

C to G

*On
Albuminuria.*

March. 1864.

1. Functional Albuminuria

2. Albuminuria from Org. Renal Disease (Diabetes)

3. Do. owing to the disease

Foot

It was originally my intention to have chosen for my Thesis, a subject of some practical importance and clinical interest, but having been laid aside from my studies through severe illness during a considerable period of last session, I have been obliged to fall back upon the usual and common place custom of making a simple compilation of a subject, in regard to which information was readily accessible, instead of carrying out my former project at a later period of my curriculum, when time is precious and one must necessarily sacrifice the chance of giving in a creditable Thesis, in order that due attention might be given to matters of more vital importance.

2
The pathological and practical importance of a minute examination of the urine in all diseases has long been recognised by our profession. It is only, however, within comparatively recent times, that, by the aid of the microscope and the progress of organic chemistry, we have arrived at a thorough knowledge of the histology and pathological chemistry of the urine; and thereby have rendered the diagnosis and treatment of diseases in which that fluid is altered in its composition, much more certain and satisfactory. I hope therefore that the perusal of this paper may not prove unprofitable, giving, as it has ventured to do, some particulars regarding one of the most common and interesting pathological conditions to which the urine is liable, namely

Albuminuria. The occurrence of albumen in the urine has only been noticed within comparatively recent times, although some observers think that Hippocrates was aware of its occasional presence in that fluid. If this be the case it is certainly very interesting, for he had no doubt learned its connection

with serious renal disease, for in his 31st aphorism we find him stating, that, "when bubbles settle on the surface of the urine they indicate disease of the kidneys, and that the complaint will be protracted." Whether or not the "Father of Medicine" knew that the urine was albuminous in certain states of the body, is, we may say, undecided, but certain it is that his observations on the urine are most interesting, and indicate clearly the wonderful amount of knowledge he had on the subject. The first unequivocal notice of our subject, is in the works of Fordyce published in 1771. He there states that "any extraneous substance soluble in water, that may get into the bloodvessels may be evacuated along with the urine; such as acids, alkalies & other saline substances.

..... If the kidneys are relaxed, chyle, serum, coagulable lymph, and even the red part of the blood may be thrown out"

Several authors contemporaneous with Fordyce, but more especially Coticchio have referred to the presence of albumen in the urine. The first physician who entered fully into the

subject and showed its connection with important morbid conditions, but more especially Dropsies, was Blackhall, who in 1813 published an excellent work entitled "the Nature & Cure of Dropsies." More recently the researches of Bright, Christison, Rees and many others in this country, & of continental observers but more especially Rayer and Solou, have added to our knowledge regarding it. Within the last few years others have written on the subject, but not with the result adding materially to our knowledge regarding it, or of controverting the observations of the distinguished authors already mentioned.

It is clear that the causes of Albuminuria will reside in some part of the mechanism by which the urine is excreted from the system. Accordingly, we find, that, to some disease organic or functional, either of the genitourinary apparatus, or of the blood, we can trace the occurrence of albumen in the urine. At the same time we must bear in mind that the primary cause in many instances may reside in the nervous system, which, by its mysterious influence, may so

modify the function of the blood and the renal capillaries, that the serum of the blood passes off, in considerable quantity by the kidneys. For the sake of convenience merely ^{we} will divide the diseases causing albuminuria into Organic & Functional.

Of the Functional causes, Congestion is perhaps the most common, and that it is really a cause of the condition in question, few are now disposed to doubt, for we find that Dr. Robinson has experimented on the subject and found that by tying the renal vein of a dog or rabbit, albuminous and bloody urine was produced. Frerichs has repeated his experiments with a peculiar result. So that we find the minute blood-vessels of the secreting structure of the kidney, may become distended with blood, and as a result, a fibrinous exudation take place which fills the urinary tubules, making casts of them and entangling blood globules and epithelium along with them, ultimately becomes washed away with the urinary secretion, and appear in the urine after its is voided, all this then, we find may happen and yet the

De Ischiade Nervosa Comment.

Diseases of the Kidney (Johnson)

Kidney substance may be quite healthy. The causes of the congestion may be numerous. The removal of the cause, if it has not been in operation a very long time, is in general sufficient to cause the albumen to disappear. It is just a question whether a persistence in the cause, however slight, resulting in the manifestation of albumen in the urine, might not ultimately lead to some organic permanent change in the structure of the kidney.

