

papers.

The concepts of central control of diaphragm are well supported by the reports of Dr Korczyn. However, we preferred the other more accepted entity, viz, phrenic nerve palsy, to explain our findings.

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Iron-Deficiency Pruritis

To the Editor.—I read the article "Pruritus: A Manifestation of Iron Deficiency" (236:2319, 1976) and would like to draw attention to work on iron deficiency and generalized pruritus dating back to 1967. Then Sneddon and Garretts¹ described the relationship between itching and iron deficiency.

Also, in 1972 Rook, Wilkinson, and Ebling² described this condition, and in 1974 I published a paper³ describing the relationship of iron deficiency to generalized pruritus in 87 patients.

I could entirely agree with your authors but would disagree that this condition has not been described.

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Infection and Total Joint Replacement

To the Editor.—Total joint replacement, particularly of the hip, is rapidly becoming one of the more commonly performed orthopaedic surgical procedures. Deep infection, involving the prosthetic devices and their anchoring acrylic cement, is the greatest threat to the success of these operations.

We have observed, from our own experience and the reports of others, that a small but substantial proportion of the late postoperative infection—that is, those becoming apparent several months to several years after surgery, can be attributed to hematogenous seeding of the prosthetic joint from distant primary sources

of acute or chronic infection. Broadly speaking, two categories seem to be involved: substantial bacteremia from infections of lung, kidney, skin, and other foci of acute infection, and surgical or dental manipulations, such as abdominal surgery, genitourinary procedures, and periodontal and exodontal surgery.

We are taking this means to suggest that all patients who have had total joint replacement, particularly those at high risk of infection (patients with rheumatoid arthritis, on continual corticosteroid dosage or immunosuppressive medication, and with debilitating diseases including malignant neoplasms) be promptly and vigorously treated with appropriate antibiotics for any acute infectious process of bacterial origin. We also suggest that they receive prophylactic antibiotics before, during, and after any surgical or dental manipulation that can produce a substantial bacteremia.

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Late Effects of Botulinum Intoxication

To the Editor.—After reading the article by Barker et al (237:456, 1977) regarding the outbreak of botulism and the subsequent management of the involved patients, we had occasion to examine their case 1 3/4 years after his intoxication. He was seen because of persistent fatigue, intermittent diplopia, and decreased sexual ability. Prior to the patient's botulism intoxication, he was physically and sexually active for his age; subsequent to this, although not incapacitating, these symptoms remain substantially distressing and have resulted in multiple consultations with different specialists.

Barker et al reported good, immediate response to the trivalent botulinum antitoxin and further commented that all cases of intoxication returned to normal after a few weeks. Although this is usually the case with botulism intoxication, we believe it is quite easy to overlook, at times, the subtle disturbances that may persist but are not incapacitating. Cherington¹ notes, for example, that recovery may be prolonged but nearly total in all patients. Other authors² have noted pathological fatigability in long-term survivors of botulism intoxication. Sexual dysfunction, al-

though uncommon, is also not a unique presentation.³

We would like to emphasize that despite the fact that most patients subsequently do have a normal general physical examination, important symptomatic complaints may persist, as noted in the aforementioned case and others.

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Laryngeal Coccidioidomycosis

To the Editor.—Platt (237:1234, 1977) is indeed correct that *Coccidioides immitis* is seldom recognized as a cause of pathogenic conditions of the upper respiratory tract. However, his assertion that there are only two other published reports of coccidioidomycosis of the upper respiratory tract, one of endolaryngeal and the other of epiglottic involvement, is erroneous. Oliver¹ described a case of coccidioidomycosis in a 34-year-old man, involving nose, left hand, left index finger, larynx, and epiglottis. Biopsy of cutaneous as well as laryngeal and epiglottic lesions was positive for *C immitis*.

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Considerations on Etiologic Factors in Meat Wrappers' Asthma

To the Editor.—A recent letter (237:1826, 1977) reports interesting clinical and respiratory-function findings in meat wrappers and a nonexposed control population.

Irritative respiratory symptoms and the meat wrappers' asthma syndrome have generally been thought to be etiologically related to decomposition products of polyvinyl chloride (PVC), such as hydrochloric acid and/or minute amounts of phosgene, and not to PVC itself or to the monomer vinyl chloride.

The distinction is important to avoid confusion, especially since different mechanisms seem to be involved.

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Thermoactivated Price-Label Fume Intolerance

A Cause of Meat-Wrapper's Asthma

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REACTIVE airway disease has been reported to occur with increased frequency among meat wrappers. Prolonged exposure to pyrolysates of polyvinyl chloride (PVC) soft-wrap films was initially implicated in the cause of this occupational disorder.¹ Severe asthma developed in a meat cutter after repeated occupational exposure to fumes of thermoactivated price-label adhesives.

Report of a Case

A 43-year-old man with a history of heavy cigarette smoking (45 cartons annually) was employed as a meat cutter for 25 years. He was asymptomatic until 1968 when he noted recurrent episodes of chest tightness and productive cough. Initially, these attacks developed only at work and appeared to be closely related to exposure to fumes of PVC meat-wrap film generated when the PVC resin was cut by the hot wire of the meat-wrapping console. His symptoms intensified at the end of the work week, decreased on weekends, and were virtually absent during vacation. In mid-1973, he had a severe asthmatic attack at work and required hospitalization. His chest x-ray film showed moderate hyperinflation, and results of pulmonary function tests indicated mild restrictive and moderate obstructive disease with noticeable improvement following isoproterenol hydrochloride inhalation. Intradermal skin testing detected no reactivity to a variety of allergens.

See also pp 915 and 943.

He was readmitted a year later with a similar attack. The patient was afebrile, his respirations were 28/min, and severe bronchospasm as well as sibilant and sonorous rhonchi were noted bilaterally. The hemogram disclosed a hemoglobin value of 15.9 gm/100 ml, and white blood cell count of 9,000/cu mm, with a normal differential cell count except for 6% eosinophils. Sputum and nasal smears were negative for eosinophils. There were bilateral inter-

stitial pulmonary infiltrates on chest roentgenograms. Sputum cultures and bronchial washings obtained at bronchoscopy did not disclose a substantial number of pathogens. Immunologic evaluation included normal levels of immunoglobulins and third component of complement.

A survey of the patient's work environment showed the presence of PVC fumes as well as thermoactivated price-label adhesive fumes. The latter were generated when label adhesive was activated on the heating element of the label machine.

Two weeks after the acute bronchospasm was controlled, a series of work-simulated inhalation provocation studies were initiated to assess the effects of fumes of PVC soft-wrap film and thermoactivated price-label adhesive on the patient's ventilatory capacity. Base-line studies at that time showed moderate restrictive and severe obstructive pulmonary disease. The forced vital capacity (FVC) was 72%; forced expiratory volume in one second (FEV₁), 25%; forced expiratory flow (FEF)_{25%-75%}, 11%; and FEF_{75%-85%}, 27%, of predicted normal values. The Pao₂ was 60 mm Hg, and white blood cell count was 9,000/cu mm, with 5% eosinophils. The total eosinophil count was 576/cu mm. Sputum and nasal smears remained negative for eosinophil cells.

The patient was challenged with PVC soft-wrap fumes operating a meat-wrapping console for three hours. Rhinorrhea, cough, and transient bronchospasm developed after 20 minutes of exposure, but improved without treatment while the provocation study was in progress. Immediately after the three-hour challenge and during the four-hour observation period, his pulmonary function, arterial blood gases, and hematologic indexes were essentially unchanged from prechallenge values.

One month later, the patient was exposed to thermoactivated price-label fumes for 15 minutes. The fumes were produced with an electric heating element at a temperature of 106 C. After five minutes of exposure, progressive dyspnea, increasing bronchospasm, paroxysmal cough, tachycardia, diaphoresis, and extreme nervousness developed. Exposure was discontinued after 15 minutes. His FVC and FEV₁ decreased to 36% and 31% of prechallenge values, respectively. The Pao₂ decreased from 80 to 43 mm Hg. Subcutaneous epinephrine did not relieve his bronchospasm,

which gradually remitted after four hours of treatment with intravenous aminophylline and isoproterenol (Isuprel) hydrochloride by inhalation. Approximately 12 hours following exposure, the patient had a delayed, but less severe, asthmatic reaction.

Comment

The major components of thermal decomposition of PVC soft-wrap film include phthalate plasticizers, hydrochloric acid, toluene, benzene, several hydrocarbons, CO₂, and CO.^{2,3} Preliminary inquiry into the composition of price-label adhesives indicated the presence of elastomers, thermoplastic co-polymers, sulfonamide stabilizers, and phthalate plasticizers. The sensitizing substance, if any, of PVC and price-label fume intolerance has not yet been identified. Pulmonary function tests done on 17 meat wrappers before and after a work shift showed no substantial difference from 21 normal controls.⁴

The occupational history of our patient suggested a close relationship between his symptoms and exposure to meat-wrapping fumes. Our inhalation provocation studies indicated that the recurrent episodes of severe asthmatic attacks, paroxysmal cough, and mucous membrane irritation were primarily related to the price-label fumes. Intolerance to fumes of heat-activated price-label adhesive in meat wrappers had not been identified prior to our initial report.⁵ His peripheral eosinophilia, transient non-infectious interstitial pulmonary infiltrates, and severe deterioration in ventilatory function following work-simulated inhalation provocation suggests a hypersensitive reaction to one or more components of thermoactivated price-label fumes.

These studies were supported by grant RR-334 from the Clinical Research Centers Branch of Research Resources.

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Bilateral Renal Artery Reconstruction

A Ten-Year Arteriographic Follow-up

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RECENT reports have indicated that operative treatment of renovascular hypertension in patients over 50 years of age is not warranted because of high morbidity, high mortality, and poor response.^{1,2} This has not been our experience; of 162 patients with renovascular hypertension who underwent operative treatment, 70 were over 50 years of age and 56 (80%) of these were either cured or improved one year later.³ The overall operative mortality was 8.6%, but five of the six operative deaths occurred in patients who were simultaneously undergoing operative treatment for abdominal aortic aneurysm or for occlusive disease. Only one death (1.9%) occurred in a patient in whom operative treatment was limited to the renal arteries.

We describe a patient with severe renovascular hypertension and bilateral renal artery stenosis who was treated with bilateral aortorenal bypass grafts and who has had a ten-year serial arteriographic follow-up.

Report of a Case

A 52-year-old man was first admitted to the Vanderbilt Medical Center in October 1963. The duration of his hypertension was unknown, but it was first recorded two

months before admission. He had had frequent occipital headaches and was easily fatigued, symptoms referable to hypertension. He denied having vertigo, blurring of vision, syncopal episodes, angina, or epistaxis. There was no history suggestive of heart disease or peripheral vascular disease, but he had had a left-sided stroke two years previously. All antihypertensive medications had failed to control diastolic blood pressures ranging from 110 to 130 mm Hg. There was no known family history of hypertension.

