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ON THE RELATION BETWEEN

ANASARCA AND THE RENAL AFFECTION,

AT THE COMMENCEMENT OF THE

SO-CALLED ACUTE RENAL DROPSY;

AND

ON THE SEQUENCE OF THE STRUCTURAL CHANGES WHICH TAKE PLACE IN THE KIDNEYS.

(A THESIS FOR A MEDICAL ACT IN THE UNIVERSITY OF OXFORD.)

BY

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"Cum hæc per multa volumina, perque magnæ contenti nis disputationes a medicis sæpe tractata sint atque tractentior; subjiciendum est, quæ proxima vero videri possint.—Sine ambitione verum scrutantibus."

LONDON:
PRINTED BY JOHN E. ADLARD,
BARTHOLOMEW CLOSE.

1864.

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A longitudinal Section of a contracted Kidney, "showing the hard and granulated texture of the whole cortical part, and the striking manner in which the tubular portions are drawn towards the surface of the Kidney."

From Dr R. Bright's reports of Medical cases, pl. III. fig. 2.

ON

ANASARCA AND THE RENAL AFFECTION,

AT THE COMMENCEMENT OF THE

SO-CALLED ACUTE RENAL DROPSY.

"The morbid appearances which present themselves on the examination of those who have died with dropsical effusion, either into the large cavities of the body, or into the cellular membrane, are exceedingly various; and it often becomes a matter of doubt how far these organic changes are to be regarded as originally causing, or subsequently aiding, the production of the effusion, and how far they are to be considered merely as the consequences either of the effusion or of some more general unhealthy state of the system. If it were possible to arrive at a perfect solution of these questions, we might hope to obtain the highest reward which can repay our labours,—an increased knowledge of the nature of the disease, and improvement in the means of its treatment." (Dr. R. Bright, '*Select Reports of Medical Cases*,' p. 1.)

It is not intended in this essay to enumerate and discuss the various relations which anasarca and effusion into the serous sacs hold to morbid changes in the structure of the kidneys: relations which differ widely, not merely in the several distinct forms of renal disease, but even at different periods in the progress of the same malady. They will be touched upon only so far as may be necessary to avoid the misapprehension of statements strictly applicable to the early period only of one particular disease, that, viz., whose onset is marked by the all but simultaneous occurrence of dropsy, and of certain well-marked symptoms of renal derangement, accompanied by more or less of constitutional disturbance.

It is difficult to fix, with anything like precision, the exact meaning which any one of the many writers on the subject attaches to the term, "Bright's disease;" it is all but impossible, even when this term is given up, to harmonise the discrepancies

between different authors. In the following table an attempt has been made to base the classification of renal diseases upon their pathology. The execution of such an attempt must necessarily be at first extremely imperfect; but the plan seems to possess the advantage of assigning a natural place for most, if not all, of the known forms of disease; however widely opinions may differ as to the exact position which certain kinds of kidney, *e.g.*, the gouty, or the alcoholic, &c., ought to occupy in it. So soon, however, as the pathology of any one of the numerous forms of renal disease is conclusively established, there can be no difficulty in assigning to each its proper place in a scheme drawn up on this principle. It is also evident, from the mere inspection of the table, that the main classes, into which the disorders of the kidneys from this point of view naturally divide themselves, are not less clinically than pathologically distinct.

Of the disease indicated in the first line of this table, and of it alone, this essay treats.

The local changes in the kidneys are so intimately connected with the more general phenomena of the malady that their separate treatment, though necessary to the clear apprehension of the whole, is not without some serious disadvantages.

As, however, the former may be considered in themselves, without reference to their original cause, and apparently run their course, in obedience to certain simple laws, but slightly, if at all, except in chronic cases, modified by specific influence, it may be more convenient to describe them first, before attempting to ascertain the real nature of the disease, and the relation in which the different manifestations of diseased action at its commencement stand to each other.

Whatever may be the nature of the exciting or proximate cause of these changes, the first in the series would seem to be some alteration in the nutrition of the epithelial cells lining the Malpighian capsules and the tortuous portion of the tubuli uriniferi. It is not easy to determine whether the epithelium of the straight tubes is, now or subsequently, similarly affected, owing to the difficulty of distinguishing between appearances due to alterations originating in that portion of the tubes, and those due to the presence there of materials which have come down from the convoluted portions; but, from certain facts connected with the congestion and the subsequent changes, the pyramids are probably not affected, or only slightly so.

- **Morbid changes in the kidneys must have their starting point in one or more of the tissues composing them.**
  - **1. Epithelium**
    - Hypertrophy of (from irritation conveyed by blood).
      - Followed by fatty degeneration and pressure upon vessels, leading to atrophy and destruction, more or less complete, of epithelium.
        - Kidneys presenting appearances occupying every possible step between the large red, and the pale contracted kidney. The consistence of the larger forms is soft, and the later changes are most marked opposite the bases of the pyramids: *i. e.*, at the greatest distance from the entrance of the vessels.
          - Gravity of disease depends upon intensity or permanence of cause, *e. g.*, in decreasing ratio.
            - Acute Renal Dropsy.
            - Scarlatina.
            - Fevers.
            - Catarrh.
      - Not followed by atrophy. Ending in large fatty kidney.
      - Simple hypertrophy; as when one kidney is destroyed.
    - Atrophy of, leading to small kidney without previous enlargement.
  - **2. Tubules**
    - Impediment to exit of urine, more or less complete.
      - General: *e. g.* from stricture of urethra, with atrophy of secreting structure. — pressure upon ureters, &c., producing dilatation of pelvis and calices, in extreme cases, kidney presents the appearance of a cyst.
      - Local: as from concretions in tubuli uriniferi, *e. g.*, gouty kidney.
    - Extension of morbid processes upwards along excretory ducts, as of suppuration from bladder.
  - **3. Vessels**
    - Interference with the circulation leading to changes in the nutrition of the organ, with alterations in size, form, and consistence of the affected portions, consequent on
      - Complete occlusion: *e. g.*, embolism, arterial, or capillary, producing fibrinous wedges.
      - Interference with function by
        - Diminution of calibre, or thickening of walls, *e. g.*, of Malpighian tufts.
          - Atheroma.
          - Amyloid degeneration.
      - Increase of pressure in vessels.
        - From obstruction to return of blood.
          - General: *e. g.*, in mitral disease (produces firm, congested, somewhat enlarged kidney, with fatty degeneration of epithelium, and exudation into matrix).
          - Local: *e. g.*, pressure of gravid uterus, thrombosis of renal vein, or of some of its branches.
        - In active congestion. (Is this ever the first step?)
      - Reflex nutrition.
  - **4. Matrix**
    - Plastic exudation into: its results varying according to the subsequent changes (*e. g.*, the degeneration or the more or less complete organization, with contraction), of the exuded material.
      - Kidneys of all degrees from large red to small pale, but firm, and the capsules adherent.
    - Fatty degeneration.
    - Morbid growths (Tubercle carcinoma).