The next of what we have ventured to term the functional causes of albuminuria, is Diabetes. The presence of albumen in the urine of this disease was first pointed out by Cotunnus. Of the proportion of cases in which it exists we are uncertain. Heller found it in 37 percent of his cases, Garrod in about 10 percent and Dr. Von Sarsch in 28 percent. Although these figures are somewhat discrepant, still they serve to show the fact, that albumen is present in many cases of diabetic urine. Dr. Johnson accounts for its presence by saying, that the continued separation from the blood, by the renal cells of sugar (an abnormal ingredient)

so alters the secreting structure of the kidney as to produce organic renal disease. We must call to mind however, that in diabetes the probability is that the lesion is of central nervous origin, for by the experiments of Brown Sequard, Schiff & Bernard, saccharine urine has been produced by irritating a portion of the 4th ventricle, upper part of the spinal cord & sympathetic; and Bernard also states that he has produced albuminuria by injuring the sympathetic in the neck. If such be the fact then, the albuminuria might be referred to the same or a similar lesion of the central nervous system, as that causing the presence of sugar.

It is well known that the urine of healthy individuals may become temporarily albuminous under the use of peculiar kinds of food or certain medicinal agents, which for the time being have produced irritation, probably congestion in the kidneys. Whether the albuminuria be caused directly, by irritation of the renal substance or by an altered condition of the

*On Granular Degeneration of the
Kidneys p. 36.*

blood, is a disputed point, and will require further observations to warrant us in forming a decided opinion. Dr. Christison has occasionally known a temporary albuminous impregnation produced in healthy individuals by eating freely, cheese, pastry & such other indigestible articles, as are known to have in general the effect of increasing the usual solid ingredients of the urine & occasioning a large deposit of Lithic acid & Lithate of Ammonia. Dr. Solon says that in individuals so affected, a predisposition must be admitted, in order to account for its production. Dr. Blackhall thinks that the use of alkalis & their salts "disposes the serum of the blood to pass off by the kidneys", and this statement seems to be by no means improbable, for Dr. Copland has shown that when these medicines are used for a lengthened period, the blood becomes deteriorated, in fact gets into a sort of hydroemic condition, somewhat analogous to its state in Scorbutus, in which we know the occurrence of albuminuria is by no means uncommon.

It is undoubted that the application of a cantharides blister to any part of the body will produce a transient albuminuria. This I think most acknowledge, but at the same time all agree, that, the result is by no means invariable & that it only occurs in certain constitutions.

It has been affirmed that the use of Mercury caused albuminuria, but the experiments in favor of this view are hardly satisfactory, for they were performed on syphilitic subjects, and in one of the cases there was a trace of albumen in the urine before the Mercury was administered; so that we would require the experiments to have been made under more favourable circumstances, before giving our adherence to this assertion, especially when it is affirmed that there is no more common thing in Syphilis than albuminuria, which, when the Syphilis is cured, instantly disappears: it no doubt having been the result of some disease of the kidney depending upon the constitutional affection.

Hæmaturia, may be mentioned as

the next cause, but the fact of having referred to it, I shall consider sufficient, as it is self-evident that albumen in a soluble state will enter the urine along with the blood, and be there recognised in the usual way.

Lastly may be mentioned certain casual causes of coagulability of the urine from the accidental admixture of Menstrual fluid, Prostatic secretion or Semen. We know that in certain cases of paralysis, the seminal secretion escapes involuntarily into the urethra. The same result may be occasioned by venereal excesses, or when the bladder is evacuated immediately after coition. The urine in passing along the urethra, washes the seminal fluid away with it, or a reflux of the semen may take place into the bladder immediately after coition in cases of stricture. Mr. Rayer has noticed that he had two cases, in which the persons were labouring under obstinate constipation and voided semen from their urethras while at stool.

