



INTERNAL CORRESPONDENCE

CHEMICALS and PLASTICS

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To: Mr. Dean E. Richardson
Division:
Location: Texas City, Texas 77590

Date: August 20, 1969

Subject:

Copy to: Dr. C. W. McGary
Dr. A. B. Steele
Dr. C. U. Dernehl

Dear Mr. Richardson:

Your request for the "Implementation Section" arrived on 8-19-69. Without benefit of consultation with Dr. Dernehl, who is out of his office until September 8, we submit the enclosed Interpretation section. I trust it will be an adequate justification but I predict that the work will not be accomplished in one year nor for the amount of money named in the proposal. It will serve as a starting point, hopefully, to unravel a seemingly complex problem.

Very truly yours,


Charles P. Carpenter, Ph.D.
Administrative Fellow

CPC/ald

UCC 100716

① Jack Field
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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

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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 al² (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.

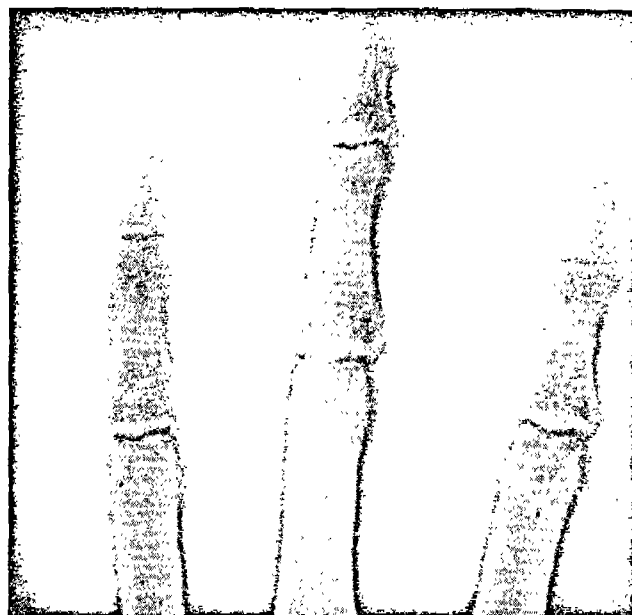
We have not observed any loss of calcium salt in the bones of the wrist and remaining bones of the hand and phalanges in any of these individuals, and there has been no evident sclerosis of the wrist and hand bones.

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

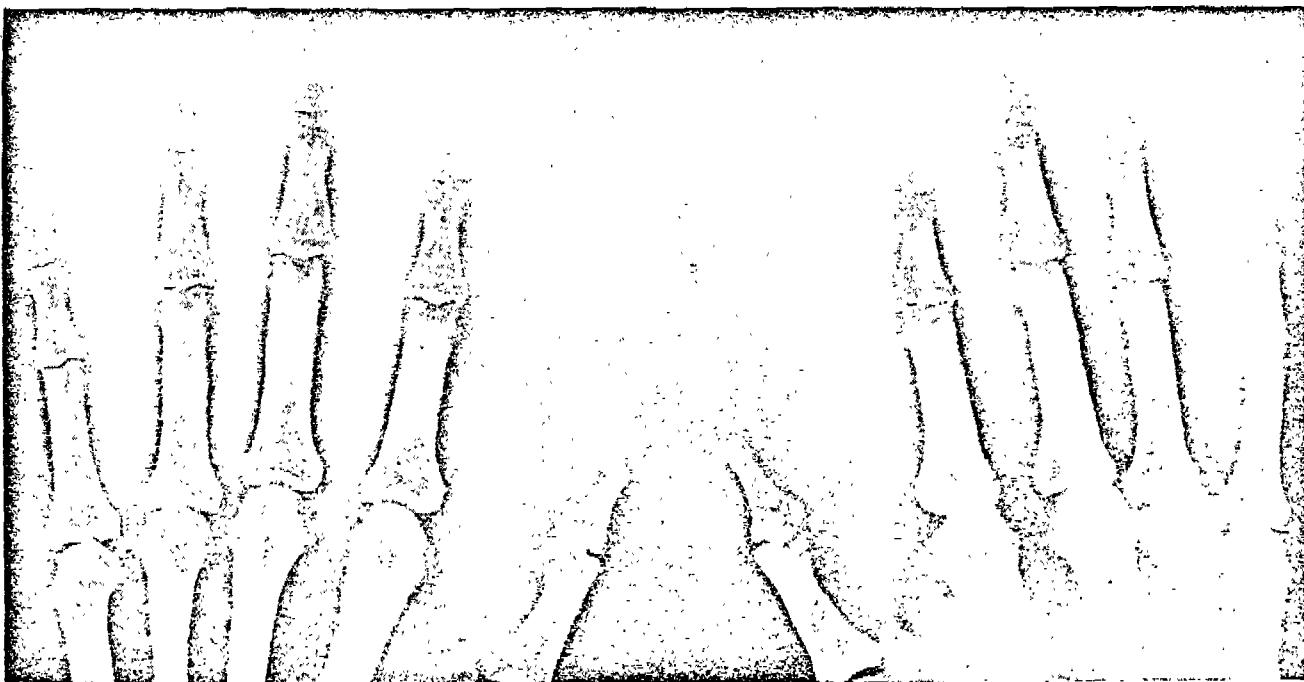
Table 1.—Summary of Symptoms and Findings

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.

