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✓ Research

Deutsche Medizinische Wochenschrift, 98 (43), p. 2034-2037,
1973

"On the So-called Vinylchloride Disease"

By S. Jühe, G. E. Lange, G. Stein, and G. Veltman

University Skin Clinic of Bonn

Director: Prof. Dr. Leinbrock

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

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internal examination to determine if visceral participation was also present. Recently, we reported completely (18) on the results found up until the end of 1972. These reveal new aspects to be used in the judgement of this disease and, as we believe, also may give new suggestions in the research.

The 13 workers examined in the April-December 1972 time period were 29 to 52 years old (average age: 39 years), and had worked at least two, and at most 18 years (average period: 7 years) in a PVC-manufacturing plant at alternating jobs, although mainly as autoclave cleaners. The first disease symptoms appeared one and one-half to three and one-half years after first working there in eleven patients, and in two cases seven and eleven years after first working.

Symptoms and Findings

The most frequent initial symptoms of the anamnetical details are increasing sensivity to coldness in the hands and feet, a feeling of deafness, and crawling parietosis. In addition, pressure pain in single fingers, a thickening of the end finger joints and weakening of the nails as well as general complaints of excessive tiredness, forgetfulness and slowing down, syncopal dizziness, nausea during work, increased perspiration and upper abdominal pain.

A major role in the diagnosis of this disease is played by the alteration of the skin: Seven patients proved to have drumstick-like (clubbed) thickened finger end phalanges (club procurements and shortening, watch-glass nails, shortening of

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 Processus 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 "thrombosytopenia", 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 thrombopenia 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 led 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% vinylchlorid (6) and often leads to leaden tiredness and short-lasting disorientation in the employees.
3. From the polymer precipitation on the walls of the k ttles. 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 pre-narcotic 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

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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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Translations Unit/TR.12.897b/MTB/VS

8 January 1974

PVC GAS: 40 MEN TAKEN ILL

Doctors say: "Very serious"

Reference: Kölner Stadt.-Anzeiger, 14.12.73

EB Troisdorf - More than 40 workers at the Dynamit-Nobel Works in Troisdorf bei Siegburg have been attacked by a severe illness which is brought on by gases released during the production of the plastic polyvenyl (sic) chloride (PVC). Doctors at the Bonner Universitäts-kliniken (Bonn University Teaching Hospitals), who have been studying the PVC-sickness for some time, describe it as very serious. It can, in severe cases, prove fatal, particularly in younger men. The most serious symptoms are said to be sensations of giddiness and cold, headaches, swollen finger joints, bone atrophy, difficulties in breathing, reduced blood clotting capacity and liver damage.

(See Panorama)

Circulation

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Ref: Weser-Kurier, No. 300, 20.12 1973, p. 11

Insidious Disease

Chemical Workers threatened by Hideous Disease due to
PVC Gas Poisoning

Bonn Ministry sets up Special Committee of Enquiry

Bonn (our own correspondent). Chemical workers directly engaged in PVC autoclave production in large chemical factories are threatened by a new and serious disease. At least 40 employees of a Troisdorf factory are reported to be poisoned by dangerous vinyl chloride gas. "A serious prognosis" for the victims, according to the Bonn skin specialist Professor Gunther Veltmann. Mortality from PVC gas poisoning is reported to be "relatively high" and particularly serious in young male workers.

According to the medical specialists the frightening consequences of the gas poisoning are reflected in the softening of the bones in hands and feet, enlargement of liver and spleen, severe effects to blood formation and coagulation, and associated grave lung disorders. The victims have increasing difficulty with breathing, and varicose veins can form in the esophagus.

This previously unknown disease, according to Professor Veltmann, is "irreversible," i.e. incurable. No remedy has so far been discovered, and the only thing that can be treated is the defective organ. The victim can only look forward to increasing disablement and insidious encroachment of the disease.

Experiments on animals are now being commenced to study the causes and course of the illness and to find antidotes. This evil disease is not even recognized yet as an occupational illness. As a result of the alarming medical reports, Federal Labour Minister Arendt has set up a special committee to investigate and report back. The more seriously affected victims are now claiming disablement pensions. However, they have as yet no entitlement to a pension, since this particular illness is not yet officially recognized as an occupational disease by the health authorities.

