

# PREVENTION AND MITIGATION OF FLUOROSIS (ENDEMIC)—PART II

BY T. K. WADHWANI

*(Section of Pharmacology, Indian Institute of Science, Bangalore-3)*

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## SUMMARY

(1) Methods have been discussed for the prevention of endemic fluorosis.

(2) Results have been presented to indicate the ameliorative role that Vitamin C can play in humans in mitigating the toxicity of ingested fluorine.

The supply of fluorine-free water would obviously be the best method of preventing the incidence of fluorine poisoning. Though, in some cases, such a method can be resorted to, considering the very wide distribution of fluorides in nature, it cannot be recommended as one universally feasible. Besides tapping of the new sources of fluorine-free water, it would involve either long distance connection with the source of fluorine-free water, or large migration of people from one site to another, or in other words, the regrouping of villages in accordance with the availability of fluorine-free water. It may not be found difficult to adopt the first two methods, but the difficulties inherent in the last procedure are such as are very likely to render it impracticable, and in some cases, even well-nigh impossible.

Under such circumstances, the alternative would be to remove fluorine from the available source of water. Various methods have been developed for this purpose, and some of the methods have attained a considerable measure of practical success in other countries, but under the conditions obtaining here, the methods will be found almost prohibitive in cost. Considering, besides the high cost, that, for the successful working of these methods, a certain degree of technical knowledge and skill is required on the part of the operator, and considering also that every house or locality has got its own water-supply, the use of these methods does not seem to be immediately possible. It, however, cannot be ruled out that, in areas, where the arrangements can be made for the provision of a common water-supply, some of these methods may be found feasible.

Owing to the limited applicability of the above two methods under the existing conditions in this country, the only remaining approach to the problem of fluorosis, that is the one requiring the mitigation of the toxicity of ingested fluorine with dietary and chemical methods, acquires an added importance. Particularly in areas where there is no immediate prospect of eliminating fluorine from drinking water, it has become highly imperative that attempts should be made to lessen the severity of the disease with dietary and chemical means. In this context, it needs to be mentioned that it has been shown (Wadhvani, 1952) that, in monkeys, placed on normal diet and receiving fluorine in the concentration of 10 mgm. of NaF per kg. of body weight, per day, the daily administration of 20 mgm. of vitamin C, as revealed by X-ray examination, prevents the development of fluorosis of bones, and in monkeys, suffering from severe bone fluorosis, in conjunction with the simultaneous withdrawal of fluorine from the rations, restores the skeletal structures to some sort of normalcy. Such findings would normally suggest a method for the prevention and cure of human fluorosis; but it may well be argued that endemic fluorosis is not quite identical with the experimental one. Fluorosis in experimental monkeys has been produced under normal dietary conditions, and its cure, though the term cannot be employed in the strict sense of its meaning, has been effected by the administration of large quantities of vitamin C and the simultaneous cessation of fluorine intake. No studies have been carried out to investigate the effect of administration of large quantities of vitamin C in monkeys suffering from severe bone fluorosis and still receiving fluorine in the concentration mentioned. Endemic fluorosis is sometimes complicated by dietary deficiencies, and for its mitigation with vitamin C, at least under the present circumstances, the prevention of ingestion of fluorine cannot be accomplished on any big scale by supplying fluorine-free water. For such reasons, it may be inferred that the administration of vitamin C in endemic cases may not yield results similar to those obtained in monkeys, but that is only one side of the picture. For the other side of it, there are the following observations and arguments to be taken note of.

1. The interference of fluorine in the metabolism of nitrogen, calcium and phosphorus represents, in part only, the action of fluorine in the system. The protective action of high calcium and phosphorus, and high protein diets is due to the partial neutralisation of some of the effects of fluorine, and is determined by the degree of this partial neutralisation. As fluorine is a systemic poison, and fluorine toxicosis a generalised systemic reaction, the ameliorative effect of any constituent will be maximum if the particular constituent is as systemic in its effect as fluorine is in its toxicity. From such

a view-point, vitamin C should be considered as one of the most useful agents in the mitigation of the toxicity of ingested fluorine.

