would lead to a high slowly falling alimentary hyperglycaemia. Now it is known that hunger pains are brought about by injecting insulin and that these are accompanied by gastric contractions of the normal type and an increase of hunger; therefore, hyperglycaemia should lead to failure of hunger and loss of gastric tone. The administration of liver, by improving sugar tolerance, should produce a fall in blood sugar and stimulate appetite, and if, after the appetite is stimulated, a high carbohydrate diet is given, improvement should occur. Treatment on these lines was carried out with great success in a child aged 12, weighing 40 lb. After seven weeks she increased in weight to 67 lb., and her intravenous glucose-tolerance test became normal. We have also used liver extract or campolon for restoring appetite and increasing weight in wasted infants and children. The results have been most encouraging, and almost as dramatic as in the case of anorexia nervosa which I have just described.

Conclusion

There are many other deficiencies of nutrition in coeliac disease, which time does not permit me to deal with, but I thought that an account of the work on liver and carbohydrate metabolism which was inspired by a study of coeliac disease, and of its applications in the treatment of nutritional states, might prove interesting.

A SYSTEM OF RADIUM DOSAGE

BY

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It will be generally admitted that success in the treatment of malignant growths by radium depends upon accuracy of dosage, and that this again depends upon two factors. In the first place the radium must be so arranged that every portion of the region under treatment receives an equal amount of radiation. In the second place the total amount of radium and the time for which this is employed must be such that the total radiation received at each point is adequate for the destruction of the cells forming the tumour.

It is usual and convenient to define the total radiation received in r units, and in general it is found that a radiation of from 6,000 to 7,000 r is sufficient to destroy the cells of a squamous carcinoma. A milligramme of radium screened by 0.5 mm. of platinum may be taken to deliver at a distance of one centimetre a radiation of 8.4 r units per hour. For many reasons it is convenient to make the standard time of treatment 133 hours, or about five and a half days. In this case our one milligramme of radium will have delivered 1,120 r units at a distance of one centimetre. Moreover, there will have been evolved and discharged just 1 millicurie of emanation, so that we can describe our source as 133 mg.-hours, or as 1 millicurie destroyed, whichever is the more convenient. We assume throughout a screenage of 0.5 mm. of platinum. Our calculations are greatly simplified if we accept five and a half days as the standard time of treatment when radium element is employed, as then the number of milligrammes of radium and the number of millicuries destroyed are represented by the same figure. To this fundamental figure, which represents the total energy delivered by our combined sources, we shall apply the term "Index."

The problem before us is so to distribute our sources and to adjust the amount of radium they contain that every portion of the region treated receives a radiation of at least 6,000 r . In general this means the use of complicated charts and most intricate calculations. To avoid this I propose to suggest certain simple rules by which we can reach an approximately accurate solution, setting up certain standard distributions which can be modified to meet the requirements of any special case.

Simple Rules for Calculating Dosage

The two methods of radium treatment in most general use are by plaques and by insertion. Plaques may be constructed of any size in wax or other material on which the radium is supported, and they are generally applied externally. We have, however, recently employed small plaques made of dental wax and inserted temporarily into the tissues. One advantage of a plaque is that the radium can be distributed upon it in an exact manner, so that we can know with great accuracy the effect which will be produced.

In order that this effect should be as uniform as possible over the region of application, the radium must be distributed in a certain manner, and it can be shown that remarkably flat and uniform fields of irradiation are obtained if one-half of the radium is distributed uniformly over the surface of the plaque and one-half around its circumference. Moreover, with this arrangement the intensity falls off roughly as the distance from the plaque, and not as its square.

Assuming such an arrangement, how are the amount of radium required and the time of exposure related to the size of the plaque, or, in other words, what is the Index of the plaque? For circular plaques we suggest the very simple rule that the Index is the diameter of the plaque in millimetres. Plaques so constructed and employed give over a large range almost identical depth doses—that is to say, they form appliances of similar power for the treatment of tumours of different dimensions. Their exact characters will be clear from the accompanying table, from which it will be seen that they form convenient standards requiring only slight modification to meet special circumstances. In most cases plaques are built up by mounting needles or seeds directly on a model of wax or other plastic material, when it will be seen that the rules we have laid down form a very useful guide. Even where the plaque is not circular we have a sufficiently accurate approximation if we take its average diameter as a basis for calculation. Where, however, it is bent upon itself, as, for example, in treating a carcinoma of the alveolar margin or the lip, allowance must obviously be made for the effect of cross-fire.

Table for Calculating Depth Dose

Diameter (Centimetres)	Index	Depth from Active Surface of Plaque in Centimetres					
		0.5	1	2	3	4	5
3	30	24	13.9	6	3.1	1.9	1.3
4	40	21	13.4	6.7	3.8	2.3	1.6
5	50	19	12.8	7	4.2	2.7	1.9
6	60	17.2	12	7	4.5	3	2.1
7	70	15.7	11.2	7	4.6	3.2	2.3
8	80	14.5	10.5	6.7	4.6	3.3	2.5
9	90	13.5	10	6.6	4.6	3.4	2.6
10	100	12.5	9.4	6.4	4.7	3.5	2.7

Depth dose in units of 1,000 r for standard plaques.

Turning now to the methods of insertion, it often happens that what we are really constructing is an inserted plaque, when the above rules still apply. This is the case, for example, in the treatment of carcinoma of the breast, where in effect a plaque is formed on the chest wall, or in the treatment of some cases of secondary glands in the neck. In other cases, however, where we are dealing with a localized tumour it is better to regard the problem from a different aspect.

