Illus. 1968[recd. 1969]. [In Jap. with Engl. sum.]--For the pollutants produced by exhaust gas from motor vehicles and blasting gas from dynamite, carbon monoxide, nitrogen oxides and dust were determined inside the Nihonzaka Tunnel under construction for the Tokyo-Nagoya Expressway. The pollutants obtained near the blasting place showed high concentrations of carbon monoxide, nitrogen oxides and the dust, with levels of 350-1,200 ppm, 10-35 ppm, and 5.3-60.5 mg/m^3, respectively. These results were due to defective ventilation.

43940. MIRKINA, K. S., and V. I. ERMOLINSKII. O sluchayakh otravleniya rtut'yu sredi meditsinskikh rabotnikov. [Cases of mercury poisoning among medical workers.] SB NAUCH TR KUIBYSHEV NAUCH-ISSLED INST EPIDEMIOL GIG 5, 82-83. 1968. Translated from REF ZH OTD VYP FARMAKOL KHIMIOTER SREDSTVA TOKSIKOL, 1969, No. 5.54.725.--Observations were made of 4 cases of Hg poisoning in medical personnel as a result of infraction of the rules for working with apparatus containing Hg. The studies, which were carried out in several medical institutions, revealed the presence of Hg in washings from equipment, walls, floors and in the air of the location. In a number of cases the concentration of Hg significantly exceeded the maximum allowable concentration. Working with apparatus containing Hg can be a considerable danger when the rules for safety techniques are not observed.

43941. IVANOVA, I. S., and M. M. MEL'NIKOVA. (Cent. Inst. Postgrad. Med., Moscow, USSR.) K voprosu o sostoyanii zdorov'ya rabochikh v proizvodstve nitrofoski. [Problems regarding the health conditions of workers in nitrogen-phosphorus-potassium fertilizer factories.] GIG TR PROF ZABOL 12(12): 49-50. 1968.--Observations conducted on 187 workers, disclosed the presence of different degrees of bronchitis, which were observed in marked and functional disorders of the nervous system in the form of vegetative dysfunction. The effect of a number of substances, having a stimulating effect (such as chlorine and sulfurous compounds) had a significant role in the development of bronchitis. Changes occurring in the nerve system are connected with the effect of a complex of chemical substances.
--L. G. G.

43942. BUSHUEVA, T. I., E. A. ZABOZLAEVA, and A. Ya. YAKUBOV. K voprosu o deistvii yadokhimikatov na aktivnost' syvorotochnykh fermentov i belkovuyu kartinu krovi. [The action of chemical poisons on the serum enzyme activity and the blood protein picture.] TR KRASNOYARSK MED INST 58, 138-142. 1968. Translated from REF ZH OTD VYP FARMAKOL KHIMIOTER SREDSTVA TOKSIKOL, 1969, No. 5.54.938.--When cotton was being sprayed with organophosphorus insecticides, the concentration of them in the air of the working zone was 0.00002-0.002 mg/l. In the air of warehouse locations it was 0.0006-0.002 mg/l. When cotton was dusted with DDT from tractors, the concentration of it in the air of the working zone was 0.002-0.04 mg/l. Ninety persons were examined before the beginning of the field work season when the chemical poisons were used and 38 were examined during the season (6 of them were working with chemical poisons for the 1st time and the remainder had exposure histories from 1 to more than 5 yr). Before the beginning of work organophosphorus insecticides were not found in the blood of those examined. They were found in the blood of 50% of them during the working season. A decrease was noted in the serum cholinesterase and alanine aminotransferase. There was also a decrease in the serum albumins and an increase in the α_1 and gamma globulins and in the albumin-to-globulin ratio. In some of those examined the thymol test was positive. These results are evaluated as the result of a disturbance of liver function.
--E. T.

43943. POKROVSKII, V. A., A. S. FAUSTOV, and S. V. IVANOV. O peresmotre i utochnenii predel'no dopustimykh kontsentratsii benzola, toluola, etilbenzola i dietilbenzola v vozdukhe proizvodstvennykh pomeshchenii. [Review and refinement of the maximum allowable concentrations of benzene, toluene, ethylbenzene, and diethylbenzene in the air of industrial locations.] TR VORONEZH MED INST 73, 13-18. 1968. Translated from REF ZH OTD VYP FARMAKOL KHIMIOTER SREDSTVA TOKSIKOL, 1969, No. 4.54.869.--From the literature and experimental data on the toxicohygienic estimation of aromatic hydrocarbons, reduction of the maximum allowable concentration in the air of industrial locations is recommended as follows: benzene, from 20 to 5 mg/m^3 and toluene from 50 to 10. The maximum allowable concentration for ethylbenzene as 5 mg/m^3 and for diethylbenzene 10 mg/m^3 remains the same. When estimates are made of the toxic action of the substances of a single homologous series, methods should be used which are adequate for this group of substances and they should be used in all the laboratories developing the maximum allowable concentrations. While their value is being decided, there should be obligatory consideration of the clinical material.

43944. PARAMONCHIK, V. M., and V. I. PLATONOVA. O funktsional'nom sostoyanii pecheni i zheludka u lits, podvergayushchikhsya vozdeistviyu khlororganicheskikh yadokhimikatov. [Functional state of the liver and stomach in people, affected by organochloride chemical poisons.] GIG TR PROF ZABOL 12(5): 27-31. 1968. [Engl. sum.]--Investigations covered functional state of the liver and stomach in 70 persons handling organochlorous compounds (DDT, hexachloran, ether sulfonate). Persons with a relatively short service record (up to 10 yr) had increased acidic and pepsinogenous gastric functions and slightly pronounced disorders of the liver function. Inhibition of the acidic and pepsinogenous gastric functions, along with a marked derangement of the proteidine, carbohydrate, pigmental, antitoxic and secretory function of the liver occurred in persons with a long service record (in excess of 10 yr) exposed to effects of organochlorous compounds.--C. M. M.

43945. VAZIN, A. N., and E. I. PLOKHOVA. K sozdaniyu eksperimental'noi modeli "toksicheskogo angionevroza", voznikayushchego pri khronicheskom vozdeistvii na organizm parov vinilkhlorida. [Creation of an experimental model of "toxic angioneurosis" developing from the chronic action of vinyl chloride vapors on an organism.] GIG TR PROF ZABOL 12(7): 47-49. 1968.--In rabbits the chronic action of vinyl chloride vapors at concentrations of 9-10 mg/liter alters the rate of cardiac contractions, disturbs the electrical and mechanical activity of the heart, changes the level of maximum arterial blood pressure and causes a reduction in the rate of linear blood flow. The changes described in the functions of the cardiovascular system in the experimental rabbits indicate that the model of the pathology which develops from the chronic action of vinyl chloride on an organism can be useful for studying questions of the pathogenesis and experimental therapy of toxic angioneurosis.

43946. GRATHANSKAYA, L. N., and E. N. SOLOV'EVA. Prichiny dittel'noi invalidnosti pri khronicheskikh professional'nykh intoksikatsiyakh. [Reasons for prolonged invalidism during chronic occupational intoxication.] GIG TR PROF ZABOL 13(8): 18-23. 1968. [Engl. sum.]--Case histories of 187 persons incapacitated by chronic poisoning with Hg, gasoline, benzene substances and Pb were analyzed (starting from the beginning of invalidism). The follow-up period averaged 8.5 yr. Investigations showed persistance of clinical manifestations of poisoning despite discontinuation of any exposure to the effects of toxic substances. Causes responsible for the continued incapacitation of individuals trained and untrained for new occupations were analyzed. A medical approach to treating these 2 groups of patients was suggested.
--C. M. M.

43947. APEL', Ya. A. Materialy k toksikologii nekotorykh promezhutochnykh produktov pri proizvodstve izoprenovogo kauchuka. [Information on the toxicology of some intermediate products in the production of isoprene rubber.] SB NAUCH TR KUIBYSHEV NAUCH-ISSLED INST EPIDEMIOL GIG 5, 87-88. 1968. From: REF ZH OTD VYP FARMAKOL KHIMIOTER SREDSTVA TOKSIKOL, 1969, No. 1.54.885.

43948. TILLER, J. R., R. S. F. SCHILLING, and J. N. MORRIS. (London Sch. Hyg. and Trop. Med., London, Engl., UK.) Occupational toxic factor in mortality from coronary heart disease. BRIT MED J 4(5628): 407-411. Illus. 1968.--Between 1933 and 1962 42% of 223 deaths of male workers exposed to carbon disulfide in 3 viscose rayon factories in England and Wales were certified to coronary heart disease--compared with 24% of the deaths in the other workers of the same age, 17% of the deaths in other local men, and 14% in the Registrar General's Tables. Of men with more than 10 yr in the rayon industry employed in 1 of the factories, those exposed to carbon disulfide had death rates from coronary heart disease between 1950 and 1964 2 1/2 times that of the other workers. This evidence of an occupational risk of coronary heart disease from long-term exposure to low concentrations of CS_2 was strongest in the 1940s and slight in 1958-62; it may relate to wartime plant conditions. Current and prospective biochemical and morbidity surveys of exposed workers are now needed. These may also throw light on general issues of atherosclerosis and coronary heart disease.--J. W. S.

