THE BROWN LECTURES ON PATHOLOGY.

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It having fallen to my lot to deliver the annual course of five lectures on Pathology, prescribed by the conditions of the will of the late Mr. William Brown, I originally chose as my subjects three topics of practical surgical interest, namely, the operative treatment of goitre, simple traumatic pyrexia, and urethral fever. The issues hanging upon that now much debated question, the surgical treatment of goitre, are really so wide, that experimental research soon showed the necessity of a greater breadth of view; and thus it comes about that I am prepared, in my first two lectures, to support the dictum (first completely enunciated by my friend, Dr. Felix Semon) that cretinism, congenital or acquired myxœdema, and cachexia strumipriva, are merely phases of one and the same state, and due to the same cause, namely, arrest of the function of the thyroid gland. I have artificially produced myxœdema in the monkey, and therefore hope to show you, in the following lectures, that the evidence in favour of the foregoing dictum rests on a sound basis of experimental fact. In my third lecture, I shall treat of the etiology of traumatic fever, as illustrated by the pyrexia following simple fractures; and in my fourth, I shall consider the varieties and pathology of urethral fever, so called. The fifth lecture will be delivered at the Brown Institution, and will be a practical demonstration of the working of that laboratory and hospital, as directed in the provisions of Mr. Brown's will. Further notice of this lecture will be given on the evening of the fourth lecture.

LECTURE I.

THE THYROID GLAND: ITS RELATION TO THE PATHOLOGY OF MYXŒDEMA AND CRETINISM, TO THE QUESTION OF THE SURGICAL TREATMENT OF GOITRE, AND TO THE GENERAL NUTRITION OF THE BODY.

VARIOUS as have been the surmises as to the function of the thyroid gland, it is not a little surprising that, although arrest of it had been vaguely known for hundreds of years to be connected with the cretinous state, it was not, until eighteen months ago, that it was suspected to be of serious importance to the animal economy.

The extraordinary condition, known as cachexia strumipriva, into which patients relapsed, in whom the operation of extirpation of goitres had been performed, was first discovered and published by the Swiss surgeons, Reverdin (quoted by Kocher; see foot-note, p. 274) and Kocher (*Archiv für Klin. Chirurgie*, Band xxix, p. 254, 1883); and the pressing need of settling the practical question of the justifiability of this surgical procedure has led to new discoveries in the relation of the thyroid body to the general nutrition of animals.

We are, consequently, able to study the whole subject from the scientific stand-point of facts, deduced from exact experiment, and I shall arrange the matter of these lectures in the following way.

First, I must very briefly allude to the anatomical position and structure of the thyroid body; secondly, various theories concerning its function, which have been put forward up to 1883, must be passed in review; thirdly, I shall fully describe the phenomena which follow the excision of the gland in the higher animals; next, the relation of the gland to the pathology of myxœdema, cretinism, and cachexia strumipriva; while, fifthly and lastly, will come the practical surgical point, namely, the operative treatment of goitre, with a fitting summary of the foregoing facts and arguments.

Structure.—The thyroid gland consists as is well known, of a bilobed organ, surrounded by a fibrous capsule, with trabeculae of connective tissue derived therefrom, penetrating the interior of the mass, and forming a stroma with large alveolar spaces. The stroma demands special attention, since running in it is so rich a network of blood-vessels and lymphatics that the sum of the sectional area of the thyroid arteries is more than half that of the cerebral arteries, as you see by the transverse sections of these vessels, which have all been distended at exactly the same pressure, and afterwards dried; while the lymphatics have been shown by Frey (Communication to Medical Society of Turin), Boéchat (*Recherches sur*

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la Stricture Normale du Corps Thyroïde; Paris, 1873), and Baber (*Proc. of Roy. Soc.*, vol. xxiv, p. 240), to form huge lacunar spaces immediately outside the margins of the alveoli. But also must be noticed the large lymphatic nodules lying along the blood-vessels, as they will be shown to play an important share in the formation of the blood. Hitherto the nerve-fibres, coursing in the meshes of the stroma, have not been shown to be more than vaso-motor in function.

It is, however, to the acini of the gland (for gland we ought to call it, it seems to me, in view of most recent researches) that I wish to draw especial attention. It is only necessary to mention that, in development, the thyroid follows a course exactly similar to that of a racemose gland, for us to remember that belief in the intercommunication of the acini is still held by Virchow and Boéchat (*loc. cit.*), although the anatomical proof of such communication, by means of injection, etc., is still wanting. It is interesting to couple with this idea the statements of the older writers, especially Theophile de Berdeu (*Rech. Anatomiques sur la Position des Glandes et sur leur Action*; Paris, 1751) and Ricou (*Recueil de Mémoires de Méd. et Pharm. et de Chirurg. Militaires*, July, 1869), who believed that they had discovered slender ducts leading from the gland into the mucous membrane of the trachea, according to the former, and of the larynx, according to the latter.

