III. BIOLOGIC EFFECTS OF EXPOSURE

Extent of Exposure

Allyl chloride is a volatile, highly reactive, liquid halogenated hydrocarbon. A number of its important properties are presented in Table XI-1. [1]

The high-temperature chlorination of propylene is believed to be the only production method used commercially although other reactions leading to allyl chloride formation are known. [2 (pp 1-2,26)] This synthesis involves the direct substitution of chlorine for a hydrogen atom on the saturated carbon at a minimum operating temperature of 300 C. In 1973, total allyl chloride production in the United States was about 300 million pounds. [3]

Commercially, allyl chloride is used as an intermediate in chemical reactions. [4] The major commercial derivative of allyl chloride is epichlorohydrin which is used in the manufacture of epoxy resins. [2 (pp 1-2,26)] Allyl chloride is also important in commercial glycerol production.

NIOSH estimates that approximately 5,000 workers are potentially exposed to allyl chloride in the United States.

Historical Reports

Allyl chloride has been known for over 100 years. The lack of an economical means of synthesis hampered its early commercial use. An economically feasible synthesis of allyl chloride by high-temperature

chlorination of propylene in the 1930's led to the commercial production of allyl chloride beginning in 1945.

Effects on Humans

In 1959, Torkelson et al [5] exposed 13 volunteers in groups of two or three to allyl chloride at a concentration of 3 ppm. The exposure chamber was a stainless steel, vault-like room with two hinged doors sealed with Silastic gasketing. The room was equipped with an air pump, circulating fan, and temperature-controlled metering equipment to deliver the toxicant. Air samples were drawn directly from the chamber using Saran plastic tubing. The allyl chloride was converted by pyrolysis to the chloride ion and measured with the micro-Volhard method. [6] The length of exposure ranged from 1 to 3 minutes. Of the 13 volunteers, 10 reported an awareness of a definite odor but no sensory irritation at 3 ppm. The exposure period was too short to draw any conclusions regarding other adverse effects from allyl chloride at this level.

Unpublished data from Shell Chemical Company [7] indicated that after exposure to allyl chloride at 3-6 ppm only half of an unsuspected number of volunteers could detect its odor, but at 25 ppm all detected its characteristic pungent odor. Eye irritation occurred in 50% of the people tested at a concentration of 50-100 ppm. Nasal irritation and pulmonary discomfort thresholds were reported at an allyl chloride concentration of less than 25 ppm (exact concentration not given). Tests were conducted on unconditioned personnel for 5 minutes. No further experimental details were provided.

Shell Chemical Company [7] has reported no evidence of chronic intoxication or acute pulmonary irritation coincident with their manufacture of allyl chloride. However, data supporting this conclusion have not been made available. The most frequent complaint following suspected overexposure to allyl chloride vapor involved the eyes. Irritation of the conjunctivae and eyelids has been observed after exposure to relatively high vapor concentrations. Orbital pain, which generally occurred 2-6 hours after exposure, was relieved somewhat by limiting the patient's exposure to bright lights. Skin contact with liquid allyl chloride was responsible for dermatitis and blistering including damage to the subcutaneous tissues. Deep-seated pain (described as bone-ache type) beneath the point of skin contact was reported with very small amounts (exact quantity not given) of allyl chloride. Pain persisted for up to 8 hours after exposure. One case of first- and second-degree chemical burns of the skin reportedly was caused by the wearing of allyl chloride-contaminated clothing for protracted periods. All findings by Shell Chemical Company were based on industrial experience but were not correlated with any known environmental concentrations of allyl chloride.

Shell Chemical Company [8] reported in an industrial hygiene bulletin summarizing literature on allyl chloride that the compound may produce varying degrees of local irritation or injury to the tissues of the respiratory tract. Complaints of eye, nose, or throat irritation, and, in the more severe cases, sneezing and epistaxis have been reported among allyl chloride workers.

Dow Chemical USA [9] has conducted medical surveillance of employees exposed to allyl chloride and epichlorohydrin. Annual blood profile tests

included hemoglobin, hematocrit, red blood cell (RBC) and white blood cell (WBC) counts, platelet count, and lactic dehydrogenase (LDH), SGOT, SGPT, blood glucose, blood urea nitrogen (BUN), bilirubin, albumin, globulin, and other determinations. Chest X-rays and pulmonary function tests (FVC and FEV 1) were given every 2 years to employees over the age of 40 and every 4 years for those under 40. Results of these tests for all allyl chloride workers were not made available. However, the Texas Division of Dow Chemical USA has identified 33 employees who were stated to have been overexposed to allyl chloride, 7 by inhalation, 11 by eye contact, 11 from skin contact, and 4 by skin and eye contact. Followup SGOT and SGPT levels of these employees were reported to have been within the normal ranges of two testing laboratories.

