

Chronic Oral Toxicity to Rats of a Vinyl Chloride-Vinyl Acetate Copolymer

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High molecular weight polymers are generally accepted as safe for food contact, although there is a dearth of published evidence. In particular, no reports of long-time experimental feeding of polyvinyl resins, widely used in food packaging, appear in the literature. In order to fill this gap, a study completed in 1947 is presented.

METHODS

Sample. The sample was then characterized as vinyl resin VYNU.¹ It was a copolymer of 95% vinyl chloride and 5% vinyl acetate, with a molecular weight of 25,000 to 30,000 as determined by the Staudinger method, or 200,000 as measured by osmotic pressure. The resin was produced in the form of particles with a diameter of 0.1 μ that tended to agglomerate loosely.

Animal management and observation. Each of the parental generation group consisted of 12-15 Wistar-strain albino rats of each sex, approximately 6 weeks of age at the first dose. They were housed 4-6, half of each sex, in wire-bottom cages. Ten to 12 offspring of each sex, consisting of the first filial generation, were fed the diets until the end of the study and, as no differences were found from the parental generation rats, both generations were considered together.

For the first 18 months the basic diet consisted of a mixture of 100 parts of ground whole wheat, 5 parts of dried whole milk, and 2 parts of iodized table salt. Wheat then became unavailable to the local miller, and during the last 6 months a commercial ground laboratory chow² was utilized. The growth curves of the rats showed no appreciable upset from the shift in basic diets.

One group received the basic diet, one had 1.5% VYNU added, the third had 12% VYNU added, with no attempt made to correct for high nonnutrient content. The respective intakes of VYNU averaged 0.61 and 5.75 g/kg. day.

The observations made during the feeding were (1) tone and behavior of animals, (2) average food consumption, (3) body weight, (4) occurrence of death and infection, (5) red, white, and differential white blood cell counts, and (6) occurrence of pregnancy, number of pups born, and survival and growth of the pups.

At death or sacrifice gross pathology was recorded, and neoplasms were sought. Body length was measured, and livers and kidneys were weighed. Organ weights were calculated as a percentage of body weight.

Adrenal, small intestine, kidney, liver, lung, pancreas, spleen, testis, and neoplasms

¹ Manufactured by a company known at that time as Union Carbide Plastics Division.

² Purina Laboratory Chow Meal, Ralston Purina Company, St. Louis, Missouri.

TABLE 3
LIVER AND KIDNEY WEIGHT RATIO DATA ON RATS RECEIVING RESIN
VYNU IN THE DIET FOR ONE AND FOR TWO YEARS

Period of feeding	Dietary level (%)	Organ weight as percentage of body weight ^a	
		Liver	Kidney
1 Year	12	4.08 ± 0.43 ^b	0.79 ± 0.18
	1.5	3.05 ± 0.37	0.66 ± 0.05
	0	3.12 ± 0.35	0.64 ± 0.12
2 Years	12	3.06 ± 0.31	0.59 ± 0.17 ^b
	1.5	3.05 ± 0.35	0.66 ± 0.06
	0	3.34 ± 0.43	0.70 ± 0.10

^a Mean ± SD.

^b $P < 0.05$.

histologically normal, and at two years livers of rats in the same group were numerically but not significantly lighter. Similarly, a slight, but statistically significant, decrease in mean relative kidney weight was seen at two years, but not at one year, with all sections histologically normal. Neither was considered to be a deleterious effect from the inclusion of VYNU in the diet.

Table 4 summarizes the reproduction results and does not suggest any effect.

TABLE 4
REPRODUCTION OF RATS^a RECEIVING RESIN VYNU IN THE DIET FOR TWO YEARS

Dietary level (%)	Females of parental generation		Females of F ₁ generation		Total per female	
	Total	Infertile	Total	Infertile	Litters born ^b	Pups born alive ^b
12	5	1	6	1	6.3 ± 3.5	47.8 ± 28.7
1.5	5	1	4	0	5.5 ± 4.0	45.2 ± 30.4
0	10	1	6	1	8.4 ± 5.3	51.6 ± 41.0

^a Alive at 365 days of age.

^b Mean ± SD.

The tissues of the 38 rats sacrificed for examination after one or two years were histopathologically normal. An infective or traumatic cause of death was clear for all rats dying, and none of their tissues showed any histopathology not directly related to this cause. Careful search of all rats dying or sacrificed revealed only 6 neoplasms, possibly because half of the rats did not survive the lung infection into the second year of feeding. At the 12% level of VYNU there were two neoplasms in the mesentery, at the 1.5% level one uterine neoplasm, and the controls had one in the mesentery and two in the lung.

DISCUSSION

This study, completed 20 years ago, differs in many respects from the design one would expect in a current study of the safety of a food-packaging resin. In particular, it would be preferable to add to animal diets only that fraction of the resin which transfers to food packaged in a formulation.

Furthermore, were reproduction considered of sufficient importance to be studied, a separate group of animals would be desirable, with opportunity for mating provided only at estrus.

SUMMARY

Starting in 1944, albino rats of both sexes caged together were maintained for two years upon diets containing 1.5% and 12% of a vinyl chloride-vinyl acetate copolymer. No effect attributable to the resin was found.