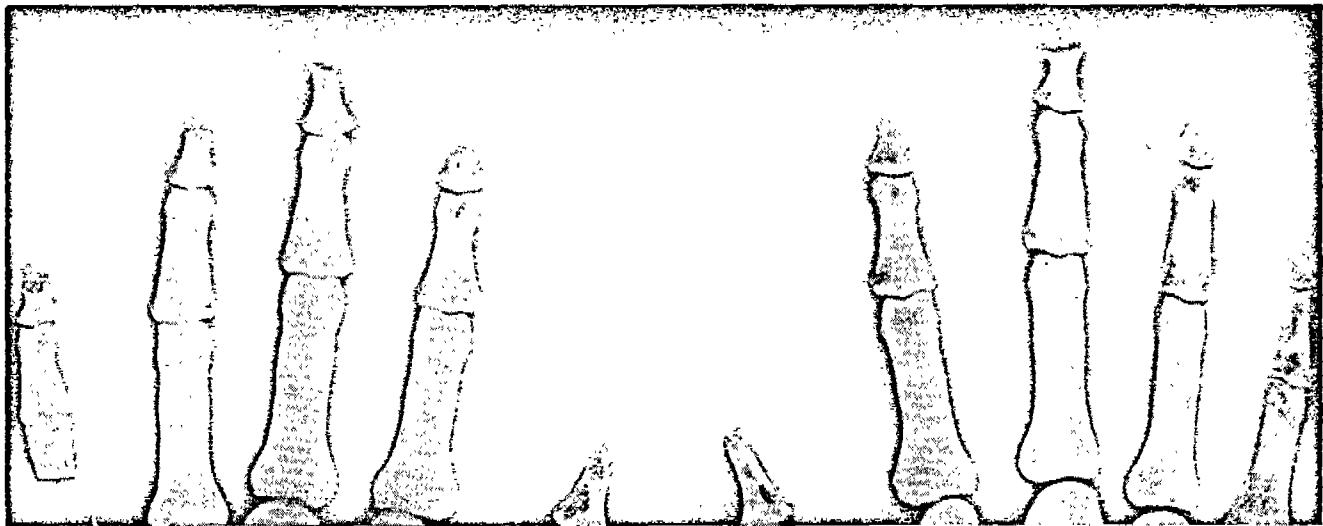


distal phalanges, or a so-called slice effect along one or more of the tufts. Figure 2 illustrates the small, half-moon cut in the cortex of the distal phalanx of the mid-finger.

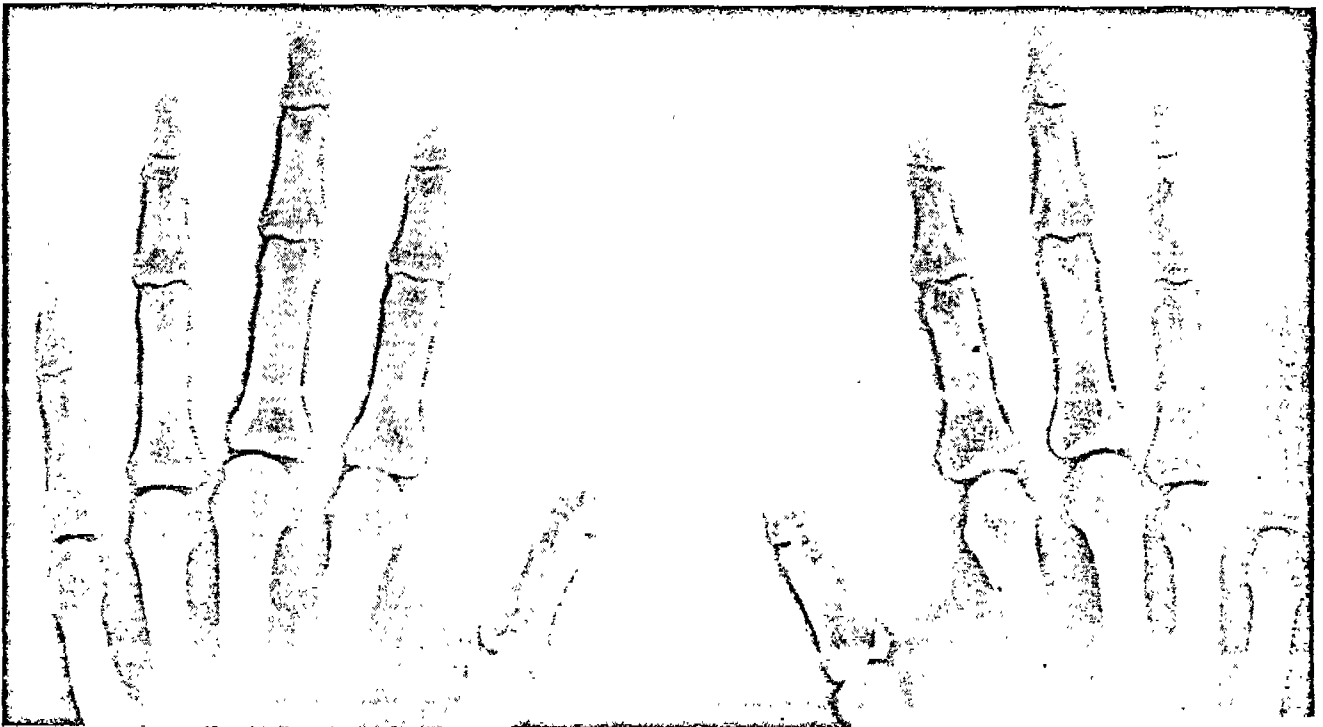
3. Advanced stage: A more severe lytic destruction may be a complete loss of the tuft and a portion of the shaft of one or more distal phalanges as illustrated in Fig 1 in which the tuft of the distal phalanx of the right thumb and the tuft of the distal phalanx of the left fifth finger are completely 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 Suciú 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 $(CH_2CHCl)_x$ 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