Karmazin [10] reported that 50% of human volunteers detected allyl chloride dissolved in water by taste at a concentration of 0.75 mg/liter and by odor at a concentration of 0.33 mg/liter. Allyl chloride was tasted by all subjects at a level of 1.0 mg/liter and smelled by all subjects at a level of 0.66 mg/liter. Allyl chloride concentrations were estimated, not measured. The number of subjects and methods of testing employed were not given.

Epidemiologic Study

Hausler and Lenich, [11] in 1968, studied the effects of chronic allyl chloride exposure on 45 men and 15 women working in an allyl chloride-manufacturing plant. Allyl chloride concentrations varied within the plant depending on the types of processes in the immediate area. Measured levels ranged from a low of 1 ppm in the laboratory to a

high of 113 ppm in the pumproom. The extent of employee exposure during the 16-month exposure period was dependent upon their duties. Effects were determined during medical examinations as described in the East German "Medical Serial Examinations of the Workers" with additional urinalyses and liver function tests, including enzyme activity determinations. Liver function was measured by thymol, cadmium, and serum bilirubin tests. Enzyme activity tests included LDH, SGOT, SGPT, sorbose dehydrogenase (SDH), and glutamic acid dehydrogenase (GDH) determinations. The only unusual finding on physical examination was the presence of a garliclike odor of the body and in the exhaled air in 20 of the exposed workers. No similar complaints had been reported in serial examinations performed in 1965 and 1966.

Urine tests [11] disclosed that two individuals had passed traces of protein, a few erythrocytes, epithelial cells, and leukocytes. Five individuals had slightly elevated urobilinogen levels. According to Hausler and Lenich, [11] the presence of allegedly abnormal results in liver function tests, including enzymatic tests, was indicative of early stages of liver damage. Although individual test findings were not reported, the criteria used to judge these abnormal results along with the number of persons exhibiting each type of abnormal result were provided and are given in Table III-1. However, in the absence of preexposure control values, a definite conclusion that these results are indicative of abnormal liver function cannot be made. The plant subsequently was remodeled so that the allyl chloride level was 1 ppm or less in all areas except in the pumproom, where the concentration was 15-36 ppm. The authors stated that all individuals previously reported to have abnormal findings in the liver

function and urine tests returned to normal within 6 months, but the results of these tests were not presented to support their conclusion.

TABLE III-1

RESULTS OF LIVER FUNCTION TESTS
PERFORMED ON MALE AND FEMALE EMPLOYEES

Test Finding	Men (n=45)	Women (n=15)	Total (n=60)
Cadmium positive	6	1	7
Total bilirubin over 1 mg%	9	1	10
Thymol positive	7	3	10
SGOT above 45 U	5	-	5
SGPT above 17 U	19	6	25
LDH above 83 U	6	6	12
GDH positive	20	5	25
SDH positive	16	5	21

From Hausler and Lenich [11]

Animal Toxicity

Smyth and Carpenter [12] developed an acute range-finding procedure to determine the approximate lethal dose of toxic chemicals. This method was used to estimate the single-dose, oral and dermal LD50's for allyl chloride in rats and rabbits, respectively. [13] Mortality during a 14-day observation period after administration of the compound was reported. In the oral tests, single doses of allyl chloride were administered by stomach

tube to rats weighing 90-120 g, and the oral LD50 was estimated by a comparison of these results with the LD50 data of a structurally similar compound (not identified). Rubber cuffs described by the Food and Drug Administration were used in the skin absorption tests to ensure maximum contact of the material with the skin of the rabbits. An oral LD50 of 700 mg/kg in rats and a dermal LD50 of 1,900 mg/kg in rabbits were reported. Since range-finding LD50 studies provide approximate values, these values should be used only as preliminary laboratory data.

