to protect workers from exposure in this procedure. However, prior to 1954 high pressure water guns were not available and the lower pressure was not sufficient to completely remove the latex residue so some manual chipping and scraping was involved. Ventilation was provided under these circumstances.

After the SBR latex is piped from the reactors unreacted monomers are removed. The butadiene is removed by flash-stripping at reduced

pressure, and the styrene by steam-stripping under reduced pressure in a stripping column. These monomers are pumped back to the tank farm for recycling or possibly returned to the manufacturer for purification. A slight odor was noted throughout various degass and stripping tank areas. These are located inside and outside the building and operators are not required to spend much time there. Cleaning of these tanks is performed periodically by flushing with water and scraping. Precautions are taken by continuous exhaust ventilations of the tank before and during this cleaning operation.

The pH adjustment area was located in a separate wing of the plant. Plant personnel indicated this area used to be the old SBR dry system which housed the coagulation tanks and below this section were the drying units. This wing was enclosed with high ceiling and windows down each side, giving the appearance of being a fairly well ventilated area.

Formaldehyde is added as a preservative to the concentrated latex (600 ppm) before it is stored for shipment. The major portion of shipping of the finished SBR latex takes place in a separate section of the plant. Latex is pumped from storage tanks to rail tank cars. One operator usually oversees this operation. During the survey, tanks were not being filled, however, there was a slight odor in the area. This odor could have been coming from the outside through the open door used for rail tank cars entering the building.

Synthetic Rubber Pilot Plant

The synthetic rubber pilot plant began production in 1945 as a research and development facility primarily for SBR dry rubber and latex. The facility now has approximately 8000 square feet of floor space on three floors where the complete process is performed--from raw materials to latex or dry rubber. Until 1957 the major materials use in

this building were butadiene and styrene. In 1957 some solution polymerization was added using hexane and benzene as solvents. These solvents were piped directly to enclosed vessels and then to small reactors from outside storage tanks. Benzene exposure was probably greatest in the past in reactor areas due to batch sampling and in the cement processing area as the solvent was removed.

General room ventilation appeared to have received considerable attention in the past. Fifteen-inch exhaust fans are mounted at floor level throughout the plant and windows which can be opened are located around all walls. The experimental reactors are centrally located on the second floor of the original building.

In 1958 a separate building was constructed especially for solution polymerization. In 1968 it was enlarged to its present size and all solution polymerization is now performed in this new building. The solvents used depended upon the product being made. Benzene usage varied from none to as much as 1 to 2 tank cars per month. Other solvents, mostly aliphatic, were also used. Benzene use continued until 1973 when it was replaced by other solvents. Exhaust ventilation in this building appears to have received considerable attention in the past.

This synthetic rubber pilot plant employs seven hourly workers per shift and operates 4 shifts per day. These employees are trained to operate all phases of the operation so substitution among jobs is easily accomplished. Salaried employees such as engineers and researchers are constantly in the work area also.

Chemigum Plant

The Goodyear Tire and Rubber Company built a production plant in 1940-41 to manufacture a nirtile rubber (NBR) under the trade name, "Chemigum". NBR may be broadly defined as a copolymer of a diene and an

unsaturated nitrile. NBR production began in 1941 with peak production being reached in the 50's. At present, NBR is only 10 percent of the plant's production. Latices, mainly the high conversion styrene type, are the major products, approximately 55 percent, at the present time. Latices began production in 1945 with a gradual increase to present times. Resin production also began in 1945 and presently is approximately 35 percent of the plants production. The main portion of the 35 percent involves production of a high styrene resin. Several other types of latices and resins such as vinyl pyridine, styrene, and butadiene are a minor portion of plant production.

The Cheminum plant employs approximately 85 hourly production workers, operating on a 24 hour, 6-7 days per week schedule with 4 six hour shifts. Production employee turnover rate is less than 1 percent. Maintenance personnel, which number approximately 30, have a much higher turnover rate because of the centralized service of the Plant 3 complex.

Polymerization of the monomers, styrene, butadiene and acrylonitrile takes place mainly in batch reactors. These monomers are stored after being piped from rail tank cars or truck tanks to storage tanks outside the process building. Few employees are involved with piping the monomer, taking samples for quality control and overseeing the pumping operation. However, maintenance personnel such pipe fitters, are mostly involved with maintaining pumps, valves and replacing pipes. Odors in these areas during the survey were minimal.

Polymerization takes place primarily in batch reactors located in two enclosed reaction wings. There are nine 1,600 gallon resin reactors in the West Wing and fifteen 2,750 gallon latices and NBR reactors in the East Wing. Within each of these reaction areas different latices or resins may be produced at any given time. These variations may be monthly or yearly.

According to plant personnel, operations during the initial phases (1942) of production caused higher exposure of workers to odorous materials than is now detected in the plant. Within the first few years, odors were reduced by increased ventilation throughout the plant. General ventilation still exists and appears to be adequate at the time of the survey. No strong odor of styrene, butadine or acrylonitrile was detected during the survey.

Cleaning procedures for the reactors varies according to the type resin or latice being run. Several of the resins adhere more firmly to the reaction vessels than do others and require some scraping by personnel. Evacuation of the vessels by vacuum followed by flushing with water is standard procedure before high pressure water guns or manual scraping of the resins or latices residue is employed. Prior to 1956-57 high pressure water guns were not available and lower water pressure was not sufficient to remove the residue so manual chipping and scraping was involved. Ventilation was provided under these circumstances.

Ventilation throughout the plant and precautions in cleaning reactor tanks originated in the late 40's due to the potential exposure to workers while cleaning reactors using acylonitrile monomer. The concern for potential exposure is mainly from residual acrylonitrile (vinyl cyanide) in the polymer deposits of the reactor.

After the various products are piped from the reactors unreacted monomer are removed. In the production of high conversion styrene (99 percent conversion) there is little residual styrene as compared to SBR latex which involves only 60 to 75 percent conversion. Vacuum flash stripping tanks and stripping columns are utilized in the removal of various monomers. Only a slight odor was noted in these areas which are outside the building and which require little worker time other than for tank cleaning. Tank cleaning is accomplished in much the same way as is reactor cleaning.

Other steps involved in the manufacture of the dry NBR and resins are coagulation, washing and drying. The latex is transferred to coagulating tanks at which point the rubber latex is coagulated into fine crumbs by the addition of various salts and acids. There did not appear to be any identifiable exposure at this point in operation. Salts and acids were added by means of pipes feeding into the latex mixing vessel. The slurry of rubber particles is then extracted by filtration, washed and finally dried and baled. After baling talc is added to prevent the bales from sticking. This station was well exhaust ventilated and talc did not appear to enter the work area. Resins are coagulated into fine particles utilizing vacuum filtration for the dewatering step. After drying the resins are packaged into 50 lb. bags.

In the production of latices and resins, it is necessary to add additional stabilizing agents in the blow down tank prior to the stripping operations, then remove the excess butadiene, styrene, and acrylonitrile. The final step is concentration or removal of water to the desired final total solids.

These latexes are then pumped to storage and tanks awaiting shipment in rail tank cars or tank trucks. The filling of these rail tank cars and tank trucks involves one employee and appears to involve minimal exposure to odorous materials.

Solution Polymer Semi-Works Plant

The solution polymer plant began as a semi-works plant in 1972. Production by continuous or batch polymerization for both polyisoprene and polybutadiene involves hexane and/or pentane as primary solvents. Polybutadiene and polyisoprene are produced in bale form as a final product.

Styrene-butadiene and divinyl benzene are polymerized in cyclohexane solvent at the rate of 100 lbs. per day since February 1976.

The complete process of polymerization to drying takes place in a two story building containing 13200 square feet per floor. Exposure to solvents appears to be minimal. In cases of large spillage personnel evacuation and complete exhausting of the building air would take place. All facilities within this process appear to be very well maintained and modern. Sixteen hourly employees work at this operation.