REFERENCE

- FISHER, R. A. (1938). *Statistical Methods for Research Workers*, 7th ed. Oliver & Boyd, Edinburgh and London.

contained 20 mg./m.³-884 mg./m.³ of fluororg. impurities, and after them only 3.5 mg./m.³ St. Janderka

68686w Hygienic evaluation of new technological processes in chemical industries. V. S. Filatova. *Gig. Tr. Prof. Zabol.* 10(11), 3-7(1966)(Russ). In a hygienic examn. of a new poly(vinyl chloride) (PVC) plant the most frequently occurring concns. of vinyl chloride, the chief noxious factor, were 10-44 mg./m.³ (30 mg./m.³ is a permissible threshold limit), compared with 100 mg./m.³ in old plants. The concn. of PVC dust after introduction of fluidized-bed drying was smaller by a factor of 27 than in the old Stroganov system VIS-75 ovens. A favorable hygienic effect of continuous production was observed in a hexamethylenediisocyanate plant, esp. after mechanization of labor-consuming operations and installation of remote control. Most frequently occurring concns. of hexamethylenediisocyanate in the air were 0-0.1 mg./m.³, compared with the highest permissible concn. 0.05 mg./m.³. Analogous conditions were found in the production of AG salt (one of the initial materials in the production of nylon 66), where the intermediate product, hexamethylenediamine, is obtained by hydrogenation of adiponitrile under a pressure of 150-180 atm., where the concn. of hexamethylenediamine, adiponitrile, and NH₃ in the air were in all cases below the permissible, limit. Also in the production of MeOH from coke oven gas the concn. of CO in the vicinity of circular pumps operating at 300-20 atm. did not exceed the sanitary limit. In a plant producing Cl by the continuous method under vacuum and equipped with new hermetic electrolyzers BGK-17, the generation of heat for 1 ton of the product was 2 times and liberation of Cl gas 3-40 times lower than in plants with old electrolyzers. No Cl was detected in most samples and the Hg level was within the standard. But some of the new chem. plants are not yet up to sanitary standards, e.g. the concn. of vinyl chloride in the polymerization area of a PVC latex plant exceeded by 100% the limit, 2.28 kg. of vinyl chloride was liberated by 1 reactor in 1 hr. in the air. Sanitary measures are proposed to improve the conditions.

St. Janderka

68687x Occupational hygiene in the production of resins from furfural. G. N. Nazzyrov and Kh. Ya. Vengerskaya (Inst. Sanit., Hygiene, and Occup. Diseases, Tashkent). *Gig. Tr. Prof. Zabol.* 10(11), 56-60(1966)(Russ). The concn. of furfural, Me₂CO, and PhOH vapors in the air of the Fergan chemical plant engaged in the production of furfural resins was detd. In the furfural-Me₂CO monomer plant, the most frequent concn. of furfural vapors was within the 0.0008-0.003 mg./l. range, and that of Me₂CO 0.007-0.01 mg./l., while in the furfural-Me₂CO-epoxy resin plant, the usual concn. of furfural vapors ranged from 0.0 to 0.004 mg./l., and that of Me₂CO 0.0-0.01 mg./l. In the furfural-Me₂CO-PhOH-HCHO resin shop, the most frequent concn. of furfural vapors averaged 0.0-0.002 mg./l., while the concn. of Me₂CO and PhOH vapors were 0.0-0.006 and 0.0-0.002 mg./l., resp. To improve the existing conditions, it is recommended to improve the general and local ventilation systems, as well as to shift to more mechanized and automatic procedures.

A. A. Horvath

68688y Prevention of air pollution with mercury inside industrial premises of synthetic fiber plants. M. N. Korshun. *Gig. Tr. Prof. Zabol.* 10(11), 18-22(1966)(Russ). Av. concns. of Hg fumes in the air of the chem. labs. of the synthetic fiber plant examd., in the mercerization and precuring areas at 27-9°, was 400-500% that of the permissible limit. It decreased gradually in the conditioning and xanthation areas. Higher concns. of Hg fumes were found in places where alkali or alkali cellulose came in contact with the air. At the opening of precuring and conditioning tubes, in which alkali cellulose is held the longest, the concns. of Hg fumes was the highest, 0.17 and 0.20 mg./m.³. Decreases of Hg fumes in the xanthation and subsequent stages may be due to treatment of alkali cellulose with CS₂, binding Hg and pptg. its sulfide. Analysis of lab. samples of 100 ml. of NaOH and 50 g. of alkali cellulose, kept 48 hrs. in hermetically sealed glass flasks, revealed that NaOH-treated cellulose acquires the ability to liberate Hg fumes; alkali cellulose liberates during prematuration most of the Hg; alkali cellulose treated with CS₂ did not liberate Hg fumes during an exposure of 48 hrs. But there is no method for the detn. of Hg in alkali cellulose; the methods recommended by GOST did not give pos. results. Lab. analyses have revealed sorbed Hg on the walls of soda station, mercerization, and precuring area. Secondary Hg sources may be also wooden construction elements and furniture. Measures are proposed to improve the condition.

St. Janderka

68689z Problems of industrial hygiene in the production of ANP chemical flotation agents. S. Ya. Krivshin. *Gig. Tr. Prof. Zabol.* 10(11), 28-32(1966)(Russ). Chem. flotation agents ANP-1 and ANP-2, used for the enrichment of iron, phosphorite, talc-magnesite, and other ores are hydrochloride salts of tetra- and pentadecylamines and begin to decomp. at temps. above 100°. Despite their wide-spread use, there are no data on their toxic characteristics. They cause dystrophic lesions of liver and kidneys, affect the permeability of wall vessels, disturbances in

central nervous system, and irritation of mucous membrane of the eyes and upper respiratory tract. The permissible limit recommended is 1 mg./m.³. Starting raw materials in their production are high mol. paraffins, HNO₃, and HCl. The plant atm. is polluted by MeOH, N oxides, HCl, amines, and their salts. Pentadecylamine is liberated in all stages of production esp. in the synthesis of the flotation reagent and its purification the concn. of pentadecylamine was 3-5 mg./m.³. Escape of these substances into the atm. was caused by corrosion of the seals to amines and their salts. App. and building constructions were polluted by amines and their salts at the rate of 0.01-1.00 mg./cm.². In dermatological examn. of 120 workers cases of professional dermatitis, chiefly in app. operators and locksmiths were observed. The amines and their salts had a pronounced sensitizing effect on the skin. Arterial hypotension (90-6 mm. 55-60 mm.) was found in 68% of 25 persons examd.; 48% had increased permeability of vessel walls. Introduction of sanitary measures (full mechanization of the process, sealing of the app., replacement of rubber seals by Teflon, shielding of samplers, use of "biol. gloves" or IEP-1 paste) helped to improve the conditions.