The Committee for Dangerous Raw Materials of the Federal Labour Ministry considers that regular medical inspection of workers engaged in plastics production is essential. Guidelines

for technical countermeasures in respect of health hazards are also being drawn up. Local factory inspectors have already ordered individual firms to introduce appropriate safeguards.

Meanwhile, the Troisdorf workers have levelled the serious accusation that they were used as guinea-pigs. One employee, aged 39, a sufferer for some 18 months, is reported to have swollen hands and feet with no more feeling left in them, and is afraid to venture on the street because of dizziness. He first became aware of the unusual symptoms when cleaning out a PVC autoclave three years ago.

Another 47-year-old chemical worker attributes his chronic liver trouble to the poison. According to Professor Veltmann, the effects of the gas on the liver resemble the liver complaints suffered by chronic alcoholics.

The 160 workers on the Troisdorf autoclaves have become particularly uneasy about the situation. However, both management and works council have emphasized that the employees directly involved are not really worried, in view of the fact that none has accepted the offer of transfer to other work on the site. A different explanation, on the other hand, is that these same workers are the top earners in the industry. It is they who are responsible for producing the material which is subsequently processed by their other 2,500 colleagues.

PVC is one of the most widely used plastics, with countless applications in the home and in industry. However, medical specialists emphasize that nobody can suffer ill effects due to contact with PVC products. The only people at risk are the workers directly engaged on the plants in which the colorless vinyl chloride gas obtained from petroleum is liquefied under pressure and converted into powder in large reactor. The danger arises from the gas, which can escape during the process either as a result of leaks, carelessness, or during the cleaning of the reactors. The maximum permissible concentrations of such leakage gases have repeatedly been reduced by the responsible authorities.

According to the Troisdorf works, "nobody has yet died and production has not been irresponsibly pursued at the expense of workers' health or safety; moreover, no efforts have been spared to safeguard the interests of their employees."

Hans Wüllenweber

Translation from Der Spiegel No 50/1973

MEDICINE

Dangerous Plastic

A new and deadly occupational disease has been discovered by Medical Specialists in Bonn: workers engaged in the production of PVC risk incurable diseases of the liver.

Pipes and venetian blinds, curtains and films and whole host of articles in common use are made from PVC, a hard, durable plastic which can be moulded into almost any product. German producers alone have distributed almost a million tonnes of polyvinyl chloride over the country in the last year.

PVC has so far been responsible for the death of as yet unknown numbers of chemical workers. For the production of this much desired material, which can be combined in so many different ways with plasticisers, fillers and pigments that it has become one of the leading products of the plastics age within the last twenty years, is apparently very much more dangerous than had been previously been assumed.

Medical specialists of the Bonn University Clinics have this year diagnosed a "vinyl chloride disease" in at least 40 of the 120 PVC workers in a labouring chemical factory. However, the number of cases is probably considerably higher than this. According to preliminary comments made by the doctors this newly discovered "occupational illness" is characterised by a "serious prognosis and a relatively high mortality rate in men of predominantly younger age groups". According to Prof. Günther Veltman writing in the "Deutsche Medizinische Wochenschrift": "Certainly more than 10% as revealed by our enquiries".

This occupational disease first came to the notice of dermatologist Veltman and his team in the form of characteristic changes to the skin, particularly in the fingers. However, they were soon forced to the conclusion that still worse was to be revealed by this already well-known PVC symptom: vinyl chloride harms blood and blood vessels, bones, nerves, liver and lungs. As summed up by Veltman: "A disease of the system".

This plastics material apparently places at risk only those individuals actually present when the colourless vinyl chloride gas, obtained from mineral oils, is liquefied under pressure and compressed to form powder in the large reactors known as "autoclaves". This "polymerisation process" is necessary to produce the PVC which is then sold as "Hostalit" (Farbwerke Hoechst) or "Vinoflex" (BASF): Products which are not toxic as far as the end consumer is concerned, unless, in the words of plastics experts, "Plasticisers migrate from them". Those cases in which these toxic substances have been liberated from such materials have indeed been reported for a considerable period of time.

