The action of picrotoxine upon the temperature of the body is very uniform and constant. Immediately after its administration, there is a slight rise, attributable to the agitation attending the exhibition of the drug, and subsequently there is a steady fall, amounting sometimes to as much as seven or eight degrees of Fahrenheit's scale, but usually more moderate, and not at all comparable with the fall which is caused by many other agents. In some instances, trifling fluctuations in temperature occur, a slight rise attending each fit, and a heavy fall marking each interparoxysmal period. As a rule, however, the fall is a steady one, and becomes slower in proportion as it recedes from the normal standard. No close relation exists between the dose of picrotoxine and the reduction of temperature, as that is sometimes as great after a small and non-fatal, as after a large and fatal, dose.

The observations made on the actions of picrotoxine may be summed up in the following conclusions.

1. It is an energetic poison, and acts chiefly upon the encephalic centres.
2. It causes first, sudden excessive and paroxysmal discharges of certain gradually widening areas of the cerebrum; secondly, continuous but remittent discharges of the corpora quadrigemina, cerebellum, pons Varolii and medulla oblongata; and, thirdly, exhaustion of all the centres discharged, coma, and death.
3. It diminishes the activity of the reflex centres, and general sensibility, by paralysing the posterior columns of the cord and the peripheral sensory nerve.
4. It first quickens, and finally retards, the movements of respiration, and the cardiac contractions.
5. It produces a decided lowering of the temperature of the body.
6. It increases the secretion of the salivary glands, and the peristaltic movements of the intestines.
7. It causes great venous congestion of the encephalon, and occasionally extravasations of blood upon its surface.

(To be continued.)

ON ARTERIO-CAPILLARY FIBROSIS.*

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DURING the short time I hope to occupy your attention this evening, I purpose considering the subject of Arterio-Capillary Fibrosis, as it occurred to me that a brief examination of this—if I may use the term for the time being—popular subject, illustrated with such specimens which I, from the limited sources at my command, could bring forward, might not prove uninteresting to those who, from the various engagements of active professional work, may not have leisure to inquire into the subject for themselves, withdrawn as it is from the beaten path of medical literature.

The first notice of this novel doctrine regarding the changes in the vascular system which are found to accompany chronic Bright's disease appeared in a paper by Sir William Gull and Dr. Sutton, read before the Royal Medical and Chirurgical Society, and published in the fifty-fifth volume of the *Transactions* of that Society. In this paper, the authors allege that the renal lesion in chronic Bright's disease, with contracted kidney, is only a part and parcel of a general morbid change throughout the vascular system, characterised by the deposit of a finely fibrous or granular material, to which they have given the name of hyalin fibroid, outside the muscular layer of the small arterioles and capillaries, and in some cases by a thickening of the inner coat also, accompanied generally by hypertrophy of the heart, and in many cases by a "fibrosis" of other organs of the body also. As the renal lesion is, from the effects it produces, be they primary or secondary, the most important element in the affection, I think it may be interesting, in the first place, to briefly examine the morbid histology of that organ when affected with the disease under consideration. In order to facilitate this, we may conveniently consider the morbid changes under three heads, as occurring—1. In the tubes; 2. In the intertubular tissue; 3. In the vessels. The changes occurring in the tubes are of two kinds; namely, those taking place (1) in the epithelium, and (2) in the basement-membrane. The changes in the epithelium are essentially of a degenerative nature; in the earliest stages of the disease, the cells appear to be shrivelling up, becoming granular, and losing their regularity of outline; and, as the morbid process progresses, they become transformed into masses of granules, filling up the tubes, and being cast out in the urine in the form of the well known "granular casts", leaving

the tubes bare and desquamated. These different degrees of degeneration are well seen in this drawing taken from the specimen under No. 1 microscope (Fig. 1), which also exemplifies the other changes taking place

Fig. 1.—Transverse Section of Kidney. (Granular contracted) — in Glycerine — $\times 400$.