Whether the notion of the acini all forming part of a ductless racemose gland will be proven or not, it does not alter the claim of the thyroid to be regarded as a gland, anatomically speaking; since, apart from the evidence of development, we have cavities lined with an epithelium, columnar in an early stage, and later cubical, the walls of the cavities surrounded by a rich capillary network, while the lumina of the acini contain a glairy fluid containing mucin, according to Kühne and Eichwald (*Lehrbuch der Physiolog. Chemie.*, 1868); while Gornp-Besanez states that, although very similar, it yet differs from mucin in being soluble in acetic acid. Everything seems to favour the view advanced by Baber (*loc. cit.*), with many authors, namely, that the mucinoid contents of the acini are excreted from the blood by the lining epithelium, and that reabsorption into the circulation is effected by means of the large lymphatics.

Function.—We must leave for a moment the argument respecting the excretory function of the thyroid gland until the second lecture, when we shall have seen the results of extirpation.

Two further distinct views respecting the functions of the thyroid gland have been advanced by different writers, arguing from different points of view; first, that it was a regulator of the cerebral circulation; and, secondly, that it secreted something necessary to the perfect nutrition of the brain. The first of these was originally advanced by Mr. Simon, but is generally attributed to Liebermeister and Guyon, and rested partly on the anatomical relationship which the gland bears to the carotid arteries in the human being; it also found support in the exceedingly elaborate researches of Mr. Simon, who found that, in all vertebrates which he examined, it was in close relation to the cerebral arteries. Guyon, relying on the fact that the pulsation of the carotidean branches disappears on prolonged effort, believed that this was beneficial to the central nervous system, by diminishing the flow of blood in those parts where venous stasis of course was already occurring from the prolongation of the effort; and considered it to be effected by the pressure of the thyroid gland on the common carotid artery, such pressure being produced by the contraction of the neck-muscles upon it. The physiological fact of the diminished pulsation in the carotid arteries anyone can at once confirm by experiment, but the explanation given above must be criticised by means of experiment in persons or animals deprived of their thyroid gland.

The argument is sometimes adduced that the blood-supply in the thyroid and brain are nearly equal, as I have just shown you; but this, of course, has no value; for, to imagine a paradoxical converse, the brain might be regarded as a mechanical regulator of the circulation in the thyroid gland. Luschka, indeed, regarding it as a mechanical structure, considers it to act as an elastic bolster, keeping off the pressure of the muscles from the important structures.

The idea that it may secrete something peculiarly necessary to the nutrition of the brain arose with Mr. Simon (*loc. cit.*); but, as will be shown, although profound changes occur in the nervous system, still the whole body is affected (whether secondarily or not is uncertain), so that we must rest content with simply stating the view expressed without further comment.

An idea, which scarcely can be considered as ever formulated into a definite theory, has from time to time been put forward, namely, that the thyroid gland is, in some way or another, hematopoietic. I must consider this point at length in discussing the course of the

oligæmia produced by thyroidectomy, and only now refer to the existence of lymphatic nodules (which were described above) as lending support to this notion.

So much for what was known and surmised up to 1883. I shall now proceed to lay before you evidence that this highly vascular mucin-secreting gland has a far wider relation to our general health than is even suggested in the foregoing theories.

Effects of Excision.—This brief retrospect of our knowledge up to last year will serve as an introduction to the next question, namely, what happens if you remove the thyroid body completely.

Kocher (*loc. cit.*) has shown that, under these circumstances, the human being becomes a cretin. Schiff (*Servus Médicale de la Suisse Romande*, February and August, 1884), Wagner (*Wiener Medizin. Blätter*, 1884, Nos. 25 and 30), and the Italian experimenters, Sanquirico and Canalis (*Archivio per le Scienze Mediche*, vol. viii, Fascic. 2, Turin, 1884), have shown that dogs exhibit great nerve-disturbance, become idiotic, and die comatose; while I think I shall be able to demonstrate, from my observations during the last three months, that this operation produces, in monkeys, the disease first accurately described by Dr. Ord (*Medico-Chirurgical Transactions*), and called by him myxoedema. I shall afterwards attempt to show that this is only a phase of a loss of nutrition determined by the destruction of the thyroid gland, and, like cretinism, is the effect of some as yet undetermined law. I wish here to state that, during the first few days, I enjoyed the collaboration of Mr. Godlee, who was unable to continue the research, owing to numerous engagements, and that the first four experiments were thus begun with him.

