

Occupational Acroosteolysis

Report of 31 Cases

Rex H. Wilson, MD, William E. McCormick, MS,
Carroll F. Tatum, MD, and John L. Creech, MD

R&S 028195

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 scleroderma.

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

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

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 al⁷ (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.

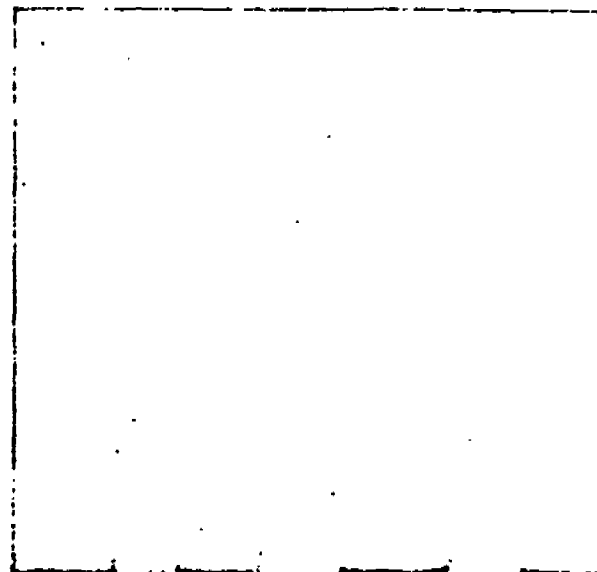
We have not observed any loss of calcium salt in the bones of the wrist and remaining bones of the hand and phalanges in any of these individuals, and there has been no evident sclerosis of the wrist and hand bones.

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

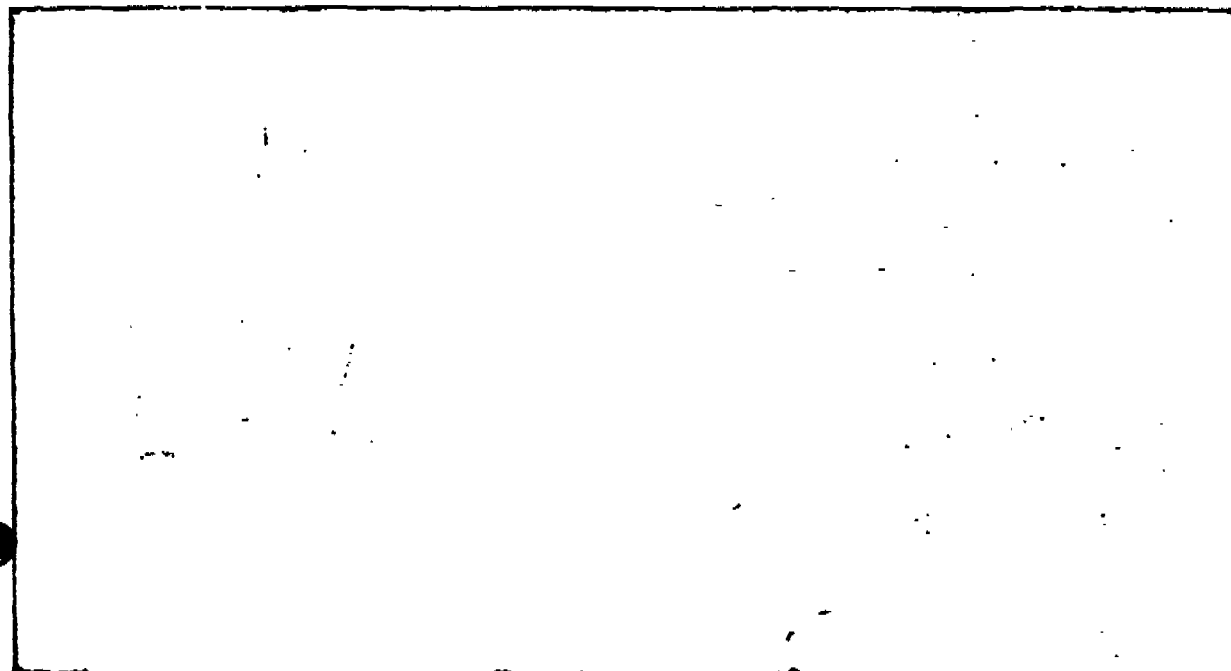
Table 1.—Summary of Symptoms and Findings

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.