A. Renal Tubules filled with "degenerated epithelium". B. Fibroid material surrounding Tubules. C. Renal Tubules (desquamated). D. Renal Tubules filled with granular debris.

in the organ, and which was taken from a typical case of this disease. The basement-membrane is found to be thickened and rendered coarsely fibrous, the desquamated tubes appearing as rings of various shapes and sizes in transverse section. Passing now to the intertubular tissue, we find it to be enormously increased in many parts of the organ, surrounding and separating the tubules, and rendering their outline irregular and distorted, appearing in some parts granular, like ground glass, and in others coarsely fibrous and wavy. This substance also exists in great density about the Malpighian bodies, and attains its maximum about the arterioles, to which we next come. The walls of these, which are of primary importance regarding the present subject, are found much thickened, the lumen often contracted, and their course tortuous and twisted. This specimen shows a transverse section of one of these vessels, its walls thickened and surrounded with the fibroid material above mentioned, which is also seen between the tubules in the drawing of the transverse section of the kidney.

Having thus glanced at the anatomical condition of the kidney, I will next, leaving until the sequel the pathological explanation of these phenomena, proceed to consider the changes occurring in the arterioles throughout the system generally, first detailing the observations of Sir William Gull and Dr. Sutton, and then examining, on experimental and pathological grounds, the correctness and tenability of their views. Sir William Gull and Dr. Sutton, at the commencement of the observations from which they finally evolved their theory of the so-called arterio-capillary fibrosis, considering the pia mater as the most suitable, both from its transparency and facility for microscopical examination, chose that membrane for the subject of their researches. Portions of the membrane taken from the bodies of those who had been the subjects of chronic Bright's disease, with contracted kidney, having first been tinted with carmine and mounted in glycerine and camphor-water, were then examined with powers ranging up to 750 diameters, and the following appearances were observed. In the larger vessels, where the three coats are distinct, the inner one was found in some cases to be thickened to a marked degree, and to have a fine fibrous or molecular appearance. The muscular coat was also found variously altered, the nuclei not absorbing carmine as readily as in healthy vessels. In some of the vessels, this coat was found to be relatively increased, while in others it was decreased, the nuclei being irregular in shape, and often

* Read before the South of Ireland Branch.

reduced to globular bodies, like fat-granules; and nowhere, it is stated, can the evidences of muscular hypertrophy described by Dr. Geo. Johnson be found. Outside the muscular coat, and immediately in contact with it, was a more or less "hyalin" formation, closely resembling the finely fibrous structure found in the kidney. This formation outside the muscular coat varied according to the size of the vessel examined, being in the larger arterioles more fibrous-looking, while in the smaller ones and in the capillaries the granular or hyalin appearance predominated. In this hyalin fibroid substance, ill-defined nuclei or corpuscles are found irregularly disposed, and wanting the regular arrangement of normal elements.

The following is a summary of these microscopical observations.

1. In chronic Bright's disease, with contracted kidneys, the arterioles throughout the body are variously altered.

2. This change is due to hyalin fibroid formation in the walls of the minute arteries, and a hyalin granular change in the corresponding capillaries.

3. This change occurs chiefly outside the muscular layer, but also in the tunica intima of some arterioles.

4. The degree in which the affected vessels are altered, and the extent to which the morbid change is diffused over the vascular system, varies much in different cases.

5. The muscular layer of the affected vessels is atrophied in a variable degree.

In order to examine how far this morbid change existed alone, the pia-maters of a number of persons who had died of various diseases were examined, and in some the same appearances were observed, while in others no change had occurred; further, the hyalin fibroid change was not found in the bodies of those who were killed accidentally, or who had died of phthisis, and other diseases not allied to the cachexia of the so-called chronic Bright's disease, with contracted kidneys.