We have now to refer to albuminuria existing in organic disease of the genito-urinary

apparatus

The first that merits our attention is Inflammation of the secreting structure of the Kidney. The disease may be either acute or chronic; in either case the urine becomes loaded with albumen and other abnormal ingredients. The simplest form of the acute variety is met with in some acute diseases as a complication, scarlatina being perhaps one of the most common of these diseases. Whether it occurs as a complication or as an idiopathic disease (which is uncommon), it is ushered in by all the symptoms of an inflammatory affection. Chills and rigors are soon followed by heat of skin, frequency of pulse, thirst, loss of appetite, pains in the loins &c. Dropsy is generally an early symptom, the face becoming pallid and puffy, and the whole body, but more especially the lower extremities being more or less dropsical. The urine is scanty, sometimes almost entirely suppressed, of a dirty brownish colour and highly coagulable. On microscope examination of the urine, distinct casts of the tubules are seen containing

epithelium cells, often blood corpuscles and a large quantity of secreting renal epithelium cells. Sometimes inflammation of one or other of the serous membranes comes on, or considerable dyspnoea is produced by effusion into the air cells of the lungs. If the case goes on well, one of the first signs of recovery is an increase in the quantity of urine & its diminished coagulability; & gradually the other symptoms disappear as the urinary function returns to its normal standard. Too often, however, we find that instead of running an acute course, the disease lingers on and becomes chronic. The complaint is very often of a chronic nature from the very first. It has perhaps been insidiously making progress under cover of some other malady from which the patient may have been suffering, and often remains for a time unknown to him or his medical attendant. Perhaps in no other form of disease more commonly than in puerile affections does this form appear. The chief symptoms which attract our notice are gradual weakness & emaciation, the latter

however being often masked by the oedematous state of the body. The complexion of the patient generally presents that pallid, dusky or waxy appearance, which is so characteristic of patients suffering from chronic renal disease. Dropsy is not by any means so constantly present in this form, cases having proved fatal in which no dropsy occurred. A pretty constant symptom is that, of the patient desiring frequently to micturate, and that more frequently at night, from some irritable state of the bladder. This indeed may be the first symptom which directs the patient's attention to the state of his urinary organs. In the early stages of the disease and in the intervals between a gouty paroxysm, the urine generally contains very little or no albumen; in the second stage the urine is much more albuminous & remains so for some time during the interval between the attacks; in the more advanced stage the urine becomes permanently coagulable. What are the changes which the inflammatory process has been effecting in a kidney producing these symptoms? Most authorities on the subject, agreed that

they consist in a preternatural production of the epithelial cells lining the urinary tubules, and their subsequent desquamation. The cells along with a few blood & pus globules collect and block up the tubes. As a consequence of this, the cells are unable to perform their functions properly, so that the solid ingredients of the urine are secreted in diminished quantity, the watery part of the urine is however, freely separated from the blood by the Malpighian bodies, and, making its exit through the tubules often washes them free of their contents, which are found in the urine after it is passed.

The morbid condition of the urine which is more characteristic and interesting, is the presence of fibrinous moulds of the tubules, which are always found in greater or less quantity along with the desquamated epithelium.

The next disease of the kidney which claims our notice, is not of an inflammatory nature, but a degeneration. It is generally termed "Bright's Disease" or granular degeneration of the kidney. The pathological consequences to the structure of the kidney, are much the

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same as those in the inflammatory affections, the essential difference being the formation & deposition of oil globules in the epithelial cells, distending them & allowing their contents to escape into the tissues of the organ. The secretion of urine is of course interfered with, and altered as to the relative quantity of its solid & watery constituents, and as it washes through the tubules it carries their contents away with it. An examination of the urine shows the presence of epithelium cells with oil globules in them & generally some free oil globules. The composition of the blood in the diseases just referred to has been carefully studied by Dr. Christison. In acute nephritis the serum was diminished in density, the albumen deficient, the density being the lowest when the urine was most albuminous. The solids may be reduced to 68 in 1000 parts, instead of about 100 which is normal. The colouring matter at the outset shows no particular change, but as the disease advances & becomes chronic it becomes much diminished. The same observer has further demonstrated, that the blood, in addition to the changes already

referred to, contains a large quantity of urea. In Chronic Nephritis, the density and solid constituents instead of being much diminished, are often normal and sometimes exceed the usual quantity. The proportion of salts and albumen was found to be from 816 to 853 in 10,000 parts. In the middle stage of the disease when the urine is moderately albuminous, the salts and albumen range from 630 to 660 in 10,000 parts; in the furthest advanced stage when the urine is only slightly coagulable, the albumen ^{is} ^{found} ^{to} ^{be} found to be from 973 to 980 in 10,000 parts. The colouring matter in this form was found highly deficient.