The range finding method has also been used to determine the approximate mortality rates of exposure to a variety of chemicals by inhalation. [12] Allyl chloride at a concentration of 2,000 ppm caused one death in a group of six rats within 4 hours. [13]

Using a stomach tube to administer allyl chloride in an unidentified oil solution, Karmazin [10] obtained oral LD50 values of 450 mg/kg for albino rats, 500 mg/kg for white mice, and 300 mg/kg for rabbits. Observation times were not reported. Microscopic examination of animal tissues disclosed mild degenerative changes in the myocardium, liver, and kidneys.

In unpublished data of experiments on mice, Shell Chemical Company [7] reported LC50's of 1,455 ppm for 60-minute and 24,633 ppm for 10-minute exposures. All mice exposed to allyl chloride at a concentration of 73,900 ppm for 10 minutes died within 24 hours. Two of four mice survived ten 60-minute exposures (sequence not stated) to allyl chloride vapor at a concentration of 129 ppm. All mice dying or killed after one or more exposures at 129 ppm showed "profound" pulmonary damage (details not given), considerable injury to the liver, and slight changes in the kidneys

and spleen. No other experimental data were provided.

In 1938, Silverman and Abreu [14] studied the toxic and anesthetic properties of allyl chloride (3-chloropropene) and three other monochlorinated compounds (1-chloropropene; 1-chloro,2-methylpropene; 3-chloro,2-methylpropene). Ten white mice in each of three groups were subjected to 10-minute exposures of allyl chloride at concentrations of 1.0 millimole/liter (24,200 ppm), 2.0 millimoles/liter (48,400 ppm), or 3.0 millimoles/liter (72,600 ppm) in a 2.5-liter glass bottle. The age, sex, and weight of the mice were not reported. After exposure, the animals were examined periodically for 48 hours. Necropsies were performed immediately on all animals dying within this time period. Animals were selected randomly from groups in which no deaths occurred, and killed for examination. Allyl chloride was highly injurious to pulmonary tissues and moderately so to the tissues of other organs, but the nature of the damage was not specified. All 10 mice exposed at 3 millimoles/liter died, some within 5 minutes from the start of exposure and the rest within 24 hours after termination of exposure. Nine of 10 mice exposed at 2 millimoles/liter died within 6-47 hours, and 4 of 10 mice exposed at 1 millimole/liter died within 26-46 hours. Anesthetic effects were noted in mice exposed at concentrations of 2 or 3 millimoles/liter. Onset of anesthesia was 2-8 minutes after the start of exposure at 2 millimoles/liter in 9 of 10 mice and 1-2 minutes at 3 millimoles/liter in all 10 mice. Recovery from anesthetic effects occurred 20 seconds-4 minutes after the termination of exposure at 2 millimoles/liter and 6 minutes at 3 millimoles/liter. No anesthetic effects were observed at 1 millimole/liter. In other tests on mice exposed at a level of 0.5

millimole/liter (12,100 ppm), allyl chloride caused prompt and profound mucosal irritation. From these findings, Silverman and Abreu [14] concluded that allyl chloride is potentially dangerous to persons working with it and estimated that in humans a single 10-minute exposure at a concentration of 22,000 ppm could result in death.

In 1940, Adams et al [15] exposed guinea pigs and albino rats in groups of four or five for varying lengths of time to allyl chloride at concentrations of 290, 2,900, 5,800, 14,500, and 29,300 ppm to determine the shortest exposure producing 100% lethality of the group and the longest exposure permitting 100% survival of the group. Exposure times varied from 10 minutes at 14,500 ppm to 9 hours at the 290-ppm level. Initial concentrations were obtained by spraying the walls of the test chamber with a premeasured amount of allyl chloride. To maintain the desired levels, allyl chloride was introduced into the chamber by a continuous-flow system. The method of checking allyl chloride concentrations within the chamber was incompletely described, but levels were reported to be quite constant. The 100% lethal exposure times and 100% survival exposure times for rats and guinea pigs are listed in Table III-2. Gross reactions of the guinea pigs and rats to varying concentrations of allyl chloride are given in Table III-3. Microscopic examination showed significant lesions in the lungs and kidneys of animals that died or were killed after acute exposure to allyl chloride vapor at all concentrations tested. Renal lesions included prominent changes in the glomeruli showing distended capsular spaces, marked damage to the convoluted tubules characterized by distention of the lumina, and moderate congestion of the kidneys with hemorrhage of the intertubular capillaries. Pulmonary damage consisted of moderate-to-marked

congestion with frequent hemorrhage into the alveolar spaces, marked interstitial edema, thickening of the mucous membrane of the bronchioles, and desquamated epithelial cells, leukocytes, and erythrocytes in the lumina. Lesions were more severe in the kidneys than in the lungs. Only slight changes were recorded in the liver, the most prominent being congestion of the central vein and adjacent sinusoids. Renal damage was most severe under the conditions of low concentrations and long exposures. Higher concentrations were more irritating to the lungs. Animals allowed to recover for 4 weeks were essentially normal, with a few exhibiting slight-to-moderate fibrosis and scarring of the lungs and kidneys.