A few words are absolutely necessary regarding the details of the experiment, as futile discussion has arisen from want of knowledge on this point.

From a frozen section of a normal Macaque monkey's neck, you will see that the thyroid body rests in a mass of fat and connective tissue, forming the so-called outer sheath or false capsule; and that it is separated by a considerable distance from the jugular vessels and nerves. The steps of the operation obviously had to be conducted so as to ensure healing by the first intention, and the avoidance of injury to, or irritation of, nerves; therefore it was performed under strict antiseptic precautions, and in the following way, the animal being under ether. The superficial structures were divided exactly in the middle line, and the sterno-hyoid muscles separated and held aside gently, while the fascia covering the isthmus was divided with the knife. The isolation of the isthmus was effected by a blunt instrument, a seeker, and a loop of catgut was passed beneath it to produce traction when required. The separation of the false capsule was then cautiously performed by holding the gland in forceps, and stripping off the tissues with the seeker or forceps. In this way, the gland was completely enucleated, except where the arteries entered. To avoid ligaturing these, they were seized in forceps, and torn out of the gland, so that the ruptures prevented hæmorrhage; and, as it occurred in the gland, the proximal portion of the trunk, with its surrounding nerves, was left uninjured. In all my experiments, I have only seen the thyroid arteries spurt three times, and this would, therefore, seem a practical means to adopt when one-half of a goitre has to be excised; all bleeding stopping in a few seconds with light pressure of carbolised wool, no ligature was ever employed. The total bleeding was usually not more than half a drachm to a drachm. The wound was then completely closed with, usually, fifteen horseshair-sutures, and dressed with a small piece of dry gauze and collodion. It was invariably healed absolutely in three days; and, as the seat of operation could be handled on the second day without the animal appearing disturbed, I think we may assume that it practically suffered no pain.

Post mortem observation showed that the gland was always completely removed, and that in no case was there any injury to the recurrent laryngeal nerve. The only one lying within two millimetres of the gland. In fact, as you may see in the specimens under the microscope, the sympathetic and other structures are perfectly normal; so the theories which would base the pathology of myxoedema on a primary disease or injury of the sympathetic, are, to my mind, inadequate.

Schiff's first series of experiments was performed septically; the wound was often not healed at the death of the animal, so that they cannot be accepted as trustworthy; but his second series, he states, was performed antiseptically, and although the duration of healing is not mentioned, I think we may assume that it was rapid; and it is these experiments that I shall quote. Wagner (*loc. cit.*) and the Italians (*loc. cit.*) obtained union by the first intention; and as they simply confirm Schiff (*loc. cit.*), I shall quote all together in comparing the results obtained from dogs with those seen in monkeys and man.

The phenomena which follow thyroidectomy in monkeys are very striking, and may be summarised as follows. At a variable period after the operation, but averaging about five days, the animal is found to have lost its appetite for a day or two, and, on closer examination, to exhibit slight constant fibrillar tremor in the muscles of the face and hands and feet more especially. These tremors disappear at once on voluntary effort. At the same time, the animal is noticed to be growing pale and thin, in spite of the appetite returning quickly, with great increase; rapidly the tremors increase, affect all the muscles of the body without exception; the animal becomes languid, paretic in its movements, and imbecile. Then puffiness of the eyelids and swelling of the abdomen follow, with increasing hebetude. During these last stages, the temperature, gradually falling, becomes subnormal; and then the tremors gradually disappear as they came. Meanwhile, the pallor of the skin often becomes intense; and, leucocytosis having been well marked, oligæmia follows, and the animal dies perfectly comatose in a variable period, but usually about five or seven weeks after the operation.

I will now describe these symptoms in detail before enumerating the appearances found after death. It will have been noticed that the most obvious effects arise from disturbance of the nervous system; and, therefore, we will take the motor symptoms first.

In the dog, these are almost exactly similar to what I have described, but beyond that, in that animal, they are usually paroxysmal, and very frequently tetanic, we have no further information as to rate, etc. Wagner (*loc. cit.*), however, distinctly observed them to commence by fibrillation, and then by clonic spasm to pass over into tetanus and rigidity.

The same condition was observed in cats, but proceeding much more rapidly.

