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"On the So-called Vinylchloride Disease"

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Since 1958, when the first information on the hazardous health aspects to workers in the vinylchloride manufacturing industries was found, and especially since 1963, when the same effects were found affecting workers in the polyvinylchloride industry (PVC), and through further reports on this subject (3, 4, 7, 8, 12, 28), attention has been drawn to this branch of the chemical industry. This deals with a disease similar to a skin and bone affecting scleroderma, but a disease unexplainable in etiology and pathogenesis. The main symptoms of this have been the Raynaud syndrome, nodular to large area dense skin alterations and band-like osteolysis in the finger phalanges.

We could report our first observations on this disease type in Germany in 1972 (15, 16, 17). As the clinical picture was at first comparable to a specialized form of progressive scleroderma, we submitted all employees to a painstaking

the nail plate). We saw scleroderma-like skin alterations in 8 patients: small knots or more spread out; very coarse and relatively sharply defined, usually covering the surface skin projecting infiltrate on the outstretched hands, the distal third of the arms under the elbow, and the area of the cheeks. Three patients had no clinical skin alterations.

The histology findings of the excision specimens (from the left or right hands) of all patients were relatively uniform. Besides hyperorthocytosis and epidermidosis, there was an expansion and increase of capillaries in the upper cutis. An increase, widening and homogenation of the collagen bundle and a clear rarefaction and fragmentation of the elastic fibers was evident. The same findings in the epidermis and the fibers of the upper cutis were proven to exist in the patients without clinical skin alterations. The histology alterations in the epidermis and the collagen connective tissues are similar to the edematosis to infiltrative stage of progressive scleroderma. Here, however, a clearly defined border is seen between that of possible but to some extent considerable injury of the elastic fibers and the vessel alterations.

So far, circulation disturbances are the most common symptoms: Nine of thirteen patients complained of this, and in fact eight of them gave this complaint as their first symptom. The degree of complaint ranged from increased sensitivity to the cold and "akrozyanose" to the Raynaud

syndrome (four patients). The circulation obstruction could be judged objectively with the aid of temperature measurements, determination of the time required to rewarm after exposure to the cold, capillary microscopy, and arm-hand arteriography. In no case did oscillography and plethysmography result in a certain pathological prognosis. From this, one can ascertain that the origin of the circulation obstruction is in the periphery and not in immediate range of the large blood vessels. This consideration is supported by the angiographic and capillary microscopy results. Four patients with sensitivity to the cold were proven to have ampule-like widenings of the capillaries in the nail joints just as described in the Raynaud syndrome (14). All seven patients who underwent arteriography showed pathological vessel images. The alterations ranged from a slight narrowing of the Aa. digitales palmares propriae et communes with single segmentary localized closures, to a high degree of stenosis and segmentary closures, and even to the extent of the loss of contents by the arteries in the entire length of the finger and clear stenosis of the entire hand joints.

After the examination until this point, it appeared that a direct relationship existed between the length of exposure and the amount of vessel damage.

The most obvious x-ray results of this disease were the band-like osteolysis between Processul unguicularis and the phalangen on single or all fingers in six of the patients.

In addition, fragmentation and border defects of the Processus unguiculares could be found in six patients. It is also possible to determine different degrees of bone alteration: in light cases only a small lytic zone is visible, and in the advanced stage the phalange is almost fully destroyed and the Processus unguiculares mounts onto the basis of the phalanx cap-like. A full restitution of the bone is not to be expected based upon the facts at this time (23,24). Remarkable herein is the solid correlation of acroosteolysis and the club-like expansion of the end phalanges. Thus, the "drumstick fingers" are an expression of the lytic bone process and not of an internal disease.

