PB 274 789

NIOSH

TECHNICAL INFORMATION

A STUDY OF METHYL METHACRYLATE EXPOSURE AND EMPLOYEE HEALTH

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE / Public Health Service
Center For Disease Control / National Institute For Occupational Safety And Health

A STUDY OF

METHYL METHACRYLATE EXPOSURES

AND

EMPLOYEE HEALTH

John Cromer, M.D.
Kenneth Kronoveter, M.S.

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Center for Disease Control
National Institute for Occupational Safety and Health
Division of Surveillance, Hazard Evaluations, and Field Studies
Cincinnati, Ohio 45202

November 1976

For sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402

Mention of trade names or commercial products does not constitute endorsement by the National Institute for Occupational Safety and Health.

DHEW (NIOSH) Publication No. 77-119

CONTENTS

ACKNOWLEDGEMENTS

The assistance of the NIOSH Division of Technical Services in providing statistical support, the Division of Physical Sciences and Engineering in providing analytical services, the Division of Surveillance, Hazard Evaluations, and Field Studies in providing manpower for the environmental surveys, and the Appalachian Laboratory for Occupational Safety and Health in providing assistance with the medical surveys is appreciated. Also, without the whole-hearted interest, efforts, and cooperation of management and labor at the private sector establishments surveyed, the study could not have been accomplished.

ABSTRACT

This study screened employees for health effects potentially resulting from exposures to monomeric methyl methacrylate vapor. Ninety-one exposed and forty-three nonexposed workers were evaluated at five plants manufacturing polymethyl methacrylate sheets. Significant acute effects developing over the work shift were not detected as measured by symptomatology, blood pressure, and pulse rate. Chronic effects were sought for in past symptomatology, blood pressure, respiratory function testing, hemoglobin and white blood count, urinalysis, and blood chemistry. The data suggest that effects may occur in the higher concentration exposure groups with regard to serum glucose, and blood urea nitrogen, cholesterol, albumin, and total bilirubin values. Although not of statistical significance, the data also suggest possible alterations in skin and nervous system symptomatology, urinalysis findings, and serum triglycerides. Extensive air sampling revealed mean 8-hour time-weighted average exposures by job category ranging from 4 to 49 ppm, for the workers studied, at the individual plants.

INTRODUCTION

The National Institute for Occupational Safety and Health (NIOSH) recently conducted a short-term study directed towards elucidating the health effects upon industrial workers resulting from exposure to monomeric methyl methacrylate (MMA) vapor. The study was conducted during the first six months of 1975 and included a comprehensive literature review, screening surveys at 27 establishments, and comprehensive studies at five facilities. The comprehensive studies included occupational histories, medical evaluations of workers, and detailed air sampling to determine exposure levels.

MMA, a clear, colorless liquid with a distinctive odor, polymerizes readily to form polymers or copolymers. Since the first commercial production of MMA in the United States over 40 years ago it has come into wide-spread use in the plastics industry. The Chemical Marketing Reporter estimates that demand for MMA in the U.S. will rise to approximately 950 million pounds annually by 1980.[1] The major uses of this plastic are cast sheet products, surface coatings, and molding or extrusion powders. The spectrum of application for MMA is quite extensive and growing. NIOSH's Office of Health Surveillance and Biometrics, in 1974, estimated that some 30,000 workers in the U.S. were exposed to MMA.

TOXICOLOGY REVIEW

Monomeric methyl methacrylate is widely used in the plastics industry but relatively little research has been conducted concerning its biological effects on man. In recent years human exposure to MMA has come under closer scrutiny, principally by orthopedic surgeons, because of effects noted on the cardiovascular system, but also by others interested in the effects of exposure to MMA.

Early research by Deichmann[2] and Spealman et al[3] showed that in rats and rabbits MMA was a mucous membrane and skin irritant. MMA also caused hypotension after intravenous injection and hyperpnea after inhalation and intravenous administration.[2-3] Deichman[2] found lung congestion and other systemic effects in rabbits whereas Spealman et al[3] described liver and kidney degeneration in mice, rats, guinea pigs, and dogs after inhalation exposures. Of particular interest was the demonstration by Spealman et al[3] that MMA is a cutaneous sensitizer in man. However, patch testing with polymethyl methacrylate (PMMA) in 10 male medical students who had developed skin hypersensitivity to MMA demonstrated no reactions to the polymer.[3] Finally, Spealman et al[3] implanted PMMA, subcutaneously and intraperitoneally, into mice for a 9 month period. None of the animals showed growths or other abnormalities on gross postmortem examinations at the end of the 9-month period.

Harris[4] described a case of dermatitis in which a 42-year old man who had considerable skin contact with MMA developed a dry, scaling hand eczema. It is unclear from his description whether this was a primary irritant or allergic contact dermatitis. He noted isolated cases in which workers complained of cough and pharyngitis from inhaling the fume or powder of PMMA and mentioned that handling of the dust of PMMA was found to cause dermatitis, possibly of an allergic nature.

In recent years a number of investigators, principally orthopedic surgeons and anesthesiologists, have noted the effects of MMA on the cardiovascular system.[5-8] The most pronounced effects noted have been on arterial blood pressure: Within seconds to minutes following the surgical insertion of partially polymerized MMA bone cement, marked decrements in blood pressure occurred, leading in instances to the patient's death.[9] Some investigators have suggested that the hypotension appears to be due to vasodilatation of peripheral vessels[6] which is caused by absorption of MMA from the cement at the time of the operation. There has been considerable correspondence in the medical literature regarding this effect and the factors influencing its frequency of occurrence.[10-12]

Bright et al[5] measured MMA concentrations in whole blood in 4 patients undergoing total hip arthroplasty and found the concentrations to be 1 mg/100 ml or less; no significant ECG or blood pressure changes were noted in these patients. In experiments on 6 sheep, 3 dogs, and 1 chimpanzee, blood concentrations of MMA were correlated with ECG and blood pressure changes. The following responses were noted:[5]

MMA Concentration in Blood	*Effect*
0-5 mg/100 ml	*No change*
10-50 mg/100 ml	*Immediate hypotension with depressed cardiac contractility (necropsy: focal pulmonary vascular congestion with fluid-filled alveoli)*
100 mg/100 ml	*Rapid cardiovascular collapse with terminal ECG changes (necropsy: marked pulmonary hemorrhage)*

These effects and the corresponding blood concentrations of MMA are of interest. The relationship that this type and degree of MMA exposure (i.e., by intravenous administration) has to inhalation exposure to MMA is unclear, for there are no published data on measurements in humans or animals of blood concentrations of MMA resulting from exposure by inhalation.

To investigate the possible pulmonary effects from systemic absorption, Hughes et al[13] *evaluated 37 patients undergoing total hip replacement in which PMMA bone cement was used. Forced expiratory volume in one second ($FEV_{1.0}$), forced vital capacity (FVC), and diffusing capacity (D_{LCO}) were measured pre-operatively and in the early and late post-operative period. No statistically significant differences were seen in the exposed and control groups. These authors cautioned that great care be exercised in implanting PMMA in young patients or patients with pre-existing pulmonary disease until further studies have established the long term safety of the material.*

A recent study[14] *looked at the potential hepatotoxic effects of MMA by comparing the frequency and severity of liver injury in mice using direct esophageal instillation of (1) varying concentrations of monomer in olive oil; (2) varying concentrations of chloroform in olive oil; and (3) olive oil only. With increasing concentrations of MMA, mild to moderate liver changes such as fatty infiltration and disruption of nuclei were noted. Chloroform produced evidence of liver toxicity in all animals even at the lowest concentrations, whereas the olive oil control group demonstrated no histological hepatic changes. These authors pointed out that the blood concentrations of MMA following total hip replacement are certainly much lower than those found in their study. They also indicated that their study "is not relevant to proper clinical applications, and (is) strictly a question of learning about the upper limits of harmful effects of the monomer."*

Effects of MMA vapor on gastric motor function have recently been reported by Tansy et al.[15] *These investigators exposed rats to* *less than LD_{50} doses of MMA vapor and produced "abrupt cessation of gastric pressure activity and a fall in gastric tonus." Marked effects were noted at an MMA air concentration of 93.6 mg/l (93,600 mg/M^3) with less pronounced effects noted at concentrations as low as 1 mg/l (1000 mg/M^3) for a 1-hour period. These investigators inserted an open-tip catheter by the oral route in the region of the gastric antrum of a volunteer dental student. They found almost immediately upon exposure to MMA vapor a gradual depression of both amplitude and frequency of intragastric pressure activity. Unfortunately the air concentrations of MMA were not measured during the student's exposure.*

The significance of these findings may relate to comments made by dental students which Tansy and his colleagues mention in their paper. When using MMA in the laboratory some dental students "indicated they felt nauseated both during the exposure and thereafter." Some also said that they experienced a lack of appetite after such laboratory classes.

Another important finding by Tansy et al,[16] as yet unpublished, is a marked absence of visceral and subcutaneous fat noted on necropsy of 24 rats exposed 8 hours per day, 5 days per week for 3-months to 116$\pm$ 2.7 ppm (475 mg/M^3) of MMA. This finding was not present in 24 non-exposed control rats also sacrificed at the conclusion of the 3-month experiment. The experiment included 6 months exposure and control populations. The results, including blood analyses for a number of biochemical parameters, are in the process of publication.

A few researchers have looked at the carcinogenic potential of MMA and PMMA. Laskin et al[17] and Oppenheimer et al [18] used PMMA film for implantation into the lateral abdominal wall of test animals and found a 20-25% incidence of fibrosarcoma. The latter researchers also painted the liquid monomer on the back of the necks of 10 rats 3 times a week for 4 months and noted no tumor production. The significance of these findings may be questioned because alteration of the surface texture and form of the implanted material can cause significant differences in its carcinogenic activity. Furthermore, the application of MMA for a period as short as 4 months in as few as 10 test animals is a less than satisfactory means of evaluating MMA's carcinogenic potential.

Lavorgna et al[19] studied the implantation in rats of polyethylene plastic, as well as epoxy resin and glass. They found the same incidence of fibrosarcoma formation from implantation of PMMA, polyethylene, and glass; no tumors were found in the epoxy resin group. As the authors point out "the relationship of this form of (testing) and human experience remains unclear.... Unless a more perfect test system is designed, the final answer will have to be generated by data obtained from man."

Borzelleca et al[20] added monomeric MMA to the drinking water of rats in concentrations ranging from 0 to 200 ppm for a period of 2 years.

Histopathologic findings revealed no lesions attributable to MMA and mortality was unaffected in the exposure groups. However, these authors failed to mention which organs or tissues were examined at necropsy.

Several studies from the Russian literature merit discussion. Karpov,[21,22] after investigation of industrial workers and laboratory animals, suggested that the tolerance for industrial establishments be 0.05 mg/l (50 mg/M^3). Raines[23] later found "signs of chronic intoxication" in workers exposed to concentrations ranging from trace amounts to 0.06 mg/l (60 mg/M^3). These signs and symptoms included hypotonia, somnolence, headaches, and anorexia, which were similar to those described earlier by Karpov.

