On the proximate cause of albuminous and dropsy, and on the pathology of the renal blood-vessels in Bright's disease / [Sir George Johnson].

7.

ON THE PROXIMATE CAUSE

OF

ALBUMINOUS URINE AND DROPSY,

AND ON THE

PATHOLOGY OF THE RENAL BLOOD-VESSELS IN BRIGHT'S DISEASE.

BY

GEORGE JOHNSON, M.D.

ASSISTANT PHYSICIAN TO KING'S COLLEGE HOSPITAL.

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The two communications on the subject of Renal Pathology, which the Society has done me the honour to publish in its Transactions,[1] had reference chiefly to morbid changes occurring in the *secreting cells* of the kidney.

Subsequent observations have confirmed the opinion expressed in those papers, that the various forms of disease which are generally included under the name *Bright's Disease*, and which are in most instances associated with an albuminous condition of the urine, have this common feature, that the first morbid change which can be detected in the kidney consists in an altered condition of the secreting cells.

Much light has, within the last few years, been thrown upon the process of secretion; it is still, however, in a great degree, involved in mystery. We do not yet possess a complete and accurate history of the secreting cells, of their development, decay, and reproduction, and of the exact process by which they separate from the blood and discharge into the excretory ducts the materials which constitute the secretions of the various glands. It appears probable, that a careful study of the pathological changes occurring in the gland-cells may throw additional light upon their healthy and

[1] Vols. XXIX and XXX.

normal action, and that in this, as in many other instances, the sciences of physiology and pathology may together produce results to which neither could attain singly.

Before entering upon the immediate subject of the present communication, it may be useful to mention briefly certain facts connected with the epithelial cells of the kidney.

1st. The true secreting cells occupy the inner surface of the convoluted tubes, those portions of the tubes which form the great mass of the cortical substance of the kidney. Neither the Malpighian bodies nor the straight tubes which form the medullary cones contain the true glandular or secreting epithelium.[1]

2d. No renal cells can be detected in normal and healthy urine. The presence of renal epithelium in the urine affords unequivocal evidence that the secreted products are abnormal. Thus, for example, when during an attack of jaundice the kidneys eliminate bile, the urine contains renal cells deeply tinged with biliary matter. The bile conveyed by the blood to the kidneys has so modified the secreting cells, that they are thrown off entire, and thus appear in the secretion. Various other matters produce a similar modified action of the secreting cells of the kidney,—the fever poisons, particularly that of scarlatina, of measles, and of erysipelas,—certain morbid matters which infect the blood of persons who have had repeated attacks of gout,—others which exist in the blood of cholera patients,—and, again, others which result from an insufficient supply of nutritious food. In these and in some other cases, which do not require special mention, although the poisons are recognised only by their effects, while their essential nature is unknown, there is yet abundant evidence to justify a belief in their existence.

3d. But it is not only by a process of desquamation that the kidney-cells afford evidence of their having eliminated abnormal products. The cells undergo various other modifications which can be detected by a careful microscopical examination of the kidneys after death. They are sometimes

[1] On the Structure and Use of the Malpighian Bodies of the Kidney. By W. Bowman, F.R.S. Phil. Trans., 1842.

gorged with oil, and this is a condition which may readily be detected by an examination of the urine during life, when, as frequently happens, the desquamative process accompanies it. In other cases the cells are remarkably opaque, and appear to contain an unusual quantity of a finely granular material. I have observed this condition in the kidneys of diabetic subjects, in which cases, probably, the long-continued secretion of sugar has modified the action and appearance of the cells. It is of the utmost importance to bear in mind, that there is a most intimate relationship between a secreting-cell and its secreted product,—there is reason to believe, that a change in one will be invariably accompanied by a corresponding modification of the other.

The various changes in the secreting-cells, just now enumerated, produce one common result; viz. an imperfect elimination of the renal secretion. The acute desquamative process rapidly fills the tubes with epithelial cells. The chronic desquamation destroys the life of the cells, arrests their reproduction, and leaves the tubes denuded.[1] The fatty engorgement of the cells tends to obstruct the tubes, and so to impede secretion; and probably each visible deviation from the normal appearance of the epithelial cells is attended by a corresponding imperfection in the performance of their function.

There are, besides, certain other morbid conditions, such as the replacing of the normal epithelium by a deposit of pus or unorganized fibrine in the tubes, which tend to the same result as the more common changes before mentioned. In every instance, excretion is imperfectly performed, and the urinary constituents are partially retained in the blood.