On the other hand, the "closed system" of the autoclaves gives rise to dangerous leakages. The Bonn Medical Specialists have been investigating "possibilities of gas leakages and associated inhalation risks" at numerous points in the production process. VC-gas escapes when the reactors are discharged and opened as well as through "leaks in the autoclaves". For many years doctors have been aware of the toxic nature of the gas and its narcotic effect. Almost without exception personnel engaged on the cleaning of autoclaves complain of feeling "dopey", giddiness and headaches. For this reason the "maximum allowable concentration" ("MAK") of the VC gas has been repeatedly reduced. According to Veltman, however, "we have so far not been aware of regular gas concentration measurements being carried out on production sites."

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Personnel responsible for cleaning the autoclaves - such as the majority of the diseased chemical workers - apparently inhale many times the quantity of the acceptable tolerable dose of the toxic substances. Industrial doctors in America have repeatedly measured gas concentrations of 1,000 ppm * in the neighbourhood of PVC autoclave walls, which is ten times the MAK value.

The symptoms suffered by the diseased Bonn workers show that the air in German chemical factories is not very much better. The following changes in bodily organs has frequently been observed after only 18 months employment :

Enlargement of liver and spleen with lasting destruction to the structure and function of their cells - collective tissues proliferate in the organs.

Reduced circulation in the hands due to diseased narrowing of the arterial vessels.

Finger bones gradually deteriorate, and were almost completely destroyed in cases of advanced disease.

Blood formation and coagulation were affected and breathing was found to become increasingly difficult.

The majority of these illness-induced changes are considered non-curable by reason of the fact that the increase in connective tissues in all vital organs is "irreversible". Specialists in internal diseases accordingly hope at the most for a "defective healing" in diseased livers. The chemical workers are left with a thick-skinned and deformed organ such as that found in chronic alcoholics after many years over-indulgence in alcohol.

According to Prof. Veltman, the necessary "consequence" is "compensation for all diseased workers" and the recognition of the illness as an occupational disease. Neither he nor his colleagues have so far ventured to estimate the numbers of the victims of the PVC disease.

Basic research into the medical problems of VC is also badly lagging. In the 100 year after the ability of vinyl chloride to polymerise was first discovered - in 1878 - the doctors in Bonn are now demanding "experimental investigations in animals on the effects of the vinyl chloride with particular reference to skin, bone, lungs, liver and spleen".

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- * PPM : abbreviation for parts per million = parts (by volume) per million : a measurement unit used to indicate the quantity of trace substances eg in a gas mixture.

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PVC DISEASE TO BE INVESTIGATED

Reference: Frankfurter Allgemeine Zeitung, 20.12.73

Bonn/Troisdorf 19 December

Many cases of illness among persons employed in the PVC plant at Dynamit Nobel AG in Troisdorf have caused concern among the local population. As Dynamit Nobel AG confirmed on Wednesday, 43 workers so far have shown symptoms of the mystery illness, which is known only as "PVC disease" at present. Two foreign workers are said to have become completely incapable of working already. PVC (polyvinyl chloride) is a widely used plastic that is produced by a number of other chemical companies apart from Dynamit Nobel AG.

How seriously the situation is regarded is apparent from a statement issued by the West German Minister of Labour on Wednesday to the effect that the government had instructed investigations to be carried out into the hitherto unknown causes of the disease. Details are to be laid down in January by a panel of experts. According to the Ministry of Labour, the relevant employers' association is working on the assumption that the disease is caused by vinyl chloride.

It was stated that the Ministry of Labour Committee considers that operatives working in the neighbourhood of PVC autoclaves must be medically examined. When the various cases of illness became known local factory inspectorates ordered steps to be taken to provide increased health safeguards on the plant.

The symptoms of the condition are unconsciousness, attacks of dizziness, changes in the hands and feet, headache and nausea. According to a report from the works in question, the first cases of physical damage to workers in the PVC plants were observed in Germany in the Spring of 1972. Dynamit Nobel have been producing PVC since 1951.

The Press Section at the Troisdorf works stated that: The government industrial medical officer, in agreement with the Chemical Industry Employers' Association, has instructed Professor Rudolf Gross, who holds the chair of Medicine at the University of Cologne to examine some of the affected persons and to produce a report.

6 patients from the PVC plant have now been examined by Professor Gross at the university teaching hospital. A report on some of his findings will be issued in December.