

Brannan (J. W.)

The Varying Significance of
Intermittent Albuminuria.

Report of Autopsy of a Case.

BY

JOHN WINTERS BRANNAN, M. D.,

Physician to Out-Patients, French Hospital; Assistant
in the Nervous Department of the Vanderbilt
Clinic, College of Physicians and Surgeons.

REPRINTED FROM

The New York Medical Journal

for July 4, 1891.



THE VARYING SIGNIFICANCE OF INTERMITTENT ALBUMINURIA.

*REPORT OF AUTOPSY OF A CASE.**

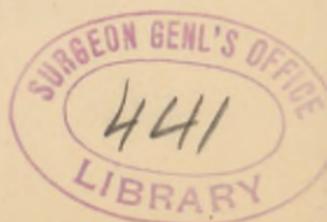
BY JOHN WINTERS BRANNAN, [✓]M. D.,

PHYSICIAN TO OUT-PATIENTS, FRENCH HOSPITAL;
ASSISTANT IN THE NERVOUS DEPARTMENT OF THE VANDERBILT CLINIC,
COLLEGE OF PHYSICIANS AND SURGEONS.

UNTIL within very recent years the presence of albumin in the urine, if at all constant, or recurring at short intervals, was taken to indicate structural change in the kidneys. In the year 1878 Leube (1) described what he called "physiological albuminuria," or albuminuria in healthy individuals. Other observers have confirmed his statements, so that now the presence of albumin in the urine of apparently healthy persons is a generally accepted fact.

What is the pathology of this condition? The answers to this question are various. This does not seem strange when we consider how varied are the theories advanced as to the pathological significance of true renal albuminuria. Even the physiology of the normal urinary secretion is still a matter of dispute. Senator (2) and T. Lang (3) have been

* Read before the Harvard Medical Society of New York City, May 2, 1891.



engaged for over a year past in a rather acrimonious controversy as to whether the fluid in the glomerulus of the kidney is a filtrate or a secretion. This may not seem a very important question, and yet upon its answer depends our conception of the nature of albuminuria. If the glomerular fluid is a filtrate, it contains albumin in the normal condition, like the other filtrates of the body, and it follows that albumin is a constituent of normal urine. If the fluid is a secretion, then the glomerulus must have the selective power common to all secreting glands, permitting certain substances to pass through its epithelium and retaining others. Without entering into a discussion of this vexed question, I will give a brief statement of the view now held by most pathologists. The epithelium of the glomerulus in the normal kidney secretes the urinary salts and water, but prevents the passage of albumin from the blood into the urine. If this epithelium suffers in any way in its nutrition, it no longer performs part of its function, and filtration of the albumin takes place. Senator (4) believes that in venous stasis albumin enters the urine through the tubules also, as the epithelium there is first affected by the increased pressure.

Such being the mechanism of the secretion of albumin, we have now to consider the general conditions which call this mechanism into play. The three factors in the production of albuminuria are :

1. Changes in the composition of the blood.
2. Changes in the blood-pressure or rate of flow.
3. Changes in the structure of the kidney.

1. *Changes in the Composition of the Blood.*—Semmla (5) is the chief exponent of the dyscrasic or hæmatogenic origin of Bright's disease. He holds that albuminuria is generally due to a dyscrasic condition of the albumins in the blood. Whenever these albumins become capable of dialysis they

are eliminated from the system by all the emunctories, but mainly by the kidneys. Such albuminuria is unaccompanied by histological alteration of the epithelium of the glomeruli. The passage of these diffusible albumins does, however, cause irritation in the kidneys and, if long continued, leads to the secretion also of serum albumin, and eventually to structural changes—nephritis. He shows that the chief cause of an excess of dialysable albumin in the blood is deficient activity in the functions of the skin. We have, then, as a sequence—1, deficient activity of the skin; 2, an excess of diffusible albumin in the blood, or hetero-albuminæmia; and 3, albuminuria, which, if allowed to continue for a certain length of time, sets up changes in the structure of the kidneys. Deficient action of the liver may also cause hetero-albuminæmia. Imperfect digestion of albuminous bodies in the alimentary canal may be followed by their absorption and excretion by the kidneys in the unchanged state. An excess of urea, or uric acid, or the oxalates, may lead to the presence of albumin* in the urine.

