Clinical lectures on albuminuria.

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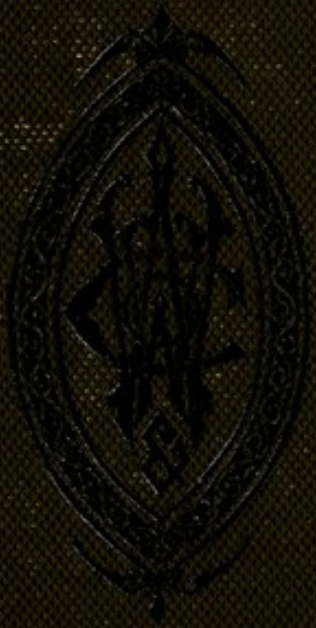

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Dr. Walter B. James

CLINICAL LECTURES

ON

ALBUMINURIA.

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ON

ALBUMINURIA.

BY

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NOTE.

THE Lectures comprised in the present series have been delivered at various times during the past two years, and several have been published in journals.

It has often been suggested that I should issue a third edition of my book upon "Bright's Diseases of the Kidneys," the second edition of which has now for many years been out of print. I have sought to embody in these Lectures the views which I entertain regarding the chief clinical questions discussed in that volume.

My thanks are due to numerous friends for help, and especially to Drs. Stevens and Gulland for aid in making the observations. Dr. Gulland has also revised the sheets and prepared the Index.

T. GRAINGER STEWART.

19 CHARLOTTE SQUARE,
EDINBURGH, *April*, *1888*.

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LECTURES ON ALBUMINURIA.

LECTURE I.

ON THE FORMS OF ALBUMEN MET WITH IN THE URINE, AND THEIR TESTS, QUALITATIVE AND QUANTITATIVE.

Introduction.

The Varieties of Albumen.—Serum Albumen.—Serum Globulin.—Peptone.—Propeptone or Hemialbumose.—Acid Albumen.—Alkali Albumen.—Hæmoglobin.—Fibrin.—Mucin.—Lardacein.—Composition of Albumen.

Tests for Albumen.—Heat.—Cold Nitric Acid.—Metaphosphoric Acid.—Acidulated Brine.—Picric Acid.—Potassio-Mercuric Iodide.—Potassium Ferrocyanide.—Dilution with Water.—Magnesium Sulphate.—Fehling's Solution.—Randolph's Test.

Comparative Delicacy of Tests for Serum Albumen.—Heat.—Cold Nitric Acid.—Metaphosphoric Acid.—Picric Acid.—Potassio-Mercuric Iodide.—Ferrocyanide of Potassium.

Quantitative Analysis of Albumen.—Separation, Drying, Weighing—Esbach's Method.—Roberts's Method.—Oliver's Percentage Method.

GENTLEMEN,—In commencing a series of lectures on albuminuria as a symptom, it is necessary first to go over some ground familiar to many of you, for I must indicate the various albuminous substances met with in the urine. I purpose in the present lecture to enumerate these, and briefly describe the source and nature of each, and then discuss the value of the different tests by which they may be discovered. In doing so I shall give you the results of a

careful and prolonged inquiry which, along with Dr. Stevens, I have made as to the comparative delicacy of the leading tests for serum albumen, and as to the value of the different methods of quantitative analysis by which the amount of albumen may be determined. In the urine we may meet with the following proteids, or bodies closely related to them.

I. *Serum Albumen*, a substance which, according to Hammarsten,[1] constitutes 4·516 per cent. of the blood serum. It is almost constantly present in urine which contains any variety of albumen. Although a less diffusible body than serum globulin, it is capable of passing through membrane.

II. *Serum Globulin or Paraglobulin*, the globulin of the blood serum, of which it constitutes 3·103 per cent.[1] It is met with in almost all albuminous urines, its proportion to the serum albumen varying in different instances.

III. *Peptone*, a product of gastric and pancreatic digestion of albuminous substances, also occurring in the process of transformation of tissues and of inflammatory effusions. It is a readily diffusible substance, occasionally met with in the urine in association with and probably apart from serum albumen.

IV. *Propeptone, Albumoses, or Globuloses*, a group of substances intermediate between proteids and peptone, constituting stages of transformation from the one to the other. They are highly diffusible, and many varieties may be met with in the urine. One of them is the peculiar form of albumen which was discovered by Dr. Bence Jones[2] in the urine of a patient suffering from osteomalacia.

V. *Acid Albumen or Syntonin*, one of the derived proteids obtained by the action of acids upon albumen. It is easily produced artificially by the addition of acid to albuminous urine, but may occur naturally in certain cases.

VI. *Alkali Albumen*, another derived proteid, produced by the action of alkalies upon albumen. It may be readily artificially prepared, but also occurs in the urine.

VII. *Hæmoglobin*, the combination of hæmatin and globulin naturally existing in the red corpuscles of the blood. It sometimes appears in the urine, particularly in cases of hæmaturia and hæmoglobinuria; also in certain septic conditions, after inhalation of arseniuretted hydrogen, transfusion of blood, and under other conditions.

VIII. *Fibrin*, a proteid substance which does not normally exist as such in the blood. It is met with in the urine in hæmaturia, in some cases of chyluria, and in certain varieties of renal casts.

IX. *Mucin*, the chief constituent of mucus, is a derived proteid substance, not an albumen but an albuminoid. As mucus is secreted from the urinary tract in greater or less quantity, it becomes superadded to the urine after its secretion in the kidney.

X. *Lardacein, Waxy or Amyloid Material*, familiarly known as a pathological substance within the body, is said to be occasionally demonstrable in renal casts.

Of these ten varieties, the last four are evidently of little practical importance—mucin alone being indeed worthy of special comment, and that mainly because of the difficulties which its presence raises in regard to the reliability of certain tests for serum albumen.

As to the composition of the various albuminous substances, it is scarcely necessary that I should say anything, but I may quote the statement of Hoppe-Seyler,[3] that their percentage composition varies from

C 51·5 H 6·9 N 15·2 S 0·3 O 20·9 to
C 54·5 H 7·3 N 17·0 S 2·0 O 23·5

The Tests for the Albumens.—I have put in tabular form the chief tests for the different varieties of albumen, with their actions upon each variety.

TABLE I.—SHOWING TESTS FOR THE CHIEF FORMS OF ALBUMEN.

	Serum Albumen.	Serum Globulin.	Peptones.	Propeptones, &c.	Acid Albumen.	Alkali Albumen.
Heat, . .	Opacity.	Opacity.	0	0	0	0
Heat with HNO_3.	Opacity.	Opacity.	0	0	0	Opacity.
Heat with $\bar{A}$	Opacity.	Opacity.	0	0	0	Opacity.
Cold HNO_3, .	Opacity.	Opacity.	0	Opacity dissolved by heat.	Opacity.	Opacity.
Metaphosphoric acid.	Opacity.	Opacity.	Opacity diminished or dissolved by heat.	Opacity diminished or dissolved by heat.	0	Opacity.
Acidulated brine.	Opacity.	Opacity.	Opacity diminished or dissolved by heat.	Opacity diminished or dissolved by heat.	Opacity.	Opacity.
Picric acid, .	Opacity.	Opacity.	Opacity dissolved by heat.	Opacity dissolved by heat.	Opacity.	Opacity.
Potassio-mercuric iodide.	Opacity.	Opacity.	Opacity dissolved by heat.	Opacity dissolved by heat.	Opacity.	Opacity.
Potassium Ferrocyanide with $\bar{A}$.	Opacity.	Opacity.	0	Opacity dissolved by heat.	Opacity.	Opacity.
Ammonium sulphate.	Opacity.	Opacity.	0	Opacity.	Opacity.	Opacity.
Dilution with water.	0	Slight opacity.	0	0	0	0
Magnesium sulphate.	0	Opacity.	0	0	Opacity.	Opacity.
Fehling's solution.	Brownish-red or mauve.	...	Rose pink or purple.	Rose pink or purple.	...	...
Randolph's test,	...	...	Yellow opacity.	Yellow opacity.	...	...

The oldest test for albumen depends upon *its coagulability by heat.* Heat coagulates the serum albumen (opalescence occurring at 140° Fah., coagulation at 162° to 167°), and also the serum globulin (opalescence occurring at 154° Fah., coagulation at 167°); has no effect upon the peptones or

propeptones, nor upon acid or alkali albumen, unless an alkali or acid has first been added. It, however, produces cloudiness with earthy phosphates, by driving off carbonic acid, which holds them in solution, but the further addition of nitric acid, by redissolving them, clears up the opacity. A preliminary acidulation with acetic or nitric acid prevents this cloudiness, but may convert albumen into acid albumen, and so make the test fail. But, on the whole, if cautiously employed, heat gives satisfactory results. A further security may be obtained by using both acetic acid, and a concentrated solution of magnesium sulphate, or of sodic sulphate, or of common salt, for these prevent the undue action of the acid upon the albumen.

The *Cold Nitric Acid Test* ranks next in date of introduction and in general popularity to that by heat. When a layer of nitric acid is brought into contact with a layer of albuminous urine, a white coagulum is formed at the line of junction of the fluids. The acid coagulates serum albumen and serum globulin ; has no effect upon peptones ; gives an opacity with propeptones, which, however, disappears with heat ; has no effect upon acid albumen, but gives distinct reaction with alkali albumen. One or two sources of fallacy must be kept in view when one employs this test. It may give an opacity with urates (but it dissolves with heat), with urea (but it occurs only in concentrated urines, and shows a crystalline arrangement), or with resinous substances.

Metaphosphoric Acid is an excellent test for albumen, but as it is only serviceable when pure, and difficult to keep in that condition, it has not come into general use.

Acidulated Brine is also a test of considerable value, acting upon all varieties of albumen, but it is not likely to become greatly trusted, because of its frequently giving some reaction with normal urine.

Picric Acid is a test which has been brought into use in

this country mainly by the recommendation of Dr. George Johnson.[4] It produces an opacity with all the forms of albumen; but while those with serum albumen, serum globulin, acid and alkali albumen persist or become more distinct with heat, those with peptone and propeptone dissolve. It must be remembered, also, that alkaloids, such as quinine, give a cloud with this reagent, but one which rapidly disappears on heating. On the whole, I believe this to be the most reliable and delicate test which we at present possess.

It has been objected to this test, that it precipitates mucin as well as serum albumen, and that this is a source of fallacy, particularly when it is used by the contact method. As this question appeared to me important, I have taken a good deal of pains to satisfy myself regarding it. By the kind permission of Dr. Sinclair, I examined, along with Dr. Stevens and Dr. Boddie, the urine of a number of inmates of Craiglockhart Poorhouse, in whom previous examination had shown that minute traces of albumen were frequently present, and in which, as in most urines, mucin was also to be found. My object was to see how far the reactions of the characteristic tests for mucin corresponded to, and how far they differed from those of picric acid. The specimens, fifty-four in number, derived from twenty-seven individuals, were tested with nitric acid, picric acid, a solution of citric acid of specific gravity 1005, and the solution of citric and picric acids together used in Esbach's method for determining the quantity of albumen. The contact method was adopted in all cases as being the most delicate. The nitric acid was used in order to show when albumen was present in considerable quantity; the picric acid to discover minute traces of albumen, and with the special view of watching for the reaction with mucin; the citric acid as the best test for mucin; and the combined citric and picric acids

for the purpose of comparison with the reactions obtained with the other tests. Of the fifty-four specimens, twelve showed a reaction with nitric acid, thirty-four with picric, thirty-eight with citric, and forty-one with Esbach's combined solution. The most important fact which we ascertained was that, while a large number of the specimens gave distinct reactions both with picric and citric acids, there were three which gave an opalescence with picric and not with citric, and seven of those which reacted with citric acid gave no reaction with picric. From these facts we conclude that mucin may be demonstrated by citric acid when no reaction is produced with picric, and that picric may show minute quantities of albumen in urines in which citric acid fails to show mucin.

But, on the other hand, picric acid often produces an opalescence in urine apparently free from albumen, and Dr. Stevens made a series of careful experiments with the view of getting at an explanation of this fact. He selected a urine which gave a faint and slowly developed reaction with picric acid, and a distinct opacity with citric acid. Having coagulated its mucin by means of citric acid and filtered off the coagulum, he found that the urine no longer gave any reaction with picric acid. Again, to another specimen of the same urine he added picric acid and then filtered off the precipitate; he found that the urine then gave either no reaction, or a very slight one, with citric acid. These experiments seem to indicate that picric acid does act upon mucin, although more slowly and in a less degree than citric acid. I suspect that the degree of acidity of the urine is an important element in relation to this reaction with picric acid; that where acid is present in quantity the opalescence is distinct, where it is in slight amount it is comparatively or completely absent.

On the whole, we seem to be warranted in believing that although picric acid often affects mucin, it does not do so in such a way as to render it unreliable as a delicate test for

albumen. Its precipitate with mucin is, even when applied by the contact method, a slight, slowly developed haze. A precipitate indicating albumen is more marked and more quickly produced. A little practice in the use of the test will soon render you familiar with the degree and rate of formation of the opacity which indicate albumen as distinguished from those which mark the presence of mucin.

Potassio-Mercuric Iodide, which was first proposed as a test by M. Tanret,[5] corresponds in its action to picric acid, giving opacity with serum albumen, globulin, acid and alkali albumen, and an opacity dissolved by heat with peptone and propeptone. But it will be found to give a reaction with a very large proportion of normal urines, and as the addition of an organic acid—citric or acetic—is required to bring out the reaction, it is clear that mucin must, in many cases give a degree of opalescence. It may be that other sources of fallacy exist in regard to these slighter reactions. It is true that Dr. Oliver's[6] method of applying this test greatly reduces the chances of error, but it has disadvantages which render it, in my opinion, inferior to picric acid.

Potassium Ferrocyanide, first suggested by Dr. Pavy,[7] also resembles picric acid in its action, except that it does not give any indication with peptones. The objections to the reagent last described apply equally to this.

Ammonium Sulphate has been shown by J. Wenz[8] to be a valuable test for proteids, for it precipitates all of them, excepting the peptones, and Halliburton[9] recommends it highly as a test of special value.

Dilution with Water is a convenient but not very reliable test of the presence of serum globulin, as it produces a milkiness, that substance being soluble in weak saline solutions, but not in pure water or extremely dilute saline solutions. It produces no effect upon other forms of albumen.

Magnesium Sulphate is a valuable test for serum globulin,

as it produces with that substance a milky opacity, which speedily deposits as a precipitate. It has no action upon serum albumen, peptone or propeptone, but produces an opacity with acid and alkali albumen. It is best used in saturated solution by the contact method. By using it also, according to methods described in works dealing with the subject of physiological chemistry, the globulin may be separated nearly pure, and its amount determined.

Fehling's Solution, or other alkaline solution of copper, is a most convenient test for peptone and propeptone, giving with these a rose pink or purple colour at the point of contact of the solution with the supernatant urine, and producing no effect upon the others, with the exception of serum albumen, with which it sometimes gives a brownish-red hue. With all albumoses in solution a pink colour is obtained with a solution containing a trace of copper sulphates and an excess of potash. This is known as the Biuret reaction.

Randolph's Test[10] for peptone and propeptone, which consists in the addition of one drop of saturated solution of iodide of potassium and then of two drops of Millon's reagent (an acid solution of nitrate of mercury) to a drachm of urine, gives a yellow instead of a red precipitate when these substances are present; but, as Dr. Oliver[11] has pointed out, it gives the same colour reaction with bile salts, which are frequently present in considerable amount in the urine. Therefore we cannot esteem it so highly as the copper and alkali test.

Although you are probably familiar with the general outline of the facts I have thus brought before you, I have thought it well to draw them up in a tabular form, and to make these comments upon them. I shall only add, that the presence of hæmoglobin may be detected by the guaiac test; and its derivations, such as methæmoglobin, by the spectroscope: that the presence of fibrin may be ascertained

by its decomposing hydrogen peroxide with effervescence; that mucin may be discovered by means of citric or acetic acid; and that waxy material may be shown (if it is ever present) by iodine, iodine and sulphuric acid, or by methyl-aniline violet.

I shall now show you the results of the investigation which we made with the view of determining the comparative delicacy of the chief tests for serum albumen. The method which we adopted was to take an albuminous urine, determine the proportion of albumen by Esbach's tubes, dilute it by successive additions of normal urine, and note the point at which each test failed to give its characteristic reaction. I wish you to observe that we employed normal urine as our diluting fluid, as we found that the substitution of water produced a misleading result. Indeed, I was led into error by this circumstance in a series of observations which I made a number of years ago—cold nitric acid giving a much better result with water than it would have done with healthy urine.

TABLE II.—SHOWING THE COMPARATIVE DELICACY OF TESTS FOR SERUM ALBUMEN.

Tests.	Dilutions.	Percentage.	Grains per Ounce.
Boiling, . .	300	0·0005	0·00218
Acidulation with acetic acid, and boiling.	500	0·0003	0·001311
Cold nitric acid, .	50	0·003	0·01311
Metaphosphoric acid.	500	0·0003	0·001311
Picric acid,. .	1000	0·00015	0·000655
Potassio-mercuric iodide (Test papers).	500	0·0003	0.001311
Ferrocyanide of potassium.	500	0·0003	0·001311

In Table II. I show you the results. In parallel columns I have represented the effects of each of the tests ; showing in the first the dilution up to which the action of each reagent remained distinct, in the second the percentage of albumen as calculated from the total quantity in the undiluted fluid and the number of dilutions, and in the third the grains or part of a grain per ounce as calculated from the same data.

The urine with which we worked contained albumen to the amount of 1·5 grammes per litre, which is equal to 0·15 per cent., or 0·655 of a grain per ounce.

Our results show that the *boiling test*, carefully applied, is an excellent one, revealing the presence of so little as 0·00218 of a grain per ounce, and continuing to show up to the 300th dilution of our standard specimen. But heat, with preliminary acidification with a little acetic acid, was still more delicate, showing 0·001311 of a grain per ounce, and giving a perceptible haziness up to 500 dilutions.

The *Cold Nitric Acid Test* falls far short of this in delicacy, for we found that it does not give distinct reaction beyond the 50th dilution, and therefore shows only with 0·01311 of a grain per ounce. It is true that if the specimen is allowed to stand, the reaction may gradually manifest itself, with more minute traces of albumen : but this is inconvenient, and for practical use tests are to be valued in proportion to their rapidity of action.

Metaphosphoric Acid gave the same results as heating after acidulation with acetic acid, giving opalescence up to the 500th dilution of our standard urine, and showing 0·001311 of a grain per ounce.

Picric Acid proved the most delicate test, giving a faint but perceptible reaction up to the 1000th dilution of our standard specimen, which is equal to 0·00015 per cent., or 0·000655 of a grain per ounce.

The *Potassio-mercuric Iodide* and the *Ferrocyanide of Potassium Tests* gave the same results as metaphosphoric acid, showing albumen up to the 500th dilution of our standard specimen, equal to 0·001311 of a grain per ounce.

From these and other observations I am led to conclude that picric acid is the most delicate of all the reagents which we possess for albumen, and that next to it rank the potassio-mercuric iodide, the heating after acidulation with acetic acid, the ferrocyanide of potassium, and the metaphosphoric acid. Boiling and adding nitric acid is less delicate, and still less so is the cold nitric acid test.

But delicacy is not the only quality required of a test. Indeed, a test may be too delicate for clinical purposes. And again tests otherwise suitable may be practically inconvenient. Nitric acid is difficult to carry about, and picric acid presents a similar disadvantage, although in a minor degree. The test pellets devised by Dr. Pavy[12] of London, and the test papers of Dr. Oliver[13] of Harrogate, are extremely convenient, being easily carried about, and very delicate. But it may be held that they are too delicate, for few urines fail to show some reaction with them. Indeed, you will find that many of them, as I have told you (and the same is true of tungstate of soda), show some reaction with practically normal urines. The smallest quantity of mucin, or a quite infinitesimal trace of albumen proper, may suffice to produce the reaction. Therefore, I should advise you to learn to use the tests with discrimination, and not to attach much importance to their fainter indications, and always remember that albuminuria is rarely a serious condition unless it is sufficiently pronounced to be made out by the cold nitric acid test.

The last point to which I shall direct your attention to-day is the results we have obtained by a series of experiments comparing the methods most used for determining the quantity of albumen in any given sample of urine. A rough plan often adopted is to boil, then add a little nitric acid, set the test tube aside for twenty-four hours, and then note the proportion of the coagulum to the whole height of the column. This may be useful in determining the progress of a case day by day, but is of no scientific value. We have carefully compared the results obtained in this way with the ingenious plan suggested by Dr. Oliver for bringing out the result without waiting twenty-four hours. This is known as Dr. Oliver's fractional method.[14] He uses a graduated tube, a paper ruled with dark lines, and his mercuric iodide or potassium ferrocyanide test papers. The graduation on the tube is so marked as to correspond with the fractions of a column in an ordinary test tube. The test papers are put into the tube along with 60 minims of water, and urine added until it is no longer possible (on account of the increasing opacity of the fluid) to make out the lines behind; the mark reached by the urine is intended to correspond to the fraction which would have settled at the end of twenty-four hours. Now we found that Dr. Oliver has hit this very correctly, for when our coagula stood in the test tubes at one-fourth to one-third, we found that we got by Dr. Oliver's fractional method an almost identical result. But this is only of service for comparison of the progress of a case day by day, and in good clinical work we have to aim at something more definite.

Various plans have been suggested for giving more accurate results. Those which we tested were coagulating, drying, and weighing, and the methods of Esbach, Roberts, and Oliver, applying each to samples of the same urine.

I. *The Separation, Drying, and Weighing of the Albumen.*

—This, which is the fundamental and best method for ascertaining the amount of albumen, is somewhat difficult, and requires considerable time for its performance. It is much too laborious to be freely used as a clinical method. One has to acidulate the urine slightly with acetic acid, then place it in a water bath at a temperature of 100° C., stirring frequently, so as to prevent the formation of bulky clots. The coagulated albumen is then allowed to settle, carefully separated from the fluid, and placed upon a filter previously weighed. It is then put into a hot air bath and slowly dried. After cooling it is weighed, then again put into the hot air bath, and the process is repeated until the filter ceases to lose weight. Thereby the amount of albumen is accurately determined. In the urine which we used we found 3·84207 grains in the cubic centimetre, equivalent to 1·0911 grains per ounce.

II. *Esbach's Method.*[15]—This plan requires certain special tubes, graduated so as to show the height to which the urine to be tested, and that to which the reagent (a solution of picric and citric acids) should reach, also the number or proportion of grammes of albumen per litre. The urine (diluted with water until the specific gravity is not above 1010, and acidulated with acetic acid if necessary) is filled up to the level indicated by the letter U, then the test fluid to the line marked R, and the fluids, having been thoroughly mixed, are set aside to stand for twenty-four hours. At the end of that time the level reached by the coagulum enables us to read off the grammes per litre. Our observations brought out a result, as is seen in the table, of 2·5 grammes per litre, which is equivalent to 0·25 per cent., or 1·0837 grains per ounce. It thus very closely corresponded to the results obtained by the first method.

III. *Sir William Roberts's Dilution Process.*[16]—In this plan nitric acid is used by the contact method. The urine

is diluted with water until it is found that the opacity begins to appear between thirty and forty-five seconds after the fluids have come together. Each dilution, with an equal quantity of water, represents what he terms one degree of albumen, and he finds that each degree corresponds to 0·0034 per cent., or 0·0148 of a grain per ounce. By this method we found 175 degrees, which corresponds to 2·5 grains per ounce. Careful repetitions of the experiment confirmed this result.

IV. *Dr. Oliver's Percentage Method.*[17]—This method consists essentially in coagulating the albumen in urine by the mercuric iodide, or the ferrocyanide of potassium test papers, and diluting until it reaches an opacity exactly corresponding to that of a standard fluid enclosed in a tube. Both tubes are flattened, and are held in front of a white card ruled with black lines, and it is easy to decide when the lines are seen with equal indistinctness through the two tubes. The standard fluid is arranged so as to correspond to the opacity produced by 0·1 per cent. of albumen when precipitated by the mercuric or the ferrocyanic test papers. Fifty minims of the urine (undiluted or diluted) are put in the flattened test tube, reagent papers are dropped in, and the contents are shaken up. The card is then placed behind the two tubes, and their opacities are compared. If the urine being tested is more opaque, water is added until the opacity of the standard is reached. The percentage of albumen is calculated by multiplying 0·1 by the number of times the volume of the urine (50 minims) has been increased by dilution. On applying this method to the urine which we investigated, we found 0·64 per cent. of albumen, which corresponds to 2·8 grains per ounce.

I have put the results in tabular form so as to permit of ready comparison. It is, of course, understood that the same urine was employed in each observation.

TABLE III.—SHOWING THE RESULTS OBTAINED BY DIFFERENT METHODS FOR QUANTITATIVE ANALYSIS OF ALBUMEN.

		Grains per Ounce.
I. Drying and weighing.	3·84207 grains in 100 cc.	1·0911
II. Esbach's method,	2·5 grammes per litre; 0·25 per cent.	1·08375
III. Roberts' method,	175 degrees.	2·5
IV. Oliver's percentage method.	0·64 per cent.	2·8

From our observations, it appears that Esbach's method brings out results closely corresponding to those obtained by the elaborate drying and weighing process, and I am glad to know that Dr. George Johnson's observations[18] have led him to the same conclusion. As the method is easily worked, as well as so reliable, it is certainly the one which I advise you to adopt, and make yourselves familiar with. Its only disadvantages are that one must wait twenty-four hours before the result can be obtained, and that it does not enable us to measure less than 0·5 grammes per litre. The methods of Roberts and Oliver have given, in our hands, results closely corresponding to one another, but considerably different from those obtained by separating, drying, and weighing; and, therefore, although they give their results at once, I cannot so heartily commend them to you.

LECTURE II.

ON THE INCIDENCE OF ALBUMINURIA AMONG THE PRESUMABLY HEALTHY.

Introduction.—Contrariety of Opinions.—Questions to be discussed.—Is Albumen a Natural Constituent of Urine?—Proportion of presumably Healthy People showing Albumen.—Method of Testing.—General Result.—Distinction between Soldiers and Civil Population.—Between Children and Old People.—Condition in New-born Infants.—Results of Insurance Experience.—Effects of Diet, of Muscular Exercise, of Severe Exertion, of Playing Wind Instruments, of Cold Bathing, of Mental Excitement.—Incidence of Peptonuria.—Conclusions.

GENTLEMEN,—I shall devote this lecture to the discussion of the question of the incidence of albuminuria among the presumably healthy. It is one which you will often find of great practical importance, in relation to diagnosis and prognosis, in the course of your ordinary work, as well as in questions of life insurance.

Great diversity of opinion exists as to the frequency of the occurrence of albuminuria in healthy people, and elaborate inquiries have led different observers to conspicuously contradictory conclusions. Posner[19] has said that his observations satisfy him that traces of albumen exist in every normal urine, and may be demonstrated if sufficiently delicate methods are employed. One of the most distinguished authorities on the subject, Dr. Senator of Berlin, says that his observations supply good reason why he "should consider it not improbable that, if we were to examine the urine for long periods at different

hours of the day, and with great care, we should sooner or later find it to contain albumen in the case of every healthy man."[20] Dr. Kleudgen,[21] in the course of a special study of albuminuria in relation to epilepsy, came to the conclusion that traces of albumen could be demonstrated in any urine above a certain degree of concentration. Dr. de la Celle de Chateaubourg[22] found albumen in the urine of 592 out of 701 healthy people whom he examined; that is, in 84 per cent. Dr. Capitan[23] found that among 98 French soldiers 44, or 44·9 per cent., had albuminuria. Professor Leube,[24] on the other hand, found among 119 German soldiers whom he examined, that only 4 per cent. showed albumen on rising in the morning, and 16 per cent. in the forenoon after a march of several hours' duration. Dr. Van Noorden[25] states that he found it vary under different conditions among healthy German soldiers from 3 to 35 per cent. Dr. Munn[26] found albuminuria in 24 out of 220—that is, in 10·9 per cent.—presumably healthy people examined for life insurance in the United States of America. And Dr. Leroux[27] found it only 19 times among 330 children, or in 5·76 per cent.

Such contrariety of results made me think it desirable to make a fresh series of observations upon this point, with the view of determining, *first*, whether Posner is right in saying that albumen is present in every urine; *second*, what proportion of presumably healthy people have albumen in the urine in quantity sufficient for demonstration by the tests ordinarily in use; and *third*, what effects various physiological conditions, such as diet, exercise, severe exertion, and cold bathing, produced upon the discharge.

I have, with the aid of Dr. Stevens, made some experiments with the view of determining the first of these questions, and have tried to repeat Posner's observations. I do not feel sure that our results were absolutely satisfactory, but the conclusion

to which I am led in the meantime is, that albumen, if present at all in normal urine, is in such extremely minute amount as to be barely discernible, or not discoverable at all with the most delicate tests, even after considerable concentration ; and that, at least in some of the cases in which minute traces occur, it is accounted for not by transudation with the urine but by the after-addition of epithelial and other cellular elements from the urinary passages.

With the view of obtaining evidence as to the second question—that is, the proportion of presumably healthy people who have albumen in their urine in quantity sufficient for demonstration by the tests ordinarily in use,—I have examined, with the assistance of Drs. Stevens and Boddie, several series of presumably healthy individuals. By the kindness of Dr. Mills and Dr. Fayrer, medical officers of Edinburgh Castle, and of the Colonel and Adjutant of the Seaforth Highlanders, I was enabled to examine a series of 205 soldiers and applicants for admission to the army. I also got specimens of urine from 100 healthy male adults engaged in civil employments. By the kindness of Dr. Sinclair and his resident assistant Dr. Helme, I examined 150 (100 being men about or above 60, and 50 children), healthy inmates of Craiglockhart Poorhouse ; and by the kindness of Dr. Halliday Douglas and Mr. Munro, I had opportunity of examining the urine of a large number of the inmates of the Orphan Hospital. We had thus in all 505 presumably healthy individuals, with regard to whose urine we made the most careful examination, sometimes on one, sometimes on several occasions.

The plan of testing adopted was in all cases the same. Urines which were cloudy from any cause were carefully filtered. Those which were clear were tested as passed. Each specimen was tested first with nitric acid by the contact method, by which, as previous experiment had shown, we

could discover albumen in the proportion of 0·003 per cent., or 0·01311 of a grain per ounce; and by picric acid, using the contact method, by which we could discover albumen in the proportion of 0·00015 per cent., or 0·0006555 of a grain per ounce. Each specimen was also carefully tested for peptones, using Fehling's solution by the contact method, a plan which certainly shows the presence of peptones very distinctly when they are added to urine, and is regarded a reliable test in cases of peptonuria.

Taking specimens of urine passed by 505 presumably healthy individuals, during the forenoon or about midday, we found that albumen was present in 166, or a little over 32·8 per cent. Of these it was in quantity sufficient to be discovered by the cold nitric acid test in 76, or 15·5 per cent. In Table IV. the general results are shown—

TABLE IV.—SHOWING INCIDENCE OF ALBUMINURIA IN 505 PRESUMABLY HEALTHY INDIVIDUALS (FORENOON OR NOON SPECIMENS).

Urines Examined.	Albumen shown by HNO_3.	Albumen shown by Picric Acid.	Total.	Per cent.
505	76	90	166	32·8

But it was evident that a marked difference existed between various groups of individuals examined, as between soldiers and men of corresponding age following civil occupations, and between children and men about or above sixty years old. It is therefore necessary to consider these groups separately. Among the soldiers and recruits examined, 205 in number, 77, or 37·56 per cent., had albuminuria; while of 100 adults in civil employments, 10 showed the symptom. Of the former group it was shown by nitric acid in 47, or 22·92 per cent.; by picric acid only in 30, or 14·63 per cent. Of the latter group it was shown by nitric acid in 7, or 7 per cent.; by picric acid only in 3, or 3 per cent. Table V. shows these results—

TABLE V.—SHOWING THE INCIDENCE OF ALBUMINURIA IN SOLDIERS AND CIVIL POPULATION.

	With HNO_3.	With Picric Acid only.	Total.	Per cent.
Soldiers, . . 205	47	30	77	37·56
Civil Population, . . . 100	7	3	10	10

In seeking to compare the facts in the case of children and old people, I thought it desirable to get access to individuals in similar position in life, and living under somewhat similar conditions, and I was glad to avail myself of the opportunity afforded of examining the inmates of Craiglockhart Poorhouse and the Orphan Hospital. We got specimens of the urine of 100 men, about or above sixty years of age, resident in the poorhouse, but not on the sick list. I found that albumen was present in 62 of them. We also examined a series of 100 healthy children of various ages, and found that it was present in 17. Nitric acid showed it in 17 of the old men, picric acid in other 45; while in the children, nitric acid showed it in 5, and picric acid in other 12.

When these results are shown in a tabular form, we see at a glance how striking is the contrast between the two groups.

TABLE VI.—SHOWING INCIDENCE OF ALBUMINURIA IN 100 CHILDREN, INMATES OF CRAIGLOCKHART POORHOUSE, AND 50 OF THE ORPHAN HOSPITAL, AND 100 OLD PEOPLE (ALL PRESUMABLY HEALTHY), INMATES OF CRAIGLOCKHART POORHOUSE.

	With HNO_3.	With Picric Acid.	Total.	Per cent.
Children, . .	5	12	17	17
People about or above sixty, .	17	45	62	62

It thus appears that of the four groups the old men in the poorhouse showed albuminuria most frequently, the soldiers next, the children in the poorhouse next, and the least frequently affected were the young men engaged in civil occupations.

As it has been asserted that the urine of newly born children is always albuminous, we obtained specimens from twelve infants in the Maternity and Simpson Memorial Hospital, and found that two showed albumen with nitric acid, and three showed a very faint trace with picric acid. Our results indicate that albuminuria is not universal, but that traces are not unfrequently present during the first days of life.

It was not in my power to determine the cause of the albuminuria in the persons examined, but I took care to exclude cases due to accidental contamination with pus, and in only four cases had I any reason to think that I might have admitted such—viz., two soldiers and two of the old men. In none of the cases was the albuminuria due to cardiac or pulmonary diseases, and in very few was there occasion to suspect the existence of Bright's disease. On the other hand, there were few cases whose clinical history corresponded to Pavy's cyclical albuminuria or Moxon's albuminuria of adolescents.

Being anxious to supplement these observations, I asked two of my former assistants, who are well known to me as careful and accurate observers, Dr. James Ritchie and Dr. Graham Brown, to give me the results as to albuminuria met with in the last 200 cases which had proposed for insurance in the two companies for which they are medical referees. The tests employed had been heat or cold nitric acid, and it was found that in one series of 200, 5 per cent. showed albumen, and in the other series only 1 per cent. did so. The former result corresponds pretty closely to what nitric acid revealed in my own series of young men following civil employments, but is considerably below the results brought

out by Dr. Munn in his American statistics. The second series gives a much lower percentage.

It is interesting to compare the results obtained in my other categories with those given by other observers. Leube found among German soldiers examined during the forenoon and after marching, 16 per cent. albuminuric. Van Noorden, under like conditions, found it in 35 per cent. Capitan found it among French soldiers 44·9 per cent., and I have found it among the Highlanders (including recruits) in 37·55 per cent.

The Craiglockhart and Orphan Hospital children gave a result less favourable than that obtained by Leroux, for while he found albuminuria in only 5·76 per cent., I found it in 17.

I am not aware of the publication of any series of observations on old men corresponding to my Craiglockhart series.

In answer, then, to our second question, it appears that a trace of albumen may be discovered by delicate tests in the urine of nearly 1 in 3 of the male population, if it be examined during the active period of the forenoon, an hour or two after breakfast, although before breakfast the proportion would be considerably smaller.

The third question is as to the effects produced by diet, exercise, severe exertion, and cold bathing upon the discharge of albumen.

In order to determine the effects of diet, I obtained specimens of the urine of 32 soldiers before and after breakfast, and found that of these 5, or 15·625 per cent., had albuminuria on rising in the morning; while 13, or 40·525 per cent., showed it after the morning meal. Thus 8, or 25 per cent., who had not had albuminuria in the morning, acquired it after breakfast.

Among 40 old men examined in Craiglockhart Poorhouse we found that 15, or 37·5 per cent., showed albuminuria before breakfast; while after that meal 27, or 67·5 per

cent., showed it. Thus 12 who had not had albuminuria on rising in the morning acquired it after breakfast.

Among 40 children, we found that 5, or 12·5 per cent., showed it before breakfast, and 7, or 17·5 per cent., showed it after breakfast. Thus 2 who had not albuminuria on rising in the morning acquired it after breakfast.

Among 48 boys, inmates of the Orphan Hospital, we found that before breakfast albumen was present in 7, or 14·6 per cent.; after breakfast, in 10, or 20·83 per cent.

Taking the four groups together, we have a series of 160 cases examined before and after breakfast, and we find that of these 32, or 20 per cent., discharged albumen before breakfast, while 57, or 35·6 per cent., showed it after the meal.

TABLE VII.—SHOWING THE INFLUENCE OF BREAKFAST ON THE DISCHARGE OF ALBUMEN FROM THE KIDNEYS.

	No.	Before Breakfast.		After Breakfast.	
		No.	Per cent.	No.	Per cent.
Soldiers, . . .	32	5	15·625	13	40·625
Old Men, . .	40	15	37·5	27	67·5
Children . . . (Craiglockhart).	40	5	12·5	7	17·5
Children . . . (Orphan Hospital).	48	7	14·6	10	20·83
Total, . .	160	32	20	57	35·6

I have put these various results in a tabular form, which shows very clearly that at all ages, and in the various conditions investigated, the taking of breakfast is followed by an increased frequency of albuminuria, but that the increase is greatest among the old men and the soldiers.

In connection with this it is worthy of notice that in most of the cases of after-breakfast albuminuria, the quantity of albumen was too minute to be shown by the cold nitric acid test, and also that when it was present before, it was generally

increased in amount after the meal. But on the other hand, there were two cases among the children in which breakfast was followed by the disappearance of albuminuria which had been present on rising. I have met with facts corresponding to this in some of my albuminuric patients. A gentleman who is at present under my care, for example, shows copious albumen in morning urine, and a comparatively small quantity after breakfast.

Contrary to what one might expect, considering what is usually taken for breakfast as compared with what is taken for the other meals, it appears that breakfast more frequently induces albuminuria, or an increase of albumen, than the others. The attempt to explain the influence of food in this respect, raises problems of considerable difficulty. But I shall not at present seek to determine whether an alteration of the blood, or the blood pressure, or of the vascular walls, or epithelial structures is the cause.

It may also be remarked that the mucin in the urine likewise increases after food, although not to the same extent as the albumen.

The next point investigated was the effect of muscular exercise on albuminuria. It appeared desirable to distinguish between the effects of moderate exercise and of severe and prolonged exertion. Observations were therefore made upon soldiers before and after their weekly march of seven to ten miles, and before and after the fatigue duty of coal-carrying.

