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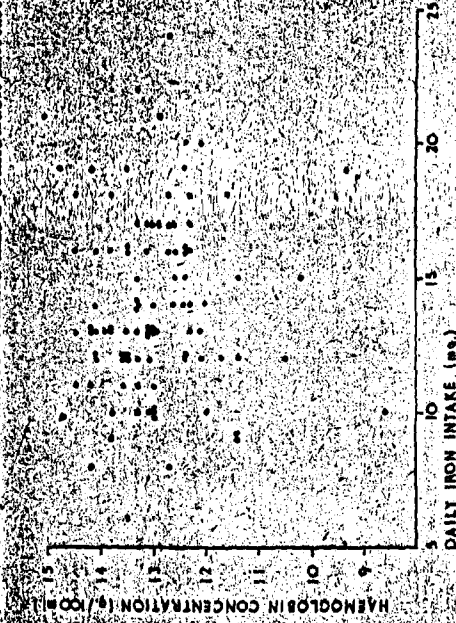
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though not to the same degree as fully ionized iron (Hussain, Walker, Layrisse, Clark, and Finch, 1965). Elwood (1963) has shown that the iron normally added to white flour is very poorly utilized. The present data suggest that the iron content of food is not a limiting factor in maintaining iron balance in normal individuals, and it must be assumed that a considerable increase



DAILY IRON INTAKE (mg.)

Dietary iron intake and haemoglobin concentration in healthy women aged 20-69 years.

in absorption from dietary sources is possible under the stimulus of iron deficiency. The total amount of iron in the diet may be more important at levels of intake below 6 mg. daily and in individuals with impaired absorption.

Mean iron intake and haemoglobin levels are both higher in than in women, but there is no correlation between these two factors in either sex. In women anaemia is almost entirely confined to those still menstruating. Though haemoglobin levels are significantly lower under the age of 45 years there is no significant difference in iron intake between the younger and older women. These findings suggest that dietary iron

intake may be a less important factor than menstrual blood loss in the aetiology of iron deficiency in women. They are in keeping with the observation of Hallberg, Hogdahl, Nilsson, and Rybo (1966) that there is a fall in haemoglobin concentration in women when menstrual loss exceeds 80 ml. (equal to 2 mg. of iron daily) and a fall in serum iron level when it exceeds 60 ml. (equal to 1 mg. of iron daily). Garby (1966) states that only a few individuals are in negative iron balance on a daily intake of 10-13 mg. It seems likely that in a normal population iron loss from the body is the most important determinant of iron status and that dietary iron is only limiting at very low levels or in individuals with a high iron loss.

Summary

A dietary survey in apparently healthy subjects showed no relation between iron intake and haematological status. It is suggested that iron loss from the body rather than dietary iron intake is the major determinant of iron status in normal individuals.

We should like to thank Professor H. Scarborough for his encouragement and the Medical Council for a grant to R.H.D.

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Acro-osteolysis Occurring in Men Engaged in the Polymerization of Vinyl Chloride

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[WITH SPECIAL PLATE BETWEEN PAGES 708 AND 709]

Brit. med. J., 1967, **3**, 712-714

The polymerization of vinyl chloride has been undertaken in this and other countries for over 20 years without apparent harm to the workers, apart from some accidental exposure to the vapour of vinyl chloride, the anaesthetic effects of which have been well known for years. The process consists, briefly, in submitting a mixture of liquid vinyl chloride and water in the presence of a catalyst to the effects of heat in large pressure vessels known as autoclaves. This produces polyvinyl chloride in a solid or latex form which is discharged from the vessel and can be elsewhere to be dried into a powder. When the autoclave is emptied at this final stage a deposit of white polymer is found on its inner wall. Air is then blown through the open vessel for at least a quarter of an hour, after which an atmosphere test for vinyl chloride is done inside it. If the autoclave is found to be clear of vinyl chloride vapour the cleaner enters to scrape the wall with a small hand pallet.

An unusual condition affecting two men employed as autoclave cleaners in this process was first reported by Cordier *et al.* (1966). After doing this work for several months they developed symptoms resembling those of Raynaud's phenomenon and later a skin eruption of the hands, and in one case of the forearms, together with general asthenia and drowsiness. The most striking sign, however, was the radiological evidence of lysis of some terminal phalanges of the hands, and in one case of the feet. Most of these abnormalities disappeared and the bones showed signs of healing a year or two after the men had stopped work.

