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Occupational Acroosteolysis

I. An Epidemiological Study

Bertram D. Dinman, MD; Warren A. Cook; Walter M. Whitehouse, MD; and
Harold J. Magnuson, MD, Ann Arbor, Mich; and Theodore Ditzsch, MD, Phoenix, Ariz

An epidemiological study was performed covering 5,911 employees with 21,810 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 (AOL) was 28; 16 other individuals were under suspicion. This condition is clearly associated with the hand clamping of polymers. Workers engaged in either 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.

WITH THE emergence of a new clinical entity, occupational acroosteolysis (AOL),¹ it became a manifest responsibility of the polyvinyl chloride (PVC) industry to define more clearly the character, extent, and possible causes of this disorder. Though individual corporations might survey their employees, a statistically valid construction of the problem could not be developed without collation of the health experience of all PVC producers. To maintain the privacy of pro-

pietary information associated with details of manufacture, some disinterested group was needed to evaluate operating processes, as these might relate to the causation of AOL. Accordingly, the Manufacturing Chemists' Association requested the Institute of Industrial Health (Institute of Environmental and Industrial Health as of Jan 1, 1970) to conduct an epidemiological survey of the PVC industry in the United States and Canada to meet their responsibility to the workers and the public.

The institute was requested to determine the extent of the problem among PVC workers. By establishing a specific job association with AOL, it was hoped to determine where the risk of incurring AOL arose within the PVC process. It was important to determine whether AOL was associated only with the synthesis stage or if those handling the finished polymer also might be affected.

The primacy of this consideration stems from the widespread use of the polymer in the fabrication of a multitude of manufactured goods that enter general commerce. While the number of workers engaged in the chemical synthesis of PVC is relatively small, there are thousands of small manufacturers engaged in the fabrication of products derived from this versatile plastic.

Further, it was hoped that the epidemiological and industrial hygiene² investigation might define more precisely how variations in manufacturing processes might relate to variations in the prevalence of AOL among PVC producers. Medical and industrial hygiene studies might furnish some clue to the precise etiological agent(s) as well as suggest preventive measures that might be applied in the industry.

In addition, it was planned that a small,

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From the Institute of Environmental and Industrial Health (Dr. Dinman), the Department of Environmental and Industrial Health, School of Public Health (Dr. Cook), the Department of Radiology, School of Medicine (Dr. Whitehouse), and the School of Public Health (Dr. Magnuson), University of Michigan, Ann Arbor, and the Department of Radiology, Good Samaritan Hospital, Phoenix, Ariz (Dr. Ditzsch).

Reprint requests to Institute of Environmental and Industrial Health, University of Michigan, Ann Arbor 48104 (Dr. Dinman).

NAME _____ Soc. Sec. No. _____ (8-13)

RACE W H Other _____ AGE _____ SEX M F
(14) (15-16) (17)

DEPT. NO. _____ (18-19)

COMPANY SERVICE DATE _____
Month Year
(20-21) (22-23)

Do Not Write in This Box

Corp. _____ (1-3)

Plant. _____ (3-4)

ARE YOU (RIGHT) (LEFT) HANDED?
(24)TO ANSWER THE FOLLOWING QUESTIONS, PUT A CIRCLE AROUND YOUR
ANSWER. FOR EXAMPLE: MONDAY IS THE DAY AFTER

SUNDAY (YES) (NO)

Have you noticed SUDDEN whiteness, blanching, or
paleness of the fingers of your RIGHT HAND (YES) (NO) 25
LEFT HAND (YES) (NO)Have you noticed a sudden redness or blueness of
the fingers of your RIGHT HAND (YES) (NO) 26
LEFT HAND (YES) (NO)IF YOU HAVE NOTICED ANY OF THE ABOVE,
are these changes brought on by (YES) (NO) (DON'T KNOW) 27
coldHAVE YOUR HANDS OR FINGERS BEEN BOTHERED
WITH ANY OF THE FOLLOWING:

Tingling or pins-and-needles feeling	RIGHT HAND (YES) (NO)	28
	LEFT HAND (YES) (NO)	
Warm feeling in hands or fingers	RIGHT HAND (YES) (NO)	29
	LEFT HAND (YES) (NO)	
Cold feeling in hands or fingers	RIGHT HAND (YES) (NO)	30
	LEFT HAND (YES) (NO)	
Numbness, fingers fall asleep	RIGHT HAND (YES) (NO)	31
	LEFT HAND (YES) (NO)	
Stiffness, fullness, or tightness of fingers	RIGHT HAND (YES) (NO)	32
	LEFT HAND (YES) (NO)	
Frequent tenderness, soreness, or pain at fingertips	RIGHT HAND (YES) (NO)	33
	LEFT HAND (YES) (NO)	

Thickening of the skin * (YES) (NO) 34
*If yes, is it on (HANDS) (WRISTS) (ARMS)

Whitish pimples * (YES) (NO) 34
*If yes, is it on (HANDS) (WRISTS) (ARMS)

Shiny skin patches *(YES) (NO) 37
 *If yes, is it on (HANDS) (WRISTS) (ARMS)

Small, raised areas, or lumps
less than 1/2 inch around * (YES) (NO) 38
(NOT including warts)
*If yes, is it on (HANDS) (WRISTS) (ARMS)

Pits or scars of the fingernails	(YES) (NO)	39
Ridges or cracking of the fingernails	(YES) (NO)	40

(DAILY) (ONCE A WEEK) (LESS THAN ONCE A WEEK) (NEVER) 41

If yes, was it the	(RIGHT)	or	(LEFT)	hand?	
Which finger was injured	(Thumb)		(Thumb)		
	(Index)		(Index)		
	(Middle)		(Middle)		43
	(Ring)		(Ring)		
	(Little)		(Little)		

selected sample of workers affected with AOL be studied in the clinical research unit of the University of Michigan Medical Center.² Previously, Rousch and co-workers¹ performed an extensive clinical evaluation of a group of such workers. Subsequent examinations have been designed to determine whether any new clinical features had developed since those prior studies.

Polyvinyl Chloride Manufacturing: A Brief Review

A more definitive description of the process whereby PVC is synthesized, finished, and compounded is reported elsewhere in this issue.³ A brief review of the operation is appropriate to the premises underlying the epidemiological considerations.

Vinyl chloride (VC), together with water, peroxide catalysts, and other additives, are placed in a reactor where polymerization is completed after ten to 16 hours. Unreacted VC is exhausted from the reaction vessel and the suspension or emulsion of the plastic transferred to equipment for dewatering and drying. Following ventilation of the reactor, one or two workers enter the vessel to remove the residues from its surfaces, using putty knives or chisels.

Sixteen plants, in addition to synthesizing, also compound PVC while five plants are engaged only in compounding the resin.

Methods

Survey Techniques.—Nineteen corporations known to be engaged in the polymerization of VC were assessed. The workers who served as the study populations were employed in 32 plants in the United States and Canada. All employees who worked at the time of the survey, or in the past, in any capacity in plants manufacturing VC, PVC, or in compounding such resin were surveyed. In multiple-product plants, all workers having any possible exposure to the PVC process were studied. This population underwent medical survey, work history questionnaire, and hand x-ray filming.

The self-completion medical questionnaire was designed to probe for signs of Raynaud's phenomenon or symptoms associated with peripheral vascular insufficiency. In addition, questions were posed to disclose skin or dermal appendage abnormalities, use of power tools, and hand-injury history.

X-ray films of both hands were requested from the cooperating plants; specific directions

concerning film type, exposure factors, technique, and identification were sent to each plant. The x-ray films, when forwarded to the institute, were coded and transmitted without identification to two radiologists for independent interpretation. The findings were recorded on a specifically designed checklist which was then returned for statistical collation. Hand x-ray films that served as controls were drawn from 2,697 men over age 18; this represented the entire male population of the town of Tecumseh, Mich.

Work history questionnaires were completed by each individual employee or by the personnel department at each plant or both. These forms recorded work assignments between Jan 1, 1961, through Dec 31, 1966; each worker noted the first and last month of assignment for each specific assignment during that period. At each plant, a team of investigators converted local job designations to standard job titles. These are listed in the paper on the industrial hygiene aspects.³

Pilot Run

In order to determine the reliability of survey techniques and recording methodological patterns, a pilot run was carried out at one large plant. Following this, minor modification of procedures and forms was accomplished.

Epidemiological Design.—Acroosteolysis appeared to consist of characteristic x-ray film abnormalities and Raynaud's phenomenon. Since the latter would be expected to occur only infrequently in a population not at risk of developing AOL, it could be used as a prime indicator of the existence of AOL. Thus, we hoped to establish an initial distinction between two populations, ie, one having AOL and the other not having it.

Comparison of prevalence of defects with the Tecumseh control population of 2,697 men suggested that all defects occurred in the PVC population with a greater frequency than in the control population (Table 1). However, the significance of this finding was clouded by an unavoidable bias which minimized the value of the Tecumseh population as a control group, ie, identification marks which could not be readily obliterated were present on these control films.

Furthermore, as is apparent from previous discussions of the x-ray film abnormalities, linear radiolucent defects could be confused with old trauma, the absence of a tuft might

follow amputation, or shortened phalanges could be consistent with a congenital defect. Defects such as sclerosis of the shafts, widening of the tufts, and soft-tissue clubbing were each susceptible to subjective reader error. Furthermore, each of these defects could arise from other bony disease or injury. Even multiple finger involvement could be consistent with these etiological possibilities. Because these problems did exist, significant divergencies in x-ray film interpretations were found (Table 2).

Because of these complications, for the purposes of first appraisal, marginal defects of the phalangeal tuft (defect 1) were not considered as indicative of AOL unless both roentgenologists independently concurred as to the presence of this abnormality. The existence of marginal defects with residual fragment(s) (defect 2), transverse defects (defect 3), transverse defect with distal fragmentation (defect 4), and total resorption of distal portion of phalanx (defect 5) were considered as possibly diagnostic of the bony defect of AOL if found by only one radiologist and if other causes for these defects could not be eliminated. Every man with any of these five aberrations was followed up subsequent to the field survey. If there was a history of trauma involving the involved finger or if the appearance of these x-ray film lesions was clearly consistent with trauma, these individuals were eliminated from suspicion.

Other x-ray film defects of an even less specific nature are known to be associated with the later stages of AOL but are not in themselves considered diagnostic. These x-ray film findings included sclerosis of the phalanges (defect 7), widening of the tuft (defect 8) or of the shaft (defect 9), and soft-tissue clubbing (defect 10). Finally, we looked with suspicion upon any bony defects involving multiple fingers regardless of whether they were AOL-specific (i.e., defects 2 to 5).

