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SOME NUTRITIONAL PROBLEMS OF CHILDHOOD*

BY

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It is within the discretion of the Trustees of the Dawson Williams Prize to ask the recipient to deliver a lecture on the subject of his researches, and since this is the first occasion on which they have exercised that discretion, it is surely fitting that I should pay homage to the memory of Sir Dawson Williams.

Dawson Williams achieved outstanding success in two spheres of medicine: first, as a paediatrician; and, secondly, as a medical editor. He edited the *British Medical Journal* for thirty years and won for it a position in the forefront of medical literature, and both it and the *Archives of Disease in Childhood*, of which he was one of the sponsors, are abiding memorials to his name. He was a great man physically and intellectually, and withal somewhat of an autocrat, as all who knew him will bear witness. The last sentence he ever wrote for publication was, "Its motto might be 'Thorough,'" and such certainly was his own motto. When he retired from the editorship of the *Journal* it was felt that his work should be commemorated by some form of testimonial, and he, true to his first love, wished that this should take the shape of a scholarship or prize for research in paediatrics. Unfortunately, before the testimonial could take form he died, and later the Dawson Williams prize in paediatrics, open to the British Empire, was founded in his memory. It is to this man that I pay in this lecture an inadequate but sincere tribute.

I wish also to express my thanks for the great honour conferred upon me by the award of this prize; an honour which gives me the greater pleasure in that I follow in the footsteps of my two distinguished teachers, Dr. F. J. Poynton and Sir Frederic Still.

In looking back over my work I find it difficult to choose a comprehensive title for the problems investigated, but since the majority have been associated with some disturbance of nutrition the title "Some Nutritional Problems of Childhood" will cover what I wish to say. I propose to use coeliac disease as a text, because the investigation of that condition has led to a consideration of many other deficiency disorders of childhood. In a paper of this nature it is obviously difficult to keep out "I." In some places "We" has been substituted, and in others the name of a colleague, because I have been assisted by an enthusiastic band of workers who have combined first-class executive and clinical ability with a high degree

of critical and constructive reasoning. My thanks are also due to the Medical Research Council for the generous help which they extended to me for many years.

Beginning my study of coeliac disease with the assumption that deficient absorption of fat was the key to its symptomatology, I now realize that its diverse symptoms are due to impaired absorption of many factors in the diet which are necessary for normal nutrition. At different times the subjects of coeliac disease show symptoms of all the well-known deficiency diseases, as, for instance, rickets, tetany, cataract, scurvy, night blindness, pyoderma, xerophthalmia, atrophic tongue, beriberi, microcytic and macrocytic anaemia, dental hypoplasia, stunting of growth—manifestations which Minot has called "conditioned deficiency diseases."

Coeliac Rickets

Diets severely restricted in their fat content have been used in the treatment of coeliac disease for many years, and although I observed the occurrence of rickets in coeliac disease in 1913, I did not connect its appearance with the diet until it was forcibly brought home to me ten years later by the following case:

In 1919 a girl aged 5 years was found to have coeliac disease and was given a fat-free diet with considerable benefit, but in 1921 she experienced the first of several attacks of tetany, and in 1922 developed knock-knee, which increased so rapidly that a year later walking became impossible. These symptoms were regarded as due to rickets, a diagnosis that was confirmed by radiographs. I was thus placed in the extraordinary position of having, by my treatment, improved one but produced another even more crippling disease; furthermore, if the treatment were continued, it seemed impossible to cure the rickets. Fortunately at this time ultra-violet irradiation was beginning to be widely used in the treatment of rickets; therefore in March, 1925, this form of treatment was started, and nine months later the child who had been bed-ridden for three years was once more able to walk.

Since then we have successfully treated coeliac rickets by other methods—for example, irradiated cholesterol dissolved in paraffin, irradiated cholesterol in powder form, irradiated ergosterol and calciferol in tablet form dissolved in as little fat as possible and usually given in large doses. We have found that by employing such treatment as a routine in coeliac disease both tetany and rickets can be prevented; otherwise rickets is apt to occur at the growing periods and when the dietetic treatment of coeliac disease has produced a resumption of

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growth, for, although osteoporosis may be present, rickets cannot develop unless the child is growing.

