Dr. BRUCE (Toronto), in speaking of propaganda, mentioned that in Canada, where methods of educating the people had been in vogue for some years, the effect was noticeable in so far as the people did go to the doctors with suspicious "lumps" much earlier than they formerly did. He advocated strongly the campaign for propaganda purposes, so as to educate the public in the early symptoms and signs of cancer, no matter where situated. The results of surgery had advanced enormously in Canada. Dr. Bruce cited a case in which excision of the tongue had been performed by the late Sir Henry Butlin, and in which he himself had removed infected glands fifteen years later.

Mr. HERBERT PATERSON, in reply, agreed with Mr. Childs that statistics might be very misleading, but in this instance statistics supported his own experience that the remote results of operation for carcinoma to-day did not seem better than was the case twenty-five years ago. Sir StClair Thomson was to be congratulated on the excellence of his results in laryngeal cancer. Mr. Paterson thought his statistics were of great value in showing what could be effected by early operation, and they were of special interest from the fact that in none of his cases were the lymphatic glands removed. It was significant that in only two instances were the glands subsequently the seat of new growth.

STANDARDIZATION OF COMMERCIAL PREPARATIONS OF THE PARATHYROID GLANDS.

BY

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WHILE it is desirable that all substances used for therapeutic administration should be prepared in forms with a known content of the active principle, at the present time such standardization is especially requisite in the case of the organotherapeutic preparations. Though the list of such substances is now very extensive, there are only three of them in which any form of standardization is undertaken as a routine practice—namely, preparations of the thyroid gland, adrenaline and pituitary extracts.

Such a state of affairs constitutes a very real drawback in the scientific aspect of organotherapy, because in so many cases the physician does not know whether the preparation he is using contains any active substance, or if it does he can never be sure that any two preparations will have similar activities, although the stated dosage may be the same. Again, the manufacturer has no means of checking his materials; he treats the fresh tissue according to what he considers to be the best method, but he has no means of determining whether the fresh substance supplied has any activity to begin with or how far its activity may have been altered by the processes he uses. It is not to be wondered at that the results of organotherapy are apt to be variable and contradictory in such circumstances, or that such forms of treatment should be open to derisory criticism.

The following account of a method for the standardization of commercial parathyroid preparations is given as briefly as possible, with the omission of details having a purely scientific bearing. It is hoped that a more detailed account of the reactions involved may be published later, but since it is possible to standardize these preparations, at least to some extent, it is desirable that the method should be thoroughly tested and utilized while the preparations are in demand.

It is generally held that the parathyroid glands have two functions: they regulate calcium metabolism and they are in some way able to prevent intoxication by guanidine and its derivatives. On this second property the standardization method is based. The principle is as follows: if an active parathyroid preparation is incubated at 37° C. with a known amount of guanidine in solution, the amount of guanidine reckoned as picrate at the end of the incubation period is found to be less than at the beginning of the test. Only one function of the glands is therefore tested, but there is reason to believe that if the preparation is deficient in this function it will also be deficient in the other.

Method.

The following solutions are required:

1. A solution of guanidine acetate of approximately 1 per cent. strength; this may be made by dissolving 10 grams of guanidine carbonate in distilled water, neutralizing with acetic acid and making up to one litre.
2. A 1 per cent. solution of calcium chloride.
3. An aqueous saturated solution of picric acid.

The formula for the test solution is as follows:

0.85 per cent. NaCl solution ...	...	20 c.cm.
Guanidine acetate solution ...	...	10 c.cm.
Calcium chloride solution ...	...	1 c.cm.
Phenol red solution ...	...	3 drops
Thymol ...	...	q.s.