On admission, blood pressure was 205/

110 mm Hg, supine, and 180/100 mm Hg, standing. Class 3 hypertensive retinopathy with hemorrhages and exudates was present. Cardiac examination disclosed no abnormalities, and all peripheral arterial pulses were present and normal. There was no abdominal bruit.

Laboratory analysis disclosed the following levels: serum creatinine, 1.17 mg/100 ml; total serum cholesterol, 346 mg/100 ml; and serum potassium, 5.2 mEq/liter. Urinary protein excretion was 1.55 gm/24 hr. Urinary catecholamine levels and a rapid sequence intravenous pyelogram were normal. The radioisotope renogram made with iodohippurate sodium I 131 (Hippuran I 131) showed bilateral disease. There was a prolonged functional segment and an abnormal excretory segment but a normal vascular segment. The Howard test of split renal function showed a decreased urine volume and increased creatinine concentration on the right side. The preoperative transfemoral aortogram revealed bilateral proximal renal artery atherosclerotic ste-

Fig 1.—Severe right and moderate left renal artery stenosis preoperatively.



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The prognostic paradox of subendocardial infarction needs explaining. Why should a limited area of myocardial damage be potentially more lethal than an area involving the entire thickness of the myocardium? A recent observation by Fuster et al² may provide a clue to the answer. Having performed coronary angiography within one year of a coronary infarction in 73 patients with transmural and 63 with subendocardial infarction, these investigators correlated the presence of collateral vessels supplying the distal segment of the occluded artery with the occurrence of angina. Ninety-three percent of all patients with subendocardial infarction had abundant collaterals; they also had angina. Collaterals were also frequent in 78% of the 32 patients with transmural infarction who had angina, but contrastingly they were evident in only 35% of the 28 patients who did not. Apparently, collateral circulation prevents necrosis but keeps alive an ischemic perinfarction zone. The latter favors development of angina and potentially lethal ectopic beats. The greater frequency of collaterals in subendocardial infarction may thus account for its unfavorable prognosis.

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Neonatal Mortality

As repeatedly noted in *American Medical News* from reports provided by the National Center for Health Statistics, infant mortality in the United States has declined dramatically during the past three decades. Although the factors contributing to the improvement are not disclosed by the cold, overall statistics, analysis by states or by census tracts within states has suggested that low socioeconomic status of mothers contributes substantially to infant mortality risk.

The latter fact gives special meaning to a report by Lee and co-workers¹ of experience at the Bronx Municipal Hospital Center (BMHC), an affiliated teaching hospital of Albert Einstein College of Medicine. The hospital is representative of the kind of US municipal institution that draws its patients predominantly from a population of low socioeconomic class. For purposes of comparison, the authors analyzed neonatal mortality (birth through 28 days of life) during the years 1966 through 1973, with special attention to two periods—1966 through 1971 (period 1) and 1972 through 1973 (period 2). Important changes

occurred at BMHC in 1970 with conversion of the hospital's center for premature infants to a complete neonatal intensive care unit and initiation of an active abortion program.

During the entire period there were no significant trends in number of deliveries and mean annual stillbirth rate. However, the incidence per 1,000 live births of infants weighing 2,500 gm or less (low birth-weight) was consistently lower during period 2, and the frequency of live births of infants weighing 1,500 gm or less (very low birth-weight) declined sharply in 1973. Also, there was a significant reduction in mean neonatal mortality during 1972 and 1973. Throughout the study period, neonatal mortality correlated closely with the very low birth-weight rate ($P < .001$).

From these and other data, Lee et al concluded that 75% of reduction in neonatal mortality resulted from a decline in the proportion of very low birth-weight infants, while 25% of the reduction could be attributed to improved neonatal medical care, to improved health status of the infants at birth, or to both. The authors also concluded that comparison of neonatal death rates among different populations (infer also nations) "may lead to falsely reassuring or alarming conclusions, while rarely pinpointing the critical determinant variables."

For some years, proponents of drastic changes in the method of financing health and medical care in the United States have often used comparisons of neonatal mortality reports in our nation with those in other countries, for example, Sweden, where nationalized health insurance prevails. The fallacies of such comparisons have been recorded repeatedly by spokesmen for the American Medical Association and by other careful observers of available data. As Lee et al have shown for a single hospital and as Geijerstam² had earlier confirmed, the difference in neonatal mortalities for the two nations could be explained primarily by differences in birth-weight distributions in the two populations.

In any event, however one studies the data about neonatal mortality in the United States—whether by analyzing socioeconomic factors, infant birth weights, variations in ages of childbearing women, availability of abortion and satisfactory means of contraception, or some, or all, or more—comparison with facts about Sweden or a similar nation will vary like statistical mixtures of oranges and apples. Perhaps orange juice and applesauce would be more apt as a simile.

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editorials

Meat-Wrapper's Respiratory Tract Disease

In 1973, Sokol et al¹ reported three instances of respiratory symptoms (dyspnea, cough, wheezing) occurring in women exposed to fumes produced when the polymer, polyvinyl chloride, was cut with a hot wire during the course of their work as meat wrappers in supermarkets. Although all three patients were cigarette smokers and had been employed for years in the same line of work, they had no respiratory symptoms prior to introduction of the polymer as the meat-wrapping material. All patients had evidence of airway obstruction, reversible or preventable by stopping work or by inhaling bronchodilating drugs. The authors speculated that they were describing a new syndrome, which they named meat-wrapper's asthma; however, historical evidence suggested that the syndrome was not new but simply not reported previously.

In this issue of *THE JOURNAL*, Andrasch and Bardana (p 937) report the case of a meat cutter who was exposed to both the fumes of polyvinyl chloride and the fumes from thermoactivated price-label adhesive. Symptoms of respiratory-tract irritation were intensified at the end of the work week, decreased on weekends, and were virtually absent during vacation. On one occasion, his symptoms at work culminated in a severe asthmatic attack that led to hospitalization. Results of pulmonary function tests indicated mild restrictive and moderate obstructive disease, with improvement following isoproterenol hydrochloride inhalation. There were transient bilateral interstitial pulmonary infiltrates on chest roentgenograms.

Two weeks after the asthma had been controlled, the patient was exposed to polyvinyl chloride fumes, and one month after that exposure, he was challenged with thermoactivated price-label adhesive fumes. On the first occasion, rhinorrhea, cough, and transient bronchospasm developed after 20 minutes of exposure but improved without treatment while the provocation study progressed for a total of three hours. In contrast, exposure to thermoactivated price-label adhesive fumes soon evoked progressive dyspnea, increasing bronchospasm, cough, and tachycardia to the extent that the provocation study was terminated after 15 minutes. One must suppose that, although the patient was possibly sensitive to polyvinyl chloride fumes, the major cause of his respiratory tract symptoms lay with fumes from thermoactivated price-label adhesive.

In a companion article (p 915), Falk and Portnoy were stimulated by reports of two cases of meat-wrapper's asthma to conduct a more thorough assay of the prevalence of the syndrome among meat wrappers in the Houston area. A questionnaire was delivered to a large number

of meat wrappers and to control persons, namely, supermarket grocery checkers and meat cutters. About 10% of the meat wrappers exposed to polyvinyl chloride fumes had multiple, rather severe respiratory tract symptoms (wheezing, dyspnea, chest pain or tightness), and a considerably larger number had lesser respiratory tract symptoms. Falk and Portnoy concluded that the spectrum of symptoms is too broad to merit the exclusive designation, "meat wrapper's asthma." Rather, a substitute term such as "meat wrapper's respiratory tract disease" seems more appropriate.

Prevention of an illness that has proved to be surprisingly prevalent might include the installation of proper ventilating equipment and use of lower-temperature cutting wires. However, Falk and Portnoy emphasize that the best solution to the problem would be to use mechanical-blade cutting machines that do not create fumes.

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Subendocardial Infarction: A Prognostic Paradox

The absence of Q waves coupled with the presence of depressed rather than elevated ST segments, characteristic of the "current of injury," used to convey a modicum of reassurance. True, the patient suffered an acute myocardial infarction, but it was after all only subendocardial, not transmural. The extent of the damage was limited, and the associated clinical manifestations and complications were less severe than in infarcts involving the entire thickness of the myocardial wall.

Although still reassuring with regard to short-range complications of shock and congestive heart failure, the long-range prognosis of subacute myocardial infarction—Levy et al¹ inform us—is anything but heartening. Comparing data on 119 patients at a mean follow-up period of 36 months with corresponding data on 36 patients whose infarcts were subendocardial, these investigators found that the latter group had a higher (33% vs 15%) incidence of sudden death from other cardiac causes. Survivors of subendocardial infarction also had a higher (61% vs 35%) rate of angina and of recurrent infarction (26% vs 12%).

In view of this unexpected malignant course of what previously appeared to be the lesser evil, Levy et al recommend coronary arteriography and serious consideration of coronary bypass surgery for patients with subendocardial infarction.

Polyvinyl Chloride Toxicity in Fires

Hydrogen Chloride Toxicity in Fire Fighters

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Polyvinyl chloride, of all the plastic polymers, has been implicated primarily in causing the most serious problem in fire fighting today because it releases hydrogen chloride gas when burning. One hundred seventy fire fighters who experienced symptoms from its toxicity have been studied from 1970 to 1975. One died.

(JAMA 235:393-397, 1976)

A RECENTLY identified hazard that is of paramount importance to practicing physicians is that of chemical injury incurred by persons exposed to fumes from fires. Specifically, such injuries are caused by the inhalation of vapors created by the thermal degradation of polyvinyl chloride, a plastic polymer. Such substances have now become widely used in the construc-

See also p 390.

tion of homes, furnishings, office equipment, electric wire, telephone and cable covering, and vehicles. A particular hazard exists in the case of the fire fighter, although it could be equally serious in any circumstance in which an individual might be exposed to such plastic combustion products.

THE FIRE

At 10:30 AM on Jan 6, 1970, an alarm sounded for a fire reported to be on the sixth floor of Building 213 at the Washington, DC, Navy Yard. Units of the District of Columbia Fire Department arriving on the scene found the floor filled with a heavy concentration of toxic fumes. Although all of the fire fighters carried masks, none were used, since neither the fire nor

the smoke was so excessive as to prevent entry without masks. The fire, which was confined to an office copying machine constructed of plastic and Teflon parts, was quickly extinguished.

The fire companies entered the building via the elevator, placed several portable fans for ventilation, and left the building about 20 minutes later. On returning to their quarters, many of the fire fighters experienced unusual and unexplainable symptoms, including a constricting tightness localized to the anterior part of the chest. This chest discomfort was described as a searing, burning sensation accompanied by dyspnea as well as a "burning sensation appearing to close off the throat." These symptoms were in addition to the usual headache, dizziness or vertigo, and nausea, which, in our experience, is frequently seen in cases of nonchemical smoke inhalation. Some symptoms persisted over a course of several days following exposure to the fumes. The dyspnea was noted on mild exertion and was associated with moderate apprehension by all of the affected fire fighters. A number of the fire fighters exposed at this fire experienced severe conjunctivitis, lacrimation, and dyspnea persisting for 24 hours after the fire. An intense headache, localized anteriorly and persisting about 24 hours, was also common.