An observation made on one of these early cases of coeliac rickets is interesting in connexion with more recent investigations. This observation was the ineffectiveness of sunlight in the Birmingham area to cure rickets. The child to whom I refer was, when first seen, so black from exposure to the summer sun that he looked like an Ethiopian, yet there was clinical and radiological evidence of the most extreme and severe rickets without the slightest sign of healing. The inadequacy of Birmingham sunshine has been demonstrated by a series of experiments in which three groups of rats were given a rickets-producing diet for a period of four weeks: one group was kept in the dark; another exposed daily from 11 a.m. to 1 p.m. (Greenwich mean time) to the open sky, but not the direct sunshine; and the third group exposed for the same time to whatever direct sunshine was available. Brown and Tisdall found that when rachitic rats were thus exposed to direct sunshine healing should become obvious when the sun is about 35 degrees above the horizon, which, in Birmingham, occurs for about twenty-eight weeks in the year. In the first year the rats were exposed in the centre of Birmingham. In spite of the fact that the summer was hot and sunny, healing only occurred in the "sunshine" rats over a period of seventeen weeks and in the "skyshine" rats for a period of nine weeks. It was thought that this limitation in the healing powers of the sunshine and skyshine was due to the considerable smoke pall which hangs over Birmingham, and therefore in the following year we exposed a series of rats in the country on the north-east side of Birmingham about ten miles from the centre of the city, and another series in the centre of the city, and were amazed to find that healing in Birmingham was better than in the country. Therefore, during a third summer three series of rats were exposed; one in the country to the south-west and some seven miles from the centre of the city; one in Birmingham itself; and one in the same situation on the north-east side of Birmingham as in the last experiment. The results showed that healing was slightly better on the south side than in Birmingham and considerably better in Birmingham than in the country on the north-east side of the city. The explanation of these facts is, we believe, that the prevailing south-west winds carry the smoke from Birmingham and the surrounding Black Country to the north-east of Birmingham and that this cuts off much of the curative ultra-violet rays. The child to whom I have referred had been an in-patient at a country hospital situated ten miles to the east of the city centre, and subject to the same smoke drift.

Some deficiency symptoms appear more commonly than others in coeliac disease: for instance, rickets and tetany occur more often than xerophthalmia, scurvy, and beriberi; again, microcytic anaemia is the commonest deficiency symptom, whereas megalocytic anaemia is one of the rarest. The explanation of these vagaries cannot be the inability of the coeliac child to absorb fat, because xerophthalmia is rare, and scurvy and beriberi occur, but it may be that the "threshold level" required for their development is lower with some deficiency symptoms than with others.

Anaemia in Coeliac Disease

Hypochromic microcytic anaemia occurs so often as to constitute a characteristic symptom of coeliac disease. It is an iron-deficiency anaemia, and essentially similar to Wits's anaemia of adults, since hypochlorhydria is also a common finding. In a few cases megalocytic hyper-

chromic anaemia has been found; in one case this was apparently due to the absence of intrinsic factor, in others to the lack of absorption of the haematinic factor, since improvement occurred when the diarrhoeal period was over. This type of anaemia can be cured by giving liver extract orally or parenterally.

In investigating the anaemias of coeliac disease, my colleague, Dr. Smallwood, discovered in three children a condition of microcytosis without anaemia, the cell count being normal and the cells deeply stained. This he thought was probably due to spherocytosis, the cells being thicker and more globular than normal, as in acholuric jaundice. In view of more recent clinical and experimental investigations, however, I would suggest another explanation. During the cure of nutritional anaemia a condition known as Hagen's phenomenon sometimes occurs in which the red cell count rises to six millions or more per c.mm. before the haemoglobin reaches normal figures, but when the haemoglobin does become normal the red cells fall to the normal number. Recently Dr. Cleland has found that sometimes, after the progressive diminution in the red cells which is known to occur in early infancy, the cells increase to more than the normal number, while the haemoglobin still continues to fall—that is, the reverse of Hagen's phenomenon. In our opinion both this and Hagen's phenomenon are manifestations of a mild degree of iron-deficiency anaemia.

We believe that the first change in an iron-deficiency state is an increase in the number of cells but a decrease in their size without any alteration in the percentage of haemoglobin, probably because the available haemoglobin is used to better advantage if a small cell is well filled than if a large cell is relatively less well filled (Smallwood). I think, therefore, that the condition found by Smallwood was a manifestation of this early iron-deficiency anaemia. The experimental evidence on which my explanation is based was obtained by feeding rats on a diet which, although deficient in iron, is not so deficient as to produce a definite nutritional anaemia. Rats fed on such a diet from weaning at the age of 3 weeks until 3 months old showed practically normal growth and did not appear pale or anaemic. Their haemoglobin was 100 per cent., but the red cells showed an increase of about two million cells per c.mm.; moreover, the red cells were smaller than normal. This combination of microcytosis, polycythaemia, and normal haemoglobin can be cured by adding iron and a trace of copper to the diet, thus proving that it is a response to a deficiency of iron.