TABLE III-2

EXPOSURE TIMES (IN HR) FOR SURVIVAL AND LETHALITY IN RATS AND GUINEA PIGS EXPOSED TO ALLYL CHLORIDE VAPOR

Concentration		Rats		Guinea Pigs	
mg/l	ppm	100% Survival Exposure*	100% Lethal Exposure**	100% Survival Exposure*	100% Lethal Exposure**
100	29,300	0.25	0.50	-	-
50	14,500	0.50	1.25	0.25	0.75
20	5,800	0.50	2.00	-	-
10	2,900	1.00	3.00	1.00	2.00
1	290	3.00	8.00	1.00	4.00

*Observation period of 4 weeks
**Deaths within 24 hours

Adapted from Adams et al [15]

TABLE III-3

GROSS REACTIONS OF GUINEA PIGS AND RATS TO ALLYL CHLORIDE VAPORS

Animal	Conc (ppm)	Exposure Time	Effects
Guinea pigs	290	1 hr -4 hr	Drowsiness, unsteadiness, death in 24 hr
		6 hr	Eye irritation, unconsciousness, death in 24 hr
Rats	290	2 hr -9 hr	Similar to guinea pigs at 290 ppm, but more resistant to the narcotic action; death in 24 hr
Guinea pigs	2,900	30 min-2 hr	Slight eye and nose irritation in a few min; death shortly after exposure
Rats	2,900	30 min-2 hr	Same findings as for guinea pigs at 2,900 ppm; 6 of 10 rats exposed for 2 hr died
		3 hr -4 hr	Mortality 100% during exposure
"	5,800	30 min-2 hr	Rapid development of eye and nose irritation, death in 24 hr for 1- and 2-hr exposures
Guinea pigs, rats	14,500	10 min-1 hr 30 min-2 hr	Eye and nose irritation, drowsiness, weakness, instability, labored breathing; some deaths in a few hr, all dead in 24 hr
Rats	29,300	15 min-1 hr	Eye and nose irritation, unconsciousness, death in 1 hr

Adapted from Adams et al [15]

Torkelson et al [5] repeatedly exposed 10 rats (5 of each sex), 4 male guinea pigs, and a female rabbit to allyl chloride at an average concentration of 8 ppm (range 7.9-10 ppm). Air samples drawn directly from

the chamber through Saran plastic tubing were heated at 1,000 C to form the chloride ion, which was collected in a solution containing 1% sodium formate and 1% sodium carbonate and was measured by the micro-Volhard method. [6] A total of twenty-eight 7-hour exposures in a glass-walled chamber was scheduled 5 days/week over a 35-day period. Matched controls were exposed daily to room air under similar conditions. Observations on general appearance, behavior, growth, and mortality failed to show any appreciable differences between the treated group and the controls. Microscopic examination of tissues from the lungs, heart, liver, kidneys, spleen, and testes showed definite tissue damage in the liver and kidneys of essentially all the exposed animals. Damage to the liver was characterized by dilation of the sinusoids, cloudy swelling, and focal necrosis; kidney damage included changes in the glomeruli, necrosis of the epithelium of the convoluted tubules, and proliferation of the interstitial tissues.

Further tests were conducted by Torkelson et al [5] on a larger scale using the same procedure as in the 8-ppm tests. Each of three groups of animals (selected by age and weight) was composed of 48 rats, 6 rabbits, 18 guinea pigs, and 2 dogs, with equal numbers of males and females. The study group was exposed to allyl chloride at an average concentration of 3 ppm (range 1.8-3.9 ppm), 7 hours/day, 5 days/week, for a total of 127-134 exposures over 180-194 days. One of two control groups was exposed to room air under conditions similar to those of the exposed animals. The other (unexposed) control group was held in the animal quarters. At the end of the exposure period, the rabbits, guinea pigs, and dogs were killed. Microscopic examinations revealed no abnormalities. The rats were divided

into two groups after the exposure period, and one group was allowed to recover for 2 months while the other was killed. In the latter group, BUN and blood nonprotein nitrogen determinations were within normal limits in all animals. No other measurements of kidney function were made. Microscopic examination of the kidney and liver tissues of rats killed immediately after exposure revealed only a slight central lobular degeneration in the livers of the female rats, but none in males. The number of female rats exhibiting this change was not given. This change was of a type normally seen in control groups. However, because of its absence in male rats and other animal species, the authors concluded that the effect was due to the allyl chloride exposure. The absence of this change in all rats allowed to recover for 2 months was interpreted as an indication that the damage was reversible.