From these preliminary remarks, I pass on to the main subject of this communication, which is to offer an explanation of two of the most common and important symptoms of renal disease, viz. Albuminous Urine and Dropsy; and this will lead me to describe a remarkable pathological condition of the blood-vessels of the kidney, which, so far as I know, has not hitherto been noticed. The observations which

[1] Med.-Chirurg. Trans., Vol. XXX, p. 165 et seq.

I have to offer on this subject will, perhaps, be rendered more intelligible by a previous brief reference to one of those lucid and valuable essays bequeathed to us by the late lamented Dr. John Reid.[1] The essay to which I allude is that 'On the Order of Succession, in which the Vital Actions are arrested in Asphyxia.' The principal facts and arguments therein contained, and which concern us in our present inquiry, are the following:—when the trachea of an animal has been obstructed, by the insertion of a tube with a closed stop-cock, dark blood is at first transmitted freely through the lungs, and reaches the left side of the heart, by which it is driven through all the textures of the body. As the blood becomes more venous, its circulation through the vessels of the brain deranges the sensorial functions, and rapidly suspends them, so that the animal becomes unconscious of all external impressions. For about two minutes after the animal has become insensible, and when the blood in an exposed and unobstructed artery is equally dark as that in the accompanying vein, the large arteries become more distended and tense than before the stop-cock in the trachea was shut, and when the animal was breathing atmospheric air freely. At the same time, a hæmadynamometer being placed in the artery of one limb, and a similar instrument in the corresponding vein of the other, the former indicates an increase, and the latter a diminution of pressure, as compared with that observed in the same vessels before the air was excluded from the lungs, this evidently resulting from an impediment to the passage of the venous blood through the systemic capillaries. At the expiration of the time before mentioned, viz. about two minutes, the instrument in the artery indicates a diminution of pressure; the mercury, at first falling very gradually, and at last very rapidly, in consequence of the blood being arrested in the pulmonary capillaries, ceasing to pass through the lungs, and so stagnating in the right side of the heart and in the veins.

Dr. Reid then quotes some observations by Dr. Alison[2]

[1] Physiological, Anatomical, and Pathological Researches, p. 17.

[2] Pathology and Practice of Medicine, p. 120.

tending to show that the arrest of the blood in the pulmonary capillaries "is to be referred to an interesting law in physiology, by which the movement of nutritious juices is influenced by the chemical changes; or, as Dr. Alison terms them, the vital attractions connected with the chemical changes constantly going on in the capillary vessels between these juices and the surrounding tissues, by which nutrition and secretion are effected. Before arterial blood can be transmitted freely through any tissue or organ, it is not only necessary that the contractions of the heart be performed with a certain amount of force, but that the actions of nutrition and secretion be also in operation; so in the same manner, before the blood can be transmitted through the lungs, it is not only necessary that the right side of the heart retain its contractility, but that the chemical changes between the blood and the atmospheric air should proceed." This doctrine is still further illustrated by Dr. Reid's experiment, before described, which demonstrates, that when the blood in the systemic circulation becomes decidedly venous, it passes less freely through the capillaries into the veins. Finally, Dr. Reid refers to some observations by Mr. Wharton Jones, which seem to accord with the explanation here given of the arrest of the pulmonary circulation during asphyxia. Mr. Jones observed, that when a solution of common salt, or a stream of carbonic acid gas, was applied to the lung of a living frog, the circulation of the blood was there arrested by the red corpuscles agglomerating together, and applying themselves here and there flat against the wall of the vessel. The same phenomena were observed, when a solution of common salt was applied to the web of a frog's foot.[1]

The observations and inferences of Drs. Reid and Alison seem to be applicable, by way of analogy, to the subject of renal disease, and will, I think, assist us in our attempt to arrive at the immediate cause of the albuminous condition of the urine and the general dropsy, which are so commonly associated with disease of the kidney.

[1] British and Foreign Medical Review, vol. xiv, p. 600.

In tracing the progress of a case of acute dropsy occurring as a consequence of scarlatina, it will commonly, but not invariably, be found that the patient has been exposed to cold. The natural process of elimination by the skin has thus been checked, and the poison is driven inwards to the kidney. It reaches the inter-tubular capillary plexus, and an effort is made to eliminate it by that modified action of the secreting cells which we have called desquamation. The cells are formed and shed rapidly and in large numbers; so that in the course of a few hours, many of the tubes may be completely filled by their accumulated solid contents. This condition of the tubes must obviously impede the secretory process; the blood is imperfectly purified, and excrementitious matters accumulate in it.

