Conclusion

Man in his own estimation is the most important and culminating result of evolution in nature. How far this may be from the truth past events in the evolution of living things, which for a time dominated the earth and passed away, has shown, and as for the future, we cannot see it, so it behoves us to take a humble view, especially in the light of the most recent achievements of *Homo sapiens*. From our immediate point of view, however, we must consider man as just one unit in the vast complex of nature and realize that too great success may be disastrous. If he eliminates all the pests and diseases which afflict him he may multiply and eat up the earth and so destroy himself as the result of his success.

For these reasons, I would like to sound a note of warning against the danger that pests such as I have described should be treated, when preventive measures are considered, as if they produced their harmful results without reference to accompanying factors in their natural surroundings. Control measures must be devised in relation not only to destruction of a specific pest but in relation to all other circumstances which might follow the elimination of a single important unit in an ecological complex. Thus if the object in some areas is the complete removal of trypanosomiasis or piroplasmiasis we must first consider whether this would not involve the production of a still more serious problem of soil erosion. Preventive or eradication measures in such a case would have to be carefully planned in collaboration with experts on land usage *before* being put into operation, or we might find ourselves in the position of regretting the results of successful eradication when irreparable damage to the land had supervened.

In other words, an all-round approach must be made, and only after careful preparatory research should important measures of control be undertaken.

It must be remembered that in the case of bovines, which alone I have been able to consider, the chief evil at present is overstocking, and this is due to limitation of grazing lands by parasites of one sort or another. The scientific way of approaching the problem when eradication of pests is undertaken would be, in the first place, to use the method to reduce overstocking in areas already free of the particular pest or pests, and only then to try to increase the total head of cattle by extending still further the use of pasturage made safe by the eradication measures.

The theme, therefore, on which I would wish to close my address is a quotation from the report by H. E. Hornby on *Animal Trypanosomiasis in East Africa, 1949*, because I am sure that he would agree that his words have a wider significance than the context in which they were used. The quotation is: "The point to be driven home is that animal husbandry demands both pasture management and disease control. Improvement of pastures often encourages parasites by giving these protection from the sun, therefore it must be accompanied by disease control. This alone leads to overstocking, so it must be accompanied by pasture management to save the soil."

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RADIATION CANCER OF THE PHARYNX

BY

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There have been many examples of radiation cancer of the skin, but only a limited number of cases have so far been reported in which a tumour has developed in the deep tissues as a sequel to external therapeutic irradiation. The case histories of four patients who developed tumours in the laryngopharynx many years after irradiation of the neck may therefore be of some interest.

The majority of radiation tumours in the deep tissues have been sarcomata, which have arisen in bone. Hatcher (1945) reported three cases of sarcoma developing in irradiated bone, and reviewed the literature on the subject. He found a total of 24 cases. In 17 of these the condition primarily treated by irradiation was tuberculous arthritis, and the interval between irradiation and the appearance of a tumour varied between 3 and 12 years. There was a tendency for these tumours to develop when irradiation had been carried to excess in the form of repeated doses administered over a long period of time.

The only other cases in which cancer has been recorded as developing in the deep tissues after external therapeutic irradiation may conveniently be considered together, since their sites of origin lie within a somewhat limited anatomical field. Four of these tumours occurred in the laryngopharynx, one arose in the larynx, and one in the thyroid gland.

The first case was reported by Lossen (1936). A man was given x-ray treatment from 1919 to 1922 for tuberculous glands in the neck. In 1929 he developed a necrotic ulcer in the skin of the neck, and in 1935, 13 years after treatment, he developed a carcinoma of the larynx.

Kruchen (1937) reported the case of a woman aged 65 who developed a tumour on the posterior wall of the hypopharynx 20 years after irradiation of the neck for a goitre. The tumour had the structure of a carcinoma simplex. The skin on the anterior aspect of her neck was grossly telangiectatic.

Kindler (1944) reported two further cases. In the first of these a man of 54 developed an adenocarcinoma in the left lobe of the thyroid gland 24 years after x-ray treatment for tuberculous glands in the neck. He had marked post-radiation atrophy and scarring in the overlying skin and subcutaneous tissues. His second case was that of a woman of 59 who developed a tumour almost completely surrounding the pharynx at the post-cricoid level 20 years after irradiation of her neck for thyrotoxicosis.

Den Hoed (1946) reported two cases he had seen, both within the space of a year. The first was that of a man aged 43 who developed a carcinoma of the aryepiglottic fold 27 years after irradiation of his neck for tuberculous adenitis. He had a necrotic ulcer in the irradiated area of skin. The second case was that of a woman of 41 who, 28 years after irradiation for tuberculous glands in the neck, developed a squamous-celled carcinoma involving the aryepiglottic fold and arytenoid cartilage. Three years before this a basal-celled carcinoma behind the ear and within the irradiated area had been excised.

The following patients were all seen in this department within the space of eighteen months, and came from various parts of the area served by this Centre. They were given x-ray treatment many years ago, and it has not been possible to obtain details of dosage or other factors relevant to irradiation.