43949. ZAEVA, G. N., L. P. ULANOVA (Inst. Ind. Hyg. Occup. Dis., Acad. Med. Sci. USSR, Moscow, USSR.), and L. A. DUEVA. Materialy k peresmotru predel'no dopustimoi kontsentratsii formal'de gida v vozdukhe proizvodstvennykh pomeshchenii. [Materials for a reexamination of the maximal permissible concentration of formaldehyde in the air of industrial establishments.] GIG TR PROF ZABOL 12(7): 18-20. 1968. [Engl. sum.]--In a concentration of 5 mg/cubic m formaldehyde produces general toxic and irritative effects and some manifestations of sensitization. Clinical and hygienic observations made in a number of woodworking and textile industries demonstrated that on the level of 5 mg/cubic m formaldehyde provoked irritation of the upper respiratory tract and increased the incidence of disease among workers. The maximal permissible concentration of formaldehyde should be reduced to 0.5 mg/cubic m.--C. M. M.

43950. LOPEZ-ARRAL DEL AMO, LUIS (Mut. Asitubere. Indust., Bilbao, Spain.), and ISAAC FERNANDEZ MARTIN GRANIZO. Neumoconiosis seudotumoral por talco y caolin. [Pseudotumoral pneumoconiosis by talc and kaolin.] ENFERM TORAX 17(6?): 395-410. Illus. 1968[recd. 1969].--A pneumoconiosis in a 64 yr old rubber worker was discovered after he had worked in the rubber industry for 10 yr. Radiological manifestations included pleural thickening; the diagnos-

R&S 028201

tion of the rate of loss of lindane from both leaf and glass surfaces as influenced by temperature and humidity.--Authors.

122382. STRELETS, N. N. K voprosu o genezе smerti pri alkogol'nom op'yanenii. [The problem of the cause of death in alcoholic drunkenness.] TR LENINGRAD INST USOVERSH VRACH 49: 154-155. 1966. From: REF ZH OTD VYP FARMAKOL KHIMIOTER SREDSTVA TOKSIKOL, 1967, No. 12.54.1058. (Translation)--A description is given of the angiotropic edema of the soft palate and uvula occurring repeatedly in subjects observed after nervous stimulation and alcoholic drunkenness. It is suggested that the cause of death in alcoholic intoxication in some persons can be mechanical asphyxia.

122383. TERESHOV, Yu. A., and E. S. LEVASHOV. Ekranirovannaya kamera dlya toksikologicheskikh i fiziologicheskikh issledovaniya. [A screened chamber for exposure to toxic substances for toxicological and physiological studies.] TR UFIM NAUCH-ISSLED INST GIG PROF ZABOL 13: 334-335. 1966 [1967]. From: REF ZH OTD VYP FARMAKOL KHIMIOTER SREDSTVA TOKSIKOL: 1968, No. 2.54.736.

122384. TOSTANOVSKAYA, A. A., V. S. LAPCHENKO, V. E. RODIENKO, V. I. SVATKOV, and G. P. EGOROVA. Nekotorye dannye o kombinirovannom deistvii smesi DDT i khlorofosa v ostrom eksperimente. [Some data on the combined action of a mixture of DDT and chlorophos in acute experiments.] In: Gigiena pitaniya. [The hygiene of nutrition.] Kiev, 151-153. 1966. From: REF ZH OTD VYP FARMAKOL KHIMIOTER SREDSTVA TOKSIKOL, 1968, No. 2.54.864. (Translation)--The DDT and chlorophos were given once, separately or mixed, intraperitoneally, to rats at 1/2 of the LD_{50}. The rats were killed 15 min. later when marked symptoms of poisoning had developed. There was a rise in the blood sugar of all the animals, especially those given chlorophos, in which it reached 124.4 mg%; there was a reduction in the liver glycogen concentration which was greatest in rats given chlorophos (1.64%) and least in rats given DDT (2.89%); there was a reduction in the concentration of lipids, chiefly in the zona fasciculata when the mixture was given; the mixture also decreased the cholinesterase activity of the erythrocytes but less than DDT alone, while chlorophos alone increased its activity. In all the rats histological studies showed generally marked hemodynamic disorders. The differences in the action of chlorophos and DDT given separately from the action of the mixture are emphasized.

122385. TOSTANOVSKAYA, A. A., V. S. LAPCHENKO, V. I. SVATKOV, G. P. EGOROVA, and V. E. GORDIENKO. (Kiev Res. Inst. Nutr. Hyg., Kiev, USSR.) O kombinirovannom deistvii DDT i khlorofosa, tiofosa i khlorofosa. [Combined action of DDT with chlorophos and of thiophos with chlorophos.] VOP PITAN 27(3): 69-73. 1968. [Engl. sum.]--Tests were conducted in albino rats by instituting acute, subacute and chronic experiments with peroral introduction of the poisons. LD_{50} was adopted as an initial dose in the mixtures taken at a ratio 1: 1. With a single introduction of the mixture comprising DDT and chlorophos there is an antagonism with prevalent action of chlorophos, whereas in multiple administration, DDT appears predominant. The mixture of thiophos with chlorophos is more potent than each one of these substances taken individually.--Authors.

122386. VAZIN, A. N., and E. I. PLOSHOVA. (Inst. Ind. Hyg. Occup. Dis., Gor'ki, USSR.) K patogenezu zabolevaniya, vozniknyushchego pri khronicheskom vozdeistvii na organizm khloristogo vinila. [Pathogenesis of a disease, developing during chronic action of vinyl chloride on the organism.] FARMAKOL TOKSIKOL 31(3): 368-372. Illus. 1968. [Engl. sum.]--Tests were conducted in rabbits to study the bioelectric activity of the brain cortex, anterior and posterior groups of the hypothalamus nuclei, along with the pulse, arterial pressure and circulation rate during chronic poisonings of animals with vinyl chloride (in a concentration of 9--10 mg/liter. Evidence was produced showing that, parallel with changes in the bioelectric activity (appearance of β-rhythms with a frequency of about 80 per/sec, rising mean bioelectric activity of the anterior and posterior groups of the hypothalamus nuclei) there appeared also changes in the circulation functions under study. It is inferred that in the mechanisms underlying the development of pathology secondary to a chronic effect of vinyl chloride a definite role is played by the functional condition of the hypothalamus.--Authors.

122387. VINOKUROVA, M. K., and S. A. STEPANOV. Toksikologicheskaya kharakteristika gerbitsida khlorazina. [A toxicological characterization of the herbicide chlorazin [2-chloro-4,6-bis-diethylamino-s-triazine].] In: Gigiena i toksikologiya pestitsidov i klinika otravleniya. [The hygiene and toxicology of pesticides and clinical aspects of poisoning.] Zdorov'ya: Kiev, 4, 173-178. 1966. From: REF ZH OTD VYP FARMAKOL KHIMIOTER SREDSTVA TOKSIKOL, 1968, No. 2.54.887.

122388. WEINSTEIN, I. (Vanderbilt Univ. Med. Sch., Nashville, Tenn., USA.), L. WILLHITE, H. A. KLAUSNER, and M. REITBERG. The requirement of free fatty acids for the fatty liver of CCl_4 intoxication. PROC SOC EXP BIOL MED 127(3): 850-854. Illus. 1968.--Livers isolated surgically from normal animals and from rats intoxicated with CCl_4 were perfused in vitro with a medium into which palmitic acid was infused continuously. Livers from normal rats were also treated with CCl_4 in vitro by direct addition of the chlorinated hydrocarbon to the medium. Under these conditions, poisoning with CCl_4 resulted in inhibition of net release of triglyceride by the liver into the perfusate and simultaneous accumulation of triglyceride in the liver. These observations support the hypothesis that the fatty liver of CCl_4 intoxication results primarily from interference with the biochemical mechanisms involved in formation and release of the triglyceride in the very low density lipoprotein of the serum.--Authors