We have now to consider the influence which the materials, thus retained in the blood, exert upon the circulation through the kidneys.

Assuming that the renal circulation is affected by an imperfect elimination of the urinary constituents in a manner analogous to that in which the pulmonary circulation is influenced by the retention of carbonic acid in the blood, we should expect to find, that the circulation would first be retarded in the inter-tubular capillary vessels, the obstruction, which will be in proportion to the extent of morbid change in the contiguous tubes and cells, will, of course, exert an influence extending backwards in the order of the circulation; so that the Malpighian capillaries and the arteries which supply them will become gorged with blood. This engorgement is exactly analogous to that of the right side of the heart and venous system observed in animals after death from asphyxia.

There are certain facts which afford a remarkable confirmation of that which, as just now propounded, might seem to be a mere hypothesis, or at best only a probable analogy.

That the circulation through the inter-tubular capillaries is retarded, and that the Malpighian capillaries are consequently subjected to a greatly increased pressure and distension, seems to be indicated by the escape of serum and blood which so

constantly occurs during an attack of acute desquamative nephritis following scarlet fever. The serum flows into the tubes, mingles with the urine, and renders it highly albuminous; while the colouring matter and fibrine coagulate in the tubes, and afterwards escape in the form of cylindrical moulds, in which epithelial cells are commonly entangled. There seems no reason to doubt, that the blood, in these cases, escapes from the Malpighian capillaries, which lie within the dilated extremities of the tubes. The result is precisely similar to that obtained artificially by Dr. George Robinson,[1] who observed, that when a ligature was placed upon the renal vein of a rabbit, the urine became albuminous and bloody. Dr. Robinson performed this experiment several times, and with an almost uniform result.

But still more satisfactory and conclusive evidence of impeded circulation, and of the precise point at which the impediment occurs, is afforded by the condition of the renal blood-vessels in cases of chronic disease of the kidney.

I have observed in all cases of chronic renal disease, which I have examined since my attention has been directed to the condition of the blood-vessels, that the coats of the arteries and of the Malpighian capillaries are remarkably hypertrophied, while the coats of the inter-tubular capillaries and of the emulgent vein present no appearances of hypertrophy or thickening. I have examined the vessels in different cases, both injected and uninjected, and I have compared them with corresponding vessels in the healthy kidney, and the result has been uniformly such as I have stated. I will now detail the appearances which I have observed in each of these sets of vessels, viz. the arteries, the Malpighian capillaries, the inter-tubular capillaries, and the veins.

Arteries.—I have observed, in accordance with the description which Henle[2] has given of the arterial tunics, that the minute branches of the renal arteries have two fibrous coats, the inner being longitudinal, and the outer

[1] Medico-Chirurgical Transactions, Vol. XXVI.

[2] Allg. Anat.

circular; in the healthy vessel the inner coat is thinner than the outer, but in the diseased condition I have generally found them of nearly equal thickness. The two coats appear to be of the same nature, and in all probability they are

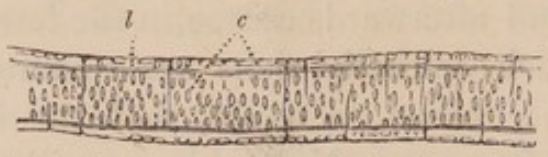

Fig. 1.—Portion of renal artery in the normal state, showing the relative thickness of its coats.
c. Circular fibres. *l*. Longitudinal fibres. Magnified 200 diameters.

muscular. The thickening appears to be proportionally greater in the smallest arteries, *e. g.* the afferent vessels of the Malpighian bodies, and gradually diminishes in passing towards the arterial trunks. I have frequently observed the coats, at least three or four times exceeding the normal thickness. The canal of the artery is of the normal size,

Fig. 2.—Portion of artery from a diseased kidney, showing great hypertrophy of its coats.
c. Circular fibres. *l*. Longitudinal fibres.
The canal of the vessel is filled with injection. Magnified 200 diameters.

and pervious until the last stage of this interesting series of changes; when, the secreting cells in the tubes being destroyed, and their vital attraction upon the blood ceasing, the circulation is arrested, and oil globules collect here and there in the canal of the arteries.

