should be set up in all children's hospitals. It can be said that attempting to manage premature babies in the general wards of children's hospitals is almost waste of time, as they will tend to become infected and die.

We have dealt here with the management of the premature baby exclusively, and so far have said nothing in regard to the prevention of the condition. This is largely a social matter that can no longer be ignored. The maternity centre in New York has been able, by pre-natal care, to reduce the percentage of premature births by one-third. In a certain home for unmarried women in Oslo the proportion has been reduced to 2%, compared with 32% still prevailing among women of the same class attending the ordinary obstetrical clinic. Nutrition, sufficient rest, and relief from strain are the most important predisposing factors. In this connexion it is well to mention that cerebral haemorrhage is a common cause of death among premature babies, and recent work suggests that one of the reasons for this is lack of vitamin K in the mother's diet. Women suffering from even mild types of the toxæmias of pregnancy are usually placed upon deficiency diets. In the past obstetricians have often failed to recognize the importance of adding vitamin concentrates to these diets. In all such cases it is wise to give special injections of vitamin K.

Finally, we may sum up the position in regard to prematurity by saying that when a combined effort is made by the obstetrician and the paediatrician a considerable reduction will occur in its incidence and its death rate, and as a result we may expect a general improvement in the whole neonatal mortality.

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TREATMENT OF WOUNDS AND INFLAMMATION BY X RAYS AND RADIUM RAYS

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The use of x rays and other radiations in the treatment of wounds and inflammations has been much neglected. Dr. Leopold Freund of Vienna, who was the first to employ x rays for any form of therapy, used them for inflammations more than 40 years ago. One of us treated such cases as long as 36 years ago, and the other has done experimental research work on the basic principles underlying this treatment. The causes of this neglect are various. First, the indications for the treatment were so universal that it came to be looked at askance by the profession, who feared that it was a semi-quack treatment. Secondly, the discovery of the value of x rays and radium γ rays in malignant disease overshadowed their other uses. Thirdly, incorrect dosage was used in the earlier days. It was not until 1928 that it came to be universally realized that the doses previously given were too large and either produced inferior results or caused the late development of telangiectases and atrophy of the skin. Fourthly, it has been found that the action of ultra-violet and sunlight increases the liability to these late changes if larger doses have to be given, as in keloid. Finally, in the earlier days of the use of x rays the penetration, in treating deep-seated conditions, was much too low, so that the surface received an overdose and the deep part an underdose. Also, in those days accurate measurement of the dose, except that administered to the surface, was impossible.

With the very small doses now employed by some radiologists it is possible to carry on treatment, if necessary, for very long periods without the slightest risk of after-effects: this necessity, of course, arises only in the most chronic inflammations. Success has been obtained by ray therapy in such diverse conditions as carbuncle, erysipelas, suppurative parotitis, tuberculous glands, tuberculous peritonitis, actinomycosis, chilblains, whitlow, gas gangrene, osteomyelitis, and many others.

Basis of Treatment

In wounds there are two purposes to which irradiation can be put. One is the acceleration of the healing of clean wounds and the prevention of keloid; the other is to check the local inflammatory reaction, if there is no foreign body or sequestrum present. It does not matter whether the infection is acute, subacute, or chronic, except that one tends to use even smaller doses in acute cases. Experimental research work was done on the mode of action of small doses of x rays at the Holzknecht Institute in Vienna by one of us and by Shuichi Fukase. This gave the following results:

(1) Under treatment with small doses of x rays polymorphonuclear leucocytes in exudates break down more quickly than they usually do. Some think that this increased breakdown of polymorphs may be combined with the liberation of immune bodies and that the acceleration of healing is achieved by this means. (2) Wounds of the skin and of the cornea of animals heal sooner in the part treated locally by x rays. On the shaved skin of rabbits incisions were made about 12 cm.