An examination of the blood building system and coagulation draws our attention to this remarkable finding: all thirteen patients showed light to serious thrombopeny. The thrombozytic count lay repeatedly between 30,000 and 119,000/ μ l (under a normal limit of 150,000/ μ l). In a sternal puncture given to six patients in search for an explanation, there resulted in no case a reference to the obstruction of the "thrombocytopoiesis", osteomyelofibrosis, or osteomyelosclerosis. The other examinations showed no deviations from the norm, except for a slight reticulocytosis in eight patients (between 16 and 26 %), and a slight leukopenia in five patients (2350 to 3950 leucocytes/ μ l). Reticulocytosis and leukopenia may be caused by the splenomegaly in the twelve patients. At this time, it is not clear if

the thrombopeny is also so caused, but it is probable that it deals with a turnover disturbance or an increase in disintegration in the periphery.

It was observed in the anamnesis that three patients reported recidivistic pain in the left upper abdomen and one patient reported pain in the right upper abdomen and a feeling of fullness, as earlier diseases of "Leber and Milz," yet long-time intake of medicines or extreme alcoholism were not discerned. However, three patients without the scleroderma-like skin condition and acroosteolysis had record histories pointing to a chronic liver ailment (Esophagus varices bleeding, splenoral anastomosis; portal hypertonus; esophagus varices, splenomegaly.). The bromosulfaline retention was clearly increased, but by comparison the values for serum-transaminase and-phosphates were for the most part nothing out of the ordinary. This discrepancy could also be proven in the other ten patients. Four patients had esophagus varices, and in twelve cases splenomegaly was proven scintigraphically. The laparoscopic and liver biopsy results of five patients, which were available to us at the end of 1972, showed remarkable agreement: surface area of the liver clearly or finely waved, capsule fibrosis, increased blood- and lymph-vessels, histologically a slight to clear fibrosis of the portal system and individual cell necrosis, and slight coarse fat droplets. The result, that we could further verify at this time let us express the following theory: Except

for the slightly toxic alterations of the liver cells, this results from the expansion of the connective tissues in the portal system into the diffuse circulation in the liver. In advanced stages this leads to an interhepatic block (most likely because of the hinderances in the height of the portal system, possibly similar to a sinusoidal block), with esophagus varices. It remains to be found if the splenomegaly is only a secondary condition or if this ^{is} primarily the direct result of toxic changes.

Of nine patients examined in the lung functions (anamnese, x-rays, spirometry, entire body plethysmography, and blood gas analysis) after references pointed to mainly restrictive alterations, eight of these patients showed partial insufficiencies. Further research must be undertaken to determine if these disturbances can be traced back to the fact that similar changes occur in the lungs as in the collagen and elastic supporting tissues of the skin, that is, that a beginning diffuse lung fibrosis is the cause of these disturbances.

The Initiating Factor

This paper is concerned with an industry-caused disease, in which the symptoms include (arranged in order of most common occurrence) thrombopeny, splenomegaly, toxic liver damage, ventilation blockage, circulation obstruction, and skin and bone alteration. This complex of symptoms has not yet been

been assigned to a known syndrome. It is unexplained etiologically and pathogenically.

Is it possible to obtain a certain insight in the etiology and pathogenesis by a comparison of our results with those previously recorded in literature? What is then possible to be the initiating factor?

At a simultaneous pressure and temperature increase, liquid vinylchloride is polymerized to polyvinylchloride with the addition of water and various additives, depending upon the different properties desired. In different countries, independent of the additive type, the Raynaud syndrome and acroosteolysis was present in workers cleaning autoclaves. The symptoms appear so characteristic that it lead in the past year to the disease designation of "occupationally-conditioned acroosteolysis" and was advanced to a diagnosis position (28). It is not assumed that the additives, differing by type, country of production and methods, play an important role, but the harmful combination of these with the vinylchloride can not be completely excluded. Therefore vinylchloride, the substance present in the largest amount, becomes the main point of our interests. The monomer vinylchloride is pumped over a closed system of an autoclave. The exit possibilities of the gas - and thus the inhalation possibilities - consist then in more places within the production process:

1. Permeability of the autoclaves (intake and offtake)

during polymerization and recovery processes.

