tissue; however, moisture seems to slightly reduce the rate of loss in the latter. With regard to the compound tissue—compact-spongy, the changes which its conductivity undergoes present simply a varying mean of those of its two components. After long exposure to the air, the bone being well dried, the conductivities of compact and of spongy tissue are found to closely approximate each other.

*Experiments on Brain.*

The experiments on this tissue had reference only to the changes of its conductivity, due to exposure to the air, and to the effect of moisture and fresh animal liquids on these changes.

Like liver and kidney, the tissue of brain quickly loses its power of conduction after death, and neither moisture or fresh animal matter can restore this loss, although they may diminish its rate.

## II. "Further Researches into the Function of the Thyroid Gland and into the Pathological State produced by Removal of the same." By Professor Victor Horsley, B.S., F.R.C.S. Communicated by Professor Michael Foster, M.D., Sec. R.S. Received December 10, 1885.

In December, 1884, I showed that the thyroid gland was intimately connected with the process of mucin metabolism, that if the thyroid gland in monkeys was removed with antiseptic precautions (the same ensuring healing of the wound in three days) the consequences to the animal were—(1) symptoms of general nervous disturbance evidenced by tremors, paroxysmal convulsions, functional paralysis, mental hebetude, and finally complete imbecility; (2) profound anæmia coupled with leucocytosis; (3) all the symptoms of the disease discovered within the last decade and termed myxœdema; (4) that just as in the acute form of the disease just named there was found to be a great accumulation of mucin in the connective tissues throughout the body (mucinoid degeneration), and in the blood, and as a consequence the same post-mortem appearances; (5) that at the same time there was a great activity in the mucin-secreting glands, and, further, that the parotid gland under these abnormal circumstances secreted mucin in large quantity, the gland cells at the same time disintegrating.

During the past year I have confirmed my previous observations, and greatly extended them, and have firm basis for my original opinion that the function of the thyroid gland is indispensable to the higher animals, and that it is duplex, since, in the first place, it regulates the formation of mucin in the body; and, in the second

place, it aids in the manufacture of blood-corpuscles. My researches during the past year (1885) have been directed towards the investigation of (1) the circumstances which influence the course of the extensive disturbance of general nutrition which follows the loss of the gland; (2) the direct effect of the said fall in nutrition upon the nerve-centres; and (3) the hæmapoietic function of the gland.

(1.) I find that the determining factor *par excellence* of the value of the gland as regards its influence on the general metabolic processes of the animal is *Age*. The effect of removing the gland in the young animal is the rapid appearance of violent nerve symptoms and death in a few days; in a rather older animal, *i.e.*, a one-year old dog, the symptoms are less violent, later in their appearance, and the animal survives perhaps for a fortnight or three weeks; in a very old animal the removal of the gland simply hastens the torpor of old age; these observations refer to dogs and cats. In the higher animals, monkeys, the operation on a young individual produces the same result as in a young dog, but, as I showed last year, an older animal, if kept under ordinary circumstances, will survive for six or seven weeks, dying at the end of that time of myxœdema. On the whole, therefore, it appears that the thyroid gland is of extreme importance when tissue metabolism is most active, and that it diminishes as the senile state advances. Huschke has shown that the relative weight of the thyroid body to the body weight is greatest at birth, that it rapidly diminishes during the next few weeks, and that it steadily decreases as age advances. Finally, the structural degeneration of the gland in old age is well known. It is clear, therefore, that the gland plays an important and constant part in the metabolism of the body; I desire here to draw special attention to the fact that the symptoms of old age, namely, wasting of the actively functional parenchymatous tissues, atrophy, and falling out of the hair, decay of the teeth, dryness and harshness of the skin, tremors, &c., are exactly the most prominent features of the myxœdematous state, whether it occurs naturally in the human being, prematurely, as in cretinism, or artificially, as in my experiments on monkeys. It is, perhaps, well to remark here that, as might have been foreseen, the previous state of nutrition of the body determines to a large extent the rapidity of onset and the course of the symptoms.