In addition to these defects previously

Table 1.—Prevalence of X-Ray Film Defects in Control and PVC Populations

		Control, N = 2,407		PVC Population, N = 5,011	
	Defect No.	No.	%	No.	%
Marginal defect	1	44	1.83	321	6.41
Marginal defect, with residual fragment	2	5	0.21	36	0.70
Transverse defect	3	6	0.25	40	0.80
Transverse defect, with distal fragmentation	4	0	---	21	0.42
Total resorption of distal portion phalanx	5	2	0.08	9	0.18
Sclerosis, with resorption	6	1	0.04	18	0.36
Shortening	7	11	0.46	69	1.38
Widening of tuft	8	4	0.17	48	0.96
Widening of shaft	9	1	0.04	7	0.14
Soft-tissue clubbing	10	2	0.08	40	0.80
Total	86	76	3.16	594	11.87

reported to occur in conjunction with AOL, those x-ray film abnormalities unrelated to AOL were grouped as defect 11.

Combining the x-ray film findings and Raynaud's, several diagnostic criteria were set up (Table 3). The diagnostic criteria for category 0 consisted of essentially normal workers while category 1 included individuals having x-ray film abnormalities which by history or radiographic evaluation or both were found to be consistent with old trauma, disease other than AOL, congenital or familial defects, etc. The history of persons in diagnostic category 3 disclosed cold-induced finger blanching unassociated with x-ray film abnormalities, clearly meeting our criteria for AOL. Category 4 consisted of persons without Raynaud's phenomenon and suggestive, though not diagnostic, x-ray films for AOL. Category 5 included those with classical AOL x-ray film defects (2 to 5 and 1, 6, and 7 without and with concurrence, respectively) and Raynaud's phenomenon. Category 6 had typical AOL bone abnormalities (as diagnosed in category 5) but without Raynaud-positive replies to the medical questionnaire.

Computational and Statistical Analysis.—Medical and work questionnaires and x-ray film reports were checked for completeness. They were then coded, verified, punched, and stored in an electronic computer. Quality control checking of the punch cards, using a 25% sample, revealed an error of 0.1% among these cards.

Table 2.—Agreement and Number of Fingers Showing X-Ray Film Defects in 1,302* PVC Workers

Defect No.		No. of Fingers Involved										Negative for Specific Defect	% Agree
		1	2	3	4	5	6	7	8	9	10		
Marginal defect	1	Agree	20	3	0	1	0	0	0	—	—	34	981
		Disagree	237	30	11	4	3	1	1	—	—	287	
		Total	257	33	11	5	3	1	1	—	—	321	
Marginal defect, with residual fragment	2	Agree	6	1	—	—	—	—	—	—	—	7	1,267
		Disagree	27	1	—	—	—	—	—	—	—	28	
		Total	33	2	—	—	—	—	—	—	—	35	
Transverse defect	3	Agree	9	0	—	2	0	0	—	—	1	12	1,298
		Disagree	26	1	—	0	1	1	—	—	0	29	
		Total	34	1	—	2	1	1	—	—	1	41	
Transverse defect, with distal fragmentation	4	Agree	1	—	1	—	—	—	—	—	—	2	1,298
		Disagree	17	—	1	—	—	—	—	—	—	18	
		Total	18	—	1	—	—	—	—	—	—	20	
Total resorption of distal portion phalanx	5	Agree	2	1	—	—	—	—	—	—	—	3	1,298
		Disagree	5	1	—	—	—	—	—	—	—	6	
		Total	7	2	—	—	—	—	—	—	—	9	
Sclerosis, with resorption	6	Agree	0	1	0	1	—	0	—	—	—	2	1,267
		Disagree	9	1	2	0	—	1	—	—	—	13	
		Total	9	2	2	1	—	1	—	—	—	15	
Shortening	7	Agree	6	2	1	0	—	1	—	1	1	12	1,236
		Disagree	30	6	1	1	—	1	—	2	1	42	
		Total	36	8	2	1	—	2	—	3	2	54	
Shortening	7	Agree	6	2	1	0	—	1	—	1	1	12	1,236
		Disagree	30	6	1	1	—	1	—	2	1	42	
		Total	36	8	2	1	—	2	—	3	2	54	
Widening of tuft	8	Agree	0	1	—	—	—	0	—	0	—	1	1,236
		Disagree	30	3	—	—	—	2	—	2	—	35	
		Total	30	4	—	—	—	2	—	2	—	36	
Widening of shaft	9	Agree	0	0	—	0	0	0	—	—	—	0	1,236
		Disagree	3	1	—	1	1	1	—	—	—	7	
		Total	3	1	—	1	1	1	—	—	—	7	
Soft-tissue clubbing	10	Agree	3	0	—	0	0	0	—	1	—	4	1,298
		Disagree	36	1	—	2	2	1	2	—	1	43	
		Total	39	1	—	2	2	1	2	—	1	47	
Totals		Agree	57	9	2	4	0	2	0	1	2	75	986*
		Disagree	429	46	10	6	7	3	4	2	1	517	
		Total	486	54	12	10	7	3	4	3	3	592	

* The difference between these two figures and those in the defect 11 category, ie, other defects, is not shown here.

Frequently, workers performed several different duties during a period spent on one assignment. Where this existed, an estimate was made at each plant of the fraction of time spent in each segment of the job assignment. Since the fraction 1/12 was used for each month a worker spent full time in various jobs during the year, it was convenient to use this fraction of 1/12 where his daily or weekly work was divided between two or more jobs. Thus, if a worker spent one half his time performing one specific component of his assignment, the value of 6/12 was assigned to our standard job title for that time period on assignment. The remaining 50%, or 6/12, of his time was distributed over one or more applicable job components during the period of assignment. By this method, job experi-

ence on each of the standard jobs could be computed in terms of months or fractions thereof.

The computer was utilized to perform collation and statistical manipulations of data.

Clinical Evaluation of Positive Cases.—Four employees with active disease were admitted to the Clinical Research Unit of the University of Michigan Medical Center. Extensive clinical, laboratory, and physiological tests and radiographic, isotopic, nutritional, and metabolic balance studies were performed. The findings are reported in detail.²

Results

General Population Statistics.—The study population consisted of 5,011 workers, of

which 98.4% were men; 95.7% were white, 4.1% Negro, and 0.2% other. The mean age was 35.8 years, with the median and modal range being 35 to 39 years. These workers were employed by 19 corporations at 32 plants in the United States and Canada; of the 32 plants, all but six were engaged in PVC synthesis. This number of plants represented 92% of the PVC synthesis industry in this country. The population at risk represented a total of 21,510 man years.

Population Analysis.—In order to construct several population groups for attribute comparisons, we applied our diagnostic criteria for AOL (i.e., x-ray film defects 2 to 5 plus Raynaud's phenomenon). Using this approach, we found that the clearly defined cases of AOL were limited to seven plants. Using these same diagnostic criteria (Table 3), we detected another group of 21 plants which had all employees in category 0 and 1, or less than a total of two individuals in diagnostic category 3 (Raynaud's without bone change) or diagnostic category 4 ("AOL questionable" x-ray film without Raynaud's) or both. To determine whether there was a risk of developing AOL among those working with the finished polymer, we extracted for further analysis a third population group, constituted by the five plants whose employees worked exclusively with the finished PVC-producing consumer products. These three groupings left three individual plants in which there remained a question of AOL's existence. The distribution of diagnostic categories among these four populations appears in Table 4.

The reason for requiring the coexistence of x-ray film abnormality and Raynaud's phenomenon to establish the diagnosis of AOL becomes apparent upon consideration of the three individuals in diagnostic category 5 (i.e., x-ray films characteristic of AOL

Table 3.—Roentgenographic and Symptomatic Criteria for Diagnostic Categories 0 to 6

Diagnostic Category	Raynaud's Phenomenon	Hand X-Ray: Abnormal, Consistent With AOL	Specific X-Ray Defect, Consistent With AOL									
			1	2	3	4	5	6	7	8	9	10
0	—	—	—	—	—	—	—	—	—	—	—	—
1	—	±*	—	—	—	—	—	—	—	—	—	—
3	+	±	—	—	—	—	—	—	±	±	±	±
4	—	±	—	—	—	—	±	±	±	±	±	±
5	+	+	+	+	+	+	+	+	+	+	+	+
6	—	+	+	+	+	+	+	+	+	+	+	+

* Indicates only those lesions that may be seen in AOL (defects 8 to 11 though not diagnostic of AOL).

† Single finger involved, no concurrence between readers.

‡ No concurrence between readers.

Table 4.—Distribution of Diagnostic Categories Among Four Subpopulations With PVC Study Group

	Total Population	Diagnostic Categories				
		0-1	3*	4†	5‡	6§
7 plants with cases of AOL	1,673	1,598	41	9	22	3
3 plants with questionable AOL	910	893	14	3	0	0
17 plants without AOL	1,873	1,861	17	3	0	0
5 plants compounding only	567	554	2	1	0	0
Totals	5,013	4,896	74	16	22	3

* Raynaud's phenomenon only.

† Questionable x-ray, no Raynaud's phenomenon.

‡ X-rays characteristic of AOL, with Raynaud's phenomenon.

§ X-rays characteristic of AOL, without Raynaud's phenomenon at time of survey.

but without Raynaud's phenomenon at time of survey). We determined by follow-up that of these three workers, two had manifested Raynaud's phenomenon during the 1960's prior to any preexposure. The third subject was re-x-rayed subsequent to the survey and demonstrated progressive changes characteristic of AOL; however, he has never noted Raynaud's disorder. In view of this finding that 24 of 25 workers with severe AOL-type x-ray film defects had associated Raynaud's phenomenon, we believe it is appropriate to link these two aberrations in order definitively to diagnose AOL. Thus, using as our criteria Raynaud's phenomenon or finger defects qualified as above or both, 25 men were found to have clearly established cases of AOL.

Intrapopulation Differences

Signs and Symptoms.—We determined the number of workers in each of the four

Table 5.—Intergroup Prevalence of Reynaud's Phenomenon Not Associated With AOL (Corrected for Male Populations Only)

	Diagnostic Category 3 Alone		Diagnostic Categories 1-2	Total
	No.	% Male Population		
Plants with cases of AOL	41	2.50	1,562	1,623
Plants without cases of AOL	19	0.82	2,294	2,313
Plants with questionable cases of AOL	14	1.70	817	831
Plants compounding only	1	0.22	438	439

Table 6.—Abnormal Number of Cases of Reynaud's Phenomenon Occurring in Various Size PVC-Plant Populations*

Population Range	Abnormal No. of Reynaud's Phenomenon
25-44	3 or more†
45-82	4 or more
83-120	5 or more
121-180	6 or more
181-220	7 or more
221-280	8 or more
281-340	9 or more
341-400	10 or more
401-460	11 or more
461-500	12 or more

* $P = 0.01$.