FIG. 1.—Cut in back of a rabbit 5 days after Section A had been irradiated. This section is firmly united, while Section B is still ununited.

long down to the superficial fascia. One half of the incision was covered with lead and the other half was treated by x rays immediately after the wound was inflicted. The wounds were left open and the animals kept in their usual surroundings. In that part treated by x rays hardly any exudate or other sign of cellular reaction occurred either as to the naked-eye or the microscopical appearance. The treated part of the wound was healed in 8 days as if it had been sewn up. The untreated part became infected and healed slowly by granulation. (Figs. 1 and 2.) Wounds of the cornea healed without surrounding inflammation on the side treated by x rays, but with marked infiltration on the side not treated. (3) Experimentally produced fractures of both fibulae of rabbits heal more quickly on the side treated with x rays. The callus on the irradiated side is less in quantity, is formed earlier, and is more heavily calcified. (4) After the inunction of tuberculin into the skin no reaction takes place in the part of the skin treated by x rays soon after the inunction. This shows the local effect of x-ray

treatment on the immunity reaction. The most striking result in all these experiments is the prevention of gross inflammatory reactions as seen both macroscopically and microscopically. Exudates are prevented and any inflammatory cells are rapidly changed to fibrocytes and fibrous tissues. This change, which always normally occurs in inflammatory reactions when sound natural healing takes place, can be induced and accelerated artificially by *small* doses of *x* rays. If *bigger* doses are used,

doses of *x* rays mentioned. After a day or two the process of healing can be recognized by loss of pain; the exudation gradually subsides, frequently after a preliminary increase; the closure of the wound and the growth of the epithelium are both accelerated; callous chronic ulcers soon become covered with healthy granulations and heal. In fractures in which bony union has not occurred *x*-ray treatment induces

FIG. 2.—(A) Untreated wound after 5 days shows no union. (B) Treated wound after 5 days shows firm union.

reversed effects and even necrosis occur, probably on account of the fact that inflamed tissues are much more radiosensitive than normal tissues. It seems to be of specific value in checking *local* inflammatory reactions which are of no further use in defence. Sometimes a mild infective agent will elicit abundant cellular reaction in the body and thus endanger life. In these cases irradiation is most useful by cutting short this inflammatory allergic reaction.

Indications for Use of Irradiation

Delay in Natural Healing.—Wounds of the surface which do not heal are quickly cured by treatment with the small

quick calcification and bony union. Similar healing takes place in those haematomata which do not heal quickly—e.g., haematoma of the pinna of the ear.

Failure of Surgical or Medical Treatment.—In any inflammation where surgical or medical treatment fails, irradiation with small doses of *x* rays is indicated. As an example of failure of surgical treatment osteomyelitis following whitlow may be mentioned: loss of part of a finger, even in advanced cases, is generally unnecessary. With *x*-ray treatment we get regeneration of bone which is almost decalcified and destroyed by osteomyelitis (Figs. 3 and 4). Much disability in workmen, munition workers, men in the Forces, artists, housewives, and

FIG. 3.—Whitlow before *x*-ray treatment. Amputation had been advised.

FIG. 4.—Whitlow 3 months after *x*-ray treatment was begun. Seven weekly doses of 100 *r* (surface) were given, and, later, two more doses of 100 *r*.

others is prevented. All other forms of osteomyelitis are indications for x-ray therapy combined with the necessary surgical treatment. Amputations with their consequent disability may be avoided. Great claims have been made in the United States for the use of this treatment in gas gangrene. Parenthetically, as an example of failure of medical treatment post-herpetic neuralgia may be mentioned. The treatment of the posterior root ganglia by x rays is followed by quick cure. Trigeminal neuralgia also responds to irradiation of the Gasserian ganglion.

Acute Inflammations.—Carbuncles of the upper lip, some forms of erysipelas, cellulitis, lymphangitis, gas gangrene, and osteomyelitis of the skull should be treated at once with x rays. No harm whatsoever can be done by using small doses on a limited field, whereas delay may sometimes prove fatal. In very few cases of infection, however, the treatment fails to improve the condition.

Subacute and Chronic Inflammations.—The number of these conditions is very large; we will instance only a few. Good examples are actinomycosis, local tuberculous infections as of lymph nodes or mucous membrane, chronic osteitis, septic fingers, and other local septic conditions.

Prevention of Disfigurement.—Scars are much better, thinner, and less obvious in wounds that are treated by x rays, and keloid will be prevented if irradiation takes place soon after trauma. This treatment is now often employed by plastic surgeons.

Social Indications and Wartime Purposes.—Delay in healing of all kinds of inflammation may be of importance from its economical or its wartime aspect. Healing can be much accelerated by irradiation and the period of incapacity therefore considerably shortened.

Dosage

The wave-length does not seem to be of great importance if the lesion receives the same biological dose. This is not the same thing as the physical dose, because a larger number of roentgens (*r*) have to be given if the wave-length is shorter, in order to produce the same biological result. Nevertheless, Fukase has shown experimentally that the shorter wave-lengths give better results. Grenz rays* are not sufficiently penetrative to give the requisite lesion dose.