2. "Chronic fluorine toxicosis has been observed to be involved in some manner with the functions of vitamin C, either by direct interference and inhibition, or by eliminating the mechanisms through which vitamin C functions in the organism." An increase in the vitamin C content has been observed in the kidney, liver, anterior lobe of the hypophysis and the suprarenal cortex of the cattle, ingesting 0.088% fluorine with the grain mixture (Phillips and Stare, 1934).

3. The following points of similarity have been noted between scurvy and the syndrome of chronic fluorosis:—

(a) The hæmorrhages of the pyloric mucosa have been observed to be common in the rats, suffering from chronic fluorine poisoning produced by feeding sodium fluoride in the concentration of 0.15% of the diet.

(b) In some cases, mottled enamel has been found to be without the inter-cementing material, normally found between the enamel rods (Hauck *et al.*, 1933), and not observed in vitamin C deficiency.

(c) In experiments with acutely toxic doses of sodium fluoride for rats, it was found (Phillips and Chang, 1934) that 4 c.c. or more of orange juice fed with the diet prolonged the survival period of young growing rats, fed sodium fluoride in the concentration of 0.2% of the diet.

(d) In the experimental monkeys, the changes in the bones noted by Pandit and Rao (1940) are mainly of the nature of diffuse periostitis. According to Ellis (1939), the absence of vitamin C in the diet can cause diffuse periostitis in children.

(e) The urine of the experimental monkeys contained homogentisic acid, indicating an interference with the metabolism of phenylalanine and tyrosine (Pandit and Rao, 1940). The excretion of homogentisic acid and other tyrosine metabolites has been noted in the case of vitamin C-deficient guinea pigs (Sealock and Silberstein, 1939, 1940). The excretion of these metabolites in the vitamin C-deficient guinea pigs has been prevented by the administration of vitamin C, and the prevention has been found to be inherent in the anti-scorbutic activity of the vitamin.

(f) There has been noticed a drop in the activity of certain enzymes like liver esterase, phosphatase, succinic dehydrogenase, cytochrome oxidase with the depletion of the vitamin and the development of scurvy (Harrer and King, 1941). Though the opinions regarding the *in vivo* action of fluorine

on these enzymes have been conflicting, *in vitro*, fluorine has been found to inhibit these enzymes.

(g) The rate of oxygen uptake of the suprarenal tissues from scorbutic and fluorine poisoned guinea pigs has been found to be half of that of the tissue from the normal control animals. The deleterious effects of fluorine poisoning and vitamin C deficiency have been shown to result from disturbances in specific phases of cellular respiration (Phillips, Stare and Elvehjem, 1934).

4. Human fluorosis is the result of intake of fluorine in very small quantities over considerably long period. The quantities of fluorine daily ingested, as compared to those administered to experimental monkeys, are so small as might not be expected to affect seriously the ameliorative effect of vitamin C.

Based on the above observations and arguments, work was carried out on the effect of vitamin C in human fluorosis. From a village called Podili, in the District of Nellore, where fluorosis in humans and cattle is highly endemic, nine human subjects of different age and in different stages of fluorine poisoning were selected for the study. The whole skeletal system of the subjects was examined with X-ray, and the pictures of bones, showing symptoms of fluorine poisoning, were taken. All the nine subjects, who looked otherwise healthy, complained of pain in the joints, particularly in the pelvis, of tingling sensation in the extremities and considerable difficulty and pain in the movement of the limbs, in squatting and lying down. Some of them suffered from occasional bleeding from gums. In six out of the nine subjects, the skeletal picture, as revealed by X-ray, was more or less the same as has been described by Roholm (1937), Shortt *et al.* (1937), Greenwood (1940), Khan and Wig (1945) and Lyth (1946). In the remaining three subjects, the picture was different in the following respect. Roholm (1937) has characterised the disease as diffuse osteosclerosis in which the pathological formation of bone starts both in periosteum and in endosteum; whereas, in the three subjects, it was observed that the bone suffered from osteoporosis and osteosclerosis at the same time. It appeared as if the calcifying elements were taken away from one part of the bone and deposited in another, causing osteoporosis in the first and osteosclerosis and exostoses in the second.