- **Cysts due to**
  - Occlusion of tubules. (Johnson.)
  - Abnormal development of cellular elements. (Simon.)
  - Cellular interspaces, becoming lined by a secreting membrane.

Infinite varieties produced by different combinations of these forms of renal disease for — Primary affections of
- Vessels
- Tubules and their contents
- Matrix

— Lead to secondary changes in
- Tubules with contents and matrix.
- Vessels and matrix.
- Vessels and tubules with contents.

In consequence of this altered nutrition the cells become much more numerous, and, on the average, larger in size, whilst, mingled with these larger cells, are other smaller bodies, apparently cells whose development has been either arrested or not yet completed. In other respects the characters of the cells do not vary materially from those of healthy ones; they appear perhaps slightly more transparent and glistening, and yet contain at the same time a larger number of granules, the so-called oleo-albuminoid granules.

To meet the increased demand for nutriment thus set up, the amount of blood sent to the kidney is also increased, and the organ becomes congested, not primarily, but secondarily to the change in the cells, and œdematous. These causes together, increased blood supply, œdema, and increased amount of epithelium, necessarily lead to increase in the size of the organ as a whole, and to the production of a large, smooth, red, soft and watery kidney. The large amount of blood now sent to the organ, coupled with the increased difficulty of the circulation through it, which will be more fully treated of presently, leads at an early period to hæmorrhage, from rupture of the smaller vessels, and blood in greater or less quantity appears in the urine.

Together with the alteration in the epithelial elements of the organ further deviations from the healthy standard occur in the contents of the tubules. The liquid in them becomes highly albuminous, and in many a material is found, probably fibrinous, transparent, homogeneous, coagulating seemingly after its arrival in the tubes, for it is moulded to their outline, and imbedded in it, in greater or less abundance, are epithelial cells, blood discs, and occasionally some of the cystalline forms of urinary deposit. Discharged from the tubules in pieces of varying length this constitutes the so-called urinary casts; with the exception of some few, which seem to be now and then formed by the coagulation of blood poured into the tubes from some ruptured vessel. The material of which these casts consist is firm and moderately elastic, for, whilst specimens constantly occur whose sinuous outline makes it all but certain that they have been formed in the convoluted tubes, and more or less straightened in their passage through the pyramids, still it is very difficult to produce any permanent alteration in their form by pressure or movement of the cover of a microscopical preparation.

Such appear to be the morbid changes in the kidneys during the first forty-eight hours, or so, of acute renal dropsy. As,

however, death rarely if ever occurs within that period, or until the congestive stage is fully established, it is scarcely possible to give actual demonstration of them. But there are two sources, which, taken together, supply trustworthy materials for the history of this early stage, viz.:—

1st. The chemical and microscopical characters of the urine.

2nd. The ascertained history of processes in other tissues of the body, resulting in the production of morbid appearances analogous to those which present themselves in the large congested kidney.

With regard to the urea; the total amount excreted is probably always diminished, but occasionally the proportional amount is said to be increased. There seems to be little doubt, that, as in other acute febrile states, so too at the onset of acute renal dropsy, the quantity of urea formed in the system is more or less considerably increased; thus aggravating the disorder produced by the defective action of the kidneys and skin.

The uric acid is said to be increased, and the same appears to be the case also with the colouring matters.

The presence of urates in abnormal amount, even if it be not, from the diminished excretion of water, more apparent than real, does not possess any special significance.

The chlorides, sulphates, and phosphates are diminished.

The water is notably diminished.*

Coupled with these variations in its usual constituents, the urine also contains a greater or less amount of albumen. In many cases this is in part accounted for by the occurrence of hæmorrhage, but only in part, for its quantity bears no proportion to that of the blood-discs, being frequently excessive when these are all but absent. Many causes, each and all of them perhaps more or less powerful in different cases, have been mentioned as producing this albuminous condition of the urine, *e.g.*, increased intravascular pressure, perverted function of the kidney, &c.; but the most probable one would seem to be some alteration in the constitution of the blood, or in the relations between it and its containing vessels, in consequence of which osmosis of an albuminous fluid takes place. From the low specific gravity of the urine, generally far below its standard in health, it would seem that the alteration in the blood is one affecting its albumen; per-

* Dr. Parkes, 'On Urine,' page 376, et seq.

haps causing it to pass into one or other of its varieties, whose existence appears to be certain, although their exact properties are as yet unascertained. It might perhaps be thought that the occurrence of albumen is due to the morbid process going on in the kidney, and that it is analogous to the œdema which surrounds those centres of inflammatory action whose products cannot be discharged on a free surface. This may be in part the cause, but, that it is, taken alone, insufficient, would seem to be proved by the contrast between the properties of albuminous urine and those of the fluid effused in inflammation of the serous sacs, or of those of the urine itself in pyelitis. An albuminous fluid, due solely to inflammatory action, presents far more of the other products of inflammation, *e.g.*, pus cells, &c., than are to be found in the urine at this early stage, even when allowance is made for the presence of a certain quantity of the normal excretion. It is true that profuse watery discharges occur in some forms of bronchitis, but from the well-known influence of certain diatheses upon the bronchial mucous membrane, it is more rational to attribute them to some cause similar to that which has been given for the albuminous state of the urine, than to consider them as due solely to the local alteration of function.

Under the view here taken of acute albuminuria it would appear likely that there may be also present in the urine some other substance not yet detected, perhaps the "materies morbi" itself; but whether this be so or not may well remain uncertain, until we are able to isolate and demonstrate the nature of the poison in syphilis, typhus fever, variola, &c.