Of 63 soldiers about to start for their weekly march of from seven to ten miles in heavy marching order, 18, or 29 per cent., were found to have albumen in their urine. After their march, the urines of 58 of these men were examined, and 11, or 19 per cent., showed albumen. The march out, therefore, distinctly diminished the albuminuria. But as the march is taken in the forenoon, it occurred to me that some of those who got rid of the symptom during the march

might have had a temporary albuminuria induced by breakfast. I therefore examined the urine of 32 soldiers before breakfast, after breakfast, and on their return from the march. It was found that before breakfast albumen was present in 5, or 15·623 per cent.; after breakfast in 13, or 40·625 per cent.; and after the march in 9, or 28·125 per cent. It was noticed also that in several cases the amount of albumen diminished, although it did not wholly disappear. It was thus shown that in a considerable proportion of cases the march removed the dietetic albuminuria, and other observations which I have made justify the conclusion that the march out exerts a favourable influence. It must, however, be observed that in some individuals the march induced albuminuria. In one of the nine cases it occurred only after the march, the urine having been quite free from albumen on rising and after breakfast, and in at least one other case the amount of albumen was distinctly less after breakfast than it was after the march. It is thus clear that the effort of marching is sufficient to induce the symptom in some people.

But while marching proved on the whole beneficial, fatigue duty of coal-carrying brought out a very different result. This work, as carried on in Edinburgh Castle, obliges two men to carry a bucket containing 80 lbs. of coal for several hundred feet up a rather steep incline, and then up barrack stairs to the different floors. Each pair of soldiers makes six or seven such journeys during the forenoon in which they are told off to this duty. Of 36 soldiers engaged in this work we found that 16, or 44 per cent., had albuminuria before the labour commenced; while 23, or 64 per cent., had albumen at the end of it. On another day, when we were able to get the urine of 17 men engaged in this coal-carrying, 7 had albuminuria, equal to a little over 41 per cent, although the observations were made not at the end, but in the course of their work.

I have put in tabular form the facts elicited in this connection.

TABLE VIII. — SHOWING EFFECTS OF EXERCISE AND OF SEVERE EXERTION, ALSO OF BREAKFAST AND EXERCISE.

	No. Examined.		Before.		After.			
	Before.	After.	No.	P. cent.	No.	P. cent.		
March of 8 miles,	63	58	18	29	11	19		
Fatigue duty—coaling, . .	36	36	16	44	23	64		
			Before	Br'fast.	After	Br'fast.	After	March.
Breakfast and march, . .	32	32	5	15·6	13	40·6	9	28·1

In regard to the effect of violent exercise, I have thought it well to make another investigation, in order to get confirmation, if possible, of the result brought out by the coal carrying, and, by the kindness of Mr. Munro, I have succeeded in obtaining this at the Orphan Hospital. The result is given in Table IX.

TABLE IX.—SHOWING THE INFLUENCE OF VIOLENT EXERCISE (PLAYING FOOTBALL FOR AN HOUR) ON THE INCIDENCE OF ALBUMINURIA.

Meal of Bread and Milk at 5.45 P.M. *Football from* 7.30 *to* 8.30 P.M.

BEFORE FOOTBALL—7.30.					AFTER FOOTBALL—BETWEEN 8.30 AND 9.			
No.	With HNO_3.	Picric Acid.	Total.	Per cent.	With HNO_3.	Picric Acid.	Total.	Per cent.
25	0	1	1	4	3	12	15	60

Twenty-five boys played very actively at football for an hour, one evening. Their supper, which consisted of bread and milk, was taken at 5.45 P.M., and they played football from 7.30 to 8.30. A specimen of urine was obtained from

each boy before and after the game. You will observe that the result quite corresponds with that obtained at the Castle. Indeed, the effect is even more apparent. None of the first set of specimens showed any albumen with nitric acid. Three of the second series showed unmistakable evidence with that test, none of these having before the exercise reacted distinctly even with picric acid. In only one case was there any distinct trace of albumen with picric acid before the game, while after it fifteen showed albumen with that reagent. You will observe, further, that this experiment confirms the view that it is only a slight albuminuria which is produced by violent exercise in healthy people.

From the facts thus given it is shown that violent exertion may produce albuminuria, while moderate exercise tends rather in many cases to diminish it. Statements have been made as to the urine of the performers of pedestrian feats which confirm this experience. Weston's urine is said to have contained both albumen and tube casts at the end of one of his prolonged walks.

A very interesting observation has been made by Dr. W. A. Stirling,[28] in a thesis sent in for the M.D. degree this year, and he has permitted me to make use of it on this occasion. He found in the course of an investigation as to the incidence of albuminuria in 369 boys, who are being educated in the training-ship at Grays, Essex, that the boys who played wind instruments in the band exhibited albuminuria in a much larger proportion than the others. Thus, while out of 64 boys so employed, 38, or 59·4 per cent., had albuminuria, out of 305 boys, otherwise under like conditions, but not in the band, only 39, or 12·8 per cent., showed the symptoms.

These results may, as he remarks, be very naturally referred to altered blood pressure due to habitual use of musical instruments.

With the view of testing this, I examined 24 boys who play wind instruments in the band of the Orphan Hospital, and 24 boys in that Institution who are otherwise similarly placed, except in not being members of the band. It appears, so far as the numbers serve us for the purpose, that albuminuria is more frequent among the band boys than among the others; but that there is a diminution rather than increase at the end of an hour's practice with the instruments. I have put the facts in tabular form, and it is clear that no such discrepancy exists as in the training-ship boys; but still the statistics lend a certain measure of support to Dr. Stirling's observations.

TABLE X. — SHOWING INCIDENCE OF ALBUMINURIA IN 24 WIND-INSTRUMENT BAND BOYS, AND 24 OTHER BOYS (ORPHAN HOSPITAL).

	No.	Before Breakfast.				After Breakfast and Playing.				After Playing, 5 P.M.			
		HNO_3.	Pic. A.	Tot.	P.C.	HNO_3.	Pic. A.	Tot.	P.C.	HNO_3.	Pic. A.	Tot.	P.C.
Band Boys,	24	2	3	5	20·8	2	4	6	25·0	1	2	3	12·5
Other Boys,	24	0	2	2	8·3	1	3	4	16·6	...	...	...	...

Some years ago Dr. George Johnson [29] of London drew attention to the fact that albuminuria is sometimes induced by cold bathing. In order to get further information upon this question, I got from 21 boys the urine which they passed on rising at 6 A.M., and that passed at 8 after a cold plunge bath. It was found that while before bathing 4, or 19·05 per cent., showed albumen; after it 5, or 23·8 per cent., showed it.

Among the boys so examined only a small number showed albuminuria, and the amount of albumen was slight, for nitric acid failed to detect it, but there was an increase both in the number of cases affected and in the intensity of the condition, although the effect was not very pronounced.

In Table XI. I have stated the results of these observations.

TABLE XI.—SHOWING EFFECT OF COLD BATHING ON 21 BOYS (ORPHAN HOSPITAL).

Before Bath (6 A.M.).				After Bath (8 A.M.).			
With HNO_3.	Only with Pic. A.	Total.	Per cent.	With HNO_3.	Only with Pic. A.	Total.	Per cent.
0	4	4	19·05	0	5	5	23·08

I have not been able as yet to test the effects of mental excitement or emotion upon any considerable number of healthy individuals, but no doubt an investigation in suitable quarters might elicit interesting results. This is indicated by the occurrence of such cases as that recorded by Fürbringer,[30] of a medical man who never showed albuminuria as the result of long and fatiguing work, nor from the use of a diet rich in albumen, nor from the free use of alcohol, but constantly showed it in large amount when exposed to mental excitement with depression.

The remarks which I have made apply only to the ordinary forms of proteid serum-albumen and serum-globulin. With regard to the occurrence of peptones, we discovered them in only 3 out of the whole series of 771 specimens, which were carefully examined in the course of the investigations.

From the facts recorded, we seem entitled to conclude—

1. That there is no sufficient proof that albumen is normally discharged from the human kidneys.

2. That albuminuria is much more common among presumably healthy people than was formerly supposed, being demonstrable by delicate tests in nearly one-third of those examined.

3. That the existence of albuminuria is not of itself a sufficient ground for the rejection of a proposal for life insurance.

4. That traces of albumen are not unfrequently present in the urine passed during the first days of life.

5. That, excepting as above shown, the frequency of albuminuria increases as life advances; being rare in children and young adults, and common in men at or above sixty years of age.

6. That it is more common among those whose occupations involve arduous bodily exercise than among those who have easy work.

7. That albuminuria frequently follows the taking of food, especially of breakfast.

8. That moderate muscular effort rather diminishes than increases albuminuria, except in rare cases.

9. That violent or prolonged exertion often induces albuminuria.

10. That cold bathing produces or increases it in some individuals.

11. That the discharge of peptones from the kidneys is exceedingly rare in the presumably healthy.

LECTURE III.

ON THE INCIDENCE OF ALBUMINURIA AMONG THE SICK.

Introduction.—Series of Cases Examined.—Method Adopted.—General Results in Different Groups.—Categories of Causes Defined.—Series of Cases taken together.—Series of Private Cases.—Series of Indoor Hospital Cases.—Outdoor Hospital Cases.—Patients in Royal Hospital for Sick Children.—Fever House Patients.—Alcoholic Cases.—General Conclusions as to Incidence of Serum Albumen.—Peptonuria in the Different Series.

GENTLEMEN,—Having shown you the results which have been obtained as to the incidence of albuminuria among the presumably healthy, I intend to-day to bring before you the results of a series of observations which I have made as to its incidence among various groups of patients to which I have had access.

I have made careful investigation in regard to 150 consecutive private patients as they presented themselves in my practice; 150 consecutive cases under my care in the wards of the Royal Infirmary; 100 patients applying consecutively for advice as out-patients at my department; 50 patients in the wards of the Royal Hospital for Sick Children; 40 cases in Ward VI., which is mainly devoted to the treatment of patients suffering from alcoholism; 50 patients under treatment in the Fever Hospital; and 25 cases of women who had been confined in the Maternity Hospital.

For their kindness in providing me with facilities for carrying on this work, I am indebted to the physicians of the Sick Children's Hospital; to Dr. Smart, the physician in charge of Ward VI.; to Drs. Allan Jamieson and Wood, of the Fever Hospital; and to Professor Simpson and Dr. Hart, who, at the time the observations were made, were on duty as physicians to the Maternity.

In each case the urine was examined with nitric acid, picric acid, and Fehling's solution. In the case of the patients belonging to the first five categories, a single specimen was examined. In the Fever House cases we obtained specimens of the urine passed on the day on which it seemed most likely that albumen would be found in each variety of fever. In the puerperal cases, Dr. Stevens undertook a specially careful inquiry, with the view of testing the correctness of certain statements as to the occurrence of peptones in the puerperal condition. He obtained specimens of the urine of some patients before the confinement, and of all during several days after the confinement, every precaution being taken to protect the specimens from accidental contamination.

In the following table are shown the number and percentage of cases showing albuminuria, those showing it with nitric acid, and those with picric acid.

TABLE XII.—SHOWING THE INCIDENCE OF ALBUMINURIA IN GROUPS OF PATIENTS.

	No.	With HNO_3	Picric Acid.	Total.	Percent.
Private Patients, ...	150	27	9	36	24
Indoor Infirmary Patients, . .	150	53	21	74	49.3
Outdoor Infirmary Patients, .	100	16	3	19	19
Royal Hospital for Sick Children,	50	3	4	7	14
Fever Hospital, ...	50	18	15	33	66
Maternity Hospital, . . .	25	13	5	18	72

It thus appears that among the private patients 36, or 24

per cent., showed albumen; among the indoor Infirmary patients, 74, or 49·3 per cent.; among the outdoor Infirmary patients, 19 per cent.; and among the sick children, 7, or 14 per cent.; among the fever cases, 33, or 66 per cent.; among the Maternity Hospital cases, 18, or 72 per cent. In the three first groups the amount of albumen was more frequently large enough to be discovered by the cold nitric acid test,—nitric acid showing it in 27 of the private patients, picric acid only in other 9; nitric acid in 53 of the indoor patients, picric acid in other 21; nitric acid in 16 of the outdoor patients, picric acid in other 3; and among the sick children, nitric acid in 3, picric acid in other 4.

Now, it may he held that the 150 private patients were placed under conditions pretty much corresponding to those of the presumably healthy civil population referred to in the last lecture, and the proportion of 24 per cent. among the sick, and 10·8 per cent. among the presumably healthy, seems such as one would expect. The indoor Infirmary patients may be said to correspond in a general way, as to occupation and circumstances, to what we find in the presumably healthy soldiers; and we find 49·3 per cent. in the hospital, as against 37·56 per cent. among the soldiers. The difference is not so great as one might have expected; but allowance must be made for the fact that Infirmary patients are in much more favourable conditions in respect of exercise and diet than are the soldiers and recruits, and so probably often escape minor degrees of albuminuria, to which they would be liable if they were following their ordinary lives of labour. The outdoor Infirmary patients represent a somewhat different class, many of them being women engaged in sedentary occupations; and accordingly one is prepared to find them occupying a position intermediate between that of the ordinary civil population on the one hand and the soldiers and indoor hospital group on the other. The fact

that the percentage among them was only 19, while among my house patients it was 24, may perhaps be explained by the circumstance that my proportion of renal cases among the latter is considerable. The Sick Children's Hospital cases bring out a result more favourable than could have been anticipated, only 14 per cent. showing albumen ; while among the Craiglockhart and Orphan Hospital children 17 per cent. showed it. I am not prepared to offer a satisfactory explanation of this fact, and therefore simply record it with the remark that probably the rest and quiet of the life in the Sick Children's Hospital affords the explanation.

With regard to the observations in the puerperal cases, the interest turns chiefly upon the question of the peptones, and I shall speak of that at the end of this lecture ; but with regard to serum albumen it may be noted that it was present in 1 of the 2 cases tested before labour commenced, in 2 out of 3 tested on the day of labour, in 12 out of 17 tested on the second day, in 8 out of 15 tested on the third, in 6 out of 12 tested on the fourth, in 5 out of 13 tested on the fifth, and in 6 out of 8 tested on the sixth ; and that in no case was there reason to believe that serious renal inflammation existed. Certainly there never was ground for anxiety in any of the series of cases, except in one who was suffering from phthisis.

My object in this research was not merely, as in the case of the presumably healthy, to determine the frequency of the incidence of the symptom, but also to make out its causes. And I found that the causes were referable to a series of categories. Let me explain what these categories are :

1. *Bright's Disease.*—Under this head I have included all cases referable to any of the forms of renal disease, including inflammation of the tubules, stroma, and Malpighian bodies, the chronic cirrhotic process, and waxy degeneration, with

their various combinations, and even the slighter inflammatory changes which so commonly occur in the course of other diseases.

2. *Probably Bright's Disease.*—This category includes the cases in which our investigations left a margin of doubt as to whether structural organic change of the kidney was really present or not.

3. *Febrile Albuminuria.*—A category of much clinical importance, including fevers, inflammations, acute rheumatism, and other diseases with high temperature. This category passes by insensible gradations into the first, but I have sought to determine their position by careful investigation of each individual case.

4. *Vascular Albuminuria.*—This group includes cases in which the albumen appears to result from changes in the circulation in the kidney, where the outflow is hindered by increased backward pressure from disease of the heart or of the lungs, or where the circulation is altered from embolic, thrombic, or other processes.

5. *Albuminuria with Disease or Disorder of Digestion.*—This category includes a group in which the albuminuria could only be referred to morbid structural or functional changes in connection with the digestive process.

6. *Nervous Albuminuria.*—A group of cases in which the albuminuria appeared to be related to changes in the nervous system, such as apoplexy, epilepsy, and exophthalmic goitre.

7. *Albuminuria with Glycosuria.*—This group includes cases in which albuminuria was superadded to the other chemical abnormality in cases of true diabetes mellitus or of simple glycosuria.

8. *Functional Albuminuria.*—This category includes those cases in which, apart from any evidence of organic change in the kidney, exercise or exertion, diet, exposure to

cold, mental emotion, or obscure cyclic influences account for the symptom.

9. *Accidental Albuminuria.*—This group includes the cases in which albumen is added to the urine after its secretion by the kidney, owing to admixture with blood, pus, prostatic or seminal fluid during its course through the urinary passages.

10. *Probably Accidental Albuminuria.*—This category includes cases occurring especially in women, in which the presence of albumen is probably, though not certainly, accidental.

I shall ask you first to note the results brought out in the series of 450 cases of disease other than the infectious forms, which do not often present themselves in a physician's consulting-room, and are not admitted to the Royal Infirmary or the Royal Hospital for Sick Children. I have stated the results in Table XIII.

TABLE XIII.—SHOWING INCIDENCE OF ALBUMINURIA IN 450 CONSECUTIVE CASES INVESTIGATED WITH REFERENCE TO THE PROBABLE CAUSES.

	With HNO_3.	With Picric Acid.	Total.
1. Bright's Disease, . . .	43	5	48
2. Probably Bright's Disease, .	7	2	9
3. Febrile, ...	6	3	9
4. Vascular, ...	16	7	23
5. Alimentary, ...	2	8	10
6. Nervous, ...	1	5	6
7. With Glycosuria, . . .	4	2	6
8. Functional, ...	4	2	6
9. Accidental, ...	9	3	12
10. Probably Accidental, . .	7	0	7
	99	37	136

This table shows that of our 450 cases, 136, or 30·2 per cent., showed albuminuria. Comparing this with the per-

centage of our series of 505 presumably healthy individuals, we find that in that series, 166, or 32·8 per cent., showed the symptom. But when we look at the proportion of cases showing a reaction with nitric acid or picric acid respectively, we find that the difference becomes distinct, for while among the presumably healthy 76 showed with nitric and 90 with picric, among the patients 99 showed with the one and 37 with the other.

It is thus clear that the slight traces are proportionately more common among the presumably healthy, and the more distinct reaction among the sick.

On looking over the different categories we find that Bright's disease accounts for more than one-third of all the cases of albuminuria met with, and that in nearly every instance the albumen was in quantity sufficient to be made out with cold nitric acid. Nine cases were regarded as probably examples of Bright's disease. The same number of cases was referred to the category of febrile albuminuria. That only 1 in 14 of the cases should belong to this group may seem at first sight surprising, but it is to be remembered, on the one hand, that fever cases are not admitted to the Infirmary or the Children's Hospital, and very rarely present themselves in a consulting-room, and, on the other, that many cases of febrile albuminuria afford evidence of some structural lesion of the kidneys, so that a category, naturally small in such a series of cases, is further reduced by the number included in other groups. The vascular cases amounted to nearly 1 in 6 of the series, thus taking the second place in frequency. But it is to be observed that in nearly one-half of them the quantity was too small to be shown by nitric acid. The alimentary cases made up 1 in 13 of the series, and the great majority showed only the faintest trace of albumen.

The nervous included six cases, or 1 in 22½ of the series,

and except in a single case, the quantity was too minute to be made out with nitric acid. One in 22½ were also referred to the category of albuminuria with glycosuria, but the larger proportion of them had the albumen abundant. Six, or 1 in 22½, were regarded as examples of functional albuminuria, and in them also two-thirds showed a considerable quantity. The accidental group included rather more than 1 in 11, and of them also two-thirds had the albumen in good quantity. Seven cases were regarded as probably accidental in origin.

I shall now go over the different groups individually.

In Table XIV. I have shown the results obtained in the series of 150 consecutive private patients, giving the total number of cases showing albuminuria with the total number which I refer to each category, the numbers in which nitric acid sufficed to demonstrate the symptom, and those in which it only became apparent on the addition of picric acid.

TABLE XIV.—SHOWING INCIDENCE OF ALBUMINURIA IN 150 CONSECUTIVE PRIVATE PATIENTS, WITH REFERENCE TO THE PROBABLE CAUSES.

	With HNO_3.	With Picric Acid.	Total.
1. Bright's Disease,	12	1	13
2. Probably Bright's Disease,	0	0	0
3. Febrile,	1	0	1
4. Vascular,	1	1	2
5. Alimentary,	1	2	3
6. Nervous,	0	0	0
7. With Glycosuria,	2	0	2
8. Functional,	4	2	6
9. Accidental,	5	3	8
10. Probably Accidental,	1	0	1
	27	9	36

In this series the preponderance of cases of Bright's disease may be readily understood, when one considers how

often the subjects of these maladies are able to go about and to consult physicians in their own houses. The second group is unrepresented, because in every instance I was able to arrive at a definite conclusion as to the existence or non-existence of Bright's disease. The third or febrile group is little likely to appear in the consulting-room. Accordingly, only one instance was noticed. The vascular group, although so common, is also little represented in consulting-room practice. Cases referable to the fifth group, with alimentary derangements, were rather more frequent—one such showing albumen with nitric, two with picric acid. There was no case belonging to the nervous group in this series, but there were two with glycosuria, both of which showed albumen with nitric acid. There were six functional cases, four showing it with nitric acid and two with picric; with regard to these, some particulars are desirable. There were eight accidental cases and one probably accidental, six of them showing with nitric acid and three with picric.

The first of the functional cases which showed albumen with nitric acid was that of a medical man in active practice, whose urine constantly contained a considerable amount of albumen, but was of average quantity and good specific gravity, and contained at least a normal amount of urea. There were none of the other symptoms of Bright's disease present. This case, therefore, belongs to the category of the simple persistent albuminurias. The second case was that of a gentleman with slight albuminuria, who was much troubled with thirst, and who passed a large quantity of urine of rather low specific gravity, but the urea was generally distinctly above the normal amount. There were no other signs of Bright's disease present, and his case I therefore regard as also belonging to the class of simple persistent albuminuria. The third case was that of a patient who had slight constant albuminuria, with a normal amount of urea, and

who was otherwise in good health. I am inclined to place his case in the same category as the previous two, but there is also a possibility of the albuminuria having been accidental. The fourth case was that of a delicate girl, with no marked signs of disease, whose urine contained a small quantity of albumen. This case probably also belongs to the same category, though it may have been a cyclic one. Regarding the two showing albumen only with picric acid, one was a case of intracranial neuralgia, and the other a case simply of overwork.

In Table XV. I give in a similar way the results obtained in the 150 consecutive indoor Infirmary patients.

TABLE XV.—SHOWING INCIDENCE OF ALBUMINURIA IN 150 CONSECUTIVE INDOOR INFIRMARY PATIENTS, WITH REFERENCE TO THE PROBABLE CAUSES.

	With HNO_3	With Picric Acid.	Total.
1. Bright's Disease,	22	4	26
2. Probably Bright's Disease,	4	0	4
3. Febrile,	3	2	5
4. Vascular,	11	5	16
5. Alimentary,	1	5	6
6. Nervous,	1	4	5
7. With Glycosuria,	2	1	3
8. Functional,	0	0	0
9. Accidental,	4	0	4
10. Probably Accidental,	5	0	5
	53	21	74

From this table it is seen that 26 of the 74 cases of albuminuria met with in the wards were referred to Bright's disease ; 22 of them showed albumen with nitric acid, 4 only with picric acid. There were 4 cases which gave distinct reaction with nitric acid, and were probably examples of Bright's disease. There were 5 febrile cases, 3 showing albumen with nitric acid, and the other 2 with picric acid. Of these, 3 were cases of pneumonia, and 2 articular rheumatism. The vascular cases were, as might be expected

among hospital patients, numerous, amounting to 16 of the 74, and of them 11 showed albumen with nitric acid, 5 only with picric acid. Those connected with gastric disorder, such as dilatation of stomach and malignant disease of that organ, were 6 in number, 1 showing with nitric acid, and 5 only with picric acid. Cases of nervous origin were 5, 1 showing with nitric, and 4 with picric only ; 2 of the 5 were with exophthalmic goitre, 2 associated with epilepsy, and 1 in a case of multiple sclerosis. With glycosuria, albumen was associated in 3 cases, 2 showing with nitric acid, and 1 only with picric. Of the accidental albuminurias there were 4, all of which showed with nitric acid. The probably accidental were 5 in number; 4 of these cases were among women, 2 being cases of gastric ulcer, 1 a case of dyspepsia, and 1 a case of malignant disease of the stomach. The fifth was the case of a man with a functional affection of the spinal cord.

The next group is the outdoor Infirmary cases. The results are stated in Table XVI.

TABLE XVI.—SHOWING INCIDENCE OF ALBUMINURIA IN 100 OUTDOOR INFIRMARY PATIENTS, WITH REFERENCE TO THE PROBABLE CAUSES.

	With HNO_3.	With Picric Acid.	Total.
1. Bright's Disease,	8	0	8
2. Probably Bright's Disease,	3	0	3
3. Febrile,	0	0	0
4. Vascular,	4	1	5
5. Alimentary,	0	1	1
6. Nervous,	0	0	0
7. With Glycosuria,	0	1	1
8. Functional,	0	0	0
9. Accidental,	0	0	0
10. Probably Accidental,	1	0	1
	16	3	19

From this table we see that 19 out of the 100 patients showed albuminuria, and of these 8 were cases of Bright's

disease, all showing with nitric acid; 3 were regarded as probably Bright's disease. There were no febrile cases; 5 were referred to vascular changes; 4 showing with nitric and 1 with picric acid. One, which was so slight as to be shown only by picric acid, was referred to a morbid state of the alimentary system. There was no nervous case. One was associated with glycosuria; none were referable to the functional or the accidental groups, and there was only one which we regarded as probably accidental.

In Table XVII. is shown the incidence of albuminuria among 50 patients under treatment in the Sick Children's Hospital.

TABLE XVII.—SHOWING INCIDENCE OF ALBUMINURIA IN 50 SICK CHILDREN, PATIENTS IN THE SICK CHILDREN'S HOSPITAL, WITH REFERENCE TO THE PROBABLE CAUSES.

	With HNO_3.	With Picric Acid.	Total.
1. Bright's Disease,	1	0	1
2. Probably Bright's Disease,	0	2	2
3. Febrile,	2	1	3
4. Vascular,	0	0	0
5. Alimentary,	0	0	0
6. Nervous,	0	1	1
7. With Glycosuria,	0	0	0
8. Functional,	0	0	0
9. Accidental,	0	0	0
10. Probably Accidental,	0	0	0
	3	4	7

There was, as the table shows only one case of Bright's disease. Two cases in which picric acid showed albumen were regarded as being probably of that nature; three were febrile; there were none vascular or alimentary; one nervous, and none referable to the other categories.

In Table XVIII. are shown the results obtained as to the occurrence of albuminuria among 50 fever patients in the

Edinburgh Fever Hospital. I first give the statistics of the whole, and then the statistics as to scarlet fever separately.

TABLE XVIII.—SHOWING INCIDENCE OF ALBUMINURIA IN 50 PATIENTS IN THE FEVER HOSPITAL, WITH THE STATISTICS FOR SCARLET FEVER.

Total Number.	With HNO_3.	With Picric Acid.	Total.
50	18, or 36 per cent.	15	33, or 66 per cent.

STATISTICS FOR SCARLET FEVER.

	With HNO_3.	With Picric Acid.	Total.
Scarlet Fever 38	13, or 34·2 per cent.	10	23, or 60·53 per ct.

Of the 50 cases, 18, or 36 per cent., showed albumen with nitric acid, and 33, or 66 per cent., showed it with picric acid. Taking the 38 scarlet fever cases separately, we find that 13, or 34·2 per cent., showed albumen with nitric acid, and 23, or 60·53 per cent., with picric acid. In regard to the other fevers, the observations are too limited in number to afford any percentage results. But the frequency of traces of albumen in whooping-cough was noteworthy: of 6 cases, 1 showing it largely with nitric acid, while the other 3 gave the reaction with picric acid. The strain produced by the coughing is, I believe, an important factor in its production. No conclusions can, of course, be drawn from the few cases of typhoid fever, measles, and typhus which are included.

I have lastly to direct your attention to the results obtained in 40 cases of alcoholism, either acute or chronic, under treatment in the Royal Infirmary. The specimens were obtained on the morning after their admission to the wards. These results I have put in Table XIX.

TABLE XIX.—SHOWING THE INCIDENCE OF ALBUMINURIA IN 40 PATIENTS SUFFERING FROM ALCOHOLISM, EITHER ACUTE OR CHRONIC, UNDER TREATMENT IN WARD VI., ROYAL INFIRMARY.

Number.	With HNO_3.	With Picric Acid.	Total.
40	11, or 27·5 per cent.	8	19, or 47·5 per cent.

One would naturally expect a large proportion of albuminurics among such patients, and no doubt the percentage is high. Still we must remember that the class of patients of whom this group is composed is most closely related to that of the soldiers; that is, the conditions of life, such as severe bodily labour, which in soldiers conduce to make albuminuria frequent, are also in operation here. Still, the percentage of albuminurics is distinctly higher than it is amongst the soldiers, and indeed more closely corresponds to the statistics obtained among the indoor Infirmary patients. While, therefore, the albuminuria is probably mainly to be ascribed not to alcohol but to the conditions of life, the alcohol must be credited with the increase over what we would expect in healthy individuals of the same class. This may be partly a direct effect of the alcohol, but doubtless the indirect influences as regards inferior diet, and bad hygienic conditions which intemperance and improvidence involve, are also factors in the case.

The following inferences seem to be warranted from the facts that I have collected :—

1. That as in health, so in disease, albuminuria is much more common than is generally supposed.

2. That it is more common among patients of adult age than among children.

3. That cases of Bright's disease do not account for one-half of the cases of albuminuria met with in practice.

4. That they account for more than any other individual cause.

5. That next to them rank cases induced by cardiac and other maladies affecting the circulation, and those due to the accidental admixture of blood, pus, or other albuminous fluid with the urine.

6. That so far as this series of observations shows, the various forms of functional albuminuria are rare.

7. That in the waxy and cirrhotic diseases of the kidneys, the quantity of albumen is at first so slight as to be shown only by picric acid.

8. That usually in these when advanced, and in renal inflammation, the albumen is more abundant than in other varieties of albuminuria.

9. That in the digestive and nervous cases, and those due to high temperature, the quantity is often so small as only to be discovered by picric acid.

We now turn to note the results of our observations as to the occurrence of peptones in the series of cases observed. In Table XX. the results are brought out.

TABLE XX.—SHOWING INCIDENCE OF PEPTONURIA IN THE SERIES OF CASES EXAMINED.

Of 150 Private Patients,	4	gave the peptone reaction.
150 Infirmary Patients,	16	,,
100 Outdoor Infirmary Patients,	7	,,
50 Sick Children,	4	,,
50 Fever Patients,	3	,,
40 Alcoholic Patients,	1	,,
25 Puerperal after Delivery,	2	,,

It thus appears that only 4 out of 150 private patients showed this condition. These cases were, first, a case of cirrhotic Bright's disease, with gout and dyspepsia; second, a case of cirrhotic Bright with heart disease; third, a case of rupture of the kidney; and fourth, a case of acute

rheumatism. The urine also contained, in each of the cases, serum albumen.

Of 150 indoor patients at the Infirmary, 16 gave the reaction. These were a case of dyspepsia, a case of malignant disease of the liver, stomach, and lungs; a case of heart disease, two of phthisis (one of them syphilitic), a case of pleurisy, nine cases of Bright's disease, and a case of acute rheumatism. Except in the case of dyspepsia, all the urines contained serum albumen as well.

Of 100 outdoor patients examined at the Infirmary, seven showed the peptone reaction. They were—a case of phthisis with waxy disease of the kidneys, four cases of Bright's disease, one of hysteria, and one of syphilis. The urines all contained serum albumen.

Of the 50 patients examined in the Royal Hospital for Sick Children, four gave the reaction for peptones. One was a case of meningitis and pneumonia; another, a case of infantile paralysis; the third, a case of disease of the spinal cord; and the fourth, a case in which the diagnosis was doubtful. In one only of these was there distinct evidence of serum albumen.

Of the 50 fever patients, only three gave the reaction; and among the forty alcoholic patients, it occurred only once.

Among the 25 puerperal cases in which the urines were carefully and repeatedly tested after delivery, two showed a trace of peptone, and in addition there were six cases in which it was doubtful whether a trace existed or not. This result differs remarkably from that obtained by Dr. Fischel[31] in the course of his researches carried out in the wards of Professor Breisky of Prague (now of Vienna). He examined the urine of twenty-eight pregnant women, and found peptone in a fourth of the cases, but mostly in small quantity, so far as he could judge by the intensity of the red coloration in

the biuret reaction, but it was not constantly present. He examined fifty-six puerperal patients from the first to beyond the twentieth day, making one hundred and fifty-one testings. Among them he found eighty-six showing peptones; fifty-eight gave a negative result. Before the labour, and in the first twelve hours after it, peptones never appeared. In the second half of the first day usually there was none, but sometimes a trace. In the second and third days, peptonuria was almost constant (24 out of 25 cases); on the fourth, fifth, and sixth days, it was very frequent (out of 44 testings it occurred 37 times). From the seventh to the tenth day, half the cases showed it; after the tenth day, it was very rare.

Such discrepancy necessarily raises the question whether the method of testing which we adopted was sufficient. It is certainly the best plan at present available for ordinary clinical work, the methods of Schultzen, Riess, Hofmeister, and Ralfe[32] being far too elaborate for frequent repetition. On the whole we seem to be entitled to conclude either that peptones are not so common as Dr. Fischel's research led him to believe, or that if he is correct, the quantity is extremely minute.

LECTURE IV.

ON THE THEORY OF ALBUMINURIA.

Introduction.

Albuminuria may be ascribed to Changes in the Blood.—Hydræmia.—Inspissation.—Excess of Salts.—Deficiency of Salts.—Excess of Albumen.—Altered Albumen.

Altered states of the Filtering Apparatus.

Abnormal Vascular Tension.—Diminution of Tension.—Increase of Tension.

Changes in Epithelial Cells and Stroma of Kidney.

Conclusion.

GENTLEMEN, — Having in former lectures given you the results of our inquiries as to the incidence of albuminuria in presumably healthy people and in various groups of patients, I shall devote the present meeting to an attempt to explain what we at present know as to the precise mechanism of the production of albuminuria.

It is necessary before doing so, to consider the process of normal urinary secretion. I agree with those who think that the watery part of the urine, along with certain salts held in solution, transudes by a filtration process through the capillaries of the Malpighian tufts. Whether along with this a certain proportion of albumen also transudes or not, as experiments made with membranes outside the body would lead us to expect, is not with certainty ascertained. Some, for whose opinion I have much respect, believe that albumen is normally transuded in considerable quantity and reabsorbed by the epithelium lining the tubules, but the arguments and experiments adduced in support of this view are by no means con-

clusive, and I incline to think that the blood pressure in the capillary loops, and the walls of these vessels, with their thin epithelial covering, are so balanced as to permit of the transudation of fluid, and yet completely or almost completely to prevent the passage of the albumen. At all events, we may hold with certainty that the water is mainly eliminated by filtration through these structures. But the urea and other urinary solids are not discharged by a filtration but by a secretion process performed by the cells of the tubules. Along with this secretion, as in the case of other glands, a certain amount of watery fluid passes, and the capillaries surrounding the tubules, of course, afford the material from which the secreting structures draw their supplies.

It is certain that in most cases the transudation of albumen takes place at the Malpighian tufts. Posner pointed out that when inflamed kidneys are boiled, coagulated albumen is found occupying the cavity of the capsule, and the commencement of the tubules; and Ribbert[33] showed that when albuminuria had been induced in rabbits by temporary clamping of the renal artery, portions of the kidney hardened in alcohol exhibited a corresponding condition. Litten's[34] observations corroborated these results. Confirmatory evidence is afforded by the experiments of Nussbaum,[35] who, taking advantage of the fact that in frogs the Malpighian bodies have an arterial supply distinct from that of the tubules, obstructed the supply to the glomerular arteries, leaving those supplying the tubules free, and then injected egg albumen into the blood, with the result that no albuminuria followed, as would have been the case had the cortical vessels been in action.

While the seat of transudation of albumen is thus determined, there are four possible ways in which the transudation might arise. It might be due to faulty conditions of the blood; to altered states of the filtering apparatus—*i.e.*, the vascular walls and their epithelial coverings; to abnormal vascular

tension or altered circulation; or to morbid action on the part of the epithelial and other structures of the kidney. We shall go over these in their order, and indicate the share which each may be supposed to take in the process. Although I enumerate them separately, you must remember that this is warranted only on account of analysis, for the individual factors rarely, if ever, act alone.

I.—Changes in the Blood.

That the discharge of albumen in Bright's disease is not due to a peculiarity of the albumens of the blood was shown conclusively by Stokvis,[36] for he injected albuminous urine into the blood of animals, and found that no albuminuria resulted. Now, had the albumen escaped from the kidneys of the patients whose urine was employed in the experiments, in consequence of a peculiarity of the substance itself, it would have again escaped from the kidneys of the animals into whose blood it was injected. But even if it be admitted that this settles the matter as regards Bright's disease, it throws no light upon other varieties of albuminuria, and there has been so much theoretical or speculative writing upon this subject that it deserves careful consideration. If you look through the literature, you will find that the following possibilities have suggested themselves to different minds. Some have thought of undue wateriness, and some of undue inspissation of blood; some of excess, and some of diminution of its normal salts; some of excess of one or other of the albumens normally present; and some of the development of abnormal and more diffusible varieties of albumen.

Now, as to increased wateriness of the blood, the results of various experiments by Magendie,[37] Mosler,[38] and others, seemed to show that dilution of the blood with water induces albuminuria. This appeared to support the view maintained by Owen Rees,[39] that the symptom, when it occurs in the course of disease, may probably, in some cases, arise from

a like alteration. But the experiments of Herrmann[40] and Westphal[41] threw doubt upon the conclusions of their predecessors, and the careful researches of Stokvis,[36] in my judgment, finally set the theory aside. He made two series of experiments on the lines followed by Herrmann and Westphal, injecting water very cautiously in small quantities at a time, a precaution which had been neglected by the earlier observers, but gradually introducing enough greatly to dilute the blood. In the first series, which included six experiments, he simply introduced the water into the circulation of healthy animals; in the second, which included four, he first bled the animals freely in proportion to their size, and then injected the water. In none of the first, and in only one of the second series did albuminuria result. The one exceptional case threw light upon the experiments of Magendie and others, for the urine became bloody, and I cannot resist the conclusion that the occurrence of hæmaturia as well as albuminuria in the earlier experiments proved that rupture of renal vessels had occurred, so that the process could not be truly reckoned a hæmatogenous albuminuria, nor the experiments a proof of the view that they were supposed to justify.