Carbohydrate and Fat Metabolism in Coeliac Disease

A few years ago we repeated and confirmed the observation of several workers that oral glucose-tolerance tests in coeliac disease gave a flat and low blood-sugar curve. Moreover, we were struck by the similarity of these curves to the low blood-fat curves which we had found in coeliac disease after test meals of fat, and since there was considerable evidence that the latter were due to impaired absorption of fat from the intestine, we concluded that the low blood-sugar curves were also due to poor absorption, and not to an endocrine defect as suggested by other workers.

Defective fat absorption in coeliac disease has been repeatedly demonstrated by balance experiments, but this method cannot be applied to carbohydrates because bacterial fermentation in the intestine splits up carbohydrate, so that the amount unabsorbed cannot be estimated by faecal analysis. Our theory therefore could not be substantiated directly, but my colleague, Wallace Ross,

suggested that the problem might be solved by the comparison of intravenous and oral glucose-tolerance tests. He accordingly began work on those lines, and the results obtained have completely confirmed our view that carbohydrate is badly absorbed in coeliac disease, and have led to valuable advances in treatment. The suggestion that glucose tolerance should be estimated by the intravenous injection of glucose is not an original one, but in the test as devised by Ross the following points are new: the glucose (20 per cent.) is dissolved in normal saline, the amount of glucose being 5 grammes up to a weight of 10 kg., 10 grammes up to 30 kg., 20 grammes for older children; the maximum injection time is two minutes; the blood sugar is estimated directly after injection and at short intervals thereafter—namely, 2, 4, 6, 8, 10, 15, 20, 30, 40, 60 minutes—from an ear-lobe puncture, using only 0.02 c.mm. of blood.

There are certain other important points about the test: first, the child should be, as far as possible, on a normal diet from three to five days before the test; secondly, the test should be done after a night's fasting; thirdly, everything should be done to keep the child free from emotional disturbance, which itself affects the blood sugar. The diet is important because it is now recognized that the glucose tolerance of a healthy individual is directly proportional to, and solely dependent upon, the amount of carbohydrate the diet contains during the few days preceding the test. In the normal individual a low carbohydrate diet leads to impaired glucose tolerance, which is shown by a high and rather slowly falling blood-sugar curve, whether glucose is administered intravenously or orally; whereas a high carbohydrate diet will lead to the opposite effect—an increased glucose tolerance giving a low blood-sugar curve.

According to Thaysen a flat oral curve is one in which the rise from the fasting level is less than 40 mg. per 100 c.cm.; even more important, however, is the absence or great delay in the occurrence of a true peak and the failure of the curve to fall to the fasting level in two and a half hours even after a small rise. The form of an oral curve depends upon two factors: first, the rate at which sugar enters the blood—and this may be impaired as the result of gastric stasis or through failure of absorption; secondly, the rate of its removal from the blood—that is, the tolerance of the individual. In impaired absorption less sugar enters the blood, thus tending to produce a low curve; but because of this carbohydrate deprivation glucose tolerance is impaired, and this tends to produce a high curve. The resultant curve depends, therefore, on the degree and duration of the absorptive disability. A mild degree of impaired absorption, although leading to impaired tolerance, probably allows a considerable part of the test dose to enter and thus produce a high curve; whereas although as absorption gets worse the tolerance does also, the test dose cannot get in to show it. Actually during the early stages of coeliac disease the oral curve rises and then, as the disease develops, falls to the flat curve. This phenomenon was observed in a child whose symptoms when she first came under observation were failure to gain weight and listlessness, at which time a fairly high curve was obtained, whereas six weeks later, when the diagnosis of coeliac disease was obvious, a flat curve was obtained. During recovery exactly the reverse of this process has been found—namely, the replacement of flat curves by curves rising to a higher level, often with a delayed peak—these curves falling later to the normal level. It is not surprising, therefore, that some cases of coeliac disease and abdominal tuberculosis have shown almost normal oral curves, although the intravenous curves

revealed pronounced impairment of tolerance. It is just such variations in absorption which have enabled Ross to make out a strong case for his view that the correct estimation of glucose tolerance can only be made by intravenous blood-sugar curves, since they are concerned with a single factor—the removal of glucose from the blood.