REPORT OF A CASE

Approximately 24 hours after the fire, a 33-year-old fire fighter fainted in the sitting room of the truck company. It was also reported that he had a muscle spasm similar to an epileptic seizure, but recovered, was fully conscious, and got up immediately. His superior officer asked how he felt, and he replied that he was "fine" and walked into the kitchen. Following lunch, the acting sergeant on duty looked for the man to check his condition for driving and found him lying on the floor next to his bed. He was cyanotic and, despite all resuscitative efforts by an ambulance crew and the rescue squad, was pronounced dead on arrival by a fire surgeon at the George Washington University Hospital at 1:10 PM. Postmortem examination by the District of Columbia Department of Public Health Medical Examiner showed severe pulmonary hemorrhage and edema due to chemical pneumonitis secondary to exposure to chemical smoke and fire. The pathologist also reported coronary atherosclerosis.

EFFECT OF FUMES

It has been suspected for several years that the smoke and fumes from electrical fires produced greater injury now than similar fires in the past.^{1,2} It was strongly suspected that hydrogen chloride released by thermal degradation of PVC, a common electrical wiring insulation material, was the lethal product causing death in this instance. The medical examiner's report and the microscopic findings subsequently confirmed our original clinical impression of the cause of death.

Hydrogen chloride, inhaled either in the gaseous state or combined with water vapor, acts as an irritant to the mucous membranes of the eyes and

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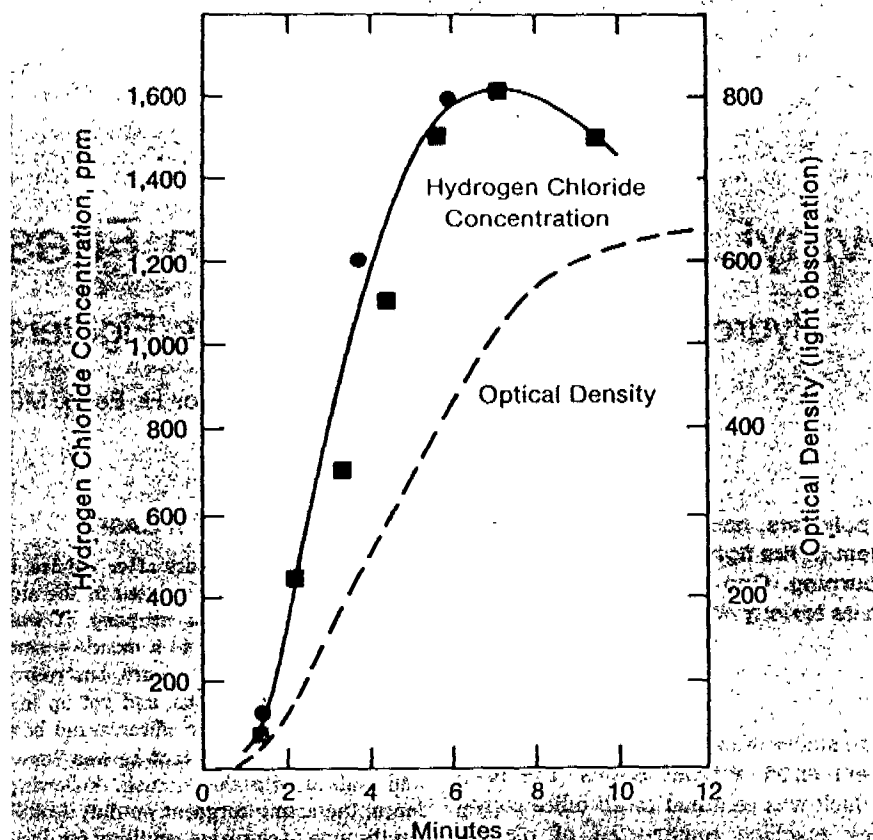


Fig 1.—Hydrogen chloride concentration and optical density of polyvinyl chloride electrical insulation decomposition products.

the respiratory tract. An HCl concentration of 15 ppm causes localized irritation to the throat after short exposure. Hydrogen chloride concentrations of 50 to 100 ppm are tolerable for one hour by humans. More severe exposures result in pulmonary edema and often in laryngeal spasm. Concentrations of 1,000 to 2,000 ppm of HCl are dangerous even with brief exposure³ (Fig 1).

Quantitative release of HCl on thermal degradation of PVC has been well documented in the scientific and medical literature. Polyvinyl chloride, of all the synthetic plastic polymers, has been implicated as causing one of the most insidious, serious problems in fire fighting today, due to its release of HCl gas while burning. Mists of hydrochloric acid are considered less harmful than anhydrous HCl because the droplets have no hydrating action.

Animal Experiments

The toxicity of PVC has been substantiated by Kishitani⁴ in his comprehensive animal experiments per-

formed at the University of Tokyo. With respect to the toxicity of carbon monoxide, Kishitani states that the injurious nature of PVC is unique. All mice exposed to harmful gas products died, but the carboxyhemoglobin concentration in the dead animals was low (average, 21.2%). This clearly indicated that the fatalities were not due directly to CO poisoning. At autopsy, the eyes of the mice were closed, their mucous membranes were injured by chemicals, and the sclerae were discolored. The latter had become white due to the action of chlorine gas. All of the mice died in a period of 15 minutes after exposure to PVC fumes. Electrocardiographic abnormalities appeared prior to generation of large quantities of smoke. This indicated that a harmful gas produced at an early stage was causing the effect. Similar results were found on exposure to polyurethane gas. Kishitani concluded that the injurious properties of burning materials such as wood, fire retardant plywood, melamine finishing board, and acrylic resin are due to CO.

In the fatalities due to CO, the average concentration of CO was 45%. The burning of cellulose material resulted in nothing but the release of CO. In the mouse study with exposure to burning building materials, the ECG abnormalities were recorded before the smoke from the burning materials was evident.

In regard to the harmful properties of PVC to mice, as well as those from polyurethane, polystyrene, and phenol, the pathologic effects of the gases, rather than those of the smoke, appeared first, as shown by atypical ECG changes. It requires less CO in combination with HCl to cause death. In conclusion, HCl and CO have a reciprocal, potentiating adverse effect.

EFFECT OF SMOKE

Smoke is a suspension of small particles in hot air and gases. It has a particulate fraction and a gaseous fraction. The particles consist of carbon and are coated with combustible products such as organic acids and aldehydes. The gaseous fraction has an extremely variable composition. Carbon monoxide and carbon dioxide are always present and constitute the bulk of this fraction.

However, a wide variety of other toxic gases are present at the scene of a fire. These may be formed by the combustion process or leak from commercial processing or storage equipment. The particulate and gaseous fractions combine to exert a large space-occupying effect and can fill an enclosed space at the expense of air. The gaseous fraction of smoke is much more dangerous to life than the particulate fraction. The nose, mouth, and throat, which filter out and trap the particulate fraction, cannot filter out the toxic gases. These gases enter the upper respiratory tract and lungs freely when inhaled. Damage to the lungs may result from exposure to a group of gases and vapors called pulmonary irritants (chlorine, phosgene, nitrogen dioxide, sulfur dioxide, and ammonia). On entering the lungs, these agents react chemically with water to produce strong acids or alkalis. A violent inflammatory response occurs, causing destruction of lung tissue.

Fire fighters and victims of fires in homes, offices, and industrial complexes are exposed to smoldering and

burning plastics and synthetics from furniture, floor and wallcoverings, textiles, and building materials. Many plastics produce large volumes of pulmonary-irritant gases when burned. Polyvinyl chloride is used extensively in furniture, both in the foamed plastic stuffing as well as the covering. Burning 450 gm of this material produces 320 gm of chlorine, phosgene, and HCl, all of which are strong pulmonary irritants. In all, there are 75 known products of PVC degradation. Practically every structure today contains plastics capable of producing lung-damaging gases when burned. Therefore, the fire fighter faces a great, new risk in almost any fire.

It became obvious that a particular pattern was emerging in which certain fire situations were productive of insidious and unpredictable fire casualties. The lethal chemical smoke was determined to be HCl resulting from the decomposition of PVC plastic used in telephone cable and electrical equipment installations.

We have found electrical and telephone cable fires to be especially hazardous to the fire fighters, due to the toxic gases produced. We have found that when a short circuit developed in a main switch, usually located in a sub-basement or penthouse of an office building or apartment house, the area was always poorly ventilated, and the plastic-covered switches quickly heat to temperatures in excess of 93.3 C. The heated conductors cause the plastic insulation to decompose and emit white, mist-like HCl fumes that resemble steam. When the temperature range of 232 to 321 C is attained, the gas may be invisible. The fire fighter may be fatally deceived if he does not know plastic-covered cable is involved in the fire he is fighting.

OVERHAUL PHASE

The period of time just after the fire is extinguished is termed the "overhaul phase." This is when the fire fighters clean up the fireground. Toxic smoke and fumes are still being emitted. This is a serious time for toxic gas inhalation to occur since many fire fighters remove their self-contained breathing apparatus during this phase. Another special hazard during this phase is the "heat sink,"

ie, concrete that retains a great amount of heat and releases fumes throughout the overhaul phase. Our testing has shown highly toxic concentrations of HCl in this concrete for as long as one hour after the fire has been extinguished.

FUEL LOADING

In the late 1960s, the type of "fuel loading" in office and high-rise buildings (ie, contents of the buildings) changed significantly and initiated a new awareness. The noncombustible buildings were not burning, but furniture within them, building insulation, ceiling tile, wall paneling, and decorations made partly or wholly of plastic were fueling disasters.

While a building may be constructed of fire-resistant elements, there is no control over the combustible material that an individual may elect to bring into the structure. This is the "fuel load" and may be expressed as kilograms of combustible material per square meter of floor area. Large differences exist in combustibility, smoke, and toxic gas release among different combustible materials. More than 50 sq m of red oak, all burning at its maximum rate, would be required to produce the same rate of smoke as 2.5 meters of acrylonitrile-butadiene-styrene plastic pipe. A fire of plastic materials develops extremely high temperatures because plastics possess a heat of combustion $2\frac{1}{2}$ times that of other combustibles. Therefore, the fire would magnify the normal problems of radiant heat, structural damage, and exposure. The fire would exhibit a very high burning rate because the flammability of plastics is much higher than that of other combustibles.

The four most common plastics produced in the United States in the past few years are polystyrene, polyethylene, polypropylene, and PVC. A chloroethylene polymer is a plastic solid marketed under a variety of trade names, and currently being manufactured at a rate over 8.3 billion kilograms annually.