† Reynaud's, as defined, is cold, white fingers brought on by hand or body chilling or both.

plant groups having one, two, three, etc., through 20 positive responses to questions concerning signs and symptoms. A graphical representation of the frequency with which respondents noted bilateral hand symptoms in those plants where AOL was believed to occur and in those free of AOL is provided in the Figure.

The one-tailed Kolmogorov-Smirnov (K-S) two-sample test⁴ was applied to the two distributions. The same analysis was directed to the compounding plant population AOL-free plant group (see above). The distribution of positive signs and symptoms were found similar in both groups. Accordingly, for the "AOL-free" population in the Figure, we have included the employees of the compounding plants. On the basis of affirmative responses concerning the presence of any symptoms, this test indicated that these two distributions did not stem from a common population pool ($P < 0.001$).

This K-S test indicates that the frequency of occurrence of the asymptomatic state (i.e.,

zero symptoms, the Figure) was different in populations believed to be free of AOL as contrasted with those probably having cases of AOL (see above). This observation could be used to screen a group of workers at unknown risk of AOL development by simply determining how many individuals reported only a single symptom. In order to determine whether more intensive scrutiny of a group of 25 or more workers at unknown risk of developing AOL is warranted, one can use a test based upon the normal approximation of the binomial,

$$\text{with } p = \frac{2}{3}$$

$$\frac{2}{3} - p$$

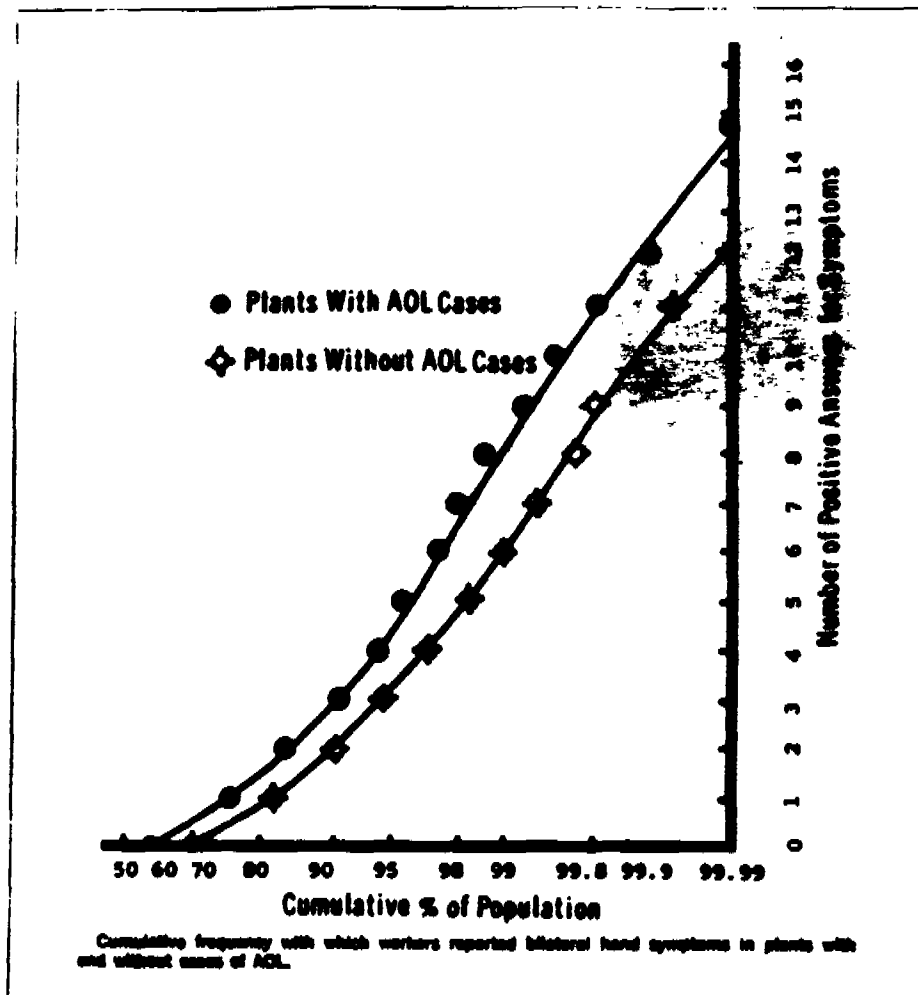
$$\sqrt{\frac{1}{3} \frac{2}{3} \frac{1}{n}}$$

where n is the number of employees questioned, where n is 24 and p is the fraction of population free of symptoms.

Should the value obtained exceed 1.65, further investigation of the population in question should be considered.

The foregoing analyses do not relate to any individual symptom sought by our medical questionnaire. These statistical approaches only considered the absence or presence of any one symptom. While these findings suggest the possibility of asking a single question to screen a population at risk of developing AOL, is there any one question that might be used as a more pertinent screening device?

Focusing once more upon Reynaud's phenomenon, we found, by the use of factor analysis,⁶ that this peripheral vascular disorder was significantly related to AOL. That is, those questions which appear to be consistently answered positively as a group constitute a cluster of symptoms or a factor. In addition, each symptom is associated with factors by scores called "loadings," which weigh the associational strength of the factor to the question at hand, i.e., the occur-



rence of AOL. The most significant of these clusterings of symptoms was found to be, by factor analysis, questions 25, 26, and 27 (questionnaire form), ie, indicators of Raynaud's phenomenon. Accordingly, this constitutes one reason for examining the prevalence of this particular symptom complex among any group at risk of AOL development.

This logically leads to an examination of the relative prevalence of Raynaud's phenomenon in our various plant-population subgroupings. However, because Raynaud's phenomenon is more frequently associated

with women and since that sex represented a relatively small part of the total study population, we first removed the female respondents from our data pool. Applying χ^2 analysis, we found that the prevalence of Raynaud's phenomenon was significantly different in the plants believed to be free of AOL ($P < 0.01$) while no difference was found between the "AOL-free" plants and the compounding locations (Table 5). If indeed the "AOL-free" plants represent a population at no significant risk of developing this disorder, one might infer that Raynaud's phenomenon may occur among the

Table 7.—Intergroup Differences Between Four Groups of PVC Plants

Question No.	7 Plants With Cases of AOL, n = 1,873 vs 17 Plants Without Cases of AOL, n = 1,873	7 Plants With Cases of AOL, n = 1,873 vs 5 Plants Compounding, n = 967	17 Plants Without Cases of AOL, n = 1,873 vs 5 Plants Compounding, n = 967	5 Plants With Cases of AOL, n = 910 vs 17 Plants Without Cases of AOL, n = 1,873	5 Plants With Cases of AOL, n = 910 vs 17 Plants Without Cases of AOL, n = 1,873
20	+	+	+	—	—
21	+	—	—	—	—
22	+	—	—	+	—
23	+	—	—	—	—
24	+	—	—	—	—
25	+	—	—	—	—
26	+	—	—	—	—
27	+	—	—	—	—
28	—	+	—	+	+
29	+	—	—	+	—
30	+	+	—	+	—
31	—	—	—	—	—
32	—	—	—	—	—
33	+	+	—	+	—
34	+	+	—	+	—
35	—	—	—	—	—
36	—	—	—	—	—
37	—	—	—	—	—
38	—	—	—	—	—
39	—	—	—	—	—
40	—	+	—	+	—

* Significant difference, $P < 0.01$, χ^2 analysis.† No significant difference, $P > 0.01$, χ^2 analysis.

general population in eight of 1,000 men. We are unaware of any epidemiological data confirming this impression.

Extending our screening approach, could one predict the number of cases of Raynaud's phenomenon which might indicate the need for further investigation? Since it appears that the general male population incidence of this circulatory disorder is less than 1% (Table 5), by application of the cumulative probability distribution of the binomial with $P = 0.01$, one can determine, for various sizes of plant population, the minimum number of positive responses indicative of a possible AOL problem. Table 6 indicates the number of cases of Raynaud's phenomenon which would only rarely occur by chance ($P < 0.01$) in various size populations.

All signs and symptoms believed to be associated with AOL were compared as to their intergroup prevalences (Table 7). There were considerable differences in the prevalence of most signs and symptoms between the plants with and without AOL, while the compounding plants appeared not to be dissimilar from the population believed to be free of AOL. By contrast, the group about which doubt existed as to the

occurrence of AOL appeared to be somewhat more like the AOL-free group than the AOL-affected population.

Work History Analysis

A detailed review of the 25 clearly established cases of AOL revealed that 18 persons had worked in reactor cleaning at some time during the study; additionally, six others, by follow-up, were found to have worked at this task prior to the study. The one man who had no history of production-line polycleaning was a laboratory technician. However, detailed review of his work history indicated experience with bench-scale reactor operation; this job included hand cleaning of small reactor vessels. Thus, the association of hand cleaning of reactors and AOL disease was striking. Because of job progression practices, practically all persons suffering from AOL had worked at other PVC production jobs at one time or another. Since the lowest paying jobs, i.e., reactor cleaning and bagging-packing, are given to newcomers, most production workers were given these jobs before progressing upward into the skilled jobs. The fact of this upward progression is underlined by work histories

Table 2.—Prevalence of AOL by Diagnostic Category and Reactor Cleaning Exposure (Job 17)

	Prevalence		
	Reporting Reactor Cleaning Experience, 1961-1966	Reporting Any Reactor Cleaning Experience, by Follow-up	Questionable or no History Reactor Cleaning
Definitive cases (ie, diagnostic categories 5 and 6) of AOL, 25			
Total workers at risk, reactor cleaning, 1,047	$\frac{18^*}{1,047} = \frac{1}{58}$ = case per 58 workers	$\frac{24}{1,047} = \frac{1}{41}$ = case per 41 workers	$\frac{1}{1,047}$ = case per 1,047 workers
Total man-years, reactor cleaning experience, 1,062	$\frac{18^*}{1,062} = \frac{1}{60}$ = case per 60 workers	$\frac{24}{1,062} = \frac{1}{46}$ = case per 46 workers	$\frac{1}{1,062}$ = case per 1,062 workers
Definitive and possible cases (diagnostic categories 3, 5, and 6), 41			
Total workers at risk, reactor cleaning, 1,047	$\frac{(18^*+10^*)}{1,047} = \frac{1}{37}$ = case per 37 workers	...	...
Total man-years, reactor cleaning, 1,062	$\frac{(18^*+10^*)}{1,062} = \frac{1}{39}$ = case per 39 workers	...	...
Total PVC work force: male			
Men at risk, 4,751	$\frac{28}{4,751} = \frac{1}{170}$ = case per 170 employees in PVC study population	$\frac{(28+61)}{4,751} = \frac{1}{140}$ = case per 140 employees in PVC study population	$\frac{71}{4,751} = \frac{1}{67}$ = case per 67 employees in PVC study population
Total man-years in PVC population, 21,510	$\frac{1}{768}$ = case per man-years in PVC study population	$\frac{34}{21,510} = \frac{1}{633}$ = case per man-years in PVC study population	$\frac{7}{21,510} = \frac{1}{3,073}$ = case per man-years in PVC study population

* By analysis of survey data.

