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CHANGES IN THE ARTERIES IN THE HAND AND FINGERS DUE TO VINYL CHLORIDE EXPOSURE

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Vinyl chloride (VC), the starting material for the world's most widely used plastic, polyvinyl chloride (PVC), was regarded as completely harmless until papers by Cordier et al (1966) and Chatelain and Motillon (1967) revealed its pathogenic effect and subsequent papers by Viola (1970), Lee and Harry (1974), Creech and Johnson (1974) and Lange et al (1974) showed that it was also a carcinogen. Earlier papers on the damage caused by vinyl chloride which appeared in Russia (Filatova et al 1958) and Rumania (Suciu et al 1963) passed unnoticed at first as they were inaccessible to the West, and the full text is still not available even today.

The literature, which was scanty at first but has become very extensive in the last few years, demonstrates that the action of vinyl chloride on the human organism primarily by inhalation but also to some extent by direct contact leads to a number of subjective and confirmable changes (Jühe and Lange 1972, Marsteller et al 1973, Stein et al 1973, Falk et al 1974, Makk et al 1974, Lange et al 1974, Lillis et al 1975, Haley 1975, Lange et al 1975, Marsteller et al 1975, Preston et al 1976, Lange and Veltman 1977, Marsteller and Leibach 1977, Gedigk et al 1977, Veltman et al 1978).

As the first phenomena to be observed were scleroderma-like changes in the skin, skeletal changes taking the form of ribbon-like acro-osteolysis in the terminal phalanges of the fingers and less commonly the toes, together with symptoms characteristic of Raynaud's syndrome, the condition was first designated "occupational acro-osteolysis" (Cordier et al 1966, Chatelain and Morillon 1967, Wilson et al 1967, Jühe and Lange 1972, Stein et al 1973). Once it was appreciated, however, that this was a multisystemic condition involving changes in the liver, spleen, lungs, haematopoietic system, central nervous system, skin and vascular system inter alia, it was given the name of "vinyl chloride disease" (Benoit 1967, Jühe et al 1973, Lange et al 1974, Preston et al 1976, Veltman and Lange 1978).

Over the past few years research workers have been increasingly concerned with the relationship, detectable both experimentally and clinically, between VC exposure and the incidence of malignant tumours. Although most of their reports deal with angiosarcoma of the liver, work was also carried out on hepatocellular carcinoma and tumours of the skin, bones, lungs and lymph nodes (Viola 1970, Creech and Johnson 1974, Lee and Harry 1974, Makk et al 1974, Lange et al 1974, Gedigk et al 1977, Konetzke et al 1978, Popper et al 1978).

More recent papers on the manifestations of the disease at the extremities that were observed initially indicate that a regression of the changes in the skin and skeleton takes place when exposure to VC ceases. The acro-osteolysis heals to some extent, but the Raynaud-type phenomena and the sensitivity of the hands to cold remain unchanged (Veltman et al 1978).

Investigations into the peripheral vascular system of the extremities in vinyl chloride disease have only been conducted in isolated cases hitherto and have either been overshadowed by other findings (Benoit 1967; Marin et al 1967, Jühe et al 1974, Walker 1976, Stewart et al 1975, Preston et al 1976) or were carried out by methods unlikely to provide information of any significance (Maricq et al 1976, Williams et al 1977). So far as we are aware no systematic angiographic investigation into the state of the blood vessels in VC operatives suffering from Raynaud's syndrome has been carried out.

PATIENTS

A striking feature of our investigations was that about a fifth of the 93 PVC production and processing workers we observed continued to complain of persistent or even increasing pains in their hands and, less commonly, feet of the type characteristic of Raynaud's syndrome even after exposure to VC had ceased and X-rays indicated manifest regression of the acro-osteolysis.

We therefore carried out arteriographs of one or both hands of 19 of these patients in order to establish the state of the blood vessels. All the patients were male in the age range 32-56 and all were employed at a neighbouring VC polymerisation plant. The exposure times varied from 1 3/4 years to 21 3/4 years. It was of course impossible to establish retrospectively the VC concentrations to which these patients had been exposed at their point of work.