Summary

Listed below are specific work areas or jobs ranked according to the UNC industrial hygienists' perceived potential for exposure to styrene and/or butadiene as the SBR process is presently being operated. These areas are ranked high (H), medium (M), low (L) and none (N) as judged from observations during the walk-through survey. As noted later, Goodyear personnel, who have long familiarity with the process, suggest some modifications to these rankings.

	Area or Job	H	M	L	N
1.	Tank Farm Area	X	- X		
2.	Pump House Operators	X	- X		
3.	Reactor Operators		X		
4.	Reactor Cleaners		X		
5.	Degas Operators		X		
6.	Strip Column Operators		X		
7.	Janitor, Trucking, and Service		X	- X	
8.	Maintenance				
	(a) Pipefitters	X	- X		
	(b) Mechanics				X

Because odors were more prevalent in the past than now, exposures to styrene, butadiene, and other solvents and/or chemicals may have been more extensive in the past in some work areas of the synthetic plant. At present the potential for high to moderate exposures to styrene and butadiene in the tank farm area are expected to be intermittent and related to sampling ports and other such sources.

Goodyear personnel suggest that actual exposure ratings may be somewhat different than those listed above for the various jobs. They suggest that the exposures of tank farm and pumphouse operators should not be categorized as high because most of the work is out of doors where a large amount of dilution takes place with wind movement. Also, pipefitters may at times experience fairly heavy concentrations should they accidentally break into a piping system which has not been adequately purged; but in their case this is an occasional type of exposure, and much of the time they may be working in the shop and have very little exposure. Goodyear points our that mechanics, listed in the Table above as having no exposure, do go into the plant area from time to time to repair equipment, and should be shown as having a potential for low exposure to vapors.

Personnel working around the SBR reactors, the operators, cleaners, supervisors and maintenance workers are expected to have a moderate exposure to styrene and butadiene. Safeguards appear to have been used in the past and presently in cleaning reactors. However, maintenance personnel may have been involved with leaks and other routine jobs involving greater exposure.

In the main make-up area where water base solutions are prepared there is little exposure to the monomers. The smaller make-up areas involved in adding and mixing accelerator electrolytes and short stops are located nearer the reactors and temperature control rooms. Here there is slight monomer exposure to the worker in addition to various other chemicals.

After the latex has been formed and monomers removed, generally there appears to be little or no exposure to the worker involved with storage and shipping.

Although a causal relationship between any particular condition of work and the occurrence of disease has not been demonstrated, an interim recommendation on industrial hygiene practice is offered.

Interim Recommendation: Work practice and equipment should be reviewed throughout the synthetic plants with the view to minimizing exposures to volatile agents including both butadiene and styrene. Particular attention should be given to (1) tank farm operations to eliminate exposures during transfers, sampling operations and maintenance; (2) to reactor operations, particularly to reactor opening and cleaning; and (3) detection and correction of leaks in process piping, pumps, vessels and other process equipment with special precautions to prevent exposure of personnel during all maintenance and repair operations.

These recommendations are based on suspicion of causal associations in SBR operations, and until the matter is resolved, special attention to good industrial hygiene practices is the prudent course.

III. TOXICOLOGY REVIEW

Introduction

Listed below are some of the ingredients used in SBR production with potential carcinogens or procarcinogens indicated by asterisk - *. A summary of toxicologic information on each compound follows:

Monomers

*Styrene

Butadiene

Initiators

Persulfates

*Hydroperoxide, e.g., p-menthane-8-hydroperoxide, cumene hydroperoxide.

Azobisisobutyronitrile (AIBN)

Sodium-formaldehyde sulphoxylate (Sulphoxylate formula)

Modifiers

Aliphatic mercaptans, e.g., n-dodecylmercaptan

(*?) p-nitroaniline

Thioethers

Chlorinated hydrocarbons

Short-stop

Sodium hydrosulfide

Hydroquinone

Phenyl-B-naphthylamine

Trialkyl phenol phosphites

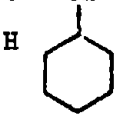
2,6-ditert-butyl-p-cresol (BHT)

(*?) Sodium dimethyl dithiocarbamate

Butadiene-Styrene Copolymers (SBR)

Production of the synthetic rubber is based on the emulsion of the purified monomers in water. An initiator is added to start the reaction, and a modifier is used to limit molecular weight and prevent cross-linking. When 60-72% of the monomers are converted to polymers, the reaction is interrupted by adding a short-stop agent. Unreacted monomer is removed and recycled, the latex is coagulated continuously with salt solutions, H_2SO_4, acetic acid, or glue. The crumbled coagulum is washed, dried, and pressed into bales. The toxicity of the compounds used, with particular reference to cancer, is summarized.

Monomers:

Styrene: (C_8H_8)  phenylethylene, vinyl benzene.

Styrene is readily absorbable into the bloodstream by all routes, although skin and lung are most important for industrial exposure. Because of its high lipid solubility, there may be extensive sequestation of styrene in fat.

Figure 1 summarizes the metabolism of styrene.

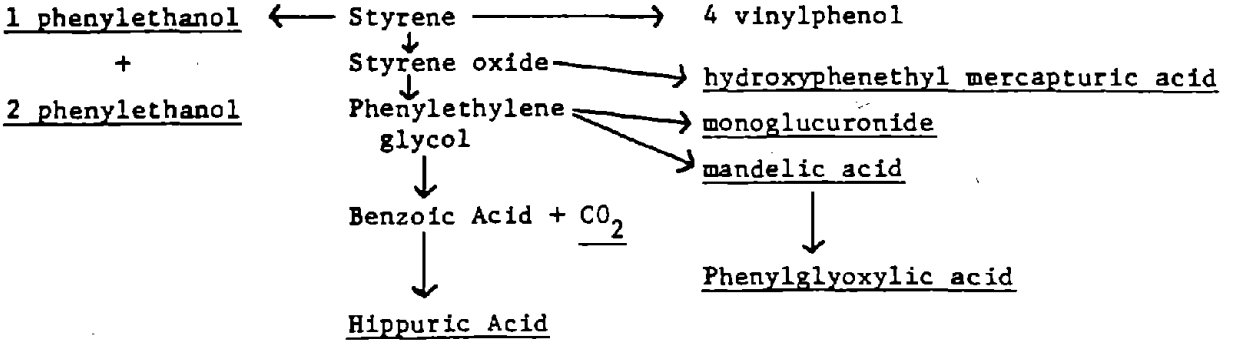


Figure 1. Metabolism of Styrene. Underlined metabolites are those excreted in urine or expired air (from 1).

The excreted metabolites of styrene metabolism are all considerably less toxic than styrene itself - at least for acute effects. [As it is with toluene, hippuric acid in the urine may provide an index of exposure to styrene (assumming no food intake of certain fruits and vegetables)]. Acute symptoms of styrene intoxication are irritation of the skin, eyes, and respiratory tract and depression of the central nervous system. Repeated 7 to 8 hour exposures to about 1300 ppm styrene resulted in no changes in blood cells in rats, rabbits and monkeys.[2] The acute toxicity of styrene oxide, however, is about 4 times that of styrene.[1,3] Epoxides have been shown to be hepatotoxins and carcinogens and exhibit radiomimetic properties such as growth-inhibitory, mutagenic, and cytotoxic activity, probably because they are alkylating agents.[1,5] Peroxides may catalyze the depolymerization of DNA and RNA in a fashion similar to ionizing radiation. Organic peroxide may also lead to the formation of epoxides, which are established carcinogens[11]. Of particular interest, styrene oxide (an epixode) was reported to produce malignant lymphomas in mice (by inhalation?) and to have carcinogenic activity when painted on the skin of mice.[4,5,6]

Butadiene: (CH_2 = CH-CH=CH_2)divinyl, biethylene.

This unsaturated aliphatic hydrocarbon forms organic peroxides on standing. At high concentrations it is an anesthetic. It is now considered to be not very toxic, and has only slight irritative effects. The TLV is 1,000 ppm.