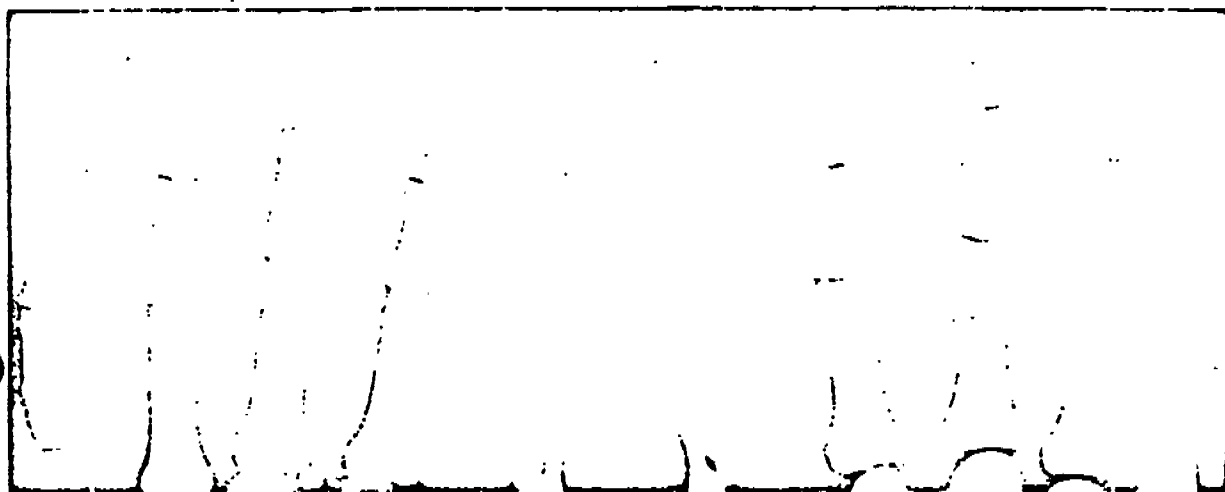


distal phalanges, or a so-called slice effect along one or more of the tufts. Figure 2 illustrates the small, half-moon cut in the cortex of the distal phalanx of the mid-finger.

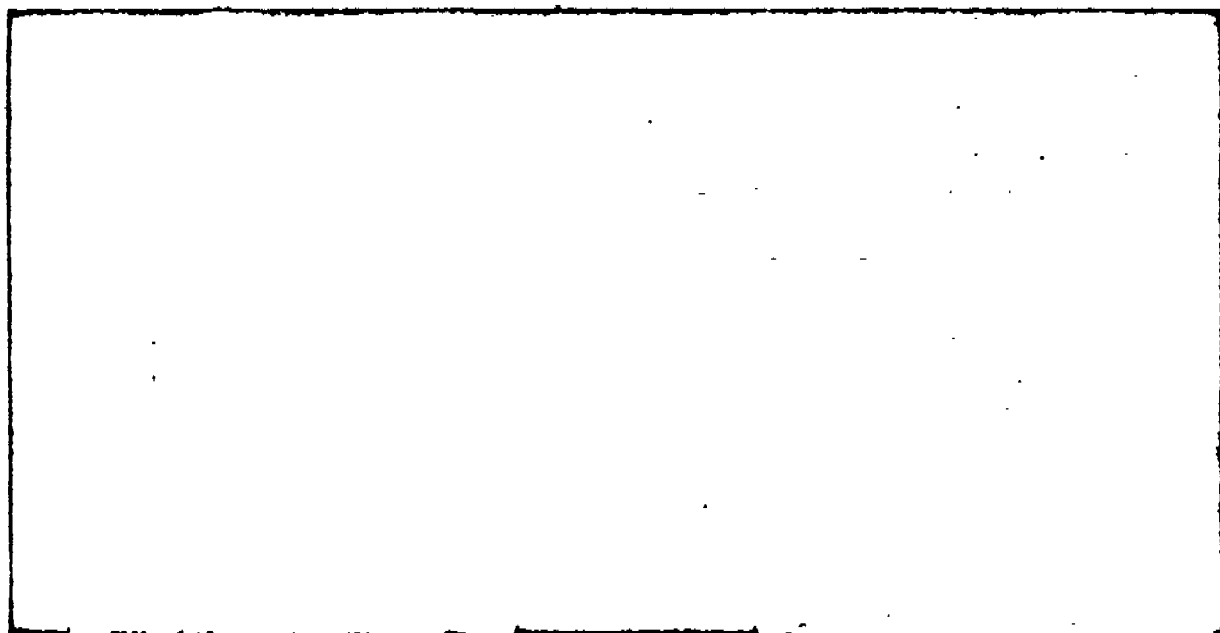
3. Advanced stage: A more severe lytic destruction may be a complete loss of the tuft and a portion of the shaft of one or more distal phalanges as illustrated in Fig 1 in which the tuft of the distal phalanx of the right thumb and the tuft of the distal phalanx of the left fifth finger are completely 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.