Malpighian Capillaries.—What has been said of the arteries applies, with certain modifications, to the Malpighian capillaries. The capillaries do not, in the normal state, present a fibrous structure, nor is there any appearance of such tissue in the diseased vessels. The coats of these vessels are greatly thickened, but homogeneous in structure, and the canal is apparently normal, or perhaps slightly

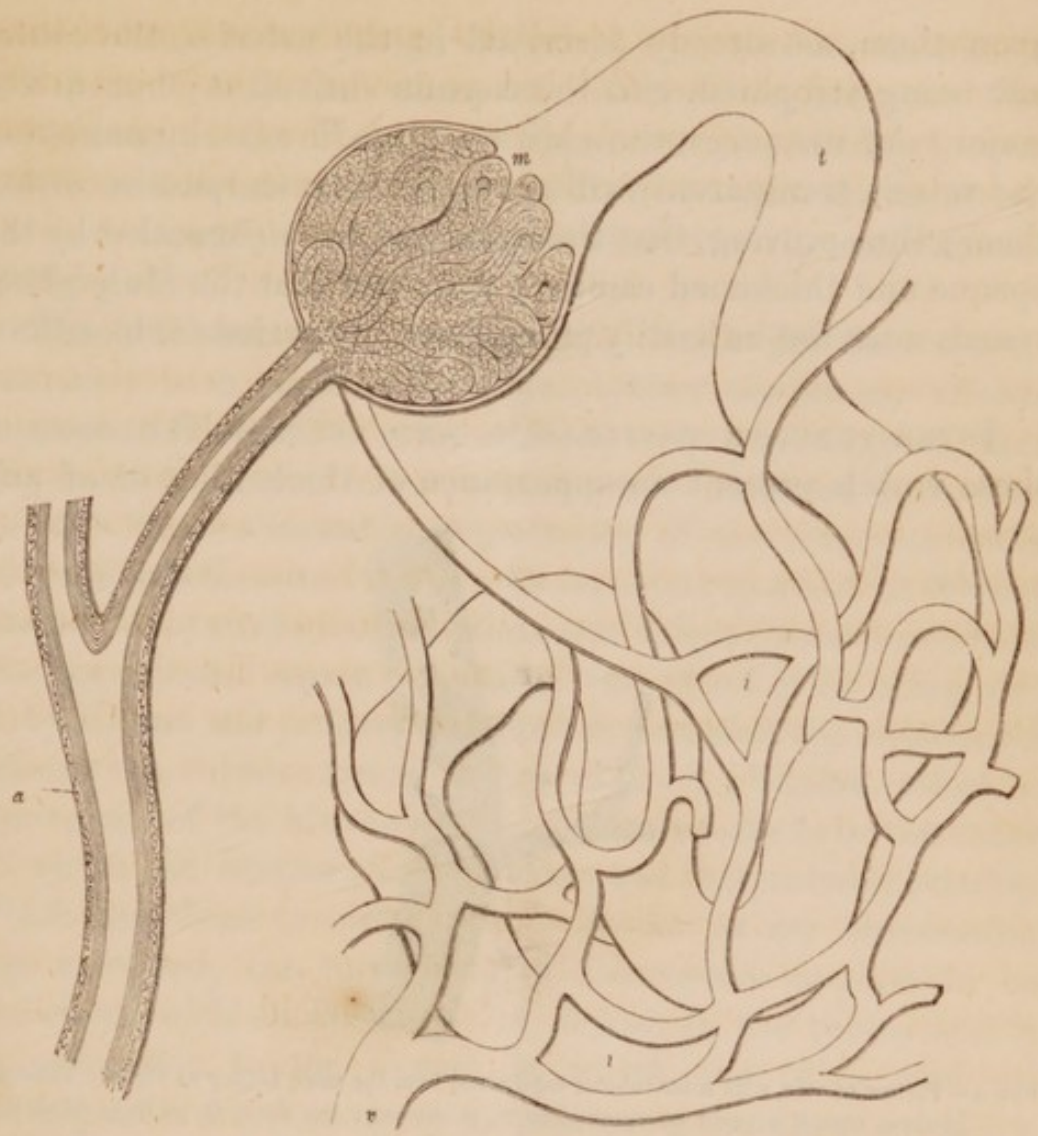

FIG. 3.—Plan of renal blood-vessels and uriniferous tube, showing thickening of the artery and Malpighian capillaries, while the inter-tubular capillaries and the vein present no appearance of thickening.

a. Artery. *m*. Malpighian capillaries. *i i*. Inter-tubular capillaries. *v*. Vein. *t*. tube.