The opposite condition of undue inspissation of the blood may be suggested as a possible explanation of some cases of albuminuria, for it sometimes occurs in the course of diseases attended by profuse watery discharges, such as violent diarrhœa and cholera, in which the water of the blood must be considerably reduced, the proportion of albumen is increased. But when we look closely into the facts as to the incidence of albuminuria in cholera the suggestion finds little support so far as it is concerned. The albuminuria of cholera is most marked in the stage of reaction, and follows upon the anuria of the period of collapse. Now, the period of collapse is that in which there must be the greatest inspissation of the blood. The inspissation has already begun

to diminish when the stage of reaction sets in, and, as it is then that the albuminuria appears, we must conclude that inspissation is not the cause. It has been asserted that during the collapse stage albuminuria is absent only because there is little or no urinary secretion, and that if a few drops can be obtained with the catheter or otherwise, it is albuminous. But, granting this, it does not follow that inspissation of blood is the cause, and, by combining the results of anatomical investigation with those of certain experiments, we arrive at a much more satisfactory explanation. The condition of the kidneys is found to correspond anatomically to what is seen as a result of temporary ligature of the renal arteries—viz., changes in the Malpighian tufts, and, taking together these facts and the sequence of symptoms, I agree with Bartels[42] in thinking that the altered blood supply, and the changes consecutive to it, afford us the best explanation of the phenomena of the disease. Making allowance for this and for the fact that more extensive inflammatory changes are often set up, we find a sufficient explanation of albuminuria in cases of cholera, and, on the whole, you will find that the blood-inspissation hypothesis rests upon no sufficient foundation.

There is more to be said in favour of the view that excess of salts in the blood may induce albuminuria. Experiments by Hoppe-Seyler[43] and others have shown that when the salts in an albuminous solution are increased, the albumen transudes more readily through animal membrane, and there is every reason to believe that this holds good in the case of the blood—that when its salts are in excess its albumen may more readily pass through the vascular walls. Urea itself has been found to exert the same influence as the salts; and it is possible that in some instances albuminuria is in this way produced, or at least that its occurrence is favoured. But of this I know no definite evidence except that afforded by Lépine's[44] experiments upon dogs, in which he found that

temporary albuminuria resulted from the intravenous injection of chloride of sodium in the proportion of 1 gramme to each kilogram of the animal's weight. Notwithstanding the interest of this result it seems unlikely that the increase of salts can in any instance be an important clinical factor.

The opposite view, according to which albuminuria is supposed to result from deficiency of salts, and especially of chloride of sodium, has been ably dealt with by Professor Stokvis,[36] who tells how Wundt,[45] having experimented upon himself by using saltless food for a number of days, induced albuminuria; his results being confirmed by experiments which Rosenthal[46] performed on animals. Stokvis made two series of experiments on himself—abstaining from the use of salt on one occasion for five days, and on another for seven; but although the urine was changed in various important respects, it never showed a trace of albumen. He experimented also upon the dog and the rabbit, feeding the animals in various ways, but without or with very little salt, with results entirely confirming the experiments made upon himself. I am not aware that deficiency of other salts has been blamed. This view must also be rejected.

As to the idea of excess of one or other of the normal albumens of the blood, there are two which might be increased, namely, — serum-albumen, and serum-globulin. Estelle[47] and Faveret,[48] working under the direction of Lépine, found that when they injected watery solutions of serum-albumen and globulin into the veins of animals, albuminuria resulted, the variety excreted corresponding to that introduced. Now, it is very natural to suppose that during digestion, when the proportion of albumen in the blood must be greater than at other times, the excess of it may in part transude through the renal vessels; and when we consider how often some trace of albumen appears after meals, and how frequently a copious dieting with eggs induces the condition, it is difficult

to resist the conclusion that in some cases this must be a cause of albuminuria. Still, there are difficulties in the way of accepting this as the full explanation of such albuminurias ; for the most albuminous meals do not seem to be the most apt to produce the symptom. An ordinary breakfast cannot be held to be as albuminous as an ordinary dinner ; and yet it seems to be after breakfast rather than after dinner that the condition is apt to occur ; and if the explanation were to be found here, albuminuria after food ought, one would think, to be even more common than it is.

As to the development of abnormal forms of albumen within the blood—forms more capable of transudation than serum-albumen and globulin—we have extremely little evidence.

Professor Semmola[49] of Naples is at the present day the most ardent advocate of this explanation of albuminuria. Indeed, he is of opinion that the organic lesions of Bright's disease are secondary results of irritation of kidneys, due to the discharge of an abnormally diffusible albumen, which he supposes to be present in the blood. But the arguments and observations which he adduces in support of his view are far from convincing. And, indeed, one feels that the suggested explanation is still simply hypothetical.

The results elicited by Stokvis in two of his injection experiments are certainly suggestive in this connection. He found that in these two instances, and in them alone out of twenty-three, albumen appeared in the urine of the animals operated upon, and in both cases the urine used for injection had been taken from a patient suffering from albuminuria without definite renal disease. It seems probable that the case may have been one of functional albuminuria, and that an easily diffusible form of albumen existed in the urine.

The appearance of peptones in the urine cannot, of course, be explained by anything occurring in the renal secreting structures or the urinary tracts. They must, whatever their

origin, be derived from the blood. They are not usually given in works on physiological chemistry as normal constituents of the blood; indeed, the researches of Ott and Collmar[50] point to the conclusion that they act as poisons, producing fever. But we are fully warranted in concluding that they are sometimes present. Otherwise how could their presence in the urine be explained? They filter more readily through animal membranes than serum-albumen or globulin, and, when introduced into the circulation, are passed out by the kidneys, and the presence of an excess of this variety of albumen in the blood may therefore be recognised as a cause of albuminuria. Egg-albumen also, when introduced into the blood, or injected subcutaneously, passes out as such with the urine; but seeing that in the artificial albuminuria induced by the ingestion of large quantities of uncooked white of egg, it is not egg-albumen which transudes but serum-albumen, we must conclude that this variety practically never occurs in the human subject. Experiments have further shown that the injection of milk or of solutions of casein into the blood of living animals is usually followed by discharge of casein or other albuminous substance with the urine, but the use of milk and cheese as articles of diet does not, unless as a result of idiosyncracy, produce albuminuria. As to the idea of other forms of albumen resulting either from transformation of the normal albumens of the serum, or of the albumen of the corpuscles, we have, so far as I know, no definite knowledge at present. There are some facts which favour the opinion that changes in the corpuscles may induce it. Dr. Ralfe[51] has worked out, with great ability and elaboration, a view which I have been in the habit of teaching, that a form of albuminuria stands closely related to hæmoglobinuria. He has shown what we may call three stages in the process of abnormal disintegration of red blood corpuscles within the liver—the first marked by increase of urea, the second by that and

albuminuria, the third by the further addition of hæmoglobinuria. The mere albuminuria in these cases might be ascribed to the action of an irritant upon the kidney tissue, but the hæmoglobinuria is not susceptible of such an explanation, and if it is not, the other also may not be so explained. Here, then, it may be that we have an altered albumen transuding more readily, but further investigation would be required to bring out fully the chemical differences between it and ordinary blood-albumens. Rosenbach,[52] working somewhat in the same lines as Ralfe, had come to the conclusion that probably in certain morbid conditions the albumens of the blood are set free from their normally close combination, and so are readily eliminated. This explanation is also, in the meantime, purely hypothetical, so far as the blood is concerned. And, even if it were proved, the question would remain for discussion, Why the kidneys should permit of its elimination ?

Lépine's[53] ingenious suggestion that the albumen may be chemically combined with foreign substances introduced into the blood, and may in such combination act as an irritant to the kidney and thereby produce albuminuria, is also, as yet, hypothetical.

Globulin transudes more easily than serum-albumen ; and Dr. Maguire[54] has found that in some cases of functional albuminuria there was relatively more of globulin than of serum-albumen, and he even met with globulin alone. In a case of purpura which many of you will remember as having been recently in my wards, and in which albumen was abundantly present in the urine, globulin was present in larger quantity than the serum-albumen ; and it is possible that, had that case been entirely free from renal inflammation, there might have been no serum-albumen at all, but simply the globulin. In that patient I believe disintegration of red corpuscles was going on far in excess of the normal. It may

turn out that, not only in purpura, but in scorbutus, in pernicious anæmia, and in simple anæmia, albuminuria may be partly due to this cause; and I have no doubt that careful clinical and chemical work in this direction would be abundantly rewarded.

In connection with the injection of egg albumen the very interesting and suggestive fact has been elicited by some of the experiments, that a greater quantity of albumen is passed out by the kidneys than had been injected into the blood. This points either to changes set up in the blood by the presence of the egg albumen, or to irritation and structural changes in the kidneys themselves.

I would have you then conclude that, while the albuminuria of Bright's disease is not of hæmatogenous origin, there is some reason to believe that certain other varieties may arise from changes in the blood, perhaps from excess of salts, or from excess of albumen, or from the presence of abnormal forms of albumen.

II.—Altered States of the Filtering Apparatus.

When we consider such a process as that of secretion of urine, it is obvious that it must be greatly influenced by the character of the membrane through which the filtration occurs; and it is natural to suppose that altered conditions of the filtering apparatus may sometimes determine albuminuria.

This apparatus is composed, as we have seen, of the loops of vessels in the Malpighian tufts, with their covering of flattened epithelium, and it is conceivable that transudation of albumen might result either from changes in the vessel walls or in the epithelium, or in both. The change in the vessel wall, with which we are most familiar, is the waxy or amyloid degeneration; and in the earliest paper which I wrote upon Waxy Kidney,[55] I suggested, as a hypothetical explanation, at once of the polyuria and albuminuria, which are characteristic of that disease, an abnormal permeability of the vessel walls.

This view has been very generally accepted as probable, but no positive proof of its correctness has been forthcoming, and it must stand as a suggestion rather than as a demonstrated fact. But Ribbert[33] has found that in cases of the kind there is, in addition to the vascular change, a distinct alteration in the cellular elements of the Malpighian bodies—in fact, a glomerulo-nephritis. He says, that in slightly affected glomeruli, where only individual loops were diseased, he found the albumen within the capsules, and undeniable changes in the epithelium, which clearly indicated a slight degree of glomerulo-nephritis. In one case, fatal at an early stage, which I lately examined, there certainly were changes of this kind superadded to the slight vascular alteration, and it may be that to this secondary, rather than to the primary change, the albuminuria must be referred. In either case, however, the starting-point is in the vessels.

In all the ordinary cases of glomerulo-nephritis, such as we see typically after scarlet fever, the filtering apparatus is manifestly at fault, and the researches of Ribbert point to the conclusion that, under a great variety of conditions, similar changes arise in the nutrition of the vessel-walls and their epithelial covering. The vessels, being nourished by the blood which passes through them, suffer whenever that blood is faulty in character or deficiently supplied. When it is loaded with such substances as phosphorus or carbolic acid, he finds that characteristic changes occur in the Malpighian bodies. So also when the renal arteries are clamped for a short time—say, for a quarter-of-an-hour—slight changes occur; if the experiment be continued for half-an-hour, the results are much more pronounced. Similar failure of nutrition has been shown to follow hindered outflow of blood in consequence of venous stasis, or of urine from obstruction of ureter, and to occur after serious hæmorrhages, after cholera, in severe anæmia, and in advanced carcinoma; and perhaps in such blood diseases as purpura and

scorbutus, there is a corresponding alteration of the filtering apparatus.

It is obvious that the causes which induce changes in what we have termed the filtering apparatus proper, cannot be limited in their operation to these structures, but must often affect the epithelium of the tubules generally, and the interstitial tissue of the kidneys as well, so that uncomplicated alterations of the filtering apparatus must be of the very rarest occurrence. For example, the effect of urinary stasis, while it induces changes in the glomeruli, has been shown by Aufrecht,[56] in his admirable work on diffuse nephritis, to extend to the epithelium of the tubules and other structures of the organ. We thus find these alterations of the filtering apparatus linked on to more extensive changes, which we shall consider somewhat later in the lecture.

I would have you, then, believe that albuminuria in waxy disease of the kidney, probably owes its origin to increased permeability of the vessel wall, or to this in association with changes in the glomerular epithelium, and that alterations of the filtering apparatus are to be recognised as the cause of albuminuria in some forms of poisoning, in fevers, and in many altered conditions of the renal circulation.

III.—Abnormal Vascular Tension and Altered Circulation.

The vascular arrangements connected with the Malpighian bodies differ from those of any other part of the economy in respect that they are composed of capillary loops covered with a layer of very delicate epithelium, and are guarded both at their entrance and their exit by arteries capable of regulating the current of blood flowing through them. Tension in the capillaries may thus be increased by relaxation of the afferent or by contraction of the efferent vessels, or diminished by spasm of the former and relaxation of the latter.

The two opposite conditions of increased and diminished tension have been suggested as possible explanations of albuminuria. The latter attracted a good deal of notice when it was first propounded by Professor Runeberg of Helsingfors.[57] He thought that when the vascular tension was diminished, transudation of albumen was apt to occur, founding chiefly upon experiments made by filtration through dead animal membranes under various degrees of pressure. It was clear enough that albuminuria often made its appearance when the blood pressure in the kidneys was diminished, as, for example, in many varieties of anæmia, and after clamping of renal arteries. Herrmann[58] and Von Overbeck,[59] had ascertained that when the renal artery was temporarily constricted, the urine secreted at the time was scanty and albuminous. And François[60] has shown that the albumen in these conditions transudes through the Malpighian bodies. It is clear that anatomical changes in the filter arise in many of these cases, and it is not improbable that the albuminuria is due to these changes rather than directly to the diminished supply of blood. But that diminution of tension is not the great cause of albuminuria has been conclusively shown by Senator,[20] Litten,[61] and others. I am not sure, however, that the views which Runeberg intended to express have always been correctly understood. I have, along with Dr. Stevens, made a number of experiments bearing on the filtering process. We found that an albuminous and saline solution placed so that it might filter through a membrane, transuded with increase of pressure a much larger proportion of the water and the salts within a given time, but that the amount of albumen was also increased, although not in the same proportion. We found moreover that when the experiments were prolonged, the membrane became so altered that transudation after a time diminished and ultimately ceased, and it appears pro-

bable that fallacies due to this fact have not always been avoided.

Recognising the fact that increase of pressure leads to increase of transudation through membranes, outside of the body, how does it stand in relation to the process within the kidneys of living animals ?

It is reasonable to suppose that increased vascular tension exists in the renal veins, and possibly also in the Malpighian tufts in cases in which the outflow of blood from the kidneys is hindered. That albuminuria results from venous stasis has been proved experimentally by many, among whom I shall name Dr. Robinson [61] of Newcastle, and it is a matter of every-day clinical observation. The stasis occurs mainly in the vessels surrounding the uriniferous tubules, and Senator [20] has demonstrated that it is from these vessels that the transudation of albumen first takes place. He found that if he ligatured the renal veins of animals, and killed them in from eight to fifteen minutes afterwards, an albuminous exudation was distinct in the tubes and not in the Malpighian bodies, and that if he continued the experiment for a longer time, exudation occurred in the glomeruli also. In cases of cardiac or other disease hindering the outflow of the venous blood, the albuminuria may be ascribed primarily to the vessels surrounding the tubules, but also to the Malpighian bodies. Although in these cases increase of pressure within the vessels may be held to exist, it does not follow that it causes the albuminuria. It may be maintained that the real cause is a slowing of the circulation, as has been suggested by such high authorities as Litten,[34] Posner,[62] Heidenhain,[63] Bamberger,[64] and Charcot,[65] but I have not been able to satisfy myself of the weight of the evidence which they adduce in support of this opinion. It may also be maintained that nutritive changes occur in the epithelium which favour transudation. But, on the whole, and especially in consideration of Senator's[20] observations, I am

inclined to ascribe the transudations to increased intravascular tension.

It is very doubtful whether increased pressure in the arterial system or within the Malpighian bodies is capable of producing albuminuria. Attempts have been made to increase the blood pressure in the renal vessels by tying the aorta below the point of origin of the renal arteries, by this and tying other vessels, also by cutting out one kidney, but it is more than doubtful whether the blood pressure is really raised by such proceedings. The results as to albuminuria have also been inconstant. Attempts have been made to ascertain whether the increase of pressure within the aorta produced by electrical irritation of the cervical portion of the spinal cord, and by the administration of such poisons as strychnia and digitalis induces albuminuria. The results show that if albumen is transuded, it is not at the time that the aortic tension is greatest, but afterwards; the explanation being that the aortic tension is due to spasm of the small arteries, and it is only when this spasm has relaxed, and the circulation become re-established, that the symptom occurs. One difficulty which attends this inquiry arises from the fact that the tension in the Malpighian bodies does not necessarily correspond to that in other vessels.

Clinical evidence also lends little support to the opinion that increased pressure within the Malpighian tufts induces albuminuria. In diabetes insipidus there must be increased blood pressure, and yet albuminuria is a rare accompaniment of this disease. Many of you have watched the case at present under treatment in the Alexandra Ward, and have noted that the urine has sometimes amounted to 600 ounces in the twenty-four hours, but you remember that the most delicate tests failed to give positive evidence of albumen. Such observations necessarily throw a shade of doubt over the occurrence of albuminuria simply from increase of tension

within the Malpighian tufts. Again, if one watches the action of digitalis and similar diuretics, one notices that so far from the quantity of albumen increasing as the diuretic action is brought out, it actually diminishes or entirely disappears, and yet the diuresis can only be explained on the hypothesis of increased blood pressure. There must also be a marked increase of pressure within the Malpighian tufts in many cases of renal cirrhosis, when the urine is excessive, and yet in such cases the amount of albumen is often trifling.

There are, however, some conditions in which increased tension may be reasonably held to be at least associated with albuminuria. Muscular exertion is one of these. With such exertion the tension necessarily rises, and we have seen how often severe muscular exertion suffices to produce albuminuria,—as among the soldiers on fatigue duty and the boys at football. I know of no explanation of these facts more satisfactory than the hypothesis that the increase of pressure suffices to produce it. We have also seen that in the course of fever albuminuria often occurs, the arterial tension being sometimes simultaneously increased; and experiment has shown that animals exposed to high temperature often exhibit the symptoms. It may be that the increased tension is one factor in its production. But at the best this could only be regarded as one of several influences in operation.

Another group of cases which might with considerable probability be referred to alterations of vascular tension is that including albuminuria from changes in the nervous system.

The influence of that system upon the kidney, and especially upon its circulation, has been the subject of many experiments, and it may be well to indicate some of the anatomical and physiological points which have been ascertained. Although the capsule and the pelvis of the organ are sensitive, the substance does not seem to be largely

supplied with sensory nerves. Neither do we know anything of nerves which influence the actual secretory processes performed by the cells. But as to the influence of the nervous system on the circulation, a good deal has been made out.

The vasomotor nerves run from the cortical substance of the brain through the crura to a centre in the medulla oblongata. Fibres reach the same centre from the cerebellum. From the medulla fibres pass downwards along the lateral column of the cord and pass out along with the anterior nerve roots, receiving fibres from independent vasomotor centres in the anterior horns. They pass out between the seventh cervical and the twelfth dorsal and enter the sympathetic, and form the sixth, ninth, and tenth thoracic ganglia. Thence they make their way through the splanchnic, cœliac, and renal plexuses to the vessels of the kidney. Their irritation contracts the vessels, producing pallor and slowness of circulation and secretion. Their paralysis dilates them ; in consequence, the kidneys swell, circulation quickens, and secretion increases.

Irritative and paralytic results may be experimentally produced at any point in the course of the fibres.

It appears also from Roy's[66] experiments that there are nerve structures within the kidneys which influence the vessels, for changes may be produced in them by passing currents of certain salts through kidneys whose nervous supply has been cut off.

That it is possible for albuminuria to be produced by the influence of the nervous system is shown by its appearance after apoplexy, epilepsy, and hysteria, as well as its experimental production by puncture of a point in the floor of the fourth ventricle. These conditions may result from vascular dilatation directly produced, or as a secondary result of spasm, or perhaps from impairment of nutrition of the filtering apparatus in the Malpighian bodies. But our present know-

ledge does not warrant our expressing a positive opinion as to what the precise connection is. Certainly we have no definite proof of its being due to increased intravascular tension.

I would have you then believe that albuminuria may result from increased pressure within the vessels of the kidney, both in cases of cardiac and pulmonary disease, which have led to hindrance of circulation, and under other conditions, but that neither increase nor diminution of intravascular tension is an important direct cause of albuminuria.

IV.—Morbid Action of the Epithelial Cells of the Tubules and of other Structures of the Kidney.

It is difficult to give absolute proof of the influence exerted by structural changes in the kidney elements proper, because it may be maintained that although they are distinct enough in themselves, they produce albuminuria only by altering the circulation, or otherwise modifying the conditions of secretion. But when we consider how everywhere throughout the body transudation of albumen takes place in connection with the inflammatory process, we perceive how this must occur in the kidney also. Indeed, it is obvious that this feature of inflammation should be conspicuous among the symptoms of disease in such an organ as the kidney.

In the severest inflammatory changes such as we see in acute renal atrophy, often associated with acute atrophy of the liver, in phosphorus poisoning, in the sudden inflammations which occasionally supervene in the course of diabetes mellitus, and with tumours of the kidney, the amount of albumen is very great. Its quantity varies in those less rapid inflammations which follow scarlet fever and other acute maladies. It is still less abundant where the process is more chronic in character or limited in extent; but, the rule is, that wherever inflammatory action in the kidneys exists, albumin-

uria is distinct. In long standing cases of chronic inflammation, the albumen may be discovered at every examination through many years.

Admitting, as every one does, the association of these clinical and anatomical conditions, two lines of explanation have been suggested. On the one hand, it is maintained that while the urine is in the healthy condition secreted free from albumen, in the course of inflammatory action albuminous materials are copiously drawn from the blood, and discharged along with the secretion. On the other, it is suggested that whereas in health the watery part of the blood which filters through the Malpighian tufts is accompanied by albumen, and only gets free of it by the absorbing power of healthy renal epithelium, so that by the time it reaches the lower parts of the tubular system it has become a practically non-albuminous fluid; in inflammation, the epithelium losing this power, the albumen passes freely down along with the watery secretion. But even the most strenuous supporters of this view seem to admit that in inflammation of the tubules inflammatory exudation must account for some of the albumen. On the whole, it appears to me most reasonable to accept the first view in its entirety as the most satisfactory explanation both of the acute and chronic inflammatory albuminuria.

To sum up the results, then, I would have you believe that albuminuria is very often due to changes of an inflammatory character in the epithelium of the tubules and in the stroma of the organ, and that in a very large proportion of the cases in which it occurs in practice it is dependent upon this cause; that increased blood pressure is a factor of some importance; that increased permeability of the filtering apparatus induces it in many instances; and that there may be some conditions of the blood which account for it or favour its occurrence.

LECTURE V.

ON ALBUMINURIA FROM INFLAMMATION OF THE KIDNEYS.

Synonyms.—Case of Acute Inflammation with Uræmia.—Varieties of Features with same Lesion.—Very Chronic Case.—Non-Infective Chronic Case.—Case with Pericarditis.—Explanation of the Albuminuria.

GENTLEMEN,—I purpose now to go over the different categories which have emerged in our study of the incidence of albuminuria, and I shall begin with the best-known and simplest forms, those in which organic change of kidney is the cause, leaving over, meanwhile, the consideration of the obscurer groups, such as the albuminuria induced among healthy people by diet or exercise. Our first category embraces various forms of renal lesion which we are accustomed still to rank as Bright's disease. It includes in our series of 450 patients (400 under my own care, and 50 in the Children's Hospital), 48 cases in all. Of these, 16 were inflammatory, 11 cirrhotic, 14 waxy, and 7 mixed. To-day I shall bring before you a series of cases illustrating the variety of renal lesion which has been termed inflammatory Bright's disease, parenchymatous nephritis, tubular nephritis, or desquamative nephritis. I shall first show you a patient who was not treated in the Infirmary, but whom I saw in private, and who has to-day come that you may judge of his condition. He is a school-boy, twelve years of age. He lately passed through an attack of

scarlet fever. The fever was never severe, and desquamation went on satisfactorily. During its continuance he was kept perhaps less strictly to milky food than one could have wished, and unfortunately was exposed one day to a draught of cold air. The next morning he had become seriously ill, his face pale and pasty, his eyelids swollen, dropsy rapidly developing in hands and feet, and throughout the body generally. His urine was scanty in amount, of dark colour, of high specific gravity, highly albuminous, depositing urates on standing, and the microscope showed it to be loaded with blood corpuscles and with epithelial, hyaline, granular, and bloody casts. The utmost care was taken, and suitable remedies employed, but the condition steadily became worse, and towards the evening of the second or third day of the illness nervous twitchings of muscles manifested themselves, and during the night uræmic convulsions and coma set in. I was asked to see him in the early morning, and immediately injected a sixth of a grain of pilocarpin subcutaneously, applied hot bottles all round the body, and put on extra bed-clothes. Under this treatment, very copious diaphoresis was established, and the uræmia began to subside. The action of the skin was kept up, while the bowels were freely relieved by a hydragogue cathartic, and the kidneys acted upon by digitalis. The quantity and quality of the urine speedily improved, and the symptoms subsided, so that, as you see, the patient now presents a healthy appearance, and the urine, which is in good quantity, shows no albumen with the nitric acid test.

This is a good typical instance of the infective form of this malady. It is not necessary for me to describe minutely the appearance which the kidneys would have presented had they been examined during the anxious days of the acute attack. Your experience enables you to depict this accurately in your own minds. Rather above the natural size,

the capsule stripping off readily, the surface generally congested, and probably marked here and there by minute hæmorrhages, they would have shown on section the cortical substance swollen, with general congestion, scattered hæmorrhages, and an altered condition of the tubules, perceptible even with the naked eye. Microscopical examination would have revealed an opaque condition of many tubules, due to swelling and rapid inflammatory destruction of epithelium, and in some parts extravasation of blood, while the glomeruli and stroma would almost certainly have shown more or less of the inflammatory changes characteristic of glomerular and interstitial nephritis. But now all that is happily changed;—if we were to examine his kidneys to-day, we should find them practically normal; perhaps here and there a tubule may still show traces of the recent inflammation, perhaps at some points the glomeruli or interstitial tissues might still show alterations, but these, if they exist, will I hope pass away and leave no trace behind.

You have seen in the wards other cases of this kind which never showed the same dangerous symptoms, and you will find, as you gather experience in practice, that the varieties of feature presented by these cases is very extraordinary. You may sometimes see the urine almost black, and scarcely any dropsy present; at others, the dropsy may be so severe, serous effusion being added to the general anasarca, that death is threatened from obstruction to respiration and circulation. You may see the illness so slight that it is never formidable, and passes away in a few days, or you may see it prove fatal in a few hours, or you may see it set up chronic changes in the kidney which, after persisting for years, at last terminate fatally. I lately met a remarkable instance of this kind of case in a lady about forty-three or forty-four years of age, whom I knew well, having frequently seen one of her relatives during a very formidable illness through which he passed.

She looked healthy, was active, full of animation, and worked night and day during the anxious months of her friend's illness. But she used casually to say, "You know that I have got albuminuria, and have had it for many years." About a year later she came to see me, looking very different from her former self. She was pale and breathless, and her feet and legs were swollen, and on going into her case, a full discussion of which she had previously wished to avoid, I elicited this history. She had been quite healthy as a child, but at eight or ten had scarlet fever. This was followed by nephritis apparently of a very serious type, but in the end she recovered to a great extent, and when she grew up showed no bad symptom except persistent albuminuria. She went on living like other people, and mixing in all the most fashionable life in London, till her marriage, at the age of two-and-twenty. She was an accomplished horsewoman, and rode regularly to the hounds. She had no bad symptom at the birth of any of her six or seven children, and I believe showed rarely anything to attract attention beyond the albuminuria, which was carefully watched by the very skilful practitioner who was her ordinary attendant. The arterial tension by the time she consulted me had become distinctly increased. The heart was hypertrophied and dilated, and the mitral valve incompetent. She had recently suffered a good deal from gout, and from the symptoms of cardiac dilatation and valvular insufficiency. She gradually lost ground, and ultimately died of a combination of dropsy with uræmia. There was no opportunity of making a post-mortem examination, but the facts which I have given afford satisfactory proof that the post-scarlatinal nephritis had initiated chronic inflammatory action, which went on for more than thirty years, and at last terminated fatally. In her case you will observe that there must have been at first extensive disease of the tubules, with affection of the glomeruli and stroma, that the tubules recovered to a great

extent, but all the while insidious changes were going on in the stroma, so that the organs underwent a very gradual atrophy. Changes were set up, and secondary complications at length ensued, which the system, enfeebled by fatigue and gout, proved unable to resist.

Besides such infective forms of renal inflammation there are non-infective varieties which present a history very similar to the above, except in respect of their etiology. I shall draw your attention to one case illustrative of certain points which I deem important, and which I watched with great care a number of years ago. When he came under my care, R. P. was a man of twenty-six, and till January, 1865, had been quite healthy. His trade had been that of a baker, and later he was a maltster, and in this, as in his former occupation, he was often exposed to vicissitudes of heat and cold. He was admitted to the Infirmary on the 3rd of March, suffering from severe dropsy and uræmic convulsions. Under treatment, by means of cupping over the kidneys and diuretics, he improved to some extent, but again relapsed, and while the head symptoms did not reappear the dropsy became very pronounced. Diuretics of various kinds, including digitalis and acid tartrate of potash, were tried without good result, but diuresis was established by the inhalation of oil of juniper, a remedy which you will sometimes find useful where other diuretics fail. Punctures were made in the skin of the legs with the view of draining off the dropsical fluid, and very good results followed. When the dropsy disappeared, the urine continued in fair quantity, the albumen became less, the casts much fewer, and the urea reached its normal standard. He was dismissed from the Infirmary five months after his illness began, in all respects well, except that his urine was albuminous. You will often see cases with histories more or less closely corresponding to this. I wish that we had it in our power either by diet or by medicine to check the lingering inflammation which is still

going on and really get the patient restored. Having left the Infirmary, he was necessarily exposed to cold, wet, and changes of temperature. Soon he got worse, and in three months returned with a renewal of all his bad symptoms. The urine was again diminished, the dropsy considerable, and uræmic convulsions recurred. Under treatment with diuretics he again improved, and was dismissed for the second time, nine months after the commencement of his illness. A few months later he came to the hospital, said he felt quite well, and there was really nothing to be detected wrong with him except that his urine contained some albumen. In March, 1871, he returned, stating that he had again caught cold, and that although during the intervening years he had been able for his work, he never had been quite strong. His urine had been up to the normal amount, but he had had occasion to rise once or twice every night in order to micturate. His heart was found to be enlarged, its muscular substance weak, the second sound was accentuated in the aortic area, and the first was muffled and rather indistinct. His vessels were thickened. His urine amounted to ninety ounces daily, was highly albuminous, and contained hyaline and granular casts. He occasionally suffered from headache, but there were no eye changes, and no tendency to fits. In June of the same year he returned in a feebler condition, but again rallied. From time to time he came into the Infirmary, gradually deteriorating in health, and with occasional returns of dropsy. At length, after his illness had lasted for eight years, his age then being thirty-four, he looked like a man of at least fifty. His face was pale and rather pinched, his general health was very poor, every system being more or less unsound. With feeble digestion, impoverished and impure blood, diseased heart and vessels, embarrassed respiration, a tendency to dropsy, deficiency of solids in urine, and disordered nervous system, he gradually became worse

and worse, and ultimately died of uræmia. His kidneys were found somewhat atrophied, granular, and uneven on the surface. The capsule tore off with some difficulty. There was a distinct relative, probably even an absolute increase of fibrous stroma, but the most interesting histological point was the blocking of many of the tubules with inflammatory products, the tubules presenting a great variety of shape, some of them altogether obliterated. It was evident that the diminution of bulk of the organ was not mainly due, as in cirrhosis of the kidney, to a shrinking of the fibrous tissue, but in part at least, if not chiefly, to the molecular absorption of the contents of the tubules, in the way that I have tried to explain in my work on Bright's Disease.[67]

It is not necessary to bring before you other individual instances of a condition which you see so frequently in the wards. It may suffice if I recall one example which must have impressed itself deeply on the minds of many of you. You remember the case of the young man who had for about seven months suffered from inflammatory Bright's disease, who had persistent dropsy, copious albuminuria, hypertrophy of heart, and extraordinary increase of arterial tension. You remember how that patient one day at our visit was observed to have an altered appearance, with marked depression. His face was pale, the tension of the pulse was gone, the action of the heart had become feeble; he had a good deal of pain in the precordia and epigastrium, and many of the members of the class had the opportunity of hearing the intense friction when they listened over the heart. In that patient pericarditis had set in, and it proved rapidly fatal.

In the course of chronic cases symptoms and complications arise which are often more immediately dangerous than the disease itself. I do not enter upon their consideration at present, as I intend to discuss them in future lectures, after I have made you familiar with the general features of other

forms of renal disease. Neither shall I at the present time go into the subject of treatment. You have seen what line was followed in each of the cases adduced, and other opportunities will present themselves of discussing it at length.

The question remains as to the cause of the albuminuria in these cases. It seems to me that there can be no reasonable doubt that it is due from first to last to the inflammatory action—that the inflammation, whether acute or chronic, leads to the transudation of serum from the blood, and so to albuminuria. No doubt the breaking down of the epithelial structures contributes to this in some measure, but that measure is small when compared with the exudation element.

LECTURE VI.

ALBUMINURIA FROM CIRRHOSIS OF THE KIDNEYS.

Synonyms.—General Features.—Case of fully Developed Disease.—Case in Early Stage.—Renal Inadequacy.—Explanations of the Albuminuria.

GENTLEMEN,—I shall show you to-day some cases illustrative of one of the most important causes of albuminuria—cirrhosis of kidney, a condition often spoken of as contracting kidney and gouty kidney, sometimes as rough granular kidney.

The first glance at this patient suggests the probability that he is suffering from chronic Bright's disease. You observe the peculiar pallor of his face, the fulness of the lower eyelids, the localised sparkle of his eyes, due to œdema of the conjunctivæ, the somewhat blank expression so common in those who do not see well, the prominence and tortuosity of the temporal arteries, and when you put your finger upon his radial artery, it feels like a cord or tendon rather than a normal vessel. Such a group of symptoms suggests at once to any one familiar with the disease, that the patient is the subject of renal cirrhosis.

But while such an appearance may be said to be pathognomonic of this condition, it is by no means constant. For you often see men, and still more frequently women, who have long suffered from the malady, whose general appearance presents nothing to attract attention. And

again, you may see a vascular congestion, or a muddiness or dirtiness of skin, or a general duskiness with congestion over the nose and cheeks, contrasting remarkably with what I show you in the present patient.

The great outstanding features of this disease are, so far as the urine is concerned, the normal or somewhat excessive quantity, the pale colour and low specific gravity, the presence of albumen in moderate amount, the deficiency of urea and the paucity of tube casts; and, so far as concerns general symptoms, the consequent changes in the digestive, circulatory, respiratory, and nervous systems.

This patient, J. S., a joiner, is in his twenty-sixth year, an earlier age than is common in the disease. Still as you gain experience you will often enough see it in young people. It is most common in its fully developed form between the ages of 40 and 55, and in lesser degree it is common at a more advanced age. I have often met with it in adolescents and sometimes even in children.

He came from Sunderland, seeking advice as to headache, and dimness of sight, having suffered from the former for two years, from the latter for eight months. Patients affected with renal cirrhosis rarely come to you complaining of their kidneys. It is after a convulsive attack, or on account of palpitation, or breathlessness, or dyspepsia, or, as in this instance, for headache and dimness of sight, that they are led to seek advice; and these symptoms do not arise until the disease has existed for a long time, even as long as from five to eight years. There is no difficulty in diagnosing the condition at this stage; it is much more difficult to make it out in the earlier part of its course.

His parents are healthy, and, so far as I could discover, there was no case of Bright's disease among his relatives. Now and then we find a different history. Sometimes one, sometimes many relatives have died of the disease. I have

met with at least one family in which its prevalence and fatality were terrible, and several in which it was recognised as a family complaint.

He never drank to excess. Indulgence in alcohol is a well-known cause of the malady, and that not only in those who indulge in drinking bouts, but also in those who habitually drink too much, although they do not become quite intoxicated. Among my cases in young people there has, as a rule, been no alcoholic taint.

It is possible that another cause may have been in operation—viz., lead-poisoning. As a ship-carpenter he may very probably have been in contact with paints containing lead, but of this we have no proof. You remember the case of the house-painter, at present under treatment on account of renal cirrhosis, in whom lead-poisoning was undoubtedly one of the chief causes ; and in not a few of your cirrhotic cases you will find that the same influence is at work.

He had scarlet fever at eight, followed by otorrhœa, but neither by dropsy nor other renal symptoms, and he says that he considered himself a quite healthy man till about a year ago. We may therefore conclude that his renal disease is not a sequence of the fever.

The headache at first used to last a day, gradually it became more persistent, and was attended by noises in the ears. Eight months ago he began to have difficulty in reading, and soon became unable to read ordinary newspaper type. The right eye was worse than the left. He suffered also a good deal from pain in the small of the back.

For three years our patient acted as carpenter on board ship. He often passed through the Red Sea, and he noticed that his headaches were worse there. We can well understand how with the stress of his work as ship-carpenter, the climate of the Red Sea should have induced headaches, or contributed to their production, but they were

doubtless mainly referable to the insidiously advancing renal disease.

When we come to examine his condition according to our usual method, we find in the alimentary system that his tongue is flabby and somewhat furred. He frequently complains of dyspeptic symptoms, such as pain after food, heartburn, flatulence, and vomiting, and he suffers from constipation. The liver is of normal size. Some enlarged glands are felt at the back of the neck, but the spleen and other blood glands are normal. The red corpuscles vary from 3,040,000 to 3,690,000, the hæmoglobin from 40 to 48 per cent. There is some dyspnœa on exertion, but the heart shows no marked increase in size, and there is no cardiac murmur. The first sound in the mitral area is impure, and has somewhat of the booming character which one expects in this disease; while in the aortic area the second sound is distinctly accentuated. The beat is somewhat irregular. The pulse is of high tension, and the vessels are thickened. The lungs are normal. The skin acts freely enough, and is not œdematous. During the last eight months micturition has been more frequent than formerly, and he has required to get up three or four times during the night. During his stay in the Infirmary the daily quantity of urine has varied from 60 to 90 ounces, and the specific gravity has usually been about 1016 or 1017. The albumen has varied from 4·2 to 9·6 grammes per litre. The microscope has revealed the presence of a few tube casts, and occasionally some blood corpuscles. The daily discharge of urea has usually been between 300 and 450 grains, but has been as low as 249 and as high as 496 grains. There is, as before stated, marked impairment of vision in both eyes. The right pupil is slightly more dilated than the left. Ophthalmoscopic examination reveals atrophy of the discs following upon optic neuritis. In the right eye

there is a white irregular patch at the macula, with small white spots round it, the result of old hæmorrhages. There is a line of hæmorrhage between the macula and disc, and a pigmented spot below the disc. The left eye shows extensive partial atrophy of the choroid at its lower periphery, from old choroidal disease. The patient, as a result of his old otorrhœa, is deaf in his right ear. He feels the pulsation of the arteries in his head in a disagreeable way. There is nothing else worthy of notice in the nervous or locomotary systems.