Initiators (Activators)

Some commonly employed initiators include:

a) Ammonium and potassium persulfate ($(NH_4)_2\ S_2O_8$, $K_2S_2O_8$) initiate polymerization (effective at $\geq$30°C). About 0.3 parts by weight was used in a typical recipe for GR-S rubber around 1942. These compounds are moderately toxic and strong irritants and oxidizing agents.

b) Organic hydroperoxide (e.g., p-menthanehydroperoxide)/iron sulfate/alkali pyrophosphate.

Peroxy compounds have been suggested as potential carcinogenic air pollutants and components of cigarette smoke[4,5,11]. At least one organic hydroperoxide has been shown to have carcinogenic activity when painted on mouse skin (5), and 620 mg/kg p-menthane-8-hydroperoxide was carcinogenic (malignant lymphomas and pulmonary adenomas) when inhaled by mice (11). 0.10 to 0.15 parts by weight of this compound is typically used in the production of cold rubber.

c) Hydroperoxide and polyamine with only slight traces of iron (peroxamine formula). 0.1 part by weight of Polyamine H (alkylene polyamine) is a typical component for cold rubber produced beginning about 1948. The peroxamine process is a redox polymerization process for SBR cold rubber, using the hydroperoxide as an oxidizing agent and a polyethylene polyamine as the reducing agent in the presence of traces of iron. No carcinogenic effects of aliphatic amines have been described (7).

d) Benzoyl peroxide [$(C_6H_5CO)_2\ O_2$]. The TLV for benzoyl peroxide is 5 mg/m^3, based on the prevention of irritation. Sensitization occurs upon skin contact (8). The lowest published toxic dose for mice is 25 gm/kg on skin contact for 42 weeks. Some neoplastic effects were observed (6).

e) Cumene hydroperoxide ($C_6H_5C\ (CH_3)_2\ OOH$). This liquid is highly toxic by inhalation and skin absorption and has been shown to have mutagenic properties (11). In the mouse, inhalation of 304 mg/kg resulted in malignant lymphomas and subcutaneous sarcomas (6,11). Cumene hydroperoxide was inactive on mouse skin, and had weakly active carcinogenic activity by subcutaneous injection (12).

f) Diisopropyl benzoyl hydroperoxide is available as a 52% solution in a nonvolatile solvent and is probably toxic. Of fifty mice exposed to 50μM, 10 died, 2 of malignant lymphomas and 3 of pulmonary adenomas (11).

g) Azobisisobutyronitrile (AIBN) [$(CH_3)_2$ C(CN) NNC (CN) $(CH_3)_2$] is a white powder that may be toxic by ingestion. No reports of neoplastic effects have been found.

h) Sodium-formaldehyde/sulphoxylate-ferrous sulphate complexes based on ethylene diamine tetra-acetic acid as the activating system (sulphoxylate formula) is used in emulsion polymerization of SBR cold rubber. Sodium formaldehyde sulfoxylate (SFS) has the formula HC HO · HSO_2 Na · $2H_2O$ and is a white solid that is probably toxic. No reports of neoplastic effects have been found. EDTA, $(HOOCCH_2)_2$ NCH_2 CH_2N $(CH_2COOH)_2$, is an organic chelating agent of low toxicity. No reports of neoplastic effects have been found.

Modifiers (Regulators)

These substances are added to regulate the average molecular weight and make possible the formation of shorter, more linear chain structures. This makes the rubber much easier to process and reduces the formation of undesirable insoluable polymers. Aliphatic mercatans such as n-dodecyl mercaptan (DDM) is the most common regulator, comprising 0.5 parts by weight in a standard recipe for GR-S (also used in NBR). DDM ($C_{12}H_{25}SH$), also known as lauryl mercaptan, is a toxic and irritant liquid that may form many isomers. Other regulators used are sodium linoleate, p-nitroaniline, thioethers, chlorinated hydrocarbon, and di-isopropyl xanthogen disulfide. Nitroaniline has a TLV of 1 ppm and is a powerful methemoglobin former with finally a hemolytic effect. It is considered more toxic than aniline. No neoplastic effects are reported for these compounds. Our literature sources do not identify the specific thioethers and chlorinated hydrocarbons are used as modifiers.

Short-stop

When the conversion of monomers to polymers is at 60-72%, the reaction in interrupted, as too high a conversion gives rise to insoluble materials that are difficult to process. In hot polymers, sodium hydrosulfide ($NaSH \cdot 2H_2O$) or sodium bisulfide is used. It may liberate H_2S; no neoplastic effects have been reported.

Hydroquinone [$C_6H_4(OH)_2$, para-dihydroxybenzene] is used in batch polymerization. The TLV of hydroquinone is 2 mg/m^3 based on levels which appear to cause no systemic effects. More toxic than phenol, subacute poisoning causes hemolytic icterus, anemia, leukocytosis, reticulocytosis, increased cell fragility, and hypoglycemia. A number of toxicity studies[6] on a variety of species suggest it is moderately toxic; one study where hydroquinone (800 mg/kg) was painted on mouse skin resulted in one tumor in 22 animals. The authors considered this to be not significant. Hydroquinone has been suggested as affecting mitosis, exerting a radio-mimetic effect. This is disputed, however (13). There are no reports of cancer in exposed human populations[8]. In very low concentrations hydroquinone is relatively safe, and has been proposed as a food antioxidant (9).

Phenols as a group, however, have been reported to be toxic to mitosis, but had no effect on body weight or leukocyte count in rabbits given 0.05 g/kg daily (subcutaneous) of hydroquinone. 0.04 gm/kg daily of hydroquinone fed to cats resulted in anemia, hemolytic jaundice, leucopenia and slight reticulocytosis; 0.03 gm/kg administered subcutaneously to rabbits resulted in anemia and luecopenia. Hydroquinone is one of the metabolites of benzene metabolism. Nomiyama (10) has suggested that the hemopoietic disturbance in chronic benzene poisoning is the formation of catechol (ortho-dihydroxybenzene), via benzeneglycol and not formation of hydroquinone.

Phenyl B-napthylamine (PNB) which acts as a stabilizer and antioxidant, is used in continuous polymerization (1.25 parts by weight). It is of low toxicity. It has been suggested as a possible bladder carcinogen.

For light colored SBR, trialkyl phenol phosphites and 2:6-ditert-butyl-p-cresol (BHT) are used. BHT is a food antioxidant with low toxicity.

Water soluble sodium dimethyldithiocarbamate [$(CH_3)_2$ NCS_2Na)] is used for redox systems. It is moderately toxic with no reported neoplastic effects. The zinc salt of dimethyl dithiocarbamates (=ziram) is a rubber accelerator and has been shown to have neoplastic effects when 1500 mg/kg is fed to mice, and carcinogenic effects in rats when 13 gm/kg is fed for 95 weeks and 60 mg/kg implanted in rats (6).

Possible or Suspect Leukemogenic Agents

Isoprene, cyclopentadiene, hexane and benzene may be used in making emulsion polymers, latex, dry rubber and solution rubber; of these only benzene is reported to have carcinogenic properties.

Any agent capable of producing aplasia of the bone marrow should be considered as potentially leukemogenic. At present, benzene seems to be the only chemical agent to have produced occupational leukemia.[14-24]

Benzene was discovered in coal tar in 1845. Since the 1890's, coal tar derivatives have become very numerous. In industry, benzene has been used in two major ways: (1) in large quantities in closed mechanical systems (distillation of coal and coal tar, blending of motor fuels, chemical industry), and (2) as a solvent or diluent (rubber industry, boot and shoe industry, artificial leather manufacture, photograve color-printing, paint and varnish manufacture, airplane, linoleum and celluloid industries, artificial manure and glue manufacture, and extraction of certain alkaloids in the pharmaceutical industry).