St. Janderka

68690t Experimental materials contributing to the establishment of hygienic standards for urea-formaldehyde resins. L. J. Dueva. *Gig. Tr. Prof. Zabol.* 10(11), 39-43(1966)(Russ). The direct relation between the damaging and sensitizing effect of resins on the skin and their general resorptive action, depending upon the amt. of free HCHO contained was established. The pollution of industrial plants with HCHO vapors, which produce harmful action on the organism of workers because of the allergic and irritative effects, may depend upon the amt. of residual monomer contained. For this reason, the max. red. of free HCHO in urea-HCHO resins is needed.

J. Pich

68691u Hygienic evaluation of some petrochemical industries. E. A. Kapkaev, L. V. Trofimova, N. A. Enikeeva, and A. K. Monkevich. *Gig. Tr. Prof. Zabol.* 10(11), 22-8(1966)(Russ). Gas impurities are the chief factor affecting working conditions in a petrochem. plant; they may contain 4-8 ingredients. Toxic substances in plants examd. for the most part did not exceed the sanitary limit, but considerable pollution of the atm. was observed in some places (opening and repair of the app. cleaning of inner surfaces, analyses of samples). In isoprene acetylene, BuOH plants, where the concn. of single toxic substances is not high, functional disturbances were observed in workers owing to the combined effect of ingredients. The highest concns. of toxic substances was in the pumping area. An important factor is corrosive substances which impair the hermeticity of the app. and sealings. Concrete, bricks, plaster walls, oil coatings, and other building materials in butadiene isoprene, α -methylstyrene, butadiene-methylstyrene, butadiene styrene, polybutadiene, and polyisoprene rubber plants adsorb many toxic substances. Benzene, isopropylbenzene, and α -methylstyrene were desorbed from building materials after many hrs. The plant atm. may be intensively polluted also by by-products, which may be more toxic than the final products. Acrolein vapors were detected in a high-pressure polyethylene plant. Toxic substances, in amts. exceeding permissible limits were found regularly on outside installations: hydrocarbons 10-520, ammonia 2-920, aldehydes 7-44, α -methylstyrene 2-56 and benzene 6-29 mg./m.³. The air in some plants involved in petrochem. synthesis was polluted to a height of 22 m.

St. Janderka

68692v Work condition and health status of plant personnel engaged in the production of epichlorohydrin. L. I. Pet'ko, E. Sh. Gronberg, L. N. Cheroval, and V. I. Filina (Inst. Ind. Hyg. Occupational Diseases, Gorki). *Gig. Tr. Prof. Zabol.* 10(11), 52-4(1966)(Russ). Examn. of chem. plants producing epichlorohydrin (I) showed higher than max. permissible concns. of I, HCl, and glycerol dichlorohydrin in the atm. Clin. examn. of 82 workers did not prove any specific pathol. changes.

Ivo Hynic

68693w Vision of workers engaged in the production of synthetic fatty acids and issues relative to setting hygienic standards for the alcohol content in the air. Yu. L. Egorov, G. A. Petropavlovskaya, E. O. Saksonova, and V. N. Ermakova. *Gig. Tr. Prof. Zabol.* 10(11), 33-8(1966)(Russ). Rabbits exposed to the effect of sprayed decyl alc. in a concn. approaching the max. permissible one (200 mg./m.³) and at 0.058 mg./l. demonstrated the presence of conjunctive keratitis, a decreased "b" wave on the electroretinogram, and lengthened retinocortical time. Degenerative alterations of the nerve cells in the brain, together with an intense proliferation of glia occurred in the optic nerve. Considering the effect of decyl alc. on the vision organs it is proposed to lower the max. permissible concn. to 10 mg./m.³ (0.01 mg./l.).

J. Pich

68694x Assessment of lead exposure in poly(vinyl chloride) manufacture and suggestions for control measures. V. Smolic (Zavod zastitu zdravlja, Split, Yugoslavia). *Arh. Hig. Rada Toksikol.* 17(3), 309-16(1966)(Croat). Pb concn. was studied in samples of air collected in 3 Yugoslav plants manufg. poly(vinyl chloride). The air was pumped through filter papers

streptomycin ascorbate, dihydrostreptomycin pantothenate, pasomycin, florimycin and kanamycin are presented. Complex compounds of dihydrostreptomycin with ascorbic, pantothenic or p-aminosalicylic acid are less toxic than streptomycin sulfate or dihydrostreptomycin. All above dihydrostreptomycin derivatives may be used in cases with side effects of streptomycin sulfate. Pasomycin is preferable since it combines 2 main antituberculous preparations (dihydrostreptomycin and PAS). Florimycin and kanamycin are more toxic than streptomycin sulfate or dihydrostreptomycin and their derivatives. These antibiotics should be limited by patients with progressive processes and streptomycin resistance. Florimycin and kanamycin are ototoxic and should be used only in stationary conditions with constant examination of hearing.--Authors.