The presence of renal epithelial cells in the urine, either free or entangled in the cylinders, these cells at first differing but slightly from their healthy standard, coupled with the condition of the secreting structure of the kidney, as ascertained by post-mortem examinations at later periods of the disorder, when the tubules are found distended to the utmost with epithelium, proves that an excessive production of gland-cells must have taken place, for the quantity thus shed is very greatly in excess of what is got rid of in health, during an equal period; and yet, in many cases, almost double the normal quantity is still found in the tubules. Again, the proportion of the free cells to those imbedded in casts is greater in the earlier than in the later stages, so that their desquamation would seem to be due to some influence, whatever its nature may be, operating in the first place

directly upon the cells themselves. It cannot be supposed that they are extruded by the formation of the casts in the tubules, for the so-called blood- and epithelial-casts, on their first appearance, are manifestly moulded in tubes not yet deprived of their epithelial lining; the outline of the cylinders being indented as if by cells still continuously coating the inner surface of the tubules, and their diameter never approaching that of the casts occurring in chronic forms of renal disease, when the tubes have been in great part completely emptied of epithelium. Again, in examining a recent section under the microscope, it is at once evident that but few of the tubes can be occupied by casts, for the cells do not cohere at all firmly either to each other, or to the walls of the tubules. From the free cut ends of these latter the epithelium pours out readily under the slightest pressure, leaving the tubes completely empty, whilst the field is covered with countless isolated cells, from which it can scarcely be freed by the most careful washing. These appearances, which are readily seen at the edge of any section, present a marked contrast to what occurs in some other forms of renal disease, *e.g.*, in the large, red, firm kidneys, coincident with long-standing obstruction to the circulation, as by disease of the mitral valve. In these, masses of epithelium, firmly cohering, are seen projecting from the cut ends of the tubules, often to a considerable distance beyond the point at which the membrane has been divided. Of course it is not meant to assert that the formation of fibrinous casts in the tubuli uriniferi, and their subsequent dislodgement, is not a most important agent in the complete removal of the epithelium which too often eventually takes place; but the above considerations do show that their influence in this respect at first can be but very slight, and that the well-marked changes in the epithelium cannot be attributed to their presence, but must depend upon some alteration in the nutrition of that epithelium itself. It may seem superfluous to lay so much stress upon the hypertrophy of the epithelium, which few, if any, would deny; but this hypertrophy, as it is the first, so also is it the most important of all the local changes, and the one to which, more than to any other, the subsequent irreparable damage to the secreting structure of the kidney is owing.

The presence of blood in the urine is of little moment, pathologically, compared with the indications of altered nutrition to which the congestion indicated by it is secondary. It generally

increases somewhat in amount for a day or two after its first appearance; but this gradual increase, though it may mark the gradual increase of the congestion, does not necessarily prove it, for it may be due to the greater number of minute vessels which, the congestion remaining the same, have given way under prolonged pressure.

The characters of the urine, then, so far, furnish evidence of the occurrence of the following changes in the kidney.

1. Hypertrophy of the epithelium.
2. Impairment, and perhaps perversion of function.
3. Congestion.

And it is generally admitted that these changes, if not identical with are certainly analogous to the early stages of inflammation. The cause of the first of these, its dependence upon some irritation communicated to the organ by the blood, will be more fittingly considered further on, at present we are concerned with the sequence of the morbid actions. It has been assumed all along that they occur in the order in which they are enumerated above; whether this be so or not depends upon the truth or falsehood of the prevailing doctrines on inflammation. It would be superfluous industry to give in detail here the arguments which prove that the inflammatory process commences in the elements of the several tissues, and that, probably in all cases, the vascular disturbance attending it is only secondary. The old axiom, "Ubi stimulus illuc affluxus," might have its terms transposed and still remain true. To quote the words of Mr. Simon, "Inflammation determines hyperæmia. When the textural changes begin, the elements of texture become increasedly absorbent of blastema, and suck more than commonly from the capillary circulation. To provide, during local necessity, for this greater local appropriation of blastema, a greater afflux of blood is required: in inflammation (as in simple hypertrophy,) the ministerial blood-vessels accordingly dilate, and ampler supplies are transmitted through them." And again, "Hyperæmia as abundant as ever exists in inflammation can go on for months without producing textural change—without causing a single pus cell to grow, or a single texture germ to die. A part does not inflame because it receives more blood. It receives more blood because it is inflamed." If this be true, it can scarcely be denied that congestion is the second and not the first stage in this disease.

Before passing to the consideration of the later structural

changes in the kidneys, there are one or two points which it may be as well to mention briefly.

The word 'hypertrophy' is not employed as the adequate expression of the affection of the epithelium, but only as the simplest term for that purpose, and one which brings prominently forward the best marked phenomenon of that affection. For though it cannot be supposed that the properties of the hypertrophied epithelium are identical in all respects with those of the same structure in health, still the increase in the number of the cells is almost the only change the reality of which can be conclusively established. At any rate I have never been able to arrive at any definite characters, by which isolated cells, obtained during the early stage, can be distinguished from normal renal epithelium. Again, if simple hypertrophy were the sole change, it might well be asked how diminished secretion could coincide with increased amount of secreting structure. But, to say nothing of the mechanical impediment to the exit of the urine in the undue distension of the tubules, it would be an exception to the ordinary laws of nutrition were increased activity of development and increased activity of function to take place simultaneously. The diminished secretion of urine is doubtless due to the combined operation of several causes, the value of each of which may vary in different cases. Change in the actual endowments of the secreting structures, obstruction to the ducts from both internal and external pressure, the nisus of the gland being directed to development rather than to secretion, would be the principal ones, although the list might be indefinitely extended.

It is unnecessary to treat, at equal length with the first, the rest of the phases through which the kidney passes in the further progress of the disease. There is no doubt as to their nature, for specimens of each of them are of frequent occurrence; there is no doubt as to their relation in time to each other, if it be once granted that they are different stages of the same morbid process. That they are really so, can scarcely be doubted if the gradual transition from one to the other throughout the series can be shown to depend upon a simple and sufficient cause.

The large red kidney gradually becomes paler, and at the same time mottled from unequal distribution of colour; the vessels on its exterior, when congested, present a stellate instead of a reticular arrangement; its size diminishes, and at the same time its originally smooth surface is, in various degrees, granular or

even nodular, and eventually it becomes a small granular kidney. But whilst its first increase in size was uniform, at least throughout the cortical portion, its subsequent atrophy is unequal, though not irregular. The peripheral portions of the cortex have almost disappeared, whilst the central masses, the pyramids of Bertini, still remain perhaps of even more than normal size. In consequence of this, the appearance of the organ as a whole is that depicted by Dr. Bright (see drawing). The changes observable under the microscope consist in gradually increasing fatty degeneration of the epithelium, ending in its more or less complete destruction, diminution in the calibre of the blood-vessels, thickening of their walls, and obliteration of many of the vascular coils, together with an increase in the fibrous stroma, partly only apparent and due to contraction, but partly also real.