Beginning in 1897, a number of deaths have occurred from the use of benzene as a rubber solvent. Chronic benzene poisoning in a British rubber factory resulted in 3 reported deaths from aplastic anemia and led to the substitution of xylene for benzene as a rubber solvent in 1918. Despite the reported toxicity of benzene, its use as a solvent increased after WWI in most industrial countries. The chief industries involved were rubber tire building, manufacture of spread rubber goods, use of rubber cements in fastening rubber heels and soles, artificial leather manufacture, dry cleaning industry, sealing of food cans with a benzene-rubber cement, and in the painting trade. In Milan, Italy, Vigliani and Saita[17] report that in 1962-3, there was a sharp rise in cases of occupationally related cases of benzene poisoning; slightly less than half the deaths were from acute leukemia, slightly more than half from aplastic anemia. In 1922, the growing menace of benzene poisoning was pointed out. In 1926, the U. S. National Safety Council ordered the improvement of rubber factory ventilation, instituted medical supervision of workers and the use of xylene as a safe substitute for benzene. This occurred 8 years after the same changes had been made in Great Britain. Around 1928, toluene was substituted for benzene in dry cleaning, thinners for quick-drying paints, and solvent for cellulose lacquers. Rubber latex was substituted for benzene in rubber cements used in the canning and boot and shoe industries. Many rubber factories returned to the use of petroleum naptha as a solvent for spread rubber goods and rubber cements.[36]

The first published cases of benzene leukemia were in 1928 and 1932. Typically, these were of prolonged exposure to benzene vapors for many years, with ultimate development of fatigue, anemia, leukocytosis, immature cells in peripheral blood, and death.

Documented cases of benzene leukemia are largely (acute?) myeloblastic leukemia, most cases being leucopenia with moderate or no splenomegely and extensive infiltration by undifferentiated cells in the bone marrow. The leukemia occurs more frequently in subjects with anemia, with the bone marrow changing from a hypoplastic to a leukemia pattern. In well documented cases of benzene leukemia in factories where aplastic anemia was also observed, the cases were all acute, the exposure was heavy and long, and the latent period long (up to 12 years).

Benzene poisoning is paradoxical in its symptomatology - being influenced by individual susceptibility, length and amount of exposure. In industry there is no explanation as to why some get leukemia, and others working alongside do not. The biological response varies from hypo- to hyperplasia of bone marrow. Chromosome aberrations, leucopenia, anemia, thrombocytopenia are the most common blood abnormalities. Studies have been reported which indicate that leucopenia is the main persisting symptoms upon removal from exposure; others indicate that thrombocytes and RBC remain low while leucocytes return to normal. Examination of 125 benzene poisoned individuals 10 years after exposure has shown that neither the severity of exposure nor the hematological changes significantly affects prognosis of those surviving the acute poisoning when compared to 86 non-benzene exposed controls. One of the 9 deaths occurring during this period was due to leukemia which occurred 7 years after initial exposure to benzene.[16]

No other aromatic hydrocarbon used industrially has yet been implicated as a leukemogenic agent. It has been suggested that the effects of benzene on the hemopoietic tissue may be due to benzene metabolites, the hydrocarbon molecule itself, or both. The metabolites seem most likely. Other alkyl benzenes (toluene, xylenes, ethylbenzene, etc.) do not appear to have

the effect of benzene on blood-forming tissue, and as a group are transformed *in vivo* to carboxylic acids and alcohols. The principal benzene metabolites however, are phenols which are protoplasmic poisons. The oxidation of phenols produces quinones which are potent mitotic inhibitors and might be responsible for the effect on blood-forming tissues.

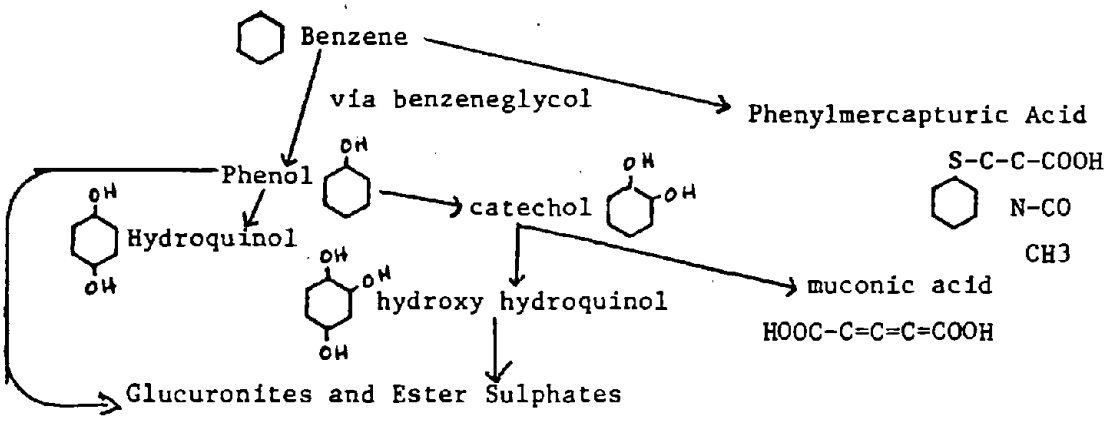


Figure 1. Metabolism of Benzene (from 34).

Nomiyama, from experiments in rats, concludes that the hemopoietic disturbances in chronic benzene poisoning is the formation of catechol via benzeneglycol.[10]

Ionizing radiation has also been implicated as a leukemogenic agent.[24,29,30,33] For leukemia there is some evidence that there is no threshold, and a linear dose-response relation may exist at lower dose levels. Acute and chronic myelogenous leukemia are usually considered the most frequent malignancies resulting from radiation exposures, although this may be due to the short latent period (<1 to 15+ years, with modal incubation time of approximately 5 years). Perhaps 5-10% of leukemia cases are caused by ionizing radiation. It has been estimated that the chance of leukemia after 1 rad of whole-body ionizing radiation is of the order of $1\text{-}2 \times 10^{-6}$/person-year. The great majority of these cases are of the myeloid type. Thus, ionizing radiation is unlikely to

account for the increased incidence of largely chronic lymphatic leukemia in older age groups.

Any bone marrow depressants or substances damaging chromosomes are possible leukemogenic agents. Other agents suggested as potential leukemogens include the following:

(a) arsenicals and sulfonamides

(b) chloramphenicol[28,35] - This broad spectrum antibiotic has become a commonly sited cause of acquired aplastic anemia. Leukemia is commonly characterized by variable degrees of bone-marrow hypoplasia. Although not usually reported, there are examples of the leukemia developing after aplastic anemia (from benzene, radiation, phenylbutazone, hypoplastic phase of paroxysmal nocturnal hemoglobmuria, and hereditary hypoplastic syndromes). Chromosomal changes have been observed in several cases of acute leukemia, similar to those following benzene and radiation exposure and in certain hereditary conditions. These may be similar to the chromosomal vacuolizations seen after chloramphenicol administration. Development of leukemia could also result from growth disturbance of the bone marrow, occurring either sequentially or together. This hypothesis suggests leukemia and aplastic anemia are different expressions of the same fundamental disturbance. Chloramphenicol is capable of destroying bone marrow - which could, for example, result in a new self-perpetuating cell line (clone), which if affecting leukocytes, could be leukemia. Three cases of acute myeloblastic leukemia that developed from chloramphenicol induced aplastic anemia have been described.

(c) hexachlorcyclohexane - This is an insecticide (Lindane) with the chemical formual $C_6H_6Cl_6$. Its effect on haemopoiesis has been reported to be similar to benzene, with one reported case of pancytopenia, and one fatal case of aplastic anemia, and failure of blood formation after

acute poisoning. Two cases of acute paramyeloblastic leukemia have been reported in blood cousins exposed to hexachlorcyclohexane 8 months prior to the onset of the disease.[27]

(d) phenylbutazone (PBZ) - This is an anti-inflammatory drug often used in the treatment of arthritis and spondylitis. Toxic side effects include those to the haemopoietic system (leucopenia, agranulocytosis, thrombocytopenia), with reported cases of aplastic anemia, depressed erythropoiesis and megaloblastosis. Complications from the blood-forming system are less common but more serious than other toxic effects.[25,26] In a retrospective study of 50 patients with acute leukemia, three patients had a history of PBZ ingestion (6% incidence), with a latent period of 15, 27 and 12 months (72, 27 and unknown grams of PBZ).[26] Since 1958, established cases of leukemia associated with PBZ administration have been reported (8 myeloblastic, 3 lymphoblastic, 1 myelomonomcytic, 2 "blast cell" leukemia, 5 chronic myelocytic leukemia). Ten of the cases had no radiotherapy. The latent period between PBZ treatment and diagnosis of leukemia varied from 4 weeks to 6 1/2 years.[26]

(e) viruses - Fowl and rodents are subject to viral leukemias. So far, it has not been shown to exist in man, although there is suggestive evidence of "microepidemics" posing the possibility of the infectious transmission of leukemia.[33]

(f) heredity - There are at least 100 instances of familial leukemia, being more common in mongoloids or feeble minded. In a New Zealand study approximately 7% of leukemia incidence could be attributed to inheritance.

