05127

AN-3998

Toxicology of Plastics and Rubber

—PLASTOMERS AND MONOMERS

REX H. WILSON, M.D., F.A.C.P., and WILLIAM E. McCORMICK, M.S.
The B. F. Goodrich Company, Akron, Ohio

THE POPULAR demand for all types of articles made from plastics has been so tremendous that literally there has been created an entirely new industry in the past several years. Many plants, large and small, are devoting their entire manufacturing facilities to "plastic" items. The demand for the compounds going into the composition of the plastic materials is so great that supplies of certain of them are short.

Because the industry is new and because of the ingenuity of modern research, the compounds making up the plastics are ever changing. Also, as demands for different types of articles made from plastics are increasing, this creates a demand for different types or kinds of plastics (Table I). Naturally, the kind of material needed for a plastic automobile body is different from the material needed for an elastic garden hose or a pair of stockings. I know of no other industry which better represents the creative genius of man than the so-called plastic industry. The creation at less cost of better things for better living is the aim of the modern business man. To achieve this, there have been brought into existence the wonderful modern-day research laboratories.

It is important to know the chemical properties of a compound and its toxicity. It is also important to know how to work with it safely. Equally important is to know the treatment for overexposure to the toxic chemical to prevent permanent damage or death.

It would be impossible to name, let alone discuss, the toxicological properties of all of the chemical compounds being used in the plastic industry. It is worth-while to discuss the properties of some of the more common resins, plasticizers, stabilizers and solvents being used. Unfortunately, the toxicological properties of all of these are not too well defined. It is to the credit of people working in industrial medicine and hygiene that industry is becoming aware of the necessity for knowing the toxicity of its materials and is taking steps to insure that its employees are not exposed to materials that would harm them.

Presented at the Eleventh International Congress on Industrial Medicine, Naples, Italy, September 13-19, 1954.

Resins

LEHMAN[1] in July, 1951, presented a list of resins both suitable and unsuitable for use as food packaging ingredients. He stated "that as a general rule resins are so insoluble as a class that the chances of contamination by the solvent action of foods are rather slight." The types of resins he considered suitable for food use are:

Polyvinyl chloride.
Polyvinyl acetate.
Polyvinyl chloride-acetate.
Polyvinylidene chloride.
Polystyrene.
Polyethylene.
Cellulose acetate.
Regenerated cellulose.
Terephthalic acid-ethylene glycol copolymer.
Butadiene-acrylonitrile (Perbunan or Hycar synthetic rubber).

Lehman classified as being unsuitable for use in food packages because of the lack of adequate data concerning their toxicity:

Polyvinyl formal.
Polyvinyl acetal.
Polyvinyl butyral.
Polymeric furfuryl alcohol.
Coumarone-indene.
Urea formaldehyde.
Phenol formaldehyde.
Aniline formaldehyde.

A. Vinyl Type

VINYL CHLORIDE, vinylidene chloride, and vinyl acetate readily polymerize. By proper combinations of one or more of these monomers, many polymer variations can be produced. These polymers, after properly mixing with plasticizers and stabilizers, are then used in hundreds of dif-

Reprinted from INDUSTRIAL MEDICINE AND SURGERY, 23:11, 479-486, November, 1954

ferent items. The three polymers, either individually or associated with each other, are relatively non-toxic.[1]

Seeler and associates studied the chronic toxicity of a copolymer of vinyl and vinylidene chloride.[2] This work was done because the copolymer was being considered for use as a constituent of a plastic film for wrapping food products. They reported that rats fed a diet containing 5% vinyl and vinylidene chloride copolymer for two years showed no toxic effects. Two dogs were fed a diet containing 5% vinyl and vinylidene chloride copolymer without evidence of toxic effects.

Some toxicological information also exists on the three monomers—vinyl chloride, vinylidene chloride, and vinyl acetate. Patty, Yant, and Waite[3] investigated the acute effects of vinyl chloride on experimental animals and found this to be essentially narcosis. Carpenter and associates,[4] in range finding studies, observed that a vapor concentration of 32,000 ppm of vinylidene chloride resulted in a portion of deaths of the six rats exposed for four hours. The vapor toxicity is reported to be of the same order as ethylene dichloride.[5] Carpenter and associates[4] also reported a level of 4,000 ppm of vinyl acetate produced some deaths under the same conditions.

B. Acrylonitrile—Butadiene Type

VARIOUS types of American made rubbers have been studied physiologically. Among those found to be acceptable for food use are Perbunan and Hycar (polymers of acrylonitrile and butadiene). However, the manufacture of these items does present some health problems.

Wilson and associates[6] reported on the toxicity of acrylonitrile in 1948. They stated that, in their observations, workmen handling cleaning operations in polymerizers with exposures varying from 16-100 ppm for 20 to 45 minutes frequently show symptoms of dull headache, fullness in the chest, irritation of all mucous membranes including the eyes, nose and throat, and a feeling of apprehension and nervous irritability. Some workmen complained of intolerable itching of the skin with no demonstrable dermatitis. Direct skin contact with acrylonitrile causes irritation and erythema followed by bleb formation, desquamation and slow healing. Wilson[7] reported several cases of acrylonitrile poisoning in which there developed mild jaundice, low grade anemia and leucocytosis. Given orally the minimal fatal dose of acrylonitrile in laboratory rats is stated[8] to be 150 mg/kilo body weight. Symptoms in these animals included respiratory changes, cyanosis, convulsions and death.