122389. ZYADNAROVA, S. A., M. N. KUKLINA, and F. V. TEPLYAKOVA. (Leningrad Sanit. Hyg. Med. Inst., Leningrad, USSR.) Gigienicheskaya i toksikologicheskaya kharakteristika preparata khlorid chetvertichnogo ammonievogo osnovaniya. [Hygienic and toxicologic features of an ammonium tetrachloride base compound.] GIG SANIT 33(5): 14-18. Illus. 1968. [Engl. sum.]--Experimental investigations of a possible effect produced by the compound 34 (ammonium tetrachloride base) on organoleptic properties of water, the sanitary regime of water bodies and the state of experimental animals in acute and chronic sanitary toxicologic tests showed that concentrations of this compound, occurring in the water as a detergent, should be limited according to its effect on the sanitary regime, its recommended maximum permissible concentration in water bodies is set at a level of 0.05 mg/liter.--Author

FOOD RESIDUES, ADDITIVES AND PRESERVATIVES

(See also Food Technology; "Veterinary Toxicology" under Toxicology, General; "Disinfection and Vector Control (Includes Pesticides)" under Public Health; "Insecticides: Chemical and Physical Control, Apparatus" under Economic Entomology (Includes Arachnids)

122390. BAYZER, H. (Biol. Forschung Osterreichs. Stickstoff, A G, Linz, Austria.) Nachweis und quantitative Bestimmung von Chlorcholinchlorid in biologischem Material. [Detection and quantitative determination of chlorocholin chloride in biological material.] MONATSH CHEM 98(5): 1828-1831. 1967. [Engl. sum.]--A method for isolation and quantitative determination of microgram amounts of chlorocholine chloride (CCC) extracted from green leaves, fruits, grains, straw, flour, etc. is described. Quaternary ammonium compounds are separated by ion exchange column chromatography. Isolation of CCC by preparative thin layer chromatography on cellulose layers is followed either by a quantitative colorimetric method using iodine reagent or by a semi-quantitative chromatographic method on cellulose thin layers.--Author

† 122391. BUGG, JOHN C., Jr., JAMES E. HIGGINS, and ERIC A. ROBERTSON, Jr. (Humble Oil and Refining Co., New Orleans, La., USA.) Chlorinated pesticide levels in the eastern oyster (Crassostrea virginica) from selected areas of the South Atlantic and Gulf-of-M[exico] PESTIC MONIT J 1(3): 9-12. 1967.--Oysters were collected from estuarine areas in South Carolina, Georgia, Florida, Mississippi, Louisiana, and Texas and analyzed for pesticide residues. Pesticide levels were determined by the electron capture gas chromatography method and were confirmed by thin layer chromatography and dual-column electron capture gas chromatography. In general, chlorinated pesticides were either not detected or were found at relatively low levels in samples collected from the Atlantic and Gulf Coast areas. Of a total of 133 samples, 94.7% contained 1 or more pesticides; 90.5% contained 2 or more; 81.3% contained 3 or more; 63.9% contained 4 or more; and 31.9% contained 5 or more. The level of sensitivity for pesticide residues was 0.01 ppm. Some correlation was found between spraying operations and pesticide levels in the oysters. --Author

† 122392. CASPER, VICTOR L. (Gulf Coast Mar. Health Sci. Lab., Dauphin Island, Ala., USA.) Galveston Bay pesticide study: water and oyster sample analyzed for pesticide residues following mosquito control program. PESTIC MONIT J 1(3): 13-15. Map. 1967.--The purpose of this study was to determine the effect of increased pesticide applications in the Houston area on shellfish and shellfish-growing waters of Galveston Bay. The study was conducted during the fall of 1964 following a large-scale mosquito control program in the Houston area. Water and oyster samples were collected in Sept. and Oct. 1964, during and after the mosquito control operations. Oyster samples collected in this study were compared to samples collected from April to July 1964, prior to the mosquito operations. Analyses included determination of levels of BHC-lindane, DDE, DDT, dieldrin, endrin, heptachlor, aldrin, chlordane, heptachlor epoxide, methoxychlor, toxaphene, and Trithion. Pesticide levels were determined by the use of electron capture gas-liquid chromatography, with thin layer chromatography for confirmation. Pesticide levels in both water and oysters were low at all times. The data indicate little or no increase in levels due to the control program in Houston.--Author.

† 122393. DUGGAN, R. E. (Food and Drug Admin., Washington, D. C., USA.) Chlorinated pesticide residues in fluid milk and other dairy products in the United States. PESTIC MONIT J 1(3): 2-8. 1967.--The findings on 12,258 objective samples of milk and dairy products examined by the U. S. Food and Drug Administration from domestic and imported lots during the period July 1, 1963, through June 30, 1966, are reported. A majority of the samples contained pesticide residues. Residues of DDT, DDE, TDE, dieldrin, heptachlor epo

R&S 028202

R&S 028203

to the fineness, dryness, only slight tendency of aggregation and good capacity of suspension, hydrophobic, precipitating silicic acid ... causes large dust concentrations in the case of open handling. ... requires certain protective measures.--J. W. S.

38121. BAGNOVA, M. D., and R. V. TEPLYAKOVA. (F. F. Erisman Moscow Res. Inst. Hyg., Moscow, USSR.) Profilaktika professional'nykh zabolevanii kozhi v usloviyakh proizvodstva novykh khimicheskikh veshchestv. [Prevention of occupational diseases of the skin in the production of new chemical substances.] KLIN MED 47(7): 114-118. 1969. [Engl. sum.]--New chemical substances, nitriles and amines, are derivatives of fatty acids, the physicochemical properties of which are still not adequately studied. According to the literature amines exert a marked effect on the skin, irritate the mucous membranes, in particular the eyes and upper respiratory tract, and are endowed with a great toxicity. Workers [211] were examined at a plant where fat-substitutes were synthesized. In 10.6% of cases occupational diseases of the skin were found. In industrial conditions the best treatment was achieved with paste on a soap basis. Polyethylene film is the best material for the manufacture of protective gloves.--C. M. M.

38122. ANTONYUZHENKO, V. A. O professional'noi intoksikatsii vinilkhloridom. [Occupational poisoning by vinyl chloride.] GIG TR PROF ZABOL 13(3): 50-52. 1969.--Experiments were conducted on workers who were severely poisoned by vinyl chloride. Only the manifestation of the stage I of poisoning, was completely reversible. Beginning with stage II, the majority of poisoning manifestations yielded poorly to treatment. In a number of cases, the poisoning was a progressive process, notwithstanding the cessation of the contact with the toxic substance and intensive treatment.--Auth. sum. transl.

38123. COMBA, G. (Inst. Nac. Med. Segur. Trab., Madrid, Spain.) Aportaciones al estudio de la incapacidad laboral en las neumoconiosis. [Study of work disability in pneumoconiosis.] MED SEGUR TRAB (MADRID) 16(62/63): 83-98. illus. 1968[rec. 1969]. [Engl., Fr. and Ger. sum.]--In the absence of substantial changes in breathing capacity, ergospirometry is an indispensible technique for determining work disability. The correlation between working ability and changes in the static and dynamic values of maximum breathing capacity was studied by determination of the various cardiopulmonary parameters during the stable state of the overload. The results are presented. --J. W. S.

38124. GABOR, S., T. FRITE, and Z. ANCA. (Institt. Hyg., Cluj, Rum.) Contribution a l'etude du metabolisme lipidique des poumons ... in silicose experimentale, chez le rat. [The study of the lipid metabolism in rat lungs during experimental silicosis.] ARCH MAL PROF MED TRAV SECUR SOC 30(7/8): 413-420. illus. 1969.--Rats which were made silicotic by intratracheal instillation of 40mg of quartz showed changes in the enzymatic activity during silica instillation. Acid lipase after an initial decrease shows an increased lipolytic activity during the stage of established silicosis. In the same way, the lipoprotein-lipase shows increased activity during established silicosis [having presented oscillations in the early stages of the experimental ...]. As for the pulmonary acesterase, its activity decreases. The rate of free fatty acids in the pulmonary tissue stays appreciably normal; on the other hand there is a noticeable decrease of these acids in the blood serum throughout the evolution of the silicosis.--E. C.

VETERINARY TOXICOLOGY

38125. CLARKE, E. G. C. (Roy. Vet. Coll., London, Engl., UK.) Poisoning in the pig [review]. BRIT VET J 125(6): 269-280. 1969.

† 38126. FRIES, G. F., G. S. MARROW, and C. H. GORDON. (Anim. Husb. Res. Div., Beltsville, Md., USA.) Comparative excretion and retention of DDT analogs by dairy cows. J DAIRY SCI 52(11): 1800-1805. illus. 1969.--Three groups of 3 cows each were fed 25 mg of p,p'-DDT, p,p'-DDD, or p,p'-DDE per day for 60 days. Concentrations of the compounds in milk fat approached, but did not reach, equilibrium during the feeding period. From 40 to 60 days, 11.8% of the p,p'-DDE, 7.6% of the p,p'-DDD, and 5.1% of the p,p'-DDT as p,p'-DDT (2.1%) and p,p'-DDD (3.0%) were excreted in the milk. When the feeding of the compounds ended at 60 days, the decline in milk fat concentrations of all compounds could be described as the sum of 2 1st-order terms. The initial partial concentrations of the 1st term were 0.61, 0.91, and 0.41 with rates of decline of 67, 41, and 31% per day for p,p'-DDT, p,p'-DDD, and p,p'-DDE, respectively. The initial partial concentrations of the 2nd term were 0.39, 0.09, and 0.59, with rates of decline of 1.3, 2.0, and 1.3% per day, respectively.