† Based on postsurvey follow-up; six workers in diagnostic categories 5 and 6 were determined to have had reactor cleaning experience; similar data not available for diagnostic category 3 population.

‡ Assumes that six workers in diagnostic category 3 had had no reactor cleaning experience.

of men with AOL; only experience as bagger-packer or reactor operator approached the frequency of experience of reactor cleaning.

Reactor cleaning has a strong association with AOL. The prevalence of AOL of reactor cleaning was one case per 72 workers at risk (total population at risk, 1,047) among all workers having a history of such job experience. For job categories larger than 500 men, the prevalence rate of AOL by job was greatest for bagger-packers (one case of AOL per 86 workers at risk out of a total population of 860) and reactor operators (one case per 69 at risk out of a total population of 893). On the basis of man-months at risk, the prevalence of clear-cut AOL was even more strikingly associated with reactor cleaners; this job had a prevalence rate of one case per 721 man-months at risk (12,984 total man-months at risk). Among those jobs reporting 5,000 or more man-months at risk, no other job category approached this prevalence rate.

The question might be asked whether plants with AOL differed from plants free of this disorder in regard to the duration of duty tours in reactor cleaning. Analysis did not indicate that men in the former group of plants worked longer tours on this high-risk job.

In addition to the 25 clear-cut cases of AOL, there remained some question whether individuals demonstrating Raynaud's phenomenon with nondescript or borderline x-ray films might have represented early or minimal cases of this disorder. Review of the x-ray films and medical questionnaires of the 74 men in diagnostic category 3 (ie, Raynaud's phenomenon) revealed 16 men who might have been manifesting an early phase or minimal degree of AOL. Eight of these men had marginal defects, about whose presence the radiologists could not agree, and two more had widening of the tuft and shaft, with soft-tissue clubbing (one of the latter subsequently developed multiple osteolytic lesions). The other eight had

three, five, six, or eight other symptoms of AOL on history but no bony abnormalities.

Among these 16 individuals about whom there is suspicion of AOL, we found that ten of them reported experience in reactor cleaning. This reported experience in reactor cleaning was somewhat similar to the work history found among those men with clear-cut AOL, i.e., 15 of the 25 cases. It would be of interest to determine the probability of finding that among 16 men chosen at random from the study population, ten or more would report such work experience. Among 5,011 individuals surveyed, 1,047, or 21%, reported experience in this specific job. (Considering this entire study population, the probability that within a random sample of 16 men we would find by chance ten or more reporting experience in reactor cleaning is only 0.00088 (i.e., 38 chances in 100,000). This determination is based upon application of the cumulative probability distribution, where

$$\sum_{i=0}^n \binom{n}{i} (0.21)^i (0.79)^{n-i}, \text{ where } n = 16$$

It is apparent that time alone will tell whether these last eight individuals will develop AOL. Nevertheless, because we know that at least one individual in this suspicious group subsequently has developed clear-cut AOL, we believe that 26 cases underestimated the total number of AOL cases in the population study. Therefore, we have considered that in addition to the 25 clear-cut cases, these 16 might also be categorized in the AOL group for statistical purposes, providing a total number of 41. On this basis, the prevalence of cases in the general plant population of AOL is calculated in Table 8.

Experience Among Compounding Workers.—One of the reasons for performing this study was to determine whether fabricators handling PVC polymer risked development of AOL. None of the cases of clear-cut AOL occurred among this group of 1,267 employees despite there being 57,657 man-months experience. Among the 557 men working as compounders, there was only one case of Reynaud's phenomenon. The prevalence of Reynaud's phenomenon among compounders was one case per 6,406 man-months experience while in reactor cleaners, this

diagnosis occurred with a prevalence of one case per 721 man-months exposure. Comparing these plants with cases of AOL with compounding plants by χ^2 analysis, significant symptoms (vs) occurred considerably more frequently in the plants with cases ($P < 0.01$) or less than in those compounding only in this group of compounders, there were no persons showing x-ray film defects of a questionable nature without Reynaud's phenomenon (diagnostic category 4). In summary, it would appear that the production of the finished PVC resin is probably not associated with a risk of contracting AOL.

Discussion

The disease acroosticosis appears to be clearly associated with heat cleaning of polymers. In these plants using high-pressure water lances or solvents for cleanup of polymerizers, there were possible cases in only one. There appeared to be a correlation between the extent of degassing prior to entry into the reactor.²

At this time, work practices, rather than any one specific ingredient or combination in the process, appear to determine whether this disease will occur. In view of the low prevalence, the probability of the occurrence of AOL is correspondingly low in a small plant. However, smaller plants without cases at the time of the survey should not consider themselves immune to this problem.

Indeed, several plants with relatively small populations do have this disease among their workers. An examination of the intimate details of their work practices might clarify these ambiguities. While plants with cases of AOL provided gloves for their reactor cleaners, we observed inconsistent usage. Furthermore, while the standard procedures used to "air out" the reactor before entry are well designed to minimize exposure, these were frequently found, upon worker inquiry, to have been "short-cut."

That host characteristics may be determinant of the pathogenesis of AOL is suggested by the low prevalence of this condition, i.e., idiosyncratic "sensitization" or "susceptibility" must be seriously considered. It will be recalled² that a number of trade-

quantely defined low molecular weight, partially polymerized materials are believed to reside in the reactor scrapings. In this connection, the smelting propensities of dextranpolyvinyl pyrrolidone plasma extenders should be recalled.⁷ While it is difficult to see how a high molecular weight (MW 10,000) compound could be absorbed percutaneously, the possibility of respiratory tract absorption and systemic distribution must remain open. In addition, because this appears to be a systemic disease, we are more inclined toward the pulmonary portal of entry rather than the transdermal route of absorption.

The possibility might be considered that this disease is caused by several agents, each one producing a specific component of the picture. In this connection, there is existent a report of Fleitner and co-workers⁸ which notes the occurrence of Raynaud's phenomenon resulting from VC exposure. Is it possible that the Raynaud's component of AOL stems from residual, unreacted VC associated with the PVC remaining on the reactor walls? Contrariwise, the bone changes in animals produced by VC monomer by Viale⁹ did not appear to be associated with vasoconstrictor liability.

To answer some of these questions, more data are required. A more complete chemical characterization of the residual PVC which remains on the reactor walls is essential. Animal exposure to these various possible components are desirable.

Finally, medical surveillance for symptoms of Raynaud's phenomenon and periodic hand x-ray films appear indicated for the present. It may transpire, as more man and man-years experience accumulate, that these manufacturers now free of AOL among their workers will, as time goes by, see development of some cases. This caution particular-

ly applies to employees in the PVC synthesis area. It must be emphasized that the limitations of any retrospective epidemiological study make impossible any definitive prediction of future consequences of PVC manufacture. Since such studies can only describe events of the past and up to instant of the survey, the recommendations as to work practices and medical surveillance become especially pertinent for the safety of these workers.

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Occupational Acroosteolysis

II. An Industrial Hygiene Study

Warren A. Cook; Paul M. Giever, MPH; Bertram D. Diaman, MD, ScD; and Harold J. Magnuson, MD, MPH, Ann Arbor, Mich

An industrial hygiene survey was conducted in respect to occupational acroosteolysis (AOL) in 22 plants engaged in production and compounding of polyvinyl chloride. This survey was limited to inspection of facilities, interrogation of technical personnel, and statistical analyses. All manufacturing processes and chemicals utilized were explored. A major objective was the identification of variables in processes and chemicals

that were peculiar to these plants affording known cases of AOL. No such processes or chemicals were found. The survey brought to light a number of situations suspected of relationship to the precise cause of AOL, some of which require additional exploration. Most positive of these was the finding that essentially all of the persons who developed AOL had served as reactor cleaners using manual methods.

POLYVINYL chloride (PVC) has been in production and widespread use for more than 30 years. An extensive account of the chemistry, methods of production, materials utilized, properties, and uses of the PVC resins was recently published in a series of technical articles by Albright.¹⁻³ Uses include such diverse products as floor tiles, films for food wrappings, sheeting for shower curtains, phonographic records, and coatings for cables.

As an indication of the magnitude of the PVC industry, the average operating capacity in this country for the year 1969 was about 3 billion lb.⁴ Much PVC is produced in other countries. Even with this extensive production involving thousands of operators, the occurrence of occupational acroosteolysis (AOL) among these workers was not recognized until about 1951.⁵

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Reprint requests to School of Public Health, University of Michigan, Ann Arbor, Mich 48104 (Dr. Diaman).

The clinical and epidemiological aspects of this condition are discussed in separate papers in this issue of the *ACRIVIA*.^{6,7}

Industrial Hygiene Survey

Surveys were made of 22 plants by the authors of this paper, most of the plants being visited by a team of one physician and one industrial hygienist. Twenty-six of these were polymer production plants. Vinyl chloride monomer production plants and plants engaged in compounding and fabricating of the polymerized resin were a part of the manufacturing complex at a number of these locations. Five plants conducted compounding and fabricating operations only, and one plant produced only the vinyl chloride monomer. These plants were located throughout the United States and one in Canada.

This survey was designed to obtain information on equipment used, procedures followed, materials involved, extent of exposure to these, and names and descriptions of jobs in order to compare practices in the plants where cases of AOL occurred with those in plants experiencing no cases.