In the monkey, I have found that, as a rule, the animal, after complete thyroidectomy, appears perfectly well for (on the average) about five days. Then there is noticed a slight fibrillation of the intrinsic muscles of the hands, feet, and jaws, following this order in successive invasion. As a rule, this fibrillation soon becomes a constant tremor, a tracing of which I now show you. (Fig. 1.) You will see that it is perfectly

Fig. 1.

steady, and having a wave-rate of 8 to 10 per second; in passing, let me first show you the tracing (Fig. 2) of ankle-clonus in a man suffering from caries of the spine, which is of exactly the same rate. I shall return

Fig. 2.

to this point directly. Occasionally, the tremor commences immediately after the operation, as will be shown presently. (Fig. 3.)

Fig. 3.

This constant tremor is soon replaced, or rather is added to, by a series of powerful clonic spasms, so that a tracing (Fig. 4) now shows large waves indicating massive movements of the trunk and limbs. Superposed on these large waves, we see a fairly constant tremor forming little undulations, the lengths of which vary from the rate just given to double and even treble that speed, usually 20 to 40, multiples of 4 and 10.

I shall refer to the large waves as paroxysms, since you can see by this tracing that the intervals between them are often very considerable, namely, half a second or more. This paroxysmal stage usually appears about the second or third day after the tremors were first noted; but they rapidly (in twenty-four hours) completely shape the curve in the way just indicated, which it preserves on the average for about twenty days. This stage of the tremors may be so violent

as to deserve the term convulsive; but I have never witnessed true tetanus in the monkey as it occurs in the dog, nor have I ever seen the spasms produce pain, as in the latter animal.

I now show a tracing where the spasms are very violent (Fig. 4). You

Fig. 4.

will notice that, although the contraction is powerful, the rate is 20 per second, and that the tonicity of the spasm (producing what I may call the "tetanoid paroxysm") is due to the summation of the effects of four waves as a rule. The force of individual contractions is variable, but always greatest during a paroxysm, and least immediately afterwards.

There is, apparently, an important point of difference between the dog and the monkey; namely, that it is the rule in the former animal for death to occur when the tetanic paroxysms are often at their height, while invariably, in the latter animal, they gradually fall in force, reassume the type seen at their onset, and disappear sometimes as much as ten days before death. Hence, if ordinates represented force and abscissæ time-intervals, a curve representing the tremors would show a rapid rise, then a constant pause, followed by a gradual fall.

It would require much more minute analysis than I have been able to give the time for, to elucidate the origin of these tremors; but a very cursory observation shows the subject to be one of immense importance, as tending to explain, not the pathology of occasional fits of trembling, such as a rigor, etc., but, what is of infinitely more importance, the causation of a constant tremor, such as in paralysis agitans. I here show you a tracing (Fig. 5) from a well marked case of the

Fig. 5.

tremor of paralysis agitans, kindly sent me by my friend Dr. Beevor, from which you will see that we have to do with a violent tremor, the rate of which is half as rapid as ankle-clonus or the early tremors I have shown you. Consequently, the wave-rate is 4 or 5 in a second. But I have found, in further observation, that there are frequently indications of each wave being a compound of two, so that the customary rate of 8 or 10 in a second is still shown to be the common one. But the field of observation does not, of course, rest with paralysis agitans, although I have only time to refer to that disease. Those familiar with paralysis agitans would have seen many similarities to it in these tremors; and, in connection with them, I may now mention that, although so-called voluntary effort abolished the tremors at their onset, it, if anything, increased them in the later stages. Then, again, Wagner has noticed retropulsion, which is an extremely suggestive observation, but one I was not able to confirm; but future research will be directed especially to elucidate this subject.

The origin and seat of these tremors must now be discussed very briefly.

Schiff showed, by division of the motor nerves, that the tremors were probably of central origin. This I have confirmed; but it has only been possible to make one experiment on this point, namely, to attempt to determine whether the stimulus affects the cortical motor area, the bulb, or the spinal cord. In one case, I removed the upper limb-centre in the cortex, producing absolute brachiooplegia, but without interrupting the tremors, as you see in this tracing (Fig. 3). The argument in favour of the symptom being due to disturbance of a lower centre in the bulb, or spinal cord, or basal ganglia, gains support from the fact that, at first, voluntary effort abolishes it; that the inhalation of ether increases it; that it disappears on reflex irrita-

tion; and that the rate is at first 8 or 10 per second, and, later, a multiple of that; while it happens to be the rate which Lovén has determined for the spinal cord in frogs, and, I have shown you, is probably the spinal cord rate in man. These experiments, however, do not disprove the possibility of these tremors being idiomuscular.