Now on examining a kidney, in which the congestion, although apparently greatest round the margins of the pyramids, owing to the larger size of the vessels there, is still uniform, *i. e.*, when the congestion is at its height, we find the capsule exceedingly tense ; on dividing it along the convex border, the cut edges retreat, sometimes even the whole kidney shells out at once from its envelope. It is plain that so long as the capsule remained entire, the organ must have been subjected to very considerable pressure, and it is equally plain that this pressure must have told with most effect upon the blood-vessels.

On examining any moderately good thin section under the microscope, it is at once seen that there are two modes in which the circulation is interfered with,—for,

First, the tubules, many of them distended to something like double their usual diameter, must exert great lateral pressure upon the main vessels and extra-tubular capillaries; and, as the pressure required to empty the tortuous tubules of their semi-solid contents must be much greater than that which would suffice to diminish the calibre of the blood-vessels lying between them, there will be brought about a more or less complete state of anæmia.

The second point at which the circulation is obstructed is in the Malpighian bodies. I have repeatedly seen the vascular tuft driven up as it were into a corner and compressed, so as not to occupy more than a third, or even a fifth, of the capsule, by the quantity of epithelium present in it, partly derived from the Malpighian body itself, partly forced up into it from the associated tubule.

From the anæmia thus produced there results a large, pale, soft kidney.

It might be thought, from looking at a kidney in the congestive stage, that the force with which the circulation has evidently been carried on would be more than sufficient to overcome these obstacles; but, when the hypertrophy of the epithelium has attained its maximum, and fatty degeneration is commencing, the demand for blood is no longer so active, the *vis à fronte* becomes weaker and weaker, and the circulation has to encounter increasing difficulties with failing force.

Now that the alterations in form which the kidneys present are principally due to the fatty degeneration of the epithelium, whatever the cause of this degeneration may be, that the so-called "Bright's granulations" owe their origin to the same change, is so universally admitted that the proofs of its truth need not be detailed here, and as it may also be assumed as certain, from the analogous changes which occur in the brain, heart, liver, and lungs, in fact wherever fatty degeneration is found, that one of the conditions most influential in its production is diminution in the amount of blood circulating through any part, we should naturally expect that the morbid changes in the kidney would be best marked in those parts of the organ whose blood supply has been the most interfered with. And this is really the case; for, it is evident on examining a contracted kidney, like that figured by Dr. Bright, (plate iii., fig. 2, 'Select Reports of Medical Cases,' vol. I), that the peripheral portions of the cortex, *i. e.*, those portions which are situated at the greatest distance from the entrance of the blood-vessels into the organ, are precisely those in which the atrophy is the most advanced. It would seem, then, that in the greater or less difficulty with which the blood reaches the different parts of the kidney, lies the explanation of the greater or less degree of atrophy which they respectively undergo. It is not brought forward as the sole cause of the degeneration in question, but as the regulator of its amount. If not in all hypertrophies, yet certainly in those where the nutrition of the part appears to have been not only exalted, but also perverted, and especially when this takes place in organs or tissues in which cellular elements preponderate, fatty degeneration follows so constantly upon the hypertrophy that it must be looked upon as its natural consequence, the last stage of a process, which, though as a whole and with reference to the organism in which it occurs,

it must be called morbid, is yet throughout governed by ordinary physiological laws. In the disease here treated of, degeneration of the renal epithelium would be as inevitable as old age, even were the circulation maintained in the highest possible activity. But the orderly inequality observable in the result coincides so closely with the different amount of blood which succeeds in reaching the different parts of the organ, that it is difficult to escape the conclusion that the change is regulated, and its degree in some measure determined by it.

I have laid so much stress upon the unequal atrophy of the cortex and its cause, because in these there may often be found the answer to the question, whether, in any given case, the morbid process, whose final result we see in a small contracted kidney, has or has not commenced with general enlargement.

There are still one or two points, connected with the structural changes, which ought to be briefly noticed here.

In the large mottled kidney the appearances of congestion are in all cases due, in great part, not to turgid blood-vessels, but to the presence of extravasated blood in the tubules, which cannot then be distinguished by the naked eye from blood-vessels, though under the microscope their nature is at once apparent.

Again, as to the condition of the pyramids at different periods. During the continuance of active congestion, they appear pale, as contrasted with the red cortical portion, whilst as this becomes pale in the progress of the disease, they appear to be, and probably are, slightly congested. Much confusion is often caused by neglecting to specify the several stages at which these appearances occur. Thus, Dr. Todd, at p. 209 of his 'Clinical Lectures on Urinary Diseases,' says, in an account of a post-mortem examination: "The kidneys were about one fourth larger than natural, and on section presented the white cortical and red tubular portions of the scarlet-fever kidney," whilst two pages further on, in treating of the pathology of the same disease, he says, "The redness of the cortical substance is in strong contrast with the whiteness of the tubular portion, which is caused by the abundance of epithelium with which the tubes are filled." The fact is that the circulation of the pyramids is, throughout, but slightly interfered with, and the different manner in which at different periods they contrast with the cortex is all but conclusive proof of Virchow's statement that the arteriæ rectæ of the medullary

cones and the afferent arteries of the cortex have a common origin from the same branches of the renal artery.

When, among other changes in the kidneys, cysts are found, my observations would lead me to believe that they are almost invariably produced in the way suggested by Dr. G. Johnson, viz., by occlusion of the tubules, and the subsequent dilatation of the portion above the obstruction.

Again, it may fairly be asked of those who believe that these morbid changes begin in consequence of an irritation conveyed by the blood to the kidneys, how it is that the operation of one and the same cause does not produce everywhere exactly uniform results. Whereas, it cannot be denied that, in examining microscopical sections of kidneys in advanced and well-marked stages of the disease, we constantly find, side by side with tubules whose structure is irreparably damaged, others which seem to be quite healthy.

In addition to the common argument in favour of a blood-poison, drawn from the fact that both kidneys are equally and simultaneously affected, it may be replied that the change is at first universal throughout the cortical substance, if not quite uniform. According to my experience, the earlier the stage at which the examination is made the greater is the difficulty of finding any tubules which can be regarded as quite healthy. The after differences between them might well be accounted for on mere anatomical grounds, such as the greater or less length of individual tubules, the greater or less sharpness of their curves, &c. Nay, even supposing that there were no such differences whatever discoverable by us, we should still expect a long and complex process to lead to different results in different parts; for, in the words of Professor Tyndall, "There seems to be no such thing as homogeneity in nature. Change commences at distinct centres, instead of being uniformly and continuously distributed; and in the most apparently homogeneous substance we should discover defects, if our means of observation were fine enough."