R&S 028197

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 Suci et al³ contains no specific information, and merely alludes to some hand problem. That of Cordier et al⁴ 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), 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-

Table 2.—Age Distribution of Cases

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

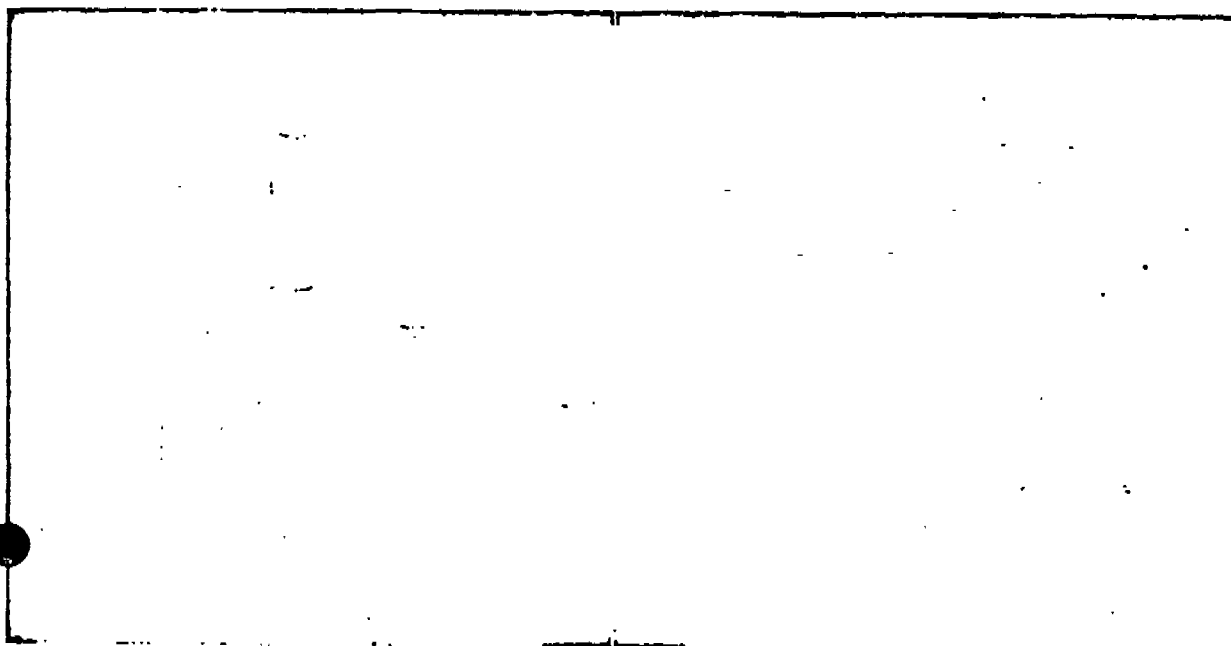
nations of 3,000 personnel performing vinyl chloride manufacturing and polymerization, we have examined more than 1,000 individuals who handle the finished resin or who process it into plastic products. *No cases of acroosteolysis have been found in these 1,000 persons.*

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.