In view of that article, the hands of 588 men engaged in the manufacture of polyvinyl chloride were radiographed in

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April 1966—150 of them were autoclave cleaners. Two cases with x-ray changes in the fingers similar to those described by Cordier *et al.* (1966) were found.

Case 1

A 44-year-old man who had worked on the autoclave section of the plant since 1950 had an interesting history in that he was diagnosed as a case of scleroderma by a consultant physician and dermatologist in 1957. The diagnosis was made on clinical grounds because of Raynaud's phenomenon, accompanied by puffiness of the face and thickening of the skin of the hands, fingers, and left forearm. The symptoms cannot have been very troublesome, because he had made no complaint, and the condition was noticed by his doctor only when he went to collect a prescription for his wife.

On being questioned about his condition during the present investigation he still made no complaints, and it was only with reticence that he admitted that his hands often felt unduly cold. Examination revealed no evidence of the skin condition that had existed in 1957, and the only abnormalities were: (a) pseudoclubbing of all the fingers of both hands; this is not true clubbing, since the angle between the base of the nail and the adjacent skin was not obliterated; and (b) the liver was palpable on inspiration.

Radiological Reports.—*Hands*: Periarticular erosions are present in the proximal interphalangeal joints. The proximal interphalangeal joint of the left little finger is disorganized. There are erosions of the terminal phalanges of index and middle fingers of both hands (Special Plate, Fig. 1). *Feet*: The fifth proximal phalanges of both feet show erosions on both their distal ends. The fifth proximal interphalangeal joint is disorganized on the left (Special Plate, Fig. 2). *Pelvis*: There is a widening of the joint space of the sacroiliac joint with cystic marginal sclerosis. *Chest*: Normal. *Skull*: Normal. *Cervical spine*: Normal. *Teeth*: Normal. *E.C.G.*: Normal.

Laboratory tests were carried out, and the only abnormality found was a persistently raised serum bilirubin.

Case 2

A 30-year-old man who had been an autoclave cleaner since 1960, having been self-employed as a window-cleaner before that date, recalled no previous serious illness, but had consulted his doctor in 1964 because of shortening of his finger-nails, which he thought to be due to biting them and "lack of calcium."

In April 1966 he had no symptoms, but radiologically he showed evidence of acro-osteolysis. Pseudoclubbing of the fingers was found to be present (Fig. 1). Raised nodules in the skin, described as "xanthomatous-like" patches, were noted round his wrists.

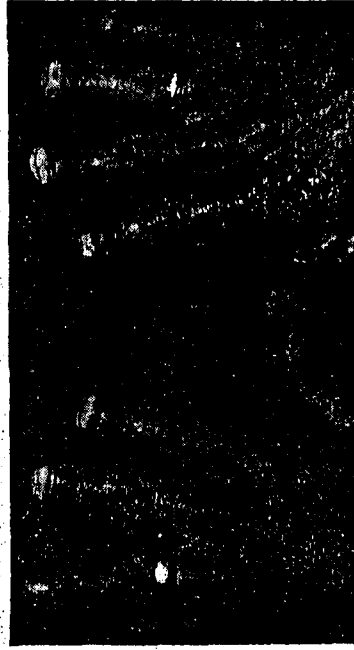


FIG. 1.—Pseudoclubbing of the fingers.

Radiological Reports.—*Hands*: Osteolysis is present in the shafts of all the terminal phalanges of the fingers and thumb, with the exception of the left ring finger" (Special Plate, Fig. 3). (Incidentally it is of interest to note that in most of the x-ray films of these cases seen by us here and in America the ring finger is unaffected.) *Sacrum*: Widening of the joint spaces of the sacroiliac joint with cystic marginal sclerosis (Special Plate, Fig. 5). *Chest*: Normal.

The most notable feature was the comparative absence of abnormal findings, apart from those shown on the x-ray films. Laboratory tests showed nothing abnormal.

In July, however, he came to see one of us (W. G. F. A.) complaining of fairly persistent pain and frequent attacks of coldness in the fingers, accompanied by pallor. On examination at this time there was some tenderness of the finger-tips, more skin nodules were seen to be developing on the dorsum of his fingers, and some thickening and coarsening of the skin of the face was noted.

In the course of the next week or two the pains in the fingers and metacarpophalangeal joints increased, and Raynaud's phenomenon was troublesome even in warm weather. He was therefore admitted to hospital in August for further investigation.