2. In the discharging and opening of the autoclaves as well as in the drying process of the finished polyvinylchloride. The residual gas consists of up to 90% vinylchloride (6) and often leads to leaden tiredness and short-lasting disorientation in the employees.

3. From the polymer precipitation on the walls of the kettles. Therefore, from the technical viewpoint, it is completely possible that vinylchloride initiates the hereby described disease.

Some facts are already known about the effect of vinylchloride on human and animal organisms. The narcotic effects have long been recognized (22). Since 1958, reports have repeatedly been made concerning the angioneurotic obstructions and the Raynaud syndrome in workers (1, 10, 21). In the literature one finds single references to the intoxication of vinylchloride, wherein a reversible dizziness, light to very noticeable giddiness, disorientation, skin appearing as a 2-degree burn, and lessened blood coagulation have been determined symptoms (6, 9, 11). One worker died as a result of poisoning.

With the use of experiments involving animals, lung odem, blood congestion in the lungs, liver, and kidneys, as well as decreasing blood coagulation could be proven (20). In long term experiments it was possible to produce centrolobular degeneration in the liver and necrosis with foamy vacuolization as well as periportal cellular infiltration (26).

Recently, reports were made concerning skin, lung, and bone tumors and obstructions in the bone structure (27). These results, based on animal experiments, lead again in 1970 to a depression of the MAK (maximum occupation concentration) to 100 ppm (13). It is not yet known to us the regulations concerning gas concentrations at the occupational site.

The symptoms related in the framework of this disease (Raynaud syndrome, toxic liver changes, obstruction in the bone compositions and prenarcotic syndrome) may then be produced by vinylchloride. Thus, in the knowledge of the occupational site we can express the conjecture that long term exposure to vinylchloride is at least a, if not even the disease-initiating factor. The fact that the name "occupationally-caused acroosteolysis" hints only at a not necessarily determining symptom shows that a new name should be coined. We have proposed the designation "so-called vinylchloride disease" for this syndrome because this disease, influenced by the participation of numerous organs, obtains the character of a system disease.

Pathogenesis

The pathogenesis is, as before, unexplained. On the basis of our research we discussed the theory that the disease as a pathogenetic principle in the furthest sense is caused by an obstruction on the connective tissue or the vessel connective tissue. In addition, as our theory shows that the toxic agent is effective not only per inhalationem, but

also perkutan, the fact exists that only uncovered main arteries exhibit scleroderma-like coatings and that the band-like osteolysis is only found on the finger phalanges. We saw scleroderma-like skin alterations as well as acroosteolysis only in workers who had worked a long period with the cleaning of autoclaves. This can perhaps be explained by the fact that 600-1000 ppm of vinylchloride could be measured in the area of the autoclave walls (5). As an indication based upon the obstruction of the connective tissues, we saw the qualitative and quantitative alterations of the skin and the multiplication of collagenic fibers in the portal system of the liver. The increase and expansion of the capillaries was visible by capillary microscopy and histology in the upper cutis, in addition to the peripheral circulation obstruction proved clinically, angiographically, and thermographically. Even the alteration of the bone (osteolysis as a result of trophic obstruction by damage to the vasa nutricia) and the lung (restrictive and obstructive ventilation blockage) can be synonomously explained. The prognosis of the disease - judged quite optimistically by earlier literature - appears quite serious to us, especially with respect to thrombopeny, splenomegaly, and portal hypertension. According to our observations of alterations in the bone, this disease should be judged with reserve.