† 30951. TAYLOR, T. G., K. M. L. MORRIS, and JEAN KIRKLEY. (Agr. Res. Coun. Poultry Res. Cent., Edinburgh, Scot., UK.) Effect of dietary excesses of vitamins A and D on some constituents of the blood of chicks. *BRIT J NUTR* 22(4): 713-721. 1968.--Groups of chicks were given diets containing 4 levels of vitamins A and D, 1, 10, 100 and 1000 times the basal level, in all 16 combinations, with the object of investigating a possible antagonism between the 2 vitamins. Only diets containing 1000 times the basal level (approx. 1700 times the dietary requirements) of 1 or both vitamins depressed growth and induced changes in the blood. The packed cell volume was substantially reduced from 4 wk of age in the chicks given the highest level of vitamin A. This was probably due to an effect of the vitamin on the fragility of the red cells and thus on their life span. Chicks given the toxic level of vitamin D showed an increase in plasma Ca and a decrease in plasma inorganic P. The highest level of vitamin A depressed plasma Ca without influencing plasma inorganic P. Increasing amounts of vitamin A given in combination with the highest level of vitamin D caused a progressive increase in the plasma inorganic P. The highest level of dietary vitamin A significantly increased the activity in the plasma of 3 lysosomal enzymes: acid phosphatase, β -glucuronidase and arylsulphatase. Excess vitamin D given in conjunction with the basal level of vitamin A significantly depressed the plasma acid phosphatase and the activity of this enzyme increased with increasing amounts of vitamin A. Excess vitamin D had no influence on the other hydrolases studied. A marked antagonism between the effects of excessive amounts of the 2 vitamins occurred only in respect of their actions on the plasma levels of Ca, inorganic P and acid phosphatase, all of which are involved in bone metabolism.--Authors.

30952. TUMARKIN, R. I. (N. F. Gamaleya Inst. Epidemiol. Microbiol., Acad. Med. Sci. USSR, Moscow, USSR.) K voprosu o mekhanizme toksicheskogo deystviya antibiotkov tetratsiklinovoi gruppy na pechen'. [Mechanism of the toxic effect of the tetracycline group of antibiotics on the liver.] *ANTIBIOTIKI* 13(7): 647-652. 1968. [Engl. sum.]--Chlortetracycline in high doses in rats increased histidine deaminase and urokinase activity. Oxytetracycline had a slight effect on histidine deaminase activity and suppressed urokinase activity. Tetracycline effect was similar to that of oxytetracycline. Chlortetracycline has a higher toxicity.--Author.

30953. TYUL'MANKOV, V. N., and B. K. LUGOVSKII. Sosudistye oslozheneniya pri lechenii psikhicheskii bol'nykh aminazinom. [Vascular complications during aminazine (chlorbromazine) treatment of mental patients.] *ZH NEUROPATOL PSIKHIAT IM S S KORSAKOVA* 68(1): 111-115. 1968. [Engl. sum.]--The main syndromes were cerebral hemorrhages and thrombotic vascular affections of vitally important organs. Aminazine probably increases coagulability. A thorough control (including laboratorial and tests) of old patients and patients with hypertensive disease must be made in the process of aminazine treatment.--From auth. sum.

† 30954. WEISS, HARVEY J. (Mt. Sinai Hosp., New York, N. Y., USA.), LOUIS M. ALEDORT, and SHAUL KOCHWA. The effect of salicylates on the hemostatic properties of platelets in man. *J CLIN INVEST* 47(9): 2169-2180. Illus. 1968.--Ingestion of 1.5 g of aspirin, but not of sodium salicylate, produced a significant prolongation of the bleeding time in 6 normal male subjects when compared with the effects of a placebo. Similar differences in the effect of the 2 drugs on platelets was also observed. Aspirin ingestion resulted in impaired platelet aggregation by connective tissue and was associated with a decreased release of platelet ADP; sodium salicylate had no effect on these values. In vitro, incubation of platelet-rich plasma with an optimum aspirin concentration of 0.045 mg/ml inhibited both the adhesion of platelets to connective tissue and the release of ADP as well as the 2ndary wave of platelet aggregation produced with ADP or epinephrine. Sodium salicylate had no effect on these reactions, which were also normal in patients with von Willebrand's disease. The inhibitory effect produced by ingesting a single 1.8 g dose of aspirin was detectable for 4-7 days at which time salicylate was no longer detectable in the blood, which suggested an irreversible effect on the platelet. Aspirin also inhibited the release of platelet ATP, but had no effect on the platelet surface charge, available platelet ATP or ADP, or the destruction of ADP by plasma ADPase. These studies support the hypothesis that ingestion of aspirin, in contrast

to sodium salicylate, prolongs the bleeding time by inhibiting the release of platelet ADP, perhaps reflecting the findings in other cell systems that aspirin alters membrane permeability.--Authors.

30955. ANONYMOUS. The kidney and oral calcium therapy. *ANN INTERN MED* 66(5): 1021-1022. 1967.--Though CaCO_3 is valuable as an antacid, severe and possibly irreversible injury to the kidney may occur from its prolonged use in conjunction with a high milk intake. Evidence of renal function disturbance may be shown by a rise in serum creatinine and renal N. During treatment with CaCO_3 a patient's serum Ca level should be watched for early signs of Ca nephropathy within the 1st 7 days of treatment.