The same tests as on the previous occasion were repeated, and once again the results were within normal limits, except in the case of the serum proteins. In this test the serum α_2 -globulin was 1 mg./100 ml. (normal 0.4–0.8 mg.). Hyland screening tests for rheumatoid arthritis and lupus erythematosus were normal. Serum transaminase was within normal limits. The E.S.R. had fallen to 4 mm. in one hour (Westergren). Blood pressure was 140/80.

Skin biopsy was performed on one of the nodules on the wrist, the histological report being as follows: "The full thickness of the dermis is incorporated in an interlacing acellular collagenous nodule, oedematous and partly hyalinized, enclosing normal sweat glands and covered by normal epidermis (Fig. II). The oedematous interstices contain a fine granular and filamentous material, meta-chromatic with toluidine blue, and staining faintly with alcian blue and periodic-acid Schiff, probably breaking up elastic (Fig. III). Two small dermal arteries are extremely thick-walled as a result of marked medial hypertrophy and intimal fibrous

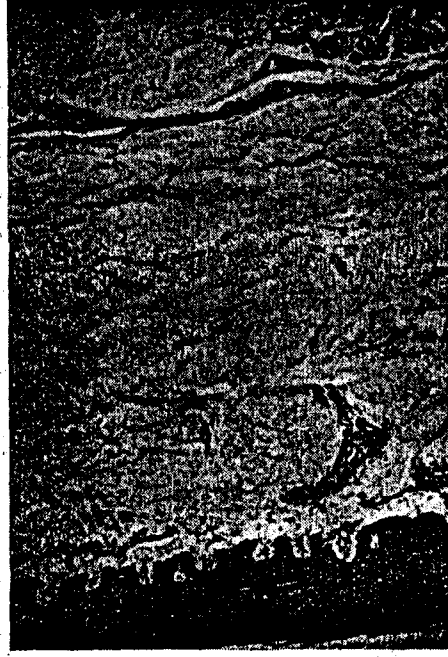


FIG. II.—Case 2. General appearance of thickened dermal collagen—also showing lymphocytic cuffing of small dermal blood vessel. (H. and E. $\times 55$.)

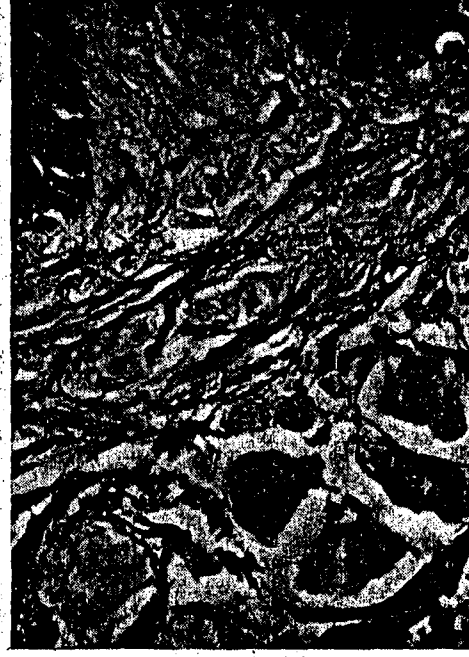


FIG. III.—Case 2. High-power view of fragmented elastic in upper dermis. (Verhoeff. $\times 270$.)

thickening (Fig. IV). The appearance is similar to those described by Cordier *et al.* (1966).

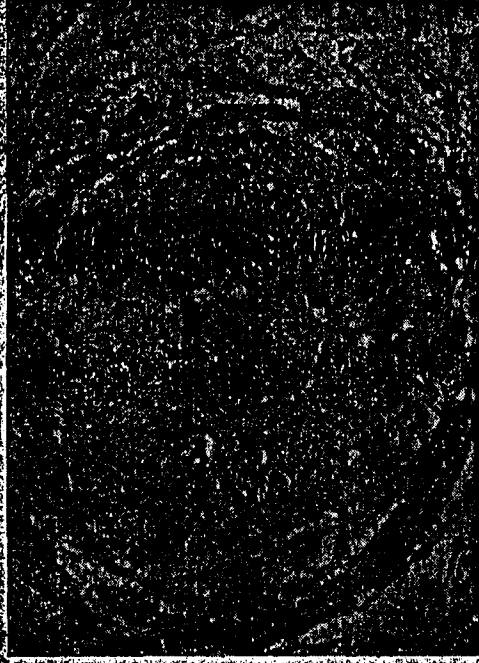


FIG. IV.—Case 2. High-power view of artery situated deeply within the zone of thickened dermal collagen. (H. and E. $\times 180$.)