Polyvinyl chloride (Fig 2) is a plastic solid widely used as a rubber substitute and as electric and telephone wire and cable covering. It is also utilized frequently in electrical fixtures, plastic drains, as well as waste pipe

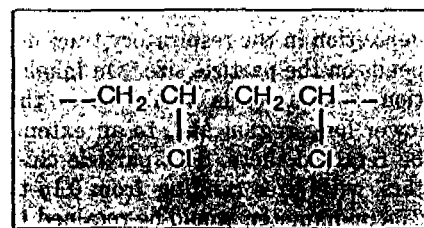


Fig 2.—Polyvinyl chloride.

for interior plumbing, pliable thin sheeting, film finishes for textiles, "nonflammable" upholstery, raincoats, tubing, belting; gaskets, shoe soles, disposable unbreakable plastic bottles, packaging materials, automobile and aircraft seatcovers, corrugated fence toppings, tarpaulins, shower curtains, phonograph records, plastic trays, baby pants, toys, curtains, and office copying-machines. It is used as an exterior finish in many vehicles, including buses and subway cars, because of its high resistance to wear and soiling.

When PVC is heated to 225 C, nothing happens. When heated above that, up to 475 C, PVC does not burn. The combustion range or flame point is 475 C. Between 225 C and 475 C, PVC loses over 60% of its weight. During this process, it thermally degrades and HCl is released. Four hundred fifty-three grams of PVC at degradation releases 320 gm of chlorine, phosgene, and HCl.

The individual toxicity factors of phosgene and the other major decomposition products of PVC, ie, benzene, toluene, total xylenes, naphthalene, and vinyl chloride, are very small, compared with the toxicity factor of HCl. Further, the total or additive toxicity factors of these minor components are also very small in comparison with HCl toxicity. Unfortunately, very little is known about the synergistic effects of toxic gases (ie, the ability of one chemical to increase or decrease the toxicity of another). The main toxic risks from the decomposition products of PVC are HCl and CO.⁶

Stone et al⁶ elucidated the nature of smoke aerosol and its role in the transport of toxic gases in fire situations. They confirmed the fact that the toxic gas, HCl, is adsorbed on soot aerosol. Possible inhalation hazards of such soot are positively related to the size of the soot particles and particle agglomerates. It has been shown that

the amount and location of particle deposition in the respiratory tract depends on the particle size.⁵ On inhalation, soot aerosols would enter the lower lung region and, to an extent, be retained there. Soot particle clusters, with sizes ranging from 0.1 μ to 2.5 μ in diameter, would be retained in the alveolar sacs to an extent of from 20% to 40% of those particles inhaled.⁶ At a breathing rate of 18 liters/min for an exposure of one hour, a maximum of 0.7 gm of soot bearing 13 mg of loosely bound HCl would be retained in the lower lungs.

The effect of HCl in the gas phase is largely limited to irritability, mainly affecting the upper respiratory tract, whereas loosely bound HCl condensed on soot aerosol gains access to the lower lungs. Experiments have shown that water droplets of respirable size rapidly adsorb HCl from the gas phase and approach equilibrium concentrations in fractions of a second.⁷

SMOKE INHALATION

Respiratory distress may develop in fire fighters or fire victims immediately or within one to two days of exposure to combustion products. The best protection against these agents is the mandatory use of the self-contained breathing apparatus by every fire fighter. When anyone without a breathing apparatus is exposed to more than a few breaths of "choking smoke" characteristic of burning or smoldering plastics, he should receive prompt medical attention.

Prior to our investigation, we considered most fireground pulmonary casualties to be due to "smoke inhalation" or CO poisoning. Carbon monoxide had long been considered the leading cause of death and pulmonary morbidity in fires. Though CO is not noxious and does not actually cause serious pulmonary injury, the amount of CO in a patient is a good indicator of whether more harmful gases are present.

Before the introduction of massive fire loads of combustible and thermally decomposable plastic products, fire surgeons usually considered the CO victim to be "home safe" in four hours after exposure due to the fast half-life of CO in the blood. After exposure to plastic degradation products, a period of one to six hours

elapses between exposure and onset of severe respiratory and chest symptoms. Treatment is most effective if given during this quiescent phase. Once the symptoms of difficult breathing, cyanosis, or other symptoms, as noted in the reported case, have appeared, it may be too late to prevent severe morbidity or even mortality. The "overhaul phase" after the fire is extinguished is dangerous with respect to fumes also.

A Harvard research team headed by Donald P. Dressler, MD, reported in 1973 that when burned, plastics and modern fibers produced colorless, odorless fumes that quickly displace oxygen and cause a dramatic rise in the CO₂ level of the atmosphere.⁸ Therefore, a person either dies or is rendered unconscious in the early stages of a fire involving these materials. If he is unconscious, he soon dies of other lethal fume inhalations.⁸ Tests performed in Cambridge, Mass, showed that fire fighters were probably affected adversely by the high level of CO₂ rather than by the initial release of toxic gases.⁸

In establishing the importance of detecting the presence of certain toxic gases, the difficulty in detecting CO has been emphasized.⁹ Some human response mechanisms are more sensitive than others to CO inhalation.⁹ Fairly high levels of CO affect a human's vision, but even higher levels do not affect his sense of timing. A research team headed by R. A. McFarland, MD, of Harvard University, found that when CO replaces 11% to 17% of the blood's normal oxygen, the peripheral vision is affected and the subject has difficulty viewing stimuli at a 20° angle from the line of sight.⁹ The Harvard team also found that at a 17% concentration of COHb, some subjects had a momentary lapse of attention and failed to respond to all the stimuli presented. This is important in disproving the once-held concept that once an individual has detected the sharp odor of HCl he can walk away. It has been our observation that the fire fighter cannot escape the HCl fumes.

Cornish and Abar reported that CO and hydrochloric acid were the major toxic products from the combustion of PVC.¹⁰ They pyrolyzed PVC polymers in a stream of air by gradually increasing the temperature from am-

bient to 600 C. Exposure to this air stream supplemented with oxygen produced pulmonary and interstitial edema in rats. Some of these animals also showed focal bronchial and intra-alveolar hemorrhage.

In a sealed environment (such as a centrally air-conditioned house, office, high-rise unit, or hospital), fumes from plastic degradation could kill, even if the fire is brought under control. It has been observed that a sleeping person needs an estimated 12 to 15 minutes to awaken, react to danger, and take appropriate action to save himself. With inhalation of fumes from burning plastic, he will not have that much time.

COHb LEVEL AND CIRCULATION

As noted by E.P. Radford (written communication), 43 deaths due to fire demonstrated that a blood COHb level of over 65% is nearly always lethal due to the depression of respiration and circulation. Ventricular fibrillation from acute myocardial hypoxia induced by a rapid rise of the COHb level in individuals with a restricted coronary circulation was found to be the likely explanation of a lower terminal blood COHb level. These individuals were found to have severe, preexisting coronary vascular disease.

We believe that any compromise of the coronary circulation, eg, atherosclerosis such as found in the fatal case, would be potentiated by highly irritating chemical fumes. We also believe that other pyrolysis products, especially HCl, have contributed to ventricular fibrillation since its concentration is comparable to that of CO in real fire situations involving plastics.

Kishitani has demonstrated that chlorine affects the myocardium more rapidly and more severely than CO. Carbon monoxide may cause changes in enzyme activities suggestive of myocardial damage. Hydrogen chloride has been found to be a more potent myocardial irritant whose effects may be difficult to determine by clinical observation. This is in conjunction with the development of pulmonary edema over a 24-hour period following exposure to HCl. This further complicates and compromises coronary artery oxygen saturation. This could lead to sudden death syn-

drome, similar to that in the reported case. Although in the cases of CO poisoning noted by G. Gordon, (written communication) the ECG changes did appear late if at all and the COHb varied in individuals at the same fire as well as in different fire situations, it has been our experience that all fire fighters exposed to PVC do manifest ECG signs of its toxicity. There are variable levels of its toxic effect on the lungs, mucous membranes (tracheal peeling effect), eyes, and other parts of the body.

CLINICAL STUDY

In Washington, DC, a clinical study of fire fighters suspected and later known to have been exposed to toxic products from thermal degradation of PVC was conducted by the DC Board of Police and Fire Surgeons between January 1970 and September 1975. One hundred seventy individuals were exposed from one to four different times to these products and reported two or all of the symptoms of acute toxicity, ie, pain in the anterior aspect of the chest, neck and throat pain, dyspnea, severe headache, dizziness, and irregular pulse within a few hours after exposure.

Initial physical examinations were performed by the fire surgeon on the fireground, in the hospital emergency room, or at the Police and Firemens Clinic. Laboratory studies including complete blood cell count, determinations of serum glutamic oxaloacetic transaminase, blood urea nitrogen, or creatinine, and a complete urinalysis were done. Electrocardiograms were performed initially when there was chest pain, extrasystoles, or cardiac arrhythmia. However, ECG studies were not incorporated as part of the physical evaluation until the latter part of the study when their importance was appreciated.

About one fifth of the fire fighters had extrasystoles during the first few hours after exposure. Fourteen of the

last 26 firemen exposed had premature ventricular contractions. Some have had recurrence of extrasystoles within the subsequent year. Chest x-ray films were done at the initial examination and have remained normal. Serum electrolyte and arterial blood gas determinations were performed on 12 of the fire fighters who were more acutely ill, or required hospitalization. Because of the excellent clinic facilities provided by the District of Columbia government, all fire fighters were observed in a holding area after exposure and examined at the clinic or the hospital emergency room after transportation from the fireground. Twelve men were admitted to the hospital for treatment. If symptoms did not worsen over the first 24 hours in the hospital, they were released and followed up on an outpatient basis at the clinic.

Specific treatment, including oxygen given intranasally at 5 liters/min, bronchodilators, antihistamines, and decongestants in oral suspension, has been utilized in controlling most of the acute respiratory symptoms. Steroids were given intravenously to three of the fire fighters during hospitalization due to the severity of their signs and symptoms of respiratory distress.

Initial and follow-up liver function tests have remained normal in all of these patients. There has been no direct correlation between severity of symptoms and history of cigarette smoking.

None of the fire fighters has had to retire for permanent airway disorders. Serial studies and follow-up examinations will continue. Since the onset of this study among professional fire fighters, the use of the self-contained breathing apparatus has been required at all fires where toxic fumes could be present. This is necessary during the "overhaul phase" also. We urge all physicians to advocate restriction of unsupervised use

of PVC products. Fire research activity should be maintained at a national level to continue study as well as preventive measures for HCl toxicity in PVC fires.

CONCLUSIONS

Hazards of Plastic Fires.—Respiratory distress may develop in fire fighters and fire victims after exposure to combustion products. The complexity of the problem is emphasized when it is recognized that the thermal degradation of PVC results in the formation of at least 75 identifiable potentially toxic compounds. Three characteristics of plastic fires are the extremely high temperatures, very high burning rates, and thick toxic smoke. The main danger to exposed fire fighting personnel at the fireground results from the massive formation of HCl gas, and in many instances, its adsorption on spherical soot particles that are carried into the victims' respiratory tracts.