2. *Changes in the Blood-pressure or Rate of Flow.*—Albumin appears in the urine when there is diminution of arterial pressure or increased venous pressure leading to venous stasis. Increase of arterial pressure does not, as was formerly thought, cause albuminuria.

3. *Changes in the Structure of the Kidney.*—The structural change may affect either the epithelium of the glomeruli and tubules (Senator) or the blood-vessels of the kidney. As already stated, any disorder of nutrition of the epithelium will allow the albumin to pass through. Such disordered nutrition may be due to either of the causes already mentioned, a dyscrasic condition of the blood, or changes in the blood-pressure or its rate of flow.

I have thought it advisable to thus run over the various factors of pathological albuminuria, as it may help us in

appreciating the varieties of the intermittent or so-called functional form.

Intermittent or "Functional" Albuminuria.—One feature characterizes all the different kinds of albuminuria not obviously dependent on organic disease—namely, intermittency in the appearance of the albumin in the urine. But pathological albuminuria is also intermittent, especially in the most serious form, the granular kidney; hence this sign alone is not sufficient for a positive diagnosis. This will appear in one of my cases in which I was so fortunate as to obtain an autopsy. Many cases of intermittent albuminuria have several elements in their causation, and any classification must be more or less arbitrary. The following is, I think, sufficiently elastic to include at least the more common varieties:

Class I. Dyscrasic.	{	Hetero-albuminæmia.
		Digestive.
		Oxaluric.
		Hepatic.
		Gouty.
Class II. Mechanical.	{	Cyclical.
		Albuminuria of adolescents.
Class III. Neurotic.	{	Mental anxiety.
		Intellectual effort.
		Excessive physical fatigue.

1. *Dyscrasic.*—Under this general heading we may include the early stages (before structural disease has resulted) of all those dyscrasic conditions of the blood described by Semmola, especially hetero-albuminæmia. In some cases the digestive system seems to be at fault. There may be oxaluria with high density of urine and excess of urea accompanied at times with traces of albumin. Or there may be congestive enlargement of the liver with catarrh; there is stasis in the portal system, the skin is dry and jaundiced,

and some bile and albumin are found in the urine. All these phenomena are especially apt to be seen in gouty individuals.

Haig (6) attributes the high-tension pulse so often noted in these cases to an excess of uric acid in the blood due to deficient action of the skin. The albuminuria following a cold bath may be thus explained by the interference with the functional activity of the skin. Glycosuria also is often accompanied by albuminuria apparently secondary to it.

2. *Mechanical*.—Cyclical albuminuria probably belongs in this class, though some observers regard it as digestive in its origin. It has also been termed the albuminuria of adolescents, but it is not confined to any particular period of life. It is generally found in individuals with a weak circulation and a general lack of tone. Position is probably the most important factor. When the patient rises in the morning the circulation is weaker and the weight of blood resting on the renal veins is suddenly increased. Hence we get a condition of venous stasis, and albumin appears in the urine, usually from one to two hours after breakfast. If the patient is kept in bed until the afternoon, the albuminuria is postponed to that time. When he is up and about during the day, the albuminuria gradually ceases, because of the stimulating effect of exercise on the circulation. Herringham (7), who has made a careful study of a case of this kind, found that there was no constant relation between the absolute or relative amounts of urea and uric acid and the albuminuria. Diet had no effect whatever. Microscopically, there were no casts, but plenty of leucocytes and some oxalate crystals. Heubner (8), who has observed this affection in three sisters, states that even forced movements of the body, provided the patient remains in the recumbent position, do not cause the albuminuria. He associates it with the developmental period of the organism.

3. *Neurotic*.—In these cases there has usually been some strain of the nervous system—such as passing examinations, in which there is the combination of mental anxiety and intellectual effort. Sir Andrew Clark (9) has seen albuminuria repeatedly follow political speaking in an individual who at other times was entirely free from it. Excessive physical exercise may also be followed by traces of albumin in the urine. Both of these varieties of neurotic albuminuria are probably due to a weakened state of the renal vaso-motor centers, causing a slowing of the circulation in the kidneys with venous stasis. Of thirty-nine cases of “albuminuria without obvious disease,” observed by Dr. Goodhart (10), seventeen were in persons of a markedly neurotic temperament. One suffered much from headache and was “highly nervous”; another had had convulsions in childhood; two others had Graves’s disease; another was a case of general paralysis. Dr. Goodhart suggests that in such cases there may be a visceral flux, comparable to that which takes place about the surface of the head and neck and hands of the neurotic woman. Perhaps even the surface and deep parts suffer together under such circumstances. He thinks that such cases support the observations made by Dr. Allbutt some years ago, that the granular kidney seemed sometimes to owe its origin to, or date its existence from, some period of anxiety or worry. The temporary albuminuria of the neurotic may possibly furnish examples of the beginning of insidious changes in the kidney, which, if unchecked, may have a serious, even if remote, ending.