The extent of exposures was estimated on the basis of general observation, a knowledge of the physical, chemical, and physiological prop-

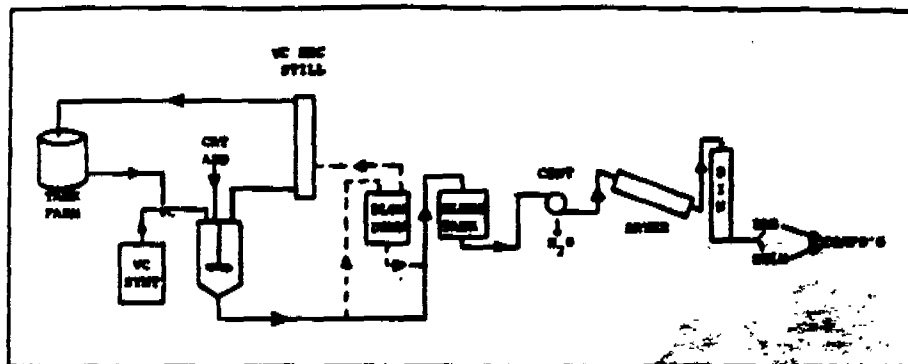


Fig 1.—Flow diagram for production of PVC from vinyl chloride monomer.

erties of the materials, and discussion with technically informed persons at the plants. By setting up three broad categories of duration and of relative severity of the exposure, semi-quantitative estimates were made. Since materials responsible for causing AOL might be absorbed either through the respiratory tract or through the skin or both, such estimates were made for each of these avenues of absorption.

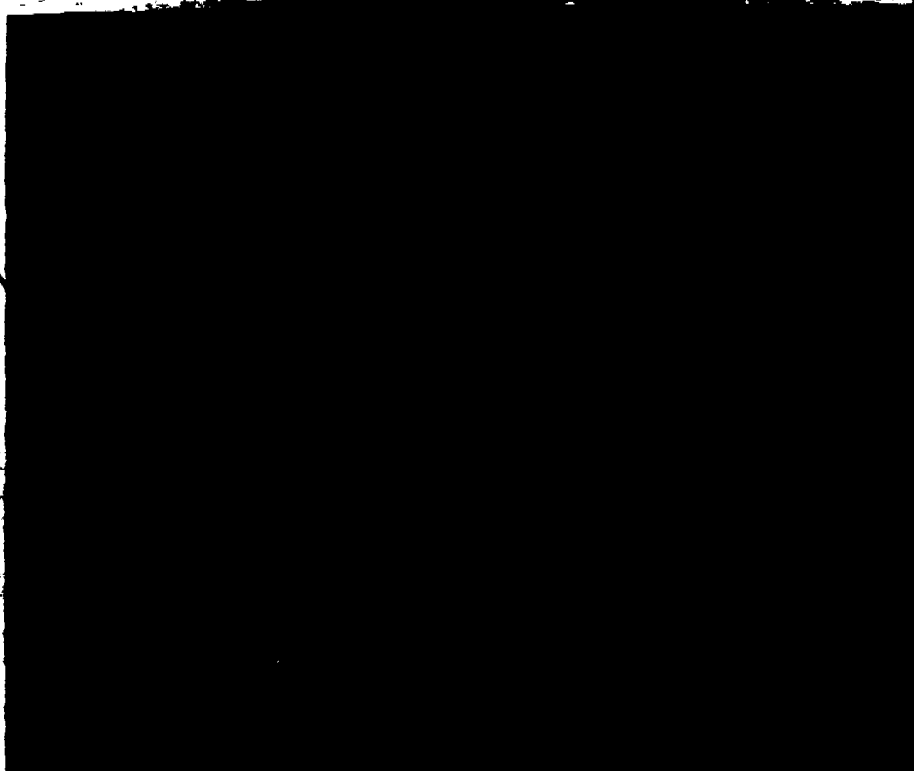
Production Operations

Vinyl Chloride Production.—The two processes for production of vinyl chloride described by Albright^{1,2} were found to be in current use. One of these involves the reaction of hydrogen chloride with acetylene in the presence of a mercuric chloride catalyst. In the other process, 1, 2-dichloroethane is pyrolyzed in the presence of chlorine as a catalyst for the production of vinyl chloride and HCl. In some plants, both methods were used, with the HCl produced in the latter of these processes being used in the former.

Polyvinyl Chloride Production.—Polyvinyl chloride can be produced in accordance with four processes, each with many variations among different plants. The final polymer may have a molecular weight varying from 50,000 to 180,000, depending on conditions under which it is produced. The production processes are designated as suspension, emulsion, bulk (or nonsolvent), and solvent. A typical procedure is presented in the flow-sheet (Fig 1). The essential steps of these operations are outlined in this paper. For more complete details, reference may be made to the papers by Albright.²⁻⁴

In the widely used suspension process, deionized water is first introduced into a large autoclave, usually glass-lined, followed by a wide variety of additives. These include suspending agents such as polyvinyl alcohol, methyl cellulose, and gelatin, emulsifying agents such as sulfonated oils, surfactants such as sodium stearate, and buffers such as sodium bicarbonate. Trichloroethylene may be added to produce the lower molecular weight polymer. Catalysts are added to initiate the polymerization. These are nearly all organic peroxides, with lauroyl peroxide and diisopropylperoxydicarbonate (IPP) being used at the greater number of plants. The reactor is then closed, evacuated to remove oxygen, and vinyl chloride, normally a gas, is piped in as a liquid under pressure from the tank farm or the vinyl chloride plant. In some plants, the catalyst is added to a charge tank from which it is introduced into the closed reactor following addition of the vinyl chloride.

The mixture is agitated with rotating propeller blades, and steam initially is directed into the reactor jacket to raise the temperature to 50 or 55 C. Since the polymerization reaction is exothermic, cooling water must be run into the jacket after the reaction has begun to avoid excessive heating. After ten to 16 hours, the polymerization is essentially complete, and the reactor is brought down to atmospheric pressure. In most plants, it is placed under vacuum for removal of unpolymersed vinyl chloride monomer and transfer to the monomer recovery area. The suspension of PVC is then discharged into a blowdown tank below the reactor. This tank is placed under vacuum for transfer of remaining vinyl chloride to the recovery area. In some plants, the blowdown tank is eliminated. The general appearance of the charging floor of a polymer plant is shown



in Fig 2. The reaction mixture is stirred or agitated by the floor blades.

The polymer slurry is pumped to the tanks, then to centrifuges for removal of water of the water. The dehydrated polymer is passed through a rotary dryer and heated to the temperature of the polymer (about 100°C) to avoid degradation. The dried polymer is passed through a cyclone separator, which separates the polymer from the air stream. The polymer is removed from the air stream by means of a filter-type collector. The polymer particles are dried by vibrating screens, and then transferred to compressing and shipping plants or shipped in bulk. In some plants, the polymer is stored in bins prior to being shipped.

In the emulsion process, the equipment and process is essentially the same as in the suspension process up to the drying operations. In order to produce the finer polymer particles characteristic of the emulsion process, a wide variety of coagulating agents is used. These may be soaps such as ammonium or sodium laurate, surfactants such as salts of naphthalene sulfonic acid, or various synthetic detergents.

Water-soluble initiators such as potassium persulfate and hydrogen peroxide are used in emulsion. Since the dry polymer particles cannot be readily separated from the emulsion by centrifuging or filtering, a spray dryer is employed in this process.

The bulk process is similar to suspension polymerization but is characterized by the production of the polymer being in a solid phase. In about 10% of the vinyl chloride monomer polymerization.

Emulsion polymerization is much the same as suspension polymerization, but no water is introduced. Instead, the polymerization is conducted in such solvents as cyclohexane, acetone, or toluene.

Copolymer and Terpolymer Production.—In addition to the production of the homopolymer PVC, many of the plants also produce copolymer and terpolymers, including vinyl chloride. The greater percentage of the monomer tends to be the vinyl chloride in all of them. The copolymer vinyl chloride-vinyl acetate is in highest production

among this group but is a minor product in comparison to the homopolymer. Other copolymers are vinyl chloride-vinylidene chloride and vinyl chloride-lauryl-vinyl ether. An example of a terpolymer is vinyl chloride-*n*-butyl maleate-dibutyl maleate.

Process, additives, and catalysts essentially identical to those used for the homopolymer are employed in the production of the copolymers and terpolymers with the addition to the reaction mixture of the additional monomers.

Vinyl Chloride Recovery.—The unpolymerized vinyl chloride removed from the batch following completion of polymerization is conveyed to a vinyl chloride recovery area by the suction pump that places the reactor and the stripping tank under reduced pressure. Here the vinyl chloride gas that is removed is placed under pressure to condense it together with water vapor in a liquid. The water and the vinyl chloride are immiscible, permitting their separation. In some plants, an inhibitor, usually phenol, is added to the vinyl chloride to prevent spontaneous polymerization during its distillation; the method used for its purification. The recovered vinyl chloride, with the higher boiling phenol remaining in the still, is then pumped to storage for reuse.

Reactor Cleaning Operations.—After the polymer has been discharged from the reactor and the pressure brought to atmospheric, the reactor is cleaned. This is accomplished by dropping a flexible duct connected to a portable blower to the bottom of the reactor, with discharge normally through the open manhole at the top of the reactor into the charging-floor area. The loose residue is washed out with water, after which one or two men enter the reactor to remove the skin of polymer remaining on the reactor surfaces. The usual method is by manual scraping with putty knives. Resi-

Table 1.—Absolute Pressure-Time Values

Absolute Pressure-Time Values Below 10			Absolute Pressure-Time Values of 10 or Above		
Plant Code	No. of Reactor Cleaners	No. of Expected AOL Cases	Plant Code	No. of Reactor Cleaners	No. of Expected AOL Cases
Plants With AOL Cases					
EE	31	0.8	B	216	8.8
			E	168	4.8
			F	16	0.4
			G	20	1.1
Plants With Possible AOL Cases					
CC	22	0.9			
Total	63	1.7		400	11.8
Plants With No AOL Cases					
P	30	0.6			0.7
O	22	0.6			0.7
V	91	2.6			0.8
W	80	1.4			0.8
			T	9	0.2
			Z	17	0.8
			AA	8	0.2
Total	190	6.9		122	2.6
Plants Started in Operation in 1965 or 1966					
DD	21	0.6	C	84	1.8
			J	13	0.4
Total	21	0.6		67	1.9

Table 2.—Classification of Standard Job Titles

Job Title	Code	Job Title	Code
Addition makeup (other than catalyst)	1	Monomer recovery operator	14
Bagging and shipping operator	2	Monomer supervisor	18
Catalyst makeup men	3	Plant guard, security officer	16
Chief, other office, staff	4	Reactor cleaner	17
Compounding and fabricating	5	Reactor cleaner, solvent	18
Dryer operator	6	Reactor operator	19
General laborer, custodial	7	Sherry blender	20
Laboratory supervisor	8	Supervisor, polymer	21
Laboratory technician	9	Tank farm operator	22
Maintenance, electrical	10	Utilities area operator	23
Maintenance, mechanical	11	(water treatment, etc.)	
Monomer maintenance operator	12	Warehouse operator	24
Monomer operator	13	Transfer operator	25
		Other than PVC	26

due on the agitator blades may require hammer and chisel for removal and sometimes even axes.