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Five of the patients had been diagnosed earlier as suffering from acro-osteolysis but our own investigations revealed that this had healed wholly or partly in some cases. 16 patients presented oesophageal varices, and histological tests revealed fibrosis of the liver in 2 cases. 14 exhibited splenomegaly and 13 patients thrombocytopenia.

Sixteen patients complained of pains indicative of circulatory disorders in the hands and fingers. They complained most frequently of paresthesia (tingling, numbness and formication) and more rarely of a sensation of cold, whiteness, blueness or deadness of the fingers. One patient found pressure on the fleshy part of the finger painful.

We were led to carry out angiography of the arteries of the hands and fingers partly because of the subjective impairment of the patients' condition, which caused considerable distress, partly because pulses could not be detected in the digital arteries and partly because of the results of the Allen test.

With one exception preliminary clinical examinations ruled out heart disease and hypertension. Two patients presented diabetes mellitus and 5 others a disruption of carbohydrate tolerance. No evidence of collagenosis was found either clinically or immunologically. Cryoglobulins or cold agglutinins of low titre were only observed in isolated cases. Elastin antibody determinations were negative.

ANGIOGRAPHIC INVESTIGATIONS

A catheter was passed into the A brachialis from the right A femoralis in 15 patients, using Seldinger's method. The catheter (right coronary catheter, 6 French, manufactured by Messrs Cook) was introduced into the transitional region of the distal A axillaris of the A brachialis. A direct retrograde puncture of the brachial artery was carried out in the case of the other four patients (Marshall et al 1966, Wegelius 1972). Just before the X-ray photographs were taken, 20 mg of Tolazolin-HCl (Priscol[®]) dissolved in 20 ml of 0.9% sodium chloride solution was introduced intra-arterially through the horizontal catheter or the horizontal injection needle to achieve maximum dilation of the arterial vessels still capable of functioning. 25 ml of a 66% solution of Meglumin-ioxythalamate (Telebrix 300[®]), or, in later tests, a solution of Meglumin and sodium ioxaglate (Hexabrix[®]), was injected by means of a mechanical injector at a flow rate of 8 ml/sec or introduced manually in a bolus. A series of large plate photographs starting 2 seconds after the injection of the contrast medium was taken of the hand and distal forearm over a period of 20 seconds with an image frequency of 1 per second.

RESULTS

Angiograms of the arteries of the fingers and hands were obtained from both hands in the case of 7 patients, the left hand only in the case of 11 patients and the right hand only in the case of one patient. Twenty-six different hands had therefore been examined. Angiograms had been taken of 2 patients in 1972 and again in 1978, while one patient had undergone angiography three times in all (1973, 1974 and 1978).

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Pathological phenomena of varying degrees of severity were observed in all 19 patients, the most frequent being vascular occlusions (17 patients), which in most cases were localised in the region of the Aa digitales palmares superficiales propriae (Figures 1 and 2) but were also found in the neighbourhood of the Aa digitales palmares communes (Figure 3) (3 patients) and the A interossea (1 patient). Fairly pronounced stenosis was also observed in 9 of these patients (Figures 4 and 5). Six patients presented striking elongated threadlike narrowing of the blood vessels with markedly inhibited perfusion (Figure 6). Fourteen patients exhibited circumscribed elongation of the blood vessels which appeared locally as coils or loops or, as in one patient, were virtually generalised in all the arteries of the fingers and hand that were examined (Figure 7). Four of the patients presented extension of the proximal or distal A digitalis palmaris transversa which was accompanied to some extent by occlusion of the associated Aa digitales palmares superficiales propriae (Figures 8 and 9) and in the case of one patient was associated with elongation and pronounced coiling (Figure 10). Hypervascularisation of the finger tip in one or more fingers was observed in 15 patients but was not necessarily associated with the presence of acro-osteolysis (Figures 1, 2 and 9). Proliferation and dilation of the arterial blood vessels in the fingertip accompanied by the occlusion of individual superficial subungual arcades were observed in 6 patients (Figure 2).