In the foregoing classification I have taken no account of “spurious” or “false” albuminuria, which originates in the urinary passages below the secreting surface of the kidney.

On studying the varieties of “functional” albuminuria

it is evident, I think, that they are due to the same general conditions that are active in the production of pathological albuminuria. The dyscrasic forms are all caused by changes in the composition of the blood. The mechanical form or cyclical albuminuria may be referred to changes in the blood-pressure in the kidneys. The neurotic forms may also be attributed to disturbances of the circulation in the kidneys. And, finally, all varieties of functional albuminuria, unless arrested, will ultimately result in changes of renal structure. Albuminuria is always pathological; the nutritive change in the glomerular epithelium may be slight or only temporary, but none the less it is not a normal process. It is not improbable that intermittent albuminuria may be due in some cases to small localized foci of nephritis. Lécorché and Talamon (11) believe it to be caused by a glomerulitis limited to a few glomeruli at a time.

The systematic testing of the urine in cases of proposed life insurance has had a considerable share in changing our views as to the nature of albuminuria. My own experience with intermittent albuminuria is almost entirely confined to cases of this character. In the course of the last seven years I have examined 365 persons, mostly males, for life insurance. Of this number, 54, or 14·8 per cent., had more or less albumin in their urine. This is probably a much larger percentage than would be found in the general population. The same fact has been noted in England, and Dr. Rabagliati (12) explains it by saying that the well-to-do who apply for life insurance suffer more from urinary diseases than the ordinary population, mainly because well-to-do people eat and drink too much. For the purposes of comparison, I examined, a few years ago, the urine of 100 consecutive male patients at the Roosevelt Hospital Outdoor Department. In not more than 5 per cent. did I find albumin without other symptoms of Bright's disease. I

have also recently looked over the histories of a number of private patients whom I had treated for minor ailments—such as lumbago, dyspepsia, lithæmic conditions, etc. There was a record of the examination of the urine in 35 cases, including men, women, and children, and in but two cases was albumin found.

One of the two cases was an old gentleman eighty years of age, who probably had some arterio-sclerosis of the kidney. The other case was a nervous lithæmic boy, in whose urine I at times found a trace of albumin, associated with crystals of uric acid and oxalate of calcium. His albuminuria may have been cyclic in character, but at that time my attention had not been called to this phenomenon.

The average age of the other thirty-three patients was but thirty-one years, which may account in a measure for the absence of albumin.

Returning to the fifty-four cases observed among applicants for life insurance, forty-nine were at the time thought to be cases of organic disease, and in five the albuminuria was attributed to a temporary derangement of function. The average age of the fifty-four cases was forty-four years. Of the forty-nine organic cases, thirty-five were called chronic nephritis, one subacute nephritis, four albuminuria associated with phthisis, three albuminuria dependent on glycosuria, and six persistent albuminuria of uncertain cause. The supposed "functional" cases I will give somewhat in detail:

CASE I.—Mr. B. W., banker, aged fifty-five, five feet ten inches and three quarters in height, and one hundred and fifty-three pounds in weight. He has always enjoyed good health, with the exception of an attack of gout in the big toe of the right foot fourteen years ago. His family history is excellent. His physical condition seemed perfect until I examined his urine, in which I found a trace of albumin by both the heat and nitric-

acid tests. The specific gravity was 1·018; there were no casts or epithelial cells. Taking into account his personal history in connection with the albuminuria, I made the diagnosis of gouty kidney. He protested that he had never had a symptom referable to any such disease, and thought that perhaps the albuminuria might be due to his habit of eating three raw eggs for breakfast every morning. I was rather skeptical as to the value of his suggestion (this was in July, 1885), but told him to give up his raw eggs and come and see me again in a few months. He returned in the following November, and his urine was free from albumin then and on several subsequent occasions when I tested it. He is still alive, and apparently in good health.