Because the mode of action of acrylonitrile in the human system appears to be similar to that of cyanide, the treatment of overexposure to acrylonitrile was outlined by Wilson and associates[6] to be the same as that for overexposure to cyanide. This treatment was proved to be life saving in several instances.

Vitamins B_1 and C have been found to be beneficial in preventing weight loss in laboratory animals exposed to acrylonitrile over long periods.

Wilson and associates[6] also suggested as a prophylaxis against overexposure to acrylonitrile that atmospheric concentrations should not exceed 20 ppm. This necessitates enclosure of processes to the maximum degree possible and the effective use of mechanical exhaust ventilation.

Skin contact should be avoided, not only because of the compound's vesicant action, but also because of possible toxic systemic effects. In the case of skin contact with the concentrated compound, immediate washing with copious quantities of soap and water is necessary. If spilled on clothing, the clothes should be immediately removed and a shower taken by the individual. The effect of chronic low-grade atmospheric or skin exposures on humans is still undetermined. It is, therefore, advisable that working personnel be given periodic physical examinations, with special emphasis on hematology and liver and kidney functions. The determination of the thiocyanate level in both blood and urine has been suggested as an index of overexposure.

Wilson and associates[6] also reported on the toxicology of butadiene. They stated that butadiene is practically innocuous, aside from its narcotizing and anesthetizing effect at very high concentrations. Human subjects who were exposed to 8,000 ppm of butadiene complained of eye irritation, blurring of vision, coughing, nasal congestion, and drowsiness.[9] Subsequent repeated exposures gave no indication of cumulative action.

A complete examination of the chest including an x-ray, blood examination and urinalysis were not informative. Subsequent follow-up examinations were also negative. In laboratory animals[9] subjected to high exposures of butadiene, irritation of all of the mucous membranes and respiratory tract occurs along with varying degrees of narcosis. Acute deaths are due to pulmonary edema. Delayed deaths are due to chemical pneumonia following pulmonary irritation. Experimentation with butadiene in laboratory animals indicates that butadiene is not a safe general anesthetic because there is not complete muscular relaxation even in the fourth stage. Death ensues rapidly when the laboratory animal is kept in deep anesthesia for any length of time.

Wilson and associates[6] stated that workmen anesthetized with or suffering from exposure to butadiene should recover completely, providing they are removed from exposure while respiration and heart action are still strong. Oxygen by inhalation should be administered until the pulse and blood pressure remain normal and the color is good. Symptomatic treatment is indicated.

Special precautions need to be observed in handling the compound from a fire and explosive standpoint. These include enclosure and mechanical exhaust ventilation and will in most cases automatically control the health hazard. There is no apparent systemic injury to humans in concentrations below 5,000 ppm. Any complaints which include eye and respiratory irritation, headache and vertigo might be considered as indicative of excessive exposure.

TABLE I.

COMMON PLASTICS	USES	PROPERTIES
Acrylics	Aircraft turrets, auto tail lights, brush backs, signs (Dynel, Acrilan, Orlon textiles).	Optical clarity, good weather resistance, wide color range, shatter resistance, machinability.
Alkyds and Rosin Modifications	Linoleum surfacings, paints for refrigerators and autos, ignition parts, magneto rotors.	Fast curing, good dimensional stability, good electrical insulation, good heat resistance.
Aminos (Urea and Melamine)	Buttons, dishes, laminated table tops, housings for kitchen appliances.	Unlimited color range, good electrical insulation, resistance to organic solvents.
Cellulose Plastic Materials	Display packaging, irrigation pipe, frames for eye-glasses (rayon and acetate textiles).	Toughness, high impact strength, ease of fabrication, lustrous finish, good electrical insulation.
Coumarone-Indene and Petroleum Resins	Asphalt floor tiles, aluminum paints, waterproof coatings, printing inks.	Resistance to water and caustic cleansers, compatibility with compounding ingredients, glass.
Epoxies	Printed circuit backing, adhesives, surface coatings, transformer and motor laminates.	Excellent adhesion, resistance to chemicals and heat, can be cured at room temperatures.
Fluorocarbons	Pump diaphragms, chemical tubing, high temperature insulation.	Extreme resistance to corrosive agents and solvents, wide temperature range, high impact strength.
Nylon	Gears, slide fasteners, combs, tumblers, tennis racket strings (nylon textile).	Good strength and toughness over wide temperature range, wear resistance, self-lubricating.
Phenolic and other Tar Acid Resins	Telephone handset, radio-TV cabinets, shell molding, dials, grinding wheels, plywood.	Hard and rigid, good temperature range, strong, good electrical insulation, low water absorption.
Polyethylene	Squeezable bottles, semi-rigid kitchenware, packaging, coaxial cables.	Inert to solvents, flexible and tough over wide temperature range, nontoxic, odorless, tasteless.
Polyester Resins	Reinforced plastics for auto bodies, boats, translucent panels (Dacron textiles).	Weather resistance, can be formed with low pressure, strong, colorful, compatible with many fillers.
Silicones	Insulation for generator coils, auto polishes, waterproof coatings, circuit breakers.	Extreme heat resistance, low water absorption, good dielectric properties over wide frequency range.
Styrene Resins	Kitchen housewares, refrigerator parts, toys and novelties, wall tiles, lighting fixtures.	Lightest of commercial plastics, excellent moldability, unlimited color range, tasteless, odorless.
Vinyl Resins	Floor tile, packaging film, rainwear, toys, upholstery material, pipe and pipe fittings, valves, electrical insulation, sponge, machine and structural parts, metal and fabric coatings.	Tough and strong, unlimited color range, excellent electrical insulation, resistance to chemicals, oil and weathering.