Having thus detailed the conclusions arrived at by Gull and Sutton, based for the most part on microscopical investigation, I will next proceed to examine on the same ground the correctness of these views. In an able paper written in answer to that of Gull and Sutton, Dr. George Johnson alleges that the hyalin fibroid material above described is entirely artificial, and produced by the distension of the outer elastic coat of the artery by the glycerine and camphor-water in which all the specimens were mounted previous to being examined. With the view of testing this for myself, I instituted the following series of experiments and observations. Having procured specimens of pia mater from subjects who had not died of chronic Bright's disease, I examined several portions in the fresh state, immediately on removal from the body, without any tinting, and immersed merely in water. I found the walls of the arterioles to be of normal thickness, and not affected with any hyaloid change. I then placed the same specimens, one portion in glycerine alone, another portion in glycerine and camphor-water, and a third portion in the last mentioned fluid acidified with acetic acid. I had also other specimens tinted with carmine mounted in the same fluids. After remaining for some time thus prepared, I again examined them, with the following results. Of the portions placed in pure glycerine, the first examined showed no change; the walls were not visibly affected, either as to structure or size. This preparation is here delineated, magnified 400 diameters, and you will be able to examine it for yourselves under the microscope by and bye. The next preparation, also in pure glycerine, which had been taken from a different subject, and also tinted with carmine, showed, on examination, very different appearances; the muscular nuclei were, if anything, more distinct than when examined in water, and outside, and in direct contact with this layer, was a fine hyalin formation, very slightly wavy, hardly at all coloured by the carmine fluid, extremely transparent, and evidently due to the distending action of the glycerine on the outer elastic coat of the vessel. The appearance presented almost exactly corresponded with the description and drawings given by Gull and Sutton, only being of less extent; the specimens which had not been stained gave precisely the same results. This preparation, which you can also examine, is figured in this drawing, magnified 300 diameters, which is quite a sufficient degree of enlargement. No drawing, however, can accurately portray the delicately fine appearance presented by the preparation itself.

Having thus proved that glycerine alone is able, though perhaps not in every case, to give rise to the hyalin formation, I next proceeded to the examination of the specimens mounted in equal parts of glycerine and camphor-water; in all, both tinted and natural, the hyalin appearance was present, and to a greater extent than in the last series, the marked points of difference being in the greater thickness of the distended outer coat, and in the diminished distinctness of the muscular nuclei, which appeared as if fewer in number and more separated. In neither series was there any appearance of distension or thickening of the tunica intima. This drawing, taken from a preparation mounted in this way, shows these appearances, the apparent

thickening of the outer coat, and the indistinctness of the muscular layer. Having thus disposed of these two series, I then proceeded to the third; namely, those put up in glycerine and camphor-water acidified with acetic acid, and here the appearances in question had attained their maximum. The entire thickness of the wall of the vessel, especially the smaller ones, appeared greatly increased, and almost perfectly transparent and hyalin; the muscular nuclei were also rendered clear, and appeared as outlines of various forms scattered through the thickened walls of the vessels. In the larger arterioles, the transverse markings were rendered sharper, more distinct, and highly refractive. I have in this drawing (Fig. 2) shown the changes

Fig. 2.—Arteriole of Pia Mater (in Glycerine and Camphor Water) $\times 400$.
E. "Hyalin Fibroid"; formation artificial. F. Muscular Layer—very indistinct.

produced by these reagents, the figure representing a rather large arteriole, in which the transverse markings are abnormally distinct. These appearances are certainly due to the ready absorption of, and consequent distension by, the glycerine and camphor-water, added to which is the clarifying action of the acetic acid on the muscular elements present. As a confirmative proof of this, I neutralised the acid with ammonia, and, on a second attempt, succeeded in producing a shrinking and contraction of the distended elastic coat.

The drawing I now hold in my hand faithfully represents the appearances produced in the natural unstained membrane by the action of the acidified glycerine and camphor-water solution, and its neutralisation by ammonia. On this side are the vessels in their normal state, examined in water immediately after being removed from the body; and on the opposite side are the same vessels acted upon by the reagents, showing to my mind in the clearest manner that, whether the so-called "hyalin-fibroid" formation exists as a true morbid product or not, it can be artificially produced by the fluids in which the specimens are immersed. I have also examined vessels prepared in spirit, but, I may say, with mostly negative results; the only appearance produced being a greater distinctness of outline and corrugation of the outer coat.

From these facts, we must necessarily come to the conclusion, apart even from any positive evidence that may be forthcoming, that any deductions based upon the examination of specimens mounted in any of these ways are untrustworthy and open to doubt, and afford negative evidence of the occurrence of this peculiar morbid condition.