There can be no doubt as to what the condition of the kidneys is. You have had many opportunities of examining such organs. They would be found somewhat reduced in size, perhaps very considerably, and not necessarily both to the same extent, for the disease does not always advance *pari passu* in the two organs. The capsule, being adherent, would be separated from the kidney with difficulty, and the surface presented would be uneven and granular, with numerous elevations and depressions. On cutting it open, the kidney would feel denser, more fibrous than usual, and on section the diminution in bulk would be seen to be mostly towards the surface. On microscopic examination the fibrous stroma would be found much increased. The tubules would show in many parts no trace of their normal structure, but would be closed up, and here and there there might be cystic dilatations in the course of some of them. The Malpighian tufts would vary in size, many of them compressed and destroyed, their capsules greatly thickened. The small arteries would be thickened, especially in their middle coat, the muscular layer markedly increased. Throughout the body generally the vessels would show considerable sclerosis, even those of the size of the radial arteries. The left side of the heart would exhibit a certain amount of hypertrophy. The gastric mucous membrane would show some evidence of catarrh.

The retina would exhibit the changes characteristic of albuminuric retinitis.

This case affords you a typical instance of renal cirrhosis as we see it at the stage at which it is usually diagnosed, and you will observe that there is no difficulty in making it out, but the case is otherwise when we have to deal with the malady in its incipient or early condition. I cannot show you an illustration of the early stage, but shall describe a case which I have had under observation for some years. The patient is a gentleman between 40 and 50, who says that as a lad he had knocked about the world a great deal and taken an excess of alcohol, but from about the age of 20, while living freely, he had not exceeded. He used to be a hard rider, many hours in the saddle almost every day. When about 40 he felt somewhat out of health, and on examination it was found that the urine was of low specific gravity, of fully normal quantity, and contained a slight trace of albumen. Very careful examination elicited no additional symptom. There was no undue tension of pulse, no enlargement of the heart or alteration either of the first or second sound, no dimness of sight, nor any retinal change. Under treatment by regulation of diet and the use of arsenic the condition improved, the albumen entirely disappearing or being present only in faint trace now and then, the specific gravity becoming more satisfactory, the amount of urea coming up to nearly a healthy standard, and all feeling of unfitness disappearing. But now and again, from some slight cause, such as a little over-exertion at tennis or in riding, a little business anxiety, or such like, a relapse occurred, and for a few days, or perhaps weeks, there would be a recurrence of the symptoms. I have watched this patient through a number of alarming attacks, including congestion of lung with considerable fever, and temporary paralysis with some aphasia. During

the febrile attack his urine became highly albuminous, and tube casts were present, with sometimes a few blood corpuscles, but the amount of urea increased considerably, and when the fever subsided, the urine returned to its ordinary condition. The nervous seizure was of quite a passing kind, but was marked by numbness in one arm with loss of power, also by twisting of face from some paralysis of the seventh nerve, and by temporary aphasia. In a few days the symptoms diminished, and ultimately passed away entirely. They were probably due to the impaction of an embolus, which gradually disintegrated. When the patient resorts to a warmer climate, his health improves in every respect, the urea comes up to a normal standard, the albumen almost entirely and constantly disappears, but when he returns to this country the symptoms become less favourable. I believe that this patient suffers from renal cirrhosis in a comparatively early stage, and that during the febrile attack some degree of inflammation of the tubules became superadded to it. In his usual condition the patient corresponds pretty closely to what Sir Andrew Clark [68] has happily described under the name of Renal Inadequacy, while during his occasional attacks an actual lesion of the kidney becomes unmistakable.

What you have seen and heard to-day may suffice to give you a general idea of the clinical features of cirrhosis of the kidneys. But in order to give you anything like an adequate knowledge of the disease, it will be necessary to go over all the systems of the body, and explain and illustrate the various symptoms and complications which occur in each as the disease advances.

I shall conclude this lecture by inquiring what is the cause of the albuminuria in this disease? Of the four possible causes we must admit that perhaps there may be alterations in the blood favouring transudation of albumen, but of this there is at present no sufficient proof.

The altered state of the filtering apparatus is obvious, and it is certain that in some degree these changes account for the production of the symptom. Increase of blood pressure from cardiac hypertrophy and from hindrance to the course of the blood through the organ may be suspected as also contributing in some measure, but I believe that the chief influence is that of the inflammatory action which is so often associated with, even if it be not in all cases an essential part of the cirrhotic process. The inflammation must be attended by an increased transudation from the vessels, and this would account at once for the slight albuminuria which is commonly present, and the more pronounced discharge which makes its appearance occasionally with the acute exacerbations.

LECTURE VII.

ALBUMINURIA FROM CIRRHOSIS OF KIDNEY—(*continued*).

Clinical Importance of the Complications.—Gastric Catarrh.—Constipation.—Morbid States of Blood.—Disorders of Circulation.—Cardiac Hypertrophy.—Degenerative Changes.—Valvular Disease.—Pericarditis.—Changes in Arterial Tension and in Vessels.—Disorders of Respiration.—Dyspnœa from Pulmonary Causes.—Uræmic Dyspnœa.—Integumentary System.—Dropsy.

GENTLEMEN,—When I gave you a general account of the clinical features of cirrhosis of the kidney, I told you that it would be necessary to return to the subject when I should have the opportunity of pointing out some of the leading complications which are apt to arise in its course. In speaking of these I shall refer also to the way in which the different complications stand related to other forms of renal disease. I show you again the patient, J. S., and ask you to notice how marked is the disturbance of his digestive system. His tongue is furred, he has little appetite, and his power of digestion is very limited. But gastric symptoms of much greater severity often arise, and they are indeed not unfrequently dangerous to life. I recall the case of a gentleman whom I saw on many occasions in the country, and who at my first visit had so severe a gastric catarrh that he was utterly prostrated. His tongue was so covered with brown fur as to resemble a piece of drab moleskin. He loathed food, and the ingestion even of a little, produced

uneasiness culminating in vomiting. A little more and the patient must have died. But in this case, as in many others, the use of bismuth with soda and a little rhubarb and aromatic powder, the application of counter-irritants, and careful dieting with small quantities of easily digested food —milk, soups, or peptonised preparations—and the use of ice, or of very hot water, sufficed to give relief, and the emergency was tided over.

Do not forget that besides such acute or subacute attacks as I have indicated, the gastric digestion is always more or less impaired, and the dietary consequently requires attention.

The state of the intestines is often of much importance. I have at present under my care a patient suffering from rather advanced cirrhosis of kidney, with disease both of the valves and muscular substance of the heart, who suffered from the most distressing constipation, with painful hæmorrhoids. This patient's journey to Edinburgh was certainly a very hazardous one, considering the degree of debility to which he was reduced, but as soon as the constipation had been relieved, the immediate danger passed away, both the kidneys and heart improving materially. In this connection I may recall to you the case of Mrs. K., whom you saw suffering from uræmia in the Alexandra Ward, in whom the toxic symptoms, which soon became fatal, were probably partly due to the prolonged constipation before the patient's admission to the Infirmary.

Functional disturbance of the liver is also a common complication of renal cirrhosis; but organic changes of that organ are less frequent than we might expect.

With regard to the gastro-intestinal complications in other varieties of renal disease, you will find the later stages of nephritis correspond very closely to cirrhosis. Sometimes digestion is extremely impaired in the earlier stages of that disease also. Diarrhœa is not common in nephritis, and

affections of the liver are quite exceptional. With waxy degeneration of the kidney the case is quite otherwise, for very intractable dyspepsia, sometimes attended by hæmatemesis, is occasionally seen,[69] and diarrhœa is, of course, the best known symptom of the degeneration as it affects the intestine. Hæmorrhage also sometimes occurs from this source, a result either of simple rupture of vessels or of ulceration. The liver frequently exhibits the characteristics of waxy degeneration or syphilitic disease.

Passing now to the hæmopoietic system we find that deterioration of the blood may also be an important element in these cases. I have seen a patient in great peril from anæmia due to actual hæmorrhage. Epistaxis is the most common variety. Sometimes it appears as an early symptom, more frequently as a late one. Some of you may remember in this connection that in the case of A. C., which we studied at the bedside, and to which I shall afterwards have to refer in relation to cerebral hæmorrhage, there was a history of a severe attack of epistaxis six months before admission to the Infirmary. Sometimes there is a continuous oozing, which may be relieved or kept in check by the insufflation of styptics, at others a gush so considerable as to require plugging of the nares.

Some of your predecessors studied with me the case of a woman who had hæmorrhages not only from the Schneiderian membrane, but into the conjunctivæ, the eyelids, and other parts of the face; and occasionally you will meet with hæmorrhage from other sources, as from the uterus or the bowel. The hæmorrhages into the retina and into the brain substance fall to be considered in another connection. Occasionally hæmorrhage from the urinary tract itself complicates the disease, for pretty copious bleeding may occur from the kidney, and sometimes I suspect from the prostate or from the vesical mucous membrane.

I have satisfied myself that hæmoglobinuria is sometimes associated with this condition of kidney, and generally as an early symptom.

Apart from considerable hæmorrhages, a deficiency of corpuscles and hæmoglobin is very common. In the blood of J. S., the hæmoglobin is only 40 to 48 per cent., and the corpuscles were once found only a little over 3,000,000 in the cubic millimetre.

But blood changes of the kind that I have discussed are for the most part, like this accumulation of urea or other waste products, secondary to the renal malady. Changes of another kind, such as increase of uric acid, often precede and probably cause the renal irritation.

In nephritis the blood shows a marked tendency to rapid deterioration, the specific gravity falling, the total solids becoming diminished, the hæmoglobin and corpuscles rapidly becoming less during the earlier stages. Later on in the history of the case the same condition persists, but I have rarely seen so marked a tendency to hæmorrhage as in cirrhosis. In waxy degeneration the blood is often in an unsatisfactory condition from causes other than the renal. I have sometimes seen a slight increase of white corpuscles, and a flabbiness of the red with tendency to tail, especially where the spleen or lymphatic glands were involved.

Complications involving the circulatory and respiratory systems are among the most important of all.

In illustration of the cardiac changes I shall show you examples of cardiac hypertrophy, cardiac failure, and of chronic endocardial disease, and shall recall to you a case of pericarditis. You observe that in the case of J. S. there is no marked hypertrophy of heart, but that the second sound is distinctly accentuated in the aortic area. In this other patient you observe the widely extended and well pronounced apex beat, and you hear that the cardiac dulness extends beyond the

line of the left nipple, while not only is the aortic second sound accentuated, but the first sound is booming and prolonged. Here we have evidence of marked hypertrophy.

So far as I have been able to make out, the more advanced the renal malady is, the more pronounced are these symptoms, and I regard them as true examples of consequent complications. In a series of cases which I tabulated many years ago I found that cardiac hypertrophy was more common in cirrhosis than in the other renal diseases, and that generally speaking the more advanced the atrophy the more distinct it was. The experience of my friend Professor Rosenstein[70] and other reliable observers brings out the same result. As to the explanation of the cardiac hypertrophy, it is to be referred partly to the obstruction of the renal circulation inevitable in the disease, partly, no doubt, to the widespread disease of arteries, arterioles and capillaries, partly to the greater difficulty experienced by the heart in its efforts to drive an impure blood through the vascular system, perhaps in part also to the spasmodic contraction of the small vessels as suggested by Dr. George Johnson.[71]

I turn now to two cases illustrative of failure of the cardiac muscle, for the hypertrophy with strong action may be followed by degenerative changes in the muscular substance of the heart, consequent failure of its power, and diminution of strength and tension in the pulse. Some of you have seen a patient who is in the private ward, and who has suffered from very distressing cardiac symptoms in the course of his renal cirrhosis. Indeed, he sought advice not on account of kidney disease, but for the heart. Its action was tumultuous and irregular, at times very rapid; the pulse beat was rather feeble, and the tension was diminished. Physical examination showed that the heart was dilated, and that its walls, although feeble, were abnormally thick. Under

treatment by means of rest, careful and nutritious dieting, and the use of cardiac tonics—digitalis and strophanthus—he has greatly improved, the action having become steady and regular, and the pulse firm and of good tension. In this other case, however, along with a degree of thickening of the vessel walls, a firm beat with great vascular tension, we find dyspnœa upon exertion, and other tokens of cardiac debility. How is this apparent contrariety of symptoms to be explained? The explanation lies in the fact that the degeneration and consequent dilatation may not affect the whole heart equally but especially certain parts of it, and that in some cases it is the right side of the heart which is mainly affected. From the comparative thinness of the wall of the right ventricle, it is evident that in such morbid conditions it is more liable to dilatation and failure than the left venticle. The explanation which I give, therefore, is that while the left ventricle continues strong enough to maintain a high tension of pulse and a firm beat, the right ventricle has become so much degenerated and dilated that it is unable sufficiently to perform its function of driving the blood through the lungs. This explanation is not definitely proved, but it is almost certain that it is correct.

Patients suffering from cirrhosis of the kidney are very liable to valvular disease of the heart. This constitutes a formidable complication, and should always be carefully looked for. I show you to-day a patient, J. G., who has cirrhosis of kidney with some tubular inflammation superadded, and who is greatly troubled with dyspnœa. That dyspnœa is in part due to pulmonary changes of which I shall speak presently, but is also in part to be ascribed to the valvular lesions. On auscultation we find a systolic mitral and a diastolic aortic murmur, and there is probably also a systolic tricuspid murmur. There is, therefore, both mitral and aortic incompetence, and probably some tricuspid

incompetence as well. You will at once perceive how greatly the difficulty of dealing with this case is increased by the existence of such complications. I cannot give you any proof that endocarditis results from the renal lesion, although they so often coexist.

But there is another cardiac complication—viz., pericarditis. When this extremely grave condition occurs, the patient is observed to be seriously ill, and is usually seized with severe pain, which may be referred to the præcordia, the scrobiculus cordis, or to some position lower in the abdomen. Friction is heard over the heart, and it is not an indistinct friction such as might be overlooked, but very marked and unmistakable. The pulse soon loses its tension, and the beat becomes weak. There may be superadded the signs of effusion into the pericardium. Pericarditis is most apt to occur when the case is far advanced, and it usually speedily leads to a fatal issue. Some of you may remember the case of a patient who was in the Paton Ward suffering from cirrhosis and slight tubular inflammation of the kidneys. In his case, not only was there pericarditis shortly before death, but there had been a previous attack of pericarditis as well, for at the autopsy it was found that in addition to the soft recent adhesions, the pericardium was thickened from old inflammation.

Besides the lesions in the heart, a variety of changes occur in other parts of the circulatory system, the increase of arterial tension and the thickening of the vessel walls being the most important. The increased tension becomes as a rule more marked as the disease advances, and is due, on the one hand, to obstruction in the smaller vessels, and on the other, to the increased cardiac action. As to the thickening of the vessels, my observations confirm the statement of Dr. George Johnson that it is situated mainly in the middle coat of the smaller arteries, a consequent complication of chronic

renal disease. But it must also be admitted that alterations of the inner and outer coats are common, and that the thickening and tortuosity of arteries are often due to them. So important is this relationship, that Sir William Gull and Dr. Sutton[72] have come to the conclusion that a vascular change, which they designate arterio-capillary fibrosis, is the real starting-point of the process rather than a renal lesion. It is certain that this change is commonly associated with the disease. It is also certain that changes around the blood-vessels often constitute the first observed lesion in the kidney itself, and in many cases not the minute vessels alone, but vessels of the size of the radial arteries and upwards show the change. But on the other hand, arterio-capillary fibrosis often exists without any renal cirrhosis. The lesion observed in the kidney is very often a simple overgrowth of the interstitial tissue, not specially perivascular, and the degree of change in the vessels varies so much that it cannot be held to stand in close and constant relationship to the state of the kidney.

The circulatory system also becomes altered in cases of nephritis. Dr. Mahomed[73] thought that before albumen appeared in the urine the arterial tension was already increased, and that its occurrence might be predicted by the rise of tension in the pulse. I have not been able to confirm his statements by my own observations. On the contrary, they show that tension follows upon renal lesion, and within certain limits I should say that the longer the nephritis lasts the more marked does the tension become. It is usually well marked within a few weeks of the commencement of inflammation, and in long-standing cases is as pronounced as it is in cases of cirrhosis, unless there is something to interfere with the development of cardiac hypertrophy. That hypertrophy itself you may often have opportunity of watching in process of development, and you will find that the more

advanced a case of nephritis is, the more distinct does it become. In a series of cases which I tabulated many years ago, I found on post-mortem examination that it was present in 12·5 per cent. of cases fatal in the first stage, in 38·5 of those fatal in the second, and in 100 per cent. of those fatal in the third.

Valvular lesions are not such common accompaniments of nephritis as they are of cirrhosis, and the retrogade metamorphic changes in the muscular substance of the heart have also occurred less frequently in my practice. Pericarditis I have met with occasionally, especially in the second and third stages of the process.

Cardiac and arterial tension changes are by no means common accompaniments of waxy disease. In my series of waxy cases they occurred only in 5 per cent. of the far advanced cases, in no case fatal in the earlier stage. Even when present, they are not very pronounced. Changes in the smaller vessels are, of course, very frequent.

Symptoms and complications affecting the respiratory system are of frequent occurrence in cases of renal disease, and dyspnœa in particular often causes great distress. Sometimes it comes on gradually, at others with great abruptness. Sometimes the air is found to be entering the lungs quite freely, at others its entrance is impeded. It may depend on various causes. I shall speak first of those proceeding from the pleuræ and the lungs.

Serous effusion into the pleural sacs takes a foremost place, and you should in every case where dyspnœa occurs make careful search for evidence of this change. It may appear when there is no dropsical effusion elsewhere, or coexist with anasarca. It may come on gradually and make the most insidious progress, or it may develop very quickly. Whenever there is dyspnœa, and even a thin line of dulness at the base of the pleuræ posteriorly, you should carefully

examine the axillary region, introduce your exploring needle, and make sure whether fluid is present or not.

Conditions affecting the lungs themselves are also very important. Chief among them, I must mention venous congestion and consequent œdema—the latter indicated by a degree of impairment of the percussion-note over the bases of the lungs posteriorly, with crepitations heard on auscultation. As a rule this complication develops gradually, sometimes, however, with great rapidity.

A few years ago a gentleman from Perthshire, who was living in one of the Edinburgh hotels, was suddenly seized with dyspnœa. He was seen by an accomplished and experienced practitioner, who found the general evidences of acute bronchitis, with œdema of the lung, and prescribed the remedies ordinarily employed in such cases ; but in the course of a few hours the condition had become much worse, and the patient died before the practitioner could again see him. A legal question of considerable interest arose in regard to the destination of his property, for he had bequeathed it by a will made not very long before his fatal illness, and, as the law then stood, the will was not valid if at the time of its execution the patient was already suffering from the disease of which he died. The opinion of various medical men was asked as to whether the patient died of an independent pulmonary malady, or of a suddenly developed sequel of chronic renal disease. Dr. Rutherford Haldane and I happened to be among those consulted, and we found evidence that symptoms had existed for a considerable time which pointed to cirrhosis of the kidney, and came to the conclusion that, although there was no autopsy, we yet were entitled to conclude that the death resulted from pulmonary œdema secondary to renal disease. This case may illustrate the sudden onset ; you have seen in the wards many instances of a more gradual invasion.

Very urgent symptoms may arise also from œdema higher up in the respiratory tract—namely, at the glottis. This may come on suddenly from slight exposure to cold, and it may be so severe as to demand operative interference.

A patient of mine in the Old Infirmary was recovering from an attack of nephritis, and had got so well as to be allowed to go out to visit some of her friends. Waiting for an omnibus at the corner of Infirmary Street she got chilled, and the same evening was taken with such dyspnœa from œdematous inflammation of the glottis that tracheotomy became necessary. This was performed by my house-physician, Dr. Coldstream, now of Florence, and the girl was rescued from most imminent danger. Such an incident is more likely to arise in connection with the acuter processes, but may occur even in chronic renal maladies.

Dyspnœa may be due to bronchitis and pneumonia; and I may just recall to your minds the grave symptoms which may arise from the occurrence of pulmonary apoplexy. You are aware also of the tendency to serous inflammation which exists in Bright's disease, and sometimes, though less frequently than the pericardium, the pleuræ are so affected and dyspnœa may result therefrom.

Embarrassment of respiration also results from the toxic state of the blood, being one of the important manifestations of uræmia. In the absence of cardiac degeneration or pulmonary change the symptom may be suddenly developed, and in either of two forms. The one variety, induced by an action upon the respiratory centre, occurs just as the case is approaching its fatal termination. I may illustrate it by an instance met with some years ago. I went to visit a patient in the south of Scotland, whose kidneys were not known to be diseased. When I arrived he was breathing rapidly and laboriously, but the air was entering the lungs freely, and there was no sign of pulmonary or cardiac change, the

pulse was tense, and the other symptoms of cirrhosis of the kidney were present, so that we had manifestly to do with a pure and simple example of uræmic dyspnœa, and it rapidly went on to a fatal result. This form is due to poisoning of the respiratory centres by the toxic substances which the kidneys have failed to eliminate. The other variety occurs in the form of temporary attacks, closely resembling ordinary asthma. The patient is awakened perhaps at one or two o'clock in the morning with a fit of coughing, and in a state of most distressing dyspnœa. After a time he expectorates some mucus, perhaps tinged with blood, and then he is relieved for the time. This variety appears to be due to irritation of the bronchi by the poisoned blood, and one cannot avoid suspecting that a cardiac element also is associated with it.

Effusion into the pleura is an important source of danger in cases of nephritis, in which dropsy is so common. Œdema of lungs, bronchitis, pneumonia, and pleurisy, are all occasionally met with, but they play a less important part in its clinical history than in that of cirrhosis. The only really important pulmonary complication of waxy kidney is phthisis, and that is a cause of the process.

The integumentary system shows a dryness, occasionally an itching, and a certain tendency to dropsy. In a pure case of renal cirrhosis there may be practically no swelling, but whenever a degree of inflammation of tubules becomes superadded, dropsy appears. It also frequently takes origin from cardiac weakness or from valvular disease. I must defer the consideration of the nervous changes to another lecture.

LECTURE VIII.

ALBUMINURIA FROM CIRRHOSIS OF KIDNEY— *continued.*

Headache.—Its Varieties.—Dimness of Vision.—Uræmic.—Due to organic causes.—Retinal Hæmorrhage.—Albuminuric Retinitis.—Uræmia.—Acute.—Illustrative Case.—Chronic.—Different Forms of Symptoms.—Illustrative Case.—Causation of Uræmia.—Paralysis and Aphasia.—Illustrative Cases.—Remarks.

GENTLEMEN,—Resuming the consideration of the complications of renal cirrhosis, which we partially overtook on a recent occasion, I purpose to devote this hour to giving you some account of the affections of the nervous system which are apt to arise in the course of the malady.

General deterioration of the nervous system seems to me always to attend upon renal cirrhosis, showing itself by irritability of temper, restlessness, diminution of power of sustained attention, consequent failure of working power, impairment of memory and of the soundness of judgment, with perhaps an increased susceptibility to the action of alcohol, and of nervine drugs. These conditions, resembling what one often notices after sunstroke or injuries to the head, mark an interference with the nutrition of the cerebral substance which the observant physician can often make out even in the early stage, and almost certainly in the later stages of the disease.

Among the subjective symptoms, headache and dimness of sight are the most frequent. The headache is sometimes

distressing, and, while it may, with sickness and morning vomiting, usher in a fatal uræmia, it may be habitual, recurring at intervals throughout a period of months or even years. Sometimes it is intense, fixed mainly in one locality, and apparently neuralgic ; sometimes it is widely distributed throughout the skull, and patients may describe it to you as a diffused, splitting headache; sometimes it is frontal, sometimes occipital. Often it is aggravated with each throb of the hypertrophied heart. I think that it may be due to different causes. It may be neuralgic or anæmic, may result from poisoning by non-eliminated tissue products, or may be due to organic change, especially in the blood-vessels. In the case of J. S., whom I again show you to-day, this was the earliest symptom. You remember how he told us that he was distressed by headache, especially when passing through hot regions, such as the Red Sea. It is now less troublesome, although he is not entirely free from it.

The impairment of vision also presents a considerable variety in its clinical features. There may be sudden dimness of sight or actual blindness. It may affect the whole field of vision or only a part. It may be associated with headache or with other uræmic manifestations, or may occur alone. It is commonly transitory, lasting an hour or two, perhaps a day, and reminding one of the dimness of sight sometimes accompanying megrim, or the temporary hemianopsia of some cases of brain syphilis. The pupils show no peculiarity, and the fundus of the eye is quite normal. This is the uræmic blindness. The attack may be precipitated by incidental circumstances, perhaps gastric derangement, and it does not necessarily herald the immediate fatal termination of the case.

But dimness of vision is often due to organic causes. You observe that J. S. has the peculiar vague and vacant expression of an amaurotic patient. His eyes do not focus

themselves readily upon objects. His pupils are dilated. It is now many months since he began to notice his sight failing. He required a brighter light when reading, and reading small type gradually became impossible. Objects appeared indefinite, blurred, and indistinct. On ophthalmoscopic examination some of you have already seen the condition of his retinæ. Perhaps they are less characteristic than those of this patient (J. G.), but from the two you can have opportunity of fully satisfying yourselves as to the retinal changes which occur in this disease. You will find that there are hæmorrhages, patches varying in size, some of a deep and some of a lighter red colour. You notice also fawn-coloured or fatty patches, and some portions that are white and completely atrophied. You will notice also the distribution of white radiating lines, corresponding to the inflammatory changes in the fibrous tissue of the structure. You notice that both eyes are affected, but usually not in the same parts or to the same extent. This is of great interest, not only in itself, but as an evidence that organic changes of a minute kind may arise in other parts of the nervous system in the course of renal maladies. The organic eye changes generally herald very serious head symptoms, but they may last for considerable periods, and indeed partial recovery may take place after they have been fairly established. Especially in the albuminuria of pregnancy does one find these symptoms prove less formidable. I have known them almost entirely disappear after delivery.

The eye symptoms are much less common in nephritis than in cirrhosis, but are occasionally seen in the early, and not unfrequently in the later stages. They are rare in waxy disease, occurring only in cases of long standing, and even there not to a great extent.

Uræmic symptoms include not only those to which we have already referred—the dyspnœa and the blindness, but

a great variety of other conditions. There is acute uræmia with coma and convulsions. It may occur in acute inflammatory disease of the kidneys, as in the first case which I showed you when speaking of that subject. It may occur in old-standing inflammatory cases, is not uncommon in cirrhosis, and is met with, although rarely, in waxy disease. I remember a patient coming to me on account of an epileptic seizure. He had been, as he supposed, in good enough health, was in a shop transacting business, when suddenly he fell down in a convulsion, and thereafter remained for some time unconscious. When I examined him it was clear that he had somewhat advanced cirrhosis of the kidney. The fit did not recur, and after a time he came stating that he had been engaged, and wishing to know whether he would be justified in marrying. He was not a young man, and the lady of his choice was of an age well suited to his own, and I said that if the circumstances and the danger of a sudden termination were fully explained, and if proper precautions as to health were afterwards taken, I thought that he might marry. His health continued fair for a year or more after the event, and then the inevitable termination came. The fits recurred; he passed into a state of coma, with stertorous breathing, and when the coma had persisted for about two days, with occasional violent convulsions, he died.

In that case I had no clue to an explanation of the sudden early attack. Sometimes the explanation is definite enough. I once attended a commercial traveller whose kidneys were cirrhotic, but who was obliged to continue his work on the road. When at home he generally managed to resist the temptations of liquor, but occasionally in a country town its attractions proved irresistible. When he had taken a little he used to become excited, and then an attack of convulsions with coma occurred. More than one of my professional brethren in different country towns had the responsibility of

treating him under these conditions. He used to recover in a day or two, and then, leading an abstemious life for a time, he enjoyed fair health. He ultimately went to live in England, and I lost sight of him. But there were three causal elements in his case. His constitution was neurotic, his renal disease was considerably advanced, and a little indulgence in liquor sufficed to precipitate the attack.

Sometimes coma and convulsions never appear till they usher in the fatal result. I was once called to see a lady who had, while, as was supposed, in the enjoyment of good health, suddenly become convulsed, and passed into a state of coma. I found her actually dying. She was pale and of a grey complexion. A cold perspiration covered her skin. Her person had a somewhat urinous odour, and I found reason to think, as was afterwards confirmed by post-mortem examination, that the kidneys were extensively diseased from cirrhosis with cystic degeneration. Thus you see that the patient may die even in the first attack. Still, the prognosis is not so unfavourable in acute as in chronic uræmia. Treatment by diaphoretics, such as jaborandi, pilocarpin, hot-air baths, or by purgatives, sometimes by venesection, may give good results. Sometimes the attack passes off without active treatment at all.

It is otherwise in the great majority of cases with chronic uræmia. The patient has had his renal lesion for a long time, and his whole system has become deteriorated. He begins to be listless, disinclined to rise, complains of lassitude, and, perhaps, a little sore throat. His articulation becomes indistinct, like that of a person slightly intoxicated. He takes little notice of what goes on around him. Gradually the listlessness passes into torpor, he is roused only when loudly spoken to, and when you ask after his health, he probably assures you that he is quite well. His torpor passes into coma. He lingers on for days, perhaps for more

than a week, and at last dies, sometimes with and sometimes without convulsions. Almost invariably this process leads up to death. Once or perhaps twice have I seen a patient rally from it.

In other cases I have known the gradually-increasing torpor associated with noisiness and with delirium. I have known a ward disturbed for days with the occasional occurrence of a loud prolonged howl uttered by a patient who, as a rule, lay quiet, and only now and then started up in a paroxysm of maniacal excitement. Sometimes there is incessant loquacious restlessness, with wild excitability, and to this again convulsions may be superadded.

Many of you have had the opportunity of seeing several examples of the head symptoms of renal disease in the wards during the present session. I shall recall one case of uræmia which, although only a short time under observation, must have interested those of you who saw it.

Mrs. K., aged forty-eight years, was admitted to Alexandra Ward on 12th April, and died on the following day. She suffered both from cirrhotic and waxy disease of the kidney. She had had phthisis for three years, but had been much worse since October. She went about, however, till the beginning of March. For sixteen days before her admission the bowels were not moved, and there had been bilious vomiting for a week. An enema was then administered, and it brought away a large amount of fæculent material. She also vomited a blackish-red fluid, and a similar fluid was passed by the bowel. There was therefore probably some hæmorrhage in the gastro-intestinal tract. She began to have fits the night before admission, and she had five altogether before she was brought to the Infirmary. During the fits the eyes were fixed, the teeth were clenched, the tongue was bitten, the legs were rigid, and the hands twitched. She remained unconscious for about half-an-hour

after the convulsions ceased. When examined on admission she was delirious, and in a drowsy condition, breathing rather rapidly. There was some twitching occasionally at the angle of her mouth. The face was flushed, and the breath had a peculiar odour. Physical examination revealed nothing additional with regard to the alimentary or hæmopoietic systems. Although the heart was not much enlarged, the first sound was loud and thumping, and the second was accentuated. The pulse rate was 92 per minute. It was regular and of high tension, and the arterial wall was thickened. There were distinct signs of phthisis at both apices. The breathing was 24 per minute, regular, but laboured. There was slight œdema over the tibiæ. The urine, which had to be drawn off by the catheter, was of low specific gravity (1009-1012), and highly albuminous. Microscopically there were a few fragments of granular and fatty casts. The sensibility to touch and pain appeared little affected. The pupils were equal and moderately contracted, and they reacted to light. The movements of the eyeballs were natural. She was certainly blind in one eye, and probably in both. There was no plantar reflex. The patellar reflex was present in both legs. Ankle clonus was present in the right leg, and to a less degree in the left. The contractions were slow, but well marked and regular. The motor power was undiminished, but any effort was accompanied with tremors. She was markedly delirious, and had hallucinations of sight. The treatment consisted in the use of vapour baths, the application of hot bottles, and the administration of full doses of digitalis.

At 10.30 P.M. she had another fit. She became cyanotic, and there was twitching, first of the left and then of the right side of the mouth, and then violent general convulsions. The tongue was bitten, the eyes were fixed and staring, and the pupils dilated. As the convulsions sub-

sided the pupils again became contracted, and then dilated slowly. The breathing was stertorous but not rapid. The pulse, 98 per minute, was less hard than before, but the heart was thumping violently. There was still some twitching at the corners of the mouth. Three-quarters of an hour after the fit she was moving her arms actively, shouting and speaking. The pupils were more dilated. The legs were cold. The ankle clonus was marked. She continued violent for some time. The twitchings and tremor persisted, and the breathing was at times laboured and dyspnœic. She was still in a semi-conscious state. This condition persisted till 3 A.M. She then slept from 3.15 to 6.40 A.M., except during occasional fits of dyspnœa, and while asleep no twitching was noticed. She awoke much stronger, sat up in bed, and answered questions more rationally, although the tremors and nervous jerkings were still sufficiently obvious. The pulse rate was 88 per minute, with the tension as before. The respiration, 30 per minute, was short and puffing. She continued in much the same condition till 4.45 P.M., convulsions not recurring, but the respiration becoming steadily more embarrassed, and fluid accumulating in the bronchi and towards the bases of the lungs. The breathing was 40 per minute. The heart continued much as before, but the sounds gradually became obscured by mucous and snoring râles. The pulse, 86 per minute, was not quite regular. The condition became gradually worse, and the patient died that evening.

The post-mortem examination revealed the following conditions:—There was slight hypertrophy of the heart, but the valves were competent. There were milk spots in front of the right auricle, and a small patch of pericardial thickening near the base of the left ventricle. The left lung was completely, and the right lung partially, adherent to the chest wall. The left lung showed a large amount of

tubercular deposit, and there was an old-standing cavity occupying about a third of the upper lobe. The right lung was also tubercular, but to a less extent. The bases were congested. Patches of pulmonary apoplexy were scattered through both lungs. The bronchi contained much mucus, were deeply congested, and of purple colour. The liver showed syphilitic cicatrices, and was adherent to the diaphragm. It was cirrhotic and waxy, and weighed 2 lbs. 4½ oz. The kidneys were large, the right weighing 9 ounces, and the left 8 ounces. Their consistence was much increased, the capsule was little adherent, but the fibrous tissue was torn on stripping. The surface was uneven. In the left kidney the surface had a mottled appearance (dirty greyish-white). There were patches of semi-translucent, gelatinous tissue, surrounded by opaque white bands. The stellate vessels were here and there distended, and so were the interlobular vessels. On section, the cortex was found to be diminished, and showed cirrhotic and waxy changes. The superficial cortex measured scarcely a quarter of an inch, and was of a pale, dirty-grey colour. The glomeruli were not specially enlarged. The pyramidal portion was enlarged — measuring one inch from apex to base—and had a striated, rosy colour, the vessels markedly waxy. The walls of the renal arterioles were slightly thickened. The right kidney was in a very similar condition, but there was perhaps more fatty change in the cortex, which was not so small as in the other. The spleen weighed 4½ ounces. It also showed the waxy change, and there was a fibrous adhesion at one extremity from perisplenitis. The skull-cap was thick, and there was no diploe. There was no erosion of the inner surface, though the grooves for the meningeal arteries were unusually deep. The meningeal arteries were thickened, and at one or two points there were small peri-arterial nodules. There was some con-

gestion of the small venules on the surface, and there was œdema of the pia mater, especially over the parietal lobes. The surface of the brain was otherwise anæmic. The arteries and membranes at the base seemed normal. On section, the brain (both grey and white matter) was very anæmic, and slightly œdematous. The lateral ventricles showed no increase of fluid, but slight congestion of the choroid plexus and velum interpositum. There was marked anæmia of the grey matter of the basal ganglia.

You had thus the opportunity of witnessing the clinical features and the post-mortem appearances in a well-marked case of uræmia, and you observe that no change was present except anæmia and some degree of œdema.

I do not intend at present to discuss with you the causes of these uræmic symptoms, and shall only express the conclusion to which I have come. I believe that in some cases they are due to poisoning of the nerve centres with excrementitious matters which the kidneys have failed to eliminate, that in others they are due to cerebral anæmia, either from vascular spasm, or as a mechanical result of serous effusion within the cranium, and that sometimes they result from organic alterations of the brain tissue of the nature of degeneration, minute hæmorrhages or softening processes.

Uræmia occurs frequently in nephritis, and that at any stage of the process. I have shown you a patient whose life had been endangered by it during the early stage, and have told you of instances in which it proved fatal after the malady was far advanced. The later stages are more apt to be attended by the chronic variety, but the acute is even then not of very rare occurrence.

Waxy kidney is much less liable to uræmic complications. In pure cases it is very rare indeed. In those which are in part waxy and in part cirrhotic or inflammatory it is relatively more common.

We proceed now to consider another set of nervous symptoms: the paralyses which are so common in Bright's disease. Such symptoms are, in some cases, due to embolism from the cardiac valvular lesions or endarteritis, in others to thrombosis of cerebral vessels, but oftenest to cerebral hæmorrhage, the result of the powerful action of the hypertrophied heart, the high vascular tension, and the degeneration of the vessel walls. Sometimes a renal case terminates with appalling suddenness by hæmorrhagic apoplexy.

A patient of mine in the Old Infirmary was well-known to successive classes of students as illustrating chronic inflammatory Bright's disease. His life had been endangered in various ways in the course of his illness, but he had on the whole improved; dropsy had disappeared, the uræmic tendency was in abeyance, and but for the cardiac hypertrophy, the tension of pulse, the pallor, and the persistent albuminuria, the patient seemed fairly well. But suddenly he was seized during the night with convulsions and loss of consciousness. When he was examined it was concluded that he was not suffering merely from uræmia, but that hæmorrhage had occurred. The grounds for this opinion were: the profound nature of the coma, no noise or pinching of the patient sufficing to rouse him, as might probably have been the case in uræmia; the deep snoring respiration contrasting with the sharper or more hissing sound produced by the rush of the expired air upon the hard palate or teeth, so characteristic of uræmia; the complete paralysis of the limbs on one side, so that the one hand, when lifted from the bed, fell like that of a dead person, while the other was comparatively less flaccid. These indications, and especially the last, justify a diagnosis of hæmorrhagic apoplexy rather than of uræmia. Sometimes the existence of bilateral paralysis from hæmorrhage into the pons or into both hemispheres deprives us of the

information to be obtained by comparing the condition of the two sides of the body, but if so, one generally finds, in the case of the pons, special paralytic features, and there are always the other symptoms to fall back upon. In the course of a few hours a fatal result ensued, and the autopsy showed extensive hæmorrhage in one hemisphere in the region of the basal ganglia and internal capsule.

But a fatal result is by no means the rule in paralysis associated with Bright's disease. You will often meet with cases in which transient attacks occur and leave no trace behind. I have already told you of a gentleman who had only slight renal symptoms, but was seized with a paralytic attack of the kind to which I now allude. On awaking one morning his attendant remarked that his face was drawn to one side, and he complained of difficulty in speaking and in raising his right arm. When I saw him some hours later the facial paralysis was distinct, there was an unmistakable degree of aphasia, and both sensibility and motion were impaired in the right arm. But within twenty-four hours the sensibility was restored, the speech a little better, and within a week the hand recovered motor power, although the face remained slightly distorted for a longer period. Whether the process was embolic or the result of a slight hæmorrhage, I cannot tell ; at all events, recovery was ere long complete, and there has been no recurrence of serious nervous symptoms during the years that have since elapsed.