Blagodatin et al[24] conducted a study of 152 workers occupationally exposed to MMA. More than 800 analyses of air samples showed exposures ranging from 2 to over 200 mg/M^3. [The Russian Maximum Permissible Concentration (MPC) is 20 mg/M^3, and the U.S. federal standard, 410 mg/M^3.] Of the 139 female and 13 male workers an unstated majority were said to have had 10 or more years of exposure to MMA. Blagodatin et al[24] noted headache in 78%, pain in the extremities in 30%, excessive fatigue and sleep disturbance in 21%, loss of memory in 20%, and irritability in 16% of the exposed workers. Other abnormalities included a decreased response to adrenocorticotropic hormone (ACTH) administration, as measured by 17-(hydro)oxycorticosteroids; a disturbed K/Ca ratio in the blood serum; a change in cholinesterase activity; a tendency toward erythrocytosis with macrocytosis; a relative lymphopenia with leuco- and monocytosis; decreased vestibular excitability on caloric testing; and "vegetative" vascular disorders. These investigators described "chronic MMA poisoning" in 14 workers with 11-26 years of exposure. This was clinically exhibited by an asthenic-neurotic syndrome, "vegetative" vascular dystonia and "vegetative" sensory polyneuritis in 12 workers, and toxic encephalopathy" in 2 workers.

Dobrinskij[25] described symptoms and signs in workers exposed to MMA. The magnitude of worker exposure to MMA ranged from 100 to 599.2 mg/M^3. The following findings were noted in 9 workers: leukopenia of 2600-2900 with a tendency to lymphopenia; hemoglobin decrease from 11.6 to 10.5 gm%; and neurasthenic syndrome (increased irritability, fatigue, headache, tearing, pharyngitis, and laryngitis). The following symptoms were reported by 300 female workers who poured MMA into forms: headache, rapid fatigue, irritability, and tearing in 70 to 75% and laryngitis or pharyngitis in 20 to 25%. Also noted were anemia in 12 workers and leukopenia in 12 workers. A tendency toward decreased blood pressure was noted at the end of the shift.

A critical review of the data from these Russian studies reveals several deficiencies: 1) no definition of terminology is given for certain items (e.g., "vegetative" vascular disorders, "vegetative" sensory polyneuritis, "toxic encephalopathy"); 2) certain findings are not well quantified or not quantified at all (e.g., decreased response to ACTH administration, a disturbed K/Ca ratio, a change in cholinesterase activity, etc.): and 3) no control group was used for statistical comparison with the exposed groups. Despite these significant limitations a few comments can be made. The exposures which Blagodatin et al[24] measured in their study ranged from 0.5% to more than 50% of the U.S. federal standard. Unfortunately, the investigators did not correlate specific adverse effects with the level of exposure. Nevertheless, the high prevalence of symptoms such as headache, fatigue, irritability, and tearing of the eyes is notable. It appears from these data that exposure to concentrations less than the 410 mg/M^3 U.S. federal standard is associated with considerable symptomatology. The work of Karpov[22] and Raines[23] supports this contention. Nevertheless, because of the limitations of the Russian studies it is difficult to comment further regarding exposure levels and associated adverse effects.

FEDERAL HEALTH STANDARD

In 1963, the Threshold Limit Values (TLV) Committee of the American Conference of Governmental Industrial Hygienists placed MMA on its "Notice of Intended Changes," thereby signaling its intent to publish a recommended exposure value.[26] In 1965, the recommended exposure value of 100 ppm or 410 mg/M^3 (referring to a time-weighted average (TWA) concentration for a 7 or 8-hour work day and a 40-hour work week) was placed on the "Adopted Values" list. Documentation for the adopted value states: "The TLV of 100 ppm is considered sufficiently low to protect against discomfort from irritation and is well below the level giving rise to any systemic effects."[27]

Following the passage of the Occupational Safety and Health Act of 1970 (PL 91-596), the Occupational Safety and Health Administration of the U.S. Department of Labor promulgated an 8-hour TWA allowable exposure for MMA of 100 ppm as one of its occupational health standards under Part 1910 of Title 29 of the Code of Federal Regulations as amended.[28]

CAST SHEET PROCESS

Since the comprehensive surveys of this study were conducted in cast sheet plants, that process only will be described. Typically, the first step in manufacturing cast sheet is the distillation of the crude MMA to remove inhibitors. The distilled or crude MMA is transported to bulk mixing tanks which vary in size. Other components such as small amounts of comonomers, pigments, stabilizers, and catalysts ("salt and pepper" additives) are usually added to the mixing tanks by hand methods. After mixing, the casting mixture is degassed and transported by tubing (gravity flow or pumped) to the molds. The molds, or cells, usually consist of two plates of tempered glass separated by a gasket of flexible material such as polyvinyl chloride. After the cells are *filled and sealed, they are heated by such means as hot water, ovens, or autoclaves for curing. When the polymerization (curing) is complete, the sheets are removed from the cells and trimmed to size. The sheets can be used "as is" or further heat treatment may follow.*

In addition to molds or cells a continuous casting process is also utilized. A continuous casting machine uses two stainless steel moving belts to form a continuous mold. The belts move through heating and cooling chambers where polymerization and other treatments occur. As the sheet is discharged from the belts it is cut to size and prepared for use or shipment.

A typical casting mixture contains 1 or 2% additives, the remainder (98-99%) being MMA. There are many formulations, each containing perhaps 10 to 15 additives with any particular additive seldom exceeding 0.5%. In addition to MMA and other momomers, additives in casting mixtures include members of the following classes of chemicals: acetates, acids, acrylates, alcohols, aldehydes, amides, amines, ammonia, carbonates, chlorates, cresols, cyanates, lactates, mercaptans, naphthalenes, nitriles, peroxides, phosphites, pivalates, polyols, quinones, salicylates, silicas, sulfates, sulfites, sulfonates, toluidines, dyes, waxes, pigments.

On the basis of relative quantities of materials, the predominant chemical work exposure of sheet plant employees is MMA.

A variety of terms is used to describe the employees, by job category, in cast sheet plants. Some of these with typical duties are as follows:

1. *Weigh-out Men - Weigh out the chemicals for the various batches of casting mixtures.*

2. *Mix Men - Add or meter the chemicals to the mix tanks. Also make connections for transfer of the casting mixture to the molds.*

3. *Mold Fillers (Head Men) - Fill the molds with the casting mixture or work at the filling end of a continuous casting machine.*

4. *Mold Filler Helpers - Assist the mold fillers in filling molds, moving racks, etc.*

5. *Mold Makers - Assemble the plate glass molds.*

6. *Distillers - Work in the distillation plant or scrap recovery plant.*

7. *Oven Men - Move racks of filled molds to and from the ovens, etc.*

8. *Inspectors - Open molds, inspect and wrap sheets, etc.*

9. *Relief, Maintenance, and Foreman - Duties as implied by job titles.*

SURVEY METHODS

The protocol for the field activities of the study provided for screening surveys and comprehensive surveys. The screening surveys were designed to provide: 1) background information on the extent and magnitude of exposures to MMA in diversified companies; 2) limited medical data; and 3) a base from which to select establishments for the comprehensive surveys. The comprehensive surveys were designed to provide data from which employee exposure categories would be developed and health effects elucidated.

The methodology for the environmental and medical phases of these surveys will be discussed separately.

Environmental Phase

Screening surveys were conducted at establishments which varied from monomer production and lens manufacturing facilities to dental laboratories. The information obtained during these surveys included process descriptions, number of exposed workers, history, duration, and magnitude of exposures, other exposures which could "confuse the issue," exposure control systems, and employee-management relationships. Air sampling was conducted to the extent that an estimate of exposures was possible. In several instances the results of air sampling conducted by the company were used to assist in estimating the magnitude of exposures.

On the basis of the screening surveys five MMA cast sheet manufacturing facilities were selected for the comprehensive surveys. The objective of these surveys was to develop employee exposure groups or categories for which medical effects resulting from exposure to MMA would be sought. The air sampling within these facilities extended over two- or three-day periods which provided multiple TWA exposure determinations for representative exposed individuals. The formulations for the sheet products were reviewed by NIOSH professional staff to identify other chemicals which might exert an additional influence (with MMA) upon the health of the workers. On the basis of the physical properties and relative quantities of chemicals used during the time of the surveys, it was deemed desirable to sample and analyze for a constituent, ethyl acrylate (EA), as well as methyl methacrylate at only one plant. The analyses for MMA and EA were performed on the same charcoal tubes. Over the years, one of the companies had sampled for such chemicals as acrylates, aldehydes, alcohols, quinones, and ketones. A review of these results did not reveal data considered to be of consequence for the purposes of this study.

Atmospheric samples for the surveys were primarily personal samples for whose collection the workers wore the sampling device for a significant portion of a work shift. The collection devices were clipped to the lapel of the worker's shirt to sample air representative of what the worker actually breathes. This type of air sample provided a reasonable degree of accuracy for determining TWA exposures.

All air samples were collected using organic vapor charcoal tubes and NIOSH approved and calibrated personal sampling pumps operating at flow rates of approximately 50 cc/min. Since an air volume of approximately 10 liters per charcoal tube was desired, it was necessary to use 2 charcoal tubes per worker-shift-sample. The results from the 2 tubes was averaged to determine the exposure of a particular worker for a specific shift.

The charcoal tubes are glass tubes with both ends flame sealed, 7 cm long with a 6-mm O.D. and a 4-mm I.D., containing 2 sections of 24/40 mesh activated charcoal separated by a 2 mm portion of urethane foam. The activated charcoal is prepared from coconut shells and is fired at 600°C prior to packing. The absorbing section contains 100 mg of charcoal, the backup section, 50 mg. At the analytical laboratory the charcoal sections are transferred to small, stoppered, glass-sample tubes and the MMA is desorbed with 0.5 ml of carbon disulfide. An aliquot of the sample is analyzed by gas chromatography.

The gas chromatograph (GC) is equipped with a flame ionization detector. The 10-foot X 1/8-inch stainless steel GC column is packed with 5% FFAP stationary phase on 100/120 mesh Supelcoport. Typical operating conditions for the GC are: helium carrier gas flow, 30 ml/min; hydrogen gas flow to detector, 35 ml/min; air flow to detector, 400 ml/min; injector temperature, 225°C; manifold (detector) temperature, 250°C; and column temperature, 70°C. The area of the resulting peak is measured by an electronic integrator, or some other suitable form of area measurement, and compared to a standard curve prepared by analyzing known concentrations of methyl methacrylate. The desorption efficiency for methyl methacrylate must be determined prior to calculating the final concentration. The desorption efficiency is determined by adding a known amount of methyl methacrylate to an amount of charcoal equal to the first section of the charcoal tube. The methyl methacrylate is desorbed with carbon disulfide (CS_2) and analyzed with the GC. The result of this determination is compared with an equivalent standard in CS_2 to obtain the amount of methyl methacrylate that can be recovered from the charcoal. A guide for determining organic solvents in air is presented in the NIOSH "Manual of Analytical Methods".[29]

<u>Medical Phase</u>

The medical portion of the screening survey entailed the administration of a questionnaire (Appendix II) to exposed workers and, when available, review of clinical data that plant medical departments had collected *on workers exposed to MMA. In most instances, the medical questionnaire was given to the worker at the plant, later filled out by him, and then mailed to the NIOSH investigators. The purpose was to identify particular complaints or problems which might warrant special attention at the time of a subsequent comprehensive survey.*

For the comprehensive survey, the evaluation of possible effects on workers exposed to MMA was divided in two areas:

<u>Evaluation for acute effects developing over the shift</u>

Pre- and post-shift testing included questions (Appendix V) as well as pulse and blood pressure determinations. The development of symptomatology and changes in pulse rate and blood pressure were compared among groups of workers with different degrees of exposure and a control group. Tests of significance were calculated for these comparisons.