INDUSTRIAL TOXICOLOGY

(See also "Pathology" under Respiratory System; "Environmental Health - Occupational Health," and "Radiation Health" under Public Health)

30956. GANDEVIA, BRYAN. (Div. Thorac. Med., Univ. N. S. W., Sydney, N. S. W., Aust.) Pulmonary function in asbestos workers: A three-year follow-up study. *AMER REV RESP DIS* 96(3): 426-427. Illus. 1967. [Span. and Fr. sum.]--Ventilatory capacity and ventilatory response to a standard exercise test were measured in a series of 41 male workers in a factory making asbestos products, and was repeated about 3 1/3 yr later. Twelve men left the industry during the interim. They had a significantly lower vital capacity after adjustment for age, and a significantly higher ventilatory requirement for exercise than those who remained in the industry. This pattern of functional abnormality contrasts with that found in subjects admitting to persistent cough and sputum, in whom a significant reduction was demonstrated in age-adjusted forced expiratory volume at 1 sec. In a control series, observed and predicted changes in pulmonary function over the observation period showed reasonable agreement. The asbestos workers showed a greater decrease in forced expiratory volume at 1 sec. than predicted, and possibly greater changes in vital capacity and ventilatory requirement for exercise. The trend toward functional abnormality is consistent with, although not indicative of, the development of asbestosis. Serial pulmonary function tests are likely to be more informative than serial roentgenograms.--From auth. sum.

30957. HARRIS, D. KENWIN, and W. G. F. ADAMS. Acro-osteolysis occurring in men engaged in the polymerization of vinyl chloride. *BRIT MED J* 5567: 712-714. Illus. 1967.--Two cases of acro-osteolysis occurring in men engaged in the polymerization of vinyl chloride are described. The bones affected were the terminal phalanges of the fingers and the sacroiliac joints, but in 1 case the patella and in the other the phalanges of the feet were involved. The condition was accompanied by Raynaud's phenomenon and skin lesions. This condition is probably a self-limiting disease.--Authors.

30958. SAMEDOV, I. G. O nespetsificheskikh proyavleniyakh deystviya uglevodorodov v malykh kontsentratsiyakh. [Nonspecific manifestations of low concentrations of hydrocarbons.] *AZERB MED ZH* 6: 56-61. 1967. From: REF ZH OTD VYP FARMAKOL KHMOTER SREDSTVA TOKSIKOL, 1968, No. 4,54,915. (Translation) --Workers were tested at a petroleum-processing plant where the concentration of hydrocarbon vapors did not exceed the maximum allowable (0.07-0.48 mg/l. Rabbits and guinea pigs were treated under various static regimes with the vapors of gasoline B-70 at 0.95-1.1 ml/l, 4 hr/day, 6 times/week for 4 mo. The workers and the animals showed a rise in the concentration of blood acetylcholine and epinephrine-like substances. Animals treated constantly and evenly with increasing hydrocarbon concentrations showed these tendencies, but they were less marked. Cholinesterase activity in the workers did not differ from that of controls, but it was reduced in treated animals, especially when the treatment was with fluctuating concentrations of hydrocarbons. Pseudocholinesterase activity did not change in either persons or animals. Daily urinary excretion of 17-ketosteroids by treated rabbits was of a phasic character: the elevated activity of the adrenocortical function was soon replaced by reduced activity. Only under the action of sharply fluctuating hydrocarbon concentrations was there a prolonged rise in 17-ketosteroid excretion. Maximum depression in the concentration of vitamins C and B₁ in the blood, urine, and organs was noted in animals treated with steadily and evenly increasing and also sharply fluctuating hydrocarbon concentrations. Changes in the electrolyte metabolism with low concentrations was insignificant. The principal changes with low hydrocarbon concentrations were in the functional condition of the autonomic and endocrine systems (changes in the metabolism of mediating substances and vitamins and in adrenocortical function). These changes are probably nonspecific and of a compensatory-adaptational nature. Over a certain period they may lead to persistent and even organic changes.

30959. SPAK, IVAR. (Dep. Surg., Lanslaasarettet, Hassleholm, Swed.) Finger injury caused by paint spray gun. *ACTA CHIR*





Occupational Acroosteolysis

Report of 31 Cases

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In 31 cases of acroosteolysis of the hands of workmen associated with vinyl chloride (CH_2CHCl) polymerization processes, the osteolysis was specific to the distal phalanges of hands and was frequently associated with Raynaud's symptoms. Affected personnel ranged in age from 26 to 47. The disorder is believed to have resulted from a combination of physical insult, chemical insult, and personal idiosyncrasy. The specific causes are unknown. The prevalence was found to be less than 3% among employees performing similar work. No cases were found in workmen using or processing the polymer or manufacturing commercial resins.

During mid-1964, several complaints came to our attention of soreness and tenderness of the fingertips of workmen in a manufacturing plant polymerizing vinyl chloride (CH_2CHCl). Comprehensive examinations of these individuals revealed nothing of significance except a "Raynaud-like phenomenon" of the hands, and in some cases, definite changes of the distal phalanges were apparent on roentgenograms of the hands. Since then we have observed additional cases of this unusual syndrome. It is the purpose of this manuscript to summarize our observations.

Description of Syndrome

To date we have observed 31 cases of hand disorders among 3,000 personnel involved in vinyl chloride manufacturing and polymerization. All have been men, between the ages of 26 and 47. We have not observed any ethnic or racial tendency for the syndrome. The great majority have been characterized by two common factors: symptoms likened to those ascribed to Raynaud's phenomenon and acroosteolysis of the distal phalanges. A few have had no symptoms but have the roentgenographic evidence of acroosteolysis. Several of the patients have external skin lesions on the dorsal surfaces of the hands and forearms, with a rope-like appearance resembling changes sometimes seen in sclero-

derma. Some have clubbing of the fingers. Only a few of the cases have sought medical attention because of symptomatic complaints; the majority have been found through x-ray examinations of the hands.