38127. WORD, J. D., L. C. MARTIN, D. L. WILLIAMS, E. L. WILLIAMS, R. J. RANCIERA, T. E. NELSON, and A. D. TILLMAN. (Dep. Anim. Sci., Okla. Univ., Stillwater, Okla., USA.) Urea toxicity studies in the bovine. J ANIM SCI 29(5): 786-791. illus. 1969.--Urea toxicity was produced in pregnant cows when dosed by drench with urea at a level of 0.44 gm/kg body weight. Symptoms of urea toxicity appeared within 10 min. This treatment proved fatal to cows which had been previously fasted and then administered a 5% v/v solution of acetic acid at the rate of 2 moles of acetic acid per mole of urea. A method was developed for handling pregnant cows to obtain high blood NH_3-N levels for a short period of time but to keep the cows alive. Cows were fed a poor-quality grass hay up to the time of urea administration. Four hr prior to urea administration, they were fed grain sorghum at a level of 5 gm/kg body weight for a standard weight of 352 kg with adjustment for greater weights being made on the basis of $W^{.75}$kg. When acetic acid was given at the rate of 2 moles/mole of urea at 15 min and at the rate of 1 mole/mole of urea 180 min after the urea was administered the animals survived. Using this procedure, 29 pregnant cows were treated and only 2 death occurred. Treated cows and their paired controls were kept under regular management conditions for another 12 mo. and treatment had no effect on number of calves born, birth weight, weaning weight of the calves, or weight changes and rebreeding performance of the cows.--J. W. S.

† 38128. CARR, S. B. (Va. Polytech. Inst., Blacksburg, Va., USA.), and DON R. JACOBSON. Bovine physiological responses to toxic fescue and related conditions for application in a biossay. J DAIRY SCI 52(11): 1795-1798. 1969.--Physiological responses were observed in 88 male Holstein calves in mostly paired comparisons for the ultimate development of a suitable biossay technique for fescue toxicity. The effects of environmental temperature, level of feed intake, ergotamine tartrate, and extracts of both toxic fescue and nontoxic orchardgrass on skin temperature of the distal portion of the tail were recorded. The 80% ethanol extract from toxic fescue caused a significant decrease in tail temperature, whereas nontoxic orchardgrass did not. Some differences in heart and respiration rates occurred. Multiple correlation and regression analysis indicated that room temperature and level of feed intake explained 57% of the variation in daily mean skin temperature of the tails of the animals in a room with continuous air movement. Complete removal of feed from the animals for 2 meals before obtaining measurements also caused reduced tail temperature, heart rate, and respiration rate. The most consistent response differences between presumably toxic and nontoxic extracts were obtained the day of treatment for intraperitoneal administration and the day following treatment for oral administration. The assay procedure described employing skin temperature appears to be the most discriminating for detecting reduced blood flow resulting from the administration of extracts of toxic fescue.

† 38129. MOUNT, DONALD J., and CHARLES F. STEPHAN. (Nat. Water Contr. Lab., Duluth, Minn., USA.) Chronic toxicity of copper to the fathead minnow (Pimephales promelas) in soft water. J FISH RES BOARD CAN 26(9): 2449-2457. 1969.--The maximum acceptable toxicant concentration of copper for the fathead minnow (Pimephales promelas, Rafinesque) in water having an EDTA hardness of 30 mg/liter (as $CaCO_3$) was found to be between 0.13 and 0.22 of the 96-hr TL_m [median tolerance limit] value, using survival, growth, and reproduction to evaluate effect. In an earlier study the application factor for copper in water with an EDTA hardness of 200 mg/liter (as $CaCO_3$) was found to be between 0.09 and 0.60 for the same species. Suggestions are made that should increase the accuracy and precision of future determinations of application factors.

38130. KRATZER, F. H., D. BANDY, M. WILEY, and A. H. BOOTH. (Agr. Res. Serv., Albany, Calif., USA.) Aflatoxin effects in poultry. PROC SOC EXP BIOL MED 131(4): 1281-1284. 1969.--A systematic study was made of the effect of graded levels of dietary aflatoxin on the performance of broilers under simulated practical conditions. No adverse effects were detected when a ration containing 400 ppb aflatoxin was fed to Arbor-Acres broiler chicks from 1 day to 8 wk of age. At higher levels (800 and 1600 ppb) adverse liver effects were detected, based on biochemical and histological studies. By chemical analysis, no evidence of aflatoxin was found in the meat, liver or blood of broilers fed 1600 ppb for 60 days prior to slaughter, nor in the eggs, meat, liver, or blood of White Leghorn hens fed a ration containing 2700 ppb aflatoxin for a period of 48 days.

† 38131. STUDIER, EUGENE H., and A. A. FRESQUEZ. (Biol. Dep., N. Mex. Highlands Univ., Las Vegas, N. Mex., USA.) Carbon dioxide. A mechanism of ammonia tolerance in mammals. ECOLOGY 50(3): 494-496. illus. 1969.--While guinea hens, Tadarida brasiliensis, inhale ammonia in air mixtures, CO_2 is passively retained in sufficient amounts to neutralize alkali excess resulting from increased blood ammonia levels. There is no change in blood CO_2 levels in house mice, Mus musculus. Little brown bats, Myotis lucifugus, are intermediate in this respect. Passive CO_2 retention is clearly related to ammonia tolerance in these animals.

† 38132. VAN KAMPEN, KENT R., and LYNN F. JAMES. (Agr. Res. Serv., US. Dep. Agr., Logan, Utah, USA.) Acute selenium poisoning of sheep. Pathogenesis of lesions. AMER J VET RES 30(10): 1779-1787. illus. 1969.--Twelve mature sheep were given a lethal dose

Reprinted from AMERICAN INDUSTRIAL HYGIENE ASSOCIATION JOURNAL
Volume 30, November-December, 1969

Monitoring Exposures to Vinyl Chloride Vapor: Breath Analysis and Continuous Air Sampling

EDWARD D. BARETTA,* RICHARD D. STEWART, M.D.,* and JOHN E. MUTCHLER†

Department of Environmental Medicine, Marquette School of Medicine, Milwaukee, Wisconsin, and Environmental Health Section, Biochemical Research Laboratory, The Dow Chemical Company, Midland, Michigan

R&S 028204

An environmental survey was conducted to determine the time-weighted average exposure (TWA) of a group of chemical plant workers to vinyl chloride (VCl) vapor. This survey featured continuous personal air sampling and analysis using an infrared spectrophotometer. The inhalation exposure data were digitized and recorded on paper tape for subsequent computer analysis and derivation of daily TWA values for each worker. A breath sampling program was conducted concurrently with the environmental survey, and a series of breath decay curves relating postexposure breath concentration to vapor exposure were derived from the data. To validate the breath curves derived from on-the-job data, postexposure breath curves were also constructed from breath data obtained following experimental human exposures to carefully controlled concentrations of VCl vapor. The close agreement between postexposure breath concentrations at the corresponding TWA's obtained by each of the methods suggests that either continuous air monitoring or breath analysis is valid for estimating the worker's individual daily exposure to VCl, and provides further evidence that breath analysis is a useful industrial hygiene technique for evaluating vapor exposure.

Introduction

THE QUESTION THAT MAY ARISE following an environmental survey is whether the chemical vapor concentrations measured are truly representative of the exposure being experienced by the workmen. Evaluation of the ranges of atmospheric concentrations and estimates of time-weighted average concentration (TWA) are all too often based on a few spot samples obtained under conditions which are not representative of all phases of a given operation. A more exact measurement of vapor exposure would have to be based on continuous monitoring of air in the workman's breathing zone during his entire work shift. Obviously this task is made difficult and often impossible by the large number and variety of tasks performed by today's modern chemical plant worker.

Recent improvements in automatic monitoring and data processing equipment have provided a means for a more satisfactory solution. Sequential samplers and automatic analyzers and recorders can now be used to continuously monitor several locations or operations to provide more valid data on which to base estimates of chemical exposure. Computers can be utilized to manage the large volume of data generated by continuous monitoring.[1]

Meanwhile a technique has been under development which more precisely defines the level of individual exposure. The realization that the total body burden of a volatile chemical is directly related to its concentration in expired air led to the development of techniques for collecting and analyzing breath samples useful in estimating the more indi-

This paper was presented at the American Industrial Hygiene Conference, St. Louis, Missouri, May 13-17, 1968.
*Marquette School of Medicine, Milwaukee, Wisconsin.
†The Dow Chemical Company, Midland, Michigan.

vidualized exposure experience of each workman. Studies by Stewart *et al.* [2-6] have shown that the excretion or "decay" of vapor in the breath can be used to characterize the exposure. Breath decay curves constructed for several chemical solvents have proved clinically useful as an index to chemical exposure.