Almeev and Karmazin [16] studied the effects of allyl alcohol and allyl chloride. They administered allyl chloride in a sunflower oil solution by gastric intubation to 84 albino rats at doses of 250, 300, 400, 750, 1,000, 1,500, or 2,000 mg/kg. Rats receiving allyl chloride at 2,000 mg/kg died within 2 hours, while rats subjected to doses of 1,500 and 1,000 mg/kg died on the first day. At doses of 250, 300, 400, or 750 mg/kg, all rats died by the third day, with most dying on the first. Results of macroscopic examination, described for allyl alcohol and stated to be similar for allyl chloride, revealed differing degrees of intumescence of the stomach and intestines, folded and swollen mucosa of the stomach, mucus in the lumen of the large and small intestines, and splenic hyperemia. The livers of these animals were flaccid and hyperemic with isolated small hemorrhages under the Glisson's capsules. The kidneys were hyperemic, and

the boundary between the cortical and medullary layers was smooth. The lungs were half-collapsed and pale red. Punctate hemorrhages were observed in some sections of the lungs. Microscopic tissue examination of the internal organs of these animals showed similar changes at the different dose levels and included mild degeneration of the myocardium, moderate hyperemia of the liver, degeneration of the connective tissues in the liver, hyperemic congestion of the stomach mucosa, and considerable edema in the submucosa. The kidneys exhibited cloudy swelling of the tubular epithelium and congestive hyperemia of the cortical- and medullary-layer vessels. The authors [16] provided only a qualitative description of organ damage produced by allyl chloride; therefore, the severity of the observed damage could not be related to the various doses.

In the subchronic portion of this study, Almeev and Karmazin [16] administered allyl alcohol or allyl chloride to rats in parallel experiments. The doses, equivalent to the LD50 or twice the LD50, were administered in 10 days by the procedures described above. For allyl alcohol, these doses were 14 or 28 mg/kg/day. The authors [16] stated that the macroscopic examination after allyl alcohol exposure included the stomach and the intestines, and no changes were apparent. The microscopic examination revealed hyperemia in the heart, liver, kidneys, and spleen, as well as degeneration of the myocardial fibrils and liver parenchyma. For allyl chloride, the doses were 45 or 90 mg/kg/day. Macroscopic examination of organs from rats given allyl chloride revealed tissue congestion. On microscopic examination, internal organs had noticeable hyperemia and mild degeneration. Although no further details were given for effects from allyl chloride, it is presumed that organs examined and changes noted were

similar to those described for allyl alcohol.

Strusevich and Ekshtat [17] determined the dynamics of activities of pancreatic lipase, amylase, and trypsin and its inhibitor in white rats after oral administration of four chlorinated compounds, including 2,3-dichloropropene and allyl chloride, at doses of 1/10, 1/50, or 1/250 of the LD50's. Because the LD50's were not identified, doses used cannot be determined. Enzymatic activities were studied on the 1st, 10th, and 20th days after each compound was administered. The administration of 2,3-dichloropropene at all dose levels changed the activities of trypsin and its inhibitor (not identified) by producing a significant increase in the level of the inhibitor with a drop in trypsin activity. These changes were most evident on the 10th and 20th days. One month after the administration of 2,3-dichloropropene, 0.05 mg of pilocarpine was given orally to each rat. There was no change in the activities of trypsin and its inhibitor at 1/10 the LD50. This may have indicated a state of inactivity of pancreatic excretory function. At the other dose levels, pilocarpine increased trypsin activity indicating that the functional activity of the pancreas was retained. The authors have reported that allyl chloride produced effects similar to those of 2,3-dichloropropene, but to a lesser degree. After the administration of allyl chloride at doses of 1/50 and 1/250 the LD50, those of lipase activity was increased when measured on the 1st and 10th days and was decreased when measured on the 20th day. At 1/10 the LD50, allyl chloride reduced lipase activity throughout the experiment. At all doses, stimulation of the pancreas with pilocarpine increased lipolytic activity. An increase in amylase activity was noted throughout the experiment with allyl chloride at 1/10 the LD50. No results were given for

amylase at the 1/50 and 1/250 dose levels.