A summary of the physical findings of the observed cases is shown in Table 1, and a detailed description of the two predominantly common symptoms follows:

Raynaud's Phenomenon.—This symptom complex has occurred in varying degrees, with one or both hands involved. Generally, its effect is observed as marked discomfort on exposure to cold. None of the cases have exhibited vascular changes of the feet. A unilateral sympathectomy performed on one of the most seriously affected cases relieved most of the symptoms on that side. The acroosteolysis was not altered by the sympathectomy.

Roentgenological Changes.—The most unique characteristic of this syndrome is the unusual roentgenological findings. These are described as acroosteolysis and are illustrated in Fig 1. It may be present in all of the fingers and readily observable, or only in one finger and barely discernible, as illustrated in Fig 2. X-ray films of the feet, as well as those of the long bones and of the skull have been made in some of these cases, with no osteolysis found other than in the distal phalanges of the hands.

Acroosteolysis is a rare clinical entity, with only 72 cases of the familial type reported up to 1965, according to Cheney in his excellent review.¹ The diagnosis of acroosteolysis requires expert roentgenological technique and knowledge. It has been our observations that early cases of acroosteolysis will be missed by the roentgenologist not familiar with this condition. All of the cases on which we are reporting have been confirmed by at least two experienced roentgenologists working independently.

We established the following roentgenographic criteria for our diagnoses. These are the result of our having viewed several thousand x-ray films of the hand in our search for the cause of the syndrome.

1. General: Roentgenographically, acroosteolysis, as found in workers who are exposed to vinyl

From the Medical Division, B. F. Goodrich Co., Akron, Ohio. Reprint requests to 500 S Main St., Akron, Ohio 44318 (Dr. Wilson).

chloride and polyvinyl chloride manufacturing processes, is somewhat different from that found in familial osteoporosis with acroosteolysis and in familial osteosclerosis with acroosteolysis. In osteoporosis with acroosteolysis there may be compression fractures in the spine, and basilar impression of the skull, along with destruction of the midphalanges. None of these findings have been seen in these workers. The changes in the distal phalanges are similar in both conditions.

Osteosclerosis acroosteolysis observed by Andren et al¹ (University Hospital, Malmo, Sweden) in twins showed diffuse sclerosis, with cortical thickening of the shafts of the long bones and clubbing of the metaphyseal ends. The phalanges of the hands and metacarpals were foreshortened, and the distal phalanges showed acroosteolytic changes. The feet showed the same changes, except that the distal phalanges were not fragmented.

There has been no evident destruction in the mid or proximal phalanges of the thumbs or fingers of these individuals and no evidence of a lytic, destructive lesion in the feet.

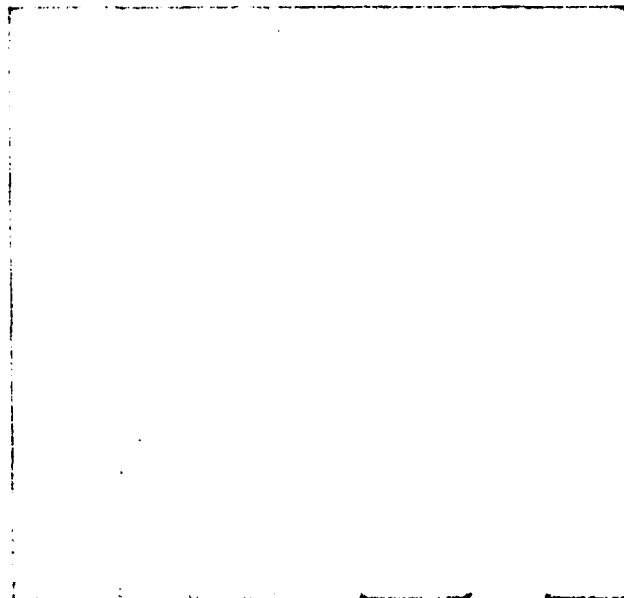
We have not observed any loss of calcium salt in the bones of the wrist and remaining bones of the hand and phalanges in any of these individuals, and there has been no evident sclerosis of the wrist and hand bones.

2. Mild stage: The earliest change found in acroosteolysis in these workers has been a loss of the cortex of one or more of the tufts of the distal phalanges, with no destruction of the tuft or shaft of the distal phalanx.

The next more advanced stage may be a small, half-moon cut in the cortex of the tuft of one or more