In brief, then, I should assert the sequence of the structural changes to be as follows:—

These changes in many cases aided, or, at any rate, a return to healthy nutrition prevented, by the continued operation of their exciting cause.	Hypertrophy of epithelium. Impairment, with perhaps perversion of function. Congestion.	Large smooth, red, soft, watery kidney.
	Fatty degeneration of epithelium. Anæmia.	Mottled kidney. Large pale kidney.
	More or less complete destruction of epithelium, with occlusion or obliteration of tubules, and consequent changes in blood-vessels and matrix.	Granular kidney. That form of contracted kidney in which the greatest amount of atrophy has taken place at the periphery, with or without cysts.

And the principles on which these changes depend are:

1. Irritation of the epithelium, causing hypertrophy, and, secondarily to that, congestion.

2. The natural tendency of hypertrophied structures to degenerate; the seat and amount of that degeneration being regulated by the varying degrees in which the supply of blood to different parts is interfered with by the mechanical consequences of the hypertrophy.

Such would be the course of a typical case advancing uncomplicated to its fatal termination. But recovery, more or less complete, might take place at any of the earlier periods, so long as the epithelium was not irremediably injured. And again, the morbid appearances of the kidney will vary with the varying duration in different cases of the several stages, and also with the presence or absence of other forms of renal disease, as in the common event of a kidney, in which the changes induced by alcohol are more or less advanced, being attacked by this malady. But it would be impossible, within the limits of this essay, to discuss satisfactorily even the more common complications and variations, for to do so would involve the consideration of nearly all the forms of renal disease.

I pass now to the second and more difficult part of my subject, viz., "The relation between the anasarca and the renal affection at the commencement of the so-called renal dropsy;" and here the incidental consideration of the real nature of the disease, obscure and hard as the question is, can scarcely be avoided.

The following clinical history, by Dr. R. Bright, will form the most fitting commencement to my present inquiry; for it is only by rare good fortune that a case can be met with, which, whilst it brings out in strong relief the points to which I would call attention, supplies, at the same time, such satisfactory materials for their elucidation.

It is extracted from 'Guy's Hospital Reports,' series 1, vol. 5, p. 104, with only one or two slight verbal alterations.

"On February 5th, 1837, I was requested to see a gentleman, about thirty-five years of age, of good constitution, who, eight days previously, the weather being very cold, came from Maidstone on the outside of a coach, and on the same evening his wife observed that his face was swollen, and he complained of some pain in the loins. The swelling has since continued, and increased, showing itself in various parts of his body. The third of a grain of elaterium, which he had taken the day before, had acted well, and somewhat reduced the anasarca. I found it, however, still well marked, both in his face and legs. His skin was dry, except the palms of the hands and soles of the feet; the urine scanty, with lateritious sediment; on the application of heat, it first became clear, and then coagulated freely. He was ordered to remain strictly confined to bed, in a warm room, to have a light milk diet, and to take a pill composed of three grains of James's powder and two of extract of conium, three times a day, and a draught containing three drachms of the Liquor Ammon. Acet. He was also to repeat the elaterium about once a week.

"February 8th. The day after my last visit he had a profuse perspiration, and has since had a pleasant moisture generally diffused over his skin; pulse 80, full; urine, two quarts, of a high brandy colour, and slightly dingy, but free from lateritious deposit; still decidedly coagulable by heat, but in a less degree than before; bowels freely open by senna draught. He was ordered to keep strictly to the rules previously laid down, but was allowed a little vegetable and a small quantity of fish. To take one third of a grain of elaterium the next morning, and continue his other medicines.

"13th.—The perspiration still continues; the urine much less coagulable.

"20th.—The perspiration has been almost constant, and he feels weakened by it. For the last few days the urine has deposited a slight brown sediment, apparently from the

presence of some of the red particles of the blood. To leave off the James's powder, but continue the other medicines.

"March 6th.—Up to this time, no alteration has been made in the plan of treatment, except that a little sulphate of magnesia has been added to his draught, and the James's powder has been resumed. He feels and looks quite well, but the urine is too abundant, and he is called upon two or three times each night to pass it. It looks pale and watery, and has a slight dingy appearance, but is not the least coagulable by heat. The perspiration is now rather deficient. Twenty minims of the Liquor Antim. Tart. to be added to each dose of the mixture, and the pill to be continued.

"13th.—In appearance, he is now quite well, though the urine has still a slight dinginess. The quantity is natural, and it is not the least coagulable. Skin perspirable.

"Three years have now elapsed, and this gentleman has suffered no return. I have, within a few days, had an opportunity of testing his urine, and find it perfectly healthy."

Now, with regard to this case, it is to be observed, that the complete and seemingly permanent recovery renders it all but certain that no disease of the kidneys existed prior to the attack; whilst the ordinary symptoms, both general and local, commenced so shortly after exposure to their most common cause, that we cannot here accept the usual statement that the renal mischief makes unobserved progress for some considerable time before the patient's attention is attracted by the more obvious features of the malady.

I would ask, therefore, when two symptoms commence so far simultaneously that the patient first notices, sometimes the one, sometimes the other; when, moreover, they follow so very closely upon the existing cause of the malady to which they belong that the one cannot possibly, on any hypothesis, have been in existence for more than a very few hours before the other,—whether, under these circumstances, they can stand to each other in the relation of cause and effect, or whether it is not more rational to regard them as co-ordinate effects of some one common cause? One great obstacle to the acceptance of this latter view lies in our natural tendency to attribute similar phenomena to the same cause, without sufficient inquiry; but similar morbid appearances do not necessarily imply the same pathological history. In the same way that each new remedy is brought forward as a panacea,

and that different authors attribute the most diverse maladies to gout, syphilis, rheumatism, scrofula, or whatever their pet cachexia may be, so in the case of renal disease, the knowledge that it is a very frequent cause of dropsy becomes a prejudice in the way of our admitting the possibility of any other relation between the two whenever they co-exist.

And yet there can be no doubt that there is no necessary connection between them.

Dropsy may, and does, not unfrequently, occur without renal disease. Of course I am not speaking here of dropsy depending upon cardiac, pulmonary, or hepatic mischief, or of instances of local œdema, such as Dr. Laycock refers to altered innervation of the part, but of those cases of more or less general anasarca in which no lesion of any one or more of the viscera can be detected. Thus in the peculiar form of general anæmia, the observation of which by Dr. Addison led to his discovery of the effects or concomitants of disease of the supra-renal capsules, more or less œdema about the ankles is one of the common symptoms; and, again, in many cases of debility in which no organic lesion can be shown to exist, anasarca of greater or less extent is of frequent occurrence, especially in women about the period of the cessation of the catamenia. Some time ago, I examined the body of a man who had been under observation for some weeks in Dr. Jeaffreson's wards in St. Bartholomew's Hospital, and failed to detect disease of any organ. Persons of far greater experience than my own agreed that none existed which appeared adequate to explain the symptoms, of which, during life, the most prominent was anasarca, so closely resembling that associated with renal disease that the urine was repeatedly and carefully examined for such disease, but always in vain.