These breath decay curves, for the most part, were constructed from postexposure breath data obtained from experimental human exposures to carefully controlled and relatively constant vapor concentrations. However, breath decay curves have recently been constructed from breath data collected from workers whose work environment was being continuously monitored.[7]

In this study of human exposure to vinyl chloride (VCl) vapor, breath decay curves constructed from data obtained during experimental exposures to the relatively uniform concentration within an exposure chamber were compared with those derived at the theoretically equal, but broadly fluctuating, concentrations encountered in a chemical plant atmosphere. A measure of the validity of continuous monitoring data and the usefulness of breath analysis in assessing time-weighted average exposure was reflected by a close similarity between the two sets of breath decay curves.

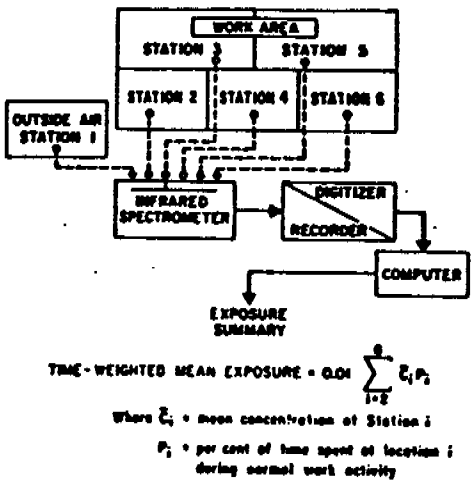

FIGURE 1. Schematic diagram of the infrared continuous monitoring system.

Procedures

Monitoring the Plant Atmosphere

The chemical installation surveyed was a closed structure housing several separate chemical processing operations. First, a job survey was conducted for each of four job classifications to determine the work areas frequented by the workmen and the time they spent in each area. For each job classification, five sampling probes were strategically placed in the work area. A sixth probe was placed outside the building, and charcoal and silica gel filters were placed in the sampling line to assure a clean air reference. The sample probes were 5/16-inch I.D. Saran tubing through which air samples were drawn by a vacuum pump at a rate of 17.5 liters/min to a centrally located infrared spectrophotometer. The spectrophotometer was equipped with a 10-meter path-length gas cell sensitive to 5 ppm of VCl at a wavelength of 10.63 microns. The VCl concentration was linearly related to absorbance up to approximately 1000 ppm.

A schematic diagram of the sampling system is shown in Figure 1. Sampling was executed sequentially with a set of six two-way solenoid valves controlled by a timer which advanced the sampling location every 5 minutes. A visual account of transmittance was recorded on a strip chart recorder. Meanwhile the data were recorded in digital form on paper tape by a tape punch and digitizer-programmed to record three equally spaced transmittances during the last half of each 5-minute sampling period.

The transmittance data furnished by the spectrophotometer was converted to absorbance and reduced to concentration according to Beer's law:

$$A = \mathrm{Log}_{10}\frac{(X_1 - X^{\infty})}{(X_i - X^{\infty})}$$

where

A	=	absorbance
X_1	=	base-line response.
X^{∞}	=	response at total absorption.
X_i	=	response at location i.
i	=	2, 3, 4, 5, 6.

R&S 028205

Finally,

$$C = KA$$

where

K = a proportionality constant,
C = concentration

The taped data were processed by a Burroughs 5500 computer at The Dow Chemical Company Computation Research Laboratory. The computer was used to calculate the mean and standard deviation of concentrations at each location for each 8-hour work shift. Finally, time-weighted average concentrations were calculated for each job classification using the time–location data obtained from the job surveys. As described elsewhere,[1] the weighted percentage of time during which concentrations exceeded several prechosen levels was also computed for use in establishing exposure profiles.

Figure 2 describes the exposure profiles (frequency distributions) for the four job classifications studied during this survey. These profiles show the percentage of time that concentrations exceeded the levels shown. They summarize several tens of thousands of individually measured concentrations and reduce them to single curves. Figure 3 shows the corrective trend brought about by actions undertaken to reduce the atmospheric concentration of VCl over the 7-month period during which the study was conducted. Only two job classifications warranted extensive study, but men in all four classifications were asked to participate in the breath sampling program.

On-the-Job Breath Sampling

Three separate breath sampling programs were conducted concurrently with the environmental plant survey, designated by the boxed portions in Figure 3. Each worker collected three breath samples daily—the first on his arrival home from work, the second 5 to 10 hours later, and a final sample before returning to work the following day. The samples were collected in pipets constructed from short lengths of 20-mm soft glass tubing to which had been welded at each end the threaded portion of a 2-dram (8-ml) screw-

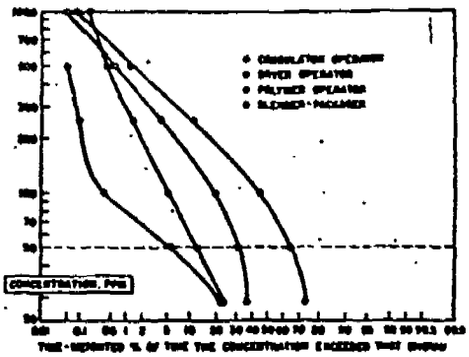

FIGURE 2. Exposure profiles expressed as VCl vapor concentration versus the exposure frequency distribution for the four job classifications.

cap glass vial (Figure 4). The overall length of the pipet was about 9 inches, so it could be conveniently and inconspicuously transported to and from work in a lunch bucket.

The plastic caps were lined with six layers of Saran film identical to that used for the construction of Saran air sampling bags. A 3/32-inch hole predrilled through one of the caps provided an access for withdrawing samples. The Saran liners provided an effective gas barrier so that vapor losses were held to less than 10% for a holding period of 3 days.

When collecting a sample the subject was asked to remove the caps, place the pipet to his lips, and breathe normally in through his nose and exhale through the pipet three

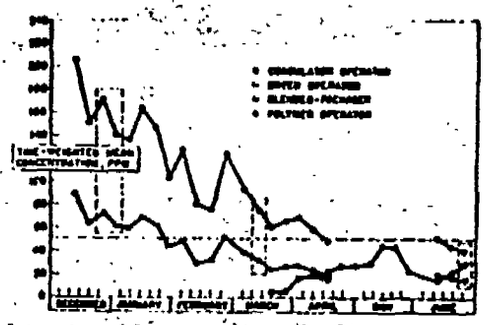

FIGURE 3. Weekly mean vapor exposure concentrations measured during the survey. Periods during which breath sampling was conducted are represented by the boxed-in areas.

R&S 028206

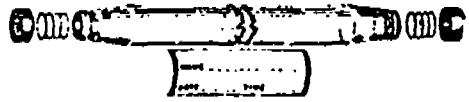

FIGURE 4. Glass pipet (50 ml) used for collecting breath samples. One cap has a predrilled hole for gas sampling. Both caps have Saran liners which seal the pipet chamber.

times. After expelling the fourth breath he quickly caps the tube, trapping a portion of alveolar air. The importance of writing the name, date, exact time of sampling, and the workshift most recently completed, on the label attached to each pipet, was stressed.

Aliquots were drawn from the pipets with a 1-ml Hamilton gas-tight syringe and analyzed in an Aerograph A-600B gas chromatograph using N_2 carrier gas and a hydrogen flame detector. Separations were made with a 6-foot, ⅛-inch I.D. stainless-steel column packed with Carbowax 20M alkaline on Chromosorb W 60/80 mesh acid-washed.

Exposure Chamber Operation

Three experimental human exposures to VCl were conducted at nominal vapor concentrations of 50, 250, and 500 ppm. The exposure chamber was a room measuring 41 feet by 6 feet wide by 7.5 feet high. The room had a continuous positive air supply and exhaust system capable of maintaining a slight negative pressure within the chamber. Continuous distribution of the chamber air was achieved by recirculating the air with a squirrel cage fan through a series of inlet and outlet ducts spanning the length of the chamber. The VCl was metered into the duct carrying air exhausted by the squirrel cage fan and entered the room atmosphere via the recirculation system at a rate sufficient to maintain the desired atmospheric concentration. The vapors were introduced from a pressurized storage cylinder through 6 feet of ⅛-inch I.D. stainless-steel tubing into a rotometer prior to entering the circulating air duct. A heating tape wrapped around the stainless-steel tubing prevented condensation of the VCl and stabilized the flow of the vapor.