For a few months after his discharge from hospital he improved, and by the end of 1966 the Raynaud's phenomenon was less marked and the skin nodules were disappearing. About this time, however, he began to develop pain in the left knee and toes. X-ray examination of the left knee showed a cortical erosion on the posterior surface of the patella (Special Plate, Fig. 4). By June 1967 he felt reasonably well, though he still complained of pain in the left knee and stiffness of the hands, particularly at the metacarpophalangeal joints. The skin of the hands and face was practically normal.

Comment

No treatment was required in Case 1, and the treatment in Case 2 was directed towards relieving the symptoms, since no specific remedy is known for the condition.

Both men were removed from the job of autoclave cleaning as soon as the diagnosis was made, but it is not yet certain how this measure will affect the course of the illness. It would appear that Case 1 went through the acute stage while still doing his normal job, and the condition has become quiescent in spite of this.

Two more possible cases were found in our most recent survey. One of these is a 30-year-old autoclave cleaner who has had Raynaud's phenomenon for three years, but in whom no bony changes have been found. The other man is an ex-autoclave-cleaner in whom a suspicious appearance has been noted radiologically in the right thumb, which had, however, been recently subjected to injury.

Discussion

In view of the similarity of the findings in these men to the cases described in the paper of Cordier *et al.* (1966), it was thought that this condition was almost certainly linked with the men's occupation. Inquiries subsequently made in America and Europe revealed that similar cases had occurred there. In all cases the features appearing most consistently were Raynaud's phenomenon accompanied by osteolysis of the terminal phalanges of the fingers, occurring mainly in autoclave cleaners and not in those engaged in handling the finished product.

Many raw materials may be used in small quantities in manufacturing the polymers but the only substance common to all cases is probably vinyl chloride. Though every autoclave is washed with water and has air blown through it at the end of each reaction, small quantities of vinyl chloride may remain and escape when the vessel lid is opened. It is also possible that very small pockets of gas may be trapped beneath the polymer adhering to the inner wall, and these can be liberated during the subsequent cleaning process. Vinyl chloride, however, has been manufactured and handled in this country for over 20 years without apparent harm apart from accidental exposure to its well-known anaesthetic action.

A point of general interest is the possible relationship of this condition to the collagen diseases. One patient (Case 1) had, in fact, been diagnosed as a case of scleroderma on clinical grounds 10 years previously. The histologist remarked on the superficial similarity of the biopsy taken in Case 2 to scleroderma, but a number of pathologists consider the appearance of the section to be unique. Cordier *et al.* (1966) mention an unusual skin condition seen in their cases. Suciu *et al.* (1963), in a paper describing conditions produced by vinyl chloride, referred to a skin lesion resembling scleroderma, but acro-osteolysis was not mentioned.

Finally, at a clinicopathological conference at the Royal Postgraduate Medical School (*B.M.J.*, 1966) it was stated that bony changes were commonly found in the terminal phalanges in scleroderma. It should be made quite clear, however, that the many radiologists who have looked at the films of our cases stated that they had not previously seen this particular lesion.

It would appear from our own and other cases that this condition is probably a self-limiting disease, which in spite of bone destruction leaves the patient with little disability. In x-ray films taken a year after the original diagnosis no further bony changes were noted in Case 1. In Case 2, however, there was evidence of partial ossification of the osteolytic bands in the terminal phalanges of both hands.

It is our intention to continue annual radiological examination of the hands of all men engaged on this work. Mechanical methods of cleaning new autoclaves have been introduced, and it is hoped in due course to extend this method to older vessels and thus eliminate the human factor.

Summary

Two cases of acro-osteolysis occurring in men engaged in the polymerization of vinyl chloride are described. The bones affected were the terminal phalanges of the fingers and the sacroiliac joints, but in one case the patella and in the other the phalanges of the feet were involved. The condition was accompanied by Raynaud's phenomenon and skin lesions.

It would seem that this condition is probably a self-limiting disease.

We acknowledge with gratitude the help given throughout this investigation by Dr. Thelwall Jones and other members of the medical staff of the David Lewis Northern Hospital, Liverpool, and by Dr. K. A. Rowley and his colleagues at Blackpool Victoria Hospital.

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