During the whole time that the animal is the subject of these tremors, there is marked rigidity of the affected muscles, and also paresis. The rigidity varies directly as the force of the tremors; but the paresis commences gradually, and progressively gets worse up to death. Occasionally the animal will appear to recover power slightly, and to be more active; but, as a rule, they steadily grow weaker.

Almost complete paralysis of the extensors of both limbs, but especially the upper, I have frequently observed; but it is never absolute, although the appearance of wrist-drop may be excessively marked. The ordinary paralytic posture of the hand is also very commonly to be noticed. A most interesting fact I have twice observed, namely, a complete attack of hemiplegia. In the best marked case, the animal presented every classical symptom. The onset was very sudden, the animal being weak, but in possession of equal motor power on the two sides, when it suddenly fell over, and was found to be absolutely paralysed on the left side (the right side was in a state of paresis, but this was

Fig. 6.

so before the attack). Rigidity was well marked; but the tremors almost entirely disappeared from the left limbs, though not from the jaw-muscles. The animal was perfectly conscious and normally emotional. In an hour, these symptoms disappeared, and the tremors became very marked. It was clear that this was an attack of functional hemiplegia, and the *post mortem* examination some days later proved it to be so.

Although we see such profound alteration in motion, the same cannot be said of sensation. It is never easy to determine the sensibility to touch in animals, or, for the matter of that, their appreciation of pain; but, from continued observation, I believe that only during the most advanced paroxysmal stage is sensation affected—perhaps delayed; and at the same time there is slight anæsthesia, but this is very incomplete.

Reflexes. Superficial.—These are diminished, with tactile sensibility; the conjunctival remaining normal. **Deep.** The knee-jerk was always marked when rigidity did not prevent its exhibition. Ankle-clonus I never succeeded in eliciting.

Centres.—The spinal lumbar centres all act normally; although, of course, in the final comatose stage, the bladder becomes overdistended, unless attended to.

I have never seen permanent bulbar symptoms, and none to indicate irritation of the general vaso-motor centre, but have observed transient difficulty of swallowing, and, as will be described directly, occasionally slight attacks of dyspnoea.

I have purposely postponed the consideration of the affection of the higher functions of the cortex cerebri until now, because, although most important, they vary directly with

the degree of severity of the foregoing symptoms. Briefly, they may be summed up as the slow onset of hebetude, terminating in complete or partial imbecility. From these lantern-photographs, the change from the well known vivacious condition of the healthy monkey is very obvious, while in this one (Fig. 6) is shown a remarkable position, which is quite characteristic, and which the animals assume in the advanced condition of imbecility following the operation. In this state they take no notice of anything going on around, and only rouse up to eat.

The same listless air is observable in severe cretinism, and, through the extreme kindness of Mr. Lunn, I had the opportunity of seeing in Marylebone Infirmary an advanced case of myxœdema assume a closely similar attitude and expression. There is little change in the emotions, except that the animals are easily enraged in the same way as idiots. There is almost complete so-called inhibition of voluntary power, as will have been seen from the foregoing facts.

Among the rarer symptoms, the importance of which will be seen hereafter, were occasional attacks of dyspnoea, never very urgent, nor occurring more than twice in the same individual.

Peripheral Nervous System.—The pupils always reacted normally.

To trace the remaining symptoms, we must describe the changes in the functions of the various systems, and will begin with the circulatory.

Circulatory System.—The blood-pressure steadily falls from the time of the operation, and shortly before death, is scarcely more than two or three millimetres of mercury; but the most noteworthy changes are those in the composition of the blood. Starting with a normal average of 61 in the field, the number of the red corpuscles steadily decreased from the time of the first operation to 48 (average) at the end of the first fortnight. About this time, it apparently found an equilibrium; and though, of course, a state of oligemia, it remained at this point, or with very slight rise (to 50), until death. But, while the red corpuscles were diminishing, the white were increasing. The normal average number in a field being 4, it rose in a fortnight to 14; then, in concert with the oligemia, it steadily diminished till death, even slightly below the normal.

In the course of very numerous observations with Gowers's hæmacytometer, I have come to the conclusion that it does not give safe results concerning the proximate number of white corpuscles, when these are only counted by means of squares. I have taken the average of ten fields, which I find more accurate; and remembering that it gives about three or four per cent. higher estimations, it is easy to convert the results.