Another instance of a similar kind rises to my recollection. A friend of mine, an active business man and zealous politician, had gone to the north of Scotland on the rising of parliament some years ago. His health was supposed to be quite satisfactory. When about to drive out one day, his speech became indistinct, he felt some weakness in the right arm, and the expression of his face became altered. With the help of those about him he got back into the house, and

although he did not lose consciousness, he became distinctly paralysed on the right side, especially in the right arm and the face, and he lost the power of speech. This probably resulted from embolism; but, at all events, gave the first indication of the existence of renal cirrhosis, which must, however, have been insidiously advancing through a period of years. Neither the slight aphasia nor the paralysis lasted long. He rallied speedily, and never during the ten or eleven months which he survived did any paralytic symptom recur.

But these slighter attacks may be better impressed upon your memories if I show you this patient, W. H., who has been for months under our observation, and has recently had a slight paralytic seizure. You know that he has renal cirrhosis, complicated with considerable inflammation of the tubules, that he has had so much dropsy as to require frequent tapping, and that certain scars on his legs and other indications have led us to suppose that waxy degeneration of the kidneys is not improbable. He was suddenly seized four days ago with a feeling of uneasiness in the face, particularly the mouth and the tongue, and he found that his speech had become indistinct. On examination we found his mouth somewhat drawn to the left side, indicating a paralysis on the right; the naso-labial fold was indistinct; he was unable to whistle, or to show his teeth, and his tongue when protruded was pushed over to the right side. But there was no difference perceptible in the eyelids nor in the forehead. There was thickness of speech, but no true aphasia, and no paralysis of arm or leg. This kind of facial paralysis contrasts with that due to lesion of the nerve, in respect that the muscles of the upper part of the face are unaffected, and there is none of the staring due to paralysis of the orbicularis palpebrarum. It thus corresponds to the facial paralysis in ordinary hemiplegia, and is, I have no doubt, due to slight hæmorrhage

involving certain fibres in the internal capsule or the corona radiata. Already I see some improvement taking place in this patient's condition, and I hope that if, by our repeated tappings and other treatment, we are able to keep him alive for another month, you will see the paralytic symptoms entirely disappear.

You perceive from what I have already said that these paralytic complications occur in nephritis as well as in cirrhosis, but they are less common in it than in the other disease, and in the early stages are quite exceptional; it is only when a stage of atrophy has been reached that you need expect to meet with them. In uncomplicated waxy disease they are of the rarest occurrence, indeed, I may say that practically they are not met with.

Let me recall to you a case which we recently studied at the bedside, and which illustrates more than one of the special features characteristic of the nervous complications of Bright's disease. The case is that of a man, A. C., aged 65 years, a maker of gas-meter indices, who, when he came under my observation, had been the subject of cirrhosis of the kidney for at least eighteen months, and probably much longer. He told us that his parents did not live beyond middle life, but he did not know the cause of their death: that at least one brother had died of phthisis; that he himself had been a temperate man, and had had a comfortable home and good food. He had enjoyed good health till he was nearly sixty, but then he began to suffer occasionally from pains in the head, and his health deteriorated in other respects; frequent nocturnal micturition, and other symptoms, giving indication that renal cirrhosis was establishing itself. About eight months before his admission to the Infirmary, he had been irritable and out of sorts for some days, and then one day, while walking on the shore at Portobello, he fell several times owing to slight paralysis, unattended by loss of con-

sciousness. He was able to pick himself up each time with a little assistance, but got home with great difficulty. From this time his power of walking and of using his hand was much impaired, his intelligence became dull, and he lost his memory very rapidly. His eyesight also became affected. Two months later he had a pretty severe epistaxis. Four months before admission he had a second attack of paralysis, this time affecting the left arm and leg and the right side of the face. The arm and leg soon recovered, but the right side of the face continued paralysed. His speech had since then been less distinct than formerly, but there did not appear to have been any actual aphasia.

When he was admitted to the Infirmary there was no dropsy, the paralysis on the right side of the face was still present, and there was also some drooping of the left eyelid. There was some muscular twitching about the mouth. The temporal arteries were prominent and very tortuous. The tongue was furred and fissured, but the appetite was good. Examination of the abdomen revealed nothing abnormal. Both the heart sounds were reduplicated, the first had a slapping character, in the aortic area the second was accentuated, while in the mitral area a faint systolic murmur was sometimes heard. The condition apparently was one in which hypertrophy had been followed by degeneration of the muscular wall. The pulse rate was 94 per minute. The vessel was very tense, and its wall was much thickened and tortuous. The lungs showed no important change. The urine was pale and of low specific gravity (1016), of acid reaction, and contained albumen which, when estimated by Esbach's method, amounted to 2·8 grammes per litre. A trace of peptone was also present. The urea amounted to 307 grains in the twenty-four hours. Microscopically there were squamous epithelial cells and some granular matter, but no distinct casts. As to the condition of the nervous

system, examination of the sensibility was difficult, owing to the mental condition, but no distinct abnormality was made out. There was a diminution in the field of vision, and considerable impairment of sight, and the fundus was hazy and the disc hyperæmic. Accommodation was deficient. The plantar reflex was well marked, and the patellar reflex was present on both sides. There was no ankle clonus. Voluntary movements were interfered with by the weakness and tremor of the limbs, but co-ordination was not otherwise affected. His power of attention, memory, and intelligence, were much impaired. There was no actual aphasia.

After being in the Infirmary for nearly a month, during most of which he was in a sort of torpid condition, the patient passed into a state of more marked uræmia, becoming drowsy, stupid, and ultimately comatose, with muscular twitchings, moderately dilated pupils (the left more than the right), and long-drawn somewhat stertorous breathing, evidently dyspnœa of the form which I have already described as uræmic, the result of the toxic action of the blood on the respiratory centres. There was also slight external strabismus. Gradually the coma became more profound, and he died.

On post-mortem examination there was no subcutaneous œdema. There was senile atrophy of the brain with gelatinous fluid in the arachnoid space. The grey matter of the hemispheres was atrophied, the white matter of the centrum ovale was very œdematous. The cortical part of both occipital lobes contained several old hæmorrhages, each of about the size of a pea. The vessels at the base of the brain were atheromatous and there were miliary aneurisms in the occipital lobe, but not elsewhere, as far as was ascertained. The heart was hypertrophied and slightly fatty. The valves were competent. There were old pleuritic adhesions. There was emphysema at the apices of the lungs and hypostatic con-

gestion at the bases. The kidneys were in an advanced state of cirrhosis—the left weighing 2¼ ounces—the right 2 ounces. The cortex was much atrophied, and contained numerous small cysts and capillary hæmorrhages. There were old adhesions about the liver and spleen.

Taking together the clinical history and the anatomical conditions, the interest attaching to this case is considerable. The nervous symptoms consisted in dimness and narrowing of the field of vision, a degree of paralysis localised in different parts and at different times during the last eight months of life, general torpor and hebetude, passing ultimately into coma. The dimness of sight I expected at first to find explained by retinal changes, but on ophthalmoscopic examination it turned out that there was no albuminuric retinitis but simply hyperæmia of the disc, with slight haziness of the fundus generally. But when the autopsy revealed hæmorrhages in the occipital lobes, it was clear that the amblyopia might very probably have been central. As to the paralytic seizures, it seemed possible that the stumbling and falling, with temporary recovery, resulted from these hæmorrhages, for one can understand how such accidents occurring in the visual centre might interfere with equilibration, but this could not explain all the paralytic symptoms, and it is possible that embolic or thrombic processes may have occurred in connection with the vessels in the motor cortex or tracts. Certainly the post-mortem examination did not reveal traces of hæmorrhages in these regions. The decay of intelligence and gradually deepening torpor was explained during life, you will remember, as suggesting to my mind what I have been in the habit of calling uræmia with organic change, and the degenerative alterations revealed at the autopsy confirmed this view. The state of the kidneys was extremely characteristic of advanced cirrhosis, and the nervous symptoms and lesions afforded examples of

more than one of the nervous complications of the malady.

I should like to impress upon you four points in relation to such hæmorrhage in cirrhotic and other chronic forms of Bright's disease. The first is, that patients with these diseases are, for the reasons which I have already stated, exceedingly liable to cerebral hæmorrhage. It is therefore very important in every case of cerebral hæmorrhage to which you are called, to satisfy yourselves not only as to the state of the nervous system, the heart and vessels, but also as to the kidneys, and in your management of cases of renal disease, it is necessary to bear these risks in mind. The second point is, that cerebral hæmorrhage occurring in this disease sometimes proves very rapidly fatal—much more so than in cases without Bright's disease. The third point is, that slight and passing paralyses are common in chronic renal cases. The fourth is, that sometimes the coexistence of other nervous symptoms with those proper to hæmorrhage makes the illness appear more formidable than the lesion would warrant, and so unexpected improvement sometimes occurs. In fact, when I am called to a case of cerebral hæmorrhage in which the condition seems almost hopeless, I am rather comforted than otherwise if I find that it is complicating a renal lesion.

LECTURE IX.

ALBUMINURIA FROM WAXY OR AMYLOID DEGENERATION OF THE KIDNEY.

Case of Waxy Disease in Early Stage.—Grounds for the Diagnosis.—Causal Complications.—Concomitant Complications.—Polyuria.—Termination of Case.—Autopsy.—Modes of Termination of the Disease.—Stages of the Process.—Explanation of the Albuminuria.

GENTLEMEN,—I take the opportunity to-day of drawing your attention to a pure example of waxy or amyloid disease of the kidneys, from which those of you who attended my wards last summer have already learned some useful lessons. The case was that of the patient A. D., who came in on 27th May, 1886, suffering from polyuria. His urine was of very low specific gravity—as a rule, about 1005, or even lower, and at the time of his admission was free from albumen. The case looked at first like one of diabetes insipidus, but very shortly after his admission it was found that, though cold nitric acid continued to give no perceptible reaction, some of the more delicate tests did give a slight opacity indicative of albumen. After a time a very faint cloud was produced by nitric acid, and gradually, but steadily, the albumen increased. Here, then, we had polyuria with slight albuminuria, and the case was on that account suspected to be one of waxy kidney. But there was no apparent cause of waxy disease, and in the absence of that kind of evidence, there was some hesitation

about the diagnosis. True, he had had chronic suppuration once, of which he still showed tokens in old cicatrices on the right side of the chest, but this suppuration had entirely ceased eight years before, and it seemed impossible for a suppurative process so long past now to set up waxy degeneration. But when my resident physician, Dr. Simpson, was examining him quietly one evening, he detected a degree of fulness and undue resistance in the region of the right kidney, and, when asked about it, the patient admitted that he had for some time felt pain in that neighbourhood. Shortly afterwards a somewhat elastic swelling appeared a little below Poupart's ligament, and fluctuation between this and the swelling in the region of the kidney gradually became perceptible. It was thus clear that an abdominal abscess of very considerable size existed, that it had been insidiously advancing, probably for a very considerable time, and thus the missing link of evidence was supplied. We had a sufficient cause of waxy kidney.

As regards the urine, the quantity was large. On the day after his admission it measured 100 ounces, about ten days later it had risen to 200, on the 2nd July it measured 270 ounces. As I have told you, it gave no reaction for albumen at the time of admission. A few days afterwards, however, picric acid showed a trace; and about ten days later nitric acid began to show it. We made a considerable series of quantitative estimations of the albumen by various methods, and found that it underwent a steady increase. On 27th June it had reached 0·17 per cent., as estimated by Esbach's method; on 6th August it reached 0·32 per cent.; and on 9th August, 0·6 per cent. The urea in 24 hours amounted on 29th May to 518 grains; after this it underwent a gradual diminution, till on 10th June it amounted to only 307 grains. Peptones although absent at

first, were detected on 23rd June, and from that time their amount increased.

The question has been asked whether there is anything in the form of albumen present diagnostic of waxy disease. A number of years ago Senator[20] stated that in cases of waxy kidney serum-globulin was more abundant in the urine than serum-albumen, and that waxy Bright's disease could thereby be diagnosed. This statement, however, has not been confirmed by others. In the present case a quantitative estimation of these two forms of albumen was made by separating them, by neutralising the urine, and saturating it with sulphate of magnesia. The estimation was then made by Sir William Roberts's dilution method. It was found that there were 50 degrees of serum-albumen present, and 20 degrees of serum-globulin. The serum-albumen was therefore in much larger proportion than serum-globulin. I would therefore have you believe that there is evidence quite sufficient to rebut the statement of Senator to which I have referred.

What, then, were the grounds for diagnosis in this case? These I shall give you under three heads:—

In the first place, we had the existence of a causal complication. As I have told you, the patient had, eight years before, suffered from suppuration on the right side of the chest, most probably due either to bone disease or empyema. He also had an abscess on the back of the right thigh. But these would not have sufficed for our purpose unless we had also found evidence of the more recent and still existing suppuration. Every one who has written on Waxy Disease has admitted the importance of this as a point in diagnosis. We look, in all cases of suspected degeneration, for the presence of, or at least a history of, some chronic wasting disease, such as syphilis, prolonged suppuration, disease of bone, or phthisis.

The second ground for diagnosis of waxy disease is the existence of concomitant complications—the presence of waxy disease in other organs. There was in this case no evidence of waxy liver or spleen, or of waxy disease of the stomach or intestine. This kind of evidence was therefore awanting. There is in regard to it, also, general agreement amongst authorities on the subject; but I would advise you not to trust absolutely to it. Ten or twelve years ago Fürbringer[74] published a paper on waxy disease, in which he gave the report of the post-mortem examination in four cases in which a wrong diagnosis was made by over-estimating the importance of concomitant complications, such as enlarged liver and spleen. On the other hand, there may, as in the present case, be no other waxy change, and yet you may correctly, and even in an early stage, diagnose waxy kidney.

The third ground of diagnosis, and one in which I have great confidence, is the existence of polyuria. In pure cases this is always present, but it is not to be expected in every case in which there is waxy disease, for its occurrence may be prevented by complications. Thus, the severe and intractable diarrhœa which results from waxy disease of the intestine, and sometimes from tubercular disease, drains the system of water, and necessarily prevents the discharge of a large amount of fluid from the kidneys. The coexistence of wide-spread inflammation of the tubules along with the waxy disease also prevents polyuria. I wish further to impress upon you the fact which this case illustrates, that polyuria may give the clue to diagnosis of waxy kidney even before a trace of albumen be detected in the urine. Of these facts I was able to satisfy myself many years ago when first making a study of this subject.

There has been a strange contrariety of opinion on the subject of polyuria in waxy Bright's disease, and I shall now

bring under your notice the views of some of the leading authors who have written upon it, and explain, as far as that is possible, how the differences of opinion have arisen: Dickinson,[75] Rosenstein,[70] Sir William Roberts,[16] Ralfe,[76] and Purdy[77] concur in regarding it as a characteristic symptom. In the first edition of Ziemssen's "Cyclopædia of the Practice of Medicine," the article on this subject was written by Professor Bartels[78] of Kiel, and he also substantially agreed with the above-named authorities. In the second edition the subject was taken up by Professor Wagner[79] of Leipsic, and he divided cases of waxy kidney into three groups, in relation to the amount of urine. In his first group the urine presented no peculiarity—was neither increased nor diminished in quantity, and did not contain albumen. In the second group, there was an increased flow of urine, containing more or less albumen. In the third group, the urine was diminished in quantity, and albumen was very distinctly present. These three groups can, I think, be easily explained. In the first Wagner included every case which exhibited even the slightest waxy degeneration of the vessels of the Malpighian tufts or of the vessels supplying the tubules. In such cases the urine may not be changed, either because the waxy disease is so slight, or because it is not in the right place to produce symptoms. The state of the urine in the second group of cases corresponds to what seems to me typical of waxy Bright's disease. The small amount of urine present in the third group of cases appears to be explained by the waxy disease being complicated with inflammation of the tubules or other disease. Lecorché,[80] again, holds the peculiar view that waxy disease is not attended by albuminuria, but that the albuminuria, when it occurs, is due to complication with inflammatory disease of the tubules. My own observations do not at all warrant such a conclusion, whether regarded in the light of the purely waxy or of the

mixed processes. Professor Charcot,[81] again, appears to attach very little importance to this symptom. He says, indeed, that in the amyloid disease there are no symptoms directly characteristic. I cannot but think that if these authors were to watch pure instances of the disease such as we are studying to-day, they would come to different conclusions, and take the view broadly stated by Dr. Murchison,[82] that he found in waxy cases, as a rule, an increased quantity of urine, the patient voiding not uncommonly from three to five pints in the day, throughout the greater part of the course of the malady.

If one of you were to ask me in how far I had found polyuria a reliable symptom of waxy disease, I should answer that by looking for it I have again and again made out the presence of waxy disease in cases in which the diagnosis would otherwise have been missed. In a few cases also I have been enabled by it to make out the presence of waxy disease before the occurrence of albuminuria. I have also escaped error in a number of cases in which there was enlargement of the liver and spleen, and in other respects good grounds for diagnosing waxy disease, by refusing to commit myself to a diagnosis, seeing that there was neither polyuria at the time nor a history of its previous existence.

The polyuria is not a mere result of polydipsia, for the urine discharged is often in excess of the whole measurable liquids taken in. In many cases of cirrhosis, and in some of inflammation of the tubules, there is also increased flow of urine, but it is only when these diseases are well advanced that the symptom arises, whereas it is the earliest renal symptom in many waxy cases.

As regards the further history of our patient, the abscess was opened by Professor Annandale. The drain of pus was very great, and the patient went downhill pretty rapidly.

Another abscess developed, and shortly before death there appeared to be commencing suppuration in the region of the right hip-joint. He died on August 13th, not from the waxy disease but from exhaustion produced by the suppuration. Unfortunately we could not get a complete post-mortem examination, but we were able to secure the kidneys. They were pale, and the Malpighian tufts and many of the small arteries showed the degeneration very distinctly. There were also slight traces of inflammatory change in some of the tufts and in patches of the stroma.

I have told you that the patient did not die of the waxy disease, and indeed it is not as a rule the waxy disease which kills. Let me, therefore, explain the usual modes of termination of this malady.

In many cases the patients die of other diseases, especially of one or other of the causal complications. Thus most of you must have seen patients die of chronic abscess, of phthisis, or of caries of bone, whose kidneys turned out, on post-mortem examination, to be waxy.

Now and then you will observe that a superadded inflammation of the tubules brings about the fatal result.

Sometimes there is slow advance, and ultimately death in a more or less distinct uræmic condition. I have seen a few cases in which this occurred, without there being much to indicate the supervention of other renal disease.

There may be a partial or complete recovery. If the causal complication can be removed, the kidneys may gradually improve and again become sound. For upwards of twenty years I have known this fact both as to the liver and the kidneys, and my conviction has been more firmly established by the writings of Sir Dyce Duckworth[83] and others on the point.

All my experience tends to confirm the impression that the waxy process in the kidney passes through what we may,

for convenience of description, call three stages. I have examined after death a large number of bodies in which the kidneys appeared almost natural to the naked eye, but in which the microscope and suitable colouring materials revealed evidence of the degeneration. This corresponds to what we may term the first stage. If the disease has gone on for a considerable period, say from six months to one, two, or three years, the organs are found large and pale, constituting one of the varieties of what is still termed, by some writers, the large white kidney. The waxy disease is in such cases extensively distributed throughout the kidneys, but in addition there are secondary alterations. Many of the tubules are blocked by a hyaline or colloid material, and the epithelium is extensively altered, sometimes with ordinary inflammatory, and sometimes with simple degenerative processes. This transudation is the cause of the enlargement and the pallor of the organ, and the condition corresponds to the second stage. In cases which have lived on, say for three years or upwards, the organ is found to be more or less diminished in bulk, it may be only slightly, or to an extreme degree. If far advanced, the kidneys closely resemble those of advanced cirrhosis, but they differ in being less fibrous, in having the Malpighian bodies far more prominent, these structures being preserved while the surrounding tubules are completely destroyed, and the remaining tubules are seen in various stages of collapse consequent upon the absorption of their contents molecule by molecule. The fibrous stroma is relatively, nay, is absolutely increased, but not in the same measure as in the purely cirrhotic process. This constitutes the third stage. Of the correctness of this description I have no doubt, and while I quite admit that interstitial inflammatory changes may arise, and in some cases mainly account for the shrinking of the organ, it appears that the intratubular process is the more important cause.

We have next to inquire as to the cause of the albuminuria in cases of waxy kidney ?

May the cause be in the blood ? Of this we have no evidence. It is ordinary serum-albumen and globulin which transude, not any special form of albumen, and we know of no blood change whatever in cases of waxy kidney which could have the effect of producing albuminuria.

May the cause be in the blood pressure ? Here again we have no evidence in support of such a view. There is not the hypertrophy of the left side of the heart and the thickening and tension of the arteries which are present in cirrhotic Bright's disease. In fact there is no evidence of any marked alteration of blood pressure.

It has been maintained that changes in the epithelium of the tubules and of the Malpighian bodies may have to do with it. Undoubtedly, in many cases there are changes in these parts owing to the coexistence of inflammation, more or less extensive, or to degenerative changes secondary to the waxy degeneration proper. In some cases therefore we must ascribe waxy albuminuria to these causes, but they do not afford the whole explanation.

The great cause of albuminuria in waxy kidney is in all probability the alteration of the vessel walls. We know that their structure is markedly altered, and we can readily understand that though thickened their walls may have become more permeable. We have, indeed, an analogous phenomenon which lends a measure of support to this view. In waxy disease of the intestine there is profuse and persistent watery diarrhœa probably owing to the excessive transudation from the waxy vessels ; and this symptom, like the albuminuria, finds a ready explanation in this hypothesis.

LECTURE X.

ON ALBUMINURIA FROM FEVER AND OTHER CAUSES.

Febrile Albuminuria.—Statements of previous Observers.—Explanation of the Albuminuria.

Albuminuria from Diseases of Circulatory System. — Explanation.

Albuminuria associated with Diseases of the Alimentary System.—Explanation.

Albuminuria associated with Diseases of the Nervous System.—Explanation.

Albuminuria with Glycosuria.

GENTLEMEN,—Leaving now the consideration of the forms of albuminuria due to renal conditions of vital importance, we proceed to consider groups of cases in which the symptom appears in association with a variety of morbid processes, does not as a rule indicate serious disease of the kidney, and is a comparatively unimportant element in the morbid action.

The first group is that of *Febrile Albuminuria,* under which I include all forms dependent upon elevation of temperature whether the process be idiopathic or symptomatic, with the exception of such as are referable to renal inflammation or other categories. In Table XXI. I show you the results brought out in the different groups of cases examined.

TABLE XXI.—SHOWING THE INCIDENCE OF ALBUMINURIA ASSOCIATED WITH FEBRILE CONDITIONS.

	No. of Patients.	With HNO_3.	With Picric Acid.	Total.	Per cent.
Fever House, . .	50	18	15	33	66
Private,. . . .	150	1	0	1	...
Indoor Infirmary, . .	150	3	2	5	...
Outdoor Infirmary, .	100	0	0	0	...
Royal Hospital for Sick Children, . . .	50	2	1	3	...

You observe that in the Fever House cases, 33, or 66 per cent., showed albumen with picric acid; while 18 of these, or 36 per cent. had it in such quantity as to show distinctly with nitric acid. The proportions thus correspond pretty closely to those obtained on examining the old male paupers, the soldiers after fatigue duty, and the boys after violent and prolonged exertion. The proportion of febrile cases in the other groups was small, and in a number of these in whom pyrexia existed, the albuminuria was due to other causes. Among the indoor hospital patients, five showed albumen—two with picric, and three with nitric acid. Among the patients in the Sick Children's Hospital, three showed the symptom—two with nitric acid, one only with picric. Among the private patients, one only showed it, and that with nitric acid.

In giving these statistics I do not in the least assume that they afford ground for important conclusions; such results could only be obtained by one who had access to a much more extended series of febrile cases, and could work out a complete account of the facts in each variety of fever, examinations being repeated daily, or, still better, upon each micturition, so as to determine the precise incidence in each variety and in each stage of the process. I am not aware that this has been done more thoroughly by any observers

than by Dr. Stevenson Thomson,[84] in regard to scarlet fever, and Dr. George Middleton,[85] in regard to typhus and typhoid.

The former made observations on 180 consecutive cases of scarlet fever, three specimens from each case being examined daily for a period generally of about fifty-six days. According to the period of its occurrence he distinguishes between initial and late albuminuria, in the former the albumen being detected during the first week, in the latter not till after that time. He found 40 examples of initial albuminuria out of a total of 112 cases of albuminuria of all kinds in 180 cases of scarlatina. This variety is not itself dangerous —only becoming so when it passes into the late albuminuria, as it did in 9 out of the 40 cases. In 31 cases the initial albuminuria was speedily recovered from, but in 21 late albuminuria followed. Late albuminuria may occur at any time from the ninth to the forty-eighth day, but has a preference for the beginning of the second, third, and in a less degree, the sixth week. Of the 180 cases, 112 or 63·2 per cent. showed by the presence of albumen or blood in the urine more or less distinct signs of renal inflammation, 55 being cases of pure albuminuria, and 57 cases of hæmaturia. Of the latter some contained blood only, and it was in these that he sometimes found what has been called a "pre-albuminuric stage," by which is meant a "stage in nephritis, characterised by increased vascular tension, and, as a result, the presence of blood crystalloids in the urine *before* albumen makes its appearance." In some cases there was dropsy without albuminuria,—albumen appearing in some of these after the dropsy has become manifest.

His figures you observe correspond pretty closely to those which I obtained in the 38 cases of scarlet fever which we examined in the City Fever Hospital. His proportion being 63·2 and mine 60·53 per cent., but then his results refer to

the whole process, while my observations referred only to the early period, and corresponded to his initial variety only. I believe that the incidence of albuminuria in scarlet fever varies greatly in different epidemics, apart altogether from the surroundings of the patients.

Dr. Middleton reported that he had examined a series of 30 cases of typhoid and 27 of typhus as to the occurrence of albuminuria, in most instances daily for several weeks. He found that it appeared in 86·6 per cent. of his typhoid cases, and in 88·8 per cent. of the typhus; that it usually proved temporary, but in seven cases of typhoid and eight of typhus persisted as long as the patients were under observation. He found that the albuminuria tended to be more considerable in typhus than in typhoid, and that in both it was more severe than in scarlet. It was usually accompanied by tube casts, and other tokens of distinct organic renal lesion.

If we could obtain with regard to each of the fevers similar series of observations, we should be able to define the relationships of the individual fevers to albuminuria in a way that we cannot at present accomplish. My object in seeking opportunity for examining at the Fever Hospital was simply to get a general idea of the frequency of the occurrence of the symptom in idiopathic fevers, and of course the subject naturally emerged in analysing the other groups of cases.

An interesting relationship, not as yet by any means cleared up, exists between malarious fever and chronic malarial poisoning on the one hand, and albuminuria on the other. I have no means of knowing in what proportion of cases of malarious fever the symptom occurs, but certainly it is not uncommon, and one often meets with cases in which albuminuria has developed itself in those who have suffered from malarious poisoning, even although they have not had ague. It appears often to be associated with a degree of inflammation of the tubules, and to be attended by dropsy

and the presence of a few tube casts ; but often tube casts are difficult to find, or entirely absent, and there is no other token of renal disease. The patients often improve under treatment with quinine, arsenic, and iron.

It has long been known that albuminuria occurs in the course of fever. Among the first to draw attention to the fact was Dr. Warburton Begbie.[86] In a paper on "Temporary Albuminuria, more particularly as occurring in the Course of certain Febrile and other Acute Diseases," published in 1852, he pointed out the frequency of its occurrence without organic renal change. He met with it in scarlet fever, in typhus, in typhoid, also in cholera, and in erysipelas, pneumonia, and other inflammations. Since that time the fact has been universally recognised by the profession as a matter of every day experience. Idiopathic fever in all its forms, septic inflammations, erysipelas, diphtheria, inflammations of less definitely septic character, particularly pneumonia, have all been found to be frequently attended by it.

It is possible that relationships may be discovered between albuminuria and individual local inflammations. This possibility has been impressed upon me by the interesting and valuable paper published a few years ago by Dr. Matthews Duncan,[87] on "Albuminuria with Parametritis." He showed that of 16 uncomplicated cases of that disease, 6, or 37½ per cent., showed albuminuria, the albumen gradually disappearing as convalescence from the parametritis was established, and it appeared to be most frequent in cases which ultimately went on to suppuration. Dr. Matthews Duncan was satisfied that the albuminuria was neither due to cystitis nor inflammation of the kidneys, for no excess of mucus, no pus, and no tube casts were to be found. In a series of thirty-two cases of perimetritis, on the other hand, he found that albuminuria did not occur.

Drs. Englisch [88] and Frank [89] have drawn attention to the relationship between albuminuria and strangulated hernia. The latter observer found in 39 cases of hernia that albumen was present in 24, or 61·5 per cent., but of the 39, 12 were reduced by taxis, and in them only one showed albuminuria, while in 26 in which operation was required 22 showed the symptom. In the one remaining case the skin was already gangrenous, and albumen was present. He further found that the more severe the strangulation the more constant was the albuminuria; the patients did not exhibit the ordinary signs of nephritis; neither the history, the microscopic examination of the urine, nor the progress of the cases, corresponded to that disease. As soon as strangulation was relieved albumen disappeared or began to diminish, and it was always gone by the end of three days. The urine was never bloody, but blood-corpuscles and blood-casts were sometimes found on microscopic examination. Whether albuminuria occurs with obstruction of the bowel from other causes I am not prepared to say. It is curious to notice that Dr. Matthews Duncan did not find it in his cases of pelvic peritonitis, while the strangulation is evidently an important element in its production in the cases of hernia. It was very natural for Dr. Frank to suggest as an explanation that in connection with the obstruction a special poison might be elaborated and absorbed capable of producing the renal irritation, but it is difficult to frame an hypothesis which might serve to explain Dr. Matthews Duncan's facts.

The explanation of the clinical facts has been the subject of much speculation, observation, and experiment. To begin with, it is certain that in a large proportion of these febrile and inflammatory cases, congestive and inflammatory changes in the kidneys exist, the changes affecting mainly the epithelial structures, and sometimes the stroma of the organ. On post-mortem examination of the fatal cases we find every variety,

from the slightest cloudy swelling to the most pronounced alterations. But how does this inflammation arise? Some have supposed that it is caused by the direct action of fever germs upon the renal tissue. Others think it more probable that poisons produced by these germs, either from themselves or their action on the tissues, are the actual irritants. Some experiments seem to point to the conclusion that the renal change may be induced by mere elevation of temperature. Senator found that albuminuria was always produced when the bodily temperature was raised above the normal by from 3·4 to 6·7° F., "with sufficient rapidity, or the heat continued for a sufficient length of time." Blood even might be present if a very high temperature were rapidly induced. Even when there were no blood-corpuscles, pale hyaline casts, and sometimes finely granular ones, were found in the urine. He satisfied himself that the albuminuria was really due to the high temperature, and was not a secondary phenomenon manifested while the temperature was falling. The kidneys were hardened by boiling, and it was found that in those least affected there was only a very slight deposit of albumen, not visible in all the capsules; whereas in the more violent cases there was not only a morbid deposit of albumen, but likewise hæmorrhages in many capsules and uriniferous tubules, whilst in others there was no abnormality, with the exception of more or less marked hyperæmia. It appears to me probable that it may arise in various ways: sometimes, as perhaps in diphtheria, from irritation by septic organisms; sometimes by poisons evolved in their action; and sometimes by the influence of elevated temperature; or by the co-operation of more than one of these influences.

But besides these cases where inflammation of the kidney arises, there are others in which we are unable to demonstrate such a condition; and the question is, How is the albuminuria in these cases to be explained? It may be thought

that it is really a result of slighter degrees of irritation, and so it no doubt is in many cases; but, apart from this, we have to recognise some other possible causes. Experiment has shown that the processes of transudation through membrane become quickened when temperature is raised. If you take a membrane and set a saline or albuminous fluid to percolate through it, you will find that the process goes on much more quickly when the temperature is at or a little above 100° Fahr. than it does at the normal temperature of the air. It may be supposed, then, that with the rise of temperature in fever the renal walls become more permeable than they are in health. But the rise of temperature operates in another way, for it modifies the blood pressure. As we increase the heart's action the arterial tension rises, and such increase of tension may in some measure favour transudation through the vascular walls. The internal congestion which arises when the temperature is raised must have its influence in this respect also. But it is to be observed that it is not during the period of high arterial tension in fever that albuminuria is most apt to occur. It is rather at a later stage, when arterial tension has become lowered either from degenerative changes in the muscular substance of the heart, or the debilitating influence of high or prolonged fever, that the albuminuria is most apt to occur, and then the congestion is rather in the venous system, and it must be due to transudation through the capillaries surrounding the tubules, if due to vascular changes at all. Lastly, we must recognise as another possible factor in the production of febrile albuminuria the presence of albuminous substances in the blood different from normal serum albumen and globulin, and perhaps more capable of transudation through vascular walls. This, which is at present purely hypothetical, may one day be demonstrated to be an important cause of this albuminuria.

It is important to inquire what degree of danger attends albu-

minuria in fever. It seems to me that the mere presence of the substance is of little moment so long as it is merely transient, and does not lead to persistent organic change in the kidney.

Albuminuria from Disease of Circulatory System.—In Table XXII. are shown the results of our observations as to the incidence of albuminuria from these causes in the different groups of patients examined.

TABLE XXII.—SHOWING THE INCIDENCE OF ALBUMINURIA FROM DISEASE OF THE CIRCULATORY SYSTEM.

	No. of Patients.	With HNO_3.	With Picric Acid.	Total.	Per cent.
Private, . . .	150	1	1	2	...
Indoor Infirmary, . .	150	11	5	16	...
Outdoor Infirmary, .	100	4	1	5	...
Royal Hospital for Sick Children, . . .	50	0	0	0	...

This table shows that in a considerable proportion of the cases in which albuminuria occurs in hospital and ordinary medical practice, the condition is due to alterations in the circulatory organs. You will find, when you watch such cases closely, that the albuminuria comes and goes with the disturbance and recovery of the balance of circulation. The greater the backward pressure in the systemic veins, the more pronounced is the albuminuria; the more compensation becomes established, the less is the symptom apparent. Any effort tends to increase the amount of albumen; rest in bed diminishes it. The urine presents other changes worthy of notice: it is apt to be diminished in quantity, of high specific gravity, dark in colour, depositing urates, but containing a good amount of urea. One often fails to find tube casts in such cases after the most careful search, but sometimes hyaline or epithelial, or finely granular casts,

are met with; but wherever epithelial casts are distinct, we have a token that a measure of renal inflammation is present.

When we ask ourselves how this variety of albuminuria is to be explained, increased backward pressure is at once suggested as the direct cause. In all the cases of the kind there is such a disturbance of the balance of the circulation; and experiments by ligaturing the renal veins and otherwise obstructing the circulation have shown clearly enough that albuminuria may be thereby produced. Ludwig has shown that when the renal vein is closed, the capillaries round the tubules become overfilled, so distended, he says, as sometimes to close the urinary tubules. This over-distension gives rise to transudation of albumen, and that not occurring in the Malpighian bodies so much as from the capillaries surrounding the tubules. The experiments of Senator[20] afford conclusive proof as to the seat of the transudation. He ligatured the renal vein for a few minutes, and found that the tubules contained albumen, while the glomeruli remained clear, but that if he allowed the obstruction to last for a longer time they also in turn became the seat of transudation. Clinical observation affords a beautiful piece of evidence that the albumen does not escape from the glomeruli in patients suffering from cardiac disease. When we administer digitalis to such a patient the quantity of urine rises, and the albumen at the same time frequently diminishes, not only relatively, but absolutely. Now, the diuresis is explained by increase of pressure within the Malpighian tufts. This increase would necessarily be associated with increase of albumen if the capillary loops of the Malpighian tufts were to blame. The evidence seems to me quite sufficient to prove, if the proof were still required, that increased pressure in the vessels surrounding the tubules is the main cause of this form of albuminuria. It is true that changes not unfrequently occur

in the epithelium and the interstitial tissue, but many cases exhibit no such alteration; and when they do exist, they are to be regarded as further additions to the morbid process. I know of no evidence pointing to alterations of the vessel walls or altered conditions of blood as favouring the production of the symptom in cardiac cases.

Albuminuria associated with diseases of the alimentary system is much less common than the groups of which I have hitherto spoken. In Table XXIII. its incidence is shown in my different series of cases.

TABLE XXIII.—SHOWING THE INCIDENCE OF ALBUMINURIA FROM DISEASE OF THE ALIMENTARY SYSTEM.

	No. of Patients.	With HNO_3	With Picric Acid.	Total.
Private, . . .	150	1	2	3
Indoor Infirmary, . .	150	1	5	6
Outdoor Infirmary, .	100	0	1	1
Royal Hospital for Sick Children, . . .	50	0	0	0

Alimentary derangements which are thus shown to associate themselves with albuminuria are very various. Functional and catarrhal gastric affections, organic disease, such as cancer of stomach, intestinal disease with diarrhœa, strangulated hernia, and perhaps other causes of obstruction, and various functional and organic alterations of the liver, are known to stand in relation to it.

One is necessarily reminded in considering this group of the fact that the ingestion of food in many healthy people is followed by slight transient albuminuria. It is natural that in conditions where the digestive process is interfered with this should be still more frequent. We have some reason to think that the albuminuria in these cases may be

referred to altered blood pressure, or to altered chemical composition of the blood serum, or to both. But, in some cases, it would appear that ulcerated surfaces may permit of the absorption of albuminous materials, which come to be discharged by the kidneys unchanged. The observations in regard to the relationship of ulcerating carcinoma of the stomach and peptonuria are in this respect specially worthy of attention.

The albuminuria attending upon diarrhœa, as well as that so often observed in cases of cholera, might perhaps be referred in part to the diminished amount of water in the blood; but, as I have shown, it is much more likely that it results from changes in the state of the filtering apparatus.

The variety met with in association with hepatic derangements may, I think, be ascribed partly to morbid materials introduced into the blood in consequence of these derangements, partly to irritation of the kidneys by such morbid products, and partly to coincident alterations of the circulation in the kidney corresponding with those existing in the liver.

The late Dr. Murchison[90] and Dr. George Harley[91] have both pointed out very distinctly the tendency to albuminuria in diseases of the liver. Murchison refers to this tendency in many diseases affecting that organ. In some, as in cirrhosis, the kidneys are liable to be affected similarly to the liver. In others, he points out that renal degeneration may be induced by the continued elimination of products of faulty digestion through the kidneys. In others albuminuria may result from a mechanical effect on the kidneys, as when the venous outflow from them is obstructed by the pressure produced by ascites. There is also, he says, reason to believe that albuminuria may be induced by hepatic derangement independently of structural disease of the kidneys, the symptom being very often intermittent or remittent. The

albumen in this condition, he finds, has certain peculiarities, the addition of a little acid very readily preventing coagulation by heat. The urine is of normal quantity, of high specific gravity, habitually loaded with lithates, lithic acid, oxalates, and pigments. The albuminuria may be explained either by the liver having too much proteid to transform, or by deficiency of the chemical activity of the liver—in either case albumen being discharged unchanged. You will remember what I have elsewhere said as to the liberation of albumen from the red blood-corpuscles destroyed during their passage through the liver. I have only to mention this here to bring to your mind its bearing in relation to the production of albuminuria from hepatic derangement.