Turning now to the examination of the vessels in cases of chronic Bright's disease with contracted kidney, we have here some instructive examples. This drawing (Fig. 3), taken from a transverse section of an

Arteriole of Skin (outer coat distended, muscular layer hypertrophied) in Glycerine $\times 100$.
H. Outer Coat. I. Muscular Layer.

arteriole of the skin from a subject with granular kidneys, shows first the muscular coat greatly thickened and deeply stained. Outside this is a

fibroid and somewhat transparent membrane, less deeply coloured, and equal in thickness to the layer within it. This preparation being mounted in glycerine for some time, I naturally infer from the experience gained by the above experiments that this external membrane is nothing more than the distended elastic outer coat of the vessel. That the inner thickened portion can be nothing else than the muscular layer hypertrophied, is evident both from its anatomical *locus* immediately within the elastic outer coat, which is here rendered so evident, and also from the radiating appearance peculiar to the muscular coat, which is present in some parts. In order to ascertain correctly the actual degree of hypertrophy present, I made comparative micrometric measurements, and found that the muscular wall of the diseased vessel was almost twice as thick as that of a healthy cutaneous arteriole of the same size and character.

Now, returning to the arterioles of the kidney, we find the same results to obtain even to a greater extent than in the skin; the canal of the vessel being very much reduced in calibre, owing to encroachment on it by the hypertrophied walls. The outer coat is not here seen, owing to its almost entire absence from the walls of the vessels of this organ.

We thus see that a true morbid thickening of the walls of the vessels does exist in this disease; and its presence may be demonstrated, along with the hyalin formation produced by the action of the glycerine mounting fluid. Whether a real thickening of the outer coat or morbid deposit in it does exist in chronic Bright's disease with contracted kidney, in company with the muscular hypertrophy, is still to my mind *sub judice*; and it is only by endeavouring to examine carefully specimens of vessels taken from persons who had laboured under the disease in question, in fluids which will not act as above on the tissues under observation, that we can ever hope to arrive at the truth.

Leaving now the experimental side of the question, let us turn and examine briefly the pathological grounds for a belief or disbelief in the occurrence of "arterio-capillary fibrosis" as a morbid state *per se*. When speaking of the morbid histology of contracted kidney, I deferred the pathological explanation of the appearances there described to a later period; and I will now proceed, with your permission, to shortly discuss this, upon which the whole question, looked upon from a pathological point of view, hinges.

Upon this point, there are at present three rival theories, each maintained by men of equal repute, and on arguments which appear in each case almost convincing. Gull and Sutton, and their followers in this controversy, hold that the renal affection is only part and parcel of this general morbid change which they allege to have discovered, and explain its almost constant occurrence in the kidney by stating that it commonly commences there, but not necessarily so, as it may begin primarily in other organs. Dr. Dickinson and his party, while agreeing with Gull and Sutton as to the occurrence of this fibrous material in the organ, differ from them in maintaining that the change is here primary, and due to an "intertubular deposit"—being, in fact, a true cirrhosis of the kidney. In opposition to these views, Dr. George Johnson and a large number of pathologists deny that the appearances, which they both similarly describe, are due to this intertubular deposit, be it primary or secondary; and assert that the changes produced are the result of a wasting and shrinking of the tubules from primary intratubular changes. From the facts which I have already adduced, the theory of Gull and Sutton cannot be at present accepted, as, if their views of a primary arterio-capillary fibrosis are fallacious, it naturally follows that a diseased condition which is part and parcel of that change cannot be maintained. With regard to the relative merits of the other theories, many cogent arguments are brought forward on either side; but, as I fear I have already overstepped my time, I cannot now discuss these as I should wish. Suffice it to say that the theory of a primary intratubular change appears to have the greatest weight of evidence.

Turning once more to the arterial changes, let us shortly examine, on pathological grounds, the correctness of the theory of a primary arterio-capillary fibrosis. As I have already shown, it is on experimental grounds untrustworthy; so also on pathological ones it is fallacious and doubtful. Supposing even that the appearances present in the pia mater examined were morbid, and not probably artificial, does it not appear that such results, as betokening a general morbid condition, are unreliable in the extreme, as the pia mater, from its peculiar office of affording a nidus or matrix for the support of the enormous number of vessels ramifying upon it, must often be the seat of local changes occurring in these vessels, the result of chronic congestions, such as may occur in emphysema, heart and brain disease, and notably in that form of renal lesion in question; such diseases being present in many of the cases examined by Gull and Sutton, and placed amongst the list on which they ground their doctrine? As an illustration of this, I have here a drawing of a vessel of the pia mater from a subject who had been for