The accurate modern methods of measurement enable us to calculate the dose received by the lesion whether it is superficial or deep. Though a very large dose is definitely harmful and the optimum dose is very small, there is considerable latitude. Thus, double the optimum dose will still give a good result, though not the best. The dose to be received by the lesion lies between 30 *r* and 80 *r*. The former dose may be applied twice a week and doses from 50 *r* upwards once a week. This dose presumes the use of x rays of about 140 kV constant current with a filter of Al 5 mm. With higher voltage and filtrations the number of *r* must be larger to give the same biological dose; with lower voltages and filtration the number is smaller. Radium γ rays filtered by Pt 0.5 mm. necessitate a lesion dose double that used with medium x rays.

In acute cases it is best to use the smaller dose, repeating in 3 days, and again in 4 days if necessary. With chronic cases treatment may occasionally have to continue a long time—two or three months or even more. A case of extensive abdominal actinomycosis even took one of us a year to cure finally. The dosage rate is 10 to 80 *r*/min. The necessary dosage is so small that even the routine fluoroscopy is occasionally enough to stop the inflammatory reaction. Children with enlarged bronchial glands and constantly raised temperature sometimes lose this temperature rise if screened for about 5 minutes. A repeated dose of 150 *r* or more is likely to be followed by bad results.

Conclusions and Summary

Owing to the war the present is an important time to bring this method of treatment forward. The use of radiations in these cases is a very valuable one, and will without doubt much increase in the future, when experience has confirmed

* X rays of very long wave-length on the border (Grenze) of the ultra-violet.

the good results, which cannot be achieved by any other means.

The treatment of acute, subacute, and chronic inflammations by small doses of x rays is described, as well as the experimental and research work on which this treatment is based. The accelerated healing of wounds and fractures by irradiation is also described. The effect of x rays is due to the influence on local cellular reaction and local immunity. The reasons for the neglect of this treatment are gone into. The necessity for small doses is stressed, both for the better results and for the absence of late bad effects.

THE USE OF SULPHAGUANIDINE IN BACILLARY DYSENTERY

BY

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The cases surveyed in this paper were selected for treatment from 600 patients suffering from bacillary dysentery admitted to a general hospital in the Middle East over a period of 8 months. Of these, 77 were treated with sulphaguanidine. Its use was authorized only in severe or refractory cases. Hence the acute cases described represent those which from general experience of dysentery could not be expected to do well on standard treatment, and the chronic cases those which had already failed when so treated. There was occasionally a temporary shortage of supply, but every effort was made to give what was considered to be an adequate course of the drug. Sulphaguanidine consists of sulphanilamide in which one of the hydrogen atoms of the amino group is replaced by a guanidine ring, and is thus homologous with sulphathiazole and sulphapyridine. Experimental investigation has shown that sulphaguanidine, although water-soluble, is poorly absorbed by the intestinal mucous membrane. This would allow large concentrations to be maintained in the gut, with only a low tissue fluid and blood concentration resulting, and a correspondingly slight danger of toxic poisoning from large or prolonged dosage.

Of the 77 cases 26 were classed as acute and 51 as chronic. This differentiation was based mainly on the day of disease, and all cases giving a history of less than 2 weeks from the onset were considered acute. Duration of symptoms in the cases termed chronic varied from over 2 weeks to many months.

The Acute Series

Treatment and Routine

In these cases the malaise and toxæmia were severe and the motions very frequent, consisting of blood and mucus only. The majority had not received any treatment, although a few had had castor oil and sodium sulphate during their evacuation to this hospital.

Dosage of Sulphaguanidine.—With no previous experience as a guide the following arbitrary indications were used as a means of gauging the dosage required: 3.5 g. 4-hourly until (a) the patient's general condition showed marked improvement as evidenced by a drop in temperature, clean moist tongue, absence of toxæmia, and general feeling of well-being; and (b) the stools had been reduced to five or less in 24 hours and were faecal. 3.5 g. 4 times a day until the infrequent stools became a semi-solid with only slight traces of blood and mucus present. 3.5 g. 3 times a day until 2 or 3 days after the stools had become normal. Stools were considered normal when not more than two solid or nearly solid stools without blood were passed in a day. No particular attention was paid to a small excess of mucus, which was almost invariably present. In the early cases treated this latter part of the plan was not strictly adhered to and sulphaguanidine was stopped on the day the stools were free from blood.