Prevention.—The mandatory use of the self-contained breathing apparatus by all who will be vulnerable to toxic smoke will aid in the prevention of plastic fires. Control of hazardous building designs, including equipment and ventilation is also necessary. Protection by masks during the "overhaul phase" should be required. Sophisticated air-sampling techniques are required for definitive study, including gas chromatography. Electrocardiographic studies utilizing base line tracings directly after HCl exposure are stressed.

Areas of Future Study.—All atmospheres should be suspected by the fire fighter. There should be a search for an effective gas analyzer that can immediately assess gas concentrations released by burning or smoldering plastics. Further definitive cardiologic studies are indicated. The term "smoke inhalation" should be abandoned and replaced by "inhalation of toxic combustion products."

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Paint-Remover Hazard

Richard D. Stewart, MD, MPH, Carl L. Hake, PhD

• The in-home use of paint removers containing methylene chloride results in the absorption of this solvent, which is metabolized to carbon monoxide. Exposure for two to three hours can result in the elevation of carboxyhemoglobin (COHb) to levels that stress the cardiovascular system. The metabolic formation of COHb continues following the paint-remover exposure, doubling the duration of the cardiovascular stress produced by a comparable COHb level after exposure to CO. Patients with diseased cardiovascular systems may not be able to tolerate this unexpected stress.

(JAMA 235:398-401, 1976)

THE REMOVAL of old paint from wood by applying a liquid paint stripping formulation, long regarded as a laborious, messy task, has not been considered particularly hazardous to health. However, recent research has shown that the main ingredient in most paint removers, methylene chloride (dichloromethane, CH_2Cl_2), is rapidly metabolized to carbon monoxide.¹⁻⁶ The amount of CO formed in the body is directly related to the amount of CH_2Cl_2 absorbed during the paint stripping operation and can be sufficient to produce a substantial stress on the cardiovascular system.

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The first case illustrates the tragedy that can occur when a patient with coronary heart disease is exposed to a paint and varnish remover containing CH_2Cl_2 and the solvent is metabolized to a toxic amount of CO. The second case is the one in which the in vivo metabolism of CH_2Cl_2 to CO was first observed.

REPORT OF CASES

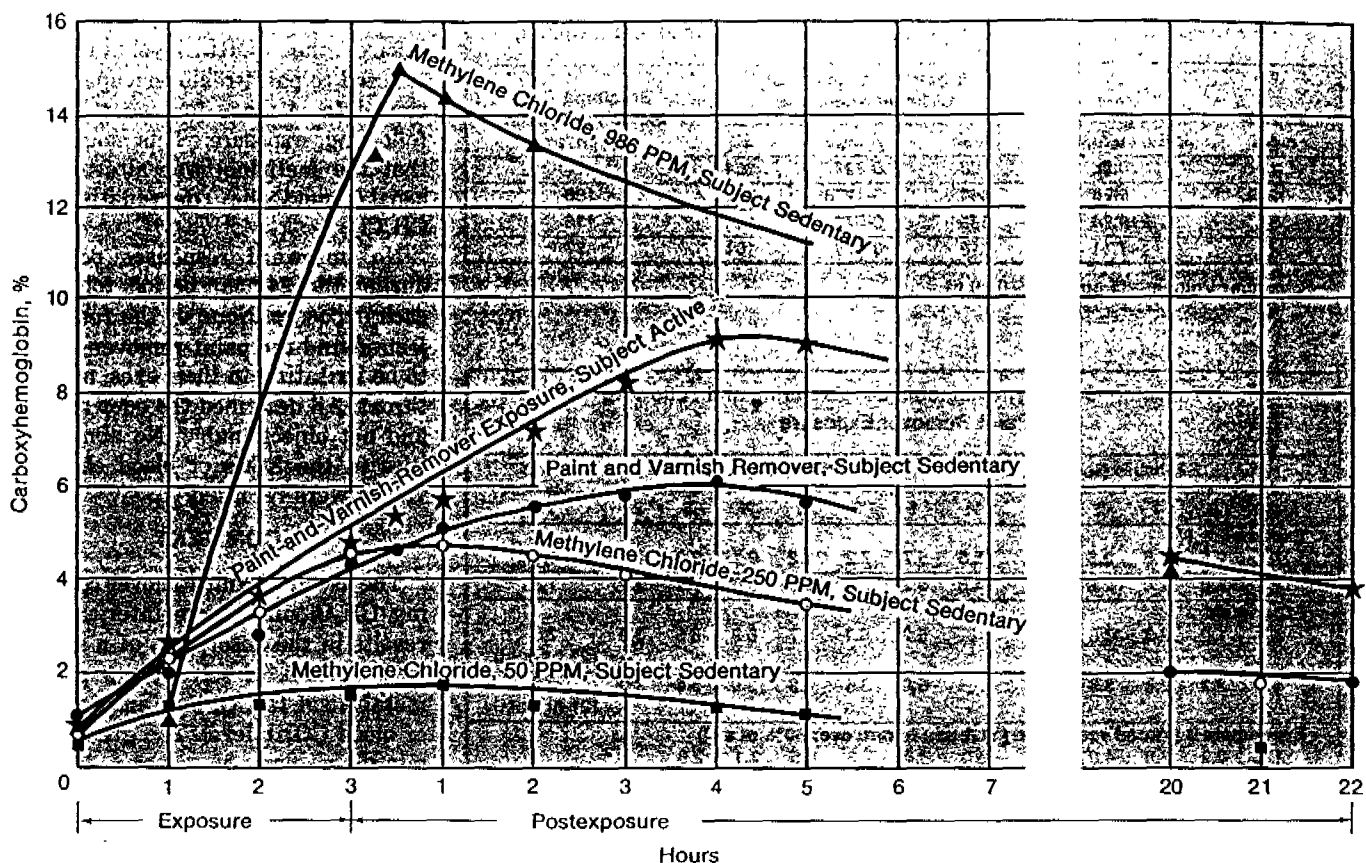
CASE 1.—A 66-year-old man with no prior history of heart disease, was admitted to the coronary care unit with severe, crushing retrosternal pain of two hours' duration that radiated to his shoulder and left arm. The patient was a recently retired executive who had chosen furniture refinishing as a hobby. Six hours prior to admission he had applied a commercial liquid gel paint and varnish remover to part of a large wooden chest of drawers. He had worked at this task for three hours in his basement workshop, which was a room

measuring 10.7×6.1×2.7 meters and was heated with hot air from a gas furnace. One hour after leaving the basement, he experienced the onset of his chest pain.

The patient related the history of the paint stripping to the attending physician who examined the paint and varnish remover container. The label cautioned that the product contained 80% methylene chloride by weight and was to be used only with adequate ventilation. No causal relationship between the inhalation of the paint remover vapor and the acute anterior myocardial infarction was made.

The patient had an uncomplicated hospital course, and two weeks following discharge he elected to strip the remaining paint from the chest of drawers. He again applied the paint remover, working for three hours in his basement workshop. The severe retrosternal pain developed again, and he was readmitted to the coronary care unit. His hospital course during this second acute myocardial infarction was complicated by cardiogenic shock, dysrhythmia, and heart failure. The patient survived, and six months after discharge returned once again to his basement workshop to complete the paint stripping operation. Assisted by his wife, he worked slowly for two hours. Two hours later he experienced chest pain, collapsed, and died before the arrival of the ambulance.

CASE 2.—A 35-year-old male cardiologist, who was enjoying excellent health, volunteered to participate in a research project, the purpose of which was to correlate the subject's carboxyhemoglobin (COHb) level



Short exposures to methylene chloride result in formation of carboxyhemoglobin (COHb) that continues to increase after exposure before slowly returning to normal levels. The presence of methanol further prolongs period of COHb elevation and cardiovascular stress.

with the air pollution in his section of Milwaukee. This nonsmoker was discovered to have a COHb saturation of 6%, and of 8% on each of the two mornings following a two-hour exposure the previous evening to paint-and-varnish-remover vapors. After a fruitless search to discover the exogenous source of CO, the cardiologist was exposed for one hour to a low concentration of methylene chloride vapor in a controlled-environment chamber.² The subject's COHb level rose from a preexposure level of 0.4% to 2.4%. Because there was no evidence of a hemolytic process, it was presumed that the CO was a metabolite of CH_2Cl_2 . To confirm this isolated observation, a series of experiments were conducted in which 21 male and nine female volunteers were exposed to CH_2Cl_2 vapor concentrations of 50, 100, 250, 500, and 1,000 ppm for varying periods of time. A prompt elevation of COHb was observed in each subject exposed to CH_2Cl_2 .^{2,7}

EXPERIMENTAL PROCEDURE

Paint Remover Exposure.—To investigate the potential of paint and varnish removers that contain CH_2Cl_2 to elevate COHb to toxic levels, four three-hour paint stripping operations were carried out in a controlled-environment

chamber where the ventilation rate could be regulated, the CH_2Cl_2 vapor concentration accurately monitored, and careful medical surveillance of the four volunteer participants was possible. Two individuals participated in each experiment. One actively applied the paint remover and did the stripping while the second subject remained sedentary, making it possible to assess the effect of alveolar ventilation on absorption. Three room-ventilation rates were studied. The first simulated the air turnover commonly encountered in home basements, while the other two simulated the higher rates of air turnover that could be encountered in industrial settings. In each three-hour experiment, one quart of a liquid gel paint remover was applied to a baby crib with a paint brush and later, scraped off. The volatile components of the paint remover were 80% CH_2Cl_2 and 20% methanol by weight.

Subjects.—Four healthy men ranging in age from 19 to 47 years volunteered for the study after the purpose, procedure, and risks of the

investigation had been fully explained. None of the subjects used drugs or consumed alcohol during the 24-hour periods preceding and following each experiment. One subject, who was a smoker, abstained for 12 hours prior to the experiment and was not permitted to smoke until a final COHb determination had been made.

Exposure Chamber.—The four experiments were conducted in an 817-cu m (2,680-cu ft) controlled-environment chamber.^{2,7} Air flow was adjusted so that the half-life of the CH_2Cl_2 vapor would range from 33 to 11 minutes. Air temperature was 22.3 to 23.3 C and the relative humidity was 55%.

Analysis of Exposure Chamber Atmosphere.—The CH_2Cl_2 vapor concentration in the breathing zone of the subjects was continuously recorded by an infrared spectrometer equipped with a 10-meter path-length gas cell. This gas cell was continuously supplied with air drawn from the subject's breathing zone through a polyethylene tubing that measured 0.635 cm in diameter.^{2,7} The absorbance of 13.3 μ

Table 1.—Concentration of Solvents in Breathing Zone During Paint Stripping

Experiment	Ventilation Rate, cu m/hr*	Breathing Zone CH ₂ Cl ₂ Concentration, ppm			Breathing Zone Methanol Concentration, ppm
		Mean	Range	SD	
1	70.28	788	0-1277	354	...
2	70.28	654	0-1278	358	186
3	210.84	368	0-576	122	115
4	147.11	216	0-379	101	77

*Chamber Volume=75 cu m (2,680 cu ft).