<u>Evaluation for chronic effects</u>

A. An extensive questionnaire inquired into the worker's smoking habits, occupational and medical history, and respiratory, renal, hepatic, gastrointestinal, dermatologic, and neurologic symptomatology (Appendix V). Responses to the questions were compared by tests of statistical significance.

B. The mean blood pressure of individuals in the control and exposure groups was compared with predicted values from the U.S. National Health Survey 1971-1972 data.[30] Tests of significance were calculated for differences between the observed and predicted values in the various exposure groups.

C. Pulmonary function test results for the control group were compared with those of each of the exposure groups. Smokers and nonsmokers were analyzed separately. Since age is a part of the determination of the individual's predicted values, the problem of group differences in mean age was not of concern. The Student's "t" test for independent data was used to compare the mean differences of predicted minus observed values between the control and exposure groups.

The pulmonary function test procedures dictated that each subject perform at least five trials on a Hewlett Packard Model VR500 lung function analyzer. The volume-time tracings were recorded on a MFE 100-mm recorder. The FEV_1, FEV_3, peak flow, FVC, and maximal midexpiratory flow (MMF) were obtained from the best trial. Usually the best trial was the trial with the largest FVC, or the FVC was the most important factor used to determine the best trial.

The pulmonary function technician performing the test was instructed to obtain at least five trials with at least two reproducible trials; i.e., second largest FVC within 5% of the largest, second largest FEV_1 within 7.5% of the largest FEV_1, and second largest peak flow within 15% of the largest peak flow. All of these parameters were available for inspection by the technician after each trial.

D. Mean white blood cell (WBC) counts and mean hemoglobin (Hb) values were compared among exposure groups. Tests of significance were computed.

E. Urinalysis findings were compared for the exposure groups. The chi-squared (X^2) test was used for analysis of significance for WBC counts. Tests of significance were not performed for red blood cells, protein, and glucose because of the low incidence of abnormalities in all groups.

F. Blood chemistry results for triglycerides, calcium, phosphorus, serum glucose, blood urea nitrogen (BUN), uric acid, cholesterol, total protein, albumin, total bilirubin, alkaline phosphatase, lactic dehydrogenase (LDH), and serum glutamic oxaloacetic transaminase (SGOT) were first compared among the exposure groups. The mean value of the control group was compared with the mean of the exposure group (t test). It should be noted that there were small differences between the limits given as normal by each of the 3 laboratories that performed the biochemical blood tests. Since these differences were considered not to be significant, comparisons of the mean values of the different tests are included. Secondly, the frequency of abnormal test results for the control group was compared with the exposure groups (X^2 test). The laboratory differences did not matter since the ranges were considered. Abnormal was considered to be above or below the range values. The blood samples were drawn pre-shift, the workers having been asked to fast for the previous 12 hours.

FINDINGS - SCREENING SURVEYS

Environmental Phase

A summary of results from the screening surveys is presented in Table 1. These data illustrate the type of facility surveyed, the approximate number of employees at that facility exposed to MMA, and the approximate 8-hour time weighted average exposure levels. It was primarily on the basis of the expected exposure levels and the number of exposed employees that five polymethyl methacrylate sheet manufacturing facilities were selected for the comprehensive surveys. Moreover, it was apparent that a high degree of cooperation would be extended by management and labor at these firms.

Medical Phase

Approximately 350 completed questionnaires were received by the NIOSH investigators from employees at the various facilities. The complaints primarily referrable to MMA were eye and upper respiratory irritation, headache, light-headedness (a feeling of being "high"), and skin rash or burn. These were occasional complaints, the symptoms usually occuring *during MMA spills when air levels of MMA were likely to be high.*

Unremarkable prevalences of gastrointestinal complaints, chronic headache, nervous system complaints, high blood pressure and low blood pressure were reported. However, the prevalences of complaints referrable to the cutaneous (19%), respiratory (30%), and genitourinary systems (25%) were noteworthy. Cutaneous problems most often were described as irritating or burn-like in nature. A few individuals reported long-standing dermatitis or eczema of a severe degree. Respiratory complaints such as shortness of breath, cough, and/or phlegm production were fairly common, but nearly all were from individuals who were currently or had been smokers. A number of individuals reported a history of genitourinary complaints including frequency of urination, urinary tract infections, and/or urinary tract calculi at one time or another during the years they had worked with MMA. Whether this finding is of consequence is difficult to know because of the limitations of the data. That these data came from self-administered questionaires often lacking in pertinent detail; that the degree and duration of the employee's exposure to MMA, as well as to other chemicals, was usually unknown; and that no appropriate control group was present for comparison, make these findings tenuous. The investigators recognized this fact and used these "indicators" to focus their subsequent evaluation toward the cutaneous, respiratory, and genitourinary systems.

A finding of interest involved a comparison of three serial complete blood cell count values taken from a group of 67 MMA exposed workers and 61 non-exposed workers over a several year period on a yearly or bi-yearly basis (company data). Comparisons were made for Hb, WBC, and differential count. No significant differences were noted between the exposed and non-exposed groups for the Hb or differential count values. However, a significant difference ($p < 0.002$) was noted in the mean WBC values: where the mean value for the exposed was $8.44 \times 10^3/mm^3$, and $7.78 \times 10^3/mm^3$ for the nonexposed.

A comparison of the two groups for the number of abnormal values in each (a WBC value $\geq 10.8 \times 10^3/mm^3$) showed a 12.5% prevalence in the exposed group and a 6.2% prevalence in the non-exposed group. Chi square (statistical) analysis with Yates correction indicated a difference approaching significance ($p = 0.074$).

The higher WBC count values in exposed vs. non-exposed tends to support a similar finding by the Russian investigators, Blagodatin et al.[24] However, the Russian data are limited, particularly because the degree and duration of exposures of a number of the MMA-exposed workers were unknown. For this reason a more accurate hematologic picture for MMA-exposed workers was planned for the comprehensive evaluation.

FINDINGS - COMPREHENSIVE SURVEYS

Environmental Phase

The relevant survey results are shown in Table 2. These data illustrate, by plant and job category, the number of men sampled, the mean sample time, the mean, range, and standard deviation of the MMA exposures, and the mean, range, and standard deviation of the ethyl acrylate (EA) exposures which were determined for one facility. Where necessary, the sample results have been adjusted to reflect 8-hour TWA exposures.

The control group subjects were employed on the same plant premises as the exposed group subjects but for the most part in different buildings. To be certain that the control group exposures were essentially zero, a number of air samples were taken in those areas where the control group subjects worked (Table 3).

Medical Phase

From the environmental results of 8-hour TWA exposures to MMA, 4 exposure groups and 1 control group were empirically developed. The groups were:

1. *Current exposure of less than 5 ppm or less than 2 months (13 persons)*
2. *Current exposure of 5 to 25 ppm (20 persons)*
3. *Current exposure of 25 to 50 ppm (33 persons)*
4. *Not currently exposed but exposed in the past for over 1 year (25 persons)*
5. *Control group with no exposure (43 persons)*

Although the results (Table 2) show a job category with an 8-hour TWA exposure to MMA of greater than 50 ppm, none of the employees in that group volunteered for the study. The number of persons in each category varies slightly for the various medical tests completed. For example, 2 persons of the control group were eliminated from the pulmonary function data because they had been welders in the past; also several of each group did not volunteer for the blood tests.

Characteristics of Control and Exposure Groups

The control group should have the same distribution (within reasonable limits) as the exposed groups for sex, age, color, and smoking history. Whereas there were differences for the percentage of white or black between the control group and the exposed groups, none were significant. All participants in the study were male.

Table 4 shows the mean ages for the control group and exposed groups as well as the probabilities resulting from the t test for independent data. The latter determines whether the mean of the comparison group is different from each of the means of the exposed groups. There are significant differences between the control group, the "25 to 50 ppm" group, and the "not current" group. The results of the subsequent analysis should be interpreted in light of these differences.

Table 5 shows the proportion smoking for the control and exposed groups. The probabilities are those resulting from a X^2 test (with correction) and indicate significant differences between the control group and each of the exposed groups for the proportion smoking. There is a significant higher percentage of smokers in the "5 to 25 ppm" group than in the control group. Again, the results of this study should be interpreted in light of this difference.

Evaluation for Acute Effects Developing Over the Shift

A. Symptomatology (Pre-and Post-Shift)

Tests of significance were not computed due to the small number of individuals who developed or lost symptoms over a work shift. The data indicate that acute symptomatology rarely occurred at the air concentrations of MMA measured during the NIOSH visits (Table 6).

B. Blood Pressure and Pulse (Pre and Post-Shift)

In Table 7, the differences between pre- and post-shift measurements have been written so the sign indicates an increase (+) or decrease (-) during the shift. The control mean shift difference was compared to the various exposed mean shift differences using the "t" test. No significant differences were found for blood pressure or pulse rates.

Evaluation for Chronic Effects

A. Past Symptomatology

Table 8 presents a summary of the symptom findings -- i.e., cough, expectoration, hepatic and gastrointestinal problems, skin and allergic problems, and nervous system problems -- and also indicates the percent frequency of individuals with one or more of these symptoms. There were significant differences between the control group and the "under 5 ppm" group for cough, and between the control group and the "5 to 25 ppm" group for expectoration. A probable explanation for these differences is that the percentages of smokers in the "under 5 ppm" (62%) and "5 to 25 ppm" (70%) groups are markedly higher than for the control group (39%).

For symptoms referrable to the liver and gastrointestinal tract, no significant differences were noted between the control group and each of the exposed groups.

For skin and allergic problems, no significant differences were detected. However, a greater percent of individuals in the "25-50 ppm" (30%) and "5-25 ppm" (25%) groups reported such problems than did the control group (14%). One might expect such a difference, knowing that MMA is both a contact skin irritant and sensitizing agent. Further study using larger groups of individuals would clarify this matter.

For urinary symptoms, significant differences were not noted between the control and exposure groups.

Looking at past nervous system symptomatology, one sees that workers in the "5-25 ppm" (50%) and "25-50 ppm" (46%) groups demonstrate considerably more positive responses than the control group (23%). Whereas the differences are not significant, they are notable nonetheless. A review of the responses showed the greatest differences in regard to dizziness, shakiness, and drowsiness.

B. Blood Pressure

Chronic, long term effects on blood pressure were evaluated in the workers exposed to MMA. Predicted age-sex-color specific blood pressures were calculated for individuals in each exposure group and in the control group. Mean differences in the systolic and diastolic values between predicted and observed were calculated for each group. As noted in Table 9, no significant differences were noted between the exposure groups and the control group.

C. Pulmonary Function Tests

Since smoking history has considerable influence on pulmonary function, smokers and nonsmokers were analyzed separately for each of the groups. Tables 10 through 13 show a comparison of the findings for forced vital capacity (FVC), forced expiratory volume in one second ($FEV_{1.0}$), $FEV_{1.0}$/FVC ratio, and maximal midexpiratory flow (MMF).

For FVC significant findings were not noted in any of the groups (Table 10). For $FEV_{1.0}$ there were likewise no significant findings noted in any of the groups (Table 11).

For $FEV_{1.0}$/FVC ratio (Table 12), one result is noteworthy. Among the smokers, the "under 5 ppm" exposure group demonstrated a significant difference - i.e., they had a significantly better predicted minus observed difference than the controls ($p=0.001$). Whether this represents a medically significant finding is uncertain since the number of individuals in this group was quite small ($n=8$). Re-examination using a larger number of individuals is required to determine the significance. Among the nonsmokers, no significant differences were found.