C. Miscellaneous Types

SOME of the newer synthetic resins which have been physiologically studied are the silicones, the polyethylene gylcols (carbowax compounds), and teflon (polytetrafluoroethylene). Rowe *et al*[10] found upon feeding guinea pigs for 50 days in amounts up to 3% of the daily diet no indication of toxicity with DC resins 993 and 2102. They also found that DC Pan Glaze possessed a very low order of oral toxicity when fed to the rat. Shaffer and Critchfield[11] concluded from their study of carbowax compounds 1,000, 1,540, 4,000 and 6,000 that no significant gastrointestinal absorption occurred when fed to rats. They also administered intravenously compounds 1,000 and 6,000 to humans and found they were readily excreted to a high degree.

Polytetrafluoroethylene (Teflon) is a synthetic resin with exceptional resistance to both heat and chemicals. It is being used for electrical insulation, for special types of tubing, for coating molds and bread pans, and for gasket materials in jet engines. Stokinger[12] has described the ill effects which may result when Teflon is heated to about 360° F as well as from exposure to the finely divided polymer itself. These effects resemble, in the case of the polymer, those of metal fume fever; in the case of the sublimate (resulting from heating the polymer) those of hydrogen fluoride poisoning. In using Teflon, adequate ven-

tilation is necessary to avoid ill effects. Lehman[1] reports that baking tests have shown no significant increase of the fluoride level of bread baking pans which have been coated with Teflon.

Plasticizers

LEHMAN in July, 1951,[1] stated that plasticizers presented more serious toxicological problems than the resins because there is always the possibility that these materials may be leached out by food substances. The plasticizers which have had adequate pharmacological study demonstrating their harmlessness in the amounts now used in finished commercial films are:

Ethyl Phthalyl ethyl glycollate.
p-tertiary Butyl phenyl salicylate.
3-(2-Xenoxyl)-1,2-epoxypropane.
2-Ethylhexyl diphenyl phosphate.
Butyl phthalyl butyl glycollate.
Glycerol monooleate.
Acetyl tributyl citrate.
Di-iso-butyl adipate.

Lehman classified as unsuitable for food use the following:

Dicyclohexyl phthalate.
Dibutyl phthalate.
Methyl phthalyl ethyl glycollate.
Di-iso-octyl phthalate.
Dioctyl adipate.
Dibutyl sebacate.
Dioctyl sebacate.
Dicapryl sebacate.

Seifter in 1943[13] made acute toxicity, chronic toxicity and skin irritation studies on dibutyl phthalate. His summary and conclusions were:

1. Dibutyl phthalate is a mild primary skin irritant for animals and humans.
2. Dibutyl phthalate taken by mouth is acutely toxic.
3. Dibutyl phthalate ingested daily over long periods of time in amounts up to 2.5 gm. per kilogram of diet, does not produce chronic poisoning.

Smith[14] studied dibutyl phthalate and found the acute lethal oral dose to be about 8 gm. per kilogram. When administered chronically in the diet the maximum concentration which did not significantly reduce normal growth was 0.25%. The feeding of dibutyl phthalate even in the highest dietary concentrations did not provoke specific gross or microscopic pathologic changes. His findings also suggested that dibutyl phthalate was metabolized in the body in much the same way as the fat normally ingested in the diet. He did not feel that it was safe to incorporate dibutyl phthalate in films for wrapping foods even if the calculated safety factor was in excess of 1400.

Seifter[13] in studying dicapryl phthalate made the following summary and conclusions:

1. Dicapryl phthalate is not a primary skin irritant for animals or humans.
2. When taken by mouth dicapryl phthalate has a low acute toxicity.
3. Ingested daily over long periods of time, in amounts up to 2.5 gm. per kilogram of diet, dicapryl phthalate does not produce chronic poisoning.

Seifter in 1943[13] came to the following conclusions concerning triethylene didecoate:

1. It is not a primary skin irritant for animals or humans.
2. When taken by mouth, it has a low acute toxicity.
3. Ingested daily over long periods of time in amounts up to 2.5 gm. per kilogram of diet, it does not produce chronic poisoning.

Smith[14] found that the acute lethal oral dose of butyl stearate was greater than 32 gm. per kilogram. When butyl stearate was administered chronically in the diet, the maximum concentration which did not significantly reduce normal growth was more than 6.25%. Butyl stearate in the highest dietary concentration did not provoke specific gross or microscopic pathologic change and in dietary concentrations of 6.25% had no adverse effect on fertility or the number of viable young in the litter. There was in this concentration slight retarded growth of the young. He felt that, based on the above data, butyl stearate when incorporated in films for wrapping food appeared to possess little, if any, potential hazard for humans, the calculated safety factor being in excess of 1,400.