To carry out a test with a desiccated powder of parathyroid gland, 0.065 gram of the powder is added to the above test fluid, and the whole incubated at 37° C. with aeration for four days. In tests carried out until recently the aeration has been intermittent, being stopped at night, and the figures to be quoted will refer to experiments of this type. More recent experiments tend to show that if the aeration is continuous rather higher activity figures may be obtained. During the incubation period the test solution tends to become alkaline and neutrality should be as far as possible maintained by the addition of 2 per cent. acetic acid from time to time. At the end of the period the solution is made up to its original volume, if necessary, and filtered through glass-wool to remove the undissolved parathyroid powder. Half the original volume of the fluid is then taken from the filtrate and at least an equal volume of saturated picric acid solution is added; the excess guanidine is precipitated together with a certain amount of dissolved protein. The picrated fluid is brought just to the boiling point and the guanidine picrate passes into solution; it is filtered hot through glass-wool, the filter washed with boiling water, and the filtrate allowed to stand overnight. The guanidine picrate crystallizes out, and the crystals are collected in a weighed filter-paper, washed with cold water, dried at 100° C. and weighed. The weight of guanidine picrate obtained is compared with that from a control test to which parathyroid substance has not been added, but which has otherwise been identically treated. The difference in weight in milligrams between the two has been taken as an arbitrary activity figure of the parathyroid substance tested.

Results.

1. *Control tests.*—Recovery of guanidine picrate from test solution where inactive substances other than parathyroid have been used.

Substance.	Picrate Recovered.	Known Picrate Content.
Horse serum ...	215 mg.	220 mg.
Lecithin ...	220 "	"
Acetone soluble fats from ...	216 "	"
parathyroid ...	214 "	"
Iodized lecithin ...	226 "	"
Unknown tissue ...	208 "	"
	222 "	"
	246 "	260 mg.

These figures show that there is a small error in the method of guanidine estimation, but it is not sufficient to interfere when active parathyroid preparations are tested.

2. The following figures indicate the necessity for adequate aeration of the test fluid; the same parathyroid preparation was used in each case under the standard test condition described above.

	Activity Figure.
No aeration ...	52, 54
Intermittent aeration ...	82
Continuous aeration ...	93

In the next table the values given are those found with intermittent aeration.

3. For the standardization of commercial preparations, the unit of weight for the test has been taken as 0.065 gram, or one grain of the desiccated powder. Where tablet preparations have been tested, a sufficient number of the tablets has been used, according to the strength indicated on the bottle, to make up the unit weight of dried gland.

Preparation from	Activity Figure.	
	Powders.	Tablets.
Group 1:		
Firm A	(100) (93) (100)	{60, 82, 68, 84, 68, 68 76, 69, 78, 66, 74, 59 63, 74, 58
Firm C	86	—
Firm G	—	67
Firm I	—	60
Group 2:		
Firm A	67	—
Firm B	66	—
Firm C	66	—
Group 3:		
Firm F	56, 50	—
Firm E	38	—
Firm H	—	31

With the exception of the preparations from Firm A, who have kindly supplied me with numerous samples, these preparations were obtained at random to gauge the average value of the products on the market. The results obtained have been divided into three groups on the basis that all tablet preparations should have an activity index of over 50, and powders over 70. This is based on the following:

	Activity.
Whole glands	106
Desiccated powder from same	93
Tablet from same	76

With the preparations in Group 1 good results were obtained clinically in suitable cases, whereas with one of the Group 3 preparations no therapeutic effects were obtained in similar cases. In another instance samples of dried tissue, submitted as parathyroid glands were tested by the method described. Of these samples, specimens A and B were histologically unlike parathyroid gland; specimen C was known to be parathyroid gland by dissection and histological appearance. The activity figure was as follows:

	Activity.
Specimen A	23, 29
Specimen B	14
Specimen C	71

4. Differentiation of parathyroid preparations from other gland preparations. It must be remembered that substances may be present in tissues and tissue extracts which prevent the precipitation of guanidine by picric acid in varying degree. Of these arginine is known to be one and nucleic acid is very probably another. There is also the possibility that other gland substances may have some degree of activity upon guanidine salts.

The following gland substances have been tested under the standard conditions; in all cases desiccated powders were used.