DISCUSSION

The changes in the blood vessels of the hands and fingers revealed by angiography are an important aspect of VC disease. They show it to be an occupational disease of the peripheral vascular system classifiable with

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other diseases of the peripheral vascular system attributable to toxic or mechanical factors that can be grouped together as a nosological unit in that they were brought about by the working environment (Valčić 1976). Although chronologically speaking changes in the hands and feet had been noted when the consequences of VC poisoning were first observed and the clinical picture with its three main features of Raynaud-type circulatory disturbances, scleroderma-like changes to the skin and ribbon-like acro-osteolysis, indicated that changes had occurred in the vascular system, very few investigations from the angiological, angiographic or histological standpoint into changes in the blood vessels of the extremities following VC poisoning have been published hitherto (Benoit 1967, Marin et al 1967, Jühe et al 1974, Stewart et al 1975, Preston et al 1976, Walker 1976). Jühe et al (1974) reported spasms and constrictions of the arteries of the fingers and complete occlusion and stenoses in 7 patients. Walker (1976) describes complete or localised occlusions in 4 patients. Angiography carried out by Preston et al 1976 on a VC worker with Raynaud's syndrome who had been exposed to VC for 5 1/2 years revealed striking tortuosity of a number of digital arteries together with acral hypervascularisation and acro-osteolysis in addition to vascular occlusion, stenosis and narrowing of the blood vessels. The other authors (Benoit 1967, Marin et al 1967, Stewart et al 1975), each of whom reported on a single patient, did not observe any vascular occlusions but noted a marked narrowing of the blood vessels which they described as "vaso-constriction", "thin fragile digital arteries with retarded perfusion and slight colouring of the distal areas of the blood vessels". These casuistically reported arteriographic findings provide documentary evidence of different aspects of the manifold changes in the digital blood vessels demonstrated by us in 19 patients. In view of this morphologically detectable cause of abnormalities in the arterial circulation of the hand and fingers in VC workers it is proper to classify the phenomenon as secondary Raynaud's syndrome (Schoop 1967).

We were unable to carry out histological tests on our patients to elucidate our radiological findings on the changes in the blood vessels of the hand and fingers. We did however succeed in conducting a post-mortem histological investigation of the arteries of the toe of one patient, which exhibited a thickening of the media. So far as we are aware the pathological mechanism of the occlusion and elongation of the blood vessels has never been elucidated beyond doubt. However, the changes observed in all the organs examined histologically indicate a generalised disease process in the connective tissue that also manifests itself in the connective tissue of the blood vessels (Marin et al 1967, Jühe et al 1974). The results of histological tests on skin specimens taken from the hand and fingers reported by certain authors permit a direct assessment of the dermal arteries, arterioles and capillaries. The changes in the connective tissue also enable conclusions to be drawn on the processes that take place in the connective tissue of the blood vessels (Cordier et al 1966, Harris and Adams 1967, Jühe et al 1974, Lange et al 1977). Jühe et al (1974) who carried out biopsies on specimens from the hands of 10 patients reported an increase in low-nuclear swollen homogeneous bundles of collagen fibres and marked rarefaction, splintering and fragmentation of the elastic fibres. The capillaries were distended and exhibited endothelial swelling and the arterial vessels in the corium exhibited marked increases in wall thickness. Infiltrates predominantly of the lymphocyte type were found around the blood vessels as was confirmed by other authors (Harris and Adams 1967, Walker 1975). Tests on the blood vessels of animals that had been exposed to VC carried out by Viola in 1970 revealed corresponding pathological changes such as endothelial fibrosis, thickening and dissociation of the elastic tissue, partial hyalin degeneration and proliferation of the connective tissue, together with thickening of the media. The striking elongation and coiling of blood vessels reminiscent of cirroid aneurysms were also observed among the changes

in the blood vessels found in rheumatoid arthritis ((Laws et al 1963, Laws et al 1967, Scott et al 1967)). The post-mortem angiographs of the hand carried out by these authors which were subsequently confirmed by histological tests on pathological sections of the vessels revealed extensive destruction of the elastic tissue in the region of marked elongation of the blood vessels which was regarded as being the cause of the elongation and probably also accounts for the similar changes observed in vinyl chloride disease.