Epidemiology

We have attempted to study the relationship of job history to the occurrence of the disease. Twenty-seven of our 31 cases have either been on the "polycleaner" job assignment at the time the syndrome appeared or have had that assignment at some time in the past. This job assignment is the only one showing any positive correlation with the occurrence of the syndrome.

Attack Rate.—The syndrome has a low attack rate. Our experience indicates it occurs only in less than 3% of all production employees who at one time have had polycleaning experience.

Age Distribution.—The youngest of our cases is 26 years old, and the oldest is 47; with the majority falling in the 30 to 39 age group. The complete distribution is shown in Table 2.

The appearance of the syndrome among younger employees may be influenced by the fact that the polycleaning job is one of the initial job assignments into which employees in such plants are hired.

Incubation Period.—If this syndrome is related to occupational factors, as we believe, then the time of exposure to these factors should be significant. We have investigated the time spent on polycleaning and, although accurate job-time assignment information is difficult to develop, it appears as if none of these cases has had less than 12 months polycleaning experience.

Comment

To our knowledge, this is a unique and, with the exception of references 3 and 4, previously unreported disorder. The specific cause is presently unknown, although it appears to be related to the manufacture of vinyl chloride and polyvinyl chloride. Not only are the x-ray findings of themselves unique, but when accompanied by the symptoms of Raynaud's phenomenon, the syndrome becomes extremely specific. As far as we are aware, this has not been an observed response to any toxicant in any of the animal species. We have attempted to arrive at an explanation of its cause, as well as the physiological mechanism whereby the extreme specificity for the distal phalanges of the hands occurs, but have been unsuccessful. We believe the condition is the result of three factors, all of which must be present for occurrence: (1) a chemical insult, (2) a physical insult, and (3) a personal idiosyncrasy. The chemical insult could occur from one or more of the monomers, catalysts, and intermediate reaction products existing in polymerizers. A low degree of exposure to these could occur from contact with the solid, slightly moist, residue in the polymerizer or to small quantities of vapor, absorbed either percutaneously or by inhalation. Research studies are in progress in an attempt to verify the chemical insult factor theory.

The physical insult is present in all "polyclean-

ers" to some degree through the prolonged hand scraping operations as well as the occasional use of hammers to remove the residues. In support of the physical insult factor, we have quite recently observed the effects of a finger injury to an existing case of this syndrome. Figure 4 (*left*) shows an x-ray film of the left hand of the first of these cases of acroosteolysis (accompanied by Raynaud's symptoms and skin nodules on the dorsal surfaces of the hands). The bone damage is quite limited. Figure 4 (*right*) shows the same hand with the roentgenogram taken four months after a crushing injury to the mid finger, with lysis having resulted to the tuft of the distal phalanx. We believe this activity was stimulated by the trauma.

Personal idiosyncrasy appears to be an important factor because of the low incidence of occurrence of the disorder. This is especially significant because, although all polycleaners are subjected to essentially similar chemical and physical insults, the incidence of this syndrome is very low, and the explanation for this can only be made on the basis of personal idiosyncrasy. We suspect pertinent factors here are related to the individual's vascular system, the nerves controlling the blood supply to the fingers, and to the specific type of collagen in the individual's hands. We are in the process of investigating these factors.

We have observed no serious disability in any of these cases. A few have been partially disabled because of hand soreness, to the extent that some restriction in manual activity was necessary. Improvement in the symptoms, as well as in the roentgenological findings, has occurred in many cases without adequate explanation.

We wish to emphasize that no cases have been found, after extensive search, in individuals either working with the finished polyvinyl chloride or its copolymers, or in processing the polymer into plastic products. In these processes, more exposure to the polymer occurs than does in the manufacturing of the polymers themselves.

We presently believe that personnel assigned to polycleaning should be evaluated, prior to assignment, for any evidence of collagen disease, osteolysis of the hands, or abnormal response of the hands to cold insult. Any evidence of the existence of any of these factors should contraindicate the assignment of an individual to "polycleaning," and thus remove, or at least minimize, the personal idiosyncrasy factor.