Smith[14] came to the conclusion that the acute lethal oral dose of methoxyethyl oleate was approximately 16 gm. per kilogram and when administered chronically in the diet of rats the maximum concentration, which did not significantly reduce normal growth, was 0.01% to 0.05%. He found renal calculi in three of seven rats fed 1.25% methoxyethyl oleate for more than six months. He felt that methoxyethyl oleate was hydrolized by pancreatic lipases as rapidly as triolein. He did not feel that methoxyethyl oleate should be incorporated in films for wrapping food.

Smith[14] concluded that the acute lethal oral dose of dibutyl sebacate was between 16 and 32 gm. per kilogram and that when administered chronically in the diet of rats, the maximum concentration which did not significantly reduce normal growth was 6.25%, and that when fed in the highest dietary concentration, there were no specific gross or microscopic pathologic changes. Dibutyl sebacate in dietary concentrations of 6.25% had no adverse effect on fertility or the number of viable young in the litter. It did cause a slight retarded growth of the young. Smith felt that this plasticizer was metabolized in the body in much the same way as fat normally ingested in the diet, and that when it was incorporated in films for wrapping food appeared to possess little, if any, potential hazard for humans, the calculated safety factor being in excess of 1400. Mallette and Von Haam[15] state that dibutyl sebacate is a non-toxic plasticizer, with no irritating or sensitizing effect on the skin, and that dibutoxyethyl phthalate is a non-toxic plasticizer with no irritating or sensitizing effect on the skin.

Mallette and Von Haam[15] listed the following as non-toxic plasticizers:

Di-2-ethylhexyl adipate.
Dibutyl cellosolve azelate.

Cyclohexyl azelate.
2-ethylhexyl azelate.
Methyl isobutyl carbinol azelate.
Pentasol azelate.
Diethylene glycol dicaprate.
Dibutoxyethyl diglycol carbonate.
Octadecene nitrile.
Dibutoxyethyl phthalate.
Dicapryl phthalate.
Methylacetyl ricinoleate.
Dioctyl sebacate.
Dibutyl sebacate.
"Plasticizer 50 B" (Barrett).
"Plasticizer Ellicott H."
"Plasticizer SC" (Drew).
"Paraplex G-25" (Rohm & Haas).
"Paraplex G-40" (Rohm & Haas).
"Plastolein X-55" (Emery).

They stated that five of the plasticizers examined showed a moderately toxic effect in laboratory animals. They were dioctyl phthalate, butylbenzyl phthalate, "santicizer 140," "santicizer 141," and "flexol 8N8."

Di(2-ethyl hexyl) phthalate (commercially referred to as dioctyl phthalate, DOP, and 2-ethyl hexyl phthalate) was studied by Hodge[16] with respect to acute oral and intraperitoneal toxicity in rats and mice. He concluded that it had a very low order of toxicity. Shaffer, Carpenter and Smyth studied it in 1945.[17] Their conclusions were that it is a chemical of low toxicity and that the health hazards involved in its use as a plasticizer are slight. Such injurious action as it does exert within the body appears to be due to the alkyl part of the molecule rather than to the phthalate portion.

Mallette and Von Haam[15] found that dioctyl phthalate had a moderately toxic effect in laboratory animals and that the intraperitoneal injection of dioctyl phthalate proved fatal in doses higher than 2 gm. per kilogram of body weight. Lower doses produced weight loss, leucocytosis, severe anemia and hematuria from which the animals recovered after a month or two. No delayed effect or permanent injury was noted in the surviving animals. They also showed that dioctyl phthalate had a moderate skin irritating effect.

Carpenter, Weil and Smyth[18] reported the results of feeding Di(2-ethyl hexyl) phthalate for two years to rats and for one year to both dogs and guinea pigs. They obtained relatively uniform responses from all three species, with the two-year "no effect" level for rats falling between .06 and .20 gm. kilogram per day, and the one-year "no effect" level for both dogs and guinea pigs approximating .06 gm. per kilogram per day. Lehman[1] reports that food packaging films containing this compound as a plasticizer are satisfactory for wrapping foods with a high water content, but are unsatisfactory for use with foods having a high fat content, because of the ready solubility of the plasticizer in fats and oils. Halpern and Weiss[19] found no irritation or induced sensitivity when 200 humans were patch tested with vinyl film containing dioctyl phthalate as the plasticizer.

In 1952 Mallette and Von Haam[15] reported on other plasticizers, several of which they found to be moderately toxic to rats in acute exposures. These were:

1. Butylbenzyl phthalate was fatal in rats after intraperitoneal administration of doses higher than 1.8 gm. per kilogram of body weight. Oral administration of more than 4 gm. per kilogram of body weight proved equally fatal. The animals died after four to eight days, showing weight loss, apathy and leucocytosis. The histological examination of the organs revealed toxic splenitis and degenerative lesions of the central nervous system with congestive encephalopathy, myelin degeneration and glial proliferation.

2. "Santicizer 140" (monotolydiphenyl phosphate) proved fatal in intraperitoneal doses of higher than 1 gm. per kilogram of body weight. Oral doses up to 4 gm. were supported. Toxic animals became lethargic on the second or third day and a profuse diarrhea developed. They died with symptoms of paralysis. Autopsy showed a generalized capillary paralysis with severe edema and numerous hemorrhages in the brain.