Table 2.—Carboxyhemoglobin Levels During and Following Paint-Remover Exposure

Subject	Exposure Hours				Hours Postexposure							
	0	1	2	3	½	1	2	3	4	5	20	22
Experiment 1*												
1	0.8	2.6	3.6	4.6	5.3	5.7	7.2	8.2	9.1	9.0	4.4	3.8
2	1.0	2.0	2.8	4.4	4.6	5.2	5.5	5.8	6.0	5.6	2.0	1.8
Experiment 2*												
3	1.0	2.3	3.3	4.0	...	5.2	6.1	6.7	6.9	6.5	3.0	2.5 (21 hr post)
4	2.2	2.8	3.8	4.1	...	5.0	5.5	5.9	5.9	5.5	3.0	2.6 (21 hr post)
Experiment 3 (forced ventilation [11.1 min to turn over 50% of air])												
1	0.9	2.8	4.0	4.8	6.0	6.8	7.3	6.5	3.1	2.9		
2	1.3	2.3	3.4	4.3	5.5	5.8	5.5	4.8	1.9	1.5		
Experiment 4 (forced ventilation [15.3 min to turn over 50% of air])												
3	0.9	1.2	1.9	2.9	3.4	3.4	3.3	3.2	1.8	1.6		
4	1.5	2.0	2.7	3.7	4.3	4.3	3.7	3.5	1.5	1.6		

*Normal home-basement ventilation (33 min to turn over 50% of air).

through a path length of 2.25 meters was measured. The infrared signal to the recorder was monitored each second by an on-line computer that displayed the mean vapor concentration, as compared to standards for each 30-second interval of exposure, and calculated the time-weighted average exposures. During the final five minutes of each hour of exposure, additional breathing zone samples were collected in large saran bags for methanol analysis.

Medical Surveillance.—Each subject was given a medical examination prior to exposure. This examination included a history, physical examination, and the following laboratory studies: complete blood cell count, 18-factor automated chemical analysis survey panel, and a 12-lead electrocardiogram. Prior to each day's exposure, the subjects were given a repeat medical examination. During exposure, the subjects were under continual surveillance by a physician, and lead II of each subject's ECG was continuously monitored by means of telemetry. Serial venous blood samples were obtained for COHb determina-

tion during and after the use of the paint remover (Figure).⁸ The 18-factor automated chemical analysis and 12-lead electrocardiogram were repeated the morning following each exposure.

RESULTS

The use of the paint-remover formulation under the three ventilation rates produced the breathing zone CH₂Cl₂ and methanol concentrations listed in Table 1. The higher ventilation rates significantly reduced the breathing zone concentrations of the two solvents.

Each subject's COHb level began to increase shortly after exposure had begun (Figure). These COHb levels steadily increased during the exposure, continued to rise for several hours following cessation of exposure, and then very slowly returned to normal (Table 2). The more active volunteer in each experiment absorbed larger quantities of CH₂Cl₂, which resulted in higher COHb levels.

In contrast to the usual pattern of COHb formation following CH₂Cl₂ exposure, with peak COHb level ele-

vations occurring one hour after exposure, the COHb level in those exposed to paint-remover vapors continued to increase for several hours following exposure. This suggested that the methanol was altering the usual metabolic degradation of CH₂Cl₂.

No untoward responses occurred during the 24-hour period following each exposure. None of the four subjects found the paint-remover vapors to be irritating to their eyes, nose, or throat. All described the odor as mild and not objectionable. No abnormalities in the ECGs or blood chemical values were recorded.

COMMENT

The use of a paint remover containing CH₂Cl₂ in a large interior room results in the absorption of a significant amount of solvent, its prompt metabolism to CO, and an elevation of blood COHb level. The greater the minute-respiratory volume or the poorer the room ventilation, the greater the absorption of CH₂Cl₂ and the higher the COHb level elevation. Use of the paint remover for a period of three hours, following the directions on the label, can easily produce a COHb saturation of 5% to 10%. Exposure for periods longer than those investigated or under conditions of poorer ventilation would result in even higher COHb elevations.

It has been well documented that elevation of COHb level to saturations greater than 5% can adversely affect patients with angina pectoris or cardiovascular disease.⁹⁻¹² Exercise tolerance is decreased and anginal pain is of longer duration. Yet paint stripping for furniture refinishing purposes has become extremely popular with older persons.¹³ Until recently, a prominent Milwaukee hospital introduced paint stripping and furniture refinishing to coronary vein bypass patients in the early convalescent period.

The COHb resulting from the metabolism of CH₂Cl₂ is additive to the COHb level resulting from exposure to other exogenous sources of CO.⁷ For example, a paint-remover exposure that results in a 10% COHb saturation level when added to a heavy smoker's preexisting COHb level of 10% will produce headache and nausea in the healthy, and sufficient car-

diovascular stress in the patient with coronary heart disease to be dangerous.⁹⁻¹²

The elevated COHb level resulting from CH₂Cl₂ exposure has a biological half-life twice that of COHb produced from exposure to CO. This occurs because the absorbed CH₂Cl₂ is released slowly from storage in body tissues and then is metabolized to CO over a protracted period of time. Thus, because it is so sustained following exposure, the cardiovascular stress produced by elevated COHb levels, derived from CH₂Cl₂ metabolism, is greater than that resulting from equally high COHb levels derived from CO. The addition of methanol to paint-remover formulations extends the biologic half-life of COHb derived from CH₂Cl₂ (Figure), further prolonging the period of cardiovascular stress.

The ethical responsibility for informing the public about the potential hazard of CH₂Cl₂ in paint removers lies with the manufacturer who is obliged to market a product that can be used safely. This is the purpose of the label. It should warn the susceptible segment of the population of the CO hazard. The manufacturers of paint removers have been cognizant of the problem since 1972, yet product labels make no mention of CO. Only

one manufacturer of paint removers has acted positively. This Racine, Wis, firm has withdrawn its product from the market.

The legal responsibility for protecting the public currently rests with the Consumer Product Safety Commission. It has remained mute, as did the governmental agency originally responsible, the Environmental Protection Agency, when in 1971 the CH₂Cl₂ hazard was formally called to its attention.

The medical responsibility for protecting patients unable to tolerate the cardiovascular stress of elevated COHb levels must rest with the physician until the general public is made aware of the CH₂Cl₂ hazard and all paint-remover formulations are appropriately labeled. This is a critical duty because one sixth of the 180 million kg of CH₂Cl₂ produced in the United States is being consumed in the rapidly expanding paint-remover market.¹³

This investigation was supported in part by contract HSM-99-72-84 from the National Institute of Occupational Safety and Health.

Anthony Wu, PhD, and Sally A. Graff provided technical assistance.

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Jan 26, 1901

Gastric Disorders

[CURRENT MEDICAL LITERATURE, p 289]

After describing the anatomy of the stomach and its blood-supply, Mayo notices the methods of examination. He believes that too much attention is paid to laboratory and too little to clinical examination at the present time; the two should go hand in hand and neither be neglected. For instance, the salol test for loss of motor power is unreliable, but the finding of food in the fasting stomach regularly seven hours after taking is most practical and reliable; fourteen hours after indicates

stagnation or retention. For getting the outlines of the stomach neither the gastroduaphanoscope nor gastroscope are of real use, nor can the giving of bismuth or the using of metal sounds for X-ray examination be compared in the efficiency with simple dilatation with bicarbonate of soda and tartaric acid, or better still, a stomach-tube and a Davidson syringe with which it is easy to distend the stomach with air. If on distension the lesser curvature and pylorus remain in the normal position while the greater curvature lies below the umbilicus, dilatation is evident. If they are detected below the costal margin the stomach has descended. The history of the patient, his present condition and the chemical and biological examination of the gastric contents, taken into account with position and size of the stomach, give a basis for diagnosis and as a rule indicate whether an abdominal incision would be expedient. In the beginning nearly all operations on the stomach are exploratory; for the most important primary investiga-

tion seldom relieves the exact condition. The technique of the operation is described and ulcer and its operative needs are noticed at length. Some forms of gastrectasia of uncertain origin are also dwelt upon, such as what has been called spasm of the pylorus, of which he thinks he has met with four cases; the special forms of pyloric obstruction are described by him, in which a high lying and fixed pylorus became more and more compressed as the stomach filled, and the distension finally relieved itself by copious vomiting. He thinks this is often the cause of dilatation, and has operated on four such cases. The so-called "fish-hook" pylorus in which the opening is directed upward, increases the muscular efforts and acts in a similar manner by increasing the stomach's work. As regards operation, he says gastroenterostomy is the most generally advisable and has few contraindications. Pyloroplasty may be of benefit in certain cases. As a result of his own experience he believes that much depends on the condition of the pylorus.

Immunogenetic Factors in Preeclampsia and Eclampsia

Erythrocyte, Histocompatibility, and Y-Dependent Antigens

James R. Scott, MD; Alan E. Beer, MD; Peter Stastny, MD

• **Determination of ABO and HL-A antigens and sex ratio of infants born to 46 women with preeclampsia or eclampsia, in comparison with normal controls, disclosed no predominant blood group, HL-A haplotype, or qualitative difference in maternal-fetal incompatibility. These results suggest that a link between immunologic mechanisms and the pathogenesis of toxemia syndromes, if present at all, must be associated with feto-placental tissue-specific antigens.**

(JAMA 235:402-404; 1976)

THE CAUSE of toxemia of pregnancy remains unknown, but suggestions that it might be an immune disorder date back to the beginning of the century. Underlying immunogenetic possibilities that have been proposed include (1) an inherited tendency for the disorder, (2) pathogenesis related to maternal-fetal incompatibility, or (3) an abnormal maternal immune response to placental antigens.

A genetic predisposition has been suspected since it was shown that there is an increased incidence of preeclampsia in daughters of women who themselves were eclamptic.¹ If women in whom preeclampsia or eclampsia was destined to develop demonstrated an unusual distribution of ABO or HL-A antigens or both compared to the normal population, typing for these antigens would be a potentially useful clinical test for predicting which primigravidas are at risk for the disease. Moreover, a com-

parison of maternal and infant blood groups and tissue types, as well as the sex ratio of infants born to women with toxemia, would help to establish whether or not immunogenetic disparity between the mother and her fetus plays a role in the pathogenesis of this disorder.

MATERIALS AND METHODS

Twenty-three preeclamptic and twenty-three eclamptic primigravidas from the obstetric services at Parkland Memorial Hospital and University of Iowa Hospitals were studied. The 46 patients included 23 blacks, 11 whites, and seven Latin Americans. Preeclampsia was defined as acute hypertension developing in a primigravida whose blood pressure was normal before the third trimester of pregnancy, and persistent elevation of blood pressure to at least 140/90 mm Hg, with an increase in the diastolic blood pressure of at least 20 mm Hg above previous levels during pregnancy. Edema or proteinuria or both were present in most cases; no patients who had equivocal findings were included. Eclampsia was defined as the syndrome of pregnancy-induced hypertension further complicated by grand mal seizures that were the consequences of pregnancy and not the result of some other cause.