References

1. Cheney, W.D.: Acro-osteolysis. *Amer J Roentgen* 94:595-617 (July) 1965.
2. Andren, L., et al: Osteopetrosis Acroosteolytica: Syndrome of Osteopetrosis, Acroosteolysis and Open Sutures of Skull. *Acta Chir Scand* 124:490-507 (Dec) 1962.
3. Suciu, I.; Drejman, I.; and Valaskei, M.: Contributii Studiul Imolnavirilor Produse de Clorura de Vinil. *Med Intern* 15:967-978 (Aug) 1963.
4. Cordier, J.M., et al: Acroosteolysie et Lesions Cutanees Associees Chez Deux Ouvriers, Affectes au Nettoyage D'Antoclaves. *Cah Med Travail* 4: (Jan) 1966.

R&S 028200

wick, N.J.). *Can. J. Physiol. Pharmacol.* 1968, 46(4), 609-16 (Eng.). A series of expts. has shown that the mechanisms by which the metabolism of EtOH occurs are strongly influenced by the partial pressures of the O present in the aerating medium. For the most frequently used gas mixt., 95% O₂ + 5% CO₂, the EtOH consumption was abnormally large, and proportional to the concn. of EtOH in the perfusate. However, when the system was aerated with 18% O₂ + 5% CO₂ + 77% N₂, the consumption of EtOH was similar to that found in the intact rat. The perfusate concn. of Me₂CO, HOAc, pyruvic acid, and lactic acid was measured in all expts. When EtOH was consumed at these two different rates, increases in the lactic:pyruvic ratio and acetate levels of the perfusate were noted in both types of expts. However, the utilization of glucose by isolated perfused liver was inhibited, and acetone levels increased markedly, when EtOH was consumed at abnormally rapid rates, although no effect was noted in the perfusate levels of these metabolites when EtOH was consumed at normal rates. 27 references.

RCYD

50591p Action of beryllium ions on primary cultures of swine cells. Vegni Talluri, Maria; Guigiani, Viviana (Univ. Siena, Siena, Italy). *Caryologia* 1967, 20(4), 355-67 (Eng.). The effect of Be⁺⁺ poisoning on mitosis and morphology of swine kidney cell and lymphocyte cultures was studied. Treatment with Be⁺⁺ had a harmful effect on all the mitotic phases and abnormality of chromosomes was frequent. At high concns. the action of Be⁺⁺ was less pronounced on kidney cells than on lymphocytes. Be⁺⁺ exerts its toxic action by competition with Mg⁺⁺ either in the activation of DNA polymerase or in the binding of DNA to histones.

L. Miron

50592q Protective effect of ethyl alcohol towards allyl alcohol-induced hepatic lesions. Schwarzmann, V.; Infante, R.; Raisonier, A.; Caroli, J. (CHU Saint-Antoine, Paris, Fr.). *C. R. Soc. Biol.* 1967, 161(12), 2425-9 (Fr.). A 90-min. perfusion of isolated rat liver with blood contg. allyl alc. (0.018 ml./180 ml.) caused a release of lactic dehydrogenase, malic dehydrogenase, and glutamic-pyruvic transaminase into the perfusate and a simultaneous depletion of these enzymes from the liver; alc. dehydrogenase and glutamic dehydrogenase activities were not detected in the perfusate and were not decreased in the liver. Biliary secretion was irreversibly arrested after 18-20 min. of perfusion, and hepatic lesions occurred. A 20-min. perfusion with blood contg. EtOH prior to the treatment with allyl alc. prevented the enzyme release, the hepatic lesions and the effect on biliary secretion, and did not cause the release of alc. dehydrogenase or glutamic dehydrogenase activities. BPJF

50593r Effect of ethanol on hepatic metabolism and enzyme activities. Nelson, Patricia Ann (Indiana Univ., Bloomington, Indiana). 1967, 104 pp. (Eng.). Avail. Univ. Microfilms, Ann Arbor, Mich., Order No. 68-7228. From *Diss. Abstr. B* 1968, 28(11), 4688.