From 18th January 1950 to 28th February 1950, each subject was given 100 mgm. of vitamin C daily. During this period, the subjects consumed the same diet and water which they ordinarily do. As has been indicated in the first part of this piece of investigation, under the present circumstances,

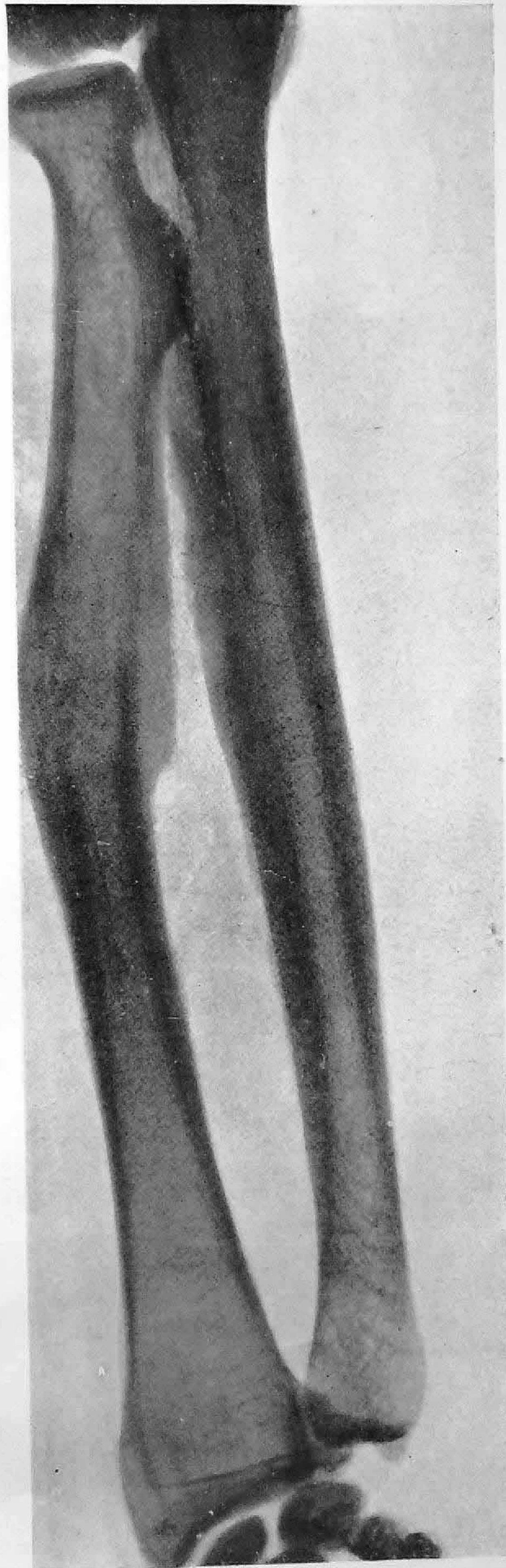
the only criteria for determining the ameliorative effect of any drug or dietary factor in fluorosis are the length of the period of survival of the subject and the degree of general improvement as evidenced by the X-ray examination of bones, or the degree of general relief as best judged by the subject or by the observer. Accordingly, all the subjects were examined again with X-ray on 1st March. All the nine subjects, irrespective of age and the severity of the disease, reported less pain in the joints, reduced tingling sensation in the extremities, and some improvement in the movement of the limbs, though, all of them, in the first three weeks after the start of the treatment, complained of severe pain all over the body, as distinguished from pain in the joints and difficulty in the movement of the limbs. In the absence of any analysis of blood, urine and faeces regarding the changes attendant upon the administration of vitamin C, it is difficult to explain the cause of the increased generalised pain in the body during the first three weeks of the administration of vitamin C. Nevertheless, it would be safe to assume that the increased generalised pain cannot be due to the intake of vitamin C as it has not been shown to exert any toxic action. The increased generalised pain might be due either to the release of fluorine from the bones in the blood where it would exert its toxic action before its excretion through the kidney, or due to some process of rearrangement taking place in the bone as a result of administration of vitamin C, or due to both these causes.