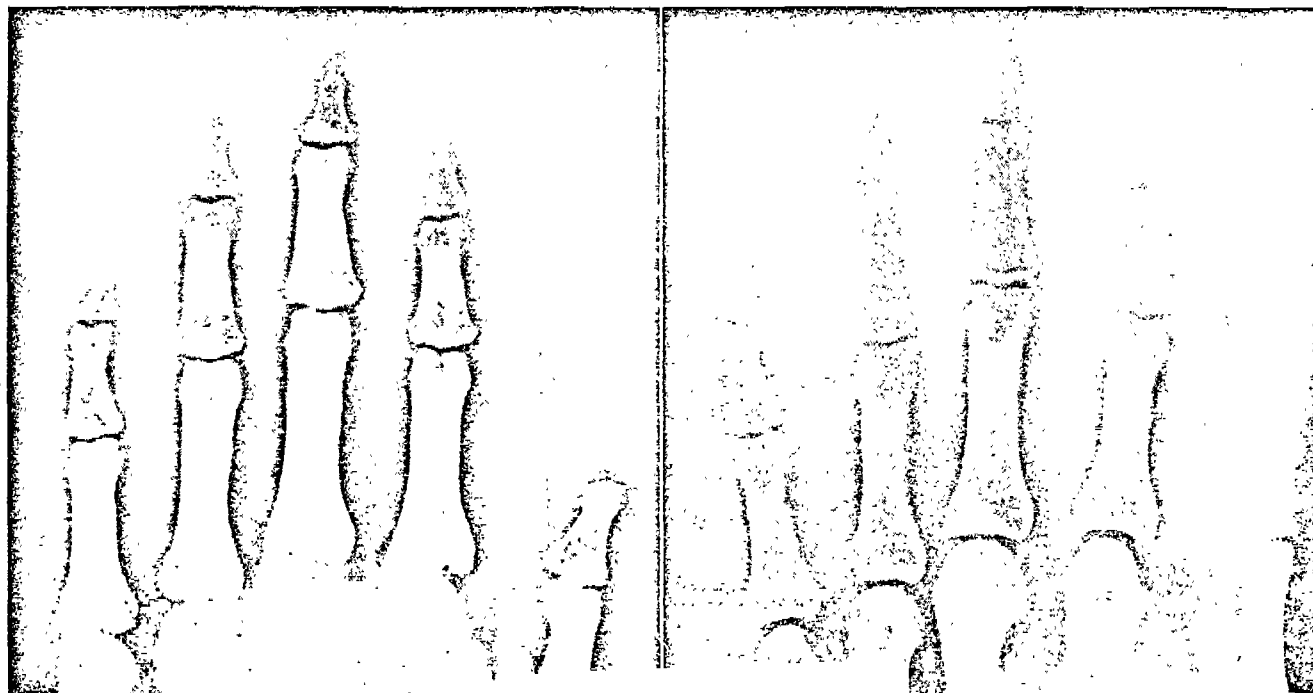
nations of 3,000 personnel performing vinyl chloride manufacturing and polymerization, we have examined more than 1,000 individuals who handle the finished resin or who process it into plastic products. *No cases of acroosteolysis have been found in these 1,000 persons.*

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.



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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* 124:496-507 (Dec) 1962.
3. Suciu, I.; Drejman, I.; and Valaskai, M.: Contributii Studiul Imolnavirilor Produse de Clorura de Vinil, *Med Intern* 15:967-978 (Aug) 1963.
4. Cordier, J.M., et al: Acroosteolyse et Lesions Cutanees Associees Chez Deux Ouvriers, Affectes au Nettoyage D'Antoclaves, *Cah Med Travail* 4: (Jan) 1966.