There are other diseases of degeneration of the kidney, in which you may have the urine coagulable, of which amyloid and fibroid degenerations may be taken as examples, but, although these forms of kidney disease are very interesting, still I think it would be some what foreign to the design of this essay to enter upon their consideration, so having referred to them I shall consider sufficient.

Lastly in connection with this section of our subject, I would just mention certain other

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affections of the genitourinary apparatus, in which the urine is generally more or less albuminous; these are Cystitis, Pyelitis, Cancerous & Serofulous diseases of the kidney & Prostatic Abscess.

Now let us proceed to consider some of the explanations offered, to account proximately for the presence of albumen in the urine. We have already seen that in renal disease there is a morbid state of the blood. Such being the fact, a question at once presents itself. Does this morbid state of the blood stand in relation of cause or effect to the kidney disease? Most I think hold the latter view. Of those adhering to the former, Dr. Walsh is one of the chief. He believes that "Bright's Disease" is a blood disease ab initio. In support of his doctrine he brings forward different statements. For instance he reminds us of an important fact in connection with the matter, that there is no positive & direct relation between the amount of albumen in the urine & the renal disorganisation, nor between the latter and the severity of the secondary diseases which so frequently accompany kidney complaints; further that albuminuria is produced by morbid states of

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the blood, other than "morbus Brightii", and that albumen may disappear entirely from the urine in the most serious cases of Bright's Disease; yet it cannot be supposed that the physical condition of the kidney, favouring filtration of serum through the vessels, has suddenly & completely changed. In fact he believes that it belongs to the same class of diseases as cancer, gout or rheumatism, that, as in those diseases, there is a peculiar disposition to imperfect organic action & a toxic condition of the blood, so, in renal disease, we have similar conditions probably brought on by errors in the primary or secondary digestive processes.

Dr. Prof. & M. Pourcaut lay great stress upon an interruption to the cutaneous function being the proximate cause of albuminuria, and this seems to be a view deserving of consideration, bearing in mind the undoubtedly vicarious action of the skin & the kidney, and the almost invariably dry state of the skin in renal disease. In support of this view, experiments have been made, with the result that when the cutaneous

function was interrupted albuminuria was produced. M. Foucault has given us at least an ingenious theory to account for this. He says that in consequence of the function of the skin being interrupted, the excretion of lactic acid by the cutaneous surface is suppressed, & this acid being retained in the blood neutralises the Soda, which in the normal state keeps the albumen in solution. The albumen, thus isolated as it were, becomes an effete product and is discharged by the kidney. Our author still backs up his assertion by another experiment, in which he injected lactic acid into the veins of an animal and produced albuminuria. If, then, these experiments be reliable and accurate, we are forced to acknowledge that albuminuria may be produced by suppressed cutaneous function. A question in connection with this, might I think, suggest itself. Whether a continuance of the interruption to the cutaneous function, might not or does not give rise to the morbid condition of the blood existing in "Bright's Disease"? This question is worthy of consideration, but I

must confess it would be one difficult to prove, for, unless we knew that a certain person were going to take "Bright's Disease" on a particular day, so that we could pay special attention to the state of his urinary & cutaneous functions for some time previously, for otherwise it is probable our attention might not be directed to it, the proposition would be extremely difficult ^{to} ascertain.

Mr. Robins in a paper which he read before the Academy of Medicine at Paris, stated that his opinion was, that in the normal state of matters albumen is burnt in the blood and the nitrogenized residue of the combustion viz urea & uric acid, are eliminated. He says that, if by any means this combustion is interfered with, the albumen would pass unaltered into the urine. In support of this he says that "in those diseases such as Croup, Complete Ascites, capillary bronchitis with emphysema accompanied by much dyspnoea, in phthisis where there is much dyspnoea or where accompanied by pneumonia, in which you have very incomplete respiration & aeration of the blood, albumenuria is present." The same

applies to cardiac disease when the patient is for a time in a semi-asphyxiated state, also to nervous diseases, which cause a diminished temperature & therefore less combustion.