It is true that the number of cases of dropsy which cannot be brought under some one or other known physiological law is being daily diminished; but it becomes, at the same time, more and more probable that the explanations of many forms will have to be sought rather in changes in the blood itself, than in definite tangible disease of any solid organ; and that such disease when it does exist is frequently but secondary to some independent change in the blood. In fact, the unmistakable tendency of most recent inquiries into the physiology of the blood is to prove not only that morbid changes may occur in it primarily, but even that many substances constantly found in it are elaborated within the

vessels, their materials only being furnished to the blood during its passage through those organs, which, at one time, were looked upon as the agents in their production.

Again, renal disease frequently exists without dropsy. No one can have made any large number of post-mortem examinations without being struck by the frequent occurrence of structural changes, more or less grave, in the kidneys, in cases where no suspicion of such changes has existed during life. With reference to many of these, it may be said that the absence of all renal symptoms is conclusive proof that extensive structural change may co-exist with unimpaired function; but, granting that this answer does not involve a too confident reliance on our present means of diagnosis, and that those means have in all such cases been employed, there still remains a class of cases, to the argument derived from which no such answer is admissible. I have myself examined the bodies of several patients whose death was undoubtedly caused by renal disease, the diagnosis having been made during life and fully confirmed by the results of the autopsy, in whom no trace of anasarca was detected whilst they were under observation, and no history of its having occurred at any former period could be obtained. They have been generally cases of renal disease induced by stricture, or instances of some forms of small contracted kidney. It may be said that the history of patients, especially of hospital patients, cannot be relied on—that the most important, and apparently striking symptoms are constantly overlooked; that persons are frequently admitted in the last stage of a chronic malady, who maintain, in good faith, that they were in perfect health but a week or two or even a few days previously. But anasarca is, of all others, the symptom which is least likely to be overlooked. A man suffering under the hardships and vices of poverty may well be unconscious of failing strength, of increasing difficulty of respiration, or of alterations in his heart's action; he may even be insensible to pain, if it exists, for the most painful diseases are sometimes all but painless; but, to say nothing of the general dread of "the dropsy," he can scarcely fail to know whether he can or cannot get his shoes on, or even to notice any great increase in the difficulty of the process. A few months ago I attended a dispensary patient who died from suppression of urine of four or five days duration, all but complete for the last two days, the consequence of a protracted debauch, in whom there was certainly no anasarca,

and no effusion into any of the serous sacs. The kidneys were small, supple, but tough, with numerous small cysts. Unfortunately, leave to make the examination could not be obtained from the friends before decomposition had advanced so far as to make any microscopical observation of the state of the renal epithelium valueless. Not to overstate my argument, I ought to add, that here, as apparently also in the case of suppression of urine quoted by Dr. Watson from Sir Henry Halford, profuse sweating took place.

Again, in the accounts of the effects upon animals of extirpation of the kidneys, there is, to the best of my knowledge, no mention of anasarca.

It may then be regarded as certain, that there is no necessary connection between renal disease and anasarca, consequently, there is no impossibility in the supposition that the two may exist simultaneously, but independently; and, when the renal disease is the cause of the anasarca, it is by virtue of some other concurring condition. This condition has been supposed to be suppression of the exhalation from the skin and lungs.

I am not acquainted with any scientific researches into the effects of interference with the elimination of watery vapour from the lungs; but there is one familiar disease, viz., pneumonia, in which the amount of fluid thus got rid of must, one would think, be greatly diminished. It is difficult to believe that the same quantity of vapour can be extricated from the solidified lung, into which little or no fresh air enters, as would be from the same structure in health; and yet, even in the most extreme cases anasarca does not occur, unless there be also present some one or other of the causes which, apart from pulmonary disease, are known to be capable of producing it. The physical conditions, too, under which respiration is carried on, are such that whenever any considerable portion of lung becomes hepatised, we can scarcely imagine that the compensative action of the remainder can keep the quantity of water excreted up to its normal amount, for the proportion of watery vapour which a given quantity of air can contain, cannot be indefinitely increased. Since, too, with regard to the carbonic acid, we have actual proof in the dusky face and livid lips that the increased rapidity of respiration is insufficient to maintain the natural balance which has been disturbed by the diminution in the amount of available lung tissue, it is but reasonable to suppose that it must be equally insufficient

with regard to the watery vapour. The possible amount of exhalation from the dry, pungently hot skin of a pneumonic patient will come, incidentally, under consideration further on.

The excretory function of the skin, no less than that of the kidneys, may be completely arrested, and that arrest may even prove fatal, without the production of anasarca. Such, at least, is the conclusion I would draw from the absence of all mention of that symptom in the records of experiments upon animals, by coating them with an impermeable varnish; if it were present, it can have been only very slight. Death is said to occur by a kind of slow asphyxia, from the seventh to the tenth day, the lungs and viscera being found gorged with dark blood. But the amount excreted by the skin is said to vary so widely, even under ordinary circumstances, that no slight interference with its function would seem to be capable of producing suddenly, at least, and by the mere retention of its excretion, any serious effect on the economy. Thus, according to one of the latest experimenters, Weyrich (I quote from the 'Brit. and For. Med.-Chir. Review,' for Oct. 1863), the extremes of the cutaneous transpiration from the same arm in summer per hour, were, in three individuals—67–740, 102–354, and 47–215 grains, respectively. And even these figures probably represent, very inadequately, the difference in the quantity of fluid got rid of during different equal periods, without this difference disturbing the balance of the circulation; for, "It has commonly been admitted that the urinary and prespiratory functions are antagonistic, and indeed vicarious of one another. In Weyrich's observations, however, there was not that agreement with this theory which might have been expected. On the contrary, it would rather appear that under similar conditions, avoiding extremes, both excretions rise and fall together; but, that when extraordinary circumstances come into play to disturb the equipoise, in all probability the law of antagonism and vicarious action comes into force. No indication, however, can in any case be drawn of the perspiratory power or amount from the amount of urine discharged."

But further, it may reasonably be doubted whether the amount of cutaneous transpiration is more than temporarily diminished in those cases where the exposure to wet and cold is followed by febrile reaction, where the skin becomes hot, dry, and, as it is commonly if not correctly added, imperspirable: in those cases, in fact, which gave rise to the term, "inflammatory dropsy."