This case answers perfectly to Semmola's description of albuminuria following hetero-albuminæmia. The gouty taint present was undoubtedly an important factor in the imperfect digestion of the eggs. Whether the albumin in the urine was the unchanged egg albumin or serum albumin I have no means of deciding. At all events, the renal irritation had not apparently gone so far as to set up nephritis.

CASE II.—Mr. J. L., hat merchant, aged twenty-six, of fair physique. Personal and family history excellent. Examination of the urine showed about one fourth per cent. of albumin, the specific gravity was 1·022, and area and urates were in excess. Later tests gave no albumin, but a continuance of the high specific gravity and excess of urea. On the last examination albumin was absent, the specific gravity was 1·030, and quantitative analysis gave thirty-three grammes of urea in the twenty-four hours' urine.

This case also apparently belongs to the dyscrasic class of intermittent albuminuria. Whatever changes may have taken place in the glomeruli, it is probable, from the amount of urea, that the tubules of the kidney are in good condition.

CASE III.—H. D., ship-captain, aged thirty-nine, apparently in robust health. Family and personal history negative. A faint trace of albumin was found by both tests in the urine. The specific gravity was 1.020; there were no casts. He stated that he had had no sleep at all the night previous, being busily engaged in loading his ship. Subsequent examinations of the urine were negative.

CASE IV.—M. L., physician, twenty-nine years old, slender and of rather nervous temperament. Record perfect, except the death of his father from Bright's disease at sixty-one years of age. On examining the urine, I found a trace of albumin by the heat test only. The specific gravity was 1.022. He was much surprised when I informed him of the fact, as he had often examined his urine himself with negative result. He said that he had been doing a good deal of hard mental work recently, but was not conscious of any unusual fatigue. I made repeated tests afterward of the urine, but failed to discover any albumin. I therefore accepted the risk, though with considerable misgiving. This was in September, 1886, and he still appears to be in excellent health, in spite of incessant work in his profession.

Cases III and IV probably represent the neurotic type of transitory albuminuria. The pathology of this type is not very clear, and in this it may be said to prove its title to be classed with other neuroses.

My next case is more complete than those preceding, in that the clinical observation is supplemented by post-mortem examination.

CASE V.—Mr. J. T., commission merchant, aged forty-one, of unusually fine, healthy appearance. He was six feet in height, and weighed two hundred and three pounds. The family history was excellent. There had been no previous illness, nor were there any present symptoms of disease. Physical examination was negative. I examined his urine with great care, as he reported that albumin had once been found in it. Of eight specimens examined during a period of six months, seven were absolutely normal in every way, while in one there was a faint

trace of albumin, only evident on filtering the urine and by the heat test. The specific gravity varied from 1.018 to 1.024. At that time (the summer of 1886) I was not in the habit of measuring the amount of urea present in the twenty-four hours' urine, relying upon the specific gravity as an indication of the eliminative powers of the kidney. There were no casts of any kind. In November, 1886, this man committed suicide by morphine, after insuring his life in various companies for a very large amount.

The circumstances surrounding his death were such that a post-mortem was required, and, fortunately, it was made by an expert pathologist, Dr. W. W. Gannett, of Boston. The record of the autopsy is as follows: Body large, well developed, well nourished. Brain and heart normal. Lungs, liver, and kidneys all show excess of blood. Aorta showed in intima numerous opaque, yellow, elevated patches and calcareous plates.

Microscopic Examination.—Kidney: marked vascular injection of glomeruli. Epithelium of convoluted tubules contained a small amount of fat in minute but distinct drops. The glomerular capsules thickened by fibrous tissue in concentric layers. Here and there small areas of round-cell infiltration.

Diagnosis.—Venous engorgement of lungs, liver, and kidneys. Chronic aortic endarteritis. Slight degree of *chronic* nephritis.

In this last case we have a man apparently in perfect health and who probably would have lived for years. The slight albuminuria, only found after filtering the urine, might well have been called functional and attributed to deranged digestion or disturbed innervation or altered conditions of the blood. And yet the autopsy showed commencing nephritis as well as marked degeneration in the vascular system. None of the cases reported by the various writers have been under observation for more than a few years, and I have found no record of an autopsy in any case.