Kaye et al [18] administered 1 ml of allyl chloride solution (10% v/v in peanut oil) by subcutaneous injection into the lumbar region of male CFE-strain albino rats weighing 200-250 g. All rats had free access to water. To test for sulfur-containing metabolites, a group of rats was kept on a diet consisting of 5% sulfur-labeled yeast. The bile duct of one rat was cannulated and the upper part of the duct intubated to avoid contamination of the bile sample with pancreatic juice. Urine and bile were collected for 24 hours prior to the administration of allyl chloride and for two consecutive 24-hour periods after introduction of the compound. Samples were analyzed using paper chromatography with a radiochromatogram scanner and gas-liquid chromatography. The urine of rats given allyl chloride contained allyl mercapturic acid, allyl mercapturic acid sulfoxide, and 2- or 3-hydroxypropylmercapturic acid. To isolate these compounds, 1 ml of a 10% solution containing 12.7 g allyl chloride in peanut oil was administered subcutaneously to each of 137 rats. Allyl mercapturic acid in amounts corresponding to 1.7% of the administered allyl chloride was recovered. The other two compounds could not be isolated. To identify whether 2- or 3-hydroxypropylmercapturic acid was present, allyl chloride was administered subcutaneously to 21 rats. Their urine was collected over the 24-hour period immediately after doses were given. The presence of 3-hydroxypropylmercapturic acid was identified on a gas-liquid chromatograph using two different columns. Radiochromatograms of urine from rats fed 35S-labeled yeast confirmed the results in rats given allyl chloride.

Correlation of Exposure and Effect

Industrial exposure observations [7] have shown that liquid allyl chloride is a skin irritant responsible for dermatitis, damage to underlying tissues of the skin, deep-seated pain, and chemical burns.

As a vapor, allyl chloride at a concentration of 3 ppm had a definite odor for 10 of 13 volunteers. [5] Odor threshold experiments conducted by Shell Chemical Company [7] showed 50% of the human subjects could detect an odor at a concentration of 3-6 ppm; at 25 ppm, the odor was detectable by all subjects. At 50-100 ppm, 50% of the subjects tested reported eye irritation. Nasal irritation and pulmonary discomfort have been reported at a concentration of less than 25 ppm. [7]

Allyl chloride vapor had a narcotic effect on rats, mice, and guinea pigs over a concentration range of 290-72,600 ppm. [14,15] Susceptibility to the anesthetic effect was species-dependent, guinea pigs being the most sensitive. Such effects were not evident in humans at a vapor concentration of up to 113 ppm. [7,11]

In an epidemiologic study, Hausler and Lenich [11] suggested that changes in the results of liver function tests in 60 employees exposed to allyl chloride coincided with changes in allyl chloride levels. No preexposure values for the liver function tests were reported; however, the test results, reported by the authors as abnormal, did "return to normal" after a reduction in exposure, suggesting that the observed liver damage may have been related to allyl chloride exposure. Renal and pulmonary changes were not observed in any of the exposed employees. Twenty of the 60 exposed employees also complained of a garliclike odor of the body and in the exhaled breath.

Acute and chronic exposures to allyl chloride in animals have resulted in hepatic, renal, and pulmonary damage. [5,7,14,15] Tables III-4 and III-5 summarize the results of these experiments. Liver damage appeared to be more significant following chronic exposure [5] while pulmonary injuries followed acute exposures. [15] Animals were exposed to allyl chloride at a vapor concentration of 3 ppm, 7 hours/day, 5 days/week, for a total of 127-134 exposures over a 180- to 194-day period. [5] Slight liver damage was observed in female rats killed immediately after exposure. Female rats allowed to recover for 2 months after exposure, as well as male rats, rabbits, guinea pigs, and dogs, did not show this effect at this concentration. Torkelson et al [5] reported extensive liver damage in rats, rabbits, and guinea pigs exposed to allyl chloride at 8 ppm for 7 hours/day, 5 days/week, for 35 days. The authors also reported renal damage at this concentration. Extensive liver and pulmonary damage occurred in mice at a concentration of 129 ppm with ten 60-minute exposures, while only slight renal changes were observed. [7] Slight hepatic changes and significant pulmonary and renal lesions resulted in guinea pigs and rats exposed to allyl chloride at 290-29,300 ppm for periods of 10 minutes-9 hours. [15]

