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 anamnese that three patients reported recidivisic 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 sclerodera-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 scintallgraphically. 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, histologicaly a slight to clear fibrosis of the portal system and indifidual 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 bleckage, 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 acroosteolytosis 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 obstrictive 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 youn men to solicit us to place the following suggestions:

1. Execution of epidemologic 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, andimprovement 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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