SNDC

50594s Energy-linked calcium transport in liver mitochondria during carbon tetrachloride intoxication. Carafoli, Ernesto; Tiozzo, Roberto (Univ. Modena, Modena, Italy). *Exp. Mol. Pathol.* 1968, 9(1), 131-40 (Eng.). In rats intoxicated by the gastric intubation of 0.5 ml. CCl₄/200 g., Ca⁺⁺ concn. in liver mitochondria increased ~10-fold within 18-20 hrs. However, i.p. injected ⁴⁵Ca was not taken up by hepatic mitochondria in intoxicated rats as rapidly as in normal animals. In vitro, hepatic mitochondria from CCl₄-intoxicated rats did not show increased Ca⁺⁺ uptake, but Ca⁺⁺ release induced by oxidative phosphorylation uncouplers was greatly decreased. This suggested that in CCl₄ intoxication, the balance between ADP phosphorylation and Ca⁺⁺ uptake is shifted in favor of the latter, thus contributing to the accumulation of Ca⁺⁺ in mitochondria. DDJN

50595t Protective effects of alpha-tocopherol on the hepatotoxicity of carbon tetrachloride: an electron microscope study. Meldolesi, Jacopo (Inst. Pharmacol., Univ. Milan, Milan, Italy). *Exp. Mol. Pathol.* 1968, 9(1), 141-7 (Eng.). The oral administration of 2.5 ml./kg. CCl₄ dild. 1:2 with liq. paraffin to rats produced severe hepatic lesions within 24 hrs. However, liver damage was markedly reduced in rats i.p. injected with the lipid antioxidant, α-tocopherol succinate (125 mg./kg.), before CCl₄ administration. This suggested that lipid peroxidn. is the primary mechanism of CCl₄ hepatotoxicity. 27 references. DDJN

50596u Distribution and toxicity of aliphatic hydrocarbons in body tissues. Shugaev, B. B. (Yaroslav. Med. Inst., Yaroslavl, USSR). *Farmakol. Toksikol.* 1968, 31(3), 360-3 (Russ.). Gas chromat. g. was used to study the distribution of 6 volatile hydrocarbons in the mouse and rat body tissues. The volatile hydrocarbon content of the brain and parenchymatous organs was similar, but the level in the fatty tissue was significantly higher than in the brain, liver, kidneys, or spleen. There was a parallel between the toxicity and effective cerebral concn. of isoprene, divinyl, and isobutylene, but not of butane, 2-methylpent-1-ene, or 2-methylpent-2-ene. The divinyl concn. was higher in the medulla oblongata than in the cerebellum or cerebral cortex. BJJR

50597v Some biochemical changes in animals following acute polyethylene polyamine poisoning. Solovinskaya, E. A. (Nauch.-

Issled. Inst. Onkol., Leningrad, USSR). *Farmakol. Toksikol.* 1968, 31(3), 364-5 (Russ.). Polyethylene polyamine (750 mg./kg.) administered s.c. to rats and mice increased the hepatic monoamine oxidase and histaminase activities, decreasing the tyramine and histamine levels in the blood and organs of the poisoned animals. The pathol. disturbances observed in mice and rats with acute polyethylene polyamine poisoning may be due to the increased oxidative decarboxination of endogenous amines with the consequent formation of aldehydes, NH₃, and H₂O₂. BJJR

50598w Effect of niacin on phagocytosis in chronic trinitrotoluene poisoning. Pidemskii, E. I.; Chukichev, E. M.; Mul'menko, A. M. (Perm. Univ., Perm, USSR). *Farmakol. Toksikol.* 1968, 31(3), 365-6 (Russ.). Trinitrotoluene (TNT) administered orally at 30 mg./kg. daily for 6 days to rats progressively decreased phagocytosis. Niacin administered simultaneously at 1 mg./kg. s.c. prevented this decrease and even increased the phagocytic activity of the leukocytes to 1.5-times the level in control rats. BJJR