Four plants use water jets with pressures of from 500 to 2,000 lb/sq in for the cleaning operation. One of these used water jets only in one of two production buildings, as the structural features interfered with movement of the portable high-pressure water unit about the building. These other plants have been using solvents for reactor cleaning. One of these started to use this method late in 1964, a second in 1965, and the third from the beginning of plant operation in 1965. The reactor is filled with the solvent which must be heated and agitated for a prolonged period, as the PVC is difficultly soluble.

Polyvinyl Chloride Compounding.—Com-

Table 2.—Magnitude of Dosage Expressed as Single Concept

Magnitude of Dosage	Severity/Duration Exposure Parameters		
	Less Than 1 hr/Week	1-6 hr/Week	More Than 6 hr/Week
Slight			
1	Negligible	None	None
2		Negligible	None
3			Negligible
4	Moderate	None	None
5	Moderate	Negligible	None
6	Moderate		Negligible
Intermediate			
7	Appreciable	None	None
8	Appreciable	Negligible	None
9	Appreciable		Negligible
10		Moderate	None
11		Moderate	Negligible
12			Moderate
Major			
13	Appreciable	Moderate	None
14	Appreciable		Appreciable
15		Appreciable	None
16		Appreciable	Negligible
17		Appreciable	Moderate
18			Appreciable

* Expressed in order of increasing dosage received from employees, which is the summation of the three columns to the right.

† Severity of exposure is estimated as none, negligible, moderate, or appreciable for indicated durations.

powdering consists of mixing PVC with a multiplicity of plasticizers, antioxidants, pigments, emulsifiers, stabilizers, and other special compounds in direct blenders and mills. The mixtures are then passed through roll mills or mixers, such as are used in the rubber industry, where the temperature may rise sufficiently to vaporize some of the plasticizer and other volatile constituents. The compounded polymer is then extruded through rolls or dies to form sheets, films, or pellets. These are used in fabricating operations.

Job Classification

Many variables were introduced in the plants surveyed and even in different units of the same plant in regard to nearly every phase of the operations. Investigation of unit jobs in the plants disclosed a wide assortment of job titles. In fact, a job title as used by the technical supervisors often differed from that for the same job in the same plant as listed by the personnel department.

Furthermore, a job assignment in one plant might include a different group of unit operations than in another plant. Also, the proportion of time devoted to the several unit operations often differed. To compound the difficulties of classification, workers would frequently rotate through several jobs

at a weekly, monthly, or other period.

A classification of 26 job titles for the statistical purposes of this study was prepared (Table 1). These job titles corresponded to comparable operations in all the plants and to a common group of types of exposure to vinyl chloride. Primary and secondary jobs in plants were classified on the basis of the nature of the work and the frequency of exposure to vinyl chloride. The classification was discussed in the accompanying paper on epidemiological aspects of PVC.²

Job Progression.—Often the first job assignment of the new employee is that of reactor cleaner. Unless there are many reactors, this work does not require the entire time of the employee. Part of his time may be spent in bagging or shipping finished polymer or in the handling of catalyst and other additives.

As job openings arise and with acquisition of seniority, this employee may progress to higher skilled jobs such as reactor, monomer recovery or dryer operator, or any combination of these at any one time.

In plants producing other products in addition to vinyl chloride polymers, employees may transfer between these product areas either as full time for a period of months or dividing their time within a given week or even day. The latter occurs particularly among maintenance personnel.

Where production of vinyl chloride is part of the operation, operators may rotate between jobs in the production of the monomer and those associated with the production of the polymer.

The length of time spent at various jobs is a function of production needs, economic conditions, plant growth rates, and activity of other product lines.

Occupational Exposures to Materials

Extent of Exposures.—Information was obtained not only on each of the materials

used or produced but also on the extent of exposure to each. Since this is a function of both duration and intensity, each of these factors was estimated. The duration of exposure was recorded as less than one hour a week, from one to eight hours a week, or more than eight hours a week. The intensity was negligible, moderate, or appreciable. Since it was not known whether the material might be absorbed through the respiratory tract, through the skin, or both, the extent of exposure as related to each of these avenues of absorption was recorded.

For statistical purposes, it was necessary to combine those two factors into a single dose value. This was done by the effect of exposure on the following differing physiological responses: heart rate, blood pressure, and respiratory rate. These were correlated with different degrees of exposure to vinyl chloride. The degrees of duration and intensity of exposure were related to increasing dose. Reactor and classified in three groups of dose: slight, intermediate, or major. These combinations are presented in Table 2.

Materials Analyzed.—A total of 10 polymer materials were used as produced in the reaction of PVC, the copolymer with vinyl acetate, and other copolymers of vinyl chloride. These materials included monomers, polymers, oligomers, oligomers, isomers, copolymers, and copolymers. These materials included monomers, polymers, oligomers, oligomers, isomers, copolymers, and copolymers. These materials included monomers, polymers, oligomers, oligomers, isomers, copolymers, and copolymers.

A computer analysis of the data was made. This has shown that the data of the polymer materials are not the same as the data of the polymer materials. This has shown that the data of the polymer materials are not the same as the data of the polymer materials.

Vinyl Chloride Exposure.—In evaluating the role of vinyl chloride as a possible influence in the causation of ALC, the estimates of the extent of the exposure of reactor chemists and reactor operators were reviewed. Since the authors conducted no air analyses, they had to judge the presence of vinyl chloride in the charging four area principally on the basis of general ventila-

Table 4.—Data of Ventilation and Vinyl Chloride

	Rate of Ventilation	
	In Reactor Charging Area	In Vinyl Chloride Recovery
Peak rate	2	2
Air change	2	2
Flow rate	2	2
Air change	2	2

The present study provided no evidence to suggest that vinyl chloride per se is the etiological agent, the measurement of vinyl chloride concentrations may serve as a useful index to the adequacy of reactor ventilation.

Inhibitor in Vinyl Chloride.—An inhibitor, usually phenol, may be added to the

When air sampling has been made in a small number of plants with more sensitive instruments, such as the gas chromatograph, it has been found that the vinyl chloride concentration in the reactor during charging operations tends to be below 100 ppm and usually about 50 ppm. With the rather sensitive new instruments vinyl chloride, and amounts of this gas are released as sampling is conducted. Air sampling has shown vinyl chloride concentrations close to the limit during sampling in the range of 600 to 1,000 ppm.

Although this study provided no evidence to suggest that vinyl chloride per se is the etiological agent, the measurement of vinyl chloride concentrations may serve as a useful index to the adequacy of reactor ventilation.

Inhibitor in Vinyl Chloride.—An inhibitor, usually phenol, may be added to the

Table 2.—Reactor Cleaning Procedures

Plant Code	Visual Scraping		Cleaning by Water Jet	Cleaning by Solvent
	After Every Batch	Less Than Every Cycle		
Plants with AOL cases				
B	X			
E	X			
F	X			
K	X		From 1965	
	(through 1964)			
N	X			
U		Every 8-12 cycles (Building A)	From 1962 (Building B)	
UE	X			
Plants with possible AOL cases				
SB		Every "approximate" cycles		On glass-lined, intermittently in 1965, entirely by September 1966
Plants with no AOL cases				
A	X			From September 1964
	(No September 1964)			
C	X			
D	X		From 1962	
H	X			
J		Every 2½ cycles		
L		Every 4-6 days		
M	X			
P		Weekly	From 1965	
		(through 1964, every 2 weeks 1965-1966)		
Q	X			
S	X			
T	X	Every 1-3 cycles (intermittent)		
	(occasional)			
V		Every 10 cycles		
Z	X			
AA		Every 4 or more cycles		
BB	X			
GB				From start of operations

vinyl chloride to prevent spontaneous polymerization in storage. An inhibitor may also be added to the vinyl chloride recovered from the reactor. The phenol is removed by treatment with caustic soda prior to its transfer to the reactor. The practice over the years covered by the study is presented in Table 2. The use of the inhibitor in the virgin vinyl chloride at two of the positive plants and three of the negative plants, with inhibitor being added in the vinyl chloride recovery operation in two positive plants and four negative plants, leads to the conclusion that inhibitors probably are not a factor in AOL causation.

Catalyst Impurities.—Since the catalysts are all active compounds, they were suspect

as a possible factor in the causation of AOL. Contact with these inorganic and organic peroxides occurs as they are handled prior to their introduction into the reactor and also during reactor cleaning if any unreacted catalyst remains in the reactor. Twenty-two of the 26 plants used liquid peroxide. Eight of these were liquid peroxide, some or none of which was used in the reactor. AOL cases were most frequent in the IPP, and it, too, was in use in both the positive and the negative plants, in four of the former and in eight of the latter. No catalyst or group of catalysts was used in all positive plants and in no negative plants.

Constituents of Scrapings.—Other suspect materials are constituents of scrapings removed from the reactor during normal cleaning. These are believed to include some partially polymerized resin, along with some unreacted catalyst and additives, and unpolymerized vinyl chloride. Little specific information is currently

available concerning these constituents. It has been reported that lauroyl peroxide is definitely associated with residual PVC particles, whereas little of the IPP remains unreacted in the polymer.⁶

Further investigation of the scrapings from the reactor may be expected to furnish information that may lead to a better understanding of the factors involved in causation of AOL. A difficulty in such investigation is that the composition of the scrapings is continually changing from the time they are removed from the surfaces of the reactor. It is obvious that comparatively small molecules of partially polymerized vinyl chloride are increasing in size with passage of time, and active constituents such as residual cat-

Table 4.—Reactor Cleaning Procedures

Method	Positive Plants	Negative Plants
Manual scraping after every reactor cycle	7	9
Manual scraping after 2-3 cycles	0	2
Manual scraping after 4-12 cycles	2	4
Water-jet cleaning	2	2
Organic-solvent cleaning	1	2

alyst and vinyl chloride monomer are decreasing or may no longer be present.

Procedures Affecting Exposure of Reactor Cleaners

Since all but one of the 25 operators diagnosed as positive for AOL had worked as reactor cleaners and the one exception had cleaned laboratory reactors,² additional inquiry was made of procedures that might affect the exposures of this group of workers.

