TREATMENT IN GENERAL PRACTICE

This article is one of a series on the management of some diseases of the blood and blood-forming organs met with in general practice.

TREATMENT OF THE LEUKAEMIAS

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There are three main varieties of leukaemia: acute leukaemia, chronic myeloid leukaemia, and chronic lymphatic leukaemia. Acute leukaemia runs its course in a few weeks or months, and is invariably fatal. It often simulates a severe infection, and no treatment beyond the symptomatic is of any avail. Haemorrhage, infiltration of the tissues by leukaemic deposits, and intercurrent infection are the most fruitful causes of symptoms, and it is easy to be misled in diagnosis and treatment unless the blood is examined. Surgical intervention, as for enlarged tonsils, foul gums, or localized tumour formation, should be strenuously avoided, as it is only too likely to lead to fatal haemorrhage or infection. Irradiation by x rays or radium is rarely well tolerated, and is of little value except for the relief of lesions which are causing pressure or pain. Necrotic ulceration of the mouth and gums may be treated on the lines laid down for agranulocytosis,* together with the intravenous injection of nearsphenamine, 0.3 to 0.6 gram at weekly intervals. Iron by mouth and injections of liver extract may be used in the ordinary dosage for anaemia. Transfusion may cause the symptoms to improve for a few days, but its effects are evanescent, and only rarely does it do more than protract a painful situation.

Chronic Leukaemia

The treatment of chronic leukaemia can be summed up as irradiation plus iron. Arsenic is often advocated, but is not as satisfactory as irradiation, nor is it free from serious disadvantages. The radiation is given in the form of x rays. Radium has been tried, and although it is probably true that the same results can be obtained by this means the large quantities of radium required and the difficulties in its application negate its general use. Chronic leukaemia cannot be cured; it is even doubtful if life is greatly prolonged by treatment. What is very important, however, is that the *quality* of the life remaining to the patient is vastly improved. Indeed, the improvement in the general condition after a course of x rays and iron is, as a rule, dramatic. The patient regains strength and appetite, he loses his breathlessness, he gains weight, and the spleen becomes reduced so that it may no longer be palpable. Most striking, however, are the changes in the blood picture. The red cells rapidly increase in number so as to approach the normal, and with them the haemoglobin. The white cells decline, even to a normal total, and the proportions of the various white cells also shift towards the normal. The latter phenomenon is more marked in myeloid than in lymphatic leukaemia, but even in myeloid leukaemia some immature cells usually persist in the blood stream after treatment, although in greatly reduced numbers.

* Professor Witts's article on the "Treatment of Agranulocytosis" will appear in a later issue.

Within a few weeks of treatment the patient returns to his work, to all outward appearance a healthy individual. Unfortunately after a period of two to three months to a year, or occasionally even longer, the symptoms reappear. Blood examination shows that the leucocytes have again increased, the red cells and haemoglobin have fallen, and further treatment is necessary. Another remission will be produced by treatment, although of shorter duration, and after a variable number of such cycles, with ever-shortening remissions, the disease finally becomes resistant to treatment, and death ensues. The total duration of the illness may be two or three years, but occasionally cases of longer duration are met with, even up to fifteen or twenty years. Spontaneous remissions may occur without any form of therapy.

The symptoms of leukaemia can be ascribed to three main causes: the infiltration of the tissues and the enlargement of glands; the presence in the circulating blood of excessive numbers of leucocytes; and the depression of the haemoglobin. Questions that not uncommonly arise are whether the patient should be treated when there are no subjective symptoms, and what level of white cells should be regarded as an indication for the resumption of irradiation. In the absence of indications to the contrary, the patient should be irradiated whenever there is gross enlargement of glands or splenomegaly, and whenever the white blood count rises above 50,000 cells per c.mm. The anaemia is usually improved by irradiation, but the improvement is much increased and accelerated by the prescription of iron.

X-Ray Therapy

Any case of chronic leukaemia, whether myeloid or lymphatic, should be treated by x rays. The rare aleukaemic cases are no exception to this rule, although in treating them the greatest possible care is necessary. Anaemia is no contraindication to x -ray therapy; a high basal metabolic rate, with nervousness, sweating, fast pulse, and loss of weight, is a definite indication. But the treatment should be interrupted at once if the clinical condition of the patient is obviously deteriorating, if the anaemia increases in severity, if the white count falls very rapidly, or if there is an increase in the number of immature white cells.

X-ray therapy in leukaemia is empirical, and the mode of action is not well understood. The rays may be applied to the spleen or to the long bones. The best results are obtained when the rays are applied to the spleen, although greater accuracy of technique and dosage is required than when the long bones are treated. Both methods lead to a gradual reduction in the leucocyte count and a shift towards normal proportions; but in the bone-irradiation method the coincident improvement in the red cells and haemoglobin is much slower. Attempts have also been made to treat leukaemia by total body irradiation. This method is a dangerous one, and no very striking results have so far been reported. In lymphatic leukaemia the glandular masses usually disappear spontaneously when the total white count is kept round about the normal level. Occasionally, however, it is necessary to irradiate the individual gland masses.