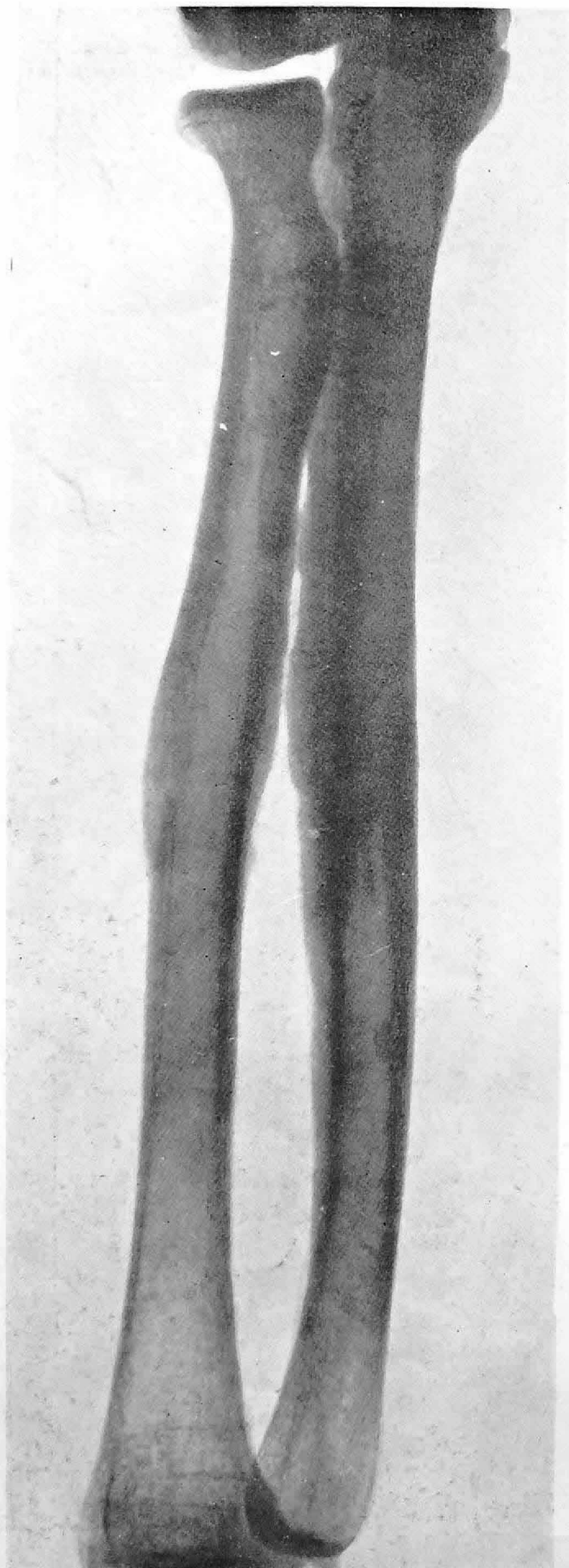
The X-ray examination of bones on 1st March 1950 showed noticeable decrease in the size of the exostoses. The decrease was more distinct in the ribs. This was observed in all except two cases, 45 and 50 years old. Though these two cases reported general relief and lessening of pain in the joints, no significant change was observed either in the general appearance of the bones or in the size of the exostoses.