(g) other agents - Chemical carcinogens such as benzypyrene, dibenzanthrocene, 9,10-dimethyl-1,2-benzanthracene and methylcholanthrene

have been shown to cause the appearance of lymphcytic leukemia in certain genetically susceptible strains of mice. Estrogens has also been established as a leukogenic agent in some mice.

Brief Summary of Agents and Some Health Effects - Other Synthetic Rubbers

NBR or Nitrile Rubber

Nitrile rubber began to be produced in this country in 1940. A nitrile rubber is a copolymer of a diene and an unsaturated nitrile, and exhibits a high degree of resistance to attack by oils, the more resistant grades having more acrylonitrile. High acrylonitrile rubber is used in oil well parts, fuel tank liners, fuel hose, gaskets, packing oil seals, and hydraulic equipment. Medium acrylonitrile rubber is used in general-purpose-oil-resistant applications, shoe soles, kitchen mats, sink topping, and printing rolls. Low acrylonitrile rubber is used in gaskets, grommets, O-rings, adhesives. The only diene used commercially in NBR is butadiene. The most common nitrile is acrylonitrile. Small amounts of styrene, methyl methacrylate, ethyl acrylate or vinylidene chloride can be used. Nitrile rubber are produced by essentially the same emulsion polymeriztion techniques used for SBR, i.e., polymerization, coagulation, washing, drying.

The components of nitrile rubber are listed below:

Monomers

Butadiene

Acrylonitrile

Initiators

Persulfate (hot process)

Cumene hydroperoxide/dextrose/sequestering agent redox system (cold process)

Peroxides (benzoyl peroxide, hydrogen peroxide)

Emulsifiers

Soaps of fatty acids (sodium salts of oleic, myristic or palmitic acid)

Anionic detergents (alkyl benzene sulfonates, dialkyl naphthalene sulfonates, higher alkyl sulfonates)

Cationic detergents (hydrochloride of diethyl amino oleomide, dodecylamine hydrochloride, lauryl pyridinium chloride).

Modifiers

Xanthogen disulfides

Higher mercaptans

Aliphatic mercaptans, e.g., dodecylamine, lauryl mercaptan (contains proportions of n-tetra decyl, and n-hexa decyl mercaptans and dodecyl mercaptan)

Short-stop

Hydroquinone

Antioxidants

Phenyl-B-naphthylamine

Alkyldiphenylamines

Hindered alkylphenols or other phenol derivatives

ABS Rubber

ABS (acrylonitrile, butadiene, styrene) is a nitrile terpolymer rubber latex (Nitrex) or a solid ABS terpolymer. Latices of acrylonitrile/butadiene/styrene terpolymers contain 10-30% styrene, 28-33% acrylonitrile. They have low water absorption and are used in impregnation, saturating agent for paper and cellulose, softener for resin latices.

ABS resin is a thermoplastic polymer blend that is used in automobile body parts and fittings, telephones, heels, luggage, packaging, refrigerator door linings, plastic pipe, building panels, shower stalls, boats and radiation grills.

Specialty Latices

1) Styrene/Butadiene/Vinyl Pyridine Terpolymer Rubber Latex. This latex is made by emulsion polymerization of butadiene, styrene and 2,3- or 4 vinylpyridine (CH_2 =CHC_5H_4N) and is used either alone or mixed with a styrene-butadiene latex for dipping tire cord, giving a stronger and more fatigue-resistant rubber/textile bond, and is especially useful for nylon and polyester cords. It is also used for belts requiring good rubber/textile adhesion.

2) Carboxylated nitrile latex - This latex is made by including 0.5 - 10% methacrylic acid in the acrylonitrile/butadiene monomer mixture copolymerization occurring in emulsion as for nitrile rubber.

The compounds used in NBR, ABS and specialty latices that are not discussed under SBR rubber, but appear to have potential significance for health are discussed below.

Monomers

Acrylonitrile: H_2C:CHCN (propenenitrile, vinyl cyanide).

This is a clear, colorless, volatile liquid with a vapor density of 1.9 and a vapor pressure of 110-115 mmHg at 25°C. It is readily absorbed through the skin and by inhalation. Acrylonitrile is moderately toxic. It is not agreed whether the toxicity of acrylonitrile is due to cyanide formation, or to acrylonitrile itself. If it acts like cyanide in acute poisoning, cellular respiration is stopped by blocking oxidative enzymes. In chronic poisoning the CN^- ion is gradually released, converted to SCN^- and excreted as the thiocyanate ion. There is some question whether chronic cyanide poisoning occurs at all. The TLV of acrylonitrile is 20 ppm, based on animal exposure data, and by analogy with the 10 ppm TLV of hydrogen cyanide. There are no reported carcinogenic effects.[7,8]

Vinyl pyridine: ($C_5H_2NCH:CH_2$) is a colorless volatile liquid with an unpleasant, pungent odor that in commercial material contains a polymerization inhibitor. It is absorbed by the GI tract, skin and respiratory tract with resultant weakness ataxia, vasodilation, respiratory distress, and convulsions. The compound is moderately toxic; no carcinogenic effects have been reported.[7]

Methacrylic Acid (CH_2 =$C(CH_3)COOH$) is an unstable colorless liquid that will polymerize readily to give water soluble polymers. Its effects are similar to acrylic acid, which is a severe skin, eye and respiratory irritant in concentrated solutions or as a liquid. No cumulative toxic reactions are known, as acrylic acid is probably a normal metabolite. The LD_{50} for intraperitoneal injection in mice is 49 mg/kg. The oral and skin LD_{50} for acrylic acid suggest it is only slightly toxic (although Chemical Dictionary indicates it is highly toxic). It is a strong acid and should be treated accordingly.[7,35]

Emulsifiers

1) Soaps of fatty acids -

-Oleic acid ($CH_3(CH_2)_7CH$ =$CH(CH_2)_7COOH$)

This is the most abundant of the natural fatty acids. There are no known hazards in its use in industry.

-Myristic acid ($CH_3(CH_2)_{12}COOH$) - No known hazard in industrial use. No sign of carcinogenic activity.[7]

-Palmitic acid ($CH_3(CH_2)_{14}COOH$)

One of the major saturated natural fatty acids. No known hazards. It is not carcinogenic.[7]

2) Ionic Detergents

-Alkyl benzene sulfonates - These are branched chain sulfonate types of synthetic detergents, usually a dodecyl benzene. They are known

as "hard" detergents because of their resistance to breakdown by microorganisms. The most widely used synthetic detergent is sodium dodecylbenzene sulfonate, also called alkyl aryl sulfonate ($C_{12}H_{25}C_6H_4SO_3Na$). This compound is only slightly toxic by I.V. or oral administration.[35] The linear alkyl sulfonates may also be used.

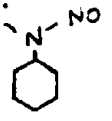
-Lauryl pyridinium chloride is a cationic detergent ($C_5H_5NClC_{12}H_{25}$) of unknown toxicity.

Modifiers

Mercaptans are a groups of organic compounds resembling alcohols but having the oxygen of the OH group replaced by S, as ethyl mercaptan (C_2H_5SH). They have a particularly strong, skunk-like odor, are strong irritants, and highly toxic by inhalation.