50599x Pathogenic effect of chronic exposure to vinyl chloride on rabbits. Vazin, A. N.; Plokhova, E. I. (Inst. Gig. Tr. Profzabol., Gorki, USSR). *Farmakol. Toksikol.* 1968, 31(3), 369-72 (Russ.). In rabbits exposed to vinyl chloride (9-10 mg./l. air) for 4 hrs. daily for 5.5 months altered β-waves (frequency >80 Hz.) appeared on the electroencephalogram from the anterior hypothalamic nuclei, and the potentials of the anterior and posterior nuclei increased by 18-30 and 70-85%, resp., over control values. Concomitant changes in the cardiovascular system (bradycardia, arrhythmia, decreased voltage of the individual electrocardiogram peaks or whole complexes, decreased duration of systole, increased arterial pressure, and retarded blood flow) also occurred. The functional changes in the anterior and posterior hypothalamic nuclei may have a role in the pathogenesis of toxic angioneurosis due to vinyl chloride. BJJR

50600r Brown FK. III. Administration of high doses to rats and mice. Grasso, P.; Gaunt, I. F.; Hall, D. E.; Goldberg, L.; Batstone, Elizabeth (Brit. Ind. Biol. Res. Assoc., Carshalton, Engl.). *Food Cosmet. Toxicol.* 1968, 6(1), 1-11 (Eng.). Acute oral toxicity studies with Brown FK gave LD₅₀ values >2 g./kg. and 8 g./kg. in mice and rats, resp. The values for i.p. injection were 1.5-2 g./kg. in mice and 0.75-1.15 g./kg. in rats. When repeated daily oral doses ranging from 0.1 to 2 g./kg. were given to rats, a precipitous wt. loss and a vacuolar myopathy of the heart and skeletal muscles accompanied by lipofuscin formation occurred with doses of 0.5 g./kg. and over. At the highest dose employed (2 g./kg.), there was also hepatic centrilobular necrosis and renal tubular degeneration. Pretreatment with antibiotics reduced the incidence of muscle lesions. Repeated i.p. injection did not have any effect on the heart or skeletal muscle. Only 2 of the 6 components of Brown FK, 2,4-diamino-5-(p-sulphophenylazo)toluene (I) and 1,3-diamino-4-(p-methoxyphenylazo)benzene (II), produced muscle damage after repeated oral doses of 0.5 g./kg. Comparable doses of mixts. contg. the other components as well as I or II were considerably less toxic. After daily oral doses of 1 g./kg., muscle lesions were found in rats, rabbits, and guinea-pigs, but none were seen in mice or hamsters. The results suggest that the intestinal microflora is responsible for the breakdown of the components of Brown FK to toxic products. Variations between species and between animals of the same species may be due to qual. and quant. differences in the intestinal microbial population. RCNP

50601s Brown FK. IV. Cytopathic effects of Brown FK on cardiac and skeletal muscle in the rat. Grasso, P.; Mair, A.; Goldberg, L.; Batstone, Elizabeth (Brit. Ind. Biol. Res. Assoc., Carshalton, Engl.). *Food Cosmet. Toxicol.* 1968, 6(1), 13-24 (Eng.). Administration of 2 or 3 massive (1 g./kg.) oral doses of Brown FK to rats induced a myopathy in cardiac and skeletal muscles characterized by multiple vacuoles ~1-2 μ in diam. Ultrastructurally, these consisted of areas of fibrinolysis, affecting initially the A-band. Histochem., the myopathy was accompanied by a moderate increase in acid phosphatase activity and by a loss of phosphorylase activity. Subsequently, complete lysis of the affected fibers ensued. In the heart, lysis was followed by macrophage invasion and fibroblastic proliferation, and in skeletal muscle, by regeneration. The occurrence of lipofuscin in muscle fibers and in macrophages was scanty and erratic. When Brown FK was given in the diet at a level of 2%, fibrinolysis and an increase in the no. and electron d. of lysosomes was observed ultrastructurally during week 2-3 of the test. These changes were accompanied by a marked elevation of histochem. demonstrable acid phosphatase. Progressive deposition of lipofuscin was the principal pathological feature during week 3-12. Initial damage to the A- and I-bands in both cardiac and skeletal muscle distinguishes the Brown FK myopathy from that known to be produced by high doses of corticosteroids, thyroxine, chloroquine, or plasmocid, from ischemic damage and from muscle damage resulting from deprivation of K, Ca, or Mg. The lysosomal changes and accumulation of lipofuscin are suggestive of primary lysosomal damage which