The concentration of VCl in the chamber was constantly monitored with a Perkin-Elmer infrared spectrophotometer equipped with a 10-meter path-length gas cell. A sampling probe, consisting of 5/16-inch I.D. Saran tubing, was centrally located during the exposure to represent the breathing zone of all subjects within the chamber. The probe was moved about prior to each exposure to detect imbalance of vapor concentrations within the chamber so that necessary corrections in the recirculating system could be made. Air samples collected periodically within the chamber throughout the exposure day were analyzed by gas chromatography for added assurance of analytical accuracy. Both the infrared spectrophotometer and the gas chromatograph were calibrated before each experiment and at intervals throughout the exposure day.

Each 7.5-hour exposure day included a 0.5-hour lunch period in an uncontaminated area outside the exposure chamber. The TWA concentration was calculated on the basis of 7.5 hours of exposure.

Clinical and Laboratory Procedures

Each subject had been under careful medical surveillance by the medical department for a number of years, and each was given a complete medical examination a few days prior to the VCl exposures. Included were a complete urinalysis and 24-hour urine for urobilinogen, complete blood count with sedimentation rate, reticulocyte count, SGOT, SGPT, LDH, alkaline phosphatase, BUN, creatinine, and bilirubin.

Each subject received a repeat physical examination 1 hour before entering the exposure chamber. This examination included measurement of temperature, blood pressure, and pulse rate, a neurological examination, and collection of blood and breath samples. A questionnaire noting the presence of any symptoms of illness (for example, headache, nausea, dry throat) completed the pre-exposure medical evaluation.

After the subject entered the chamber, total expired breath samples were collected every hour by having him breathe out through a Saran tube leading to a Saran plastic collection bag located outside the chamber. Tidal volume and total expiratory capacity

R&S 028207

were measured in the morning and again late in the afternoon exposure periods.

Subjective and neurological responses were measured before the subject entered the chamber, 15 minutes after entrance, and at 1-hour intervals thereafter. Flannagan Coordination and Crawford Manual Dexterity Tests were conducted at midmorning and again in the afternoon. Breath sampling began immediately after the subject left the exposure chamber. A 24-hour postexposure urine sample was collected and a blood sample was drawn the following morning for SGPT, LDH, alkaline phosphatase, BUN, creatinine, and bilirubin determinations.

Analysis of Breath Data

The decay curves for the breath vinyl chloride concentrations were constructed by stepwise multiple regression using a digital computer. An empirical relationship of the form Concentration = f (TWA, time) was selected from a choice of several terms, each based on TWA and/or time. The resulting regression equation best represents the ordered relationship between breath vinyl chloride concentration, time-weighted average exposures, and postexposure time.

Each breath decay curve has an associated standard error of regression which can be used to compute the confidence band for any chosen level of significance. The 95% confidence band for the mean of a group of observations was chosen in this case to describe the statistical error associated with the breath data and the regression technique.

Results

Experimental Breath Curves

A total of 13 men participated in the three experimental chamber exposures at nominal concentrations of 50, 250, and 500 ppm producing a total of 160 valid breath data points. Five of the six subjects exposed to 50 ppm were re-exposed at 500 ppm 2 days later. There was no measurable residual vinyl chloride detected on the breaths of the subjects prior to the second exposure. Serial breath sampling was initiated immediately after the subjects left the exposure chamber and continued up to 20 hours following the exposures.

TABLE I
Experimental Human Exposure to Vinyl Chloride

Chamber Concentration (ppm) $\bar{X}$	S.D.	Range (ppm)	TWA[a] (ppm)	Number of Subjects
59	2	55–63	48	6
261	8	239–245	248	4
493	7	518–471	439	4
491	5	525–475	491[b]	7

[a]Time-weighted average concentration based on 7.5 hours including a 0.5-hour lunch period in an uncontaminated area.
[b]Continuous exposure for 3.5 hours.

Table I shows the analyzed concentration to which the subjects were exposed. Calculations of the mean and standard deviation of exposure concentration are based on chart readings from the infrared spectrophotometer taken at 5-minute intervals over the two 3.5-hour exposure periods. The TWA is based on the total 7.5 hours which included a 0.5-hour lunch period in an uncontaminated area.

The final breath decay curves intended for use as an index to VCl exposures were adjusted to TWA concentrations of 50, 250,

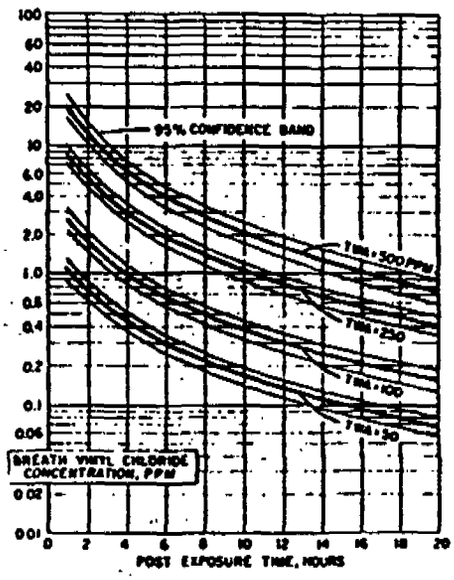

FIGURE 5. Breath decay curves based on experimental human exposures to 50, 250, and 500 ppm of VCl (7.5-hour TWA).

R&S 028208

R&S 028209

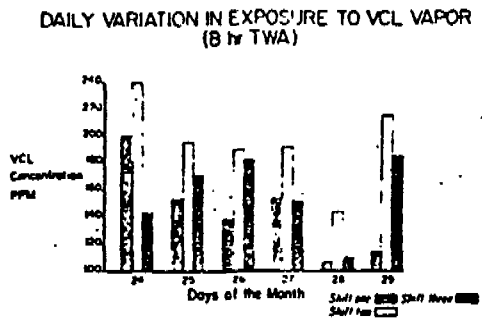

FIGURE 6. Variation in VCl vapor exposure for three shifts.

and 500 ppm (Figure 5). A 100-ppm decay curve was interpolated from the available data using regression analysis. These curves are presented with the calculated 95% confidence bands for the mean of a group of observations.

On-the-Job Breath Curves

Ten workmen participated in the on-the-job breath sampling program, producing a total of 91 usable sets of data. Ten percent of the breath samples collected were discarded because of pipet leakage or poor sampling techniques.

Absolute breath levels ranged from about 20 ppm in one sample taken less than 1 hour after an 8-hour TWA of 250 ppm, to barely detectable levels (<0.05 ppm) in samples taken after exposures at TWA's below 50 ppm.

The extremely broad variation in the TWA's experienced by workmen during one of the periods in which breath sampling was being conducted is demonstrated for three shifts of men bearing the job classification "coagulator operator" (Figure 6). Minute, hourly, and daily fluctuations in the concentration of a contaminant are most descriptively revealed by continuous monitoring. This method of sampling quickly points out the fallacy of judging TWA and peak exposure concentrations on the basis of spot sampling or periodic surveys of brief duration.

The remarkable correlation between breath concentration and corresponding TWA values made it possible to construct the series of breath decay curves shown in Figure 7. with confidence bands only slightly wider than those from controlled human experiments. The close similarity between these curves and those constructed from controlled exposure data are further illustrated in Figure 8.

Human Responses

From a subjective standpoint no significant untoward affects were noted at any of the exposure concentrations. The only complaints were those of two subjects who reported mild headache and some dryness of their eyes and nose during the 500-ppm exposure experiments.

No odor was detected by anyone entering the exposure chamber at 50 ppm. At 250 ppm all four subjects entering the chamber initially reported that they could detect a very slight odor of the chemical. Five of the seven subjects entering the exposure chamber at 500 ppm were able to detect the odor of VCl, but after 5 minutes of exposure those five were unable to detect it even with forced inspiration. Three of the four subjects reentering the chamber after lunch were able

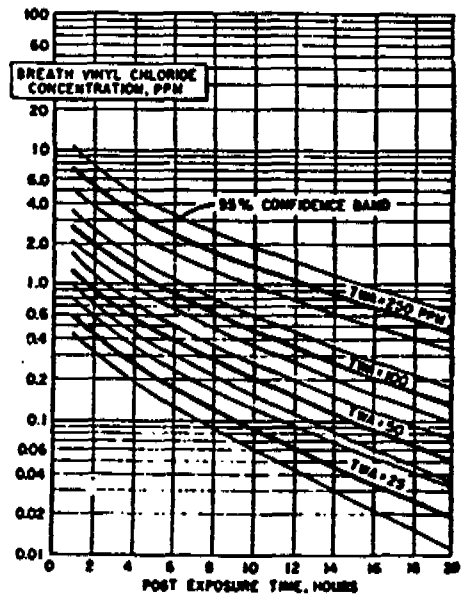

FIGURE 7. Breath decay curves derived from breath data collected from workers following on-the-job exposures to VCl vapor (8-hour TWA).