For MMF (Table 13) no significant differences were found among the smoker and nonsmoker groups comparisons.

D. White Blood Cell Count and Hemoglobin Value

Three persons had abnormal WBC counts, 1 each in "under 5 ppm", "5-25 ppm", and "not current" groups. No abnormal Hb values were detected, and no significant differences between the exposure groups were noted. The mean WBC counts for the exposed groups are shown in Table 14.

While no WBC counts for controls were available to compare with those of exposure groups, it is believed that a worker's WBC count is probably unaffected by these levels of MMA exposure. This is based upon the findings of WBC counts ranging from 6.9 X 10^3 to 7.8 X 10^3 which are well within the accepted "normal" range of 4.8 X 10^3 to 10.8 X 10^3 and no apparent relationship between the degree of MMA exposure and WBC count.

E. Urinalysis

The urinalysis results are given in Table 15. For white blood cells per high power field (WBC/HPF), the three current exposure groups were compared to the "not current" group. There was a considerably larger percent of abnormal values for the "5-25 ppm" group (35%) as compared with the not current group (5%). However, there was not a significant difference between these two (p=0.064). In view of the earlier results indicating no significant differences in urinary tract symptomatology between these two groups, this greater percent of abnormal findings is puzzling and further investigation along this line seems warranted.

Regarding the other urinalysis findings, there was an obvious lack of significant differences between the groups for red blood cells per high power field (RBC/HPF), protein, and glucose.

F. Blood Chemistry

An interpretation of the data must take into consideration that, as shown in Table 4, the exposed "25-50 ppm" group is significantly younger and the "not current" group significantly older than the control group. Additionally, small differences in the normal ranges of blood tests given by the contract laboratories may be of some importance (Table 16.) All blood chemistry results are presented in Table 17.

1. Triglyceride - A significant result (p=0.014) was noted for the "not current" group as compared with controls for mean triglyceride values. Additionally, this group showed a considerable percentage (50%) of abnormal values. That the "not current" group was significantly older than the control group may account for its higher percentage of abnormals. The other exposure groups show no *significant differences from the controls. Nevertheless, there is a higher mean triglyceride value in each of the exposure groups as compared to the controls. This is especially notable in the "25 to 50" group for which one would expect possibly a lower mean triglyceride value than for the control group, considering it is significantly younger. Further study is warranted.*

2. Calcium - The "not current" group showed a significant difference (p=0.008) in its mean serum calcium value (9.4 mg%) as compared with the control group (9.7 mg%). However, the significance of this finding is unclear and further investigation may be indicated.

3. Phosphorus - Again the "not current" group showed a significant difference (p=0.004) for its mean serum phosphorus value (3.3 mg%) as compared with the control group (3.9 mg%). No significant difference, however, was noted in the percent abnormal. The meaning of this difference remains unclear.

4. Serum Glucose - Significant differences of mean values were noted for the "25-50 ppm" exposure group (76 mg%) and the "not current" group (100 mg%), as compared with the control group (91 mg%). Because glucose intolerance is known to increase with age, one might postulate that the higher glucose value in the "not current" group is due to its older age. For the "25-50 ppm" exposure group, the lower mean glucose value might be attributed to its younger age, though a difference of this magnitude (15 mg%) is probably not attributable solely to this factor. Furthermore, the fact that 8 of 29 individuals in the "25-50 ppm" group had abnormally low serum glucose values, whereas none of the 23 controls had a similar finding, makes one suspicious that exposure to MMA may be affecting glucose metabolism in some way. More investigation along this line seems warranted.

5. Blood Urea Nitrogen (BUN) - A significant difference (p=0.011) was noted for the "5-25 ppm" group (16 mg%) as compared with controls (18 mg%). It is uncertain whether this represents a medically significant finding. Further study is necessary.

6. Uric Acid - No significant differences were present for any of the groups.

7. Cholesterol - Mean values in all the exposure groups were notably higher than the control group, and significantly so in all but the "5-25 ppm" group. However, the frequency of abnormal values in all of the groups showed no significant differences from the control group. The difference in mean values may represent an effect of MMA on lipid metabolism. An expanded study along this line would be of value.

8. Total Protein - No significant differences were noted for any of the groups.

9. Albumin - A significant difference (p=0.037) was noted for the mean value in the "25-50 ppm" group (4.6 gm%) as compared with the control group (4.4 gm%). Again, while this finding is significant, its medical significance remains unclear. No significant differences were noted in the frequency of abnormal findings.

10. Total Bilirubin - A significant difference (p=0.008) was present in the "25-50 ppm" group (0.6 mg%) as compared with the control group (0.9 mg%). No significant differences were noted in the frequency of abnormal findings.

11. Alkaline Phosphatase - No significant differences were noted for any of the groups.

12. Lactic Dehydrogenase (LDH) - A significant difference (p=0.010) was present in the "not current" group, its mean value (176 mU/ml) being lower than that of the controls (197 mU/ml). However, this group had less abnormalities than the control group (0% vs. 17%, respectively).

13. Serum Glutamic Oxaloacetic Transaminase (SGOT) - As with LDH, the "not current" group mean (29 mU/ml) was significantly lower (p=0.031) than the control group mean (37 mU/ml). The medical meaning of this difference is not apparent and requires further investigation. No significant differences were noted for the frequency of abnormals.

DISCUSSION

Environmental

The environmental portions of this study and the resultant data are not remarkable. As shown in Table 2, the mean 8-hour time-weighted average exposure to MMA by job category ranged from 4 to 88 ppm at 5 plants. The highest exposure grouping for the workers examined medically was 25 to 50 ppm as none of the subjects who volunteered for the study represented a job category for which the mean exposure was greater than 50 ppm. It would have been particularly beneficial if one of the groups studied had exposures to MMA approximating 100 ppm, the current OSHA standard or the ACGIH Threshold Limit Value. Although a variety of establishments were screened, exposures of this magnitude were not found.

With the exception of one plant using ethyl acrylate, at the time of these studies MMA was the only monomer involved and was the principal contaminant in the plant environments. The presence of other chemicals has a potential of influencing the results, but due to the diversity of such chemicals, determinations of the ambient air levels of each of them were beyond the scope of this study. Also considering the physical properties (especially volatility) and *relatively minor quantities of these other chemicals, it would not be expected that related significant air contamination levels would be reached.*

The control group was essentially not exposed to MMA as documented by air sampling for MMA in those areas where these employees worked.

Medical

In order to assess properly the health effects resulting from MMA exposure, the following questions seem pertinent:

1. *How do the findings of the present study compare with those of past investigations?*

2. *Is there a carcinogenic potential associated with chronic exposure to MMA?*

3. *What, if any, are the acute and the chronic effects of exposure to MMA?*

4. *Is a dose-response relationship evident for acute and chronic effects?*

Before the findings are discussed with regard to those of earlier studies, several remarks should be made. This research, in looking at a wide array of body systems in a rather general way, has attempted to ascertain whether a health problem exists from worker exposure to MMA. In so doing, limitations were present that deserve mention. The exposure groups and control group were small in size. The tests used to evaluate particular areas of concern were sometimes only rough tools by which a system's function could be evaluated - e.g., respiratory system evaluation by forced expiratory maneuvers, renal function by urinalysis, BUN, uric acid, etc. Effects from acute and chronic exposures to MMA concentrations of 50 to 100 ppm, yet still below the current Threshold Limit Value (TLV) were not evaluated. Effects from exposure of female workers to MMA were not investigated. Evaluation of MMA exposure and associated mortality causes, e.g., cardiovascular disease, cancer, was not carried out. Other limitations were present and are alluded to in this report.

The findings of Spealman et al[3] and Diechmann[2] that MMA is a cutaneous sensitizer in man and a skin irritant makes one suspect that skin complaints might be a prominent feature among MMA workers. However, other investigators failed to include this as an area of concern in their papers. Similarly, the present study demonstrated no significant differences between the exposure and control groups for a history of skin and allergic problems. Nevertheless, a considerably greater percentage of individuals in the "25-50 ppm" and "5-25 ppm" groups had a history of these complaints than did the controls.

The acute cardiovascular effects noted in patients with surgically inserted, partially polymerized MMA bone cement[5-9] *do not appear to be present in workers exposed to MMA vapor in this study. Also, no long term effect on blood pressure appeared to be present in the same workers. However, it is not possible to be definitive about the effect of MMA exposure on atherosclerosis and arteriosclerotic heart disease. The findings of Tansy et al*[16] *of an absence of visceral and subcutaneous fat in rats chronically exposed to MMA suggest that fat metabolism may be altered by MMA exposure. The present findings of higher mean triglyceride values in each of the exposure groups as compared to controls, particularly the "25-50 ppm" group since it is younger, lends support to the thesis that MMA affects fat metabolism, which in turn may influence the atherosclerotic process. It is recognized that shift workers can be difficult to control as regards a requested 12 hour pre-shift fasting period. Cholesterol values in the exposure groups, although higher than the control group, nevertheless showed no significant differences for the frequency of abnormal values. An expanded study utilizing larger groups and mortality data could clarify this area.*

The screening survey found no significant evidence of acute airway obstruction occurring in workers exposed to MMA. The later in-depth study looked at chronic effects on respiratory function as noted by history and as measured by FVC, $FEV_{1.0}$, $FEV_{1.0}/FVC$ *ratio and MMF and found none of consequence.*

Whether long term industrial exposure to MMA may lead to hepatotoxic effects remains in question. Whereas Mallory et al[14] *noted mild to moderate liver changes in mice exposed to MMA by direct esophageal instillation, the present study found no significant changes in liver function tests such as alkaline phosphatase, LDH, and SGOT among workers currently exposed to MMA. Two other tests of liver function (total bilirubin and albumin) both showed significant differences in the two highest exposure groups (25-50 ppm and 5-25 ppm). However, these changes were presumably "for the better" with the bilirubin values being lower and the albumin higher than normal.*

Significant gastrointestinal effects did not appear to be present in the current study among workers exposed to MMA. Specifically, the prevalence of such symptoms as anorexia, weight loss, nausea, and vomiting was no more frequent among the various exposure groups than in the control group. The research of Tansy et al[15] *in demonstrating decreased gastric motility in two mammalian species (rats and a dental student) and commenting anecdotally regarding lessened appetites among some dental students working with MMA, makes one suspicious that industrial workers exposed to similar concentrations of MMA may also experience analogous effects. The NIOSH findings, however, do not support such a suspicion.*

Further study of possible urinary tract effects from MMA exposures seems reasonable. This is based upon the suggestion of urinary tract symptomatology found during the screening survey and the considerable percent of pyuria in the "5-25 ppm" exposure group.

The hematologic effects reported by the Russian investigators, Blagodatin et al[23] and Dobrinsky,[24] were not found in this study. As cited earlier, the findings of the screening surveys had suggested that the mean WBC values of workers exposed to MMA were significantly higher than those of a comparable control group. This finding was not borne out in the comprehensive survey. A repeat study using larger groups could clarify this area.

Glucose metabolism in workers exposed to MMA warrants further research. An expanded study to measure serum glucose levels during the workshift of workers exposed to MMA, with a properly matched control group, should be carried out. This would aid in clarifying whether the significantly lower serum glucose levels found in the "25-50 ppm" exposure group are indeed related to MMA exposure and reproducible. If so, then more sophisticated studies looking at pancreatic function and insulin and glucose metabolism might next be in line.