The condition of oligemia can be recognised with the naked eye. In daily observations, one saw the animals becoming paler, until the equilibrium-point referred to was reached, and when the drop of blood was drawn for the cytometric observations, it could be seen to be thinner than normal. At the same time, it clotted with difficulty and slowly, but when it did, it formed a well marked buffy coat.

But the next important change in the blood is a chemical one. My friend, Dr. W. D. Halliburton, kindly undertook the chemical analysis of various tissues, simply estimating the quantity of mucin (extracted from known quantities of the tissue) by weighing the precipitate produced, by adding acetic acid to baryta-water holding the mucin in solution. He has found that, whereas mucin is absent from the blood of healthy monkeys, it is present (in increasing quantities, according to the duration of life after the operation) in my artificial myxœdema, as may be seen on this diagram (see Section 2).

He has also found that, while the total proteids are about normal in amount, the serum-globulin is probably increased, and that the serum-albumen is not differentiable into three varieties by heat-coagulation, as it is in the normal monkey.

Respiratory System.—The only abnormal symptom was dyspnoea. This was probably simply of bulbar origin, since it came on suddenly and disappeared soon, without any other physical signs.

There was never any laryngeal stenosis nor paralysis of the vocal cords, nor alteration of the trachea, as has been suggested, to account for the symptoms.

From the microscopic specimens, you will see that the recurrent laryngeal nerves are perfectly sound.

Alimentary System.—A point of extreme interest and novelty is to be found in the alimentary system, namely, that the salivary glands undergo an enormous hypertrophy. In this photograph (Fig. 6), you see them forming swellings, like those of mumps, on each side of the animal's neck. This swelling of the glands is quite painless, and it is simply an increase of the secretion of mucin, for not only does Dr. Halliburton show the increase to be very great (in one case sixty times the normal amount), but physiologically the condition is very interesting, because the parotid gland is normally a serous gland,

while here it is seen to become a muciparous one. This important point must, of course, be again referred to.

The condition of the appetite is a prominent feature in the disorder, namely, the post-thyroidectomy state; for, as an invariable rule, I have seen the appetite fail at the onset of the tremors, then, after a few days' depression, rise far above the normal, the animal seizing greedily everything offered it. This continues until shortly before death, when it falls again completely.

Connected with the digestive, but also with the hæmatopoietic, system, is the spleen. The observations made by Crede, Zesas, and Tauber, show that there is a connection between the thyroid and the spleen to this extent, that when one is excised the other temporarily swells. I can fully confirm this, for I have detected the swelling of the spleen by increase of the splenic dullness during life, and proved it by *post mortem* inspection.

But an important point is, that we have in these animals a gradual swelling of the abdomen, just as in myxœdema, and this is due to hypertrophy of the great omentum, and distension of the intestines. There is also always some amount of peritoneal fluid, but never enough to deserve the term ascites. This fluid also contains mucin.

Renal System.—The urine I have very frequently examined qualitatively, and have found that, as a rule, it is perfectly normal. I have, however, occasionally observed glycosuria, lasting a day or more, but this is very variable, and has occurred both before and during the stage of tremors. Throughout the life of each animal, there was always a trace of mucin in the urine, but this was not pathological.

Genital System.—I have never seen the reproductive instinct in action.

Skin.—Beyond the pallor due to the anæmia, the skin, to outward appearance, is normal. The question of perspiration is a difficult one to decide in monkeys, but I thought that the skin remained averagely moist. But we have repeated here the swelling and hypertrophy, as in myxœdema; the lower eyelids become puffy and elastic, so much so as to diminish the palpebral fissure one-half, and the face of the animal becomes very similar to that pathognomonic of the disease mentioned.

Although dryness of the skin has not been observed, here is an example of atrophy of the hair in the animal that lived longest. It was interesting to observe the bald patches appear, first, on the right side, and then on the left; and their situation just above the root of the tail is very suggestive, in view of the ordinary site of bed-sores in man. I may here remark, parenthetically, that, of course, in the monkey, these parts are never submitted to pressure.

In the way of varying the experiment, I have also cut off hair in an early stage, and found that, even after several weeks, it had grown very little.

But the most scientific method of estimating the constitutional change in the animal's condition is, of course, thermometry; and, from a complete series of morning and evening observations, I have constructed the average curve of temperature. It will be seen at once that, immediately consequent on the operation there is a slight rise, followed by a fall, in a few days, to normal; this, of course, is simple traumatic fever, as I shall explain in my third lecture. Then, as the tremors develop, there follows a condition of exaggerated morning fall and evening rise, but nothing which can be considered more than a

Temperature after Thyroidectomy; Morning and Evening.
Normal Temperature before Operation, 100.2.