Carcinogenicity, Mutagenicity, and Teratogenicity

No reports which address the subject of carcinogenic, mutagenic, or teratogenic properties of allyl chloride were found. The Manufacturing Chemists Association is currently administering a research program to study the oncogenic and teratogenic effects of inhaled allyl chloride on rats and rabbits (AC Clark, written communication, February 1976).

TABLE III-4

EFFECTS FROM ALLYL CHLORIDE INHALATION ON ANIMALS

Animals	Concentration (ppm)	Exposure Time	Effects	References
Mice	73,900	10 min	Death	Anon [7]
White mice	72,605	"	Highly injurious to pulmonary tissues; moderate damage to other organs; onset of anesthesia in 1-2 min with recovery in 6 min; all mice dead within 24 hr	Silverman & Abreu [14]
"	48,403	"	Death in 9 of 10 mice in 6-47 hr; onset of anesthesia in 2-8 min with recovery in 20 sec-4 min; damage to organs same as at 72,605 ppm	"
Albino rats	29,300	15 min-1 hr	Significant lesions in lungs and kidneys; slight changes in liver; eye and nose irritation; death within 1 hr	Adams et al [15]
Mice	24,633	10 min	LD50	Anon [7]
White mice	24,202	"	Death in 4 of 10 mice within 26-46 hr; organ damage same as at 72,605 ppm	Silverman & Abreu [14]
Guinea pigs, albino rats	14,500	10 min-2 hr	Eye and nose irritation; drowsiness, weakness, instability, labored breathing; death within 24 hr; effects on lungs, liver, kidneys same as at 29,300 ppm	Adams et al [15]
White mice	13,300	10 min	Irritation of mucous membranes	Silverman & Abreu [14]
Albino rats	5,800	30 min	Rapid development of eye and nose irritation; death in 24 hr; lung, liver, and kidney damage same as at 29,300 ppm	Adams et al [15]
Guinea pigs, albino rats	2,900	30 min-2 hr	Slight eye and nose irritation; death in 24 hr; lung, liver, and kidney damage same as at 29,300 ppm	Adams et al [15]
Mice	1,455	1 hr	LD50	Anon [7]
Albino rats	290	6 hr	Eye irritation; unconsciousness; death in short time; no organ damage	Adams et al [15]
Guinea pigs, albino rats	290	1 hr-4 hr	Drowsiness; unsteadiness; no organ damage or deaths	"
Mice	129	1 hr x 10 exposures	Profound pulmonary damage; considerable liver injury; slight changes in kidneys and spleen	Anon [7]
Rats, rabbits, guinea pigs	8	7 hrs/d 5 d/wk x 28 exposures	Extensive tissue damage in liver and kidneys	Torkelson [5]
Rats, rabbits, guinea pigs, dogs	3	7 hrs/d, 5 d/wk x 180-194 exposures	Reversible liver damage in female rats; no effects in other animals	"

TABLE III-5

EFFECTS FROM ALLYL CHLORIDE IN
ORAL TOXICITY EXPERIMENTS ON ANIMALS

Animals	Concentration (mg/kg)	Effects	References
Albino rats	2,000	Death; flaccid and hyperemic livers, degeneration of liver connective tissue; swollen kidney tissue, swelling of canal epithelium of kidney, hyperemia of cortical and medullary layer vessels of kidney; half-collapsed and pale red lungs; effects on stomach, intestine, spleen	Almeev & Karmazin [16]
"	1,000-1,500	Death on 1st day; other effects same as at 2,000 mg/kg	"
"	750	Death within 3 days with most deaths on 1st day; other effects same as at 2,000 mg/kg	"
"	700	LD50 for 14-day observation period	Smyth & Carpenter [13]
Albino mice	500	LD50, observation time not provided	Karmazin [10]
Albino rats	450	"	"
Rabbits	300	"	"
Albino rats	250	Death within 3 days with most deaths on 1st day; other effects same as at 2,000 mg/kg	Almeev & Karmazin [16]
"	45, 90	Hyperemia of organ (nature of damage and organ affected not provided)	"