The carcinogenic potential of MMA in humans is unknown. The studies by Laskin et al[17], Oppenheimer et al[18], and Borzelleca et al[20] were conducted on test animals, were inconclusive, and had limitations which prevent their generalization to human exposure. For this reason, it seems appropriate that a properly conducted mortality study of workers occupationally exposed to MMA be carried out to determine the incidence of various neoplasms.

To establish a dose-response relationship for any industrial toxicologic agent is a formidable task, especially when one recognizes all of the variables which exist in the worker and in his/her environment. Under the section "Toxicology Review" in this paper, the work of other researchers has been summarized and an attempt made to formulate such a relationship wherever possible. Having acknowledged a number of limitations, Tables 18 and 19 summarize the data for the acute and chronic effects noted in this study. It is hoped that these findings will prompt further research into the toxicological implications of occupational exposure to MMA.

REFERENCES

1. *Chemical Marketing Reporter. Chemical Profile: Methyl Methacrylate. 209(15):9. April 12, 1976.*

2. *Deichmann, W. Toxicity of Methyl, Ethyl, and N-butyl Methacrylate. J Ind Hyg Toxicol. 23(7):343-351. Sept 1941.*

3. *Spealman, C.R., Main, R.J., Haag, H.B. Monomeric Methyl Methacrylate. Ind. Med. 14:292-298. Apr 1945.*

4. *Harris, D.K. Health Problems in the Manufacture and Use of Plastics. Br J Ind Med. 10:255-268. Oct 1953.*

5. *Bright, D.S., Clark, H.G., McCollum, D.E. Serum Analysis and Toxic Effects of Methyl Methacrylate. Surg Forum. 23:455-458. 1972.*

6. *Pebbles, D.J., Ellis, R.H., Stride, S.D.K., Simpson, B.R.J. Cardiovascular Effects of Methyl Methacrylate Cement. Br Med J. 1:349-351. February 5, 1972.*

7. *Mir, G.N., Lawrence, W.H., Autian, J. Toxicological and Pharmacological Actions of Methacrylate Monomers 1: Effects on Isolated Perfused Rabbit Heart. J Pharm Sci. 62:788-782. May 1973.*

8. *Kim, K.C., Ritter, M.A. Hypotension Associated with Methacrylate in Total Hip Arthroplasties. Clin Orthop. (88):154-160. Oct 1972.*

9. *Kepes, E.R., Underwood, P.S., Becsey,L. Intraoperative Death Associated with Acrilic Bone Cement. J Am Med Assoc 222(5):577-577. Oct 1972.*

10. *Fowler, A.W. "Correspondence" - Methyl Methacrylate Cement and Fat Embolism. Br Med J. 4(5832):108. October 14, 1972.*

11. *Brittain, G.J.C., Ryan, D.J. "Correspondence" - Hypotension and Methyl Methacrylate Cement. Br Med J. 4(5841):667-668. December 16, 1972.*

12. *Ellis, R.H. "Correspondence" - Hypotension and Methyl Methacrylate Cement. Br Med J. 1(5847):236. Jan 1973.*

13. *Hughes, J.D., Convery, F.R., Drucker, J.P. Total Hip Replacement with Polymethacrylate: Lack of Early Effect on Lung Function in Man. Am Rev Respir Dis. 105:665-677. Jun 1972.*

14. *Mallory, T.H., Stone, W.A., St. Piere, R.L. Potential Hepatotoxic Effects of Methyl Methacrylate Monomer. Clin Orthop. (93):366-368. June 1973.*

15. *Tansy, M.F., Benhayem, S., Probst, S., Jordan, J.S. The Effects of Methyl Methacrylate Vapor on Gastric Motor Function. J Am Dent Assoc. 89:372-376. Aug 1974.*

16. Tansy, M.F., Kendall, F.M., Benhaim, S., Hohenleitner, F.J., Landin, W.E., Gold, M. Chronic Biological Effects of Methyl Methacrylate Vapor. Temple University, Philadelphia, Pa. (Preprint).

17. Laskin, D.M., Robinson, I.B., Weinmann, J.P. Experimental Production of Sarcomas by Methyl Methacrylate Implants. Proc Sec Exp Biol Med. 87:329-332, Nov 1954.

18. Oppenheimer, B.S., Oppenheimer, E.T., Danishefsky, I., Stout, A.P., Eirich, F.R. Further Studies of Polymers as Carcinogenic Agents in Animals. Cancer Res. 15(5):333-340. June 1955.

19. Lavorgna, J.J., Burstein, N.A., Schiller, A.L., Harris, W.H. The Carcinogenesis of Plastics Used in Orthopedic Surgery. Clin Orthop. 88:223-227. Oct 1972.

20. Borzelleca, J.F., Larson, P.S., Hennigar, G.R. Jr., Huf, E.G., Crawford, E.M., Smith, R.B. Jr. Studies on the Chronic Oral Toxicity of Monomeric Ethyl Acrylate and Methyl Methacrylate. Toxicol Appl Pharmacol. 6:29-36. Jan 1964.

21. Karpov, B.D. The Effect of Small Concentrations of Methyl Methacrylate Vapors on the Inhibition and Stimulation Processes of the Cortex of the Brain. Trud Leningr Sanit Gig Med Inst. 14:43-48. 1953.

22. Karpov, B.D. Methyl Methacrylate from the Viewpoint of Labor Hygiene. Gig Sanit. 1:25-28. 1954.

23. Raines, L.A. Toxicity of Methacrylate in the Conditions of a Dental Supplies Factory. Gig Tr Prof Zabol. 1:56-57. 1957.

24. Blagodatin, V.M., Golova, I.A., Bladokatkina, N.K., Rumyantseva, Ye.P., Goryacheva, L.A., Aliyeva, N.K., Gronsberg, Ye.Sh., Gig Tr Prof Zabol 14(8):11-14. 1970.

25. Dobrinskij, S.I. Data Concerning Problems of Industrial Hygiene and Occupational Pathology in the Manufacture of Acrylic Polymers. Gig Tr Prof Zabol 14(11): 53-54. 1970.

26. American Conference of Governmental Industrial Hygienists. Threshold Limit Values for Substances in Workroom Air. Adopted by ACGIH for 1963. Cincinnati, Ohio 1963.

27. American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values for Substances in Workroom Air. Ed 3. Cincinnati, Ohio 1971.

28. *U.S. Department of Labor, Occupational Safety and Health Administration. OSHA Safety and Health Standards (29 CFR 1910). OSHA 2206 (Revised January 1976) p. 507.*

29. *Crable, J.V., and Taylor, D.G. NIOSH Manual of Analytical Methods. U.S. Department of Health, Education and Welfare, Cincinnati, Ohio. Publication Number (NIOSH) 75-121. 1974. p.127-1 to 127-11.*

30. *U.S. Department of Health, Education, and Welfare. National Health Survey. Blood Pressure of Persons 18-74 years, United States, 1971-72. Publication Number (HRA) 75-1632. Series 11. No. 150. Rockville, Md. April 1975.*

31. *Kory, R.C., Callahan, R., Boren, H.G., and Syner, J.C. The Veterans Administration - Army Cooperative Study of Pulmonary Function. Am J Med. 30(2)243-258. Feb 1961.*

32. *Lapp, N.L., Amandus, H.E., Hall, R., and Morgan, W.K.C., Lung Volumes and Flow Rates in Black and White Subjects. Thorax. 29(2)185-188. Mar 1974.*

TABLE 1

RESULTS OF SCREENING SURVEYS FOR METHYL METHACRYLATE EXPOSURES AT VARIOUS MANUFACTURING FACILITIES

Type of Facility	Approximate Number of Exposed Workers	Approximate Time-Weighted Average Exposures to Methyl Methacrylate (ppm)*
Monomer Production	30	< 5.0
Monomer Production	50	< 5.0
Refining	10	10
Resin Mfg.	50	< 5.0
Resin Mfg.	35	< 5.0
Resin Mfg.	30	< 1.0
Resin Mfg.	10	< 5.0
Resin Mfg.	25	< 5.0
Sheet Mfg.	5	15.0
Sheet Mfg.	9	30 to 50
Sheet Mfg.	10	10 to 50
Sheet Mfg.	25	40 to 130
Sheet Mfg.	40	10 to 40
Sheet Mfg.	45	20 to 40
Reinforced Sheet Mfg.	10	2 to 40
Lens Mfg.	5	5 to 10
Lens Mfg.	135	< 1.0
Ornament Mfg.	3	20 to 90
Acrylic Coated Products	4	< 50.0
Dental Laboratory	1	< 5.0
Dental Laboratory	1	10.0
Dental Laboratory	2	5.0
Dental Laboratory	4	5.0
Dental Laboratory	3	< 5.0
Dental Laboratory	3	< 5.0
Dental Laboratory	3	< 5.0
Dental Laboratory	4	< 5.0

*Parts of methyl methacrylate per million parts of air by volume

TABLE 2

RESULTS OF AIR SAMPLING, BY JOB CATEGORY, FOR METHYL METHACRYLATE AND ETHYL ACRYLATE IN FIVE SHEET PLANTS DURING MAY 1975

Plant	Job Category	Number of Men Sampled	Mean Sample Times (hrs.)	8-Hour Time-Weighted Average Exposures to MMA (ppm)*			8-Hour Time-Weighted Average Exposures to EA (ppm)*		
				Mean	Range	S.D.**	Mean	Range	S.D.**
A	Weigh-out	3	5.5	10	3 to 20	8.7	0.5	0.2 to 1.2	0.7
	Mix Men	9	6.4	43	25 to 68	16.9	2.0	0.3 to 4.7	1.5
	Mold Fillers	9	5.7	19	15 to 24	2.6	0.7	0.2 to 1.6	0.6
	Relief	3	5.7	21	6 to 44	20.9	1.3	0.4 to 2.8	1.3
B	All Employees	13	4.7	4	1 to 12	3.9			
C	Mix Men	6	6.3	49	16 to 90	25.9			
	Mold Fillers	2	6.6	31	22 to 40	12.7			
	Mold Makers	10	6.5	4	1 to 8	2.2			
D	Mix Men	15	7.2	16	6 to 35	10.0			
	Mold Fillers	40	7.1	37	10 to 84	17.5			
	Helpers	8	6.1	20	7 to 41	12.6			
	Foremen	3	6.4	19	13 to 22	5.1			
E	Mix Men	27	6.0	49	11 to 145	26.6			
	Mold Fillers	12	6.0	15	8 to 26	4.9			
	Distillers	4	5.3	88	25 to 174	49.8			
	Maintenance	5	5.1	4	1 to 8	2.3			

* Parts of methyl methacrylate or ethyl acrylate per million parts of air by volume

** Standard Deviation

TABLE 3

RESULTS OF AIR SAMPLING FOR METHYL METHACRYLATE AND ETHYL ACRYLATE IN WORK AREAS WHERE THE CONTROL GROUP SUBJECTS WERE EMPLOYED

	Number of Work Areas Sampled	Number of Samples	Mean Sample Time (hrs.)	Number of Samples Below 0.3 ppm*	Number of Samples above 0.3 ppm	
					Number	Average (ppm)*
Methyl Methacrylate	12	20	3.1	19	1	0.8
Ethyl Acrylate	6	8	3.2	8		

*Parts of methyl methacrylate or ethyl acrylate per million parts of air by volume