Reactor Cleaning Procedures.—The number of men hours required to clean the reactors depended not only on the number of reactors but also on the frequency of cleaning. In 16 of the 26 production plants, reactors were manually cleaned after every batch. This was true of six of the seven positive plants and one of two plants with possible AOL cases. In only nine of the 17 plants with no AOL cases were reactors manually scraped after every batch.

The procedures followed in each of these plants appears in Table 4 and an analysis of the types of procedure by positive and negative plants in Table 5.

Procedures Following Completion of Polymerization.—Since vinyl chloride and other volatile components of the residues remaining on the reactor surfaces following discharge of the batch might be factors in AOL causation, information was obtained concerning the degree of vacuum applied to the reactor prior to opening it and the length of time that the reactor was under this reduced pressure. The amount of volatile materials remaining in the residues on the reactor surfaces was considered to be roughly proportional to the absolute pressure and inversely proportional to some function of the time. Since the rate of removal of volatile material would tend to decrease with time, the logarithm of this factor was used in calculating an absolute pressure-time (AP-T) value. It was hypothesized that the relative amount of vol-

atile materials remaining in the residues following application of vacuum would approximate a nondimensional value obtained by dividing the absolute pressure in inches of mercury by the logarithm of the time in minutes during which the vacuum was applied. Thus, the lower the AP-T value, the less is the amount of volatile materials remaining in the residues.

Another factor affecting removal of volatile materials is the temperature range over the period that the reactor is under vacuum. The variations in temperature ranged from as diverse that the same reactor could be used for different polymerizations in the same parameter range. Actually, variations in degree of vacuum and timing of its application were such that meaningful calculation of an AP-T value could be accomplished only for five of the seven positive plants, one of the two with possible cases, and 14 of the 17 negative plants.

In the subsequent discussion of these values, the three plants that started in operation as recently as 1965 and 1966, all with no AOL cases, are not included as it is not known whether sufficient time had elapsed for cases to have developed by the terminal date of the study period. These plants are listed separately in Table 6.

The AP-T values ranged from 0.5 to 21. The AP-T values were 10 or above (an arbitrary division line) for four of the five positive plants and for one of the two plants with possible AOL cases. Four of the negative plants gave AP-T values below 10, and seven gave values of 10 or above.

Consideration is directed to the number of reactor cleaners and the corresponding number of expected AOL cases in the two groups of positive plants as compared with those in the negative plants.

The total number of reactor cleaners at risk in the positive or possibly positive plants with an AP-T value of less than 10 is 68; that in such plants with an AP-T value of 10 or more is 436. The relation of these two totals is to be compared with that of the negative plants in which 198 reactor cleaners at risk are in the four plants with an AP-T of less than 10 and 122 are in the seven plants with an AP-T above that value.

The number of expected cases of AOL for each plant is also listed in Table 6. These values were obtained by dividing the number of reactor cleaners at risk by 36. This

figures derived from the paper on epidemiological aspects of AOLP which reports the prevalence of AOL or possible AOL as one case per 37 reactor chambers at risk.

Of the negative plants with an AP-T value of 20 or more, none of those in operation earlier than 1965 had enough reactor chambers at risk to expect an AOL case, whereas two of the four plants with an AP-T value under 10 have enough working to expect cases. Cases would be expected here, the total population of reactor chambers in the entire group of the seven negative plants with AP-T values of 20 or more, but the total number would be 22, as compared with 1.5 expected cases from the entire group of four negative plants with an AP-T value of less than 10. This compares the expected cases in the group of negative plants with an AP-T value of less than 10 at 1.7, compared with 11.2 in each plant with an AP-T value of 20 or more.

The proportion of the number of reactor chambers in the negative plants with an AP-T value of less than 20 to the total number in each plant was 28% to 58%. This proportion for the positive plants was 42% to 68%. A χ^2 test demonstrated that the probability of this difference between the negative and the positive plants coming by chance is less than 0.001.

In order to make this comparison between the positive and negative plants with AP-T values below and above 10, it was necessary to oversimplify a multiplicity of varying details of operational procedures from the time the polymerization is completed to the time the chamber enters the reactor. Accordingly, any interpretation of the findings that reduction of the AP-T value below 10 by reducing the chamber pressure or keeping the reactor at reduced pressure for a longer time or both may result in reduction in development of AOL cases should be approached with great caution.

Preventive Measures

The present knowledge as to AOL is such that adequate statements as to preventive measures are not justified. However, on a suggested qualitative basis, some measures are indicated that may be conducive to AOL prevention.

1. Although some general aspects of reducing development of AOL have been suggested, the specific details of the polymerization process, the reactor design, the reactor operation, and the reactor maintenance are all factors that may be conducive to AOL development.

2. The design of a reactor of reaction chamber should be designed with a minimum of complexity, and with a minimum of moving parts. The design of the reactor should be such that it is possible to maintain the reactor at a constant pressure and temperature.

3. The operation of the reactor should be such that the reactor chamber is maintained at a constant pressure and temperature, and the reactor is operated at a constant rate.

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Occupational Acroosteolysis

An A Clinical Study

Victor E. Nelson, MD, Robert S. Nelson, MD, Walter M. Whitman, MD, Albert H. E. Mink, MD, PhD, and Robert J. Morgan, MD, MPH, Ann Arbor, Mich.

Four subjects with acroosteolysis were studied clinically, and laboratory studies, including x-ray films of the distal phalanx of the thumb, the proximal phalanx of the middle finger, and the proximal phalanx of the middle finger, were made. The subjects were a 35-year-old man, a 38-year-old man, a 40-year-old man, and a 42-year-old man. The subjects were all white, male, and had no known occupational or environmental exposure to any known toxic agents. The subjects were all healthy, with no known medical or surgical history, and no known family history of any known disease. The subjects were all living in the same household, and all had been living in the same household for at least 10 years. The subjects were all living in the same household, and all had been living in the same household for at least 10 years.

Discussion.—The clinical and laboratory studies of the four subjects with acroosteolysis, including x-ray films of the distal phalanx of the thumb, the proximal phalanx of the middle finger, and the proximal phalanx of the middle finger, were made. The subjects were a 35-year-old man, a 38-year-old man, a 40-year-old man, and a 42-year-old man. The subjects were all white, male, and had no known occupational or environmental exposure to any known toxic agents. The subjects were all healthy, with no known medical or surgical history, and no known family history of any known disease. The subjects were all living in the same household, and all had been living in the same household for at least 10 years. The subjects were all living in the same household, and all had been living in the same household for at least 10 years.

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From the sections of Occupational and Environmental Medicine and the Department of Internal Medicine (Dr. Nelson), and the Institute of Environmental and Industrial Health (Dr. Nelson and Dr. Morgan), the Department of Environmental and Industrial Health, School of Public Health (Dr. Morgan), and the Department of Radiology (Dr. Whitman), University of Michigan, Ann Arbor.

Special reports to Institute of Environmental and Industrial Health, University of Michigan, Ann Arbor, Mich 48104 (Dr. Nelson).

The subjects were all living in the same household, and all had been living in the same household for at least 10 years. The subjects were all living in the same household, and all had been living in the same household for at least 10 years. The subjects were all living in the same household, and all had been living in the same household for at least 10 years. The subjects were all living in the same household, and all had been living in the same household for at least 10 years.

Various roentgenographic techniques were employed, including long double views of the distal phalanx of the thumb and the proximal phalanx of the middle finger. The subjects were all living in the same household, and all had been living in the same household for at least 10 years. The subjects were all living in the same household, and all had been living in the same household for at least 10 years.

Results

History.—Blanching of the hands was the first sign of AOL. In two of the men, the onset was gradual over a few weeks, and in two it was abrupt, as shown in Table 2. Cold was the leading factor in all cases. The blanching was associated with either tingling of the hands or tenderness of the fingertips. The polyvinyl work exposure-to-first-blanching ranged from one to 25

In the following table, the cases are listed in order of onset of symptoms. The cases are listed in order of onset of symptoms. The cases are listed in order of onset of symptoms.

Table 1.—Laboratory abnormalities in cases

Case No.		Laboratory Abnormalities	
1	2	3	4
5	6	7	8
9	10	11	12
13	14	15	16
17	18	19	20
21	22	23	24
25	26	27	28
29	30	31	32
33	34	35	36
37	38	39	40
41	42	43	44
45	46	47	48
49	50	51	52
53	54	55	56
57	58	59	60
61	62	63	64
65	66	67	68
69	70	71	72
73	74	75	76
77	78	79	80
81	82	83	84
85	86	87	88
89	90	91	92
93	94	95	96
97	98	99	100

months. The length of the interval has no relationship to the mode of onset or the severity of the symptoms.

A summary of the habits and dietary history of these patients is detailed in Table 2. Three of the four men were cigarette smokers with smoking histories of nine (case 1), 15 (case 4), and 25 (case 2) pack-years. Half drank coffee (three or nine cups per day). All were casual tea drinkers. Three drank between three and 15 bottles of beer each week. One (case 4) drank 120 cans of beer per month but no whiskey while the others consumed less than four

Fig 2.—Shows that further restriction of beer, resulting in abstinence of limited quantities of all liquor except 100 ml and 100 ml beer, after having abstained previously from all beer, has clear clinical results of good prognosis in patients showing a similar to chronic alcoholism.

cans of whiskey per month. Three of the men rarely drank milk, and the other (case 4) averaged two glasses each day. Dietary histories indicated calcium intakes between 1,000 mg and 1,500 mg/day except for one patient (case 2) whose usual intake was 250 mg/day. This patient's normal dietary intake of phosphorus averaged 1,000 mg/day. The other three patients had intakes of 1,000, 1,200, and 1,500 mg/day. These intakes seemed high in light of the disease.

Some patients had a history of renal calculi. Case 4, a man without a history of renal calculi, was reported to suffer the failure of the kidney in one of the four patients, and he had also had hemodialysis by nephrology with dialysis resulting in renal stone previously extracted by the doctor. Finally, the father of all four men had heart disease.

The associated symptoms and signs of joint involvement are listed in Table 5. Intermittent burning osteoarthralgia was mentioned by three of the four patients. This occurred upon rising from sitting or recumbency. The one patient not having rheumatism (case 3) had chronic postural drip, nasal stuffiness, and a prior history of childhood hemorrhoid infection.

Physical Examination.—The major physical findings were restricted to the skin and joints, as shown in Table 5. Synovial and skin thickening were observed by two or more clinicians independently. Dupuytren's contractures were present bilaterally in one patient (case 1). The extensor ligaments of the wrist were thickened in another (case 2). The distal phalanges of the hands of one patient (case 3) were shortened.