Consequences for the Practice

The triassic formation of this disease system, serious

prognosis and relatively high mortality (from our investigation certainly more than 10%) has led prevailingly young men to solicit us to place the following suggestions:

1. Execution of epidemiologic and preventative medical experimental tests. In our opinion, it is not sufficient any more to search for only Raynaud syndromes and knotty skin alterations because these symptoms, as characteristic as they are, already show the advanced stage of disease. Perhaps more important, controls to determine the thrombozytic count in regular time periods should be given to all employees of PVC-producing industries. This should take workers with a constant thrombopeny out of this branch of the industry, as this appears to be the first objective symptom, before further and more serious internal damage occurs.
2. No employment given to those with liver diseases or circulatory problems.
3. Regular gas concentration measurements in different work sites to avoid exceeding the MAK limit. Experienced technical improvement with the goal of greatest possible automation, and improvement of the ventilation conditions to reduce the possibilities of gas inhalation to the lowest amount possible.
4. Compensation to diseased workers and recognition of this disease as liable to indemnity by inclusion in the list of BKVO.
5. More research, especially with animals, using vinylchloride with special consideration to the skin, bones, lungs, liver, and spleen.

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in intracellular media in all persons under study. The Ca^{2+} level in blood plasma decreased with age. The Ca^{2+} level in intracellular media increased with age, that in intercellular lgs. was practically const. These findings agree with the literature data of the effect of occupational stresses as in this case high atm. air temp., noise, vibrations and industrial dust on electrolyte metabolism.

E. Strossberg

23182f Importance of polonium-210 determination in the urine of workers in uranium mines. Panov, D.; Parovic, D.; Novak, L.; Djordjevic, V. (Inst. Labor Med. Radiol. Prot., Belgrade, Yugoslavia). *Suvrem. Med.* 1972, 23(11): 6-10 (Bulg.). A study of 209 workers in the uranium mines of Yugoslavia who were exposed to Rn as well as rats living under the same conditions showed that it is not possible to det. the contamination by Rn and its degradation products by testing the urine for ^{210}Po . No correlation exists between the concs. of ^{210}Po in the urine and the concn. of Rn in the work environment.

J. J. Pohl

23183g Hand tremor induced by industrial exposure to inorganic mercury. Wood, Ronald W.; Weiss, Ann B.; Weiss, Bernard (Sch. Med. Dent., Univ. Rochester, Rochester, N. Y.). *Arch. Environ. Health* 1973, 26(5), 249-52 (Eng.). Hand tremor in 2 subjects with industrial Hg exposure decreased after cessation of exposure and the subjects became asymptomatic after 3.5 months. The extent of hand tremor was evaluated by requiring the subjects to maintain a force of 10-40 g with the forefinger on a finger trough attached to a strain gauge. Performance improved after the subjects were removed from Hg exposure.

Raymond Zehnpenning

23184h Sanitary-hygienic appraisal of working conditions during the welding of metal covered with protective coats. Protchenko, G. A.; Danilov, V. I.; Timchenko, A. N.; Nenartovich, A. V.; Trubilko, V. I.; Savchenkov, V. A. (Khark', Nauchno-Issled. Inst. Gig. Tr. Profzabol., Kharkov, USSR). *Avtomat. Sverka* 1973, 26(2), 65-8 (Russ.). Air samples were taken using a specially equipped welder's helmet and analyzed for dust, phenol, CO, HF, acrolein, phthalic anhydride, NO_x , Mn, and SiO_2 . Tests were run with and without general ventilation. Weldings were both hand-operated and automatic on a 10-mm coated steel plate. Gas-cutting was also examd. The coatings were a glyptalic (I) a phenol-formaldehyde (II) and a polyethylene (III), in 25 μm thickness. The results are compared with the max. permissible concns. I is the least and III the most objectionable II, with ZnO , is toxic.

Olaf Thomsen

23185j Hygienic certification of the building projects development, and reconstruction of plants producing organochlorine products. Levina, M. M.; Filatova, V. S.; Belaya, E. G.; Ashirova, S. A.; Tikhomirov, Yu. P.; Levin, A. L.; Mostinskaya, R. Z.; Kuznetskii, B. E. (Inst. Gig. Tr. Profzabol., Gorki, USSR). *Gig. Sanit.* 1973, (4), 86-7 (Russ.). Certification of building plans, development, and reconstructions of plants manufg. PVC along with a favorable solution of sanitary-hygienic problems appear to depart from hygienic requisites. Poor ventilation in plants manufg. vinyl chloride, polychloroprene, and trichloroethylene is poor and does not conform to stds. Architectural modifications should be employed to effect hygienic stds.