TABLE 4

DIFFERENCES BETWEEN MEAN AGES OF EXPOSURE GROUPS

Group	n*	Mean Age	Statistical Significance Control vs. Exposed
Control	41	45.4	---
Exposed - 25-50 ppm	33	35.3	$p = < 0.001$
- 5-25 ppm	20	40.3	NS**
- under 5 ppm	13	41.5	NS
Not currently exposed	25	51.0	$p = 0.025$

TABLE 5

DIFFERENCES BETWEEN PROPORTIONS CURRENTLY SMOKING FOR THE EXPOSURE GROUPS

Group	n	Proportion Smoking %	Statistical Significance Control vs. Exposed
Control	41	39	---
Exposed - 25-50 ppm	33	45	NS
- 5-25 ppm	20	70	$p = 0.044$
- under 5 ppm	13	62	NS
Not currently exposed	25	48	NS

* n = Number of Subjects
** NS = Not Significant ($p > 0.05$)

TABLE 6

FREQUENCY OF DEVELOPING SYMPTOMATOLOGY DURING THE WORKDAY FOR THE EXPOSURE GROUPS

Symptom and Group	n*	Symptom Developed	Symptom Improved	No Change
Nose and Throat				
Control	35	0	2	33
Exposed - 25-50 ppm	24	0	1	23
- 5-25 ppm	13	0	0	13
- under 5 ppm	9	1	1	7
Not currently exposed	18	0	1	17
Head				
Control	35	0	0	35
Exposed - 25-50 ppm	24	1	0	23
- 5-25 ppm	13	0	0	13
- under 5 ppm	9	1	0	8
Not currently exposed	18	0	1	17
Eye				
Control	35	0	0	35
Exposed - 25-50 ppm	24	0	1	23
- 5-25 ppm	13	0	0	13
- under 5 ppm	9	0	0	9
Not currently exposed	18	0	0	18
Chest				
Control	35	1	0	34
Exposed - 25-50 ppm	24	0	1	23
- 5-25 ppm	13	0	1	12
- under 5 ppm	9	0	1	8
Not currently exposed	18	0	1	17
Gastro-intestinal				
Control	35	0	0	35
Exposed - 25-50 ppm	24	0	2	22
- 5-25 ppm	13	0	0	13
- under 5 ppm	9	0	0	9
Not currently exposed	18	0	0	18

*n = Number of Subjects

TABLE 7

PRE- AND POST-SHIFT BLOOD PRESSURE AND PULSE DETERMINATIONS
FOR THE EXPOSURE GROUPS

Group	n*	Means Pre Shift	Means Post Shift	Difference, Post-Pre	Statistical Significance of Post-Pre Shift Means, Control vs. Exposed
Systolic					
Control	25	136	127	-9	---
Exposed - 25-50 ppm	20	124	120	-4	NS**
- 5-25 ppm	8	125	123	-2	NS
- under 5 ppm	7	136	129	-7	NS
Not currently exposed	15	132	126	-6	NS
Diastolic					
Control	25	82	78	-4	---
Exposed - 25-50 ppm	20	72	70	-2	NS
- 5-25 ppm	8	74	72	-2	NS
- under 5 ppm	7	81	82	+1	NS
Not currently exposed	15	78	77	-1	NS
Pulse Rate					
Control	27	74	77	+3	---
Exposed - 25-50 ppm	22	77	74	-3	NS
- 5-25 ppm	10	75	77	+2	NS
- under 5 ppm	8	70	72	+2	NS
Not currently exposed	16	71	75	+4	NS

* n = Number of Subjects
** NS = Not Significant ($p > 0.05$)

TABLE 8

STATISTICAL SIGNIFICANCE OF SELECTED SYMPTOMS
FOR THE EXPOSURE GROUPS

	n	One or More Positive Responses: Frequency	One or More Positive Responses: Percent	Statistical Significance Control vs. Exposed
Cough				
Control	43	3	7	---
Exposed - 25-50 ppm	33	5	15	NS**
- 5-25 ppm	20	4	20	NS
- under 5 ppm	13	3	23	$p = 0.029$
Not currently exposed	25	3	12	NS
Expectoration				
Control	43	6	14	---
Exposed - 25-50 ppm	33	7	21	NS
- 5-25 ppm	20	10	50	$p = 0.006$
- under 5 ppm	13	3	23	NS
Not currently exposed	25	8	32	NS
Hepatic & GI				
Control	43	8	19	---
Exposed - 25-50 ppm	33	9	27	NS
- 5-25 ppm	20	3	15	NS
- under 5 ppm	13	1	8	NS
Not currently exposed	25	8	32	NS
Skin & Allergic				
Control	43	6	14	---
Exposed - 25-50 ppm	33	10	30	NS
- 5-25 ppm	20	5	25	NS
- under 5 ppm	13	0	---	NS
Not currently exposed	25	3	12	NS
Nervous System				
Control	43	10	23	---
Exposed - 25-50 ppm	33	15	46	NS
- 5-25 ppm	20	10	50	NS
- under 5 ppm	13	6	46	NS
Not currently exposed	25	11	44	NS
Urinary Tract				
Control	43	20	47	---
Exposed - 25-50 ppm	33	14	42	NS
- 5-25 ppm	20	11	55	NS
- under 5 ppm	13	8	62	NS
Not currently exposed	25	10	40	NS

* n = Number of subjects
** NS = Not significant ($p > 0.05$)

TABLE 9

BLOOD PRESSURE (mm Hg)
COMPARISONS OF OBSERVED WITH PREDICTED[30] FOR EXPOSURE GROUPS

The predicted blood pressure values are from the National Center for Health Statistics nationwide Health Examination study and are age-sex-color specific.

Group	n*	Means: Predicted	Means: Observed	Means: P-O	Statistical Significance of P - O Means Control vs. Exposed
Systolic					
Control	40	131	127	4	---
Exposed - 25-50 ppm	33	128	125	3	NS**
- 5-25 ppm	19	130	129	1	NS
- under 5 ppm	10	128	127	1	NS
Not currently exposed	23	135	129	6	NS
Diastolic					
Control	40	84	80	4	---
Exposed - 25-50 ppm	33	82	75	7	NS
- 5-25 ppm	19	83	78	5	NS
- under 5 ppm	10	82	77	5	NS
Not currently exposed	23	86	79	7	NS

* n = Number of subjects

**NS = Not significant ($p > 0.05$)

TABLE 10

FORCED VITAL CAPACITY (LITERS)
COMPARISONS OF OBSERVED WITH PREDICTED[31,32] FOR EXPOSURE GROUPS

Group	n*	Means Predicted	Means Observed	P-O	Statistical Significance of P - O Means Control vs. Exposed
Smokers					
Control	15	4.57	4.89	-0.32	---
Exposed - 25-50 ppm	15	4.95	5.14	-0.19	NS**
- 5-25 ppm	15	4.79	5.38	-0.59	NS
- under 5 ppm	8	4.83	4.78	0.05	NS
Not currently exposed	12	4.47	4.96	-0.49	NS
Non-Smokers					
Control	25	4.68	4.86	-0.18	---
Exposed - 25-50 ppm	18	4.71	5.13	-0.42	NS
- 5-25 ppm	6	4.72	4.82	-0.10	NS
- under 5 ppm	5	4.42	4.72	-0.30	NS
Not currently exposed	13	4.39	4.53	-0.13	NS

TABLE 11

FORCED EXPIRATORY VOLUME IN ONE SECOND (Liters/Sec)
COMPARISONS OF OBSERVED WITH PREDICTED[31,32] FOR EXPOSURE GROUPS

Group	n	Means Predicted	Means Observed	P-O	Statistical Significance of P - O Means Control vs. Exposed
Smokers					
Control	15	3.63	3.53	0.10	---
Exposed - 25-50 ppm	15	4.05	3.90	0.15	NS
- 5-25 ppm	14	3.82	4.04	-0.22	NS
- under 5 ppm	8	3.90	4.00	-0.10	NS
Not currently exposed	12	3.50	3.60	-0.10	NS
Non-Smokers					
Control	25	3.69	3.67	0.02	---
Exposed - 25-50 ppm	18	3.85	4.13	-0.28	NS
- 5-25 ppm	6	3.83	3.85	-0.02	NS
- under 5 ppm	5	3.49	3.60	-0.11	NS
Not currently exposed	13	3.41	3.25	0.16	NS

* n = Number of subjects
** NS = Not significant ($p > 0.05$)

TABLE 12

$FEV_{1.0}$/FVC RATIO (%)
COMPARISONS OF OBSERVED WITH PREDICTED[31,32] FOR EXPOSURE GROUPS

Group	n*	Mean Predicted	Mean Observed	P-O	Statistical Significance of P - O Means Control vs. Exposed
Smokers					
Control	15	66.5	71.5	-6.0	---
Exposed - 25-50 ppm	15	67.6	76.1	-8.5	NS**
- 5-25 ppm	14	65.9	75.6	-9.7	NS
- under 5 ppm	8	66.8	83.6	-16.8	p = 0.001
Not currently exposed	12	64.4	71.4	-8.0	NS
Non-Smokers					
Control	25	65.0	75.1	-10.1	---
Exposed - 25-50 ppm	18	67.2	80.3	-13.1	NS
- 5-25 ppm	6	67.1	79.8	-12.7	NS
- under 5 ppm	5	64.8	76.1	-11.3	NS
Not currently exposed	13	63.9	70.8	-9.9	NS

TABLE 13

MAXIMAL MIDEXPIRATORY FLOW (L/Sec)
COMPARISONS OF OBSERVED WITH PREDICTED[31,32] FOR EXPOSURE GROUPS

Group	n	Mean Predicted	Mean Observed	P-O	Statistical Significance of P - O Mean Control vs. Exposed
Smokers					
Control	15	4.07	2.96	1.11	---
Exposed - 25-50 ppm	15	4.41	3.43	0.98	NS
- 5-25 ppm	14	4.19	3.51	0.68	NS
- under 5 ppm	8	4.37	4.43	-0.06	NS
Not currently exposed	12	3.91	2.75	1.16	NS
Non-Smokers					
Control	25	4.04	3.18	0.86	---
Exposed - 25-50 ppm	18	4.37	4.19	0.18	NS
- 5-25 ppm	6	4.37	4.03	0.34	NS
- under 5 ppm	5	3.99	3.47	0.52	NS
Not currently exposed	13	3.87	2.90	0.97	NS

* n = Number of subjects
** NS = Not significant ($p > 0.05$)

TABLE 14

MEAN WHITE BLOOD CELL COUNTS BY EXPOSURE GROUP

Exposure Group	Mean White Blood Cell Count
25-50 ppm	6.9×10^3 cells/mm^3
5-25 ppm	7.8×10^3 cells/mm^3
under 5 ppm	7.4×10^3 cells/mm^3
not currently exposed	6.8×10^3 cells/mm^3

TABLE 15

STATISTICAL SIGNIFICANCE OF URINALYSIS RESULTS BY EXPOSURE GROUP

	n*	Frequency Abnormal	Percent Abnormal	Statistical Significance of Percent Abnormals Not Current vs. Other Exposed
WBC/HPF**				
Exposed - 25-50 ppm	31	7	23	NS***
- 5-25 ppm	17	6	35	NS
- under 5 ppm	12	2	17	NS
Not currently exposed	19	1	5	---
RBC/HPF*				
Exposed - 25-50 ppm	31	0	--	NS
- 5-25 ppm	17	1	6	NS
- under 5 ppm	12	1	8	NS
Not currently exposed	19	0	--	---
Protein				
Exposed - 25-50 ppm	31	0	--	NS
- 5-25 ppm	17	2	12	NS
- under 5 ppm	12	0	--	NS
Not currently exposed	19	1	5	---
Glucose				
Exposed - 25-50 ppm	31	0	--	NS
- 5-25 ppm	17	0	--	NS
- under 5 ppm	12	0	--	NS
Not currently exposed	19	1	5	---