Radiological Technique

X-ray treatment is best carried out as a series of small doses applied to the spleen within the space of two to three weeks. Strict control of the treatment by blood counts is necessary throughout. At the beginning of the treatment one to four small daily doses of x rays are given, according to the acuteness of the leukaemic process; the more acute the process the greater the caution that has to be exercised in the treatment. A transitory increase in the white cells may occur within a few hours of the treatment, before the typical fall; it is therefore important to allow a clear interval of twenty-four hours after the last dose before carrying out a control blood count. The number and magnitude of the further doses is determined by the result of the blood count. In all, from eight to fourteen doses may be required to complete the treatment.

Treatment is stopped when the total white count has fallen to about 15,000; but in deciding when to cease treatment not only the actual blood count but also the rapidity of fall in the white cells has to be taken into consideration. The fall may continue for from two to four weeks after cessation of the treatment. As important as the effect upon the white cells is that upon the red cells and haemoglobin. Indeed, the immediate prognosis may be estimated with some accuracy by observing the effects on the latter. A steady rise in the red cells and haemoglobin gives a good immediate prognosis, while a fall in the red cells, and especially in the haemoglobin, in spite of splenic irradiation, indicates the probability of an early fatal issue.

It is desirable that the patient should be under observation in a hospital or nursing home during the first course of treatment, but when the measure of the case has been taken in this way further treatment may be ambulant. X-ray sickness may be relieved by the ingestion of fluids and glucose; by the daily intramuscular injection of 2 c.cm. of liver extract; or by the oral administration of a solution of adrenaline hydrochloride (*B.P.*), 10 minims, four-hourly, on the days when the patient is irradiated.

Iron Therapy

The patient's feeling of well-being during the course of his illness depends to a large extent upon the state of the red cells and haemoglobin. The results of treatment have greatly improved since massive doses of iron have been administered in conjunction with x -ray treatment, and iron is now usually administered throughout the whole duration of the illness. In the average case the following mixture will be found suitable, but if this is not well tolerated, other preparations may be used, provided always the dosage is adequate.

R.	Ferri	ammon.	cit.	...	...	...	gr. xxx
	Glycerin.	...	...	...	...	...	℥ xv
	Aq. chlorof.	...	...	...	...	...	ad. 3 j

3 j, t.d.s., p.c.

If there is a sudden exacerbation of the anaemia from haemorrhage or infection one or more transfusions of 500 c.cm. of blood may prove of great value.

Arsenical Therapy

The results of the administration of arsenic are similar though inferior to those of x rays, the great disadvantage being that prolonged administration may lead to the unpleasant effects of chronic arsenical poisoning. We do not recommend the use of arsenic unless x -ray treatment is not available, and we are opposed to the use of arsenic at the same time as irradiation is taking place. Arsenic is sometimes prescribed during remissions in the hope

of warding off recurrence for as long as possible, but in our experience it is better to rely on x -ray therapy, and it is unusual for a patient who has become refractory to x rays to respond to arsenic.

Treatment is begun with a dose of 3 to 4 minims of Fowler's solution three times daily. The initial dosage is continued for two days, and then the total daily dose is increased by 3 minims. This amount is given for two days. Thereafter the dose is increased at the same rate until anorexia, the first sign of intoxication, is noted. This sign, as a rule, is first noticed when the dose reaches about 24 minims daily, and the subsequent increments in the drug must be added more slowly, at the rate of an increase of not more than 1 minim to the total daily dose. By such a method medication may be carried up to 12, 15, or even 20 minims, three times daily.

The dose must be increased until the desired effects are obtained or until the limit of tolerance has been reached, for it has been shown by Forkner and others that the best results require a dose which is near the upper limit of tolerance. When the blood has improved considerably or when the limit of tolerance has been reached, the Fowler's solution should be gradually withdrawn. The total daily dose may be decreased by 1 minim daily until the patient is taking about 5 minims three times daily, which amount may be continued without harm for at least several months. If, with the larger doses, rather severe toxic symptoms develop, the drug may be entirely omitted for forty-eight or seventy-two hours, and then resumed in doses equivalent to about three-fourths or two-thirds of the amount which the patient was taking at the time of development of the symptoms. From this point the drug may again be increased or decreased as indicated by the effects on the patient. The solution should be well diluted and given with or after meals. Arsenic by mouth appears to be far superior to the injection of salvarsan or its allies.

Other Forms of Therapy

Other leucotoxic drugs such as benzol have been used in leukaemia, but they are too dangerous to be recommended. Nor should the removal of the spleen be countenanced.

Loss of weight is sometimes a troublesome symptom; the diet should therefore be as nourishing as possible, and the appetite may be encouraged by a bitter tonic before meals. Restful holidays in the open air are helpful, but excessive exposure of the body to the sun should be avoided, as it may diminish the tolerance to x rays.

The General Nursing Council for England and Wales invites applications from registered medical practitioners for examinations for the preliminary and final State examinations for the general part of the Register and for the supplementary parts of the Register, for mental nurses, nurses for mental defectives, sick children's nurses, and fever nurses. Examiners in anatomy and physiology should be medical practitioners of good standing who have held a resident or other post on the staff of a hospital, and who have had experience in teaching. Examiners in medicine or surgery must hold, or have held, a post on the medical or surgical staff of a hospital recognized by the General Nursing Council as a complete training school for nurses, and preferably should possess a university degree in medicine and surgery or hold the M.R.C.P. or F.R.C.S. diploma. Examinations are held three times a year. The names of examiners are entered on a panel, from which those selected to serve are called up as required. Forms of application and full information may be obtained from the Registrar, 20, Portland Place, London, W.1.