The next circumstance of extreme importance which influences the course of the symptoms is the *Temperature* at which the animals are kept after the gland has been removed. I showed last year that one of the most obvious features of the fall of nutrition which follows the loss of the gland was a steady diminution of the body heat, this suggested to me a line of research which has yielded a striking result. I have kept another series of animals (on whom I have performed thyroidectomy under the conditions above stated) at a constant tem-

perature of 90° F.,* and when they exhibited any nerve symptoms, *i.e.*, tremors, &c., were placed in a hot-air bath at a temperature of 105° F. The effect of this has been to lengthen the duration of life (in all but very young animals) four or five times the extent of that observed in the first series. Instead of living four to seven weeks they now live as many months. At the same time several additional facts of importance are noted, and the symptoms before referred to are so modified as to require the addition of a third stage to the two I described in 1884. (These observations refer solely to monkeys.) The animals kept under the extra high temperature above noted thus pass through three stages—(1) neurotic, (2) mucinoid, (3) atrophic. I have said that the neurotic stage under these circumstances may be scarcely marked, or if the nerve symptoms occur, and the animal be put in the hot-air bath, they soon disappear. Next the animal lives through the mucinoid stage, *i.e.*, myxœdematous condition, and arrives in the third stage—the atrophic. Now, the symptoms of the second stage are just as much subdued as those of the first, there is no excessive secretion of mucus, the parotid glands do not swell, and the post-mortem examination does not reveal the extensive mucinoid degeneration observed in the first series. Finally, the third, atrophic, stage into which the animal passes is evidenced by great emaciation, functional paresis and paralysis, imbecility, falling blood pressure and temperature, with death by coma.

I am disposed to regard this fact of the animals passing through these neurotic, mucinoid stages, and dying at the end of the atrophic, as the key to the observation that cretins in whom the thyroid gland is very slowly destroyed, and very chronic cases of myxœdema, do not exhibit much mucinoid degeneration.

(2.) I will now briefly enumerate the direct effect of the fall of nutrition produced by the loss of the thyroid gland on the nerve-centres: (*a*) Effect on cortex.† The tetanus obtained by stimulating the cortex is remarkably changed (even as soon as one day after the thyroidectomy in a dog, who exhibited violent symptoms in twenty-four hours) by the fact of the fall (when the current was shut off) being as sudden as that observed on stimulating the corona radiata. Next, that the tetanus in a more advanced case is soon exhausted, the curve approaching the abscissa soon after the initial rise; at the same time the curve is followed by clonic epileptoid spasms, which, however, are soon exhausted. Stimulation of the corona radiata and spinal cord also gave the customary tetanus, which, like that of the cortex, was rapidly exhausted. These stimulations of the nerve-centres sup-

* In my first experiments (1884) the animals were kept at a temperature varying from 60° to 70° F.

† Graphically recorded according to method described by Prof. Schäfer and myself ("Proc. Roy. Soc.," vol. 39, p. 404).

pressed the thyroid tremors just as voluntary movements do. Another evidence of the changes in the cortex is the frequency with which continuous stimulation will evoke the appearance of clonic spasms on the original tetanic curve, the latter not being followed by epilepsy when the current is shut off.

(*b.*) Effect on the spinal cord. The tetanus obtained by stimulating the spinal cord like that of the cortex rises slowly to the highest point, and then steadily falls towards the abscissa although the stimulation is maintained, and when the current is shut off the muscle completely relaxes, having absolutely lost its tone, and this tonic paralysis is not recovered from for ten to fifteen seconds. Stimulation of the spinal cord to fatigue, after some time has elapsed so as to produce exhaustion of the preliminary tetanus, evokes a tremor of eight to ten per second.

Tracings from an old animal (cat), which had survived the operation some months, and also from a dog, in which case the symptoms had been very severe for some days, exhibited only a very feeble tetanus in the former instance, and no reaction at all in the latter; this being the ultimate state of depression of function which the nerve-centres had arrived to.

(3.) I have thought it as well to add to the anatomical and physiological proofs I gave last year of the thyroid gland being a hæmapoietic structure by counting the number of corpuscles in the blood of the thyroid artery and vein respectively. After discounting any possible alteration in the relative number of the corpuscles in the two vessels by changes in the fluid constituent of the blood which may have happened in the gland, the much greater number of corpuscles in the vein (+7 per cent.) confirms the deductions drawn from my previous observations.

To sum up, the functions of the thyroid gland appears to me to be two-fold as already suggested, viz.: (1) Control of mucin metabolism, (2) Hæmapoiesis. The metabolic processes in the body may be regarded broadly as resulting in Construction and Destruction. The products of destruction are the waste products of tissue change, and being, as such, harmful to the organism, are cast out by the excretory organ. It appears to me that the thyroid gland aids in excretion of mucinoid substances or their precursors, not of course by excretion properly speaking, that is, casting them out from the body, but by metamorphosing them into some other form which is useful to the system. That this process, whatever it is, is of vital importance to the young mammal (seeing that interference with it causes death in a few days) is obvious, and such as it is the loss of it is distinctly connected with the appearances of the diseases known as myxœdema, cretinism, and senile degeneration. Finally, this defect in the circle of metabolism determines the appearance of so-called functional disorders of the nervous system.