*n - Number of subjects
**WBC - white blood cells
HPF - high power field
RBC - red blood cells
***NS - Not Significant ($p > 0.05$)

TABLE 16

RANGES OF NORMAL FOR EACH BLOOD TEST GIVEN BY THE THREE CONTRACT LABORATORIES EMPLOYED IN THIS STUDY

	Triglyceride (mg %)	Calcium (mg %)	Phosphorus (mg %)	Glucose (mg %)	BUN (mg %)
Lab 1	30-180	8.5-10.5	2.5-4.5	70-120	10-20
Lab 2	30-170	8.5-10.5	2.5-4.5	65-110	10-20
Lab 3	30-170	8.3-10.8	2.5-5.0	65-110	6-22

	Uric Acid (mg %)	Cholesterol (mg %)	Total Protein (gm %)	Albumin (gm %)
Lab 1	2.5-8.0	150-300	6.0-8.0	3.5-5.0
Lab 2	2.5-8.0	150-300	6.0-8.0	3.5-5.0
Lab 3	2.4-7.8	150-275	6.0-8.0	3.5-5.5

	Total Bilirubin (mg %)	Alkaline Phosphatase (mU/ml)	LDH (mU/ml)	SGOT (mU/ml)
Lab 1	0.15-1.0	30-85	100-225	7.5-40
Lab 2	0.15-1.0	30-85	100-225	10-50
Lab 3	0.10-1.2	30-110	100-225	10-60

TABLE 17

STATISTICAL SIGNIFICANCE OF BLOOD CHEMISTRY RESULTS BY EXPOSURE GROUP

	n*	Mean	Statistical Significance of Mean Values Control vs. Exposed	Frequency Abnormal High	Frequency Abnormal Low	Percent Abnormal	Statistical Significance of Percent Abnormals Control vs. Exposed
Triglyceride (mg %)							
Control	23	126	---	5	0	22	---
Exposed - 25-50 ppm	29	172	NS*	12	0	41	NS
- 5-25 ppm	19	210	NS	7	0	37	NS
- under 5 ppm	12	167	NS	4	0	33	NS
Not currently exposed	22	186	$p = 0.014$	11	0	50	NS
Calcium (mg %)							
Control	23	9.7	---	0	0	---	---
Exposed - 25-50 ppm	29	9.6	NS	0	0	---	NS
- 5-25 ppm	19	9.7	NS	1	0	5	NS
- under 5 ppm	12	9.4	NS	0	1	8	NS
Not currently exposed	22	9.4	$p = 0.008$	0	0	---	NS
Phosphorus (mg %)							
Control	23	3.9	---	1	0	4	---
Exposed - 25-50 ppm	29	3.8	NS	2	0	7	NS
- 5-25 ppm	19	3.6	NS	0	1	5	NS
- under 5 ppm	19	3.6	NS	0	0	---	NS
Not currently exposed	22	3.3	$p = 0.004$	0	3	14	NS
Serum Glucose (mg %)							
Control	23	91	---	2	0	9	---
Exposed - 25-50 ppm	29	76	$p = 0.001$	0	8	28	NS
- 5-25 ppm	19	89	NS	1	1	10	NS
- under 5 ppm	12	92	NS	0	1	8	NS
Not currently exposed	22	100	$p = 0.003$	1	0	4	NS
BUN (mg %)							
Control	23	18	---	2	0	9	---
Exposed - 25-50 ppm	29	17	NS	3	0	10	NS
- 5-25 ppm	19	16	$p = 0.011$	3	0	--	NS
- under 5 ppm	12	16	NS	1	1	17	NS
Not currently exposed	22	17	NS	3	0	14	NS

TABLE 17 (Cont)

STATISTICAL SIGNIFICANCE OF BLOOD CHEMISTRY RESULTS BY EXPOSURE GROUP

	n*	Mean	Statistical Significance of Mean Values Control vs. Exposed	Frequency Abnormal High	Frequency Abnormal Low	Percent Abnormal	Statistical Significance of Percent Abnormals Control vs. Exposed
Uric Acid (mg %)							
Control	23	6.6	---	3	0	13	---
Exposed - 25-50 ppm	29	6.4	NS	1	0	3	NS**
- 5-25 ppm	19	6.4	NS	2	0	10	NS
- under 5 ppm	12	6.3	NS	2	0	17	NS
Not currently exposed	22	6.4	NS	0	0	--	NS
Cholesterol (mg %)							
Control	23	190	---	0	2	9	---
Exposed - 25-50 ppm	29	211	$p = 0.043$	1	1	7	NS
- 5-25 ppm	19	206	NS	1	1	10	NS
- under 5 ppm	12	220	$p = 0.015$	1	0	8	NS
Not currently exposed	22	224	$p = 0.001$	0	1	4	NS
Total Protein (gm %)							
Control	23	7.3	---	0	0	--	---
Exposed - 25-50 ppm	29	7.4	NS	1	0	3	NS
- 5-25 ppm	19	7.4	NS	1	0	5	NS
- under 5 ppm	12	7.5	NS	2	0	17	NS
Not currently exposed	22	7.2	NS	1	0	4	NS
Albumin (gm %)							
Control	23	4.4	---	0	0	--	---
Exposed - 25-50 ppm	29	4.6	$p = 0.037$	3	0	10	NS
- 5-25 ppm	19	4.6	NS	1	0	5	NS
- under 5 ppm	12	4.5	NS	0	0	--	NS
Not currently exposed	22	4.5	NS	0	0	--	NS

TABLE 17 (Cont)

STATISTICAL SIGNIFICANCE OF BLOOD CHEMISTRY RESULTS BY EXPOSURE GROUP

	n	Mean	Statistical Significance of Mean Values Control vs. Exposed	Frequency Abnormal High	Frequency Abnormal Low	Percent Abnormal	Statistical Significance of Percent Abnormals Control vs. Exposed
Total Bilirubin (mg %)							
Control	23	.9	---	3	0	13	---
Exposed - 25-50 ppm	29	.6	$p = 0.008$	0	0	--	NS
- 5-25 ppm	19	.7	NS	1	0	5	NS
- under 5 ppm	12	.9	NS	3	0	25	NS
Not currently exposed	22	.7	NS	3	0	14	NS
Alkaline Phosphatase (mU/ml)							
Control	23	57	---	0	0	--	---
Exposed - 25-50 ppm	29	61	NS	0	1	3	NS
- 5-25 ppm	19	63	NS	1	0	5	NS
- under 5 ppm	12	62	NS	0	0	--	NS
Not currently exposed	22	62	NS	1	0	4	NS
LDH (mU/ml)							
Control	23	197	---	4	0	17	---
Exposed - 25-50 ppm	29	203	NS	5	0	17	NS
- 5-25 ppm	19	189	NS	1	0	5	NS
- under 5 ppm	12	186	NS	1	0	8	NS
Not currently exposed	22	176	$p = 0.010$	0	0	--	NS
SGOT (mU/ml)							
Control	23	37	---	0	0	--	---
Exposed - 25-50 ppm	29	37	NS	2	0	7	NS
- 5-25 ppm	19	36	NS	0	0	--	NS
- under 5 ppm	12	34	NS	2	0	17	NS
Not currently exposed	22	29	$p = 0.031$	1	0	4	NS

* n = Number of subjects

**NS = Not significant ($p > 0.05$)

TABLE 18

SUMMARY OF ACUTE HEALTH EFFECTS BY EXPOSURE GROUP

	Current Exposure		
	5 ppm or <2 months	5-25 ppm	25-50 ppm
(1) All symptomatology	(-)	(-)	(-)
(2) Blood Pressure	(-)	(-)	(-)
(3) Pulse	(-)	(-)	(-)

(-) = Not significantly different than the control group.

TABLE 19

SUMMARY OF CHRONIC HEALTH EFFECTS BY EXPOSURE GROUP

	Not Currently Exposed	Current Exposure: 5 ppm or <2 months	Current Exposure: 5-25 ppm	Current Exposure: 25-50 ppm
(1) Past Symptomatology				
(a) Cough	(-)	(a)	(-)	(-)
(b) Expectoration	(-)	(-)	(a)	(-)
(c) Hepatic & G.I.	(-)	(-)	(-)	(-)
(d) Skin & Allergic	(-)	(-)	(b)	(b)
(e) Urinary Tract	(-)	(-)	(-)	(-)
(f) Nervous System	(-)	(-)	(b)	(b)
(2) Blood Pressure	(-)	(-)	(-)	(-)
(3) Pulmonary Function Tests				
Smokers				
FVC	(-)	(-)	(-)	(-)
$FEV_{1.0}$	(-)	(-)	(-)	(-)
$FEV_{1.0}/FVC$	(-)	(a)	(-)	(-)
MMF	(-)	(-)	(-)	(-)
Non-Smokers				
FVC	(-)	(-)	(-)	(-)
$FEV_{1.0}$	(-)	(-)	(-)	(-)
$FEV_{1.0}/FVC$	(-)	(-)	(-)	(-)
MMF	(-)	(-)	(-)	(-)
(4) Hemoglobin	(-)	(-)	(-)	(-)
(5) White Blood Cell Count	(-)	(-)	(-)	(-)
(6) Urinalysis				
RBC/HPF-Protein-Glucose	(-)	(-)	(-)	(-)
WBC/HPF	(-)	(-)	(b)	(-)
(7) Blood Chemistry				
Triglyceride	(a)	(b)	(b)	(b)
Calcium	(a)	(-)	(-)	(-)
Phosphorus	(a)	(-)	(-)	(-)
Serum Glucose	(a)	(-)	(-)	(a)

TABLE 19 (Cont)

SUMMARY OF CHRONIC HEALTH EFFECTS BY EXPOSURE GROUP

	Not Currently Exposed	Current Exposure: 5 ppm or <2 months	Current Exposure: 5-25 ppm	Current Exposure: 25-50 ppm
BUN	(-)	(-)	(a)	(-)
Uric Acid	(-)	(-)	(-)	(-)
Cholesterol	(a)	(a)	(b)	(a)
Total Protein	(-)	(-)	(-)	(-)
Albumin	(-)	(-)	(-)	(a)
Total Bilirubin	(-)	(-)	(-)	(a)
Alkaline Phosphatase	(-)	(-)	(-)	(-)
LDH	(a)	(-)	(-)	(-)
SGOT	(a)	(-)	(-)	(-)

(-) = Not significantly different from the control group.
(a) = Statistical significance present as compared to the control group. Further study needed.
(b) = Not statistically significantly different from the control group. However, further investigation possibly warranted (see text).

APPENDIX I. SCREENING SURVEY MEDICAL QUESTIONNAIRE

DATE____________________
COMPANY____________________
I.H.____________________

SCREENING QUESTIONNAIRE

INSTRUCTIONS: Please answer all of the questions below as best as you can.

1. NAME____
(First) (Middle Initial) (Last)

JOB TITLE______________________________ SHIFT__________

DESCRIPTION OF WORK DUTIES______________________________

ADDRESS____
(Street)

____
(City) (State) (Zip Code)

AGE__________ SEX________

2. OCCUPATIONAL WORK HISTORY:
(Please list all of the jobs you have had since finishing school. Include only the jobs where you worked 1 year or more. Start with your present job.)