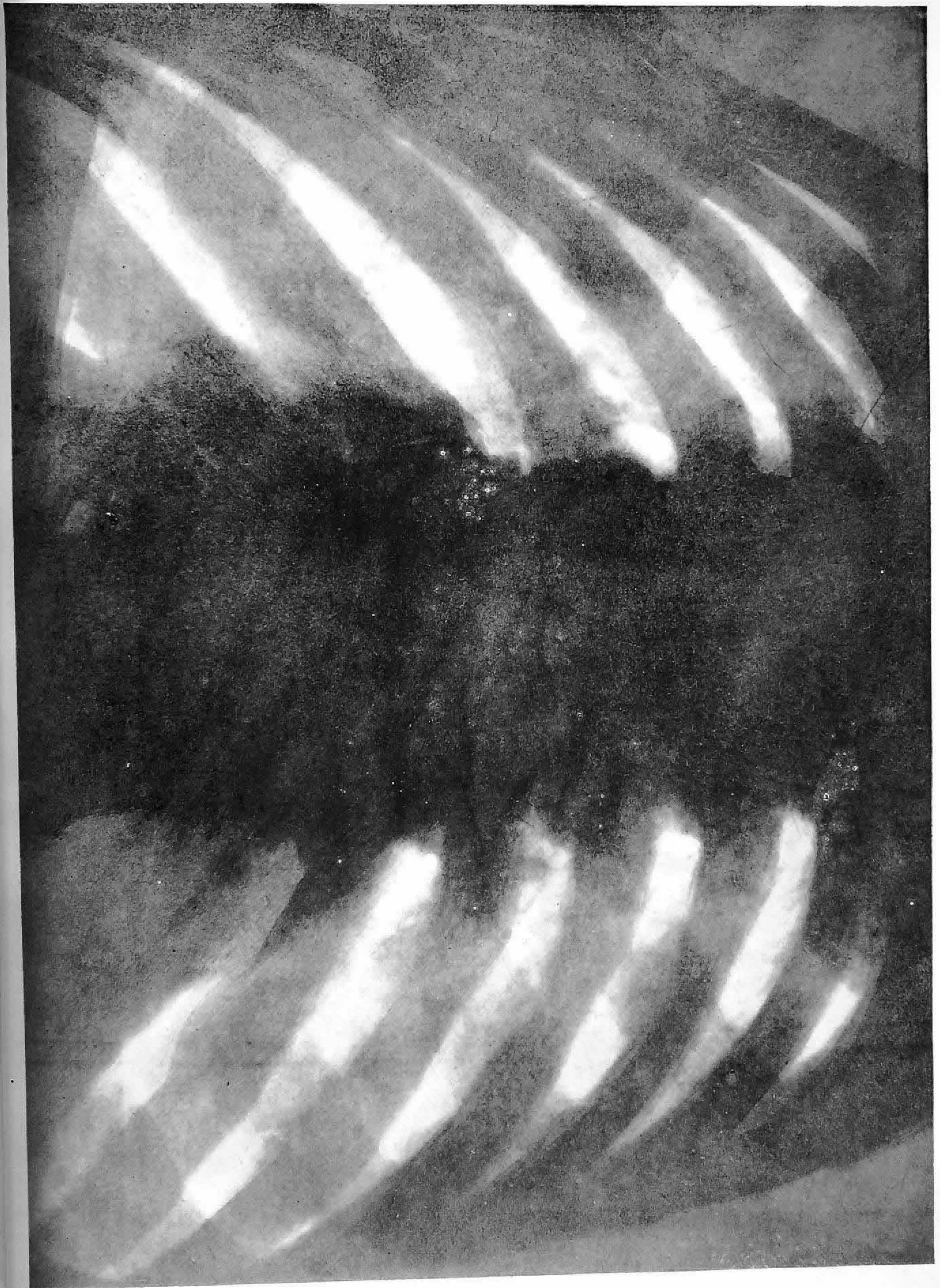
Due to circumstances beyond control, the administration of vitamin C to the subjects was discontinued on 2nd March 1950.

The results obtained, though are highly qualitative in nature, and may require confirmation under the different conditions of endemic fluorosis, are, nevertheless, sufficiently indicative of the ameliorative role that vitamin C can play in humans in mitigating the toxicity of ingested fluorine. The sole object of publishing these results, qualitative as they are, is to attract the attention of those concerned to the solution of the problem of endemic fluorosis.