Day after Operation.	M.	E.	Day after Operation.	M.	E.	Day after Operation.	M.	E.
1	101.5	100.7	16	100.7	100.6	31	98.6	98.4
2	100.6	100.8	17	101.2	101	32	97.8	96.6
3	100.3	—	18	99.4	100.9	33	96.6	100.2
4	100.4	100.8	19	99.5	100.5	34	97.1	98.2
5	100.6	—	20	99.4	100.3	35	98	99.8
6	100.4	100.3	21	99.3	101	36	98.8	99
7	100.8	101.2	22	99.9	102	37	98.4	98.7
8	100.5	101	23	99.6	101	38	98	—
9	101	101.1	24	99.7	100.6	39	95	—
10	100.8	101.3	25	100.3	101.4	40	95.2	—
11	100.3	100.9	26	100.3	102	41	96	—
12	99.9	100.2	27	100.7	101.2	42	95.4	95
13	99.2	101	28	—	101.6	43	95	—
14	98.6	100.4	29	—	100.1	44	94	—
15	100.4	101.4	30	97.0	99.2	45	92	—

superexcitable thermic condition. Schiff (*loc. cit.*) has described high fever in dogs when the tremors were most marked, but I have seen nothing of it in the monkey. After the severest stage of the tremors,

the temperature gradually falls to death, at which point it is many degrees subnormal. Clinically, this is shown by cold extremities at the commencement, followed by general coldness of the whole body-surface. I have never seen shivering excited by cold air, however: a fact not without interest.

It is difficult to express, by *seriatim* discussions of aberrant functions, the full force of the symptoms exhibited after thyroidectomy; but those conversant with the appearance and bearing of myxœdematous patients will have no difficulty in recognising a parallel condition, in which, however, some symptoms, for example, the tremors, are more exaggerated than in the human being.

Possibly, the mere rapidity of death may seem to some the most striking result, considering the hitherto undreamt-of importance of the thyroid gland; but, although the *post mortem* appearances about to be described may seem inadequate, it must not be forgotten that the perversion of nutrition indicated thereby is really profound, and is the result of a small but constantly acting force.

THE PLACE WHICH ALCOHOLIC DRINKS SHOULD OCCUPY IN THE TREATMENT OF DISEASE.

Read at the Hunterian Society.

By ALFRED CARPENTER, M.D., M.R.C.P. Lond.

I NEED not apologise for bringing this subject to your notice. It is one of the burning questions of the day, and likely to stand in the first rank, both politically and therapeutically. As citizens of a free country, we must not refuse to look at its political aspect, and to form our opinions according to the evidence which may be forthcoming as to the conditions under which the sale of such articles as wine, spirits, and beer may be carried on; but I shall avoid that side of the subject on this occasion, and restrict my observations as much as possible to the therapeutic value of these agents. I cannot shut my eyes to the necessity which exists for accurate information upon this point; a fearful responsibility rests upon our profession in this matter, and it must be faced. Our duty is threefold.

First, as members of a great commonwealth, which must override every other consideration, we must be just and honest men first, we must be true citizens. We must not do evil that good may come, in spite of any teaching to the contrary. The end will never justify the means, if the means be wrong.

The second duty is to our patient. He engages our services for a twofold purpose; first, to cure him of his disease; and, in the second place, to prevent its recurrence. The therapeutic duty is not the only one which we have to perform. If a workman be sent for to stop a leak in a water-pipe, and he content himself by plugging it with some material which stays the leak, but which is dissolved by the water, so that the waste is, sooner or later, renewed, that workman fails in the duty for which you employed him. He must not only stop the waste, but prevent its recurrence. It is so in the treatment of disease. The physician has only done a part of his duty who limits his work to the removal of the present set of symptoms, but gives no instructions for the purpose of preventing their recurrence. If he give advice which may be beneficial for to-day, but which is certain to be pernicious if it be persevered with beyond a stated time, he has only done half his duty, and that half badly.

The third and last duty of a physician is to himself, as regards pecuniary reward. He must place this in the last rank, and not in the first position. Self must be put aside. The man who follows these rules will be a blessing to his patient, and will assist to guide his country through one of the greatest dangers which can possibly beset a nation in its battle with the drink evil.

Having made these few observations upon duty, I will go to the special object for this evening's discussion.