Case Reports

Case 1.—A woman aged 69 was seen in March, 1949, with the complaint that her voice had started to become hoarse three months before. The only other symptoms she had were related to radiation dermatitis of the neck, which had been giving her trouble on and off for at least 20 years. In 1923 she had been given a course of x-ray therapy for thyrotoxicosis. The skin overlying the thyroid cartilage was telangiectatic, and the subcutaneous tissues were fibrotic. On direct laryngoscopy she was found to have a friable tumour on the medial wall of the left pyriform fossa with extension on to the aryepiglottic fold on the same side. Section showed this to be a squamous-celled carcinoma. The interval between irradiation and the appearance of a tumour was 26 years.

Case 2.—A woman aged 50 was seen in February, 1950, with a history of dysphagia, which had been progressive for the past year. In 1920, when 21 years of age, she was given a course of x-ray treatment for thyrotoxicosis. She was uncertain how long the treatment had lasted, but it was probably between nine months and a year. In 1937 she developed what she described as a growth in the skin immediately over the thyroid gland. This was excised and repaired with a skin graft. In the absence of a histological report it is not known whether the condition was malignant or necrotic. After this she remained well until the onset of her present symptoms. On examination she had a grafted area about 10 cm. square over the thyroid gland. Direct laryngoscopy revealed a tumour in the post-cricoid region, extending down to involve the first 2.5 cm. of the oesophagus and superiorly involving the pharyngeal surface of the aryepiglottic fold. Section showed the structure of the tumour to be predominantly that of a fibrosarcoma. The interval between irradiation and the appearance of a tumour was 29 years.

Case 3.—A woman aged 76 was seen in April, 1950, the presenting symptom being dysphagia. This had first been noticed about 18 months before, and had become progressively worse since its onset. More recently she had developed referred pain in the right ear. She had received x-ray treatment for thyrotoxicosis in 1922. She stated that treatment had been given once a week for a period of six months. In 1936 she had had a skin graft performed on the anterior part of her neck. On examination she had a hard tender gland in the upper part of the deep cervical chain on the left side, and there was a grafted area of skin over the thyroid cartilage. Oesophagoscopy revealed a granular bleeding stricture in the immediate post-cricoid region. Section showed the tumour to be a squamous-celled carcinoma. The interval between irradiation and the appearance of a tumour was 27 years.

Case 4.—A woman aged 49 was seen in August, 1950, and gave a history of having developed a sore throat about seven months before. This was associated with the sensation of

having a lump in her throat, which she could not swallow. More recently she had developed referred pain in the right ear. In 1919, at the age of 20, some tuberculous glands had been removed from the right side of her neck. After this she was given prolonged x-ray treatment to the neck. The total dose is not known, but treatment extended over a period of a year. On examination there were no obvious radiation changes in the skin of her neck. On direct laryngoscopy she was found to have a tumour arising from the posterior wall of the hypopharynx, just above and apparently involving the cricopharyngeal sphincter. Section of material removed at biopsy showed a highly infiltrative but moderately well-differentiated squamous-celled carcinoma. The interval between irradiation and the appearance of a tumour was 30 years.

Discussion

It may sometimes be difficult to decide whether a tumour in the deep tissues can be attributed to previous irradiation. Smith and Bowden (1948), in an attempt to determine whether uterine cancer followed the use of radium therapy for benign uterine conditions, investigated 805 proved cases of carcinoma of the body of the uterus. The criteria they adopted for the diagnosis of radiation cancer were (a) a ten-year interval between irradiation and the development of a uterine tumour; and (b) an originally confirmed negative endometrial biopsy. In only eight cases were these conditions satisfied. In the absence of any reliable figures for the natural incidence of uterine cancer they found it impossible to decide whether the irradiation of benign uterine conditions played any part in inducing cancer at a later date. It is suggested that the diagnosis of radiation cancer should be based on the following considerations.

1. It cannot be assumed that cancer has developed in response to previous irradiation unless this was used primarily in the treatment of a benign condition.

2. There must be a latent interval between irradiation and the development of a tumour. This has been a characteristic feature of all radiation tumours, and must therefore be regarded as an essential factor in the pathogenesis of radiation cancer. In a series of patients with skin cancer following therapeutic irradiation who were seen at the Radium Institute in Paris, the latent interval varied between 4 and 21 years (Lacassagne, 1945). The two cases reported by Walter (1950), in which epitheliomata developed in the skin of the neck within three months of irradiation, are without precedent and hard to explain.

3. It seems probable that neoplastic change occurs only in tissues which have suffered appreciable radiation damage. Skin cancer supervenes typically in an area of skin showing obvious radiation changes, and radiation tumours which have developed in the deep tissues have been accompanied by gross changes in the overlying skin and subcutaneous tissues.

4. There should be histological proof of any tumour which is suspected of arising as a result of irradiation. A late necrosis might simulate malignant disease.