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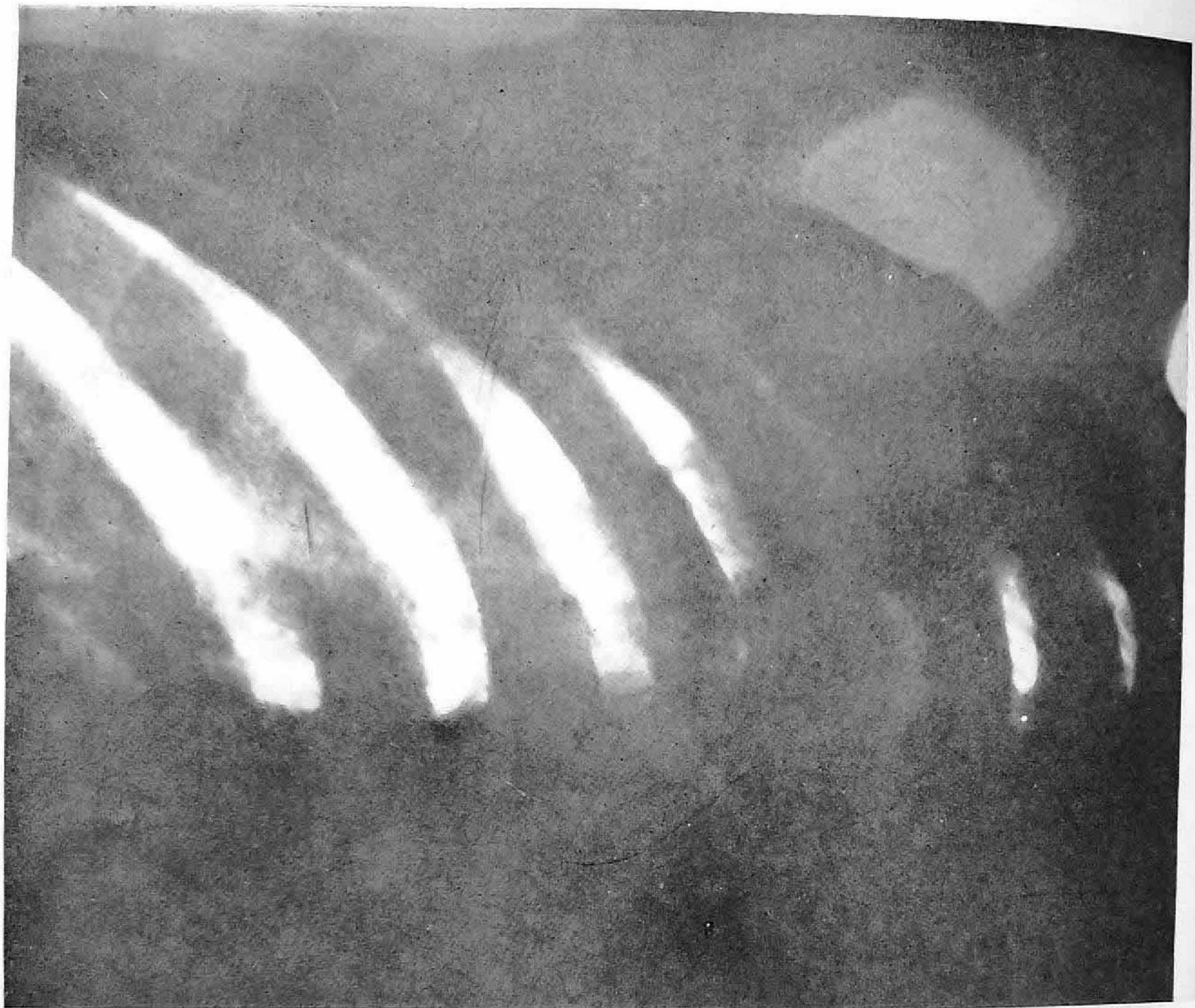
## EXPLANATION OF PLATES

PLATE VIII. Skiagram of radius and ulna of 25 years old male human subject suffering from endemic fluorosis.

PLATE IX. Skiagram of the same radius and ulna after the subject had been given daily 100 mgms. of vitamin C for 42 days.

PLATE X. Skiagram of the ribs of 40 years old male human subject suffering from endemic fluorosis.

PLATE XI. Skiagram of the same ribs after the subject had been given daily 100 mgms. of vitamin C for 42 days.



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