It is now nearly seven years since I had the privilege of delivering the oration to the Medical Society of London. In that address, I endeavoured to show that alcohol in all its forms was unsatisfactory as a diet, and that its daily use by men in health ought not to be encouraged by the earnest followers of the healing art. I was then supported by one of the greatest authorities of the time, who wrote to me a few days afterwards, and said "that he agreed with every word that I had spoken in that address, excepting, however, two lines," in which I had stated that I could not advise an old man accustomed to take wine daily to give it up. That same authority has reiterated his

view within the last month. I refer to Sir A. Clark. He says, "a healthy man is better without alcohol, which agent is not a helper but a hinderer to work." I am glad to find that Sir Andrew is very decided upon this point, as decided now as he was seven years ago. The experience of the past seven years has not led me to modify the view that I then held, but, on the contrary, to render it even more decided than it was in 1878. A close observation of effect, on families and individuals, tells me that my views, as then expressed, are essentially right on this point. I propose on this occasion to consider the position which alcohol should occupy in the treatment of disease. Before, however, we can thoroughly assess its value in the cure of disease, we must be quite certain as to its physiological action in healthy tissue. I shall, therefore, ask you to allow me to trace its physiological effect, then to consider the pathological consequence which may result from its regular and irregular use, and afterwards detail the class of cases in which it is accustomed to be used, and in which it may or may not produce beneficial effect. Having considered the physiological action, we shall then be able to say whether it does good or evil as usually presented. Finally, I propose to point out the cases in which it may be of inestimable benefit, if rightly used, and if rightly discontinued when its effect has been secured.

Physiological Action.—Take absolute alcohol, its formula being C_2H_5O ; it is an oxide of the radical ethyl. It is not met with as such in ordinary circumstances, but it is better known to us as proof-spirit. This is defined by law as a mixture of water with 49.24 per cent. of alcohol. Every 0.5 per cent. of alcohol above this corresponds to one degree over proof. Concentrated alcohol acts as a poison in whatever way it may be administered, and numerous instances are on record in which death has been rapidly produced by it, its attraction for water being the real cause of this effect. Half a pint of gin has proved fatal to an adult. Works on toxicology give numerous instances in which death has been brought about in from two to six hours, and in some cases it has been almost instantaneous in its effect.

There may be intense coma; convulsions are not uncommon; and occasionally the symptoms have all the characteristics of an irritant poison, according to the tissue affected by it. Indeed, an early, free, and active vomiting, succeeded by a sound sleep, especially if it be accompanied by profuse sweating, may be the saving of the patient's life when a deadly dose has been given.

The symptoms of alcoholic poisoning vary somewhat according to the habit of the person affected. They are immediate and decided in the total abstainer, whilst, in the habitual drunkard, at one time a large quantity produces but little effect, but at another, especially after a time of abstinence, a much smaller quantity of liquor sets up a series of symptoms which end in delirium tremens and death. I need not give you all the points in connection with this side of the subject. I cannot do better than refer you to Dr. V. Magnan's work on *Alcoholism: the various Forms of Alcoholic Delirium, and their Treatment*, which has been translated by Dr. W. S. Greenfield, entirely without reference to the temperance-question. If you will study that wonderful work, and follow the thirty-nine separate cases which are given in minute detail, and in which the symptoms have varied considerably, you will be perfectly satisfied as to the toxic character of alcohol in all its forms. The perfect pictures which the author has drawn of its numerous phases, and the ramifications which arise in its development as an irritant or narcotico-irritant poison, are described by a master hand.

Dr. Tidy says, in his *Handbook of Forensic Medicine*, "Alcohol acts as a true poison, whether the vapour be respired or the liquor swallowed, or injected into the cavity of the chest or into the cellular tissue" (p. 498).

It is certain that children at the breast have been killed by imbibing it with the mother's milk, and that convulsions have been but too often caused by an infant being nursed by a drunken mother. I labour upon this point, for recent sensation-writers have tried to altogether ignore the toxic effect of alcohol. They have tried to make out that, as wine and beer, it is not the same thing; forgetful, or rather, anxious to put the analogy which exists in nature altogether out of sight.

Morphia, however diluted, is morphia still, if it can be recovered as such from its solution. Strychnine is not altered in its constitution or its effects by subdivision; and arsenic is arsenic still, though it may be subdivided into doses of 100,000th of a grain. Two of the poisons I have mentioned are also cumulative, and will, in time, produce certain effects if the minutest doses be persevered with; and those who have thoroughly looked into the daily use of intoxicants, but too well know that there is a result from even a single glass of wine, which is shown at once by the feelings of those who, long