3. "Santicizer 141" (2-ethyl hexyl diphenyl phosphate or mono octyl diphenyl phosphate) killed animals after intraperitoneal administration of doses higher than 2.4 gm., but oral administration of 4 gm. per kilogram of body weight was tolerated. With the intraperitoneal administration the animals became paralyzed and lethargic. Recovery from non-fatal lesions was delayed. The histopathological examination demonstrated a severe acute hemorrhagic encephalopathy with cerebral edema, ganglion cell degeneration and small hemorrhages. As delayed effects, focal gliosis and persistent foci of myelin degeneration could be observed. Large fatal doses also proved a powerful hemolytic agent with marked vascular hemolysis, hemoglobinuria, and hemosiderosis of the spleen.

4. "Flexol 8N8" (N,N-di-beta-(2-ethyl hexyl) ethyl 2-ethyl hexylamide) proved fatal in doses higher than 4 gm. per kilogram of body weight. The animals developed convulsions followed by paralysis. The histological examination of the brain gave the picture of toxic hemorrhagic encephalopathy with edema, swelling of ganglion cells and small hemorrhages.

Their conclusions were that these four plasticizers proved moderately toxic in doses from 0.6 to 2.4 gm. per kilogram of body weight. The toxic reaction was displayed by the erythrocytes, the blood capillaries and the central nervous system. They also found in their studies 17 plasticizers to be slight or moderate skin irritants. Three—"Flexol 8N8," "Paraplex G-25," and "Paraplex G-40"—proved to be severe skin irritants.

A moderate sensitizing effect on the skin was found by Mallette and Von Haam[15] to exist with diethylene glycol dicaprate, methylacetyl ricinoleate, "Paraplex G-25," "Paraplex G-40," and "Santicizer 140."

Seeler *et al*,[20] in their studies on the chronic toxicity of acetyl tributyl citrate came to the following conclusions:

1. Rats showed no toxic effect after eating diets containing 200 ppm, 2,000 ppm, and 20,000 ppm of acetyl tributyl citrate for two years.

2. Dogs were given a daily oral dose of 140 mg. of acetyl tributyl citrate for two years without evidence of toxic effect.

Seeler *et al*,[21] on making chronic toxicity studies of butyl phthalyl butyl glycollate came to the following conclusions:

1. Rats fed diets containing 200 ppm, 2,000 ppm, and 20,000 ppm of butyl phthalyl butyl glycollate for two years showed no toxic effect.

2. Dogs were given a daily oral dose of 140 mg. of butyl phthalyl butyl glycollate for two years without evidence of toxic effect.

The results of both acute and chronic oral feeding, as well as skin absorption and irritation with 2-ethylhexyl diphenyl phosphate (Santicizer 141) are given by Treon *et al.*[22] These investigators found the compound to be innocuous when administered orally to rabbits and rats in a single large dose. No effects, either irritative or systemic, were found as the result of keeping it in contact with the abraded skin of rabbits for seven to 24 hours. Rats fed for two years on a diet containing 1%, 0.125%, and 0.0625% by weight of the compound showed no pathology, but did show a retarded growth rate at the 1% level. Dogs fed the compound at dietary levels of 2.5% for two years showed retarded growth, but those fed a 1.5% level grew normally.

Treon, Cappel, and Sigmon have found[23] that a high percentage of Santicizer 141 is excreted in the feces of both rabbits and humans unchanged. Halpern and Weiss[19] have shown that films plasticized with Santicizer 141 are not irritating and do not induce sensitivity in humans.

Stabilizers

MANY different materials are being used as stabilizers for plastics. The specific type of plastic with particular reference to its use, governs to a large degree the stabilizer to be selected. Obviously, uses such as that of food packaging where there might be leaching of the stabilizer into the food require materials that are not harmful if ingested. Lehman[1] states that the following are not objectionable for food packaging:

Aluminum monostearate.
Calcium acetate.
Calcium ethyl acetoacetate acetate.
Calcium carbonate.
Calcium stearate.
Calcium glycerophosphate.
Mono- di- and tricalcium phosphate.
Calcium oleate.
Calcium ricinoleate.
Magnesium stearate.
Magnesium glycerophosphate.
Mon-, di-, and trimagnesium phosphate.
Disodium hydrogen phosphate.
Ammonium potassium phosphate.

Some of the most efficient stabilizers from the standpoint of performance, particularly for the vinyl resins, are the heavy metal salts of barium, strontium, lithium, cadmium, and lead. All of these compounds, however, possess a relatively high degree of toxicity and they are objectionable for use in items involving contact with human food.[1] There are, however, many plastic formulas for uses in products where toxicity is not of particular significance and consequently, one or more of these stabilizers can be safely used. Obviously, when these heavy metals are used, adequate, safe handling procedures must be utilized in the manufacturing plant. These involve the practice of good industrial medical and hygiene procedures.

Lehman[1] has also stated that zinc oxide, zinc stearate and salts of manganese and copper are not objectionable as stabilizers in food wrapping material if not more than 50 ppm of the metal leaches out into the food.