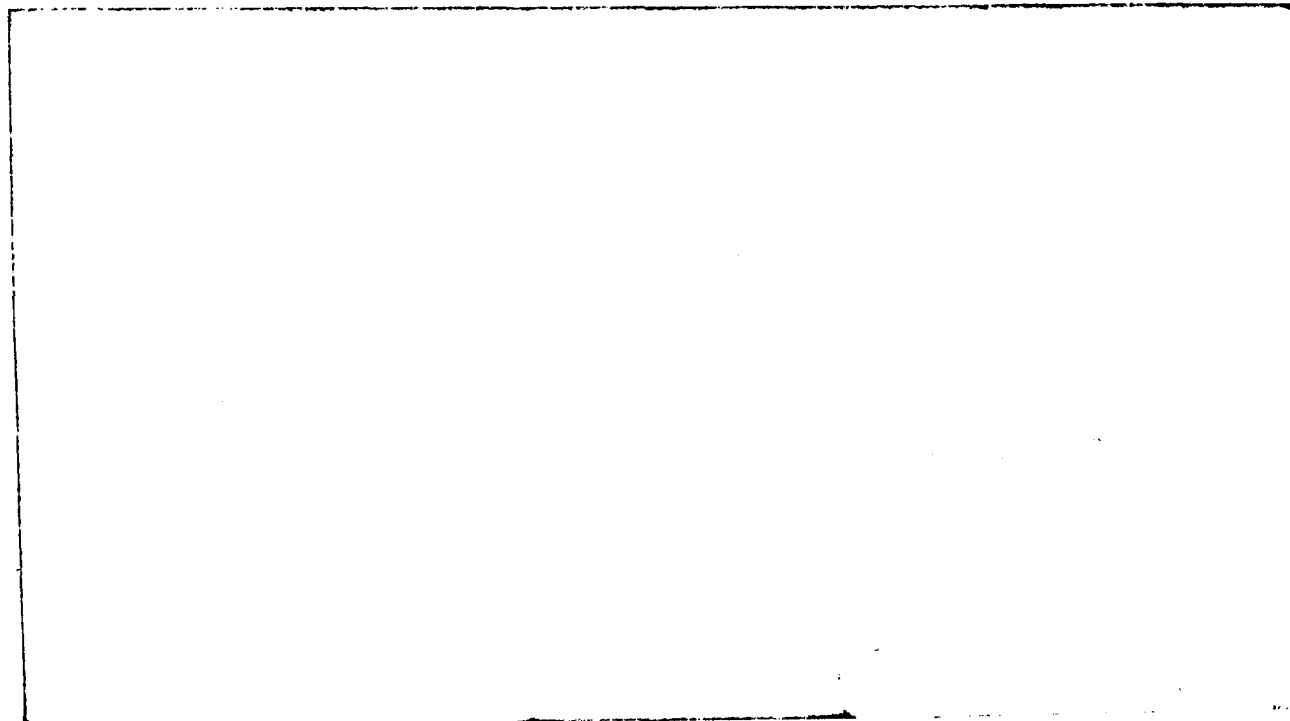
Table 1.—Summary of Symptoms and Findings

Symptoms	No. of Cases
Acroosteolysis without Raynaud's symptoms, one hand	4
Acroosteolysis without Raynaud's symptoms, both hands	5
Acroosteolysis with Raynaud's symptoms, one hand	5
Acroosteolysis with Raynaud's symptoms, both hands	17
Total	31
Clubbing of fingers	8
Skin nodules	8



2. Mild stage of acroosteolysis with half-moon defect of distal phalanx of mid finger.

1. Acroosteolysis with involvement of distal phalanges of all fingers.

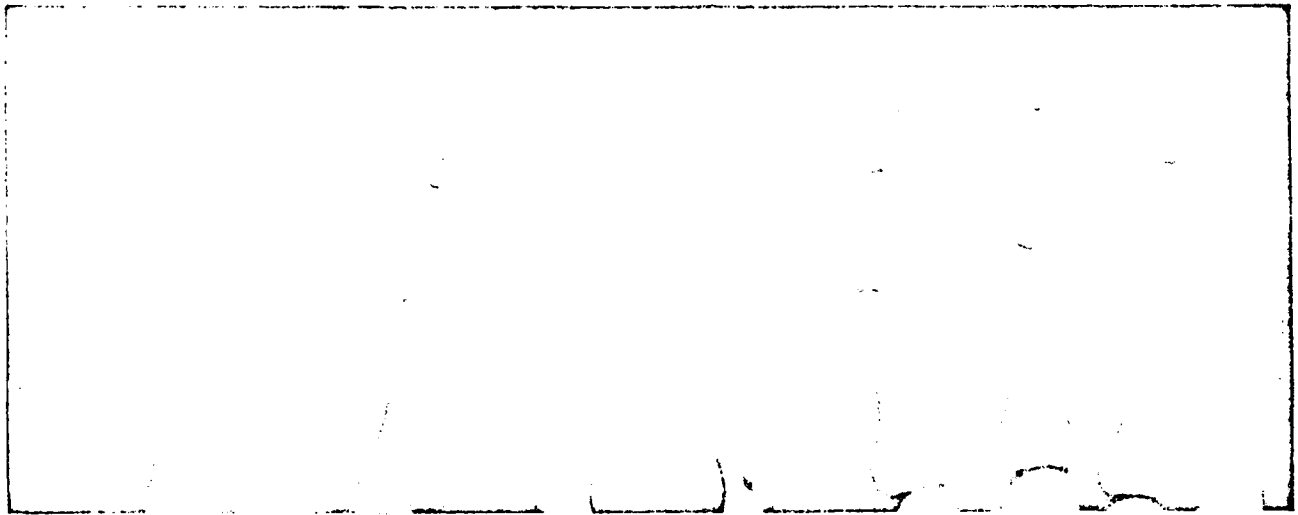


distal phalanges, or a so-called slice effect along one or more of the tufts. Figure 2 illustrates the small, half-moon cut in the cortex of the distal phalanx of the mid-finger.