Standard blood group determinations were done by testing the red blood cells (RBC) against anti-A and anti-B serum and by testing the serum against group A and group B red blood cells. The blood

groups of preeclamptic and eclamptic patients were compared with those of 4,494 normal pregnant women who gave birth at Parkland Hospital. HL-A typing was done by the microdroplet lymphocytotoxicity test for 23 specificities in all of the mothers with preeclampsia and eclampsia and in ten of the infants, as well as in comparison with the tissue types of 343 black and white control patients seen during the same period of time.

RESULTS

All maternal and fetal blood groups, HL-A antigens, and sex of the infants born to mothers who were preeclamptic or eclamptic are listed in Table 1. The male-female sex ratio of infants born to toxemic women was 1.13, which is not significantly different from the 1.06 sex ratio of normal pregnancies.² As shown in Table 2, the blood group distribution in these women did not differ from that of the normal population. Eleven of the 46 infants were ABO incompatible with their mothers, a frequency that is not greater than in nonaffected pregnancies.³ There was also no unusual distribution of HL-A antigens (Table 2) in the preeclamptic or eclamptic women or their infants, and the HL-A antigen frequencies compared well with those published.⁴ Although the number of infants with HL-A antigen determinations is too small to make any statement about a recurring haplotype, the high incidence of HL-A incompatibility between mother and fetus is not different from that in normal pregnancies.

COMMENT

Striking associations have been demonstrated between both ABO blood groups and HL-A antigens of

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Respiratory Tract Illness in Meat Wrappers

Henry Falk, MD, Benjamin Portnoy, MD

• A questionnaire survey was done in 152 Houston supermarkets to assess the prevalence of respiratory tract symptoms in meat wrappers exposed to the thermal decomposition fumes of polyvinyl chloride (PVC) film wrap and in two supermarket control groups (checkers and meat cutters). Meat wrappers had increased respiratory tract symptoms; 12% of meat wrappers who smoked (vs 6% and 2% of controls) and 5% of meat wrappers who did not smoke (vs 0% and 0% of controls) had multiple respiratory tract symptoms. It is probable that a large number of meat wrappers have mild symptoms with some progressing to more severe respiratory impairment or clinical asthma.

(JAMA 235:915-917, 1976)

A RECENT report¹ described a new syndrome called "meat-wrapper's asthma." Three women experienced dyspnea, wheezing, and coughing while at work as supermarket meat wrappers. Their jobs involved cutting strips of polyvinyl chloride (PVC) meat-wrap film by pulling the film across an electrically-heated wire. The fumes generated by this process were implicated in the asthma syndrome. In addition, the National Institute for Occupational Safety and Health has investigated a larger number of reported cases of this syn-

See also pp 937 and 943.

drome in recent years,² suggesting that the disease is more widespread than was first apparent. Since there are currently about 70,000 meat wrappers in the United States (according to a recent estimate of the Joint Labor Management Committee of the Retail Food Industry, Washington, DC), the potential for a widespread hazard exists.

In January 1974, the Houston City

Health Department was notified of two cases of meat-wrapper's asthma, and interviews with the affected women suggested that there might be other workers in local supermarkets with similar symptoms. As a result, a questionnaire study was designed to define the prevalence of meat-wrapper's asthma and respiratory tract symptoms among Houston meat wrappers.

METHODS

The five largest supermarket chains in Harris County, Texas (Houston and environs), were chosen for the study, and a total of 152 of these chain stores were included (98% of total). In each store, the meat wrapper on duty and two control employees were interviewed with a standard questionnaire. The controls included one grocery checker and one meat cutter. The meat cutters were used as controls because they work in the same refrigerated environment (most are at 10 to 12 C) as the wrappers do but do not usually wrap meat. (In this study only a small minority of meat cutters spent any portion of their time wrapping meat.) The three subjects at each supermarket were interviewed simultaneously by a team of three investigators who rotated between subjects and controls. The survey was conducted during May and June 1974.

The questionnaire was adapted for this study from a standard respiratory tract disease questionnaire used in a study of coal worker's pneumoconiosis (form HSM-591, US Department of Health, Education, and Welfare, National Institute of Occupational Safety and Health). The questions

were designed to elicit a full history of occupation, respiratory tract symptoms, and smoking.

In each store, the investigators recorded the temperature of the meat room, the type of wrapping device, and the manufacturers of the PVC film and film cutters that were in use.

Written consent was obtained from each subject. Each supermarket chain and labor union involved in the study granted written permission to the investigators to conduct the survey.

RESULTS

Interviews were conducted with 145 meat wrappers and 150 persons in each control group. All but one of the meat wrappers and most of the checkers were women, while all the meat cutters were men (Table 1). The meat wrappers as a group were somewhat older than both groups of controls.

The duration of work in their job categories was similar for meat wrappers and meat cutters, with approximately 50% having worked longer than ten years at their jobs. Checkers, however, worked fewer years.

Table 2 shows the results for the portion of the questionnaire relating to the presence of the major respiratory tract symptoms (wheezing, shortness of breath, and chest pain); the meat wrappers have a significant increase of these symptoms. This table shows that the increase is primarily in meat wrappers who smoke, although a smaller increase, while not significant in our study, is also seen in meat wrappers who do not smoke.

A comparison of smoking patterns in the three groups shows the meat wrappers and checkers to be almost identical, with both groups smoking considerably less than the male meat cutters (Table 3). Smoking by itself (or in combination with the cold environment) is therefore not an adequate explanation for the increased symptoms seen in meat wrappers. In addition, although the wrappers as a group are somewhat older than the

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controls, the increased respiratory tract symptoms are independent of age (Table 4).

The response to the question, "Have you ever had any of the following problems that you believe is re-

lated to your work?" (an unstandardized addition to the questionnaire in use that should be evaluated cautiously) suggests that irritation of the eyes and throat may be a prominent part of the meat-wrapper's syndrome

(Table 5). Nasal symptoms, however, are equally prominent in meat cutters and wrappers and appear to be related to working in the cold environment.

The data also suggest that meat wrappers have had an increased incidence of nonspecific respiratory tract illnesses (Table 6). For some of these categories (pneumonia, pleurisy, bronchitis), however, the timing of the illnesses (before vs after employment) was not dealt with in the questionnaire, and it is therefore possible, although somewhat unlikely, that these differences antedate and are unrelated to employment.

The incidence of respiratory tract symptoms in meat wrappers was unrelated to the supermarket chain where employed, duration of work, temperature of the meat room, or brand of PVC film wrap or hot-wire machine used. Seventeen of the 145 meat wrappers were working with mechanical blade machines and not with fume-producing hot wires. None of these had any respiratory tract symptoms related to work.

There were no significant differences between meat wrappers and checkers (the two female groups) in responses to the remainder of the questionnaire, including history of allergy, history of medication, previous hazardous occupation, use of hair sprays, history of cardiac or other respiratory tract illness, or level of education. The male meat cutters differed somewhat, with fewer medical complaints and use of medications, but with a slightly greater exposure to other hazardous occupations.

COMMENT

Earlier reports have shown the relationship between meat wrapping

	Meat Wrappers	Controls	
		Checkers	Meat Cutters
Mean age, yr	39.0	35.4	33.4
Race			
White	131	131	138
Nonwhite	14	19	12
Sex			
M	1	16	150
F	144	134	0
Total	145	150	150

	Controls		
	Checkers, No.(%)	Meat Cutters, No.(%)	Meat Wrappers, No.(%)
Nonsmokers			
Shortness of breath	3(5)	0(0)	3(5)
Wheezing	0(0)	0(0)	3(5)
Chest pain	4(6)	2(7)	8(13)
Multiple	0(0)	0(0)	3(5)
No. at risk	63	30	61
Smokers, past and current			
Shortness of breath	3(3)	6(5)	13(15)†
Wheezing	7(8)	11(9)	14(17)
Chest pain	6(7)	10(8)	17(20)†
Multiple	5(6)	2(2)	10(12)†
No. at risk	87	120	84
Total			
Shortness of breath	6(4)	6(4)	16(11)‡
Wheezing	7(5)	11(7)	17(12)
Chest pain	10(7)	12(8)	25(17)†
Multiple	5(3)	2(1)	13(9)†
Total at risk	150	150	145

* Shortness of breath was considered present if subject responded "yes" to (1) Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill? and (2) Do you become short of breath walking with other persons your own age on level ground? or (3) Do you have to stop for breath when walking at your own pace on level ground?

Wheezing was considered present if subject responded "yes" to (1) Do you ever have a wheezing or whistling sound in your chest? and (2) Do you get this most days or nights?

Chest pain was considered present if subject responded "yes" to: Do you ever have attacks of chest pain?

† $P < .01$.

‡ $P < .05$ (2 df χ^2 test).

No.	Controls		
	Checkers	Meat Cutters	Meat Wrappers
<1	63	30	61
1-19	38	31	35
20-39	42	64	41
≥40	7	25	8
Total	150	150	145

*Includes current smokers and former smokers when they smoked regularly.

Age, yr	Meat Wrappers		
	All, No.(%)	Any Chest Symptom, No.(%)	Multiple Chest Symptoms, No.(%)
<20	1(19)	1(2)	0(0)
20-29	32(22)	13(31)	4(31)
30-39	45(31)	12(29)	3(23)
40-49	42(29)	9(21)	3(23)
50-59	22(15)	5(12)	3(23)
≥60	3(2)	2(5)	0(0)
Total	145	42	13
Mean age, yr	39.0	37.4	38.5

*All meat wrappers and meat wrappers with chest symptoms, Houston, 1974.

Symptom	Checkers, No.(%)	Meat Cutters, No.(%)	Meat Wrappers, No.(%)
Dry or sore throat	18(12)	24(16)	41(28)†
Burning or itchy eyes	13(9)	15(10)	38(26)†
Tearing of eyes	6(4)	11(7)	28(19)†
Stuffy nose	13(9)	49(33)	42(29)†
Runny nose	9(6)	51(34)	46(32)†
Coughing	9(6)	29(19)	26(18)†
Chest tightness, soreness or heaviness	3(2)	10(7)	26(18)†
Wheezing or whistling in chest	4(3)	7(5)	15(10)‡
Shortness of breath	5(3)	14(9)	25(17)†
Chest pain	5(3)	12(8)	13(9)
Total at risk	150	150	145

*"Have you ever had any of the following problems that you believe is related to your work?"

† $P < .01$ (2 df χ^2 test).

‡ $P < .05$.