narrowed. The injection sometimes fills the Malpighian vessels very completely, in other instances the tuft is only partially filled; and again, in other cases, the injection proceeds no farther than the termination of the afferent artery. The entire Malpighian body is not sensibly enlarged, but the increased thickness of the capillary walls produces a close packing and crowding of the vessels, so that their outline can scarcely be distinguished. The surface of the vessels is usually smooth and free from deposit, and the entire Malpighian body presents a peculiar whitish opaque appearance. A hasty examination might produce an impression, that the vessels are bloodless; and in the extreme stage they actually become so, presenting oil-globules in or

upon them, as already described in the arteries, the entire tuft being atrophied, and the capsule shrivelled; but in the majority of instances, the addition of acetic acid, by rendering the vessels transparent, will show the blood-corpuscles within them; thus proving, that the blood had been concealed by the opaque and thickened capillary wall, and that the Malpighian vesesls must not be hastily pronounced impervious or bloodless.

INTER-TUBULAR CAPILLARIES AND VEINS.—The coats of these vessels present no appearance of thickening or of any

FIG. 4.—Portion of vein, with inter-tubular capillaries, from the same kidney as Fig. 2. The coats of these vessels present no appearance of thickening; the canal is partially filled with injection. Magnified 200 diameters.

other morbid change; they seem to be less numerous than in the healthy kidney, and they probably become atrophied and obliterated, in consequence of the arrested action of the secreting cells.

The pathological explanation of these changes in the renal blood-vessels appear to be this. There is an imperfect elimination of the urinary constituents, in consequence of changes in the secreting cells, produced by an effort which they have made to excrete abnormal products. Deficient excretion at once leads to impeded circulation,—the obstruction occurring at the very point where the excretion should be effected, viz. in the inter-tubular capillaries. The impediment reacts backwards upon the Malpighian capillaries, which in a sudden acute attack become ruptured, and allow the blood to escape into the urinary tubes; but when the

disease has been of longer duration, they become thickened, and permit only the serum of the blood to escape. The thickening of the Malpighian capillaries is probably preservative, and is intended to enable them to bear the increased pressure to which they are subjected during the continuance of the disease.

The thickening of the arteries, which proceeds simultaneously with that of the Malpighian capillaries, affords support to the opinion entertained by some physiologists, that the smaller arteries exert a propulsive influence upon the blood. The remarkable hypertrophy of the muscular coats of these vessels seems to have for its object to assist in driving the blood onwards through the inter-tubular vessels in which the impediment exists. Finally, the gland-cells being destroyed, and the process of secretion arrested, the circulation ceases, the tubular tissue wastes, and oil globules collect in the canals of the blood-vessels. This appears to be the order in which the various changes occur, and the probable relation which they bear to each other. So far as my observation has extended, the thickening of the vessels appears to be associated with all the forms of deposit in the tubes, and is in proportion to the degree in which the tubes and secreting cells are destroyed, as well as to the duration of the renal disease.[1]

In recent acute cases, the appearances just now described are of course not observed. Hypertrophy of the left ventricle is undoubtedly a common result of disease in the aortic valves; but we do not expect to find hypertrophy after a recent attack of acute disease producing a deposit on the valves.

The subject of renal dropsy appears now to demand a brief notice. Analogy would indicate the very great probability, that this form of dropsy is produced by an impeded circulation through the systemic capillaries, consequent upon the retention of the urinary constituents in the blood, and that the obstruction thus originating is similar to that which Dr.

[1] The best specimens for the examination of these changes are the small contracted granular kidneys, which have been the seat of that form of disease to which the term *chronic desquamative nephritis* has been applied. See a paper by the author, 'Med.-Chirurg. Trans.,' Vol. XXX.