The late Dr. Snow, in an article in the 'London Medical Gazette' for March 3rd, 1843, observes: "It is generally taught, that in fever with a hot and dry skin there is diminished cutaneous transpiration; but, reasoning by analogy from the above facts" (viz., experiments on animals similar to those mentioned above), "we may conclude that such is not the case, and that the secretion from the skin is at least equal to, if not greater than, what it is in health; and, that such is really the case, a little consideration will prove; for the patient drinks a good deal, voids but little urine, does not increase in bulk, but, on the contrary, gets thinner; therefore, there must be increased evaporation from the skin and lungs, for which the elevated temperature is sufficient cause. The heat of the surface, which is sometimes considered as a consequence of diminished evaporation, accounts satisfactorily for the dryness of the skin, where the cutaneous secretion is not very great indeed, by the increased rapidity of evaporation it must produce. I admit that this position respecting the perspiration in fever requires to be proved by experiment; but, in the mean time, I feel so satisfied that the evaporation from the lungs, which is confined by physical laws, cannot be sufficient to dispose of all the supplementary fluid, that I have no doubt, in my own mind, on the point." I have not met with any subsequent direct criticism upon these views of Dr. Snow's, but they have been accepted by Dr. W. B. Richardson, in a recently published essay on scarlet fever. It may be objected that this extract is not strictly applicable to the case of acute anasarca, for, in it the patient does most certainly increase in bulk and weight, and no reasonable person can doubt that the cutaneous transpiration is lessened, for it has been proved by direct experiment. But, in the only attempt to determine this question which I have met with, as detailed by Dr. Parkes, it is expressly stated that the experiments were not begun till the disorder had reached its height; whereas, I am speaking solely of the very commencement of the disease, and merely wish to show that a dry, hot state of the skin, is by no means such conclusive evidence of greatly diminished transpiration as it is commonly believed to be.

It must be further remembered, that the effect of the diminished excretion of fluid is, in many cases, to a certain extent counteracted by vomiting.

It appears to be uncertain whether there is any marked deviation from the normal standard in the amount of matters excreted

by the intestines. That increase, which is said to occur in the later stages of the disease, is no doubt due, in great part at any rate, to the effect of remedies.

It would be absurd to deny that dropsy would not necessarily result from the continued ingestion of fluid, if its excretion were prevented; but it is certainly well worth while to inquire, whether the commonly assigned causes of renal dropsy are really so potent as to furnish a satisfactory explanation of the symptoms at the outset of a case such as that detailed above. That combined, or even singly, they are amply sufficient by their continued operation to produce anasarca, is undoubedly true, but is, at the same time, not a sufficient answer to the question here discussed.

The theories which have been advanced as to the proximate cause of anasarca in connection with renal disease, may be classed under three main heads, viz.:—

I. Diminution of the specific gravity of the blood.

II. Increase of pressure within the vascular system.

III. Some change in the constitution of the blood, not necessarily attended by diminution of its specific gravity: such, *e.g.*, as would result from modification of the albumen, or from the accumulation in the blood of any substance ordinarily existing only in minute quantity.

They may be enumerated as follows:

1. Impoverishment of the blood, consequent on the loss of albumen.

2. Increase of pressure in the vascular system from the impediment to the capillary circulation, due to the impure state of the blood; the retention of urea being perhaps the chief element in this impurity. In chronic cases the pressure is still further increased by the compensative hypertrophy of the left ventricle.

3. Increase of pressure in the vascular system, caused by obstruction to the flow of blood through the renal arteries throwing a greater mass of blood into the general circulation.

4. Some alteration in the constitution of the blood, consequent on the accumulation in it of matters which are normally excreted by the kidneys.

5. That the anasarca is the result of an attempt at the excretion of either the urea, or of some other urinary constituent; the ordinary channels by which they are got rid of being blocked up,

and their elimination necessitating the separation, at the same time and place, of a certain quantity of water.

6. A watery state of the blood, consequent on the insufficient excretion of water; acting probably in two ways, viz., by diminution of the specific gravity of the blood, and by increase of pressure from the increased quantity of fluid contained in the vessels.

Of these, it is evident that the first two can only explain anasarca as it occurs in the later stages of renal disease. The third cannot well be supposed to be in existence during the early part, at any rate, of the congestive stage, for then the quantity of blood circulating through the kidneys is probably increased rather than diminished. The fourth would seem to require a longer period than elapses in many instances between the time when the changes in the kidneys must in all probability have commenced, and that at which the anasarca is first noticed. Beside, as there is no doubt that the elements of the urine may be retained without the occurrence of anasarca, we should still have to seek further for the special conditions under which they become capable of effecting this supposed alteration.

The fifth is liable to the same objection, for it is difficult to believe that the constituents of the urine can have accumulated, in the course of, at most, a few hours, to such an extent in the blood, as to stimulate the elements of the connective tissue to take on themselves such an unwonted function as that of secretion or excretion; especially when it is borne in mind that none of the ordinary channels for such excretion can be, except in some extreme almost impossible case, completely closed.

The sixth is that which appears at first sight to meet in the most satisfactory manner the requirements of the case. But when we remember the great variations in the proportion between the liquid and solid parts of the blood which may and do exist, even in health, without the occurrence of any serious disturbance, and the great increase in the amount of the circulating fluid which may take place in any organ or part of the body, and doubtless in the whole, an increase leading to an appreciable increase in the size of the part affected, as any one may convince himself by noting the variations in size of his own hands, and yet to nothing which can be rightly called anasarca, or even œdema in the technical sense of the word; remembering this, it seems hardly credible that the amount of fluid ingested in the course of a few hours, even supposing none of it were eliminated, can be

sufficient of itself to account for what is often the most prominent and first noticed symptom of inflammatory dropsy. It could be so, only on the assumption, surely in very many instances a groundless one, either that the vessels have been already filled up, nearly if not quite to the extent of their capacity, or that the fluid swallowed is considerably in excess of the usual quantity. And here I must again guard myself against the imputation of having fallen into the fallacy of composition. It may be true that these several causes, taken singly, are insufficient, but it does not therefore follow that their continual operation will be equally without result.