These results, and the fact that in established coeliac disease the combination of low oral and high intravenous curves has always been found, furnish important evidence in favour of our thesis that the absorption of glucose from the bowel is impaired in coeliac disease. Furthermore, if our assumption were really true it would follow that the glucose tolerance and general condition of these children should be improved by the administration of glucose. This in fact has proved to be the case, and I have seen the most remarkable success follow this treatment in the severest exacerbations of coeliac disease.

The problem of carbohydrate absorption has been attacked in another way. It is known that glucose tolerance is directly proportional to the sensitivity to injected insulin; therefore, the fall in blood sugar when estimated every five minutes for half an hour after crystalline insulin is injected intravenously into a fasting person—the so-called insulin depression curve—is less in a normal individual on a low carbohydrate diet than when the individual is on a normal diet. If there is impaired carbohydrate absorption in children suffering from coeliac disease they should therefore show an insulin depression curve similar to that found in a normal individual on a low carbohydrate diet, and this is exactly what they do show.

"Insulin Kinase"

The third phase of these investigations was based upon the assumption that insulin, whether produced in the body or injected, is inert until acted upon by a "kinase," formed, chiefly in the liver, in response to the stimulus of an elevated blood-sugar level. If this assumption is true, kinase would be deficient—either as the result of lack of stimulus consequent upon a low carbohydrate intake, such as we have postulated in coeliac disease and in diets deficient in carbohydrate, or because the liver, possibly as the result of disease, is unable to respond to the stimulus and produce kinase. Attempts were therefore made to see if the glucose tolerance and sensitivity to insulin of children suffering from coeliac disease could be improved by giving liver preparations intravenously or orally. The same results were achieved by both methods, although more rapidly with campolon than with liver by mouth—namely, that the intravenous tolerance curves became normal, an effect which was not due to campolon itself having an insulin-like action. It was therefore clear that the poor absorption of carbohydrate in coeliac disease resulted in a diminished production of something, perhaps "insulin kinase," which is supplied by campolon or liver extract. Campolon was chosen by Ross because it is prepared by simple expression methods, and therefore is more likely than the more purified products to contain the kinase; actually a more purified and concentrated preparation—anahaemin—was found to have little effect on the glucose tolerance, indicating that insulin kinase is not identical with the haematinic factor. Another interesting fact is that although the intravenous curves are rendered normal by treatment with liver, and there is ample clinical evidence of improvement in the general condition of the children, the oral glucose-tolerance curves do not improve. The reason for this improvement cannot therefore be an immediate increase in carbohydrate absorption, but,

according to Ross, it may be due to better utilization of the carbohydrate formed in the body from protein. In view of these findings we now give liver extract as a routine in coeliac disease, and have been convinced of its value, although the results obtained are in no sense dramatic, like those obtained in severe relapses by the intravenous administration of glucose.

It is interesting to note that Minot and his colleagues regard sprue as primarily a deficiency disease closely allied to pernicious anaemia, and believe that in both there is involved a failure of a reaction between an extrinsic factor in the diet and an intrinsic factor present in the gastric juice of a normal person. Moreover, they class coeliac disease and idiopathic steatorrhoea with sprue, and state that those substances in liver extracts which are effective in pernicious anaemia have a highly beneficial effect on the major features of sprue. Recently, Barker and Rhoads have investigated blood-fat curves in sprue after a fat test meal and obtained results similar to those found by us in coeliac disease, but they also found that after the parenteral administration of liver extract the curves approached normal. In one patient a single injection sufficed to produce this change, but in two other cases several daily injections were required—a result which they say suggests that liver extract exerts some specific effect in converting malabsorbing intestines to normal function. Liver treatment does not produce this dramatic effect in coeliac disease, and low blood-fat curves may be found after months of liver treatment. Again, although carbohydrate absorption gradually improves as the child approaches normal health, it does not, as I have shown, improve immediately after, or even in a relatively short time after, the institution of liver treatment; moreover, the factor in liver which improves glucose tolerance in coeliac disease is not the haematinic factor. Coeliac disease is therefore not a conditioned deficiency caused by lack of specific reaction between extrinsic and intrinsic factors, although the megalocytic anaemia of coeliac disease can be cured by the parenteral administration of haematinic factor; furthermore, the results of the American observers, if confirmed, seem to differentiate sprue from coeliac disease.