Stopping Agent

EDTA may be used as a stopping agent. This is a commonly used chelating agent and is practically nontoxic.

Nitroso-phenyl hydroxylamine (NPH)  is moderately toxic in oral administration to rats. It is added at the recovery stage in making NBR rubber to prevent "popcorn" formation.

Antioxidants

1) diethylhydroxylamine [$(C_2H_5)_2$ NOH)]. This liquid antioxidant is slightly toxic on oral administration. Also used as a stopping agent.

2) Di-tert-butyl-methyl-phenol could be either 4,6-di-tert-butyl-meta-cresol (DBMC) or 2,6-di-tert-butyl-para-cresol (BHT), both with the chemical formula $[C(CH_3)_3]_2$ $CH_3C_6H_2OH$. Both are of low toxicity. BHT is used as a food antioxidant.

3) Phenol  . The TLV is 5 ppm, sufficient to prevent systemic poisoning if skin absorption is avoided. Phenol is readily absorbed through the skin, gut and lung. After absorption, most of the

phenol is oxidized and conjugated with sulfuric, glucuronic and other acids, and excreted as the conjugated and free phenol. The toxic effects of phenol are related to the amounts of "free" phenol in the blood. Phenol is moderately toxic. Ingestion may cause nausea, vomiting, circulatory collapse, tachypnea, paralysis, convulsions, coma, necrosis of mucus membranes and respiratory failure. Chronic phenol poisoning is rarely reported. Because of its low volatility, phenol does not frequently constitute a serious respiratory hazard in industry. There is no specific evidence of human cancer attributable to phenol or related compounds. However, painting phenol (5 and 10%) on mouse skin induced both papillomas and carcinomas.[6-9]

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APPENDIX E.

CLINICAL STUDIES OF STYRENE WORKERS: PRELIMINARY REPORT

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INTRODUCTION

After the recognition in 1976 of vinyl chloride as a potent carcinogen, producing liver hemangiosarcoma and possibly other malignant tumors, the Environmental Sciences Laboratory undertook extensive clinical field surveys of vinyl chloride exposed workers, on a total population of 1,200 workers. The main purpose of these clinical and laboratory studies was to assess the prevalence of adverse health effects other than carcinogenic due to vinyl chloride. Toxicity and significant abnormalities of the peripheral circulation of liver and lung were found. Some of these abnormalities had been previously described, but no valid information on their prevalence and natural history was available. The possibility that workers developing such nonmalignant changes due to vinyl chloride toxicity may be at a greater risk for malignant tumors was thought of as being worth studying.

The possibility that other monomers widely used in the plastic industry may induce toxic changes and may also be carcinogenic was considered. Since styrene is widely used in the production of polystyrene and has a chemical structure with some similarities to that of vinyl chloride (styrene is vinyl benzene), it was decided to undertake a clinical field survey of styrene-exposed workers, in order to assess the prevalence of adverse health effects.

A thorough review of literature had shown that, although there were quite extensive data on acute toxicity in animals, there were very few reports on chronic experiments. The reports on effects in humans were few and contradictory.

MATERIALS AND METHODS

A styrene monomer and polymerization plant was chosen in which a large number of workers had had relatively pure styrene exposure for many years. We will report initial clinical findings in 494 workers. A mortality investigation of 563 long-term styrene workers is currently underway. The plant started operation in 1943 as a production facility for butadiene-styrene (Figure 1), manufacturing the monomer and conducting the co-polymerization. Since the 1950's its principal product has been polystyrene. Limited extrusion of polystyrene also is performed; the remainder of the polystyrene is extruded elsewhere. Since 1969 ethylbenzene has been the starting product. Nevertheless, some benzene has been present in

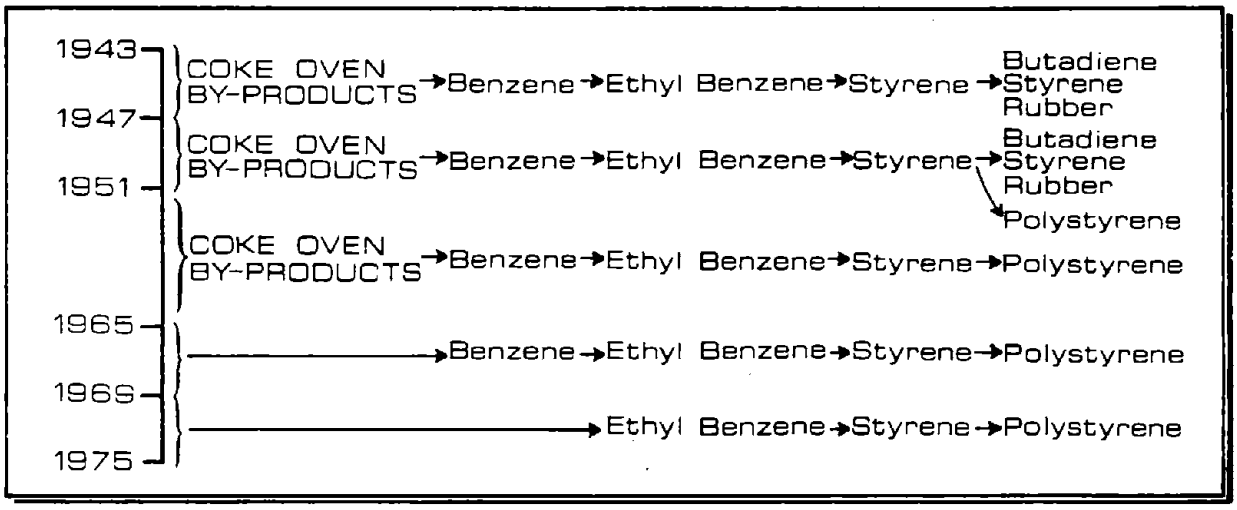

Figure 1. Plant history.

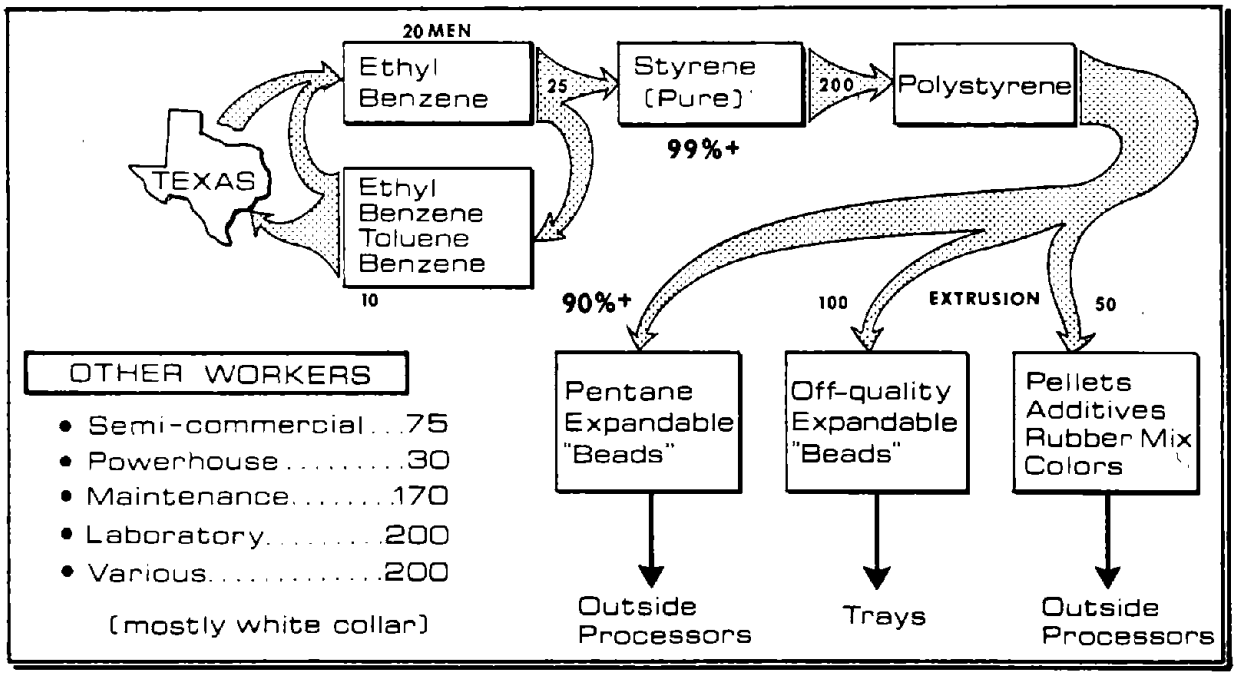

Figure 2. Current production.