Dr. George Harley expresses views very similar to those of Murchison. He describes a condition which he designates "hepatic" albuminuria, dependent on disease of the liver, and characterised by the discharge of a normal amount of urine of good or even high specific gravity, containing casts of the renal tubules. He emphasises the value of treatment of the liver in such cases.

Albuminuria associated with diseases of the nervous system is not of very frequent occurrence. In Table XXIV. I have shown its incidence in my different groups of cases.

TABLE XXIV.—SHOWING THE INCIDENCE OF ALBUMINURIA ASSOCIATED WITH DISEASES OF THE NERVOUS SYSTEM.

	No. of Cases.	With HNO_3.	With Picric Acid.	Total.
Private, . . .	150	0	0	0
Indoor Infirmary, . .	150	1	4	5
Outdoor Infirmary, .	100	0	0	0
Royal Hospital for Sick Children, . . .	50	0	1	1

Among these there were two cases of epilepsy, one showing with nitric, the other only with picric acid; there were two of exophthalmic goître, one of infantile paralysis, and one of multiple sclerosis, all showing only with picric acid. We did not happen to have cases of hæmorrhagic apoplexy or other nervous disease exhibiting the symptom during the time that the observations were made. In my cases of exophthalmic goître the albuminuria did not present the peculiar features which occurred in the case which led to the discovery of this relationship by Dr. Warburton Begbie.[92] For in his case the albumen was very copious, and occurred mostly after breakfast; in ours it was scanty. It may be interesting to those familiar with the admirable paper of Dr. Warburton Begbie to know that his patient has now for years been quite well, the goître and the albuminuria having both entirely disappeared.

With regard to the question of the relationship of albuminuria to nervous disease, there has, in my opinion, been a good deal of inaccurate observation and rash assertion, and I believe that a thorough clinical investigation of the relationship, extended over a long series of cases, is much wanted. How often does it occur in cases of concussion of brain or cord? How often is it met with in hæmorrhage or other central lesions, and what are the special seats of lesion with which it is most apt to be associated? Is it really as common an after-symptom of epilepsy as some have supposed? Such questions I should like to see answered. I have not myself been able to collect a sufficient number of facts, but as we have seen, the proportion among the usually alcoholic inmates of the delirium tremens wards of the Royal Infirmary has not been so great as might have been anticipated among the forty cases that I examined.

In regard to the explanation of the symptom in the cases in which it does occur we cannot speak very positively,

as I have already shown. Its occurrence in diseases of the cord is usually at least a result of catarrh of bladder, and therefore such cases are referable to the accidental group. With regard to prognosis it does not seem to afford any indication.

The association of albuminuria with glycosuria is one which we sometimes meet with, and in Table XXV. I give the statistics as to its occurrence in the different series of cases examined.

TABLE XXV.—SHOWING THE INCIDENCE OF ALBUMINURIA ASSOCIATED WITH GLYCOSURIA.

	No. of Cases.	With HNO_3.	With Picric Acid.	Total.
Private, . . .	150	2	0	2
Indoor Infirmary, . .	150	2	1	3
Outdoor Infirmary, .	100	0	1	1
Royal Hospital for Sick Children, . . .	50	0	0	0

Dr. Arnold Pollatschek, of Carlsbad,[93] has recently published a paper showing that during two successive years about 37 per cent. of the urines which he found to contain sugar also contained albumen. The frequency of the association would thus appear to be much greater than has been generally supposed.

The explanation of the symptom is doubtless different in different cases. In some it is due to acute inflammation of the kidney; in others, probably to nervous influence, possibly sometimes to changes in the blood. But the occurrence of albuminuria in cases of diabetes is always of very serious omen.

LECTURE XI.

ALBUMINURIA—PAROXYSMAL—DIETETIC—FROM EXERCISE—SIMPLE PERSISTENT.

Four Categories.—Sketch of Progress of Knowledge on this Subject. —Christison. — Jaccoud. — Moxon.—Gull.—Morley Rooke. — Burney Yeo. — Clement Dukes. — Mahomed. — Fürbringer. — Runeberg. — Saundby. — Leube. — George Johnson. — Quain.— Stanley Rendall.—Pavy.—Maguire.

Paroxysmal Albuminuria.—Illustrative Case.—Relation to Paroxysmal Hæmoglobinuria.—Explanation.—Treatment.

Dietetic Albuminuria.—Illustrative Cases.—Positive and Negative.— Theoretical Explanations.—Treatment.

Albuminuria from Muscular Exertion.—Illustrative Cases.—Summing up of Features.—Theoretical Explanation.—Treatment.

Simple Persistent Albuminuria.—Illustrative Cases.—Summing up of the Features.—Theoretical Explanation.—Treatment.

Prognosis in the Four Varieties.

GENTLEMEN, — In this lecture I shall discuss some varieties of albuminuria not dangerous to life of which few examples occurred in the series of cases which I selected as the basis for this discussion, but which have attracted a considerable amount of attention in recent years. They have been variously designated functional, intermittent, dietetic, cyclical albuminuria, also the albuminuria of adolescence. They may be variously grouped, but it seems clear that at present four categories at least may be defined, which, although they run into one another and mutually overlap, perhaps varying in the same individual from time to time,

may yet with advantage be distinguished. These are, 1st, paroxysmal albuminuria; 2nd, dietetic albuminuria; 3rd, albuminuria from muscular exertion; and 4th, simple persistent albuminuria. I do not know whether this classification will ultimately turn out the most satisfactory, but I can illustrate each of the varieties with cases markedly characteristic.

In a few words I may explain the substance of what I deem the most important contributions to the subject in recent literature. Many years ago Sir Robert Christison[94] pointed out that the use of certain articles of diet and luxury sometimes induces temporary albuminuria. Jaccoud[95] formulated the statement that there are cases of persistent albuminuria in which the patient is substantially in good health, and in which there is no kidney disease. He therefore distinguished between persistent albuminuria and albuminuria from Bright's disease. Dr. Moxon[96] gave definiteness to our ideas by his paper, published in 1878, on chronic intermittent albuminuria. He divided cases of this kind into two classes: 1st, the albuminuria of adolescence, in which the symptom continues during a long period in a desultory and irregular way, so that in some it is rather occasional than intermittent; 2nd, remittent albuminuria, in which the albuminuria is in greater quantity and occurs more constantly from day to day, especially in the urine passed after breakfast, but is usually wanting in that passed in the early morning. He further divided these remittent cases into two groups, in one of which there is renal disease, in the other none. With regard to the albuminuria of adolescence, Dr. Moxon pointed out that it is a state of health to which young men are subject, which from its frequency deserves a special name. The patient is out of condition, listless, and languid, sleeps too much, and yet rises unrefreshed, is anæmic, and grey and sunken about the eyes. It is simply a state of debility without any organic

disease. The urine is found to be at times albuminous—most often after breakfast—while at other times it is quite free from albumen. He had met with nineteen cases of it, and of the seven cases which he records, two pairs were brothers, while another brother in one of the families affected was under his care with a different urinary abnormality—the persistent presence of a large excess of urea. This paper, as I have said, defined our knowledge, but that the existence of non-dangerous albuminuria was an idea familiar to acute physicians may be shown by the fact that Sir William Gull had told Dr. Moxon that in his experience albuminuria is almost as common in young and growing men and boys as spermatorrhœa. Dr. T. Morley Rooke[97] drew attention to the remarkable effect of rest in the recumbent posture in removing or keeping in abeyance the albuminuria of adolescence; and Dr. Burney Yeo[98] dwelt upon the importance of muscular exercise as a cause, and of rest in bed and the effect of food and wine as means of lessening the albuminuria.

Dr. Clement Dukes,[99] discussing the albuminuria of adolescence on the basis of his experience as Physician to Rugby, pointed out that it is extremely common and presents a great variety of features, both in its causation and special characters. Sometimes a sudden change in temperature, sometimes an error in diet, sometimes excessive exertion, sometimes mental emotion induces it. He showed that sometimes the diet has no effect, at others the most marked, so that a patient who has no albuminuria when taking milk, may get it when he adds a little bread to his diet, and one who, going about, requires to limit his food in the strictest way, can eat and drink freely if he remains in bed. It may be persistent for a very long time, or it may disappear and reappear; it it may be absent at one time of the day and present at another.

I shall not detail anything of the important contributions of Mahomed,[100] Fürbringer,[30] Runeberg,[101] Saundby,[102] Leube,[103] George Johnson,[29] Quain,[104] Capitan,[23] Semmola,[105] Von Noorden,[106] Keene of Philadelphia,[107] and Stanley Rendall,[108] but pass at once to a communication by Dr. Pavy,[109] made at the British Medical Association meeting in 1885, in which he suggests the name cyclic albuminuria, and gives interesting details of a number of cases. He describes the diurnal appearance and disappearance of the albumen very much as Dr. Moxon did. There may, he says, be considerable variation in the amount of albumen on different days. It may go on for weeks, months, or years, without impairment of health. There may be sharp, unduly forcible cardiac impulse, but the pulse is soft, not hard and sustained. There is nothing, he says, to show that it is an early stage of Bright's disease, or that it leads to any serious disorder. The urine is otherwise normal as a rule, with no casts, but occasionally sugar has been detected, while oxalate of lime crystals are frequently present. The age of patients observed varied from nine to forty-nine. Three cases were in children aged nine, eleven, and thirteen respectively, two boys and one girl. Dr. Pavy offers no theory, but compares the condition with some analogous phenomena of a diurnal character. Thus, in the phosphatic diathesis the urine may be normal in the early morning, whilst for a few hours after breakfast it is turbid from the presence of phosphates, becoming clear again in the afternoon and remaining so till after breakfast next day. There is also a diurnal variation in the temperature of the body. Thus a physiological cyclic change exists of which other illustrations could be adduced. This paper has given fresh impetus to the study of these cases.

Dr. Maguire,[110] in an able and interesting communication, has suggested that we may recognise three classes of

functional or cyclic albuminuria: 1st, those accompanied by general languor, low tension pulse, and no deposit of uric acid in the urine; 2nd, those with robust health, pulse of high tension, frequently some dyspepsia, and a copious deposit of uric acid; 3rd, rare cases in which some abnormal albumen is present in the urine.

Having thus given an idea of some of the chief recent observations on this subject, I proceed to describe and illustrate our four varieties.

I. *Paroxysmal Albuminuria.* I shall perhaps best convey an idea of the features of this form of albuminuria if I describe a typical case which I studied in the wards of the Old Infirmary. A young woman was admitted on account of acute illness. She had general *malaise*, some degree of fever, and gastric catarrh, but, on examination, nothing further could be discovered amiss, excepting that the urine was rather scanty, dark in colour, and was loaded with albumen. The microscope showed tube casts in great number and of several varieties—epithelial, granular, and hyaline. There were also some crystals of oxalate of lime. There was a degree of puffiness of the face, but no dropsy, and, notwithstanding the urgency of the renal symptoms, I ventured to express the opinion that the illness would prove transient and unimportant. My reasons for so doing were the suddenness of development of the renal symptoms, and the discrepancy between them and the general condition of the patient; and the opinion was further confirmed when it transpired that similar attacks had previously occurred and had speedily passed off. The next day the patient was much better; the albumen was disappearing, the tube casts were no longer so numerous, and before many hours had elapsed she was quite well.

This form of albuminuria stands in very interesting relationship to what is called paroxysmal hæmatinuria or hæmo-

globinuria, a disease which is ascribed by many to a morbid action of the liver. The patient in the intervals between the paroxysms may appear to be in good health. The attack begins with a slight feeling of chilliness, or a rigor attended by some uneasiness in the region of the liver and in the small of the back. The urine is of a dark colour, due to the presence of blood pigment. As a rule, the colour is due simply to hæmoglobin, but sometimes blood corpuscles may be detected when the fluid is freshly passed. They, however, even when present, tend to break down, and the blood pigment is liberated. There is, therefore, in this disease a hæmolytic process, a destruction of red blood-corpuscles probably due to some temporary derangement of the liver, and the liberated pigment is discharged by the kidneys. A single micturition may discharge all the hæmoglobin which has been set free, or it may appear during two or three micturitions. Now I think I may more clearly bring out the close relationship which exists between this disease and that which I have called paroxysmal albuminuria, by relating a case described by Rosenbach.[111]

A little boy, seven years old, after a severe fall from a waggon, became subject to attacks of periodical hæmoglobinuria. The attacks occurred pretty frequently, and exhibited the features common in the disease. The most interesting point for our present purpose is that at the beginning of each attack, before the hæmoglobin appeared, the urine became albuminous. This is by no means an exceptional circumstance; indeed, it will be found in many cases of hæmoglobinuria. It is probable that the process originates either in the nervous system, inducing a morbid action of the liver, or in a primary affection of that gland; and that it causes blood changes which irritate the kidneys, giving rise to a transient inflammatory action during the process of elimination of the waste products. Whether this view of the patho-

genesis of the process be correct or not, the clinical relationship of hæmoglobinuria to the form of albuminuria we are now discussing is unmistakable. The relationship is rendered the more distinct by their etiology, for, like those of paroxysmal hæmoglobinuria, the attacks of paroxysmal albuminuria are apt to be brought on by cold and wet, sometimes by errors of diet and alcoholic intoxication.

The characteristic features of this group of cases are easily recognised. The sudden and copious occurrence of albumen in the urine with numerous casts, the process lasting only a short time and recurring at intervals with or without a perceptible exciting cause, will justify you in diagnosing the condition.

What view are we to take as to the explanation of the process? Is it to be referred to changes in the secreting structures, in the blood-vessels, or in the blood itself? Considering that we have so marked a discharge of casts and epithelial cells, it is obvious that we must admit changes in the secreting structures. Alterations in the blood pressure may exist, but only as a secondary element. Changes in the blood itself, although not demonstrated, are, in my opinion, extremely probable, and they most likely induce the alteration in the kidneys. Irritation of the kidneys from blood changes is a very common phenomenon. You must frequently have noticed how, in cases of many varieties of jaundice, albumen and tube casts appear in the urine, and this evidently as a result of irritation of the kidney by the products of the hepatic disorder. In cases of oxaluria a similar change, probably depending upon a corresponding cause, is often seen. The analogy with the hæmoglobinuria process supplies another consideration in favour of the view. Such is the hypothetical explanation which at present commends itself to my judgment.

II. *Dietetic Albuminuria* is a variety which has long been

more or less distinctly recognised. Some people suffer from it whenever they indulge in certain articles of diet. In some cases one kind of food, in others many require to be proscribed; cheese, pastry, and eggs are among the more common offenders. My first experience of such cases was obtained when I held the office of resident physician in the clinical wards of the Infirmary. A member of the staff used sometimes to make his appearance with a pasty, puffy condition of eyelids, and he found that this was associated with albuminuria. His albuminuria proved to be dietetic. If he indulged in even a moderate amount of cheese or of pastry the symptom was pretty sure to arise. Such a passing and temporary albuminuria always and exclusively following upon error of diet is easily made out and avoided. On the other hand, there are some cases in which the albuminuria is little, if at all, determined by the kind of food, but the entrance of food of any sort into the stomach suffices to induce the symptom; and there are many in which the food determines the occurrence of albumen, and in which, nevertheless, some other factor also plays an important part in its production. In dietetic albuminuria we must, therefore, recognise at least these three factors as possible exciting causes: first, the use of certain kinds of food; second, the entrance of food (of any kind) into the stomach; and, third, one or both of these, in association with other influences, such as exercise or time of day. It will be readily gathered from the examples to be described, that each of these factors has a very different amount of influence in different cases, the symptom being chiefly due to one in some cases, to another in others.

I shall illustrate this variety by a negative and a positive instance. A gentleman consulted me some years ago on account of albuminuria, and when I was searching for the cause it transpired that his dietetic habits were such as might well have accounted for the symptom. He was accustomed

to a luxurious table, and acknowledged a special partiality for cheese. I asked him which were his favourites. He named Stilton, Rochefort, and Gorgonzola. I inquired as to the quantity, and he indicated that a piece three inches long, an inch and a quarter broad, by at least an inch thick, was his usual allowance. I expected that this would prove to be an important causal element in his case, and after various other experiments I directed him to take a good piece of one of his favourite cheeses, but found that no albuminuria followed. Indeed, I found that diet had little or no effect upon his urine. On testing it after dinner on one occasion I found that, although the meal had included a good allowance of *pâté de foie gras*, chicken croquets, roast pigeon with spinach, gooseberry tart, and a pint of Marcobrunner, the urine was normal. On another occasion, when a Welsh rarebit constituted part of the meal, a like result appeared. I found also that a breakfast of fried sole, a cup of coffee with milk, and a pint of milk with bread did not produce albuminuria, and a sumptuous luncheon was alike inoperative. The only food which seemed to induce the albuminuria was newly baked hot bread. Thus, it was clear that my first impression was wrong, and that the albuminuria in this case was not of dietetic origin. I shall show further on what its cause really was.

I shall now refer to a case in which a positive effect was apparent. The patient, then a medical student, called upon me first in the autumn of 1881, complaining of headache and dyspepsia. The heart's action was not satisfactory, but gave no indications of structural change either in the organ itself or in the kidneys. There was distinct, although not copious, albuminuria, unattended by tube casts or other token of organic renal disease. I ordered him a mixture containing chloride of ammonium and tincture of perchloride of iron. In the course of a week the albumen had diminished to a faint trace, and by the end of a fortnight it had dis-

appeared entirely. It did not recur until the following summer, when his vigour was reduced, owing to the work for the final examination and to anxiety in connection with the death of his father. It was then observed that, although not present in the morning urine, there was a distinct trace immediately after food entered the stomach. The rapidity of its onset was very remarkable. As soon as food of any sort was taken albumen began to be discharged by the kidneys. Being by this time a well-educated medical man, he was much interested in this circumstance, and found by experiment that if after commencing a meal he passed a little water, it was sure to be albuminous, although that passed a few minutes before was not. But the symptom was influenced also by the season of the year and the time of the day. It occurred only in summer and, while easily induced in the morning or at midday, it never appeared during the evening or at night. It had its special periods, but even during them the ingestion of food was the determining element. The breakfast and the midday meal always produced it, but never was a trace discoverable in the evening, whatever food was taken. The nature of the diet had at all times very little effect. If he lived upon rich food the albuminuria became no worse. If he made Revalenta Arabica and such like substances his diet, it appeared all the same. Even a milk diet seemed to produce no favourable effect, but he could not persevere in its use, as it did not suit him.

The results of exercise were carefully tested. They were found distinct, but much less marked than those of food. If he fasted of a morning, no amount of exertion induced the albuminuria. But if, when the albuminuria had been induced by eating, he took exercise, the quantity of albumen at once greatly increased. On the other hand, as with food, exertion failed to produce it during what I may call the non-albuminuric portion of the twenty-four hours.

There never were any tube casts, but oxalates were frequently present. The urine was occasionally high coloured, never bloody, sometimes deposited urates but never uric acid. He never had pain in the back or other local symptoms to draw his attention to the renal functions. The albuminuria thus recurred each summer till 1885, when it was very slight, and in 1886 it did not make its appearance. The last specimen of urine examined was natural in colour, specific gravity while warm, 1·020, distinctly acid, and contained no albumen or sugar. The condition of the heart is the same as it was in 1881. The state of the vessels is also the same as before, with perhaps a little increased tension. The walls of the radials are distinctly thickened. When the albumen was present there was always, he says, some intermission of pulse, but this has continued during the last year although the albumen has been absent.

By way of treatment, various plans were tried. Arsenic failed entirely. Iron produced little benefit. Spinal douches of cold water falling from a height of eight feet did much good; while cold sitz and Turkish baths (without the cold douche) increased the albuminuria. If, however, he took either a Turkish or a cold sitz bath in the morning when he had no albuminuria, neither of them produced it. But, on the whole, nothing proved so serviceable as the combination of iron with chloride of ammonium.

Summing up the facts ascertained in this case we find—

1. That albuminuria occurred only after ingestion of food.

2. That it occurred in summer and at certain periods of the day—viz., after breakfast and after the midday meal; never before breakfast or in the evening.

3. That its onset was sudden, setting in as soon as food reached the stomach.

4. That the nature of the diet appeared to have little or no effect.

5. That exercise had a decided effect, but only secondary to that of food.

6. That the albuminuria was worse after mental excitement.

7. That cold douches applied to the spine checked it.

8. That counter-irritation to the loins by mustard or croton oil did not at all diminish the albuminuria, but rather increased it.

9. That, as regards medicines, arsenic had no effect, and while iron proved slightly beneficial, iron with chloride of ammonium was much more efficient.

The first question which arose as to diagnosis in this case was whether Bright's disease existed or not. The state of the vessels, in respect both of their walls and tension, might have corresponded to this, and the heart's action was such as one sees occasionally in renal cases. But there had never been a trace of dropsy, there were no tube casts, the specific gravity was good, and the albuminuria came and went. Therefore, there was manifestly no inflammation of the tubules. The quantity of the urine, the specific gravity, and the absence of consequent complications, such as the retinal changes, excluded a diagnosis of cirrhosis, while there was no polyuria, or any causal or concomitant complications fitted to suggest waxy disease. It was also certain that the albuminuria was not an accidental result of disease of the urinary tract. I therefore concluded that it belonged to the category of unimportant albuminurias and gave from the first a correspondingly favourable prognosis. It was only later that all the facts which I have mentioned became known to me, and now, surveying them, it is clear that we have to do with a form of albuminuria referable to the functional group, being related to the ingestion of food, influenced in an important measure by season and time of day, but also markedly, though in a minor degree, to exercise.

Deferring what I have to say regarding the causation of dietetic albuminuria, I must express the wish that I could throw definite light upon the curious annual and daily cycle observed in this case—not a cycle of albuminuria, but a cycle of capacity for dietetic albuminuria. With our present knowledge, speculation on this subject is, however, not profitable.

This patient's constitution is peculiar, combining a marked nervous excitability with a tendency to hepatic derangement. He is liable to mental depression—often suffers from what he calls an ill-defined dread. His complexion is sallow, especially during what he terms his bilious attacks. These are attended by general malaise, headache, catarrh of stomach, irregularity of bowels, and functional disturbance of the liver. He is greatly impressed with the value of chloride of ammonium in the treatment, not only of his renal, but also of his nervous symptoms and his digestive disorders.

In order, then, to clear up the diagnosis in a case of supposed dietetic albuminuria, it is necessary to experiment with various articles of diet, and watch the result.

What explanation can we offer of this form of albuminuria? Obviously it cannot be due to primary change in the secreting tissue, for, although albumen may be very copious, there is no discharge of tube casts or renal epithelium. A chemical alteration of the albumen of the blood, or of its condition in other respects, naturally suggests itself. In regard to the first of these suppositions, one can understand how, with faulty chemical processes within the body, digestion of nutritive substances and transformations of albumen might be abnormally performed, and albumens more capable of transudation produced, but I know of no sufficient evidence of the real existence of such a process. The excretion of more diffusible forms of albumen, such as propeptone and peptone, is, of course, known to be of not infrequent occur-

rence, and it may, in some cases, be related to digestion, but at present we are studying cases in which the ordinary forms of albumen—serum albumen and serum globulin—are met with.

Apart, however, from any such problematic change in the nature of the albuminous constituents of the blood, we have to consider another possible explanation. It is definitely known that changes in some of the other blood elements exert a marked influence upon the filtration of the ordinary forms of albumen. We have seen that the quantity of albumen which passes through a filter increases with the increase of the saline constituents. Chloride of sodium is the most efficacious, but nitre, chloride of calcium, and even urea exert a certain influence. We can readily conceive that, after a meal, the salts of the blood may be increased; it seems possible that in this way transudation of the albumen may be induced. The whole question of the influence of salts on the circulation is very interesting. If you attempt to pass fluids of various kinds through the vascular system of the kidneys of animals recently killed, you will find that it is much easier to pass one rich in salts than simple water. But to this subject I have already alluded, and I would say, meanwhile, that, although the fact as to diffusion is well established, its applicability in the explanation of such cases as those we are considering is not yet demonstrated.

While, however, giving these suggestions towards chemical explanations due weight, I cannot but advert to the possibility of reflex vascular influence being at work. We may conceive that, on the entrance of food into the stomach, the terminations of the vagi may be morbidly influenced, or that the nerves supplying the renal vessels respond abnormally to a normal peripheral impression. I have already accentuated the fact that the patient, whose case I have last described, says that as soon as food reaches his stomach the albumen

appears, and that the nature of the food ingested makes no difference. One can scarcely suppose that sufficient time has elapsed for absorption, chemical alterations, and excretion, and it seems reasonable to suspect that an influence exerted on the vessels through the nervous system would have more chance of bringing about the result within the time. While throwing out these suggestions, I must admit that our present knowledge does not suffice to afford a satisfactory explanation.

III. I shall now illustrate *albuminuria following upon muscular exertion*, and shall bring out its features by narrating a case at present (July, 1886) under my care. The patient is a girl thirteen years old. I show you a sample of her urine, passed on rising at 7.30 A.M. When I test it with nitric acid you see that it contains no albumen, or only the very faintest trace. But this specimen, which was passed an hour later, after dressing and moving about the house, but before any food had been taken, is, as you see, highly albuminous. Thus the getting up is followed by this extraordinary and marked albuminuria. The history of the case is as follows:—Her previous health is reported to have been good. About last Christmas, while at a boarding-school, she had an attack of diphtheria, which is, like scarlatina, a not uncommon cause of albuminuria by the production of inflammatory Bright's disease. She did well, however, and went through the whole illness without a trace of albumen appearing in the urine. I can say so with confidence, as I know that particular care was taken in regard to its examination. When, however, she was convalescent, and was getting up and going about the house (but not getting out), albumen was detected. This does not correspond to the ordinary clinical history of albuminuria connected with diphtheria. As a rule, it appears during the attack, or on exposure to cold, within a few days of its subsidence. My own experi-

ence in this matter corresponds with that of others. Dr. John Abercrombie,[112] for example, says that while he has seen it occur within twenty-four hours of the first symptoms of diphtheria, he has never seen it commence later than the tenth day of the disease. During January, a few tube casts were found on two occasions, and sugar was present once or twice in small quantity. At first no peculiarity was observed as to the albuminuria, and so it was of course believed to be constant, and regarded as a result of renal disease due to diphtheria. It was only after some considerable time that it was discovered that the urine passed on getting up in the morning, and also that passed during the night, contained no albumen. This fact was noticed the first time the urine of these periods of the day was separately tested, and from inquiry I find that, although the peculiar periodicity was only then observed, it may have existed from the first, and I think the history and progress of the case make it most probable, in fact almost certain, that it did so. I have said that traces of sugar were sometimes discovered in the early period of the illness. No trace of it has ever been detected since the patient came under my care, nor have there been any casts. In a specimen passed on rising, however, we found one morning a well-marked layer of oxalates deposited on the top of the mucus, and under the microscope octahedral crystals of oxalate of lime were seen in very large numbers. Curiously, in a specimen passed an hour later, there was not a single oxalate crystal; the urine had become alkaline, and there was a pretty copious deposit of triple phosphates.

This patient has now been for a considerable time under my observation, and I can give some interesting details as to the features of her albuminuria and as to some experiments which we have made regarding it. I have already pointed out that the urine passed on rising—and the same has been true, except on one or two occasions, of that passed during

the night—contains no albumen, or only the merest trace. Now while she is up the albumen is constant, though once or twice toward evening the quantity has been small. But the fact as to the daily cycle of the albuminuria is, that the quantity is, as a rule, largest in the morning in the urine passed before breakfast. I have many times examined samples passed forty-five minutes after she got up and before she had taken any food, and have found the albumen in them to be very copious. It would appear, therefore, that the moment she gets up there is a sudden onset of albuminuria, so that this case forms, in this respect, an interesting parallel to that which I have described in the dietetic group, in respect to suddenness of onset, although due to a different cause. During the forenoon the albumen has several times been observed to become distinctly diminished in amount. Sometimes, though not so often, it is in largest quantity later in the day—during the afternoon or the earlier part of the evening.

I have further tested the conditions of the albuminuria by experiment. On one occasion she remained in bed a whole day and two nights—about thirty-six consecutive hours, taking her ordinary diet during the time. The result was that the albumen scarcely appeared. Indeed, there was in only one of the samples passed during that period anything more than a mere trace, and in that sample the quantity was small. Curiously, in the urine passed at night after she had been all day in bed, albumen appeared in small quantity. In that passed in the morning there was a mere trace. She then got up, and in the urine passed forty-five minutes after, the albumen was found to be present in large quantity,—distinctly larger than it had usually been before. It was again present in small quantity the following night, and there was a distinct trace on rising the next morning. After that, the former cycle became re-established. Thus the rest in bed, though it

greatly diminished, did not entirely prevent the albuminuria ; and it was followed by an increased elimination of albumen when she got up, and a disturbance of the ordinary diurnal cycle. A corresponding result was elicited when the same experiment was repeated.

On another occasion an experiment of an opposite kind was made. She was asked to rise at 5 A.M., dress, and walk about the house for three-quarters of an hour. The urine passed on rising was free from albumen, whereas that passed forty-five minutes later contained abundance of it. She then lay in bed till 7 A.M., and the urine passed at that time contained no albumen or only a mere trace. She got up, and by 7.45 the albumen was again abundant.

On another morning she was asked to lie in bed and to move about the arms and legs, thus taking exercise in the recumbent posture. This she did for twenty minutes, and the astonishing result was that the urine passed after the time of exertion was, like that passed before it, perfectly free from albumen.

The next morning she was subjected for twenty minutes to very efficient massage in bed, but neither before nor after it did albumen appear.

A warm bath proved equally inoperative. Experiments were also tried with different kinds of diet, and they turned out to have very little effect. She was fed for several days exclusively on milk. It produced marked diuresis, and so, the urine being increased, the albumen seemed diminished, but the diminution was merely relative, not absolute. The subsequent addition of an egg daily and some bread and butter to the diet did not produce any evident increase in the albumen. Nor did it increase when ordinary or even rich diet was prescribed.

I have put in a tabular form, on page 157, the most important points connected with the urine in this case. The

first table shows the patient's usual cycle, the second the cycle as influenced by experiment. From these experiments it is obvious that the change from the recumbent to the erect posture is at least the main factor in the production of the albuminuria, remarkable as that may appear. Diet has only a very slight effect, and the condition contrasts strikingly with that seen in the dietetic case which I have described. This case also differs from most if not all the so-called cyclic cases which I have seen recorded, in respect of the suddenness of the onset of the albuminuria. In them it commenced, as a rule, gradually and increased during the earlier part of the day, and then gradually diminished toward night, flowing and ebbing like the quiet tide, whereas in our case, though the diminution is gradual, the onset is sudden and abrupt like the tidal wave which is seen in certain rivers.

I have now related most of the facts of the case, and will next discuss the question, What is the nature of the albuminuria from which she suffers? Is this young lady affected with, as was at first assumed, a hopeless, chronic renal disease which must almost inevitably send her to her grave before she is twenty, or has she merely an unimportant albuminuria without organic disease, which may, perhaps, disappear when she gets past her present critical period of life, and at all events gives no ground for anxiety? From a careful study of the case, I am convinced that the latter is the correct diagnosis. The grounds upon which I have formed this opinion are:

1st. That there is a period in every day in which the urine is free from albumen;

2nd. That the quantity of urine and of urea is normal;

3rd. That except on two occasions no tube casts have ever been found; and,

4th. That there is no symptom except the albuminuria at all fitted to suggest the idea of organic renal disease.

TABLE XXVI.—REPORT OF EXAMINATIONS OF URINE IN CASE OF ALBUMINURIA FROM EXERCISE, BEGINNING WITH 20TH JUNE, 1886.

	Specific Gravity.	Reaction.	Albumen. Quantitative estimation by Dr. Oliver's Percentage Method.	Percentage of Bile Salts normal = 100 per cent.	Urea in Grains.
June 20th.					
7.45 A.M., ...	1023	Distinctly acid.	Trace.	240 or 200	110·6316
8.50 A.M. Before breakfast,	1013	Faintly alkaline.	0·133 per cent.	300+	2·757
10.30 A.M. An hour after breakfast.	(Below average.)	Slightly alkaline.	Less than 0·05 per cent.	300	17·89426
6.30 P.M. After dinner and tea.	1029	Faintly acid.	0·13 per cent.	240	38·67
9 P.M. Going to bed, .	1026	Decidedly acid.	0·06 per cent.	150	66·102
Total, ...	....	....	....	....	236·0548
June 21st.					
Night, ...	1011	Distinctly acid.	Trace.	100	58·93674
7 A.M., ...	1016·5	Acid.	Very slight trace.	166	64·8
10.30 A.M., ...	1017	Very faintly acid.	0·24 per cent.	300	24·25

Neither sugar, peptones, nor bile pigment present in any of the specimens.

TABLE XXVII.—URINE BEFORE, DURING, AND AFTER THE EXPERIMENT OF RISING AT 5 A.M., GOING TO BED AGAIN AT 5.45, AND RISING AGAIN AT 7 A.M.

	Specific Gravity.	Reaction.	Albumen. Quantitative estimation by Dr. Oliver's Percentage Method.	Percentage of Bile Salts normal = 100 per cent.	Urea in Grains.
June 22nd.					
9 P.M., ...	1027	Acid.	0·08 per cent.	240	69·267
June 23rd.					
Night, ...	1020	Slightly acid.	Faint trace.	166 or less.	72·5933
5 A.M., ...	1019	Acid.	Almost imperceptible.	166	29·388
5.45 A.M. Arose at 5 A.M., .	?	Acid.	0·05 per cent.	300	5·6038
7 A.M. In bed since 5.45, .	1013	Acid.	Scarcely perceptible.	240 or 200	17·04713
7.45 A.M. Up since 7 A.M., .	1009	Neutral.	0·06 per cent.	183 (?)	4·4361
2.30 P.M., ...	1023	Slightly acid.	0·3 per cent.	200	41·40092
9 P.M. Going to bed, .	1027	Strongly acid.	0·16 per cent.	183	81·13725
Total, ...	....	....	....	....	251·60659
June 29th.					
Night, ...	1012	Acid.	Faint trace.	150	99·2715
7 A.M., ...	1024	Acid.	Very faint trace.	240 or 200	36·1269
7.45 A.M. Still in bed, before breakfast.	1024	Acid.	Very faint trace.	300	6·6111

No sugar, peptones, or bile pigment in any of the specimens.

I shall now recur to the case of the gentleman regarding whom I have already given some details. The patient is between twenty and thirty, and has travelled very extensively, riding and walking a great deal. The earliest symptom of which he complained was a painful uneasiness in the calves of his legs. The most careful examination afforded no evidence of disease in any part of the body, some degree of dilatation of the stomach and the abnormality of the urine alone excepted. On 5th June, 1885, I examined six specimens of his water. At 7.30 P.M. the albumen was copious; at 8.50 it was very distinct; at 9.30 A.M. there was a trace; at 10.30 it was distinct; at 12.30, the patient having in the meantime taken a walk, it was copious. There were no tube casts, and the amount of urea was normal. A few days later, after he had recovered from the fatigue of a long journey, I found at 1.50, 3.40, and 5.45 P.M. no albumen; at 7.30 a trace; at 8.30 A.M. a very slight trace; at 10 A.M. a slight trace. I have already pointed out that diet, even of a rich, varied, and ill-chosen sort, produced no albuminuria. On the other hand, walking, especially walking up hill, always did so. He lived in a hotel in Princes Street, and could walk to Charlotte Square with little or no effect on the urine, but if he took a walk to the Calton Hill, the Castle, or Arthur's Seat, the albumen became copious. With rest it gradually disappeared. Carriage exercise seemed to produce no unfavourable effects. Massage, which had been very carefully tried, being thoroughly carried out for forty or fifty minutes by a most competent rubber, was also without result. I tried the effect of exercise in a sitting posture. He sat in his chair and played the banjo for an hour, and then used dumb-bells for fifteen minutes. The urine passed immediately afterward was normal, but that voided half-an-hour later contained albumen. I did not think of trying the effect of muscular movement when he

was lying on his back. It was however abundantly clear that muscular exertion, and particularly active walking exercise, was the chief exciting cause in this case also, while no effect was produced by a change from the recumbent to the upright position. I need not again go over the reasons which led me in this case also to give a favourable opinion.

As to the origin of the symptom, it is worth noting that in his travels he once walked through Asia Minor in a wonderfully short space of time, and it was during or after this feat that the albuminuria was first observed. It is very probable that the great strain on his system which his feat implied was the starting-point of the albuminuria, which subsequently, when the damage had been done, could be induced by a much less amount of exertion.

Passing from the illustrative cases, I shall now direct attention to certain special points of interest connected with them :

1. The kind of albumen discharged has recently received some attention. Dr. Maguire [54] has published the results of investigations as to the forms of albumen met with in different diseases, and he concludes that the less grave the case the greater is the amount of paraglobulin in proportion to the amount of serum albumen. In three cases of cyclic albuminuria he found that the albumen present entirely, or almost entirely, consisted of paraglobulin. In a case described as one of anæmia with albuminuria, due in all probability to fatty degeneration of the kidney, both serum albumen and paraglobulin were present, but the latter was in much greater quantity than the former, while in Bright's disease the proportion of these two substances was reversed. On examining very carefully into this question, in the case of the young lady, the serum albumen was found to be in greater quantity than the paraglobulin, and, as it was

certainly functional, I cannot admit the universality of Dr. Maguire's conclusion.

2. Another observation as to the kind of albumen present has been made by Dr. Pavy. He finds that sometimes it is not ordinary serum albumen, but alkali-albumen. I am not in a position to confirm this statement from my own observations, but I have been struck with the facility and rapidity of formation of acid albumen, very slight quantities of acid sometimes preventing coagulation by heat.

3. No peptones, or any other body of that group have been found in our case, and very little is said of them in cases recorded by others. I observe, however, that Dr. Oliver,[113] of Harrogate, has met with an instance of intermittent albuminuria, in which peptones replaced the albumen for a time.

4. My patient, though she had no distinct œdema, had a pale, puffy-looking face. This was, I believe, due partly to a general morbid condition of the vessel walls, and partly to the anæmia which often accompanies this affection.

5. Occasionally sugar is found instead of or in addition to the albumen. It was detected early in the illness by good observers in both the cases last described ; and this fact, as will be seen, lends support to the hypothesis that faulty metabolism may have to do with the production of the albuminuria in such cases.

6. Other chemical changes also occur. Thus phosphates may be present in addition to, or alternately with, the albumen. Urates are sometimes very abundant, and sometimes uric acid is present in considerable quantity. The most common of all the additional chemical abnormalities is the presence of oxalates. They occur, at least occasionally, in a large proportion—I should say in the majority—of cases. It is found that ordinary oxaluria sometimes leads to temporary albuminuria and the presence of tube casts,

probably by irritating the renal tissues ; but, in addition, it should be observed that oxalates very frequently appear in the course of the cases we are considering.