In the same way he explains the occurrence of albuminuria in diabetes, as there would appear in this disease to be some central nervous lesion, causing the accumulation of such a quantity of sugar in the blood, as to prevent the combustion of albumen into urea & uric acid. He reminds us that profitable hints may be taken from comparative physiology. As a general rule, the urine of mammals & birds contains no albumen, but that of reptiles & frogs however, remarkable for the low temperature of their bodies, always contains albumen. Our author concludes his paper by saying, that if his theory be correct, the proportion of urea & uric acid contained in albuminous urine would be diminished, and such he found to be the case in the diseases, which he experimented on viz phthisis, disease of the cerebrospinal axis, extensive & acute bronchitis with dyspnoea & "Bright's Disease".

Dr. Johnson has offered an explanation of the proximate cause of albuminuria. The idea involved in his view was suggested to him by the experiments of John Reid on Asphyxia. The experiments were as follows. A pipe with a stopcock was inserted into the trachea of an animal. The stopcock was closed & unarterialised blood began to circulate through the lungs, was returned to the heart & thence sent by the systemic circulation throughout the body. Venous blood circulating through the brain suspended consciousness. For two minutes after the animal has become insensible, & when the blood in an exposed & unobstructed artery, is equally dark with that in the corresponding vein, the large arteries become more distended than before the stopcock in the trachea was shut. By the use of a haemadynamometer it was found that a diminution of the pressure of the column of blood in the vein and an increased pressure in the artery, was produced, as compared with that observed before the stopcock was closed. After relating the experiment Dr. Reid goes on to refer to the observations of Dr.

Dr. Johnson on Dis. of the Kidneys.

Alison where he says, that not only is integrity of the right side of the heart necessary in order that blood may circulate freely through the lungs, but "that the chemical changes between the blood & the atmospheric air should proceed" Dr. Johnson thinks that these principles are analogically applicable in the etiology of kidney disease, "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 intertubular vessels, the morbid change would of course exert an influence extending backwards in the order of the circulation, so that the Malpighian capillaries and the arteries which supply them would become gorged with blood. As a consequence of these changes a transudation of serum would result" And that something of the kind happens in Chronic Nephritis is extremely probable

Traite de Chim. Pathol. 1854 p. 190.

for it is found that the coats of the small arteries are considerably hypertrophied, evidently from being called upon to do increased work from some impediment to the circulation.

We now go on to notice the occurrence of albuminuria in certain fevers and other diseases, -

In a large percentage of cases of Pneumonia the urine is found to be albuminous. In fact in no other disease except perhaps Continued fever is this complication more common. We have a striking contrast in this respect also between the urine of Pneumonia and that of Bronchitis, Pleurisy & Chronic Phthisis, for in these diseases the albuminous complication is only of occasional occurrence. Looking at the proportion of cases, we notice that Feiger found the urine albuminous in 15 out of 33 cases; Becquerel in 9 out of 21; Parkes in 6 out of 13. We have then out of 67 cases, albuminuria in 30 or about 45 per cent. The particular stage of the disease at which it is liable to occur, seems to vary. Most observers had the idea

Archiv. für Pathol. Chem. NF 1852 p. 282.

that the appearance of the albumen was coincident with the resolution or absorption of the exudation, and that some of the exudation was got rid of in this way, but from statistics it appears that it is most common at or before the height of the disease. Out of the six cases related by Parkes 5 had the urine albuminous at the height of the disease or just before resolution commenced, in the other case it appeared during the stage of resolution. Heller found the albumen present during the time consolidation was advancing, when the chlorides are most deficient. Dr. Begbie has paid some attention to the matter, and has come to the conclusion that the presence of albumen bears a close relation to the so-called process of resolution in the lung. In one or two of his cases the albumen appeared before resolution began, but in the majority it was coincident with the commencement of that change, and the appearance of the large deposits of lithic acid and lithate of ammonia, which at that time generally make their appearance. Dr. Begbie has termed

it a Critical Albuminuria, as he considers it demonstrative of & coincident with a critical period in the disease.