certain areas, notably the benzene building and styrene monomer purification areas (Figure 2). Some toluene is also recovered, primarily as a side product of the ethylbenzene-styrene conversion process. About 650 workers are employed in production, performing the various chemical and physical steps in the plant. Approximate numbers of workers employed in each area are indicated on the table: about 20 workers are involved in storage of ethylbenzene, 200 in conversion of 99% + pure styrene to polystyrene. Most of the end product is polystyrene beads (polystyrene impregnated with various pentanes). When the "beads" are heated and extruded, they expand to polystyrene foam used as coffee cups and other articles. The off-quality beads are processed at the plant to form trays, used primarily in the retail packaging of meat.

The group examined numbered 494. The median age was in the 40's, but because of hiring practices the age distribution is bimodal (Table 1). The vast majority of all those examined were male; only 9 women were included.

The duration of exposure is presented in Table 2; 42% had more than 20 years since onset, but there were 30% who had entered the plant after 1970.

The examination included a complete and detailed occupational history, past medical history, a questionnaire on symptoms possibly related to exposures on the job (irritation of eyes, nose, throat, bronchi and skin, and prenarcotic symptoms), the MRC Questionnaire for chronic bronchitis, and the complete physical examination.

A broad spectrum of laboratory investigations was used in order to detect possible adverse health effects, and the following were included: SMA 25, CBC and platelet counts, routine urinalysis, metabolites of styrene in urine (mandelic, phenylglycoxilic and hippuric acid), styrene in blood and fat tissue, the carcinogenic embrionic antigen (CEA) test, chromosome studies, sputum cytology tests, chest x-ray and PFT's (including diffusion in 60 workers), nerve conduction velocity measurements, a reaction time test.

Selection was governed by trying to achieve clinical breadth while also trying to test hypotheses gleaned from literature review and from interviewing several workers and management personnel prior to the examination. Albeit, the scientific emphasis of the survey is upon hypothesis development rather than hypothesis testing. This report will deal with prevalence of certain symptoms (prenarcosis, acute irritation, chronic bronchitis) and test results (simple spirometry, chest x-ray, serum liver enzymes, hemogram, and platelet count). The above parameters will be related to estimate styrene exposure in order to develop hypotheses concerning causal relationships.

From the careful review of job descriptions and actual tasks performed by those in each job, an estimate of relative exposure was obtained (Table 3). In developing this estimate, we utilized the experience of management and of workers and had available a NIOSH Health Hazard Evaluation(35) of the facility. Of the 494 production and maintenance workers examined, 200 were judged currently to be in low exposure, 288 in relatively high styrene exposure. Significant benzene exposure was thought to be a possibility in certain job categories. The results and findings were related to length of exposure, and also to level of exposure.

RESULTS

Styrene in high doses (hundreds of ppm) produces a prenarcotic syndrome, described by the individual affected as being "light-headed" or "drunk". An attempt was made to exclude prenarcotic symptoms due to other substances (such as pentane) which also cause the syndrome. Prenarcotic symptoms attributable to styrene exposure were reported by 13% of the workers. Those with "high" styrene exposure had significantly more prenarcotic symptoms than those with low exposure (Table 4).

Irritation of mucous membranes is a common occurrence with styrene exposure and has repeatedly been reported at levels of 60-100 ppm in experimental work with subjects never before exposed to styrene. Significant tolerance may develop in industrial populations. This may explain the fact that there were no remarkable differences in incidence between relatively high and low styrene exposure groups, nor were these differences related to duration of exposure

— irritative symptoms were reported by 18% of those examined (Table 5).

The workers were also asked if they ever had wheezing or tightness in the chest related to styrene exposure. 11% of workers had such an episode. Significantly more high than low-exposed workers had had this symptom (Table 6).

The same pattern is present for recurrent tracheo-bronchial irritation, i.e. present weekly to monthly over a period of time (Table 7). Twelve percent of the workers in the high styrene area vs. 5% of those in low styrene exposures had such recurrent episodes.

The prevalence of chronic bronchitis according to the MRC definition was investigated. Nineteen percent of the workers met the criteria (Table 8). Remarkably, 6% of non-smokers had chronic bronchitis, and the probable etiologic contribution of styrene exposure has to be considered in these cases (Table 9).

Airway obstruction defined as $FEV_1/FVC<75\%$ was found in 35.3% of the examined and was more frequent in those with "high" styrene exposure. Interestingly, 31.6% of the non-smokers had evidence of airway obstruction (Table 10, 11, and 12). As expected, more obstruction was found in the "smoking population," especially in those with longer duration of exposure, but the difference in prevalence of obstructive respiratory dysfunction between smoking and non-smoking workers was much less than expected (38.4 vs. 31.6).

The x-rays were read according to the ILO U/C International Classification of radiographs of pneumoconiosis. Apart from individuals with past asbestos, coal or silica exposure, there were no findings of significant radiological changes.

Liver function was investigated using the bilirubin, alkaline phosphatase, SGPT, GGTP and SGOT determinations (Tables 13, 14, and 15). Elevated GGTP was the only abnormal test showing a relationship with level and duration of styrene exposure. No significant patterns were observed analyzing the other liver function tests in a similar manner.

The hematological changes investigated included hemoglobin, white blood count, and platelet count (Table 16). Fourteen percent of the workers had hemoglobins below 14.0 grams; 2.7% had white blood counts below 4,800; and 7.4% had platelet counts below 180,000. No clear trend according to length or level of exposure was found. Over 300 fundal examinations were performed by an ophthalmologist. No optic neuritis or other unexplained fundal abnormalities were noted. A case report of possible association between styrene and optic neuritis has been published. Analysis of the remaining tests will be reported later.

DISCUSSION

This clinical survey confirms styrene as an irritant to the mucous membranes of the upper respiratory tree. The possibility that styrene is a significant lower respiratory irritant in occupational groups must also be considered. That 32% of the workers had $FEV_1/FVC<75\%$, and that 12% of the high-exposed workers (vs. 4% of the lower exposed) had repeated episodes of wheezing and/or tightness in the chest leads one to postulate an etiologic relationship.

The analysis of results of the CEA tests and sputum cytology tests are not yet completed. Liver damage attributable to styrene exposure at levels prevalent in the plant we studied does not seem to be a major problem, although there were some indications, especially in the GGTP elevations, that follow-up is necessary.

The hematological findings have to be considered in conjunction with the past and present benzene exposure.

Table 1. Styrene workers. Sex and age distribution.

Age (years)	Number	Percent
<21	3	0.6
21-30	104	21.1
31-40	118	23.9
41-50	82	16.6
51-60	107	21.7
61-70	61	12.3
71+	15	3.0
Unknown	4	0.8
Total	494	100.0
Sex		
Male	485	98.2
Female	9	1.8
Total	494	100.0

Table 2. Styrene workers. Year of first exposure.

Onset	Number	Percent
<1950	112	22.7
1950-54	94	19.0
1955-59	25	5.1
1960-64	77	1.4
1965-69	109	22.1
1970+	147	29.8
Total	464	100.0

Table 3. Occupational distribution. High and low styrene exposure.