	COMPANY	JOB DESCRIPTION	MONTH/YEAR BEGAN	MONTH/YEAR ENDED
(Example:	Ryerson Fiberglass	Maintenance of mold mach.	7/70	Present
	Central Warehouse	Stockroom work	8/68	7/70
	etc.)			
	(continue on other side if necessary)			

3. Do you have any health complaints or problems at work or you feel might be related to your work? Yes___ No___
If "yes", list your symptoms, when they occur, what they seemed to be caused by, how long they have been present.

____
____
____

When was the last time you had this problem?____________________

____

4. Do you have any other health problems? Yes___ No___
If "yes," list the symptoms, when they occur, how often they occur, and how long you have had them.

____

____

Have you seen a doctor about them? Yes___ No___
If "yes," whatdid he say the problem was.

____

5. Are you a: Non-Smoker?_____ Ex-Smoker?______ Smoker?_______
If "smoker" or "ex-smoker":
Type?______________________________
How much___________________________
How long___________________________
When did you quit? (year)__________________________

6. Since you have been working at this plant, have you noticed:

	YES	NO	DESCRIBE (If more space needed write below or on back
a-Shortness of breath?			
b-Chronic cough?			
c-Phlegm or mucus?			
d-Pain or burning on urination?			
e-Dark colored or bloody urine?			
f-Frequent urination?			
g-Frequent nausea & vomiting?			
h-Loss of appetite?			
i-Upper abdominal pain?			
j-Rash or other skin problem?			
k-Dizziness?			
l-Frequent severe headaches?			
m-Problems with your memory?			
n-Problems with your coordination?			

o-Other problems?

7. Has your doctor ever told you that you had:

	YES	NO	DESCRIBE
a. Kidney or bladder infection?			
b. Hepatitis?			
c. High blood pressure?			
d. Low blood pressure?			

MEDICAL QUESTIONNAIRE

A. Identification

1. Name____
2. Address:____
3. Phone Number____
4. Birthdate:_______________________ 5. Age_____________
6. Sex__________ 7. Race: ___W ___B _______Other
8. Standing height: _____in. 9. Weight: ______lbs.

B. Occupational History

I am now going to ask you about the jobs you have held since you started to work regularly. I would like to start with your present job and go back to the first.

1. In what year did you start working here?_____________________
2. What exactly is your main job? (include how you are exposed to methylmethacrylate)

   Describe it____

   ____

   ____
3. In which department do you work?_____________________________
4. How many years have you worked at this job?__________________

(For the present job, enter employer and location on first line of occupational history table.)

B. OCCUPATIONAL HISTORY TABLE

Complete the following table showing the entire work history of the individual from present to initial employment. Sporadic, part-time periods of employment (6 months or less) should be grouped if possible.

Employer & Location	Tenure of Employment From Mo./Yr.	To Mo./Yr.	Specific Occupation or Job title	Ave. # of days worked per week	Average Hrs. Per Day	No./ years on Job
		Present		OMIT	OMIT	
48						

5. Have you had prolonged or repeated exposure to any of the following? (If "Yes," then describe below)

a. Asbestos (insulation, car undercoating, brake line, fire proofing building)	Yes___	No___
b. Radioactive material (uranium, radon gas, ores)	Yes___	No___
c. Arsenic (powder, insecticide, sheep dip, spray, ores)	Yes___	No___
d. Nickel or Chromium (manufacture or refining)	Yes___	No___
e. Iron and Silica (hemalite mine, foundry, sand blast, metal grinding)	Yes___	No___
f. Petroleum products (gas retorts, distillation)	Yes___	No___
g. Very dusty environment (coal mining, etc.)	Yes___	No___
h. Lead, (Storage battery repair plant, dyes, rubber factory, paint manufacturing, mercury)	Yes___	No___
i. Other________________________________	Yes___	No___

____

____

____

C. GENERAL SYMPTOMS

I am now going to ask you some questions, mainly about your chest. I would like you to answer "YES" or "NO" whenever possible.

COUGH

1. Do you usually cough first thing in the morning (on getting up*) in the winter? YES____ NO____

    Count a cough with first smoke or on first going out of doors. Exclude clearing throat or a single cough

2. Do you usually cough during the day (or at night*) in the winter? YES____ NO____

    Ignore an occasional cough.

    If "No" to both questions 1 and 2, go to question 4.

    If "Yes" to either question 1 or 2.

3. Do you cough like this on most days (or nights*) for as much as three months each year? YES____ NO____

PHLEGM

4. Do you usually bring up any phlegm from your chest first thing in the morning (on getting up*) in the winter? YES____ NO____

    Count phlegm with first smoke or on first going out of doors. Exclude phlegm from the nose. Count swallowed phlegm.

5. Do you usually bring up any phelgm from your chest during the day (or at night*) in the winter? YES____ NO____

    Accept twice or more.

    If "No" to both questions 4 and 5, go to question 7.

    If "Yes" to either question 4 or 5

6. Do you bring up phlegm like this on most days (or nights*) for as much as three months each year? YES____ NO____

7. In the past three years have you had a period of (increased**) cough and phlegm lasting for three weeks or more? YES____ NO____

If "No" to question 7 go to question 9.

If "Yes" to question 7.

8. Have you had more than one such period? YES____ NO____

BREATHLESSNESS

9. Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill? YES____ NO____ Disabled______

If "No" or "Disabled" to question 9 go to question 12.

If "Yes" to question 9.

10. Do you get short of breath walking with other people of your own age on level ground? YES____ NO____

If "No" to question 10, go to question 12.

If "Yes" to question 10.

11. Do you have to stop for breath when walking at your own pace on level ground? YES____ NO____

WHEEZING

12. Does your chest ever sound wheezing or whistling? YES____ NO____

If "No" to question 12 to go question 14.

If "Yes" to question 12.

13. Do you get this most days--or nights? YES____ NO____

14. Have you ever had: (✓or 0)

a. An injury or operation affecting your chest? ____

b. Heart trouble? ____

c. Bronchitis? ____

d. Pneumonia? ____

e. Pulmonary TB? ____

f. Bronchial asthma ____

g. Emphysema? ____

h. Other chest problems? ____________

(Expound on any (+) findings)

____

____

____

15. Do you have any present problems for which you are seeing a doctor?

Yes___ No___ If yes, what are they? ______________________

____

____

16. Are you presently taking any medication? Yes___ No___

if yes, what medication? ______________________________

(Circle ave or ad) 17. Do you have or have you had any allergies in the past? Yes___ No___

If yes, what are they? ______________________________

If present or past, did you have this before working in the plant?

Yes___ No____

SMOKING HISTORY

18. Are you presently:

a. a cigarette smoker? Yes___ No___ How Much__________How Long________

b. a cigar smoker? Yes___ No___ How Much__________How Long________

c. a pipe smoker? Yes___ No___ How Much__________How Long________

19. Were you ever:

a. a cigarette smoker? Yes___ No___ How Much__________How Long________

b. a cigar smoker? Yes___ No___ How Much__________How Long________

c. a pipe smoker? Yes___ No___ How Much__________How Long________

RENAL

Have you ever had (or do you have) any of the following? (if "yes," have worker describe below)

20. Pain or burning on urination? Yes___ No___
21. Blood in the urine? Yes___ No___
22. Pain in your flanks? Yes___ No___
23. History of kidney stones? Yes___ No___
24. Swelling of the eye lids or face? Yes___ No___
25. Kidney infections? Yes___ No___
26. History of kidney disease? Yes___ No___
27. High blood pressure? Yes___ No___
28. Low blood pressure? Yes___ No___

____

____

____

____

____

HEPATIC

Have you ever had (or do you have) any of the following?

29. Yellow skin (jaundice)? Yes___ No___
30. Abdominal pain? Yes___ No___
31. Swelling of the abdomen? Yes___ No___
32. Light colored stools? Yes___ No___
33. Diagnosis of "hepatitis"? Yes___ No___
34. A blood transfusion? Yes___ No___
35. Frequent nausea and/or vomiting? Yes___ No___
36. Recent weight loss? Yes___ No___
37. Loss of appetite? Yes___ No___
38. Alcohol ingestion? Yes___ No___
    Amount & Type____

SKIN AND ALLERGIES

Do you have:

39. Any history of skin disease? Yes___ No___ Type______________________
    When diagnosed?____
40. Any rash or other skin lesions? Yes___ No___
    Describe lesion____
    ____

NEUROLOGICAL

Do you have any of the following:
(Describe below)

41. Dizziness Yes___ No___
42. Fainting Yes___ No___
43. Crying Spells Yes___ No___
44. Problems with coordination Yes___ No___
45. "Shakiness" (Tremor of extremities) Yes___ No___
46. Tingling in hands or feet Yes___ No___
47. Trouble talking Yes___ No___
48. Feel sad a lot Yes___ No___
49. Drowsiness Yes___ No___
50. Problems with memory Yes___ No___

Describe____
____
____
____
____

☆USGPO: 1976 — 757-057/5717 Region 5-II

BIBLIOGRAPHIC DATA SHEET

1. Report No. NIOSH-77-119

2.

3. Recipient's Accession No. [illegible]274789

4. Title and Subtitle

A STUDY OF METHYL METHACRYLATE EXPOSURE AND EMPLOYEE HEALTH

5. Report Date Nov. 1976

6.

7. Author(s)

J. Cromer, M.C., and Kenneth Kronoveter, M.S.

8. Performing Organization Rept. No.

9. Performing Organization Name and Address

National Institute for Occupational Safety and Health
4676 Columbia Parkway
Cincinnati, Ohio 45226

10. Project/Task/Work Unit No.

11. Contract/Grant No.

12. Sponsoring Organization Name and Address

Same as box 9.

13. Type of Report & Period Covered

14.

15. Supplementary Notes

16. Abstracts

Ninety-one exposed and forty-three nonexposed workers are evaluated at five plants, manufacturing polymethyl methacrylate sheets. Significant acute effects developing over the work shift are not detected as measured by symptomatology, blood pressure, and pulse rate. Chronic effects are sought for in past symptomatology, blood pressure, respiratory function testing, hemoglobin and white blood count, urinalysis, and blood chemistry. Data suggest that effects may occur in the higher concentration exposure groups with regard to serum glucose, and blood urea nitrogen, cholesterol, albumin, and total bilirubin values. Also, possible alterations are suggested in skin and nervous system symptomatology, urinalysis findings, and serum triglycerides. Extensive air sampling reveals mean 8-hour time-weighted average exposure by job category ranging from 4 to 49 ppm, for the workers studied, at the individual plants.

17. Key Words and Document Analysis. 17a. Descriptors

Environmental surveys
Industrial atmospheres
Industrial hygiene
Industrial medicine
Toxicity
Acrylic resins
Polymethyl methacrylate
Plastics processing
Blood diseases
Nervous disorders
Occupational diseases
Air pollution

17b. Identifiers/Open-Ended Terms

Occupational health
Air sampling
Air quality
Exposure limits

17c. COSATI Field/Group 06/J

18. Availability Statement

Release unlimited

19. Security Class (This Report) UNCLASSIFIED

20. Security Class (This Page) UNCLASSIFIED

21. s

22. Price A04 - A01

FORM NTIS-35 (REV. 10-73) ENDORSED BY ANSI AND UNESCO. THIS FORM MAY BE REPRODUCED USCOMM-DC 8265-P74