Surprisingly there did not appear to be an unequivocal correlation between the clinical pattern of the symptoms and the morphological changes detected by X-rays in the patients affected by VC whom we examined. For instance we were surprised to find that in one patient the arteriographic findings were virtually completely negative in spite of classically pronounced symptoms, whereas in a second patient (Figure 7) who presented relatively uncharacteristic local findings and a normal stratification sample (?) accompanied by severe pain there was no evidence of occlusion of the digital arteries although he presented the corkscrew-like coiling of the blood vessels characteristic of the condition. Investigations spaced over several years which we were able to carry out with 3 of our patients did not reveal any marked change in findings. In particular, there was no evidence of a reopening of the closed vessels.

The present investigations cannot make an unequivocal contribution to the problem of the true incidence of vascular changes attributable to VC, as a precisely ordered sequence of angiographic and histological tests is out of the question on ethical grounds and because of the current absence of information on the results of therapy. Experience to date indicates that we may assume that if investigation techniques capable of providing meaningful results are used it will be found that the contribution of vascular damage to the problem as a whole

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is undoubtedly greater than has been thought hitherto and it will be possible to achieve the desired elucidation of the causes of changes in the peripheral vascular system in problematical individual cases. Our own experience shows that it is possible to detect changes in the blood vessels even after a long period during which the subject has not been exposed to VC. This is an aspect of the question that may also be significant in the assessment of cases*.

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* Translator's Note: Presumably for compensation purposes.

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CAPTIONS TO ILLUSTRATIONS

- FIGURE 1: S. O. Age 47. 11 years' exposure to VC.
Acro-osteolysis of 2nd and 3rd fingers.
Extensive occlusion of the A princeps pollicis and the Aa digit palm. superf. propriae. on 2nd and 3rd fingers radial. Localised stenosis of arteries of 5th finger. Acral hypervascularisation of 1st, 2nd and 3rd fingers.
- FIGURE 2: S. O. Age 47. 11 years' exposure to VC. Second finger of left hand. Acro-osteolysis. Occlusion of A dig. palm. superf. prop. rad. Narrowing of A. dig. palm. superf. prop. uln. Acral hypervascularisation.
- FIGURE 3: H. H. Age 48. 16 3/4 years' exposure to VC. Occlusion of Aa. dig. palm. superf. rad. and uln. of 3rd, 4th and 5th fingers. No acro-osteolysis.
- FIGURE 4: K. H. Age 56. 20 years' exposure to VC. Extensive occlusion of Aa. dig. palm. superf. ulnaris on 2nd, 3rd and 4th fingers. Opening-up of Aa. dig. transversa distalis and proximalis..
- FIGURE 5: W. J. Age 53. 15 1/2 years' exposure to VC. Left thumb. Localised stenosis of A. princeps pollicis.
- FIGURE 6: D. A. Age 32. 5 1/2 years' exposure to VC. Acro-osteolysis of 2nd and 3rd fingers of right hand. Narrowing of Aa. dig. palm. superf. prop. with retarded perfusion.

FIGURE 7: F. W. Age 54. 20 years' exposure to VC. Generalised elongation and tortuosity of Aa. dig. palm. comm. and AA. dig. palm. superf. prop. No occlusion of blood vessels.

FIGURE 8: M. W. Age 46. 1 3/4 years' exposure to VC. 4th finger of left hand. Extensive occlusion of A. dig. palm. superf. prop. radialis with opening-up of A. dig. transversa distalis.

FIGURE 9: K. H. Age 56. 20 years' exposure to VC. 2nd and 3rd fingers of left hand. Occlusion of Aa. dig. palm. superf. ulnaris with collateralisation over Aa. dig. transversae distales.

FIGURE 10: Z. R. Age 45. 8 1/2 years' exposure to VC. 2nd finger of left hand. High degree of stenosis of A. dig. palm. superf. propr. radialis. Opening-out of A. digitalis transversa distalis, which exhibits considerable elongation and serpentine coils.