Some of the newer stabilizers for vinyl resins are the organic tin compounds. Elemental tin has been used for many years as a lining for food containers and is relatively harmless. The organic tin salts, however, while not known to be harmful have not thus far been shown to be sufficiently safe for use in food container applications. The plant manufacturing operations involving the use of the organic tin stabilizers may present some industrial health problems but again the degree or extent of these is not known at the present time.

Solvents

IN THE processing of plastics into products, a number of chemicals are used. These include aromatic hydrocarbons, chlorinated hydrocarbons, petroleum distillates, ketones, acetates and alcohols. These compounds are all toxic in varying degrees and present certain medical problems in their handling. Specific methods for determining the atmospheric concentrations of these chemicals can be found in Jacob's[24] text.

The American Conference of Governmental Hygienists[25] suggested the maximum allowable concentrations of many of the more common solvents in Table II.

The aromatic hydrocarbons are used extensively in the processing of plastics. Of these, benzene (benzol C_6H_6); toluene (toluol, $C_6H_5CH_3$); and xylene (xylol, $C_6H_4(CH_3)_2$) are the principal ones. These compounds are of value because of the fact that they are excellent solvents.

As pointed out by Wilson[26] benzol poisoning may result from absorption of benzene by either the respiratory tract, the alimentary tract, or probably the skin. Cases of poisoning in human beings have been found with exposures to atmospheric conditions as low as 25 ppm. Concentrations of 50 to 100 ppm are considered to be safe for the average person. Individual susceptibility varies. *Acute benzol poisoning is rare.*

As pointed out by Wilson[27] the pathologic manifestations of exposure to toluene are a matter of controversy. The conclusions reached by various authors are in decided variance with one another. Toluene poisoning is probably caused by absorption through the respiratory system, the skin, and the alimentary tract. The absorbed

TABLE II.

SUGGESTED MAXIMUM ALLOWABLE CONCENTRATIONS
(Parts per million parts of air)

Acetone	1000
Acrylonitrile	20
Amyl acetate	200
Amyl (iso) alcohol	100
Benzene (benzol)	35
Butadiene 1,3	1000
Butyl acetate	200
Butyl alcohol	100
Carbon tetrachloride	25
Ethyl acetate	400
Ethyl alcohol	1000
Ethylene dichloride	100
Gasoline	500
Heptane	500
Hexane	500
Propyl (iso) alcohol	400
Methyl alcohol	200
Methyl ethyl ketone	100
Naphtha (petroleum)	500
Perchlorethylene (tetrachlorethylene)	200
Propyl acetate	200
Stoddard solvent	500
Tetrachlorethane	5
Tetrachlorethylene	200
Toluene	200
Trichlorethylene	200
Xylene	200

vapors exert a progressive depressant action on the central nervous system and the bone marrow. Toluene is also a pronounced irritant to mucous membranes. A factor to be considered whenever it is employed is individual susceptibility. Exposure to concentrations of toluene from 200 to 500 ppm for six to eight hours will in most persons cause tiredness and lassitude. Concentrations over 500 ppm for one to three hours are definitely dangerous and will cause symptoms attributable to depression of the central nervous system and the bone marrow.

Xylene[6] is stated to possess more severe narcotic properties than benzene. Xylene poisoning is relatively uncommon because its volatility is lower than that of benzene or toluene. Chronic poisoning does occur. There is some evidence that xylene exerts an action on the blood forming organs similar to that of benzene. Cases of aplastic anemia have been attributed to xylene vapors. There have been some cases reported in German literature of leukopenia and thrombocytopenia with no reduction in red cells.

The commonly used chlorinated hydrocarbons in the plastic industry are:

Carbon tetrachloride (tetrachlormethane) CCl_4.

Ethylene dichloride (dichlorethane) $C_2H_4Cl_2$.

Tetrachlorethane (acetylene tetrachloride) $C_2H_2Cl_4$.

Trichlorethylene (ethylene trichloride) C_2HCl_3.

Perchlorethylene (tetrachlorethylene) C_2Cl_4.

The most toxic of the group is tetrachlorethane, having, according to Matruchot,[28] a comparative toxicity of 6.0. Carbon tetrachloride is listed by the same author as having a comparative toxicity of 2.6, trichlorethylene of 1.0, perchlorethylene of 1.4, and ethylene dichloride of 1.6. According to Davis[29] and the U.S. Public Health Service,[30] the maximum allowable concentration of carbon tetrachloride is 100 parts per million. According to Elkins[31] this level is too high and should be reduced to 50 parts per million.

Many of the petroleum distillates are used. Gasoline (unleaded), hexane, heptane, Stoddard solvent, varsol, and naphtha are mixtures of hydrocarbons, paraffins, olefins, cycloparaffins (naphthenes), aromatics, and other impurities including sulphur. Cracked gasoline may also carry a fairly high percentage of benzol. These substances are frequently referred to by the general name of benzine. This is to be distinguished from benzene (benzol). These distillates are narcotics, and it is possible to produce complete anesthesia with heavy doses. However, their anesthetic properties are much less than those of the aromatic and chlorinated hydrocarbons. For this reason they may be more desirable for commercial use. Drinker and associates, in studying the effects of gasoline vapors[32] found that concentrations from 270 to 500 ppm were tolerable. Neuromuscular symptoms began at about 900 ppm; mild intoxication at 2,000 ppm.