My own feeling with regard to intermittent albuminuria is, that the derangement of function will sooner or later end

in structural change in the kidney. This impression is strengthened by the observations of Lécorché and Talamon (13). As a result of their extended pathological investigations they state that Bright's disease, of whatever form, develops, as a rule, intermittently, by acute periods of inflammation interrupted by remissions more or less complete. The remission may last for years; the albuminuria may even entirely disappear—a fact to be explained by cicatrization of the lesions of the glomeruli and their complete atrophy.

Such cicatrization in the kidneys seems the more possible in view of the results obtained in recent years by careful post-mortem examination of the lung tissue in all hospital patients, without regard to the cause of death. It is now well established that about sixty-five per cent. of all cases give evidence of old inflammatory processes which have entirely healed, leaving only a fibrous cicatrix.

I will add, in closing, that when I have spoken of albumin I have included in the term both of the two chief proteids of the blood plasma—serum albumin and serum globulin. They are both present in all forms of albuminuria, though in varying proportions, and react alike to the usual chemical tests. It has been stated that functional albuminuria is characterized by the high proportion of serum globulin, but D. Noel Paton (14) has proved that such is not the fact.

In cases of albuminuria of doubtful origin I now habitually make a quantitative analysis of the amount of urea. If the individual is excreting from twenty to thirty grammes of urea daily, it is evident that the urinary *tubules* at least are not seriously affected.

References.

1. Virchow's *Archiv*, lxxii, p. 145.
2. *Wiener klin. Wochensch.*, 1890, iii, p. 591; also, 1891, iv, p. 282.

3. *Wiener klin. Wochensch.*, 1890, iii, p. 463 ; also, 1891, iv, Nos. 9, 10, and 12.
4. *Revue de médecine*, 1891, x, p. 68.
5. *Deutsche med. Wochensch.*, 1888, xiv, pp. 409, 434, 459.
6. *Brit. Med. Jour.*, 1890, i, p. 65.
7. *Brit. Med. Jour.*, 1891, i, p. 218.
8. *Centrbl. f. d. med. Wissensch.*, 1891, p. 177.
9. *Brit. Med. Jour.*, 1884, ii, p. 312.
10. *Brit. Med. Jour.*, 1890, i, p. 1121.
11. *Semaine médicale*, 1888, annexes, p. lxxiv.
12. *Brit. Med. Jour.*, 1889, ii, p. 422.
13. *Loc. cit.*
14. *Brit. Med. Jour.*, 1890, ii, p. 197.



REASONS WHY

Physicians Should Subscribe

FOR

The New York Medical Journal,

EDITED BY FRANK P. FOSTER, M. D.,³

Published by D. APPLETON & CO., 1, 3, & 5 Bond St.

1. **BECAUSE** : It is the *LEADING JOURNAL* of America, and contains more reading-matter than any other journal of its class.
2. **BECAUSE** : It is the exponent of the most advanced scientific medical thought.
3. **BECAUSE** : Its contributors are among the most learned medical men of this country.
4. **BECAUSE** : Its "Original Articles" are the results of scientific observation and research, and are of infinite practical value to the general practitioner.
5. **BECAUSE** : The "Reports on the Progress of Medicine," which are published from time to time, contain the most recent discoveries in the various departments of medicine, and are written by practitioners especially qualified for the purpose.
6. **BECAUSE** : The column devoted in each number to "Therapeutical Notes" contains a *résumé* of the practical application of the most recent therapeutic novelties.
7. **BECAUSE** : The Society Proceedings, of which each number contains one or more, are reports of the practical experience of prominent physicians who thus give to the profession the results of certain modes of treatment in given cases.
8. **BECAUSE** : The Editorial Columns are controlled only by the desire to promote the welfare, honor, and advancement of the science of medicine, as viewed from a standpoint looking to the best interests of the profession.
9. **BECAUSE** : Nothing is admitted to its columns that has not some bearing on medicine, or is not possessed of some practical value.
10. **BECAUSE** : It is published solely in the interests of medicine, and for the upholding of the elevated position occupied by the profession of America.

Subscription Price, \$5.00 per Annum. Volumes begin in January and July.