5. Radiation tumours often display some abnormality in respect of sex and age incidence, anatomical site, or microscopical appearance when these are considered either separately or in relation to one another. It is not uncommon to find atypical forms of squamous carcinoma in radiation cancer of the skin, and tumours in this situation may be fibrosarcomatous or have a pseudosarcomatous appearance (Lacassagne, 1945). The incidence of chondrosarcomata is high in tumours which have developed in irradiated bone (Hatcher, 1945). The way in which age, sex, and site may indicate the nature of a tumour is well illustrated in one of den Hoed's cases where a carcinoma of the aryepiglottic fold occurred in a woman in the fourth decade of life. As he points out, this is exceptional.

The four patients whose case histories are presented above have certain features in common, apart from their site of origin. In all of them neoplastic change occurred after a long latent interval, which varied only between 26 and 30 years. They were all treated originally for benign conditions, and in three of them it is known that frequently repeated doses of x rays were given over a period of six months or more. In the three patients treated for thyrotoxicosis the tumours had arisen approximately 4 cm. deep to the centre of the irradiated area of skin, and these three patients had all suffered severe radiation damage to the skin, two of them requiring excision and plastic repair for either epitheliomatous change or necrosis. Case 4 alone failed to show any convincing evidence of skin damage, and for this reason it is doubtful whether the tumour can be attributed to irradiation. However, this is a comparatively uncommon site for cancer, and it is difficult to be persuaded that its appearance was purely coincidental. Radiation is only one of many known carcinogenic agents, and, although it cannot be held solely responsible, it may well have been a contributory factor in the genesis of this tumour.

The remaining three patients all seem to have developed tumours as a direct result of irradiation, and in two of them there are features which further support this aetiology. In Case 2 the tumour had the structure of a fibrosarcoma, and, although this tumour may rarely occur in the upper part of the oesophagus, it must be very rare in post-cricoid tumours. As Cade (1951) has pointed out, fibrosarcoma may develop on a basis of post-radiation scarring. In Case 1 the tumour arose in the pyriform fossa, which may be significant, as carcinoma in this site is predominantly a disease of men.

In conclusion it seems reasonable to speculate that, if the treatment of thyrotoxicosis by intense or prolonged irradiation was a common practice 25 to 30 years ago, further cases of radiation cancer in the laryngopharynx may occur, or have perhaps already occurred.

Summary

It is rare to find a tumour in any of the deep tissues following external irradiation, and the literature on this subject is briefly reviewed.

The case histories of four patients who developed tumours in the laryngopharynx after irradiation of the neck are presented. The criteria considered to be important in the diagnosis of radiation cancer are enumerated, and the reasons for regarding three of these tumours as examples of post-radiation cancer are given. In the fourth patient the aetiology of the tumour is open to doubt.

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FERROUS SULPHATE POISONING IN CHILDREN

BY

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Iron poisoning in children occurs through the temptation of attractive sugar-coated pills containing ferrous sulphate which, with good reason, are freely supplied to their mothers. The first comprehensive reports of this disaster in children were published in 1947, and, though it is difficult to believe that cases did not occur before, the first recorded case was that of a child of 16 months who died, in May, 1944, after swallowing 39 ferrous sulphate tablets (Thomson, 1947). Since this time there have been further case reports, and the clinical picture of the poisoning is becoming clear.

The daily press has recently given prominence to inquests on children who have died after swallowing ferrous sulphate tablets, and I have used this source of information to collect some details of four cases to add to the reports of four which I have seen myself. Brief reference has already been made to two of these coroners' reports (Cases 6 and 8) in a leading article in the *Lancet* (1949). The daily press has also made reference to the ignorance of parents and doctors alike concerning the effects and dangers of these tablets to small children.

It is the purpose of this paper to describe the clinical picture of iron poisoning in detail, to discuss the effects of large doses of iron, to propose a more positive therapeutic approach than has been given in previous medical articles, and to suggest a method of safeguarding children from these tablets.

The Tablets.—The most readily available tablets are green sugar-coated pills, and each of these contains ferrous sulphate, 3 gr. (0.2 g.), copper sulphate, 1/25 gr. (2.6 mg.), and manganese sulphate, 1/25 gr. (2.6 mg.). Forbes (1947) has shown by animal experiments that the effect of the copper and the manganese can be discounted, and that it is the ferrous sulphate which has the irritating and lethal effect.

The cases recorded below have, with the exception of the coroners' cases, all been treated in this department within the space of a year. In this period three other children were admitted with a diagnosis of ferrous sulphate poisoning, but they have been excluded because of lack of detail regarding what they had swallowed. One had the symptoms of poisoning, but the other two were not upset. The mother of one of the latter, aged 18 months, was quite sure he had swallowed 24 tablets, but only minute quantities of iron were recovered from the stools and stomach washings, and it was thought more probable that only a few pills had been taken than that 24 tablets had not made him ill.

In the seven preceding years during which this department has been in existence only one other such case has been admitted. This was a girl aged 2½ years who swallowed 60 tablets. Her mother thought she vomited back "nearly all the tablets," and, though she was pale and drowsy and had marked diarrhoea and vomiting, her recovery during the subsequent three days seems to