It cannot be denied that, in the great majority of cases, where the renal disease has existed for some little time, they furnish a satisfactory if not complete explanation of the associated dropsy, that they are, in and by themselves, fully adequate to the production of such a symptom, but there may be at the same time, in the history of the disease, indications, very plain ones I believe, of the existence of some other more general cause. The very number of the modes in which it has been endeavoured to establish a connection, more or less necessary, between renal disease and anasarca is in itself no slight evidence of the difficulty of doing so, and of the frequent occurrence of cases in which we are obliged either to seek for some new cause, or to accumulate acknowledged tendencies until, in their united influence, we may seem to have obtained a sufficient power. The reason which leads me to regard the ordinarily assigned causes of anasarca as inadequate to the explanation of that symptom as it occurs at the commencement of acute renal dropsy, rests, not upon their absolute inefficiency, but upon the length of time which it would seem must elapse between the beginning of the local changes in the kidneys, and the production of general symptoms secondary to those changes. This consideration is, I believe, conclusive against the claims of any one of them taken singly, and the same argument applies, though with somewhat diminished force, to their combined operation. I confess myself unable to understand how the symptoms of cases, similar to that related above, can be satisfactorily explained, except on the supposition that, prior to and independently of the renal affection, there exists a marked tendency to dropsical effusion. That this tendency, even by itself and unaided by the secondary effects of diminution or suppression of the renal and cutaneous excretion, may suffice for

the production of anasarca is, I conceive, very probable; though, from the nature of the case, it seems impossible to bring forward actual proof that such is the fact. For, admitting freely that in very many instances the relation in time of the renal affection to the anasarca is such that we are fully justified in looking upon the former as the cause of the latter, there are still many cases in which it is very difficult to believe that such a relation can exist, and in which, consequently, we must seek for some other cause. It is a great obstacle in the way of either the successful study or treatment of urinary diseases that the local changes are so easily demonstrated, and at the same time so clearly capable of producing the most fatal results, that we are led to overlook the signs of a more general malady. But it would be almost as easy to explain typhoid fever by reference solely to the intestinal affection as to explain the phenomena of many so-called renal diseases by reference solely to the kidneys. It may be difficult, perhaps impossible, in the latter case, to determine how much of the sum total of the symptoms is due to the local affection, how much to the more general malady of which this is only one of the manifestations: it is not very easy to answer the same question in many cases of typhoid fever, especially those in which a relapse occurs, apparently consequent on some error in diet, such as a premature return to solid food.

There are two periods at which there seem to be distinct indications of the existence of an element in some forms of renal disease, which does not depend upon the interference with the function of the kidneys, though this interference contributes no small share of the sum total of the symptoms, and, in so doing, masks the operation of the deeper seated cause. They are—First, the commencement of cases of acute renal dropsy; secondly, the later, or rather middle, stages of some chronic forms. It would require an experience, far longer and wider than mine has as yet been, to enable me satisfactorily to establish this view, and to support it by a sufficient number of carefully observed facts. I can at present do little more than point out the grounds for the opinion to the proof or disproof of which any future researches I may have the opportunity of making on this subject will be directed: unfortunately the nature of the inquiry is such that it appears all but impossible to submit it to direct experiment.

With regard to the first, I have endeavoured to show that there are strong reasons for doubting that one of the most

prominent symptoms, viz., the anasarca, can at first be due to the renal disturbance, in and by itself, even though aided by a considerable diminution in the cutaneous transpiration. Still, if no other cause could be assigned, we should be obliged to accept this as a sufficient explanation. But the phenomena of the renal affection itself all point to a previously existing blood-disorder, and, to some extent, indicate its nature. Thus, both kidneys are always attacked, and in all but an equal degree; whereas, if it were due to the direct action of cold, or of any local cause, we should scarcely expect this to be the case, for the kidneys are far more widely separated than any other of the double organs in the body, except the supra-renal capsules and ovaries; and yet double pleurisy, for instance, as the result of exposure to cold, is certainly the exception. Again, the appearance of albumen in the urine, at a period so early that it is impossible to suppose that any grave organic change can have taken place in the secreting structure, naturally suggests that this blood-disorder is one in which some part at least of the liquor sanguinis transudes from the smaller vessels much more readily than under ordinary circumstances; that, in fact, the albuminuria and the anasarca are both co-ordinate effects of one common cause; and stand to each other in a relation analogous to that between hæmaturia and some of the malignant forms of exanthematous diseases.

If, now, we seek for the cause of this blood-disorder, there are many ways in which it may be referred to the recognised cause of the disease itself, viz., exposure to cold and wet. It may be the result of the retention of some matters which ought to be excreted by the skin; or, it may be, that from the follicles whose orifices are constricted by cold, a part of their contents is reabsorbed, and acts as a poison; or, it may be that the action of cold upon the peripheral extremities of the nerves over a large portion of the surface of the body, influences, by reflex nutrition, the metamorphoses of the elements of the tissues, and arrests or alters the changes through which they normally pass. An indication, only in a minor degree, of this same interference with tissue change is, perhaps, to be found in the copious deposit of lithates in the urine during a common cold, and in febrile states generally.

In chronic cases of renal disease, if, in their essence, they depended simply upon the local changes in the kidneys, we should scarcely expect much benefit to be derived from measures

which lead to increased production, under ordinary conditions, of the solid constituents of the urine; for the excretion of such matters being already insufficient, this would merely add to the impurity of the blood. But, as is shown by numerous reported cases, the best results are often obtained by a sea voyage; and yet, if the experiments of Beneke as to the effect of a residence by the sea-side have any value, it would seem probable, in the absence of more direct observations, that during a sea voyage the quantity of urea and of some of the salts of the urine would be greatly increased.

Again, the remedies which appear to be most useful are rather those which belong to the class of so-called hæmatinics than those which can be supposed to exert any direct action on the kidneys.

But the adequate discussion of these questions would carry me far beyond the scope of this essay. I have endeavoured to describe the sequence of the structural changes in acute renal dropsy, and to establish the probability, at least, that the relation in which the anasarca and renal affection stand to each other, at the commencement, is that of co-ordinate effects to a common cause.

In conclusion, I would attempt a brief answer to a common objection against the view here taken of the cause of the disease. It is said that to talk of blood-disorder, dyscrasiæ, defective secondary assimilation, &c., is too vague to lead to any practical result, that to do so is but to conceal our ignorance behind long words; to impede rather than advance the progress of true knowledge. But, surely it is as unwise to deny our knowledge as to dissemble our ignorance; we need not say that we can know nothing because we do not know all. The knowledge of one single property of any substance is as conclusive proof of the existence of that substance as the knowledge of them all. No one would deny the existence of the several poisons producing ague, syphilis, typhus fever, variola, and many other diseases; and yet, as in the case of acute renal dropsy, our knowledge of their nature is all but limited to what we may gather from one single physiological reaction. To deny their existence on that ground, would scarcely conduce either to the successful study, or treatment, of the disorders to which they give rise.