Reid detected by the hæmadynamometer when black blood was circulating through the arteries of the animals which were the subjects of his experiments. There is one fact which, *per se*, is almost sufficient proof, that the systemic capillary circulation is actually impeded, in the way supposed, as a consequence of imperfect elimination of the urinary constituents. I allude to the frequent occurrence of hypertrophy of the left ventricle of the heart in cases of chronic renal dropsy, when there exists no obvious disease of the valves or vessels to account for such hypertrophy. The very frequent concurrence of cardiac and renal disease was long since pointed out by Dr. Bright.[1] In passing under review the chief morbid appearances observed in one hundred cases of renal disease connected with albuminous urine, Dr. Bright thus alludes to the subject of cardiac disease. "The deviations from health in the heart are well worthy of observation; they have been so frequent as to show a most important and intimate connection with the disease of which we are treating; while, at the same time, there have been twenty-seven cases in which no disease could be detected, and six others which, from not having been noted, lead to the belief that no important deviation from the normal state existed. The obvious structural changes in the heart have consisted chiefly of hypertrophy, with or without valvular disease; and, what is most striking, out of fifty-two cases of hypertrophy, no valvular disease whatsoever could be detected in thirty-four: but in eleven of these thirty-four, more or less disease existed in the coats of the aorta; still, however, leaving twenty-three without any probable organic cause for the marked hypertrophy generally affecting the left ventricle. This naturally leads us to look for some less local cause, for the unusual efforts to which the heart has been impelled: and the two most ready solutions appear to be, either that the altered quality of the blood affords irregular and unwonted stimulus to the organ immediately; or, that it so affects the minute and capillary circulation, as to render greater action necessary to force the blood through the distant subdivisions of the vascular system."

[1] Guy's Hospital Reports, vol. i.

The latter of the two explanations thus suggested by Dr. Bright, is the one to which analogy would point as the true one. The existence of capillary obstruction being admitted, dropsical effusion appears to be a natural and necessary consequence. It follows, too, that an albuminous condition of the urine, and dropsical effusion into the areolar tissue and serous cavities, must result from precisely analogous conditions, viz. an arrest of poisoned blood in capillary vessels. The hypertrophy of the renal arterial tunics, and that of the left ventricle of the heart, must also be considered as analogous means of overcoming an obstacle to the passage of the blood. It will be evident, that the dropsies here referred to are those which result from an abnormal condition of the blood; renal disease being the most frequent, but by no means the only cause of such abnormal condition. The dropsies produced by disease of the heart, or lungs, or liver, or by pressure on a venous trunk, differ in some respects from those before alluded to; they are all, however, alike in this one important particular—that *an impeded circulation precedes and accompanies the dropsical effusion.* There yet remain for brief notice some facts which, equally with those already mentioned, seem to indicate an impeded capillary circulation.

The first of these is the effusion into the air-cells of the lung, which occurs as a consequence of the imperfect aeration of the blood after division of the pneumo-gastric nerves. This was repeatedly observed by Dr. Reid during his experiments on the eighth pair of nerves. The same condition is found after death by slow asphyxia, consequent on an injury of the spine, which has paralysed all the respiratory muscles, except the diaphragm.

The hypertrophy of the right ventricle of the heart, so commonly observed in connexion with chronic bronchitis and asthma, probably depends upon a similar cause, viz., imperfect aeration of the blood, and a consequent impeded circulation through the pulmonary capillaries. Another instance in which the same law appears to operate is afforded by the sudden arrest of the circulation produced by the admission of air into

the veins. It appears that the pulmonary capillaries refuse to transmit the strange mixture of air and blood which is sent to them, and death is the immediate result.

The frequent connection of cerebral hemorrhage with renal disease is another fact closely related to those already mentioned, as also the occurrence of what is sometimes called serous apoplexy. Both these phenomena are, in all probability, associated with impeded circulation through the cerebral capillaries. With reference to some of these points, I may probably, ere long, have some additional evidence to offer. The subjects to which I have thus briefly alluded, are of wide extent and of vast importance, from their bearing upon the general doctrines of disease. I have endeavoured in this, and in my last communication, to trace the steps of what may be considered strictly inflammatory diseases of the kidney. If the facts are true, and the inferences just and rational, they must be applicable in a greater or less degree to the diseases of other parts; and we may hope, from a careful study of the kidney, presenting as it does facilities for pathological research, which do not exist in the case of any other organ, to obtain a light by which to remove the gloom now hanging over some of the most serious diseases with which we have to deal. In conclusion, I cannot refrain from a respectful mention of the name of William Bowman, to whom we are indebted for the accurate knowledge which we now possess of the Anatomy and Physiology of the Kidneys, —this being the only sure basis upon which to build up the pathology of the organ. To remark upon the debt of gratitude which the profession, and, indeed, all mankind, owe to Dr. Bright, would appear as presumptuous as needless; since it is universally acknowledged, that the results obtained by those who have followed in the track which he opened to them, have served only to enhance our estimate of the important discoveries made, now more than twenty years since, by that eminent physician.

Finally, I have to express my obligation to my friend Mr. H. H. Salter, to whose kindness I am indebted for the illustrations which accompany this communication.