Laboratory Parameters.—The numerous

Table 2.—Clinical Features of Patients With ABL of Hand

Clinical Features	Case 1	Case 2	Case 3	Case 4
Swelling				
Joint	Sudden	Gradual	Gradual	Sudden
Swelling	+	+	+	+
Associated symptoms				
Finger stiffness	+	+	+	-
Tingling of the hands	-	-	-	+
Joint pain				
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
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Joint swelling	+	+	+	+
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Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
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Joint swelling	+	+	+	+
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Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
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Joint stiffness	+	+	+	+
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Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
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Joint warmth	+	+	+	+
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Joint pain	+	+	+	+
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Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
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Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+	+	+	+
Joint warmth	+	+	+	+
Joint swelling	+	+	+	+
Joint pain	+	+	+	+
Joint stiffness	+	+	+	+
Joint tenderness	+	+	+	+
Joint redness	+</			

Physical Findings	Case 1	Case 2	Case 3	Case 4
Swarm-like biting insects	+	++	+	+
Swarming				
Without odor	-	-	+	+
With odor	+	+	+	+
Notes				
Swarm-like biting insects	+++	+++	-	+++
	+++			
	+++			
Incubated	Superficial ulceration under 2 weeks C. trachea	Ulceration of oral pharynx	Swarm like	

[illegible]

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[illegible]

During this period of time, there has been further resorption of bone, resulting in shortening of the terminal phalange of all fingers except the left 20th, which has remained uninvolved, and the right 19th, which has maintained its length but has developed a transverse

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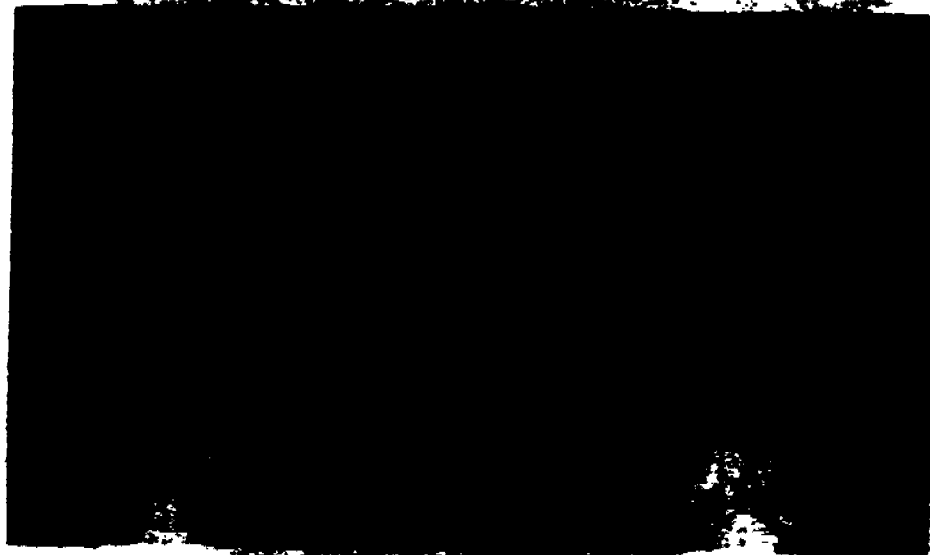
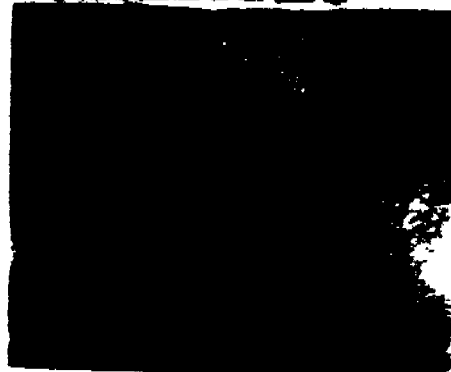


Fig. 6.—Left hand shows extensive edema of 2nd & 3rd fingers, with noticeable defect in distal phalanx of third finger. Right hand shows extensive edema in distal phalanx of second and third fingers and an additional distal marginal defect of second finger (top) (June 23). Radiograms show typical of sodium fluoride 75 percent.



Fig. 7.—Upper-limb joints show osseous and articular changes, grossly marked on left (June 23).



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Table 6.—Five-Hydroxyglutamic Acetic Acid and Calcitonin Studies in Patients With ABL

Urinary Excretion	Case 1			Case 2			Case 3			Case 4		
	Urine mg	Crat- Volume ml/min	Acid ml/min	Urine mg	Crat- Volume ml/min	Acid ml/min	Urine mg	Crat- Volume ml/min	Acid ml/min	Urine mg	Crat- Volume ml/min	Acid ml/min
Five-hydroxyglutamate												
acetic acid												
Spont-2pm	0.70	200	0.35	2.0	200	0.00				300	0.30	
Spont-4pm	0.60	400	0.40	2.2	200	0.04				1,200	0.97	
Spont-8pm	0.60	700	0.60	1.5	200	0.00				410	0.30	
Spont-12pm	0.60	140	0.10	1.0	200	0.00				400	0.30	
Total (1)	0.30	1,700	1.00	7.0	1,000	0.04				2,440	1.94	
Total (2)	0.0	0.170	1.47	...	...	...				...	...	...
Total (3)	0.0	1,700	1.00	...	...	...				...	...	...
Calcitonin	7.0											
Calcitonin												
Calcitonin												

defect. The right 20th finger has shown additional resorption of the phalanx tip. Half-time chipping is noted in the distal phalanx. Some resorption is noted along the proximal aspect of the distal phalanx. This patient also showed extensive osteoporosis throughout the entire hand, as seen in Fig 5. An amorphous lesion was also found in the proximal aspect of the 20th, as depicted in Fig 6.

Case 2.—This patient had an extensive distal survey on Feb 6, 1971, with positive findings limited to the hands and joints.

As shown in Fig 5, the left hand revealed a marginal defect at the tip of the distal phalanx of the second finger while the distal phalanx showed a transverse defect in the distal phalanx. At the same time, the right hand present-

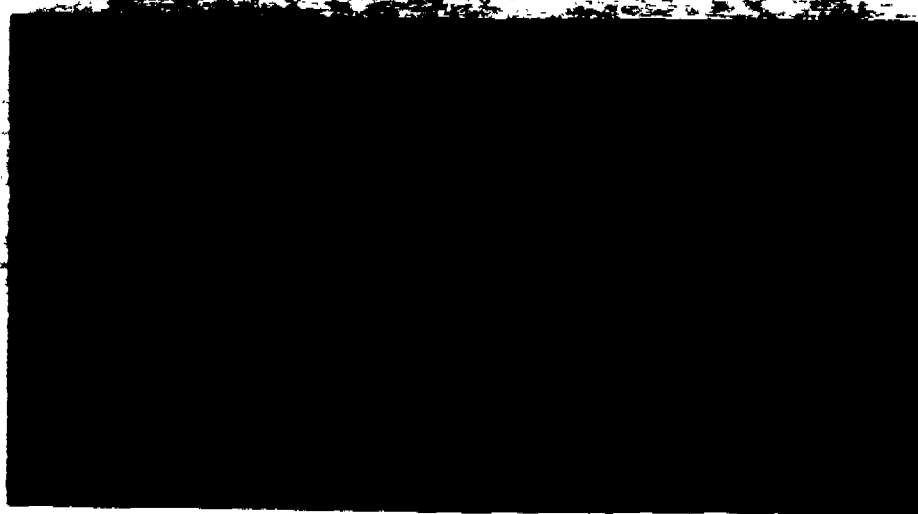
ed a similar type defect in the distal phalanx of the second and third fingers and an additional distal marginal defect of the second finger.

Figure 5 captures a typical calcium fluoride (CaF₂) radiograph of the hands and the corresponding roentgenograms. A slight increase in calcium fluoride (CaF₂) uptake is seen in the distal phalanx of the left third and right second and third fingers while the uptake is diminished over the distal phalanx of the left 20th and right fourth and 20th fingers. Generally, uptake over the remaining bones of the hands are uniform.

The mano-man joints also displayed extensive erosion and sclerotic change, more marked on the left, as shown in Fig 6.

Case 3.—Extensive distal survey on this

Fig 7.—Hands show chipping and widening of distal phalanx of all fingers, with constant chipping of all hand bones.



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When the first of the new series of stamps was issued in April 1968, the bank had no more than 100 million dollars in assets. Within a few years, however, the bank had grown to more than 1 billion dollars in assets, and its deposits had increased from 100 million dollars to more than 1 billion dollars. The bank's assets were made up of a variety of investments, including stocks, bonds, and real estate. The bank's deposits were made up of a variety of accounts, including checking accounts, savings accounts, and time deposits. The bank's growth was due to a variety of factors, including its aggressive marketing strategy, its strong financial performance, and its commitment to customer service.

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Abstract

The sodium fluoride ^{19}F solid-state data suggests that the more advanced catalytic changes with transverse defects at this time were picking up more fluorine and probably

calcium, indicating active remineralization. That the digits with marginal defects picked up less than the normal bones implies some type of uptake block or active demineralization. If the latter is true, it is all the more interesting that different bone lesions appear to be mineralizing and demineralizing in the same individual, even the same hand. The etiological agent or agents responsible and the pathological mechanisms remain obscure.

Medical Prevention.—The interval between the beginning of master cleaning and the onset of AOL appears highly variable, is, one to 25 months. Accordingly, the frequency with which one questions master cleaners has no rational basis. By contrast, the occurrence of Raymond's phenomenon should serve as a sufficient warning for further inquiry.

This is not to suggest that prudent medical practice does not require periodic examination of master cleaners and other groups of workers in whom AOL occurs. These groups should be surveyed periodically by use of hand remineralization and medical questionnaires. The form the latter might take has been discussed in the epidemiological segment in this series. But we would emphasize that prevention of AOL also requires the cooperation of supervision. This group should be alerted as to the possible significance of Raymond's phenomenon in relation to AOL.

Upon the discovery of any case of AOL among workers at risk, each individual should be removed from the job. X-ray films of the hand, back, and knee should be obtained. A medical history questionnaire, similar to those used in the epidemiological survey reported here, should also be procured. A medical evaluation for other causes of Raymond's phenomenon is in order. In view of the unpredictable course of AOL, it

would be wise to exclude any individual with Raymond's phenomenon from master cleaning. Since similarly practices usually remove workers from master cleaning with the passage of time, such excluded workers probably would not return to this particular job. In view of the low prevalence of this disease, we believe that permanent restriction of these few workers from this job does not pose any undue administrative burden. Until more is known of the natural history of this disease, guidance would dictate the course as here recommended.

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