Acetone, methyl ethyl ketone, methyl isobutyl ketone, and methyl amyl ketone are also used. In our experience no cases of occupational disease have been attributed to the ketones.

Methyl, ethyl, propyl, isopropyl, butyl and isoamyl acetate may be used. These solvents are not considered severely toxic and in most cases the allowable concentrations are based more on comfort than on toxic requirements.

Methyl, ethyl, isopropyl, amyl and butyl alcohol are all used at times in plastics manufacture. Methyl alcohol is a source of grave injury to many industrial workers. It has a specific action on the optic nerve, and with long enough exposure, blindness may result. The action is that of inflammation of the optic nerve followed by atrophy. A considerable amount of methyl alcohol poisoning was noted during prohibition days when wood alcohol was used in large amounts with subsequent optic nerve degeneration and blindness. The other alcohols, because of their volatility are not considered to be especially dangerous. Cases of narcotic poisoning have been attributed to them but not proved. The higher alcohols, like butyl and amyl, have in addition an irritant action as well as some poisonous action on the protoplasm.

Summary

THE ADVENT of a great industry for the manufacture of articles of all kinds made from various chemical compounds has created many new problems for the industrial physician and the industrial hygienist. Many of the compounds used are new and very little, if anything, is known about their toxicity. Also, since there are no set formulas or recipes, each plastic article may have a different composition.

This paper attempts to discuss the toxicity of the more common compounds now being used in

plastics manufacture. Resins, plasticizers, stabilizers and solvents are discussed in some detail in regard to their toxic properties. The scarcity of knowledge of the properties of many of the chemicals is sufficient reason for further study.

It is not enough for industry to make better things cheaper; it must also make them safely.

Resume

ARTICLES made of a variety of chemical combinations commonly called plastics have found increasing favor with the consuming public. Many useful products can be made stronger, better looking, longer wearing and at lower costs employing these versatile new materials. The imaginative creativeness of the human mind is evident in our new world of plastics. To create these manmade marvels, the research chemists and development engineers have not only used known chemicals but also have created new ones.

Unfortunately, many of the chemicals currently used are known to be highly toxic. Even worse, the toxicity of many of the newer chemicals is not even known. Thus, industrial medicine and hygiene face serious problems both from known and potential toxic hazards. Considerable information has been published concerning some of the chemicals now being used in plastic manufacture, and at the present time many chemicals are undergoing toxicological investigation.

The authors of this paper have accumulated information on many of the resins, plasticizers, stabilizers and solvents being used in the manufacture of numerous plastic articles. It will be noted that the information is meager in some instances while in others it is quite complete, but, to our knowledge, this comprehensive summary on the toxicology of plastics has not heretofore been attempted.

Among the authors' conclusions is that industry must maintain strong Departments of Industrial Medicine and Hygiene to control toxicological hazards. Many industries are diversifying manufacturing activities and entering fields of endeavor for which previous experiences may not have prepared them. Highly toxic chemicals cannot be successfully handled in a haphazard manner and it is essential to invest money for toxicological investigation, because to be without such programs is foolhardy and more expensive in the long run. No industry can afford to endanger the health of its people by knowingly exposing them to toxic materials.

It is not enough for research chemists to discover a chemical combination, which will create a new sales masterpiece. The industrial hygienist must also determine the toxicity of the chemicals involved and designate ways and means of handling them safely. If the sales potential of a new plastic does not warrant toxicological study, then the product should not be produced.

Another conclusion of the authors is that much additional toxicological study is necessary on plastics, and it is hoped that the toxicology of plastics can be added to and made more complete, year after year.

References

1. LEHMAN, ARNOLD J.: Chemicals in Foods: A Report to the Association of Food and Drug Officials on Current Developments. *Association of Food & Drug Officials of the United States*, Vol. XV, No. 3, July, 1951.

2. SEELER, ALBERT O.: Clinton, Marshall, Boggs, Joseph, Drinker, Philip: Experiments on the Chronic Toxicity of a Copolymer of Vinyl and Vinylidene Chloride. Unpublished.

3. PATTY, F. A., YANT,, W. P., and WAITE, C. P.: Acute Response of Guinea Pigs to Vapors of New Commercial Organic Compounds. *U.S. Public Health Reports*, 45:1963 (1930).

4. CARPENTER, C. P., SMITH, H. F., and POZZANI, U. C.: The Assay of Acute Vapor Toxicity and the Grading and Interpretation of Results on 96 Chemical Compounds: *J. Indust. Hyg. & Tox.*, 31:343, 1949.

5. REINHARDT, R. C.: Handling Vinylidene Chloride: *Chemical & Engineering News*, 25:2136 (July 28) 1947.

6. WILSON, R. H., HOUGH, GLENN V., and MCCORMICK, WM. E.: Medical Problems Encountered in the Manufacture of American-Made Rubber. *Indust. Med.*, 17:6 (June) 1948.

7. WILSON, R. H.: Health Hazards in the Manufacture of Synthetic Rubber. *J.A.M.A.*, 124:701 (March 11) 1944.

8. DUDLEY, H. C., NEAL, P. A.: Toxicology of Acrylonitrile: *J. Indust. Hyg. & Tox.*, 24:27 (February) 1942.

9. CARPENTER, C. P., SHAFFER, C. B., WEIL, C. F., SMYTH, H. F.: Studies on Inhalation of Butadiene with a Comparison of its Narcotic Effect. *J. Indust. Hyg. & Tox.*, 26:69, 1944.