7. The bile salts have been found present in very considerable excess. In the case recorded by Dr. Oliver, to which I have already referred, this was so. In one of my cases also they were present in marked excess, and my friend, Dr. Stevens, who has devoted much time to this subject, drew my attention to the fact that there has been a diurnal cycle in their excretion corresponding, in the main, to the cyclic character of the albuminuria. This was very distinctly made out when the patient was on ordinary diet, and nothing was done to disturb, in any way, her daily routine of life. The urine passed at night usually contained little more than the small quantity which one expects to find in the urine of healthy individuals. In the urine passed on rising they were in excess, still more in that passed before breakfast, at which time the quantity sometimes reached its maximum for the twenty-four hours. The amount, as a rule, kept up during the day, and diminished toward evening. One interesting fact thus brought out is that the excretion of bile salts began to increase during the morning before rising, so that, whereas the albuminuria appeared to be due to exercise in the upright posture, and to be little influenced by anything else, the excretion of the bile salts was partly influenced by exercise, but partly dependent on some other factor. This is further shown by the circumstance that when the patient was kept in bed for thirty-six hours the diurnal cycle in their excretion continued to be observed.

I may further state that a diurnal variation has been observed by Dr. Oliver in the secretion of the bile salts in health, and his result may be broadly stated to be that the quantity increases during fasting and diminishes during

digestion—falling rapidly after meals. But in this patient's case this is entirely altered. The night urine, during fasting, contains the smallest quantity of all. No doubt it increases toward morning, and still more when she rises before breakfast ; but then the quantity keeps up during the day while digestion is going on, and only falls again toward night. A similar change was observed by Dr. Oliver. He found that when albuminuria occurred after a meal the bile salts were excreted in increased quantity, whereas if at any time albuminuria did not occur after a meal, the excretion of bile salts was within the normal range. It will be observed that Dr. Oliver found this change in the discharge both of albumen and of bile salts to stand in relation to the diet, whereas in our case it is related to exercise. The two cases are, therefore, not similar, the one being an albuminuria from exercise, the other, as stated by Dr. Oliver, being of hepatic origin. We have in this altered excretion of the bile salts an indication of some morbid change in the chemical or absorptive processes which I shall discuss later on.*

* Until recently our only method of detecting the bile salts in the urine was that of Pettenkofer by sugar and sulphuric acid. This method, however, owing to the necessity of first extracting the bile salts from the urine, though it might be satisfactory in the hands of chemists, was impracticable as a clinical test. Dr. Oliver,[6] of Harrogate, has devised a method free from this objection, and by which a quantitative estimate can be made. It depends on the fact that the bile salts precipitate albumen or peptone when the fluid is of the requisite degree of acidity, and the test is done in specially graduated tubes with a standard solution of peptone acidified to the proper degree by acetic acid. The solution is, however, difficult to prepare, and, if much used, comes to be expensive. A simpler qualitative method, depending on the same property of the bile salts, but requiring no special reagent, was devised by Dr. Stevens (Ettles Scholar for 1884, and at present one of my assistants, in the course of his clinical work as holder of the Stark Scholarship in Clinical Medicine). The urine, if not albuminous, must first have a little albumen added to it. An albuminous urine does very well for this—care being taken that one is selected which does not itself contain any excess of bile salts. A few ounces

8. The presence of a normal amount of urea and the general absence of tube casts are specially worthy of our notice.

We have now to ask ourselves what explanation our present knowledge enables us to give of the cases of this class. While it must be at once conceded that changes of a gross kind in the secreting renal tissues are not very probable, it might be held that molecular alterations of the cells in the Malpighian tufts dependent upon congenital peculiarities might exist, permitting the transudation of albumen along with the water of the blood serum. But I am not aware of any sufficient evidence in favour of such a view, and the conditions under which the albumen appears seem susceptible of a better explanation. There are some considerations

of albuminous urine can be carbolised and kept just like other test solutions for any length of time. If now the urine be poured into a conical glass and a little cold nitric acid be run carefully down the side, there will be, if bile salts are present in sufficient quantity, a precipitate of albumen at a certain level in the urine, separated by a clear area from the precipitate of albumen produced by the nitric acid. This upper precipitate of albumen is produced by the bile salts at the level at which the urine has become acidified to the proper degree. A slight reaction may occur even with the small quantity of bile salts present in normal urine, and a similar faint precipitate may also be seen in healthy urine owing to the precipitation of mucin by the nitric acid. A little practice, will, however, soon enable you to distinguish the slight precipitate which may occur in health from the well-marked and dense precipitate which appears when the bile salts are present in excess. It is, of course, necessary to avoid mistaking a precipitation of urates by the nitric acid for this reaction; should there be any doubt, the effect of heat will set it at rest. As the test is simple and easily worked, and requires no special reagent, it is well fitted for ordinary clinical work. Another method of testing the bile acids has been introduced by Prof. Matthew Hay of Aberdeen, founded upon the discovery that when bile acids are present in urine, the surface tension is lowered. It consists in gently dropping a little sulphur on the top of the water. In normal conditions it remains on the top, when bile acids are present it sinks rapidly. Dr. Stevens found that in consequence of the diminished surface tension the drops discharged from a pipette are smaller, and he finds that by thus counting the drops from a given quantity of urine taken up in a pipette, he can pretty accurately gauge the proportion of bile acids.

which favour the supposition that chemical changes in the serum may be the cause—namely, the occasional coexistence of other morbid states of urine, such as glycosuria, phosphaturia, or oxaluria. Manifestly no change in blood pressure within the kidney or in the walls of the vessels, and no changes in renal epithelium could account for these, and it seems necessary to conclude either that the albuminuria and they are common manifestations of a faulty metabolism, or that, independently of alteration in the kidney inducing the one, we have alterations in the liver or other organs setting up the others. The other possible cause of the albuminuria, namely, vascular changes, seems to correspond most readily with the facts observed. The marked influence of muscular exercise and exercise of particular kinds, and in particular postures, does not seem readily explicable on the chemical hypothesis, while what we know of the physiology of the blood-vessels prepares us to believe that alterations of their lumen and of the blood pressure within them might readily be induced under such circumstances, and result in the symptom in question. The occasional occurrence of glycosuria and the excess of bile salts might be advanced as difficulties in the way of this explanation, but it is easy to conceive that a general change in vascular activity which in the kidney induces albuminuria, might, by its influence on the liver, induce the other abnormalities. My judgment, therefore, leans toward this hypothesis, but I cannot give positive proof of its correctness.

IV. I now proceed to consider much more briefly the fourth category of cases—those of *Simple Persistent Albuminuria.* I cannot speak so positively and definitely in regard to them, for, on the one hand, they are certainly rare, and on the other, they are difficult to differentiate from examples of slight chronic organic renal disease; still our conception of this subject would be incomplete if we did not refer to them.

I can recall the case of a student whom I watched all through his University career. He looked quite healthy. No casts were ever found in his urine and the albuminuria was only accidentally discovered. He never had any bad symptom. He successfully went through the arduous work of a four years' course in medicine, which may be taken as a sufficient guarantee that, despite the albuminuria, his health was not in any way seriously impaired. I cannot be certain that he had no intermissions, but I do not think he had.

I have at present under my care a gentleman whose case probably is referable to this category. He has persistent slight albuminuria, none of the many specimens passed at all hours having ever been found free from albumen. But he has no tube casts and he discharges a normal quantity of urea. The albumen is scarcely influenced by diet or exercise, although, as is so often seen in all albuminurias, it is least abundant during the night and early morning. There is no distinct increase of vascular tension and no cardiac hypertrophy or other consequent complication of renal change. The only competing diagnosis is slight irritation of the urinary tract, due to an old gonorrhœa from which he formerly suffered. But as there is no positive evidence of this, I incline to think that a simple persistent albuminuria is the most likely cause.

I shall now record a case which I believe to be a well-marked example of this form of albuminuria. The patient is a medical man in active practice, who consulted me in October, 1886, regarding the state of his health. He had for some time previously had enlargement of the cervical glands, and one or two of them had threatened to suppurate. By the time he consulted me, however, some improvement had occurred in the state of the glands, and suppuration seemed less likely to result. There was nothing in his condition to

suggest any renal abnormality ; but on examining the urine I found that it contained a considerable quantity of albumen. I then decided to have a very careful investigation on this point made, and for that purpose asked him to send me separately the urine of each micturition for a period of twenty-four hours. I received from him samples passed on 19th Oct., at 9.30 A.M. on rising, and at 1, 4, 7, and 9 P.M., and on 20th Oct. at 1 and 4 A.M., and at 8.45 A.M. on rising. All the specimens were albuminous, but the albuminuria was not so copious as it had been when he consulted me. The urine was normal in colour. The mixed urine of twenty-four hours measured 64 ounces, had a specific gravity of 1025, and was of acid reaction. The discharge of urea in twenty-four hours amounted to 617 grains. No sugar or peptone was present. Microscopically there were found one or two hyaline casts and mucus corpuscles. The urine was carefully examined several times after this, and it always presented the following characters :—The quantity was rather above the normal average ; the specific gravity was high ; the reaction was distinctly acid ; albumen was constantly present ; no sugar, peptone, or bile pigment was ever found ; the amount of urea was above the normal average ; a few hyaline casts could, as a rule, be detected.

It was sometimes observed that the colour reaction, produced by the action of nitric acid on the urinary pigment, was decidedly more marked than in normal urines. Amorphous urates were sometimes copiously precipitated, and occasionally uric acid crystals were present. The bile salts were not markedly affected. When the mixed urine of twenty-four hours was tested no excess was detected. When samples of each micturition were tested there was found to be a slight increase in some, but this was not constant.

In order to discover what amount of loss to the system was

involved in this drain of albumen, a quantitative estimation was made on 4th Nov. by Esbach's method. It was found that the urine contained 0·8 gramme of albumen per litre, or 0·08 per cent. The total loss of albumen in twenty-four hours was 19·25 grains — an amount really quite inconsiderable.

The characters of the urine which I have described justified us in hoping that this gentleman might, so far as his renal functions were concerned, expect to enjoy his active life in the future as he has done in the past. Unfortunately the glandular disease appears to be advancing, although the renal condition is at least no worse. With no form of grave renal disease could we have such a condition of the urine. Wherever the primary fault may be, it certainly is not in the kidneys. The presence of an excess of urea along with albumen corresponds with what Dr. Ralfe[51] has found in such cases, and I know of no better explanation of the condition than that which Dr. Ralfe has given.

The features of this kind of case I take to be persistent presence of albumen, usually in small quantity, with few tube casts, and these mostly hyaline, without diminution of urea, increased vascular tension, cardiac hypertrophy or other consequence of renal malady, persisting for a period of months or years, and little influenced by diet or exercise. I cannot say whether further experience will confirm this view or not.

The last question which occurs in regard to these cases is as to prognosis. Are these different forms likely to continue simple, or do they culminate in organic renal disease? I think that in the first category there is a slight tendency to this latter issue. In the second and third categories it is less likely. From what has been said by such eminent authorities as Dr. George Johnson,[29] and Dr. Clement Dukes,[99] we

cannot but fear that the condition does sometimes culminate in organic disease, but so considerable a proportion of my cases have gone on for long periods without doing so, that I am confident that it must be rare. Dr. George Johnson has seen several cases in which, beginning with the simple affection, Bright's disease has developed. He mentions the case of a distinguished London physician, in whom at first albumen only appeared occasionally after walking exercise, and then was present in large amount, while diet had no apparent influence. After a time the albuminuria became persistent, and in the end fatal uræmia resulted. It is, of course, possible, that this was an example of cirrhotic Bright from the first, but when a contrary opinion is held by Dr. Johnson who saw the case, we are bound to conclude that the evidence was strongly in favour of his view. Dr. Clement Dukes concludes that many cases are without doubt only transient, that probably many persist for years and yet recover, but he believes that a large proportion are simply the first stage of Bright's disease.

It must not be forgotten that one may find in some cases of cirrhotic Bright's disease the urine generally free from albumen, that abnormality occurring only when the patient has taken alcohol to excess, has been chilled, or over-fatigued with travelling. But in such cases vascular and cardiac changes, and very probably alterations in the retina will be found, which give conclusive proof of the existence of cirrhosis. Neither must it be forgotten that cases of cirrhosis may show no albumen in specimens passed during the night or in the early morning, while in the day and evening urines it is distinct enough.

The fourth category is one in which my prognosis would be less hopeful. Still, so long as the solids are in the normal quantity, and the vascular changes do not manifest themselves, we may speak hopefully even in such cases.

LECTURE XII.

ALBUMINURIA—ACCIDENTAL, &c.

Number found in Groups of Patients.—From Catamenial and other Discharges.—Discharges from the Urethra.—Hæmorrhages and Discharges from Prostate.—Seminal Fluid.—From Bladder.—From Ureters and Pelvis of Kidney.—Cases of Renal Calculus.—Hæmorrhage from the Kidney.

Albuminuria of Pregnancy.—Albuminuria from Hindered Outflow due to other causes.

Explanation of the Albuminuria in the Series of Healthy Individuals.—Renal Disease.—Accidental.—Taking of Food.—Violent or Prolonged Muscular Exertion.—Playing upon Wind Instruments.—Cold Bathing.—Mental Conditions.

GENTLEMEN,—We commence to-day by considering the group of accidental albuminurias, composed of cases in which albumen is added to the urine after its secretion, owing to admixture with blood, pus, prostatic or seminal fluid, or uterine, or vaginal discharges. Among our private patients, eight—and indoor hospital patients, four—had albuminuria, which we referred to this category. Among women we are specially liable to meet with it, seeing that vaginal and uterine discharges may so readily mingle with the urine. During the catamenia, and when hæmorrhages or discharges from other causes exist, the urine is always contaminated, and the presence of albumen is of no clinical importance. The microscope reveals in such cases blood corpuscles, mucus corpuscles, vaginal epithelium, and sometimes other cellular elements. Filtration improves the con-

dition of the urine, but does not remove the albuminuria because no filter can retain the albuminous fluid. Discharges from the urethra may be of the nature of pus or blood. In men more especially is this a common source of contamination. Bleeding from the urethra is by no means usual, but purulent discharges associate themselves with every gonorrheal infection. Pus or blood derived from this source is carried out in front of the current of urine, or with its first portion, but also comes away, especially when the urethra is pressed, apart from the act of micturition.

Hæmorrhages and discharges from the prostate are reckoned by many as common. You will not unfrequently find, particularly in men somewhat advanced in life, that hæmaturia occurs occasionally in association with prostatic enlargement. Sometimes it recurs in an intermittent way for years, and seems practically of as little importance as a slight bleeding from hæmorrhoids; but it also sometimes betokens the development of malignant disease in the gland or its immediate neighbourhood. Discharge of prostatic fluid, whether connected with simple prostatorrhœa or with prostatitis, has been supposed to produce albuminuria, and Sir Andrew Clark[114] has, in a recent paper, brought forward certain observations as to cases of acute prostatitis in which hyaline cylinders, resembling renal tube casts, and small flask-shaped hyaline masses were present during their whole course. Dr. Campbell Black[115] of Glasgow had previously recorded similar observations.

Seminal fluid also, when mingled with the urine, produces a certain amount of albuminuria, but in such cases the albumen is seen only occasionally, and the microscope reveals spermatozoa. I have known a patient advanced in years much alarmed by the occurrence of bloody seminal emissions, the hæmorrhage evidently resulting from rupture of the fragile vessels in the prostate or elsewhere. This is to

be recognised as an occasional, although rare, occurrence. Bloody, purulent, or other discharges from the bladder are common causes of albuminuria. The irritation from vesical calculus, ordinary, acute, or chronic catarrh of the bladder, malignant or simple villous growth from its mucous membrane, are all familiarly known as causes of this condition. With these maladies your surgical experience has made you familiar. Blood and pus also frequently result from disease of the ureters and pelvis of the kidney, especially from calculus, and the characteristic features of these I may illustrate by reference to an acute and a chronic case. A patient was suddenly taken ill with acute pain in the region of the left kidney. The pain varied in intensity from time to time, but was generally such as to make the patient cry out and writhe in agony. It darted down not only towards the bladder but along the front and inside of the thigh, and was associated with retraction of the testicle and nausea with violent retching. The urine was passed frequently, but in small quantities, and it contained a considerable amount of blood. Suddenly the acute pain subsided, and only a diffused aching remained. A freer micturition followed, and as it was going on, a small calculus was observed to escape, and from that moment the symptoms of irritation rapidly diminished, and finally disappeared.

Another patient, a lady of middle age, consulted me this summer on account of symptoms which clearly pointed to the presence of a renal calculus. She had for a long time lived in India, and her health had undoubtedly suffered from the climate of that country, as, in addition to less important tropical maladies, she had had abscess of the liver. During the last twenty-four years or so she had suffered from severe attacks of pain in the left renal region, and other symptoms of calculus, which, as I have already mentioned them in connection with the previous case, I need not recapitulate here.

For the first twelve years or more, the attacks of pain were of short duration, but for ten or twelve years before I saw her, she had never been free from distress, and there is every reason to believe that during all these years the same calculus was lodged in the pelvis of the kidney. While living in India, and afterwards in England, she had been seen by various medical men, and had been told that an operation would be necessary for her cure, the weak state of her health alone preventing that proposal from being strongly urged. When I saw her this summer she was in a very alarming condition. The state of the urine, which contained pus in considerable quantity, with a small amount of albumen due to that, showed plainly, along with the other symptoms, that the patient was suffering from chronic calculous pyelitis, and that probably there was a collection of pus in connection with the kidney. There was intense pain in the left renal region shooting downwards and towards the bladder, and on palpation there was great tenderness in the left loin, and a large and apparently hard solid body was felt. This was a suspicious element in the case, for, as you know, in cases of calculus the kidney does not, as a rule, enlarge, but rather contracts and atrophies round the stone. Being fully satisfied that whatever other condition might be present besides calculus, the only hope for the patient lay in surgical interference, I asked Professor Annandale to see her in consultation with me. He agreed with my opinion, and decided to operate at once. The patient having been anæsthetised, a transverse incision was made in the left loin, and the large hard mass could then be more distinctly felt. Its characters were such that we were at first suspicious that the long-continued irritation had set up malignant disease in the kidney, as I have known happen in a similar case before. Professor Annandale, however, found that towards the pelvis of the kidney fluctuation could be detected, and on making an incision at this part a

considerable quantity of pus discharged. A pretty large calculus was then felt in the abscess cavity, and, although with considerable difficulty, it was successfully removed. It consisted of a central hard nucleus, of the size of a bantam's egg, covered by a large amount of looser incrustation, which was mostly broken down in the efforts at removing it. A drainage tube was introduced, and the rest of the wound was closed by sutures, and speedily healed by first intention. The progress of the patient after the operation was in every respect satisfactory. The pain in the renal region, though severe for the first few days, gradually diminished, and so did the hard swelling of which I have spoken. Her general health steadily improved. In little more than a fortnight she was able to be removed daily to a couch in the dining-room. In three weeks we thought it safe for her to go out driving, and within a month of the operation she was able to take a pretty long railway journey home without any untoward result. The urine, till shortly before her departure, contained a varying proportion of pus, but this greatly diminished when she was put upon a mixture containing potash, hyoscyamus, and uva ursi. Since she went home the improvement has continued; and now this patient, after her twenty-four years of suffering, may hopefully look forward to the enjoyment of continued good health.

Calculus is not the only cause of pyelitis, for I have known an acute and even fatal case result from simple exposure to cold. When the kidney is the seat of suppurative nephritis, whether infective or non-infective in character, albuminuria, and sometimes hæmaturia, appear; and a like result is met with in strumous disease of the organ unless the ureter be blocked in such a way as to hinder the downward passage of the strumous products.

Hæmorrhage from the kidney itself often produces albuminuria. You may see it in cases of renal tumour and

infarction, in rupture of the kidney, in such diseases as purpura and scorbutus, and as a result of excessive use of certain medicines, such as turpentine, cantharides, and copaiba. It may also appear when there is inflammation round the kidney, as in perinephric abscess, probably usually when that is associated with suppurative nephritis. With hæmoglobinuria, also, albuminuria is associated under conditions to which I have already referred.

There remain one or two causes of albuminuria which have scarcely been brought out in the series of cases which I have tabulated. Among them I shall mention first the albuminuria of pregnancy. It may be variously related to the condition. The pregnancy may coexist with acute or chronic organic kidney disease. It sometimes also arises along with other tokens of obstructed circulation from hindrance to the outflow of blood from the renal vessels. Probably hindrance to the outflow of urine from pressure on the ureters may lead to albuminuria in such cases, and it is possible that alterations of the arterial circulation may in some instances bring about the like result.

Albuminuria sometimes occurs also in consequence of hindered outflow of urine from the kidney from causes other than pregnancy. The pressure of a tumour, or obstruction by a calculus, may lead to this result. The results of experiments show that counter-pressure to the outflow of urine speedily induces, not only some widening out of tubules, but changes in the filtering apparatus which suffice to induce albuminuria.

We have thus then gone over the causes of albuminuria in our series of patients, and have endeavoured to explain how the symptom arises in each. It only remains to ask

how the albuminuria in our various series of presumably healthy individuals is to be explained. Some of them, no doubt, were due to renal disease in various forms, some, probably, to obstructions of circulation which did not interfere with the general health, and some may have been due to accidental causes, notwithstanding the precautions which we took to avoid this source of fallacy. But these do not account for all the cases, and it remains for us to inquire particularly why the taking of food and the violent or prolonged muscular exertion induced albuminuria in so many.

I do not believe that such albuminurias can be correctly referred to mere increase of mucin, although that does occur after the ingestion of food. It is a true albuminuria, and looking at our four sets of causes we recognise, as a possible explanation, changes in the blood, either in respect of salts or its albuminous elements ; but this is not proved to be an important cause, and sometimes the symptom comes on so suddenly as to make this explanation extremely improbable. As to changes in the filtering apparatus, it does not seem probable that this affords an explanation.

If we were more certain as to the effects of modification of the blood pressure we might find in changes produced through the action of the nervous system a somewhat attractive hypothesis. Certainly it is in some cases more like the result of a nerve influence than anything else. We have no right whatever, in the present state of our knowledge, to assume a morbid action on the part of the renal epithelium.

The albuminuria following upon severe muscular exertion, on the other hand, may result from either of two causes. There may be such alteration of the blood pressure throughout the system generally, or in the kidneys, as determines the condition ; or the introduction into the circulation of an abnormal amount of albuminous or saline

waste products may induce it in individuals predisposed to albuminuria.

It may also be asked how it happens that moderate exercise brings certain dietetic albuminurias to an end. This may depend upon chemical influences, using up materials which were being poured out from the blood, or more likely upon vascular influence, a general toning up of the circulation relieving a local overfilling, a result of some weakness of the kidney.

The influence of playing upon wind instruments, of cold bathing, and of mental conditions, may be explained in the rare cases in which they do occur, the first by a reference to altered states of the circulation resulting from the effort of playing, the second by nerve influence exerted upon the vessels of the kidney, and partly by interference with the action of the skin, and the third by influence propagated through the nerves to the renal vessels.

LECTURE XIII.

ON THE DIFFERENTIAL DIAGNOSIS AND THE PROGNOSIS IN ALBUMINURIA.

Diagnosis.—Is the Albuminuria Constant, Intermittent, or Cyclic?—Quantity of Albumen discharged.—Variety of Albumen present.—Quantity of Urine passed daily.—Specific Gravity.—Tube Casts.—Other Urinary Conditions, Phosphaturia, Oxaluria, Urates.—General Considerations.—Alimentary System.—Hæmopoietic System.—Circulatory System.—Respiratory System.—Integumentary System.—Nervous System.—Locomotory System.

Prognosis.—Importance of the Drain of Albumen.—Data for estimating daily loss, and its proportion to amount of Albumen in the Blood.—Prognosis in Inflammatory Bright's Disease.—Cirrhosis of the Kidneys.—Waxy Kidney—In Febrile Albuminuria.—In Albuminuria from Alimentary Diseases.—From Nervous Derangements.—From Glycosuria.—In Paroxysmal, Dietetic, Exercise, and Simple Persistent Albuminuria.—In Accidental Albuminuria.—In Albuminuria from Blood Diseases.

GENTLEMEN,—You will find in practice that questions of diagnosis as to the cause of albuminuria frequently arise, and that not unfrequently it is very difficult to satisfy yourselves on the point. You will find also that the question of prognosis involves both difficulty and responsibility. I intend to devote this lecture to a survey of the considerations which guide the physician in determining such questions.

Starting from the general fact of albuminuria, the first question that we have to solve is whether it is constant, affecting the urine of every micturition, intermittent, appearing only now and then, or cyclic, occurring regularly at cer-

tain periods and not at others. If it be found to be cyclic, completely absent at one part of the twenty-four hours and present at others, the diagnosis of functional albuminuria is rendered probable, and this with the greater confidence the more regular the cyclic character is found to be on different days. But the mere absence of albumen from the urine passed on rising in the morning is not incompatible with the existence of most serious organic disease, for in cirrhosis this condition is sometimes seen. If a cycle of a different kind manifest itself,—if, for example, a patient gets albuminuria only during the warm part of summer, or during the cold of winter, whether it then presents a daily cycle of changes or not, the probability is that it will prove simply functional. But even with this you must remember that in some cases of cirrhosis, and perhaps in some of very slight tubular inflammation, albumen may appear during cold weather, and be ordinarily absent.

If the albuminuria be intermittent, that is, be occasionally present and occasionally absent without manifesting any distinct regularity, a certain degree of probability attaches to diagnosis of functional disease, and this especially if the albuminuria be found to stand related to special circumstances, in particular to the ingestion of food, the change of attitude of the patient from the recumbent to the erect position or to muscular exercise. Still it must be kept in view that albumen may appear and disappear under other conditions, that in the earlier stages of cirrhosis, and perhaps also of waxy disease of kidney, it may be present at one time and absent at another in the same day, or it may make its appearance for a time, say for a week or two, and then disappear altogether for a considerable period. I have known a patient, for example, showing symptoms of renal cirrhosis whose urine was ordinarily quite free from albumen, but who developed the condition under the fatigue

and excitement of a railway journey, and a visit to a physician.

If the albuminuria be constant, even although it may vary somewhat in amount at different times, there is a greater probability of organic changes in the kidney, but this consideration is far from being of itself pathognomonic, for, as we have seen, there are cases of simple persistent albuminuria, truly functional in their character, which may go on for long periods, and terminate in complete recovery.

When in any case you find that the albuminuria comes on distinctly and only after meals, on change of attitude, after more or less severe muscular exertion, under mental excitement, or after cold bathing, you may conclude with certainty that the process is functional.

The quantity of albumen discharged is of no great diagnostic importance. In many purely functional cases it is large. In some hopeless organic cases it is small. It is, as a rule, most abundant in inflammatory Bright's disease, and in the combined forms. It is small in the early stages of cirrhosis and of waxy degeneration, is almost always scanty in the cases associated with nerve lesion and usually in those of circulatory origin. In many of the dietetic and other functional varieties it is also small, but I have seen it in some of these as copious as in inflammation.

The variety of albumen present has not yet been proved to possess diagnostic importance. It may turn out that the presence of a larger proportion of globulin, or the exclusive presence of peptones, may enable us to make out certain points, but my observations do not bear out the suggestion of Senator[20] on the one hand, that globulin is specially characteristic of waxy disease, or of Maguire,[54] on the other, that it stands so related to functional albuminuria. With regard to peptones, we find them in cases of renal inflammation, chronic suppuration, and waxy disease, sometimes

in fevers, and in pneumonia about the stage of resolution, but we are not entitled at present to attach diagnostic importance to them.

The quantity of urine sometimes affords important diagnostic indications. If, apart from the effect of the atmosphere and the diet, the quantity be excessive, the case generally turns out to be either waxy disease or cirrhosis. The polyuria appears in waxy cases at an early stage, sometimes even before the albumen. It is always at a later stage in cirrhosis. I have observed in a number of cases, where the bladder has become distended from prostatic disease, that not only are there frequent calls, but that the total amount of urine is increased. Such patients pass large quantities of pale, often slightly opaque, and albuminous urine. The opacity is sometimes due to the admixture of catarrhal products, sometimes to bacteria, or to a combination of the two. If the amount be exceptionally small, we may suspect obstruction in some part of the urinary tract, either in the uriniferous tubules, in consequence of inflammatory blocking, or lower down, as from occlusion of the ureters. The quantity is also diminished in cases due to increased backward pressure on the renal vessels, and is sometimes scanty when there is catarrh of the bladder or pyelitis.

The specific gravity and amount of urea are often very important aids to diagnosis. If the specific gravity is high, we commonly find either that the albuminuria is functional or is associated with fever, cardiac disease, or glycosuria, or with a comparatively early stage of acute inflammation of the kidneys. In the other conditions it is, as a rule, subnormal. But the amount of urea discharged daily is far more important. In a considerable proportion of the functional cases it is at least up to or even above the normal standard. In waxy disease of the kidneys it is up to that standard at the beginning, but gradually diminishes as the disease

advances. In cirrhosis of the kidney it is diminished throughout, and in tubular inflammation it is generally below the normal standard. In cardiac cases it is diminished. In fevers the urea is very frequently increased above the habitual standard of the patient. Even in fever occurring in the course of renal cirrhosis I have seen it rise to the normal standard. With glycosuria there is often also an increase.

With regard to tube casts, it must, I think, be admitted that their diagnostic importance was overestimated when their existence was first recognised. Almost any condition which may give rise to albuminuria may also produce casts. Still, much may be learned from a study of their characteristics. Epithelial and fatty casts afford definite evidence of the existence of inflammation of the tubules. Hyaline casts, associated with them, or containing here and there fatty granules, results of disintegration of epithelial cells, also give evidence of a more advanced stage of the process. Casts containing blood-corpuscles or pus give definite evidence of the presence of hæmorrhage or of suppuration in the renal tissues, but the mere presence of simple hyaline casts may be associated with waxy disease or with cirrhosis of kidney, with simple persistent, with cardiac, alimentary, or other varieties of albuminuria. Sir Andrew Clark,[114] Dr. Campbell Black,[115] and other reliable observers, have recorded the fact that they have met with bodies resembling renal casts, which were really casts from the prostate. Cases of jaundice and of oxaluria frequently exhibit true renal casts, the delicate hyaline outline being rendered the more distinct in the one case by the tinging and the granular urates, and in the other by the octahedral crystals scattered throughout them.

Other urinary conditions which sometimes possess a degree of diagnostic value are the occurrence of phosphates, oxalates, or urates along with the albumen. When we find that a urine which is sometimes albuminous also shows at times a

sudden copious deposit of phosphates, we may conclude that the albuminuria is functional, and, though with less certainty, a sudden and abundant deposit of oxalates may give a like indication. Urates occur so often in association with albuminuria, in acute nephritis, in febrile and inflammatory conditions, and in cardiac cases, as well as in some simply functional ones, that their indications are unimportant.

Apart from the characters of the urine, there are certain general conditions which must be considered in relation to diagnosis. Sex is practically of no importance. Age is also of comparatively little service; only one should remember that about the time of puberty functional albuminuria is most apt to set in. Occupation and habits, also, possess no special value in diagnosis. The general appearance of the patient often affords important information. The existence of marked dropsy implies either inflammatory disease of the kidneys or cardiac disease, or great deterioration of blood. There is a peculiar appearance of the face, somewhat difficult to describe, which is characteristic of many of the functional cases. It is marked by pallor, with slight œdema of eyelids, and a certain laxity of tissue, with a general languor of circulation and unfitness for exertion. But a similar appearance often coexists with waxy disease, and, of course, is common enough apart from albuminuria. The general appearance characteristic of patients suffering from cardiac and diabetic albuminuria need not be referred to.

The condition of systems other than the urinary often throws great light on the question of diagnosis. The alimentary system may give you important hints, especially in the case of waxy disease when there is evidence of enlargement of the liver, or intractable dyspepsia indicating degeneration of the vessels of the gastric mucous membrane, or diarrhœa indicating the more common implication of the intestine. Other abnormalities, although often of clinical importance,

are of little service in diagnosis. Obviously cases in which the ingestion of food or the process of digestion induces or greatly increases the albuminuria are most likely to be referred to the functional group.

From the state of the hæmopoietic system there is little to be gained in the way of diagnosis. The enlargement of the spleen, however, if associated with other recognised complications, may give an indication of waxy disease, and a tendency of the red blood corpuscles to adhere to one another and to tail may also suggest the presence of this form of degeneration.

The circulatory system, on the other hand, affords very important indications. The tension of the pulse, the changes in the heart and in the blood-vessels, take the first place. Increased pulse tension is very characteristic of cirrhosis of the kidney, and of inflammation of the tubules in its fully developed and advanced stages. It is true that in some cases of post-scarlatinal albuminuria an increase of blood pressure is found to precede the appearance of albuminuria ; but albuminuria does not constantly follow upon this condition, and the increased pressure is not proved, as in the later stages, to be definitely related to changes in the renal circulation. It is not met with in waxy disease unless the malady be far advanced, and probably associated with cirrhosis. It is very rare in the alimentary, circulatory, nervous, and functional cases ; and though it is often seen in fever cases which are attended by albuminuria, it is not, as a rule, when these have the highest tension that the albuminuria appears. In many of the circulatory, febrile, and functional cases the tension is markedly subnormal.

The auscultatory changes in the heart, in particular the accentuation of the second sound in the aortic area, and the prolonged or booming character of the first, correspond precisely in their indications with the increased tension. The

same may be said to be true of the hypertrophy of the left ventricle when it manifests itself in other ways than the altered first sound already referred to. Thickening of vessels is more common in renal cirrhosis, and in advanced inflammation, and in cases due to heart disease, than in those connected with any of the other causes. But the diagnostic indications to be derived from it are not very important. The respiratory changes may be of moment as indicating phthisis or other chronic or debilitating process, which might cause waxy disease, otherwise they afford little diagnostic indication.

The integumentary system, by the presence of anasarca, often gives indication of the existence of organic renal or cardiac disease, while syphilitic eruptions, or the cicatrices resulting from them, may point to possible waxy disease, and subcutaneous hæmorrhages may be the token of blood diseases, such as purpura, scorbutus, and pernicious anæmia. Changes such as those characteristic of Raynaud's disease may, on the other hand, indicate other blood diseases or nervous maladies. An abnormal dryness, and sometimes a reddish-brown discoloration of the skin, may attend upon renal cirrhosis, and simple dryness upon albuminuria with glycosuria.

Among the symptoms referable to the nervous system there are many which afford suggestions for diagnosis. Dimness of vision, whether uræmic or connected with changes of the retina revealed by the ophthalmoscope, gives distinct indication of organic renal disease, and that usually in advanced cirrhosis, inflammatory, or complicated waxy cases. Uræmic seizures of whatever kind, indicate formidable organic renal disease. Headaches are often results of organic renal processes, but they also occur with functional albuminuria. Complications of the nature of paralysis often afford a similar indication, but as they are sometimes

associated with syphilis they may indicate rather, under certain conditions, a tendency to waxy disease.

The locomotory system affords little aid to diagnosis excepting where there is caries or necrosis tending to induce the waxy degeneration.

We have now to consider what is the prognosis in the different groups of cases, and I shall take them up in the same order as in previous lectures.

A preliminary question however arises as to the importance of the drain of albumen from the system. The largest amount discharged by a patient in my wards during last winter session was between 400 and 500 grains in the twenty-four hours, but in most cases the quantity was very much less. Now 400 grains of albumen is, of course, a large amount, and when we compare it with the amount of albuminous food taken in the course of twenty-four hours, or with the amount of albuminous material in the blood it is seen to involve a very formidable daily loss. The albuminous material in an ordinary diet table for twenty-four hours is about 4·25 ounces, or 2040 grains, so that a loss of one-fourth part of the amount taken occurred in that particular patient. But we have to consider that probably considerably less than the whole amount of what is taken is actually assimilated and converted into blood albumen. As to the total amount of albuminous materials in the blood, they are reckoned, apart from the hæmoglobin, as amounting to 7 per cent. Now, the total amount of the blood being held to be one-thirteenth of the weight of the body, we should calculate that a person weighing 10 stones would have about 10·7 lbs. of blood, which would contain about 12 ounces of albumen. Now my patient was losing one ounce of this material in twenty-four hours, that is to say, one-twelfth part of the elaborated albumen of the blood. Such a drain must

have involved a heavy tax upon the power of blood formation.

To give our ideas of the loss of albumen more definiteness, I have prepared a formula by which, using Esbach's method, we can easily calculate in any case what proportion of the total amount of albumen of the blood is being daily lost.

Albumen in grammes per litre.	Per Cent.	Grains of Albumen per Ounce of Urine.	Albumen in Blood per Stone of Body Weight.
0·5	0·05	0·21875	527·7 grains.

In the first column of the table is placed the smallest amount of albumen in grammes per litre, which Esbach's tubes indicate, in the next, the per cent. of albumen to which this corresponds, and in the third the weight in grains of the corresponding amount of albumen which would be contained in an ounce of the urine. In the fourth column is given an estimation from the most reliable data of the weight of blood albumen per stone of body weight of the individual. The total weight of albumen lost in twenty-four hours is obtained by multiplying the weight in the third column by the number of ounces of urine passed, and by the multiple of 0·5 grammes which the estimation of the albumen by Esbach's method gives. The total blood albumen in the body is easily obtained from the albumen per stone by simple multiplication or rule of three. By dividing this by the weight of albumen in the twenty-four hours' urine, we get the proportion of the total albumen of the blood which is lost daily. Thus, for example, in a patient suffering from a combination of the different varieties of Bright's disease, the urine contained 20 grammes per litre. His body weight was about 10 stones. The quantity of urine was 50 ounces, so that the weight of albumen lost in twenty-four hours was 0·21875 ×

$50 \times 40 = 437{\cdot}5$ grains. The patient's weight being 10 stones, the total albumen of his blood would weigh 5277 grains. Now, by dividing this by the amount lost daily, we find that the daily drain amounted to nearly one-twelfth of the total albumen in the blood. The calculation may be expressed thus :—

$$\frac{0{\cdot}21875 \times 50 \times 40}{527{\cdot}7 \times 10} = \frac{1}{12{\cdot}06}$$

This, of course, is an extreme case. The vast majority of albuminurics lose nothing like this quantity. In one, indeed, of my functional cases, which we worked out with the view of determining the daily loss, this was found to amount to only between 5 and 6 grains in the twenty-four hours, although the reaction was at certain times of the day very distinct.