John Howe Scott

23186k Studies of combustion with a sludge burner. Wiesenerberger, J. (Ger.). *Wasser, Luft Betr.* 1973, 17(1), 24-6 (Ger.). A 40 to 1500 kg/hr sludge burner burns combustible industrial waste sludges with a min. of soot or CO. The sludge is atomized in the nozzle by a stream of compressed air or steam and elec. fired. The burner fires into a suitably insulated muffle furnace chamber from which combustion products may be removed for anal. Using a 100 kg/hr model burner, old crankcase oil and lacquer solvent wastes were burned with a min. of soot or CO. Less flammable materials can be totally burned if other flammable gases are used in place of compressed air or steam. J. H. Leftin

23187m Aircraft Emissions: Impact on Air Quality and Feasibility of Control (Office of Air Programs APTD-0757). United States Environmental Protection Agency, Office of Air Programs (USEPA, Off. Air Programs: Research Triangle Park, N.C.), 1972, 60 pp.

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23189p Air Pollution Translations: A Bibliography With Abstracts, Vol. 3 (United States Environmental Protection Agency Publication No. AP-120). United States Environmental Protection Agency, Information Services Division (USEPA, Air Pollut. Tech. Inform. Cent.: Research Triangle Park, N.C.), 1973, 250 pp.

23190g Absorber for purifying sulfur dioxide-containing flue

gases. Gustafsson, K. A. G. (Aktiebolag Sulfatverken, Sved. 352,817 (Cl. B 01d), 15 Jan 1973, Appl. 6973/73, 15 May 1971; 6 pp.). The absorber consists of an absorption column with a mist-nose suspended at its bottom, a tube reaching to the top above the absorbent surface and through which the gases pass from the bottom carrying drops of absorbent to the top of the column, a circulation line from the top of the column to the bottom for returning sep'd. absorbent to the bottom, and a mill located in the circulation line for grinding the regenerated absorbent.

I. G. Zewi

23191h Determination of micromounts of some substances in air. Sotnikov, E. E.; Filippova, S. A. (U.S.S.R. 366,444 (Cl. G 01n), 1973, Appl. 14 Sep 1971, From *Otkrytiya, Izobreteniya i Sposoby, Tokennye Sovet. 1973* 50(7), 84). The analyzed sample of air was passed through an entrainment separator filled with a fine-grained absorbent (fluorocarbon) to condense the substances from analysis. The gas was then heated and blowing with a stream of air with a flow rate of 10 l/min. The gas analyzer for further analysis. The accuracy of anal., air was partially absorbed by the substances. During subsequent testing, air was passed through a separator for supplying the substances into the gas analyzer.

23192j Test tube for carbon dioxide measurement. Augengesellschaft G.m.b.H. Ger. Offen. 2,151,693 (Cl. G 01b, 19 Apr 1973, Appl. P 21 51 693.8, 13 Oct 1971; 5 pp.). The measuring range of CO_2 test tubes, useful for automotive exhaust gases, was extended by an Al_2O_3 -supported KOH prelayer. The layer was made by drying in vacuo at 100° a mixt. contg. Al_2O_3 and $40\text{-}100\text{ mm}$ 100 g and KOH (40% KOH in 72 sat H_2O) 15 ml and then reacting with H_2O 1 ml. A 10 mm long bed of this mass adsorbs 10 vol. % CO_2 at test gas concn. 0.11.