10. ROWE, V. K., SPENCER, H. C., and BASS, S. L.: Certain Commercial Silicones and Hydrolyzable Silicone Intermediates: *J. Indust. Hyg. & Tox.*, 30:332 (November) 1948.

11. SHAFFER, C. B., CRITCHFIELD, F. H., and CARPENTER, C. P.: The Absorption and Excretion of the Solid Polyethylene Glycols. *J. Am. Pharm. Assoc.*, 36:152 (May) 1947.

12. STOKINGER, H. E.: Teflon—A Plastic with an Inhalation Hazard. *Occupational Health*, 13:86 (June) 1953.

13. SEIFTER, JOSEPH: Toxicity of Plasticizers. Unpublished, 1943.

14. SMITH, CARL C.: Toxicity of Butyl Stearate, Dibutyl Sebacate, Dibutyl Phthalate, and Methoxyethyl Oleate: *A.M.A. Arch. Indust. Hyg. & Occup. Med.*, 7:4, 310 (April) 1953.

15. MALLETTE, F. S., and VON HAAM, E.: Studies on the Toxicity and Skin Effects of Compounds Used in the Rubber and Plastics Industries: *A.M.A. Arch. Indust. Hyg. & Occup. Med.*, 6:9, 231 (September) 1952.

16. HODGE, HAROLD C.: Acute Toxicity for Rats and Mice of 2-Ethyl Hexanol and 2-Ethyl Hexyl Phthalate. *Proc. Soc. Exp. Biol. & Med.*, 53:20, 1943.

17. SHAFFER, C. B., CARPENTER, C. P., and SMYTH, JR., H. F.: Acute and Subacute *Toxicity of Di(2-Ethyl Hexyl)* Phthalate, *J. Indust. Hyg. & Tox.*, 27:5 (May) 1945.

18. CARPENTER, C. P., WEIL, C. S., and SMYTH, H. F.: Chronic Oral Toxicity of Di(2-Ethyl Hexyl) Phthalate for Rats, Guinea Pigs and Dogs. *A.M.A. Arch. Indust. Hyg. & Occup. Med.*, 8:219 (September) 1953.

19. HALPERN, L. K., and WEISS, R. S.: Toxicity of 2-Ethyl Hexyl Diphenyl Phosphate. IV. Skin Sensitization Studies of Santicizer 141. *A.M.A. Arch. Indust. Hyg. & Occup. Med.*, 8:284 (September) 1953.

20. SEELER, ALBERT O., CLINTON, MARSHALL, BOGGS, JOSEPH, DRINKER, PHILIP: Experiments on the Chronic Toxicity of Acetyl Tributyl Citrate. Unpublished.

21. SEELER, ALBERT O., CLINTON, MARSHALL, BOGGS, JOSEPH, DRINKER, PHILIP: Experiments on the Chronic Toxicity of Butyl Phthalyl Butyl Glycollate. Unpublished.

22. TREON, J. F., DEUTRA, F. R., and CLEVELAND, F. P.: Toxicity of 2-Ethyl Hexyl Diphenyl Phosphate: I. Immediate Toxicity and Effects of Long Term-Feeding Experiments: *A.M.A. Arch. Indust. Hyg. & Occup. Med.*, 8:170 (August) 1953.

23. TREON, J. F., CAPPEL, B. S., and SIGMON, H.: Toxicity of 2-Ethyl Hexyl Diphenyl Phosphate: II. Metabolic Fate in Man and Animals: *A.M.A. Arch. Indust. Hyg. & Occup. Med.*, 8:268.

24. JACOBS, MORRIS B.: The Analytical Chemistry of Industrial Poisons, Hazards and Solvents: Chemical Analysis, Vol. 1, 2nd Revised Edition. Interscience Publishers, Inc., New York, 1949.

25. American Conference of Governmental Industrial Hygienists: Threshold Limit Values for 1954. *A.M.A. Arch. Indust. Hyg. & Occup. Med.*, 9:530 (June) 1954.

26. WILSON, R. H.: Benzol Poisoning in Industry. *J. Lab. & Clin. Med.*, 27:12, 1517 (September) 1942.

27. WILSON, R. H.: Toluene Poisoning. *J.A.M.A.*, 123:1106 (Sec. 25) 1943.

28. HAMILTON, ALICE, and JOHNSTONE, R. T.: Industrial Toxicology, p. 636. Oxford University Press, 1945.

29. DAVIS, P. A.: Carbon Tetrachloride as an Industrial Hazard. *J.A.M.A.*, 123:962, 1943.

30. GAFAFER, WM. (Editor): Manual of Industrial Hygiene, p. 264. W. B. Saunders Company, 1943.

31. ELKINS, H. B.: Maximum Allowable Concentrations: I. Carbon Tetrachloride. *J. Indust. Hyg. & Tox.*, 24:233, 1942.

32. DRINKER, P., YAGLOU, C. P., and WARREN, M. F.: The Threshold Toxicity of Gasoline. *J. Indust. Hyg. & Tox.*, 25:225, 1943.