R&S 028210

to detect a faint odor of VCl. One subject could detect a faint odor on deep inspiration for approximately 15 minutes after entering the exposure chamber.

The exposure had no noticeable effect on neurological responses, nor did it produce significant changes in the results of mental, coordination, or manual dexterity tests conducted during the exposure period. All clinical laboratory studies performed in the post-exposure period were normal and not significantly different from pre-exposure values.

Discussion

The object of the environmental health survey is to identify the atmospheric contaminant, determine the exposure level, and relate this to the health hazard it presents. If one is to judge hazard by ambient concentration measurements, then those measurements must accurately describe the exposure on a continuing individual basis. A carefully conducted survey combining continuous analysis of the work room atmosphere with a comprehensive job study will provide data valid for estimating time-weighted average exposure.

On the other hand, breath decay curves constructed from breath data collected during continuous plant monitoring are in close agreement with those obtained from exposure chamber experiments with VCl. These curves should therefore be useful as a second method for assessing exposure to VCl vapor.

The choice of whether one or both methods should be used depends on prevailing circumstances and on the thoroughness desired. For example, data useful in describing peak exposures are obtained from continuous monitoring. Concurrently, exposure trends and concentration gradients may help identify plant operational inefficiencies and equipment malfunctions by revealing specific sources of emission. Correcting these problems not only restores a healthful work environment but often results in bonus savings by reducing losses of raw material and product.

Continuous monitoring, however, is extremely costly both in time and in the equipment required. The scope of data acquired is limited by the number of sampling probes, and these probes are not always capable of accurately measuring the individual's daily exposure experiences, especially should these involve unusual incidences such as chemical spills or exposures outside the monitored area.

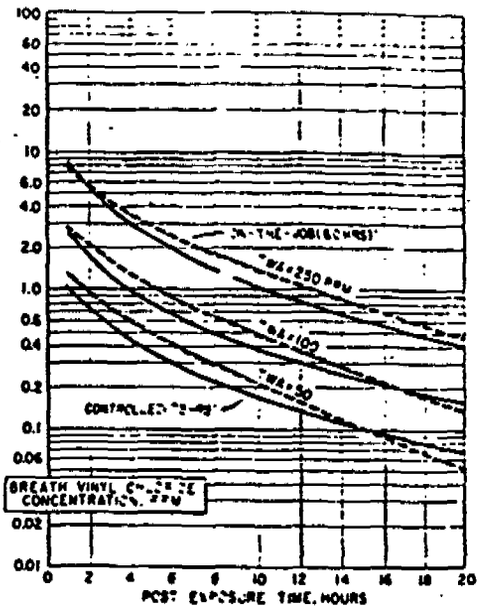

FIGURE 8. Comparison of breath decay curves derived from the on-the-job data and the experimental human exposure data.

Breath analysis has the advantage of individualizing each worker's integrated daily exposure. Breath decay curves, as an index of exposure, offer a means of estimating the average daily individual exposure on the basis of a few breath samples taken serially in the postexposure period. Consequently breath analysis can be used to diagnose as well as quantitate an exposure which has already occurred. It is a relatively inexpensive and simple method which can be put into operation without extensive and costly preliminary preparations.

However, postexposure breath analysis does not provide information on the daily fluctuations of exposure, and the peak exposure concentrations are not made evident by breath data. Finally, breath analysis is not applica-

ble to all chemicals, and breath decay curves established for one chemical are not useful as an index of exposure to any other chemical.

The decay curves presented here are intended to serve as an index of exposure to vinyl chloride vapor and are based on an exposure duration of 7.5 hours for the experimental exposures, and 8 hours for the on-the-job study. The close agreement between the two sets of curves and the narrow confidence bands obtained in each case demonstrate the usefulness and accuracy of both methods for estimating TWA exposures and indicate the importance of breath analysis and the need for expanding its use in evaluating exposures to other widely used volatile organic chemicals.

References

1. Peterson, J. E., H. R. Hoyle, and F. J. Schuttish: The Application of Computer Science to Industrial Hygiene. *Amer. Ind. Hyg. Assoc. J. 27:* 180-185 (March 1966).
2. Stewart, R. D., H. H. Gay, D. S. Erley, C. L. Hake, and A. W. Schaffer: Human Exposure to Tetrachloroethylene Vapor: Relationship of Expired Air and Blood Concentrations to Exposure and Toxicity. *Arch. Environ. Health 2:* 516-522 (May 1961).
3. Stewart, R. D., H. H. Gay, D. S. Erley, C. L. Hake, and J. E. Peterson: Observations on the Concentration of Trichloroethylene in Blood and Expired Air following Exposure of Humans. *Amer. Ind. Hyg. Assoc. J.23:* 167-170 (April 1962).
4. Stewart, R. D., and V. K. Rowe: Quinze Ans d'Etudes sur le 1,1,1-Trichloroethane. *Arch. Maladies Profess. 28:* 194-201 (1967).
5. Stewart, R. D., H. C. Dodd, E. D. Baretta, and A. W. Schaffer: Human Exposure to Styrene Vapor. *Arch. Environ. Health 16:* No. 5 (May 1968).
6. Stewart, R. D., E. D. Baretta, H. C. Dodd, and T. R. Torkelson: Experimental Human Exposure to Tetrachloroethylene. *AMA Arch. Environ. Health.* (In print).
7. Stewart, R. D., H. C. Dodd, E. D. Baretta, A. W. Schaffer, and J. E. Mutchler: Chronic Overexposure to Benzene Vapor. Presented at the Sixth Annual Meeting of the Society of Toxicology, March 23-25, 1967, Atlanta, Georgia.

Received May 26, 1968

R&S 028211

THE TOXICITY OF VINYL CHLORIDE VAPOR
A Brief Summary of the Published Literature
February 7, 1974

The following articles and abstracts, compiled by The Dow Chemical Company, are believed to include most of the significant scientific information on the toxicology of vinyl chloride in man and animals. The articles and abstracts are arranged in chronological order. Articles published in the last half of 1973 may not be included if they have not been abstracted by Chemical Abstracts or Biological Abstracts.

Important review articles which summarize much of the old literature have been used to cover the literature prior to 1961-1962. Therefore, copies of certain articles and abstracts described in these early reviews are not included in this compilation.

Since vinyl chloride (chloroethene, $CH_2=CHCl$) is a gas at room temperature and pressure, the common route of toxic exposure is by inhalation. As with many liquified gases, contact of the skin or eyes with escaping compressed vinyl chloride can produce freezing and frostbite. (Torkelson et al, 1961).

Vinyl chloride has long been considered to be very low in toxicity by acute inhalation. Lehmann and Flury (1938) summarized the literature and reported work by Schauman who considered vinyl chloride to be a candidate surgical anesthetic. Schauman reported little pathological changes even after repeated exposure to anesthetic concentrations.

R&S 028212

W. F. von Oettingen (1955) of the U. S. Public Health Service summarized the available toxicity data on many halogenated hydrocarbons in an excellent monograph.

According to von Oettingen, several authors had reported vinyl chloride to be rapidly absorbed and excreted through the lungs and to cause anesthesia. The following is von Oettingen's summary of the toxicity of vinyl chloride in animals and man:

"As to the *toxicity* of vinyl chloride, Patty, Yant, and Waite (1930) studied this in guinea pigs. They found that exposure to 20 to 40 vol. percent kills the animals in a very short time, that concentrations of 10 vol. percent are dangerous to life with exposures for 30 to 60 minutes, and that 0.5 vol. percent is the maximum allowable concentration for several hours' exposure without causing acute disturbances of severe nature. Animals exposed in this way showed some edema of the lungs and hyperemia of liver and kidneys. They considered vinyl chloride less harmful than chloroform or carbon tetrachloride and of a similar order of toxicity as ethyl chloride. Schaumann (1938) found that mice and rats tolerate repeated light narcosis for 4 hours daily on 5 to 8 consecutive days and for 1 hour daily for 4 weeks without showing kidney or liver injuries. Dogs which had been narcotized for 3 hours with 10 vol. percent on 7 occasions in the course of several weeks showed no considerable changes in kidney and liver. Higher concentrations (20 vol. percent) caused in dogs marked salivation, respiratory arrest, and vomiting after narcosis. Peoples and Leake (1933) determined the lethal range for mice with 10 minutes' exposure as 10 to 12 mM per liter, and Schaumann (1934) determined the vinyl chloride level in the blood at the time of cardiac arrest as <40 mg percent and at the time of respiratory arrest as 27 to 30 mg percent, the same value for chloroform being 60 to 70 mg percent.

