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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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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function of the thyroid; in a case of severe myxoedema in a girl of 11 years the transplant was taken from a patient whose goitre had to be removed. A few weeks later the girl developed between the peritoneum and fascia lata, where an apparently healthy piece of gland from the goitre patient had been transplanted, a hypertrophic goitre of the size of an apple, and at that time all her symptoms of myxoedema had disappeared; she was quite well for five years, when she had typhoid fever; the abdominal goitre became infected and an abscess formed which had to be opened; within a few weeks all her symptoms of myxoedema came back. Von Eiselsberg of Vienna a year ago published a similar case; the patient had been cured of myxoedema by transplanting a piece of gland of a goitre patient in the peritoneum below the liver. The patient died several years after the transplantation from pneumonia. At the *post-mortem* examination a hypertrophic goitre of the size of a hen's egg was found under the liver.

We have succeeded in demonstrating experimentally that the transplant is active. As a rule such experiments have been conducted in a way that could not give a result. The transplantation has usually been made into an animal with a normal thyroid gland; the organism had no want of thyroid and the graft did not live. We proceeded in a different way. We first removed the animal's thyroid almost totally, avoiding the parathyroids, and then waited until the animal developed characteristic symptoms of hypothyroidism. Then a piece of normal thyroid gland of a healthy animal of the same species was transplanted into the upper end of both tibial bones. We then waited until the symptoms of myxoedema in the transplanted animal had disappeared, and a few months later removed the two pieces of gland from the bones, and within a few weeks the symptoms of myxoedema reappeared. I believe that by these observations and experiments we have proved that the transplant can live and, in view of our clinical results, recommend this as the method of choice in cases of hypothyroidism. We believe that it should be tried also in cases of total absence of the thyroid gland.

Selection of Transplant.

The method of performing transplantation in our cases was that described by my father Theodor Kocher in 1909. There are three types of transplantation that can be employed: we may take (1) a normal gland of an animal; (2) pieces of a goitre from a case of Graves's disease; (3) the hypertrophic thyroid tissue around a nodular goitre. We have used all three methods. As early as 1908 we used some heterotransplants from sheep and goats. The best glands to transplant are those from pregnant animals. This method has given a good result in some cases. One of the cases of congenital total absence of thyroid gland mentioned above was entirely cured by transplantation of two pieces the size of a cherry of a normal thyroid gland of a pregnant sheep into the two tibial bones. As a rule, however, homotransplants are much better. They are best taken from the hypertrophic gland of a severe but recent case of Graves's disease, which is in a condition of exquisite cellular hypertrophy and active new formation of vesicles. The best part of the gland to be taken is the upper pole or posterior part of the gland near the superior thyroid artery. It is essential that the pieces of gland (we take usually two to four pieces of the size of a small cherry) shall be put into the receiver's body immediately after being cut out of the donor. The receiver must be ready on a table next to the donor, and the bed for the transplant must be carefully prepared beforehand and in particular all haemorrhage carefully stopped. Besides the glands of patients with Graves's disease, we have very often taken pieces of the hypertrophic thyroid tissue around goitre nodules in young healthy goitre patients. Of course, in every case the donor is examined very carefully beforehand; tests for syphilis and tuberculosis must more especially be done.

The Operation.

As mentioned above, we transplant mostly into the upper end of the tibial bone, where, with Doyen's trephine, the corticalis is opened and a bed in the bone marrow made, exactly of the size of the transplanted piece. We have chosen this bone, first, because it is very vascular and has a

special affinity to thyroid tissue, as shown by the frequent bone metastasis in malignant goitre, and secondly, because the gland is very well protected from injury in the bone. However, we also transplant into the sheath between the fascia transversa and peritoneum, or into the peritoneal cavity. But in the latter it is better to stitch the parietal peritoneum over the transplanted piece of gland and not to put the gland free into the peritoneal cavity. If the graft is to be successful, the healing of the wound must take place without any rise of temperature or other post-operative reaction. The most important of all is the pre-operative and post-operative treatment. The patient must take thyroid some time before and several weeks after the transplantation, in order to decrease his actual want of thyroid, because if this is very strong the transplanted gland tissue is simply eaten up by the organism. The non-observation of this is the most common cause of failure of transplantation, especially in cases of total congenital absence of the gland.

DIFFERENTIAL DIAGNOSIS OF RHEUMATOID ARTHRITIS AS A CLINICAL ENTITY.

BY

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ALL authorities are now agreed that an important factor in the etiology of the arthritides is some form of infective process, and a certain degree of progress has been made in the classification of this amorphous group of clinical material by the recognition of special types as being due to specific infective agencies such as the tubercle bacillus, the pneumococcus, gonococcus, etc. But there remains a large number of cases of non-specific origin which in the past have been aggregated under the term "rheumatoid arthritis." Those with experience in this class of case are not satisfied, however, with this and have preferred the more vague terms of "multiple non-specific infective arthritis," "focal arthritis," or "indeterminate arthritis." Several attempts have been made to differentiate so-called true rheumatoid arthritis from this group, and it is our purpose to report our preliminary investigations for the furtherance of this object.

We would define rheumatoid arthritis as a disease of insidious origin, affecting young adults in particular, usually running a prolonged subacute or chronic course with periodic exacerbations, but occasionally acute in its onset and manifestations, leading to serious deformity of structures in intimate relationship to joints, and associated with digestive disturbance, upset of general metabolism, alteration of the normal blood picture, and with glandular enlargement.

ETIOLOGY.

Patients suffering from rheumatoid arthritis frequently give a history of previous debilitating disease or some prolonged physical strain. A history of rheumatic fever seems to occur more frequently than can be accounted for by the incidence of this disease in the general population. But this condition does not produce chronic intra-articular disease, though repeated inflammatory reactions do occur and may cause such laxity of ligaments and impairment of joint circulation that the synovial membrane is liable to be attacked by other infective agencies. Influenza is another predisposing cause, probably acting simply by the general lowering of resistance, though serous membranes in all parts of the body are liable to inflammatory changes after this disease. Pregnancy and childbirth with their general upset of digestive and metabolic processes are recorded in many instances as the starting point of the attack.

Certain observers¹ have cited cervical and uterine infections, pyelitis, otitis media, furunculosis, etc., as the factories of infection, but we are very doubtful whether these extra-digestive foci are of any real importance in this particular group of cases except in so far as they lower the general resistance. Pyorrhoea and dental caries are frequently, if not always, present, but these conditions are so wellnigh universal that they cannot be held to be solely