I have followed Ross in postulating the existence of an insulin kinase produced chiefly in the liver. The theory that insulin requires an activator insulin kinase is due to Himsworth, but, unfortunately, with the help of McNair Scott he has recently proceeded to strangle the infant to which he had given birth. They now suggest that the reduction in carbohydrate tolerance and decreased insulin sensitivity produced by a low carbohydrate diet are better explained by an increased secretion of the anti-insulin substance of the anterior pituitary—that is, by an inhibitor rather than by an activator such as insulin kinase. It is, however, as pointed out in an annotation in the *Lancet*, possible that both inhibitor and activator may exist and that the anterior pituitary extract may act by inhibiting the production of insulin kinase. If an activator of some variety is not present in liver it seems impossible to explain the results which I have described, because Ross has quite convinced me of the accuracy of his observations.

Phosphorylation

There is, however, another interesting and possible explanation of the undoubted improvement brought about by liver extract in coeliac disease. According to Verzář, fat, glucose, galactose, and vitamin B₂ (lactoflavin) are absorbed from the intestine by phosphorylation, a process which, together with dephosphorylation, constitutes a

mechanism for the transport of phosphoric acid from one compound to another. By this process fatty acids are synthesized to phospholipoids and neutral fat in the intestinal mucosa, glucose to a hexose phosphoric acid, and vitamin B₂ to lactoflavin phosphoric acid. Furthermore, the “yellow respiration ferment” of Warburg, which is a combination of lactoflavin phosphoric acid with a specific protein, is probably necessary for phosphorylation to be carried out, and is also the form in which lactoflavin is chiefly absorbed and stored in the liver. If, therefore, phosphorylation does not take place the absorption of fat, glucose, and lactoflavin is greatly impaired, although a certain amount of glucose may be slowly absorbed by diffusion. Verzář maintains that phosphorylation is regulated by adrenal cortical hormone because it does not take place in adrenalectomized animals. Phosphorylation may also be prevented by the administration of monoiodoacetic acid, and young rats chronically poisoned by this acid become stunted in growth and show impaired absorption of fat and glucose from the intestine, a condition which Verzář regards as experimental coeliac disease. He found that this disease in rats could be cured “as effectively as in man” by the administration of yeast or liver, because these substances contain lactoflavin phosphoric acid, and he also found that injection of adrenal cortical hormone into adrenalectomized animals rendered their fat absorption normal. He therefore believes that coeliac disease may result from adrenal cortical insufficiency, and that the administration of liver extract, yeast, or adrenal cortical hormone will cure the condition by rendering fat, glucose, and vitamin B₂ absorption normal.

Now, all our patients suffering from coeliac disease are given liver and marmite (crude yeast extract) as a routine; therefore, if Verzář's theory is accurate and coeliac disease is due entirely to failure of phosphorylation, cure should be as rapid and absorption should be rendered normal as quickly as described by the American workers when patients suffering from sprue are treated with liver. Unfortunately, as I have already stated, our experience in coeliac disease has been that whereas clinical improvement undoubtedly does occur following liver treatment, there is no immediate and dramatic improvement in absorption of fat and glucose; that, moreover, absorption only approaches the normal after months of treatment; and that indeed, even after such a lapse of time, oral blood fat and sugar curves may still be low and flat.

I can therefore sum up by saying that all our work on coeliac disease supports the theory that the symptoms of the disease are the result of defective absorption from the bowel.

Carbohydrate Metabolism in Other Diseases

Observations on carbohydrate metabolism have also been made in many conditions other than coeliac disease; indeed, abdominal tuberculosis has already been referred to. I mentioned a short time ago that, accepting the formation of insulin kinase in the liver, impaired glucose tolerance might be expected to be found in cases of liver disease. This has been observed to be the case in catarrhal and chronic jaundice, cirrhosis of the liver, etc.

The suggestion has been made by J. H. Sheldon that anorexia nervosa is a “functional Simmonds disease—a pituitary black-out of psychological origin,” but Ross, in a recent paper, maintained that it could be explained on the ground of starvation. Thus, if for psychological reasons there was a brief abstinence from food, an impaired glucose tolerance would be produced, and this

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.