R&S 028213

R&S 028214

Regarding the *toxicity* of vinyl chloride *for man*, Patty, Yant, and Waite (1930) expressed the opinion that the gas does not possess adequate warning properties because of its odor or irritant action, but that it gives warning by producing symptoms of dizziness and disorientation in advance of harm, except when present in exceedingly high concentrations which would cause almost immediately helplessness and unconsciousness. Inhalation of 2.5 percent will soon cause dizziness, disorientation, and a burning sensation in the soles of the feet, which symptoms disappear immediately after discontinuation of the exposure except for a slight headache which may last 30 minutes. These authors suggested the use of vinyl chloride for narcosis in man."

As a result of two deaths in Canada, the acute inhalation toxicity of vinyl chloride was studied by Mastromatteo et al (1960) who reported that exposure of mice, rats, nd guinea pigs to 10, 20, and 30 volume percent vinyl chloride caused the following mortality:

NUMBER OF DEATHS IN DIFFERENT GROUPS OF FIVE MICE, RATS AND GUINEA PIGS EXPOSED FOR THIRTY MINUTES TO VARYING CONCENTRATIONS OF VINYL CHLORIDE IN AIR

Vinyl chloride concentration (percent by volume in air)	Laboratory animal			Total
	Mice	Rats	Guinea pigs	
10	0/5	0/5	0/5	0/15
20	1/5	0/5	0/5	1/15
30	5/5	5/5	1/5*	11/15
40	-	-	2/5*	2/5
Total	6/15	5/15	3/20	14/50

* A delayed death occurred within 24 hours following exposure.

R&S 028215

Some pulmanary hyperemia and engorgement was observed by these investigators, but liver and kidney injury were remarkably low. Deaths were due to narcosis.

The first report of studies to determine the effect of long-term repeated exposure (6 months) were summarized by Torkelson, Oyen and Rowe (1961) as follows:

"Repeated exposures of laboratory animals to several concentrations of vinyl chloride in air were conducted to determine the chronic toxicity of this material towards animals in order to assess the hazard to humans. Vinyl chloride was found to have a slight capacity to cause liver and kidney injury on repeated exposures. Male and female rats showed micropathological changes after repeated daily 7-hour exposures at 500 ppm for 4.5 months. Repeated 7-hour exposures at 200 ppm for six months resulted in micropathological changes in the livers of rabbits and statistically significant increases in the average weight of the livers of male and female rats but no detectable changes in dogs and guinea pigs. Repeated 7-hour exposures at 100 ppm resulted in slight increases in the average weight of rat livers, the other species were not affected. All species studied tolerated repeated daily 7-hour exposures to 50 ppm for six months with no detectable injury.

Repeated daily 1-hour exposures at 200 and 100 ppm of vinyl chloride were without effect, longer exposures caused a slight increase in liver weight.

The standard for evaluating regular daily 7 to 8-hour exposures may be defined as the concentration below which practically all analytical results must fall. The value of 100 ppm is suggested as this standard for vinyl chloride, with a time-weighted average for all exposures not to exceed 50 ppm."

Lester, Greenberg, and Adams (1963) took strong exception to the conclusion of Torkelson et al (1961) that 50 ppm should be a maximum time weighted average exposure for workers. On the basis of 3 months exposure of rats to 2 volume percent and 19 days to 5 volume percent, they concluded that 500 ppm was acceptable as a TLV despite minor changes which they observed in rat livers and which they considered "were within the normal range and were not pathologic in nature."

Because of these conflicting reports, the TLV Committee of the ACGIH in 1963 chose to change their TLV from 500 ppm as a maximum time-weighted average for industrial exposure to 500 ppm as a ceiling value. (American Conference Governmental Industrial Hygiene, 1963).

Since 1962, numerous European articles on vinyl chloride have appeared, particularly in the Russian literature. For several reasons, these articles are difficult in interpret in terms of chronic toxicity since the reported exposures were to mixtures or were otherwise ill-defined, the exposures are often acute, or the criteria of effect was a minimal change in response or behavior, such as a subtle change in a conditioned response.

R&S 028216

In 1967, reports appeared in the literature describing a condition known as acroosteolysis in workmen engaged in polymerization of vinyl chloride to polyvinyl chloride. Harris and Adams (1967) reported on two cases in Europe. Wilson et al (1967), reported on 37 cases in the B. F. Goodrich Company. Basalaev (1970) described the use of large frame photofluorography for diagnosis of acroosteolysis in Russia. Basalaev et al (1972) described studies in rats and rabbits and claimed to have produced the disease in these species. Fethiere and Kerzner (1972) discussed the disease as did Jühe et al of the University of Bonn (1973). Jühe et al (1973) described a syndrome consisting of (arranged in decreasing order of occurrence) thrombopenia, splenomegaly, liver damage, obstruction of ventillation, circulatory obstruction, and skin and bone alteration.

As a result of this problem, the University of Michigan in 1967 was retained by the Manufacturing Chemists Asscciation to investigate this disease in sponsoring American companies. The results of a large scale epidemiological study of workers then currently employed in vinyl chloride and polyvinyl chloride production were reported in three publications by this group (Dinman et al, (1971) Cook et al, (1971) and Dodson et al, (1971)).

Dinman et al summarized the study as follows:

"An epidemiological study was performed covering 5,011 employees with 21,510 man-years experience in various phases of vinyl chloride (VC) and polyvinyl chloride (PVC) manufacturing in 32 plants throughout the United States and Canada. The total number of definitive cases of acroosteolysis

R&S 028217

(AOL) was 25; 16 other individuals were under suspicion. This condition is clearly associated with the hand cleaning of polymerizers. Workers engaged in other phases of VC or PVC manufacturing do not appear to be at risk of developing AOL. The importance of Raynaud's phenomenon as a concomitant of AOL is emphasized. Several statistical approaches for rapid medical survey are suggested. Acroosteolysis appears to be a systemic rather than local disease. Presently, neither the etiological agent nor its portal of entry is known."

Cook et al describes the polyvinyl chloride production process in considerable detail. They concluded that although no etiological agent could be identified, "There appeared to be a correlation between the extent of degassing prior to entry into the reactor" and the incidence of acroosteolysis.

Mutchler and Kramer presented a paper at the 1968 Gordon Research Conference which was subsequently published (1972), which reported on "The Correlation of Clinical and Environmental Measurements for Workers Exposed to Vinyl Chloride " The authors drew the following conclusion:

"Our findings suggest that repeated exposure to vinyl chloride at TWA levels of 300 ppm or above for a working lifetime together with a very low level of vinylidene chloride may result in slight changes in certain physiologic and clinical laboratory parameters. The possibility of some impairment in liver function tests must be considered, even though no overt clinical disease was evident in any of the individuals studied. We shall continue our study, but suggest that similar studies to help clarify the effects of this material be performed for other worker populations exposed to vinyl chloride alone."

R&S 028218

The MCA sponsored studies by Dinman et al and Mutchler and Kramer appear to be the only two significant eqidemiological studies on vinyl chloride reported in the literature.

P. L. Viola, in an attempt to produce acroosteolysis in animals, exposed rats 4 hours per day, 5 days per week to 30,000 ppm (3%) vinyl chloride vapor. (Viola, March, 1970). In his first report on the results of 12 months exposure, he described metaplastic changes in the bones which he considered similar to the human disease acroosteolysis. He made no mention of having observed cancer in these animals until the Tenth International Cancer Congress in May, 1970. In the abstracts of this meeting, (Viola, 1970), and subsequently in May, 1971, Viola, Bigotti and Caputo (1971) reported tumors of the skin, lungs and bones occurring first after 10 months of exposure. The authors summarized this work as follows:

"Rats (Ar/IRE Wistar strain) exposed for 12 months to vapors of vinyl chloride developed tumors of the skin, lungs, and bones. The cutaneous tumors, which always appeared in the area in which submaxillary and parotid glands are located, have been histologically recognized as epidermoid carcinomas, papillomas, and mucoepidermoid carcinomas. The morphological characteristics of lung tumors, which occurred in a lower percentage, were mainly of the adenocarcinoma type, with the exception of a single epidermoid tumor originating from the epithelial covering cells. In a minor number of rats, a large proliferation of cartilaginous tissue diagnosed as osteochondroma developed in the metacarpal and metatarsal regions of the four limbs.

R&S 028219

R&S 028220

This report by Viola et al is apparently the earliest and only publication in which carcinogenic activity has been ascribed to vinyl chloride. Although there are possible deficiencies in Viola's study, such as his very impure sample, the presence of food and bedding in the exposure chamber, excessive exposure concentration as well as in the statistical evaluation and interpretation of the lesions, the report is of serious concern and has resulted in additional animal and epidemiological studies which are currently underway (MCA Press Releases).