	Checkers	Meat Cutters	Meat Wrappers
Recent illness			
In the past three years have you had a period of increased cough and phlegm lasting for three weeks or more?	14	15	30*
During the past three years have you had any chest illness that has kept you from your usual activities for as much as a week?	18	12	32*
History of illness			
Bronchitis	19	13	31*
Pneumonia	27	21	36
Pleurisy	16	9	33*
Total at risk	150	150	145

* $P < .01$ (2 df χ^2 test).

and asthma¹⁻³ and have sought to identify the toxic thermal decomposition products of PVC film wrap.⁴⁻⁷ Our study was designed to estimate the prevalence of respiratory tract problems in a large group of meat wrappers. Our results show that about 10% of the meat wrappers studied have multiple respiratory tract symptoms (wheezing, shortness of breath, chest pain, or tightness) and that a considerably larger number have lesser respiratory tract symptoms or eye, throat, or nose irritation. In most cases, this spectrum of common respiratory tract problems is not severe enough to cause workers to seek medical attention and treatment; in some, however, more severe impairment, including clinical asthma, can develop and may be severe enough to force the wrapper to quit her job (as in the case of two former workers whose illnesses prompted this study). We cannot estimate how often this more severe

form of respiratory tract illness occurs, since our study was confined to current workers at the supermarkets included; a detailed analysis of former meat wrappers is needed to answer this question.

The results also suggest that wrappers may have an increased incidence of acute respiratory tract illnesses (including illnesses characterized as pleurisy, bronchitis, or pneumonia). We suggest, therefore, that the term meat-wrapper's asthma is inappropriate in describing acute and chronic respiratory tract symptoms related to meat wrapping.

Meat wrappers who smoke appear to be at greater risk to respiratory tract problems, although a larger number of meat wrappers who do not smoke will have to be studied to evaluate fully the risk in this group. Working in a refrigerated environment, however, does not seem to be an important risk factor for the development of lower respiratory tract

disease. We cannot assess from this study the long-range effects of inhaling PVC thermal decomposition fumes or of the increased respiratory symptoms, and further studies are needed to address these problems. This study was designed to detect respiratory tract illness, and no conclusions can be drawn about disease in other organ systems.

Prior to this study there had been some discussion in the local press and among labor leaders of the potential health problems related to wrapping meat. Although all efforts were made to minimize potential bias in this study, we realize that there is a possibility for subjective bias on the part of those interviewed; it is important that additional studies, such as pulmonary function analyses, be performed on groups of meat wrappers to confirm the associations noted here.

Where hot-wire machines are still used, the installation of proper ventilating equipment and lower-temperature wires may help reduce the risk to meat wrappers. It would appear, however, that the best solution to this problem would be to use mechanical blade machines that do not create fumes.

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Rates of Cutaneous Reactions to Drugs

A Report From the Boston Collaborative Drug Surveillance Program

Kenneth A. Arndt, MD, Hershel Jick, MD

• Rates of allergic skin reactions to commonly used drugs were estimated from data obtained on 22,227 consecutively monitored medical inpatients. A total of 57 drugs were implicated in skin reactions. Five or more reactions were attributed to each of 22 drugs (or drug groups). Many commonly used drugs did not appear to cause any allergic reactions. The study provides the practicing physician with drug-specific quantitative data that can be used to value the causes of drug-induced rash, itching, or hives. (*JAMA* 235:918-922, 1976)

SKIN REACTIONS are among the most common undesired effects of drugs—occurring in 2% to 3% of medical inpatients.¹ The attribution of a cutaneous reaction to a particular drug frequently entails a difficult judgment, since patients generally receive many drugs simultaneously. This judgment requires quantitative information about the rate of such reactions to each drug received by the patient.

In order to estimate the frequency of skin reactions to commonly used drugs, we examined the records of the Boston Collaborative Drug Surveillance Program (BCDSP), which now includes data on over 22,000 medical inpatients.

MATERIAL AND METHODS

The methods of the BCDSP have been described in detail elsewhere.² All drug treatments of the consecutively monitored medical inpatients were recorded, including dates of starting and stopping, dosage, and route of administration. All drug-attributed adverse events were also recorded, together with the date of onset,

and a full description of the event was secured by the monitor regardless of whether the reaction could be attributed to a particular drug.

As a preliminary to data analysis, a detailed review of each drug-attributed skin reaction was carried out to identify those that conformed to the generally accepted concepts of "allergic" reactions. (The commonly used term "allergic" is used in this communication for convenience. It should be noted, however, that mechanisms of drug-induced skin reactions are obscure and that some may be nonimmunologic in nature.)

Case histories and descriptions on all patients who experienced drug-attributed skin reactions were examined by a dermatologist (K. A. A.). Included for further study were (1) eruptions characterized by the rapid onset and widespread, bilateral involvement with erythematous macules or papules or both, often termed morbilliform, maculopapular, or exanthematous in appearance, (2) hives, and (3) generalized itching. Some 565 drug-attributed skin reactions occurred among 22,227 monitored patients. Of these reactions, 58 were excluded because they did not appear to represent clinically typical allergic skin reactions: several were acne attributed to steroids, some were preexisting rashes, many were local injection reactions, and the remainder represented vague and ill-defined localized cutaneous changes. The remaining 507 reported events, occurring in 491 patients, were considered to be "allergic" drug-induced skin reactions, and

the review of the data was confined to these.

Data analysis was first directed to the qualitative identification of allergenic drugs. (Cephalosporins, [cephalothin, cephaloglycin, cephalexin, and cephalexin], barbiturates [secobarbital, pentobarbital, phenobarbital, barbital, butabarbital, amobarbital, butethal, and mephobarbital], mercurial diuretics [meralluride and mercaptomerin], and semisynthetic penicillins [methacillin, nafcillin, oxacillin, cloxacillin, carbenicillin, and dicloxacillin] were examined as groups rather than individual drugs.) A major principle in this analysis was the removal from the data base of patients exposed to known allergens. The procedure was a sequential one: In the first stage, all patients receiving any penicillin or blood product were removed. This removal was based on an a priori recognition of these products as major causes of skin allergies on medical wards. It involved 8,401 (38%) of the patients and 357 (70%) of the skin reactions.

In the remaining patients, the detection of individual drugs that produced skin reactions was based on two criteria. First, the frequency of reactions in patients receiving the drug had to be at least twice as high as the frequency of reactions in the remaining patients at large. Second, there had to be a characteristic cluster of rashes in the days following the first exposure to the drug. The application of these criteria was based on computer-produced scattergrams that showed, for recipients of any given drug, the occurrence of allergic skin reactions in relation to first exposure to that drug. Additional causative drugs were detected by these criteria, and the recipients of these drugs were also removed from the data base to provide for the detection of the next set. The procedure was repeated until all skin reactions were accounted for.

Having identified a set of apparent allergens, the next step was to assign each reaction to a single drug in order to obtain

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Polyvinyl Chloride Implicated in Liver Ills

By R. S. GRIMSHAW, JR.

Medical Tribune Staff

NEW YORK—Preliminary indications that workers involved in the fabrication of plastics from polyvinyl chloride (PVC) may be at risk for impaired liver function were presented here by West German investigators.

Drs. C. E. Lange and W. K. Lehlbach, of the University of Bonn, told a conference on vinyl chloride toxicity sponsored by the New York Academy of Sciences that of 15 persons employed in the manufacture of PVC floor tiles, six had evidence of "vinyl chloride disease," including sensations of pain in the upper abdomen, slight to moderate thrombocytopenia, increased BSP retention by the liver, reticulocytosis, and liver fibrosis upon peritoneoscopy—lesions that, in one case, were termed possible precursors of a more advanced, perhaps malignant lesion. Leukocytopenia was noted in one case, as was splenomegaly, although selective splenograms were done.

Exposure to Monomer Postulated

Dr. Lehlbach postulated that the workers had probably been exposed to vinyl chloride, the monomer of PVC, which could have been leached from PVC when the material was heated in the tile-forming process.

Exposure to vinyl chloride gas has been found to be strongly associated with angiosarcoma of the liver, and is presumed to be the source of 13 such cases found so far in persons employed in vinyl chloride manufacture or polymerization in the United States.

While the number of persons working directly with the monomer is small—approximately 6,500—the number working with PVC is many times greater.

Dr. Irving J. Selikoff, Professor of Medicine at the Mount Sinai School of Medicine and cochairman of the conference, termed the reports "our first hint," although still unconfirmed, that vinyl chloride risk extends beyond the monomer workers.

Dr. Cesare Maltoni, director of the Institute of Oncology of Bologna, Italy, reported new animal studies demonstrating oncogenicity of vinyl chloride at a level of 50 parts per million. At that level, Dr. Maltoni found cases of liver angiosarcoma, peritoneal angiosarcoma, and nephroblastoma in very old rats, while no malignancies were found in control animals.

Fifty parts per million is the current emergency temporary standard of exposure set by the U.S. Department of Labor's Occupational Health and Safety Administration. This agency has proposed a new job safety standard that would allow "no detectable level" of occupational vinyl chloride exposure.

The Food and Drug Administration and the Environmental Protection Administration have recently acted to limit consumer exposure to vinyl chloride, requesting recall of aerosol products that use vinyl chloride as a propellant, specifically hair sprays and indoor-use pesticides.

In addition to potentiating malignancies, vinyl chloride appears to be associated with other clinical manifestations, according to reports presented by investigators from Germany, Japan, and Romania. These include skin lesions, acroosteolysis, Banti syndrome and Banti fibrosis, pulmonary lesions, nervous system lesions, impotence, and hormonal imbalances.

"We have," said Dr. Selikoff, "a multisystem disease."

Evidence of Oncogenicity Was Available in '72

Medical Tribune Report

NEW YORK—Evidence that vinyl chloride causes a variety of cancers in rats and mice was available as early as 1972, one and a half years before action was taken to determine its toxicity in man, Dr. Cesare Maltoni, director of the Institute of Oncology of the University of Bologna, told MEDICAL TRIBUNE in interviews here and in Italy.

Dr. Maltoni, who began studies on the oncogenicity of vinyl chloride under the sponsorship of several European chemical companies in 1971, said the results were communicated to the Manufacturing Chemists Association, an American industry trade group, by the end of 1972. A team of M.C.A. scientists visited his laboratory in January, 1973, he said, and the National Institute of Occupational Safety and Health was notified in July. Yet, he charged, nothing was done about possible vinyl chloride effects in man until the death, from liver angiosarcoma, of a worker at the Louisville plant of the B.F. Goodrich Company last December.

Dr. Maltoni said that the experience with vinyl chloride underscores the need to accept animal studies of carcinogenicity and the need to perform bioassays "for all new products that are developed."

Reduced Drinking Age Raises Highway Toll

Medical Tribune Report

WASHINGTON—State laws reducing legal minimum drinking ages to 18 years represent "social policy that carries a price in increased fatal motor vehicle collisions," a research report by the Insurance Institute for Highway Safety declared.

The study compared fatal-crash implication of drivers under 21 in Michigan, Ontario, and Wisconsin—where the legal drinking age was dropped

from 21 to 18 in either 1971 or 1972—with corresponding figures for Indiana, Illinois, and Minnesota, where the age was 21.

The investigators estimated that for each 100,000 of their numbers in the population, 15-to-20-year-olds were a party to 2.6 to 3.3 more fatal crashes in the first year after the legal drinking age was lowered than would have been expected from prior experience.