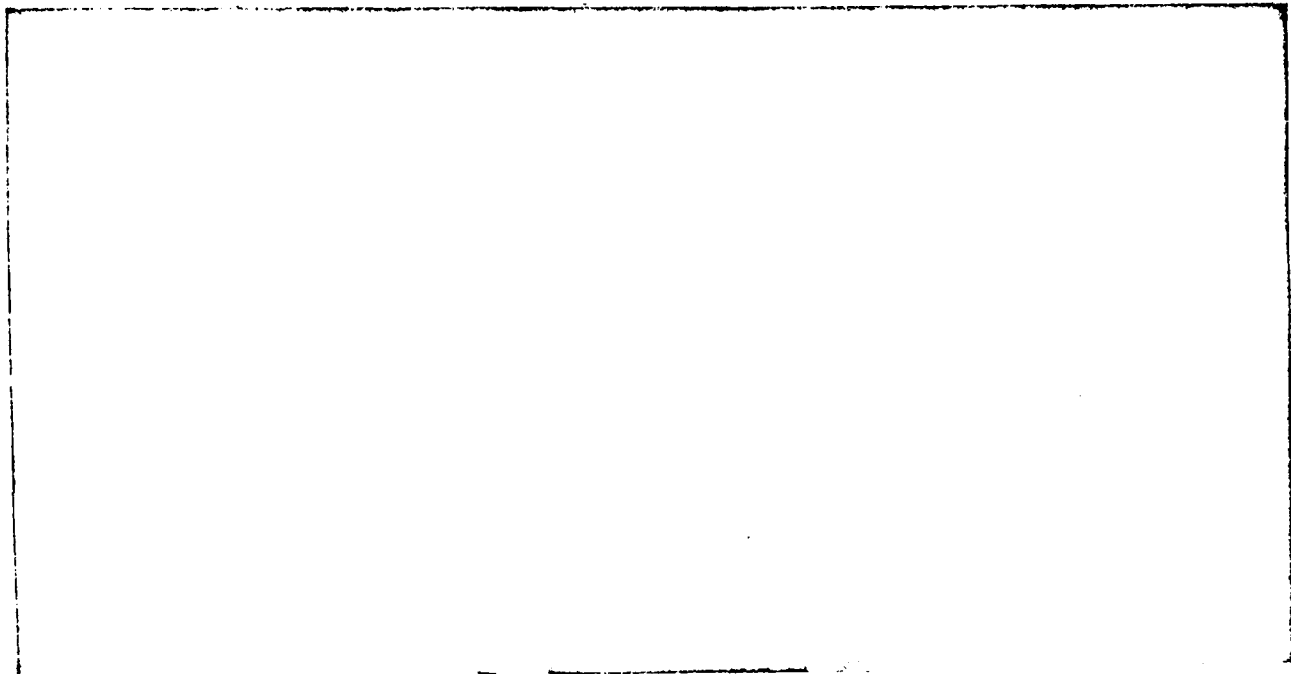
3. Advanced stage: A more severe lytic destruction may be a complete loss of the tuft and a portion of the shaft of one or more distal phalanges as illustrated in Fig 1 in which the tuft of the distal phalanx of the right thumb and the tuft of the distal phalanx of the left fifth finger are completely absent. Additionally, there may be in the same hand a portion of the distal rim of the tuft remaining, with loss of the proximal portion of the tuft and a portion of the shaft of the phalanx, which can also be identified in the remaining phalanges in Fig 1. This loss may be of a transverse nature through the

shaft and the tuft, or of an oblique type loss of bone structure.

4. Healing stage: In this phase, there is often definite fragmentation of the remaining tuft and of the filled-in area where the previous destruction was noted through the shaft of the distal phalanx. This may go on to a complete bony union or remain as a fibrous union with fragmentation. In Fig 3 and 4, x-ray films of the same individual well demonstrate this. This employee had almost complete reunion of the multiple fragments when first seen in November 1965 and again in November 1966 (Fig 3). In the latter, the completely healed shafts and tufts of the distal phalanges are indicated by no residual fragmentation with fibrous union. There is a definite shortening of the shaft and a widening of



3. Above, Acroosteolysis with marked fragmentation of distal phalanges in November 1965. Below, Same individual in November 1966.



the shaft and tuft, both in the transverse and the anteroposterior diameter. This is most likely due to a combination of constant pressure, and by the normal tension of the soft tissues, particularly the tendons to the distal phalanges.

Occupational Aspects of Syndrome

Based upon our observations of these 31 cases, it appears as if this syndrome may be of occupational origin and is somehow related to the process of vinyl chloride polymerization. Its specific cause is not presently known. We are performing extensive research in an effort to find the cause. Two other papers referring to the condition have appeared in the literature. The publication by Suciu et al¹² contains no specific information, and merely alludes to some hand problem. That of Cordier et al¹³ presents case histories with symptoms similar to many of the cases we describe. This syndrome differs from idiopathic and familial acroosteolysis in that only the hands are involved.

Vinyl Chloride Polymerization Process

Polyvinyl chloride is a widely used synthetic resin. It has been manufactured commercially for more than 30 years and is used in upholstery fabric, floor and wall tile, wire insulation, phonograph records, and many other commonly used commodities. For many of these uses, the resin $(CH_2CHCl)_n$ is mixed with other materials to achieve the desired physical characteristics. The hand syndrome occurs apparently only in those people exposed to vinyl chloride or to other chemicals used in the manufacturing process of the resin itself or both. In addition to our exami-

Age Group	Acroosteolysis Without Raynaud's Symptoms	Acroosteolysis With Raynaud's Symptoms
20-29	1	4
30-39	4	12
40-49	4	6

nations of 3,000 personnel performing vinyl chloride manufacturing and polymerization, we have examined more than 1,000 individuals who handle the finished resin or who process it into plastic products. *No cases of acroosteolysis have been found in these 1,000 persons.*

Basically, the manufacture of polyvinyl chloride consists of polymerizing vinyl chloride. The reaction is accomplished in closed containers (polymerizers) with suitable catalysts and emulsifiers.

Copolymers, formed by combining vinyl chloride with other monomers, create variations of the homopolymer. These are commercially produced. Following polymerization, the resin is washed, dried, and sold as a finely divided white powder.

The polymerization operations are carried out in closed processes and provide little opportunity for employee exposure. Following the completion of the polymerization reaction, periodic cleaning of the walls and agitator of the polymerizer is necessary. The frequency of this cleaning and its method varies with the type of material used in these vessels and with different manufacturers. The most common practice has been to accomplish the cleaning manually by using hand scraping techniques, with workers spending several hours each day on this job assignment. Personnel performing this job are commonly referred to as "polycleaners."

4. Left, Healed acroosteolysis with only minor roentgenographic changes. Right, Same individual one month after crushing injury to midfinger.