many years insane, and whose brain showed the appearances of former congestions. Again, in certain cases, where thickened arterioles were coexistent with hypertrophy of the heart without any affection of the kidneys, brought forward by Gull and Sutton as proof of the independent existence of this morbid change apart from renal disease, the cardiac hypertrophy was due to other and extraneous causes, such as degenerative changes in the larger arteries and chronic disease of the lungs. And, finally, the authors in one part, having stated that atrophy of the surrounding tissues is an accompaniment of the hyalin fibroid condition, yet describe cardiac hypertrophy as one of its most prominent conditions. From these and other facts, it is evident we must look further for some better theory to explain the undoubted thickening which occurs in many cases of chronic Bright's disease in its advanced stages; and this, I think, will be found in that of "muscular hypertrophy", an example of which, and the histological appearances present, I have already described. And it now remains to offer the pathological explanations which have been given by its original discoverer, Dr. Johnson, and others who have followed him. His explanation is as follows. "In proportion to the destruction of the renal gland-cells, and the consequent diminution of the secretory power of the kidney, there is less demand for blood to be acted upon by the gland; the small arteries, by virtue of their muscular coats, consequently contract upon their contents, so as to maintain the balance between the blood-supply and the diminished secretory action of the kidney. This continued over-action of the small arteries in antagonism to the heart results in hypertrophy of their muscular walls: as it is now well known that the minute arteries through the body have the physiological power, by the contraction of their muscular coats, of diminishing and retarding the blood-stream, and adapting to the different organs the amount of blood required by them at different periods, the heart itself finally, by its resistance to this retarding force, becoming in turn hypertrophied." If this explanation be correct, it follows that the renal condition in this disease is primary, the arterial secondary, and the hypertrophy of the heart tertiary. Traube and Ludwig, while agreeing in the main with Johnson in this explanation of the muscular hypertrophy, differ from him in considering that, besides a true hypertrophy, there also occurs a degeneration of the coats. This he explains by the fact that the heart and minute arteries, acting against each other, lead to a distension of the elastic vessels between them, and so to atheroma. I may add that Bamberger and others dispute this explanation of Johnson, asserting that the hypertrophy develops in a stage of the disease when no obstruction of any importance to the circulation of the kidney exists. A more extensive collation of facts will be necessary to decide this disputed point; but at any rate, whatever be the explanation, there can be no doubt of the existence of hypertrophic thickening of the minute vessels throughout the body, but whether accompanied by other changes has not, in my opinion, yet been determined.

In conclusion, I have to thank you for the kind attention with which you have listened to this, what, I fear, to some must have appeared a long and tedious paper. The nature of the subject, however, from the various and opposite views brought to bear on it, must be my apology. It is in itself a subject of narrow limit—in fact, a microscopic atom of our science, which requires a high power, as it were, for the unravelling of its mysteries; and it is only by patient investigation and laborious study that a true understanding of its complex nature and intricate working can ever be arrived at; and it is with an earnest hope that, as opportunities for such study present themselves, they may not be lost sight of, but carefully examined and worked out, that I have brought the subject before you.

NATIVE OIL OF MALE FERN.

HAVING failed lately in several cases in expelling the whole of the *tænia solium* by the ordinary foreign oil of male fern, I was induced by Messrs. Wyley and Co. of Coventry to give their native oil a trial. I have used it now in seven cases, in six of which it has proved entirely satisfactory; the seventh case being that of a young child, in which it was not retained many minutes. I administer it in the following manner. Two days previously, I give a brisk aperient, and order a strictly fluid diet. On the evening of the second day, I direct about two ounces of new milk to be brought in a wide mouthed bottle, to which I add for an adult male two drachms and a half of oil of male fern, agitating the oil and milk, which readily mix, and direct the dose to be taken early in the morning fasting, and to be followed by a dose of castor-oil in three hours. In all six cases, the worm has been expelled whole in from four to six hours. Three of the cases had been treated in the same manner previously by the foreign oil, kamala, and other anthelmintics, but with no more effect than to bring away a few feet *minus* the head.

HERBERT C. P. MASSER.