Suppose that we require to treat a spherical mass of growth and that it is possible to distribute our radium both around it and throughout its substance, how should it be distributed and how much should we employ? Again two very simple rules can be formulated. As regards the distribution, arrange one-quarter of the radium uniformly through the growth, and three-quarters just outside its palpable limits—that is to say, just beyond the growing edge. In this way it can be shown that every point of the growth received a nearly equal dose. As regards amount, the number of milligrammes required for a treatment extending over five and a half days or, what is numerically the same, the number of millicuries destroyed—that is to say, the Index—is given by the square of the diameter of the growth in centimetres.

This simple rule depends upon the physical fact that in the case of a sphere such a distribution gives a very uniform irradiation throughout, and at its centre a total irradiation of exactly 6,720 *r* units, whatever the diameter of the sphere may be. For clinical purposes where a tumour is only roughly spherical we obtain a sufficiently accurate result by taking its average diameter.

Comment

It is not, of course, suggested that the rules we have laid down form an infallible guide to radium dosage, or that they can in any way replace experience or the exact calculations of the expert. It is, however, felt that they form standards which even the expert may use as a starting-point, and which he can readily modify to meet any special requirements. The conception of the Index certainly simplifies calculation, and in effect reduces all our problems to a single scale.

The 1938-9 programme of the West London Medico-Chirurgical Society opened on October 7 with the presidential address by Dr. Maurice Shaw on heredity and medicine. Other meetings have been arranged as follows: Friday, November 4, 8.30 p.m., clinico-pathological meeting at West London Hospital. Friday, December 2, 7.45 p.m., at De Vere Hotel, Kensington, W., Discussion: "Illegal Operations." To be opened by Mr. Cecil Binney, Dr. C. P. Blacker, Mr. Aleck W. Bourne, and Dr. W. J. O'Donovan. Friday, January 13, 7.45 p.m., at De Vere Hotel, Discussion: "Some Aspects of Medical Folklore." To be opened by Dr. J. D. Rolleston. Friday, February 3, 8.30 p.m., clinico-pathological meeting at West London Hospital. Friday, March 3, 7.45 p.m., at De Vere Hotel, Discussion: "Pre- and Post-operative Treatment." To be opened by Dr. E. H. Hudson, Mr. Cecil Joll, and Mr. A. Simpson-Smith. Friday, April 14, 7.45 p.m., at De Vere Hotel, Discussion: "Sex Glands in General Practice." To be opened by Professor E. C. Dodds and Dr. L. P. E. Laurent. Friday, May 5, 7.45 p.m., at De Vere Hotel, Discussion: "Some Recent Advances in Medicine." To be opened by Professor Henry Cohen. The Cavendish Lecture will be delivered at Kensington Town Hall on Wednesday, June 7, at 8.30 p.m., and the annual dinner will be held at the Trocadero Restaurant on Wednesday, July 5, at 7.45 p.m.

THE ANTI-PERNICIOUS PRINCIPLE: SOME EXPERIMENTS WITH URINE

BY

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(From the University Medical Clinic, Lausanne, by permission of Professor L. Michaud)

We have no proof that the anti-pernicious principle circulates in the blood, although some authors explain in this manner the partial efficacy of blood transfusions in pernicious anaemia. Its presence in organs other than the liver cannot be deduced from the experiments of Whipple and Robscheit-Robbins (1925), which established that the haematopoietic power of the kidneys, for example, is equal to that of the liver, that of the brain one-third as great, etc. The experiments of Whipple were based upon the rate of blood regeneration in dogs exsanguinated by successive haemorrhages, and in no way prove the presence of *anti-pernicious* principle in the organs concerned. It remained for Minot and Murphy to apply clinically the discoveries of Whipple and to show that pernicious anaemia was peculiarly responsive to the action of liver. Furthermore, since the introduction of therapeutic extracts (Cohn, McMeekin, and Minot, 1930) of increasing purity it has become possible to distinguish the specific action due to anti-pernicious principle from that which causes blood regeneration in non-pernicious anaemia and is due to other haematopoietic substances (Farrar and Sturgis, 1936; de Jong, 1938).

The presence of an anti-pernicious principle has, however, been demonstrated in the kidneys (McCann, 1928), the lungs (Hitzenberger, 1934), the brain, salivary glands, and pancreas (Dakin, Ungley, and West, 1936), and the saliva (Tempka, 1936). This substance, as emphasized by Wakerlin (1937), cannot be precisely identified with that of the liver, since the methods employed in preparing active extracts of liver are ineffective when applied to other organs.

Briefly, although we are in the realms of hypothesis, it would not appear unlikely that the anti-pernicious principle, widely diffused throughout the body and present in the kidneys, should be eliminated, like so many hormones, in the urine. In 1935 Wakerlin reported favourable results from the treatment of pernicious anaemia by intramuscular injections of a concentrated extract of normal urine, while Decastello (1935) obtained similar results with urine administered both by injection and per rectum. Wakerlin, however, in a more recent work (1936), based upon a greater number of cases, was unable to confirm his previous results.

The confirmation of such a fact as the presence of an active anti-pernicious principle in normal urine would not only possess a considerable theoretical interest—in establishing that the metabolism of the principle is not confined to the alimentary tract and liver—but would have a practical application in suggesting the elaboration of a method of biological diagnosis of pernicious anaemia based upon the absence of anti-pernicious principle from the urine. It is for this reason that the experiments to be described were attempted.