23193k Oxidation catalyst for exhaust gases. Seito, Uchida, Sumio; Kori, Yoshizo; Kawaguchi, Kiyohiko; Okamoto, Osamu (Hitachi Makuseru Co., Ltd., Japan). Kokai 73 27,988 (Cl. 13(9)G11), 13 Apr 1973, Appl. 73 10,534, 12 Apr 1971; 3 pp. A perovskite-type $\text{A}_2\text{B}_{1-x}\text{MeO}_{3-x}$, alk. earth metals; B, rare earth metals; Me, Fe group metals; x, 0.0-0.9) oxid. catalyst for exhaust gases from a car of chem. products is prep'd. by heating the acetate mixt. at 900° for 6 hr, powdering, mixing with NH_4HCO_3 , pressing in a pipe-form, and heating at 1200° for 1 hr to obtain a sinter of 85% porosity. The catalyst is even at 1000° for long periods and is not poisoned by Pb, S and N compounds.

23194m Adsorbent of poisonous gases. Inoue, Shiro (Japan). Kokai 73 27,989 (Cl. 13(9)G11), 13 Apr 1973, Appl. 73 10,535, 13 Aug 1971; 4 pp. N and S oxides in exhaust gases are adsorbed on a spinel-type oxide contg. one or more of the alk. earth metals, e.g. Cu, Ti, V, Cr, Mn, and Fe groups and alk. earth metals on active carbon and desorbed by CO or H_2 at 400° .

23195n Device for recycling exhaust gas from a heat engine. Cusson, Charles (Pan American Chemical Co. Inc., S. Africa). 72 01,665 (Cl. C 10k), 25 Oct 1972, Fr. Appl. 71 15,730, 09 Apr 1971; 6 pp. The exhaust gases of a heat engine are recycled to reduce the amt. of NO_x in the final effluent. The exhaust gases are recycled below the discharge for return to the intake; the gases are passed into a catalytic purifier unit where the vol. recycle of exhaust gases is varied with supply of fuel to the engine.

Henry H. Ginzberg

23196p Smoke abatement in the desulfurization of pig iron. Braetsch, Peter; Domalski, Willi; Behrens, Manfred (Zahlwerke Peine-Salzgitter A.G.). Ger. Offen. 2,150,905 (Cl. C 21c), 26 Apr 1973, Appl. P 21 50 965.9-24, 13 Oct 1971; 5 pp. The development of smoke in the desulfurization of pig iron was reduced by adding soda-cement-fluorite mixts. contg. 50-70% Na metasilicate for fixation of the volatile Na_2CO_3 formed by decompos. of the soda. A mixt. contg. soda 63, portland cement 28, and fluorite 9% was suitable for the desulfurization of Fe at $1350\text{-}1400^\circ$.

23197q Removal of sulfur oxides from chimney gas. Tanaka, Takushi; Hattori, Hiroshi; Matsumoto, Seiji (Sakai Chemical Industry Co., Ltd., Japan). Kokai 73 26,689 (Cl. 13(9)F2), 07 Apr 1973, Appl. 71 52,227, 13 Jul 1971; 6 pp. SO_2 in chimney gas are 94% removed by passing, at 10 ml/min for 30 hr, through a column of 800 g of 4-6 mm diam. pellets contg. SrCO_3 , which are prep'd. by mixing SrCO_3 with bentonite, diatomaceous earth and pitch, molding, and igniting. The pellets are regenerated by treating with 20% Na_2CO_3 sol. for 3 hr. CaCO_3 and BaCO_3 are unsuitable.

23198r Potassium sulfate recovery in the purification of sulfur dioxide-containing waste gases. Von Schlabilla, Eduard; Strowe, Wolfgang (Udde, B. & Co., Germany). Ger. Offen. 2,147,427 (Cl. B 01d), 23 Mar 1973, Appl. 72 14,427.1, 23 Sep 1971; 7 pp. The waste gases containing SO_2 , N_2 , CO , and CO_2 containing dust with SO_2 are purified by washing with a KOH-KCl soln. obtained by washing from a diaphragm electrolyte plant. The K_2SO_4 formed in the countercurrent washing process is oxidized by an O_2 stream in air at $50\text{-}100^\circ/3\text{-}24\text{ atm}$ and KCl is added to the oxidized soln. to lower the soly. of K_2SO_4 . The K_2SO_4 is filtered off and the KCl