Substance.	Activity.
Parathyroid	100, 93, 100, 86, 67, 66, 66
Thymus	110, 114, 106, 116
Lymphatic glands	88
Thyroid	26, 11, 16
Suprarenal, total	37, 32
Pituitary, anterior	33, 30
" posterior	39, 42
Orchitic	45
Ovarian, total	18
" residue	28
Corpus luteum	43

The difficulty therefore lies in the means of differentiating between parathyroid, thymus, and lymph glands. This can be done by estimating the activity every day over the period of the test, instead of only at the end. If the figures so obtained are plotted in the form of a graph, quite dissimilar pictures are obtained. (See figure.) The appearance of the thymus and lymphatic gland curves suggests that some substance is dissolved which prevents guanidine precipitation and which gradually disappears under the conditions of the experiment. The parathyroid curve, on the other hand, suggests the possibility of some ferment-like action upon the guanidine.

These are some practical points in connexion with the test, and it is hoped that this method may be found of use in controlling the therapeutic value of parathyroid preparations.

THE TREATMENT OF HYPOTHYROIDISM BY THYROID TRANSPLANTATION.*

BY

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BERNE.

It is to-day generally admitted by physicians and surgeons that transplantation of thyroid gland tissue, from man to man, or from animal to man, is not successful, and therefore most surgeons do not do it.

It is now forty-five years since my father, the late Professor Theodor Kocher of Berne, introduced this method and made some experiments with it. Since then there have been some successes and many failures. The failures are due, in my opinion, to insufficient technique, especially pre-operative and post-operative technique.

Congenital Absence of Thyroid Gland.

We have, up to date, done 214 thyroid transplantations in man, and it is possible therefore to state the practical result, which is more important than any theory. Amongst the 214 there were about 10 cases of congenital total absence of thyroid gland; in these cases the results are, as a rule, not satisfactory, but 3 out of the 10 cases have benefited so much that they have been able to follow the school normally. One boy has even been able to take a university degree.

Congenital Thyroid Insufficiency.

All the other 204 were cases of hypothyroidism, more or less severe. In such cases the thyroid gland is not absent, but there is greater or less degree of congenital insufficiency. In about half of the cases the condition is not diagnosed early in childhood, because distinct clinical symptoms occur only later in life, when the gland should work more, or when it has been hurt or overdone. Thus, distinct clinical symptoms appear at the age of development, after multiple pregnancies, in the menopause, or at the time when a goitre develops, or when chronic bacterial or toxic thyroiditis sets in, or, more especially, after severe general infections such as typhoid, influenza, dysentery, furunculosis, syphilis, tuberculosis, etc., and also after gynaecological operations, when the ovaries have been partially or totally removed.

Clinical symptoms and the methods of diagnosis of these cases were first described by Theodor Kocher in 1909, under the name of "Slight thyroid insufficiency." For diagnosis the method of choice is Kocher's functional thyroid test; it depends on the change in the white cells and coagulability of blood and the influence of thyroid feeding on it; basal metabolism is very little changed in these cases. Hypothyroidism is not yet sufficiently known; very often severe rheumatism, neuralgia, stomach, intestinal, and heart trouble of unknown origin are due to hypothyroidism and cured by transplantation of thyroid tissue. This is the method of choice in these cases, as thyroid feeding often causes stomach trouble and is never carried on long enough.

Of our 204 cases of hypothyroidism, 26 per cent. have been entirely cured by transplantation and have not taken any thyroid since; 21 per cent. have been very much better since and have to take only now and then a small quantity of thyroid, whilst before the transplantation they had to take continually much more thyroid and never felt so well; 39 per cent. are much better since the transplantation; they have to take thyroid internally, but only about one-half or one-third of the quantity they took before the transplantation. There were only 14 per cent. failures—that is, cases which did not benefit from the transplantation. There is no doubt that this result, in such a number of cases, proves that the transplant is active, at least for several years. In most of the cases the patient's own thyroid gland resumes a normal function after some years and he is cured; if not, another transplantation can be done. In twenty of our cases transplantation has been done twice and they got well; in eight cases three, and in one four transplantations have been made.

In addition to these clinical results, I can produce direct evidence that the transplanted thyroid tissue takes up the

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