Low exposure	(Total 175)
Retired or working elsewhere	41
Power house	22
Handling of extruded polystyrene or finished beads:	
Sheet plant	41
Polystyrene handler	16
Packaging operator	
Handling and transportation, miscellaneous packaged materials	22
Maintenance, low exposure	22
Other	11
High exposure	**(Total 288)**
Production:	
Styrene manufacture	16
Styrene purification*	14
Styrene polymerization	
to polystyrene	70
to co-polymers, special processes*	38
Miscellaneous production workers*	25
Polystyrene extrusion	14
Maintenance:	
Pipe fitters*	29
Millwrights*	19
Electrician	15
Laborer	13
Welder	11
Other	20
Other high exposure*	4

*Significant benzene exposure possible.

Table 4. Acute prenarcotic symptoms in styrene-exposed workers.

Styrene exposure, years	0.1-7.0	7.1-20	>20.0	Total
Low	15/143 (11%)	2/61 (3.3%)	13/102 (13%)	30/305 (10%)
High	3/34 (9%)	11/53 (21%)	20/95 (21%)	34/182 (19%)
Total	18/177 (10%)	13/114 (11%)	33/197 (17%)	64/488 (13%)

For high as compared with low:

$\chi^2 = 7.81$ $.001 < p < .01$

$\chi^2 = .08$ NS (0.1-7.0 years)

$\chi^2 = 8.57$ $.001 < p < .01$ (7.0-20.0 years)

$\chi^2 = 2.43$ NS (>20.0 years)

Table 5. Mucous membrane irritation in styrene-exposed workers.

Styrene exposure, years	0.1-7.0	7.1-20	>20.0	Total
Low	28/143 (20%)	6/61 (10%)	17/102 (17%)	51/306 (17%)
High	4/34 (12%)	11/53 (21%)	22/95 (22%)	37/182 (20%)
Total	32/177 (18%)	17/114 (15%)	39/197 (20%)	88/488 (18%)

Table 6. Acute lower respiratory symptoms in styrene-exposed workers.

Styrene exposure, years	0.1-7.0	7.1-20	>20.0	Total
Low	9/143 (6.3%)	5/61 (8%)	8/102 (8%)	22/306 (7.2%)
High	4/34 (12%)	13/53 (25%)	17/95 (18%)	34/182 (19%)
Total	13/177 (7%)	18/114 (16%)	25/197 (13%)	56/488 (11%)

For low compared with high:

$\chi^2 = 14.84$ $p < .001$ (overall)

$\chi^2 = 1.21$ NS (0.1-7 years)

$\chi^2 = 5.69$ $.01 < p < .02$ (7.1-20.0 years)

$\chi^2 = 4.49$ $.02 < p < .05$ (>20.0 years)

Table 7. Recurrent acute lower respiratory symptoms in styrene-exposed workers.

Styrene exposure, years	0.1-7.0	7.1-20	>20.0	Total
Low	6/143 (4.2%)	3/61 (4.9%)	6/102 (5.9%)	15/306 (4.9%)
High	2/34 (5.9%)	8/53 (15%)	12/95 (13%)	22/182 (12.1%)
Total	8/177 (4.5%)	11/114 (9.6%)	18/197 (9.1%)	37/488 (7.6%)

For low compared with high:
$\chi^2 = 8.41$ $.001 < p < .01$

Table 8. Chronic bronchitis in styrene-exposed workers.

Styrene exposure, years	0.1-7.0	7.1-20	>20.0	Total
Low	16/143 (11.2%)	11/61 (18.0%)	21/102 (20.6%)	48/306 (15.7%)
High	5/34 (14.7%)	16/53 (30.2%)	22/95 (23.2%)	43/182 (23.6%)
Total	21/177 (11.9%)	27/114 (23.7%)	43/197 (21.8%)	91/488 (18.7%)

Table 9. Chronic bronchitis in non-smoking styrene-exposed workers.

Styrene exposure, years	0.1-7.0	7.1-20	>20.0	Total
Low	2/31 (6.5%)	2/15 (13.3%)	0/26 (0%)	4/72 (5.6%)
High	1/10 (10.0%)	0/12 (0%)	2/20 (10.0%)	3/42 (7.1%)
Total	3/41 (7.3%)	2/27 (7.4%)	2/46 (4.4%)	7/114 (6.1%)

Table 10. Obstruction ($\frac{FEV}{FVC^1} < 75\%$) in styrene-exposed workers.

Styrene exposure, years	0.1-7.0	7.1-20	>20.0	Total
Low	29/143 (20.3%)	21/61 (34.4%)	45/102 (44.1%)	95/306 (31.1%)
High	13/34 (38.2%)	19/53 (35.8%)	45/95 (47.4%)	77/182 (42.3%)
Total	42/177 (23.7%)	40/114 (35.1%)	90/197 (45.7%)	172/488 (35.3%)

For low compared with high:
$\chi^2 = 6.34$ $p \approx .01$

Table 11. Obstruction ($\frac{FEV}{FVC^1} < 75\%$) in non-smoking styrene-exposed workers.

Styrene exposure, years	0.1-7.0	7.1-20	>20.0	Total
Low	9/31 (29.0%)	2/15 (13.3%)	11/26 (42.3%)	22/12 (30.6%)
High	4/10 (40.0%)	3/12 (25.0%)	7/20 (35.0%)	14/42 (33.3%)
Total	13/41 (31.7%)	5/27 (18.5%)	18/46 (39.1%)	36/114 (31.6%)

For low as compared with high:
$\chi^2 = .09$ N.S.

Table 12. Obstruction ($\frac{FEV}{FVC^1} < 75\%$) in smoking styrene-exposed workers.

Styrene exposure, years	0.1-7.0	7.1-20	>20.0	Total
Low	14/82 (17.1%)	15/28 (53.6%)	19/33 (57.6%)	48/143 (33.6%)
High	3/13 (23.1%)	9/27 (33.3%)	24/36 (66.7%)	36/76 (47.4%)
Total	17/95 (17.9%)	24/55 (43.6%)	43/69 (62.3%)	84/219 (38.4%)

For low as compared with high:
$\chi^2 = 4.00$ $.02 < p < .05$

Table 13. Liver function tests in styrene exposed workers.

Tests	No. positive*	%
Bilirubin ≧ 1.0 mg %	15	3.2
Alkaline phosphatase ≧ 41 units	28	5.9
SGPT ≧ 70 units	19	4.0
GGTP ≧ 45 units	23	4.9
SGOT ≧ 50 units	16	3.3

*96th percentile or higher as compared with a group of 993 non-hospitalized men aged 40-44 done at same laboratory.

Table 14. Elevated GGTP in styrene exposed workers.

Styrene exposure, years	0.1-7.0	7.1-20	>20.0	Total
Low	1/83 (1.2%)	1/60 (1.7%)	4/75 (5.3%)	6/218 (2.8%)
High	1/62 (1.6%)	2/72 (2.8%)	14/119 (12%)	17/253 (6.7%)
Total	2/145 (1.4%)	3/132 (2.3%)	18/194 (9.3%)	23/471 (4.9%)

For high compared with low:
$\chi^2 = 3.97$ $.02 < p < .05$

For over 20 years compared with under 20 years:
$\chi^2 = 13.72$ $p < .001$

Table 15. Elevated GGTP* in styrene exposed workers.

Styrene exposure, years	0.1-7.0	7.1-20	>20.0	Total
Low	0/68 (0%)	1/53 (1.9%)	2/56 (3.6%)	3/177 (1.7%)
High	1/52 (1.9%)	2/60 (3.3%)	12/96 (13%)	15/208 (7.2%)
Total	1/120 (0.8%)	3/133 (2.3%)	14/152 (9.2%)	18/385 (4.7%)

For high compared with low:
$\chi^2 = 6.53$ $.01 < p < .02$

For over 20 years compared with under 20 years:
$\chi^2 = 13.01$ $p < .001$

*Excluded: Those drinking ≧ 400 proof ounces/week alcohol

Table 16. Hematological parameters in styrene-exposed workers.

Parameter	No. positive	Percent
Hemoglobin < 14.0 grams	66/486	14.0
White blood count < 4,800	13/486	2.7
Platelet count < 180,000	36/486	7.4

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