In the urine of Bronchitis & Pleurisy, we have Solon, Walsh, Peghie and others noticing the occurrence of albumen, but, as these diseases are so often complications of or secondary to renal disease, it is not improbable that the kidneys might have been affected in the cases noted. As far as I have been able to look, there are none of the observations on the subject accurate enough to prove that albumen is present in the urine in simple uncomplicated cases of either disease. One circumstance apt to mislead in regard to Pleurisy, would be the use of blisters, which as we have seen produces albuminuria in a large number of cases.

In Phthisis the data about the matter are very contradictory, Pruzer having found albumen in 24 per cent of his cases and Parker in only 4 per cent.

In Diphtheria albuminuria is by no means uncommon. Lee found it in 50 per cent of his cases; Pouchot in 66 per cent;

Brit. & For. Med. Chir. Review Jan. 1860

Mon. Jour. of Med. Science 1854. p. 255.

Sanderson in all the cases he examined, Parker has also noted its occurrence. It was 7 or 8 years ago that Dr. Wade first called attention to the albuminous complication in this disease, and he along with Bouchut considered it a serious complication and significant either of the approach of Pyæmia, or of its suspending the function of the kidneys & producing symptoms of poisoning consequent upon retained excreta. Dr. Sanderson on the other hand considers it a symptom of no great moment and that in many cases it is coincident with amelioration of the patient's condition. From these observations it would appear probable, that the albuminuria is simply a result of the toxic condition of the blood, its occurrence being quite analogous to that which takes place in other morbid conditions of the blood seen in many diseases.

In Typhus & Enteric Typhus the urine is not infrequently found albuminous. In Typhus Dr. Sidney of this City noticed it "in a very large proportion" of his cases in the Royal Infirmary. Dr. Edwards in

14 cases examined before the 14th day, found albumen to be invariably present. In Dr. Sides's cases it always occurred about the critical period & generally lasted 4 or 5 days. In regard to Enteric Typhus Parkes found the albuminous impregnation in 7 out of 21 cases, in 5 of which the albumen had entirely disappeared before the patients left hospital, in the other cases it still remained. Pecquerel & Andral & others have also noticed albuminuria in this fever.

The next disease and practically the most important, in regard to the albuminous complication, is Scarlatina. The presence of albumen in the urine of certain cases of this affection has always been noticed, but it was not until a few years ago, from the researches of Dr. W. Begbie & others, that we became alive to the fact that in almost every case albumen was present in the urine for a certain time. The period of its occurrence seems to be after the first week and during desquamation, the albumen in general, being present only in sufficient quantity to render the urine "slightly coagulable."

The coagulability generally lasts a few days & after disappearing, does not recur. These characteristics are of importance as they contrast strikingly with the state of the urine in Scarlatinal Dropsy. On making a microscopical examination of the urine a good deal of renal epithelium is found, besides often deposits of urates & not unfrequently octahedral crystals of oxalate of Lime. The absence of tube casts serves to distinguish it from the urine of Scarlatinal Dropsy. Pathologists & physicians are not quite agreed as to the proximate cause of the albuminuria in this affection. All of course agree that it is a result of the specific action of the poison upon the kidneys, but whether this be direct or indirect is the question. The direct action may be caused by the condition of the blood, the result of the presence of the poison, or by a hypercemia of the kidneys caused by the passage through them of the poison, as it is eliminated from the body. Dr. Johnson holds the latter to be the correct explanation, but that this does not happen in every case, but only in those

instances in which, from exposure to cold the excretion of the poison has been diverted in its channel from the skin to the kidneys, the former of which he considers is the natural course for excretion of the poison under ordinary circumstances.

Those who disbelieve this view, hold that the albuminuria is a natural symptom of the disease, occurring during a desquamatory process in the kidney, and being just as common a symptom as the desquamation of the cuticle.

I must now conclude, although there are many other matters of interest that might have been touched upon, for instance the various questions which might be discussed about the albuminuria of Pregnancy. Before concluding however, the question very naturally presents itself, "What is the diagnostic value of albumen in the urine?" Many years ago such a question would have received a very different answer from what it does now, for at that time albumen in the urine was accounted a very serious symptom & probably pathognomonic of Bright's

Disease. Now we know that albumen may be present in the urine from such a variety of causes, that as a symptom per se it is of comparatively little value, but, taken in connection with other signs & certain symptoms, it forms a most valuable addition to our means of building up a diagnosis of certain diseases.

James Carmichael.