In regard to Bright's disease, the prognosis varies greatly according to the form or forms present. In uncomplicated acute inflammatory Bright's disease, whether infective or not, the prognosis is, as a rule, favourable. By proper treatment a complete recovery may be obtained in a large proportion of cases, and this even after the patient has passed into a state of acute uræmia with general convulsions, coma, and complete, or almost complete, suppression of urine. Some cases, however, especially those of the glomerular variety, prove very rapidly fatal by uræmia or by some of the other complications, such as pericarditis, œdema of the brain, &c. Other cases do not recover, but pass into the chronic form of nephritis. One further remark I have to add is that the prognosis of acute nephritis in pregnancy is, as a rule, favourable. Even after eclampsia and organic eye changes have become developed, complete recovery may be obtained. Still in some of these also the disease passes into the chronic stage. In some cases of albuminuria in pregnancy, however, the nephritis is

more chronic from the outset, and in these, of course, the prognosis for complete recovery is less hopeful. In regard to chronic nephritis in other conditions, while in some cases complete recovery may be obtained, as a rule, the case pursues a slow course, with gradually increasing impairment of the general health, and with the development of complications which I have described, some of which, such as the cardiac and cerebral, may at any time prove rapidly fatal. The course is not usually very prolonged, but it may be so, authentic cases being on record in which a period of thirty years has elapsed from the onset of the acute inflammatory attack till the fatal issue of the chronic disease supervened.

In regard to cirrhosis of the kidney, the prognosis is, I need scarcely say, hopeless, so far as complete recovery is concerned. The course may be comparatively rapid in some cases — a tendency to acute inflammation being frequently present — while in others it is very chronic — the patient living for many years after the detection of the disease. Careful treatment and guidance as to climate, mode of life, food, and medicine, and attention to the complications apt to arise in special cases, may in this form, and in the chronic inflammatory also, greatly prolong the life of the patient, and diminish his discomfort. Still we can do nothing to arrest the progress of the malady. As to the prognosis of the probable duration of any individual case, we must be guided mainly by the condition of those organs affections of which are known to lead to a fatal issue. The state of the cardiac muscle, not so much as regards hypertrophy, but rather as to the presence or absence of degeneration and failure of its power, is important. The importance of cerebral and eye symptoms also I need not further impress upon you. I would only remark in addition that, cirrhosis being often complicated by the superaddition of inflamma-

tion of the tubules, we can often, by the cure of the latter, tide the patient over periods of urgent danger.

In waxy disease the prognosis must be regarded as grave, especially as we seldom have it in our power to remove the cause of degeneration. Still, when this can be achieved we need not lose hope, for I have seen a patient with well developed waxy degeneration brought to a fair state of health, the waxy material being evidently replaced by more healthy tissue. The treatment of the cause, with the improvement of the general tone and the avoidance or cure of complications, constitute our best means of prolonging the life of the patient.

In the other diseases in which albuminuria is met with as a complication, the prognosis depends as a rule very little on that symptom. The presence of a well marked albuminuria in fevers increases the gravity of the case. But when it is associated with a strong, bounding pulse and vigorous cardiac action, it is much less grave than when the pulse becomes feeble and perhaps irregular, and the heart's action flags. It is most grave of all in cases where there is a septic process going on, as in pyæmia and in fevers with typhoid or putrid symptoms.

Albuminuria in circulatory diseases indicates marked failure of circulation, and backward pressure in the veins. This may be overcome by rest, cardiac and other tonics, diuretics, and means of removing œdema and collections of fluid in serous cavities. If these remedies fail, the prognosis is very grave, but the albuminuria is not the cause of danger.

Albuminuria is associated with such varying conditions of the alimentary system that the most that can be said is that the prognosis depends on the nature of the disease present. Where that is simply a functional derangement, of some part or other of the digestive system, as in dietetic albumin-

uria, suitable treatment may remove the condition. Where the disease is organic, though appropriate treatment may do good to the patient, and lessen or even remove the albuminuria, the ultimate prognosis is bad.

Almost the same remarks apply to albuminuria from nervous derangements. In functional diseases, such as exophthalmic goître, as I have pointed out, the disease may be cured and the albuminuria disappear with it.

Albuminuria is a very serious complication of glycosuria, but its gravity in each case must depend on the condition of the kidney producing it, and on the state of the patient in other respects. If the glycosuria is only temporary, the albuminuria may pass off with it; and I may remind you that the two symptoms are sometimes associated in cases of functional albuminuria, in which, as you are aware, the prognosis is good.

In paroxysmal and dietetic albuminuria, in albuminuria from exercise or muscular exertion, and in simple persistent albuminuria, the prognosis is good, less so, perhaps, in the last than in the other three. In that variety the difficulty is greatest of differentiating it with certainty from forms of albuminuria due to more grave conditions. The points to which I have referred in speaking of these forms of albuminuria must be borne in mind in making the differential diagnosis. If such cases do not yield to treatment, but persist for long periods, there must be a fear lest, though only functional at the first, and even though the albumen only appears at certain periods of the day, ultimately the continuance of this abnormality may, through impaired health and renal irritation, lead to the development of organic disease of the kidneys. My own observations lead me to think that this is not a very frequent termination, still it is one to which we must not shut our eyes. A careful watch must be kept in such prolonged cases to see that none of the

complications indicating organic disease are manifesting themselves, for then the prognosis would be entirely changed. A fuller discussion of this subject will be found in the lecture devoted to these forms of albuminuria.

In regard to albuminuria due to accidental causes, the prognosis must depend on the prospect of curing the disease on which it depends. I must remind you that even the most simple case of albuminuria due to irritation of the urinary passages is not without serious danger, for the irritation may spread upwards from the urethra to the bladder, from the bladder to the ureters and pelvis of the kidney, and from thence to the kidney itself; or an attack of nephritis and even suppression of urine may result from reflex irritation from some inflamed area of the urinary tract. Especially if the process has become septic is this danger present. Thus, in some of the diseases of the bladder, such as enlarged prostate, stone, &c., septic mischief may extend to the kidney and lead to the development of what is called "surgical kidney," with the characters of which you have doubtless become acquainted in the post-mortem room. In diseases with obstruction to the outflow of urine, such as stone or enlarged prostate, renal changes, somewhat of the nature of cirrhosis, are not infrequently developed, and I need not impress upon you the influence which such conditions have upon the prognosis.

The only remaining class of diseases to which I need allude are those affecting the hæmopoietic system. In several of the diseases affecting this system, such as purpura, scorbutus, hæmophilia, pernicious anæmia, and even simple anæmia, albuminuria is not infrequent, and in some of them there is actual hæmorrhage from the kidney or the urinary tract. In such cases the prognosis is simply that of the general disease. If the morbid process can be cured, so will the albuminuria and hæmaturia. In such cases we are,

generally at least, justified in regarding the renal symptom as a blood albuminuria, which will be cured by improving the state of the blood or of the glands which act upon it. When there is superadded a degree of renal inflammation, the prognosis is, of course, influenced thereby.

LECTURE XIV.

ON DIET IN ALBUMINURIA.

Introduction.—Production of Albuminuria by Diet.—Evidence of Stokvis, Lehmann, Lauder Brunton, Maguire, Claude Bernard, and Others.—Experiments with Egg Diet; Cheese; Walnuts.—Diet in Bright's Disease.—Views of Dickinson and Bartels.—Experiments.—Various Diets.—Results in Bright's Disease and Mixed Forms of Albuminuria.—Alcohol.

GENTLEMEN,—I purpose to-day to bring before you the question of the influence of diet on the different varieties of albuminuria. It is a subject which, although often and carefully studied, is well worthy of further investigation, and I shall, after indicating the views generally held by the profession, bring under your notice the results of some observations which, with the aid of my resident physicians, Drs. Gulland and Pirie, I have made with the view of testing the accuracy of current opinion. We have sought to throw some additional light upon the question of the possibility of producing albuminuria by diet in persons whose kidneys were healthy, and as to the effect of various forms of diet in patients affected with albuminuria.

I shall speak first of the production of albuminuria by diet. The facts with which you are already familiar regarding the frequent occurrence of slight, and the occasional occurrence of marked albuminuria after meals in healthy

people, have prepared you to expect that interesting results might be obtained by means of experiments on diet. We have seen that in certain individuals the mere ingestion of food of whatever kind is followed by albuminuria, and that in others particular kinds of food produce this effect, while most articles of diet do not. Precise experiments have been made, especially with regard to the influence of egg-albumen, with the view of ascertaining whether that substance introduced into the system in large quantity induces albuminuria, what the variety of albumen is when albuminuria does appear, in what condition the egg-albumen must be introduced, and by what channels it must enter the circulation.

The experiments of many observers, of whom I shall mention Stokvis[36] (whose work I have always found careful, and his conclusions trustworthy), showed that the injection of egg-albumen into the veins of animals invariably produces albuminuria, while the injection of serum-albumen of an animal of the same species produces no such result, unless the quantity is such as to produce a signal rise in the blood-pressure ; and in these experiments it was found that egg-albumen appears as such in the urine, so that it manifestly passed out of the system unchanged.

It may also be accepted as demonstrated that the injection of egg-albumen into the rectum is followed by a similar albuminuria.

But as to the effect of introducing it into the stomach there is more doubt. Thus, it may be introduced either in its natural condition or coagulated by cooking, and it is necessary to distinguish the results of each method. We, of course, set aside the cases in which, from an idiosyncrasy, the ingestion of eggs is always followed by constitutional disturbance, with derangement of the stomach, and sometimes albuminuria. Apart from such cases, considerable difference of opinion exists as to the facts. Senator[20] states that the

investigations of Lehmann, Stokvis, and Creite show beyond doubt that egg-albumen is really excreted as such, and that in the majority of cases the albuminuria disappears when it is completely excreted, the investigations having been performed on the observers themselves, on other persons, or on dogs and rabbits. Dr. Coats[116] expressed, in 1884, the same opinion, and quoted the experiments of Nussbaum to show that egg-albumen (however introduced into the system) passes out by the glomerular tufts, which retain the serum-albumen. Dr. Lauder Brunton[117] failed to produce albuminuria in himself by swallowing six raw eggs in succession, but violent headache and sickness were produced ; while D'Arcy Power,[117] on the other hand, succeeded in producing albuminuria in this way. Regarding the explanation of the albuminuria thus produced, these authors remark that "it is only when the digestive powers are overtaxed—as by swallowing many raw eggs together, or deranged so as to digest the food partially but not completely—that such an event occurs." Dr. Maguire,[54] in his able paper upon the albumens of the urine, states that he failed to produce albuminuria by swallowing the whites of twelve raw eggs, a slight headache being the only effect produced. He rightly points out that the severe digestive disturbance indicated by diarrhœa, and the appearance of bile in the urine, which was produced in the animals fed by Stokvis for several days upon raw egg-albumen, may account for the albuminuria, and he doubts whether observers have taken sufficient care to ascertain whether egg-albumen or albumen in another form appeared in the urine. Dr. Dobradin[118] found no albumen in his own urine after he had eaten nineteen raw eggs in thirty-six hours. These remarks apply to the result of dieting with raw eggs. But Claude Bernard[119] and (I suppose) others have found that albuminuria may be produced by eating large numbers of cooked eggs. This of course stands on a different footing from the experi-

ments made with uncooked eggs, for however the latter might be absorbed into the system unchanged, the former must necessarily be digested.

As our information upon this matter seemed to me somewhat unsatisfactory, I thought it well to institute some experiments on the point. I selected for the purpose four individuals whose urine showed no albumen even when tested with picric acid, and whose condition offered no objection to such a trial being made. In the first case—one of locomotor ataxia—the patient took ten raw eggs daily, in addition to his ordinary diet, for a period of nine days. In two days from the commencement albumen appeared. It was not in large quantity, but quite sufficient to be demonstrated by picric acid. On two occasions it was demonstrable with nitric acid, and on each of them the addition of excess of the acid redissolved the coagulum, showing that it was not egg-albumen, but blood-albumen that was present. The albumen persisted from the second day to the end of the experiment, but disappeared on the day in which the eggs were stopped. In the second case—one of mitral incompetence—nine eggs were given daily for a period of seven days. Albumen appeared on the first day, persisted throughout the experiment, and disappeared when the eggs were discontinued. Although distinct with picric it never showed with nitric acid. In the third case—one free from organic lesion—ten eggs were given daily for three days in addition to the ordinary diet. On the first and third days albumen was distinct with picric acid. On the second day it was in such quantity as to be shown with nitric acid, and in this case also the opacity readily disappeared when an excess of the reagent was used. In the fourth case—one of chorea—the eggs were not well borne by the stomach; only three were taken, and the experiment was continued only for three days. But in it also albumen showed itself with picric acid

on the third day, and disappeared when the patient resumed his ordinary diet.

The results of these experiments go to confirm the impression that the introduction of raw egg-albumen into the stomach induces albuminuria; that the albumen is always in small quantity; that it disappears when the ordinary diet is resumed; and that it is not egg-albumen, but serum-albumen which is discharged. Explanations of this kind of albuminuria on the theory of absorption of egg-albumen as such into the blood, and its discharge from the kidneys, must be set aside, and with it also the speculation—so far as this question is concerned—as to the minute size of the molecules of egg-albumen and its greater transfusibility. In these experiments also it was clear that the albuminuria was not a result of gastric disturbance produced by diet, for no gastric disturbance manifested itself in the cases in which the albuminuria was most distinct. Two suggestions may be offered by way of explanation. One is, that owing to the large amount of albumen digested and absorbed, the blood becomes surcharged with that ingredient, and some of the excess escapes by the kidneys. The other explanation stands in relation to some recent investigations on allied topics by Dr. Ralfe,[51] Dr. Noël-Paton,[120] and Dr. Thomas Oliver[121] of Newcastle. Dr. Ralfe has shown in an interesting way the relation of functional albuminuria and hæmoglobinuria to the rate of destruction of the red blood-corpuscles, and of the formation of urea. Dr. Noël-Paton has brought out some of the relations which exist between bile secretion and urea formation. Dr. Oliver has shown that the urea is mainly formed from the red blood-corpuscles, and that the most active period of urea formation is when the liver is actively secreting during digestion. It seems, in the light of all these observations, reasonable to suppose that in our experiments the liver was stimulated to excessive activity owing to the

excessive amount of proteids ingested, that thus the red blood-corpuscles were more rapidly destroyed, and that the albumen liberated from them not being all transformed into urea was in part discharged by the kidneys. This suggestion receives some confirmation from the facts which we observed in regard to the urea discharge. In the first case there was a marked increase in its amount after the eggs were commenced, followed by as marked a fall on the day after ordinary diet was resumed. In the second case the urea was over the normal, except on one day, during the whole time that the eggs were taken, and for two days afterwards. Then followed a fall to the normal amount. In the third case also an increase of urea was distinct, although the results were less striking from the brevity of the experiment. In the fourth case the effects were doubtful, but it will be remembered that only three eggs were taken daily.

Apart from the egg-albumen diet, I was anxious to get information as to other food substances which are supposed to stand in close relationship to albuminuria. Remembering the prominence which Sir Robert Christison's[94] remarks in regard to *cheese* had given to that substance in this respect, I arranged to give a good supply of it to twenty healthy boys, and to test their urine before and after its use. I show you in tabular form the results brought out by this experiment. Two ounces of Cheddar cheese were taken by each boy soon after twelve o'clock, breakfast having been taken at eight, and a specimen of urine passed before taking the cheese was compared with one voided shortly afterwards.

[Table xxviii.

TABLE XXVIII.—SHOWING THE EFFECT OF CHEESE ON THE INCIDENCE OF ALBUMINURIA IN 20 PRESUMABLY HEALTHY BOYS.

BEFORE CHEESE.				AFTER CHEESE.		
Number.	With Nitric Acid.	With Picric Acid.	Total.	With Nitric Acid.	With Picric Acid.	Total.
20	1	6	7	0	6	6

You observe that while one showed albumen with nitric acid (only a trace) and six with picric before the repast, none showed it with nitric and six with picric afterwards; but the latter six did not exactly correspond to the former, for one boy who showed no albumen before the repast showed it afterwards. The boy who showed it with nitric acid before, showed only with picric acid afterwards. Two others who had had a distinct picric acid reaction before, showed only the faintest trace afterwards. And in one it disappeared in the later though present in the first specimen. These results point to the conclusion that cheese, when eaten in reasonable amount, has little or no effect in producing albuminuria in healthy people. Those in whom it has this effect must be regarded as the subjects of idiosyncrasy. It is possible that the large proportion of albuminuria in the twenty boys before the cheese was eaten was due to the effect of the breakfast not having yet passed off at the time of the earlier micturition.

I thought also that it might be well to try the effect of *walnuts* in this respect, and accordingly gave ten presumably healthy boys six walnuts each. They were taken apart from meals, and a specimen of urine was obtained before and some time after they had been taken. The result showed that while before taking the walnuts one showed albumen with nitric acid and other two with picric acid,

afterwards a different one showed with nitric acid who had only showed with picric before, and other three showed with picric acid. Thus there was an increase on the whole number showing albumen. The boy who had shown with nitric acid before, showed only with picric afterwards. From this experiment it appears that the use of such articles of diet, even in moderate quantity, may suffice to produce albuminuria in some individuals, and certainly, at all events, it proved more active than cheese. The six walnuts weighed, without their shells, only five drams, and yet the effect was very distinct.

Our general conclusion as to this part of our subject is, that while the ingestion of food has been shown frequently to produce albuminuria from idiosyncratic peculiarities, particular articles of diet induce it in some people, and while we may succeed in inducing it by the use of special articles of diet, yet the quantity of albumen is usually minute, and it has little tendency to persist after the resumption of ordinary food.

Proceeding now to consider the second part of our subject, I shall speak first of the diet in Bright's disease. The profession is for the most part agreed as to what is most suitable. I shall content myself with quoting the statements of one or two of the most judicious writers on the subject. Dr. Dickinson[122] says that in the *inflammation of the tubules* spare diet, with plenty of water, abundance of milk, and sufficiency of light broth or beef-tea, is best. In *cirrhosis* the food should be as non-nitrogenous as is consistent with the proper nutrition of the patient. Purely vegetable diet has not succeeded, and the anæmic tendencies forbid a non-nutritious regimen, but the patient should be kept upon the smallest amount of food on which he can thrive. In the *waxy disease* he recommends that the diet should be

generous and varied, and that extra supplies of beef-tea and Liebig's extract should be given for the sake of the saline constituents.

The late Professor Bartels,[123] of Kiel, recommended in *acute tubular inflammation* a milk diet, with all its possible modifications, as the ideal bill of fare. If the digestive organs and the appetite permitted, he recommended a more solid diet, consisting of easily digested meats, light vegetable food, and good bread. In *chronic inflammation of the tubules* the milk seemed to him more essential, especially where there was loss of appetite, which he ascribed to œdema of the gastric mucous membrane. In *cirrhosis* of the kidney he advises to sustain the strength by abundant meat, milk, and mixed vegetable dietary. In *waxy cases* he praises the effect of vigorous diet of meat and milk with the use of good wine.

It were tedious for me to quote to you the very similar conclusions of Johnson, Roberts, Rosenstein, Purdy, and other writers. You may assume that the two whom I have quoted represent the views generally held by judicious practitioners.

It will be apparent from the results which I have now to lay before you that these views are generally confirmed by our observations. I wish that the importance of our results had been more commensurate with the amount of time and labour expended upon them.

The diets which we employed were five in number :—(1) ordinary, (2) large, (3) milk, (4) low, (5) low diet with eggs. The annexed tables show the composition, weight, and the amount of carbon and of nitrogen contained in each :—

[TABLE XXIX.

Table XXIX.—Ordinary Diet.

	Ounces.	Carbonaceous.	Nitrogenous.	Total.
Meat (minced collops),	8	1·2	1·61	2·81
Bread, . . .	12	6·18	1·26	7·44
Potatoes, . . .	12	2·94	0·30	3·24
Sugar, . . .	2	2·00	0·00	2·00
Milk, ...	24	1·92	1·08	3·00
Butter, . . .	1	1·00	0·00	1·00
Total, . .	59	15·24	4·25	19·49

Table XXX.—Large Diet.

	Ounces.	Carbonaceous.	Nitrogenous.	Total.
Meat (minced collops),	16	2·40	3·22	5·62
Bread, . . .	16	8·84	1·08	9·92
Potatoes, . . .	12	2·94	0·30	3·24
Sugar, . . .	2	2·00	0·00	2·00
Milk, . . .	24	1·92	1·08	3·00
Butter, . . .	1	1·00	0·00	1·00
Total, . .	71	19·10	5·68	24·78

Table XXXI.—Milk Diet.

	Ounces.	Carbonaceous.	Nitrogenous.	Total.
Milk, . . .	80	6·4	3·6	10·0

Table XXXII.—Low Diet.

	Ounces.	Carbonaceous.	Nitrogenous.	Total.
Bread, . . .	12	6·18	1·26	7·44
Potatoes, . . .	24	5·88	0·60	6·48
Sugar, . . .	4	4·00	0·00	4·00
Milk, . . .	24	1·92	1·08	3·00
Butter, . . .	1	1·00	0·00	1·00
Total, . .	65	18·98	2·94	21·92

TABLE XXXIII.—LOW DIET WITH EGGS.

	Ounces.	Carbonaceous.	Nitrogenous.	Total.
Eight raw eggs, .	14½	4·35	5·8	10·15
(Otherwise as in Table XXXII.)				

The following are short notes of the cases, in regard to which the points determined were: the weight of the patient, the daily amount of urine, its specific gravity, the amount of urea, and the amount of albumen in grammes per litre as determined by Esbach's method.

I. INFLAMMATORY BRIGHT'S DISEASE.

T. T., æt. 19, a gardener, was admitted to Ward XXII. on 24th December, 1886, suffering from dropsy, and had been ill for eight weeks. Early in October the patient had scarlet fever. During desquamation he went out and was exposed to cold. He then took dropsy, with diminution of urine, and the other ordinary features of post-scarlatinal nephritis. As the symptoms did not yield, he was sent to the Infirmary.

In this patient trial was made of the effects of ordinary diet for seventeen days, milk diet for eight days, and low diet for eight days. The analyses showed that each of the three brought out essentially the same result, both in respect of the urea and the albumen. I should not have considered it right to give the large diet to this patient, as it might have proved irritating to the kidneys.

L. M., æt. 52, an unmarried woman, was admitted to Ward XXV. on 7th December, 1886, suffering from subacute inflammatory Bright's disease. She had been ill for about a month. Her chief complaints were of dropsy and debility. Her urine was on admission 22 ounces in the 24 hours. It was of pale straw colour, its specific gravity 1016; it con-

tained 131·12 grains of urea and 1·25 grammes of albumen per litre, and deposited a few blood-corpuscles and a good many granular, epithelial, and hyaline tube casts. The dropsy was distinct, although not severe. The pulse was regular and rather tense, but there was a systolic murmur most audible in the aortic area. In this case it was somewhat difficult to judge of the effects of the diet, as the patient was making throughout steady although rather slow progress towards recovery. The ordinary, the large, the milk, and the low diets were tried in succession, and we came to the conclusion that the two latter did better with her than the first two, and that the low diet was the best of all. While under ordinary diet she was passing 46½ ounces of urine, containing 270·7 grains of urea, and 1·75 grammes of albumen per litre ; under the large she passed 50½ ounces, containing 247·5 grains of urea, and about 0·2 gramme of albumen per litre ; under the milk she passed 48 ounces of urine, with 301·4 grains of urea, and about 0·1 gramme of albumen per litre ; and under the low diet she passed 48½ ounces of urine, 187·5 grains of urea, and only once a trace of albumen. She also gained weight slightly while taking the low diet.

R. M., æt. 45, a carter, was admitted to Ward XXII. on 15th December, 1886, suffering from chronic inflammation of the kidneys, chiefly affecting the tubules, but probably to some extent the stroma also. The quantity of urine was about 52 ounces, of dark colour, specific gravity 1018, containing 303·5 grains of urea, and albumen in the proportion of 3·2 grammes per litre. There was a considerable amount of dropsy, some tension of pulse, sclerosis of arteries, the heart was not enlarged, and there was a slight systolic murmur in the aortic area. In this case the ordinary, the milk, and the low diets were used. Under their use no difference emerged as to the amount of urine, or the specific gravity, and there was

very little effect on the urea. But the albumen diminished under the milk, and continued to do so under the low diet.

It is clear that these experiments, although I may claim that they were carried out with extreme care, were far from sufficient of themselves to warrant our arriving at any general conclusion. Still they afford some support to the view generally held by the profession, that milk diet or low diet are better suited to such cases than ordinary or ample diet.

II. Cirrhotic Bright's Disease, with Inflammatory superadded.

S. R., æt. 40, a waiter in an hotel, was admitted to Ward XXII. on 15th January, 1887, suffering from cirrhosis of the kidneys, with some degree of inflammation of the tubules superadded. He was passing at the time of his admission only 15 ounces of urine. Its specific gravity was 1036. It contained serum-albumen, globulin, and a trace of peptone, 144 grains of urea, and hyaline, granular, and fatty casts. The dietetic experiments were commenced on 18th January, and he had ordinary and milk diet in succession for periods of six days respectively. No effect was discernible upon the quantity of urine or of urea, and the albuminuria was certainly not diminished by the milk diet.

III. Pure Cirrhosis of the Kidneys.

J. S., æt. 26, a joiner, was admitted to Ward XXII. complaining of loss of sight and headache. His case has been referred to in one of my earlier lectures, and I shall now say only that it presented all the features characteristic of renal cirrhosis. His urine was in good, although not excessive, quantity. It contained albumen and a few casts, with about 150 grains of urea in the 24 hours. The heart was hypertrophied, the pulse firm and tense. The

blood was somewhat poor in corpuscles, and the eyes showed the characteristic features of albuminuric retinitis. It was clear that the renal disease was advanced. Ordinary, large, milk, low, and egg diet were given in succession, and it was found that with the first four of these the urine remained in all respects unchanged. In trying the egg diet, I gave eight raw eggs daily, in addition to the ordinary allowance of low diet. The quantity of urine was unaltered; its specific gravity became somewhat higher. The urea showed a decided increase during the first four days that the eggs were used, and diminished again in the later three days of the observation. The albuminuria showed a relative increase during the first two days, and during the rest of the time the amount was about the same as it had been before the experiment commenced.

In the cases of T. M. and R. D. F., both suffering from cirrhosis of kidney, the egg-diet was carefully tried, and no material change resulted.

From these and other observations I am inclined to think that in the cirrhotic form of Bright's disease the diet is a less important element than it is in the tubular inflammation.

IV. Waxy or Amyloid Form of Bright's Disease.

I have not had opportunity, since entering upon the present investigation, of carrying out an elaborate and extended series of observations; but by the kindness of Dr. James Ritchie I have had it in my power to ascertain the effect of egg diet upon a well-marked example of this disease. The patient, a young lady, was suffering from chronic abscesses connected with vertebral disease, and had for some time exhibited the ordinary features of waxy degeneration of the kidneys. Six raw eggs were taken daily for two days, in addition to her ordinary food. The urine was 120 ounces before the eggs were taken, and 100 ounces on the second

day of the egg diet. Its amount of urea was 200 grains before and 210 grains after, thus showing a slight increase, notwithstanding the diminution of urine. The albumen was, before the eggs were used, 3·8 grammes per litre, or 199·5 grains in the 24 hours, afterwards 7·2 grammes per litre, or 315 grains in the 24 hours. This increase of albumen was very marked, and it was found not to be egg-albumen but ordinary serum-albumen which was present.

In a doubtful case of waxy disease complicated with other renal disorders a succession of ordinary, large, milk, and low diets was tried, and we satisfied ourselves that there was no effect upon the amount of urine, its specific gravity, or the discharge of urea. With regard to the albumen, however, it was found that the use of the large diet was attended by some increase, and the low diet gave a diminution, that suiting the patient better than the milk diet.

In waxy cases, then, so far as my evidence goes, I am inclined to think that the good nourishment which is otherwise indicated in that disease is not contra-indicated by the state of the kidneys, even although their vessels appear to be in a condition permitting of more ready transudation of albumen than is the case with healthy vessels.

I shall speak more briefly of the forms of albuminuria which are, comparatively speaking, not dangerous to life. Some of them may be indeed dismissed in a few words.

In cases of *febrile* albuminuria, the question of diet is usually of little moment, but in some, and especially in scarlet fever, there is a special liability to the occurrence of actual inflammation of the kidney, and there is no doubt that the use of a copious diet rich in nitrogenous substances is very dangerous, but that something of the nature of low diet or milk diet is best for such fever cases during convalescence as well as during the continuance of the fever.

The albuminuria due to *heart disease* is, as a rule, comparatively slight, and in the presence of the organic changes in the circulatory system, scarcely deserves attention.

As to the forms of albuminuria which accompany *derangement of the digestive system,* I have already referred to the idiosyncratic relations of some individuals to particular articles of diet. As I have made no special observations regarding these cases, I shall merely say here that albuminuria due to digestive derangements is necessarily influenced by the kind of food which produces the disturbance in each particular case, and that the effect of different diets upon the albuminuria must depend on the effect they have on the digestive derangement.

Albuminuria connected with *nervous disease* and with *glycosuria* also demands little attention in this respect. There thus remain only the functional and accidental groups for consideration.

As to the four great varieties of *functional* albuminuria —the paroxysmal, the dietetic, that due to exercise, and the simple persistent—the first requires no special notice. Of the second, it is obvious that each individual case must be studied, and the diet prescribed for the patient in accordance with what may seem best to suit his individual peculiarities. In some cases referable to the third group—that of albuminuria from exercise—I have made careful trial of different kinds of food, and I do not think that much difference was induced by it. It is true that in the case of the young lady whose case is given in detail in the eleventh lecture of this series, there was a relative diminution of albumen when she was under the milk diet. But the diminution was merely relative, the water was increased to a large extent, while the daily discharge of albumen remained unaltered. I have had opportunity during the present summer of making observations as to

the effect of diet in a case which I regard as one of simple persistent albuminuria. The patient is a young man of twenty, who is suffering from asthma, bronchitis, and backward pressure on the right side of the heart. Although his urine is always albuminous, it shows no tube casts, and has rather an excess than a diminution of urea. He has also no evidence of the usual consecutive complications met with in true renal cases. This patient was kept upon his ordinary diet for two days. He then took for ten days ten raw eggs in addition to other food. He was then kept upon a purely milk diet for seven days, and thereafter his ordinary diet was resumed.

The egg diet had no effect upon the quantity of urine. There is some doubt as to the effect on the urea at first, but certainly towards the end of the period of experiment it underwent a distinct increase. The albumen also increased both relatively and absolutely, especially towards the end of the experiment. It may be worthy of mention that we examined four specimens of the water daily—one before breakfast, one after it, one in the afternoon, and one in the evening—and found that while the albumen was usually more abundant after breakfast, it was not more so than one usually finds apart from special egg dieting, and on some days there was no increase after breakfast.

The milk diet increased the quantity of urine considerably. The urea remained as high as it had been at the end of the period during which the eggs were given—and twice it was distinctly higher. The albumen was on one day larger than on any previous occasion, but on the whole was less than it had been under the egg diet.

During the first five days on which ordinary diet was again given the quantity of urine was about the same as on the ordinary diet at first, the urea was less than under the milk and during the latter period of the egg diet, but

larger than under ordinary diet at first, and during the first part of the egg diet. The albumen showed a relative increase over what it had shown under the milk—being at least in as large a proportion as during the egg diet, but the absolute amount lost during the twenty-four hours showed little difference from what it had done during the milk diet.

From this and similar cases I am inclined to think that little is gained by very special dieting in cases of this kind, but that the physician should keep his eye upon the effect of each kind of food in each individual case.

In the treatment of accidental albuminuria, diet is often, as most practitioners well know, of great importance. Above all, in cases of catarrhal inflammation of the urinary tract, bland and milky diet is to be recommended. I have often seen great advantage in such cases from the adoption of an exclusively milk diet. In some of the accidental cases of course ordinary dietetic arrangements are best.

As to the use of alcoholic stimulants, I think that it is best to avoid them in all organic renal disease and in cases of inflammatory accidental albuminuria, unless when the condition of the circulation or nervous system directly requires stimulation. I have not seen alcohol prove injurious when used in moderation in circulatory albuminuria, nor in the other less dangerous groups.

LECTURE XV.

ON THE EFFECT OF MEDICINES IN ALBUMINURIA.

Introductory.—Treatment of Nephritis.—Renal Cirrhosis.—Waxy Degeneration. — Combined Forms. — Febrile Albuminuria. — Albuminuria from Circulatory Disease. — With Alimentary Derangement. — With Nervous Disease. — With Glycosuria. — Functional Albuminuria.—Accidental Albuminuria.

GENTLEMEN,—Having recently laid before you my views as to the dietetic treatment of the different varieties of albuminuria, I shall devote our present meeting to a description of the general, and especially the medicinal, treatment of each of the forms.

The question as to the power of medicines to control the discharge of albumen with the urine has attracted the attention of many observers, and numerous drugs have enjoyed a certain reputation with some, while they have failed in the hands of others. I shall give you as briefly as possible a general idea of some recorded observations on this question.

Dr. Lauder Brunton,[124] in discussing the influence of medicines upon albuminuria, states that a similar effect to that of temporary ligature of the renal artery (which, as you know, produces albuminuria), may be produced by causing the vessels temporarily to contract by such drugs as digitalis. He and Mr. Power found that the urine which was first secreted after the temporary arrest induced by digitalis was albuminous, and in poisoning by strychnia a similar effect is noticed. Such drugs as cantharides and

turpentine, which irritate the kidney, may produce albuminuria and even hæmaturia. Lead and mercury produce albuminuria by inducing chronic interstitial nephritis. Chlorate of potassium and glycerine in large doses produce hæmaturia, and the tubules get blocked up with plugs of broken-up corpuscles.

As regards the much more important question of the effects of medicines in diminishing albuminuria, Dr. Brunton speaks favourably of tannin and tannate of sodium, which have been experimentally found useful in this way by Ribbert. Arbutin, the active principle of uva ursi appears, he says, to be still more efficacious, and fuchsin has a similar action. In a case of intermittent albuminuria,[125] which he believed to be due to imperfect intestinal digestion, arsenic and pancreatine were both efficacious in stopping the albuminuria. Arsenic has also been found useful in this respect in the hands of others, and in another lecture of this series, I relate a case in which chloride of ammonium was similarly efficacious. He also points out the value of purgatives, such as elaterium, which in cases of renal congestion, lessens albuminuria and increases the flow of urine.

Dr. Fothergill[126] is very sceptical as to the value of medicines in diminishing albuminuria. He says, "It is questionable how far the drain of albumen is ever sufficiently serious to endanger life, and it is even more questionable if the drain can be checked by astringents unless they be ferruginous." His favourite treatment consists in warm baths, warm clothing and poultices, plasters and cupping to the loins, regulation of diet; and the medicines which he prefers are cathartics, containing potash, the potassio-tartrate of iron in buchu, and mercury in limited doses, the last of which, he says, Dr. Broadbent has found very useful in removing the traces of albumen which often persist for

a long time towards the decline of inflammatory Bright's disease after fever.

Dr. Allard Memminger[127] finds that in Bright's disease chloride of sodium reduces the albuminuria, increases the urea and chlorides, removes œdema, and otherwise improves the patient.

Dr. Sydney Ringer[128] states that Dr. George Lewald has found that lead diminishes to some extent the amount of albumen lost in twenty-four hours in Bright's disease, while it increases the amount of urine. The same observer has found that tannin acts in a similar manner.

Senator[20] says there is at most one drug, iodide of potassium, which must be allowed to possess a certain amount of efficacy in some forms of chronic nephritis.

One of the most careful writers on the subject is Dr. Saundby[129] of Birmingham, who has made an elaborate and valuable series of observations in order to test the effect of a large number of drugs on albuminuria. He made a careful quantitative estimation of the albumen by Esbach's method, and after having tried all or nearly all the important drugs from which some result might have been expected, including alkalies, astringents, benzoates, cardiac tonics, pilocarpine, turpentine and similar remedies, fuchsin, cantharides, iodide of potassium, iron preparations, and purgatives, he says that he cannot affirm that any one of them can exercise control over the quantity of albumen lost with the urine. Some advantage appeared to follow the use of certain medicines, for example, alkalies and tannate of sodium in chronic cases; nitro-glycerine in acute cases. Digitalis and other heart tonics increased the albumen. So also did iron in various forms. Perchloride of mercury in very minute doses ($\frac{1}{1000}$th grain), although it has been highly praised, was found useless. Purgatives and diaphoretics, though of great value in treatment, did not appear directly to influence

the amount of albumen excreted in chronic Bright's disease.

Sir William Roberts and Professor Rosenstein have come to the same general conclusion as Dr. Saundby as regards the inefficacy of drugs in diminishing albuminuria, and I have satisfied myself by a long series of careful observations that we have no right to credit any drug with the power of directly diminishing the discharge of albumen.

Passing now to consider the treatment of the different groups of cases, I shall embody the results of a series of elaborate and prolonged observations made for me mainly by my resident physician Dr. Gulland, and partly by Dr. Pirie. We arranged to try the action of different remedies of repute in cases of different groups; and, after determining the amount of urine, urea, and albumen passed on an average by each patient, we tried different drugs in succession, noting the effects of each, in each particular, of the cases. The labour involved in this research was very considerable, but the results are interesting, and in some respects important.

I shall speak first of the renal inflammations.

In albuminuria from acute or subacute inflammation of the kidneys the treatment must vary according to the severity of the disease. Some cases get well without any interference; in others, the life is saved only by careful medication. In all cases the patient must, in the early stage, be kept in bed. The action of the skin must be favoured by warm clothing, while the diet is of the bland and simple kind already described. When dropsy is considerable, the quantity of urine is almost invariably diminished, and the two important indications are to remove the one and increase the other. If we can succeed in establishing diuresis, we attain three valuable results—viz., we clear the tubules of inflammatory materials blocking them; we relieve

the blood of excrementitious matter, which would otherwise be retained; and we drain away the dropsical fluid. The first of these, in particular, seems to me to be of great importance; for, if the tubules remain blocked, an absorption of their contents, molecule by molecule, takes place, and the organ shrinks in corresponding degree; whereas, if the tubules are cleared out, opportunity is afforded for the formation of new epithelium, and a restoration of the tubules to structural and functional health. Some writers have maintained that the use of diuretics is dangerous, because they may tend to increase the renal inflammation. This may be true of some diuretic medicines, but it certainly is not true of all. Diuresis may be obtained, as Dr. Dickinson[122] has shown, by the administration of water, two or three pints of pure, or, best of all, distilled water being taken daily, and you will find that milk is useful in this way, as well as in the way of supporting the nutrition. But medicines are often required, and digitalis is certainly a safe and non-irritating diuretic. You will find that digitalis, at least when given in medicinal doses, never produces albuminuria; that in cardiac cases it often leads to its disappearance; and that in inflammations of the kidney it does not increase the albumen, even when it is exerting an active diuretic influence. Strophanthus and other members of the cardiac tonic group may also be employed. Saline diuretics, such as acid tartrate of potassium and acetate of potassium, must be more cautiously employed during the acute stages, but often do good when the acute is passing into the chronic. Combinations of these, with broom-top and digitalis, are eminently serviceable. It is better, in the acute stages, not to use juniper, as it is apt to prove too irritating; but in the later stages both it and such remedies as gin and copaiba sometimes act when others fail. The action of diuretics may be helped by the use of nux vomica. Iron, or iron combined with arsenic, is

frequently of great service. Much relief may be afforded to the kidneys by acting upon the bowel. Perhaps a free purge sometimes suffices to avert renal inflammation, and certainly salines or other aperients do good in the way of eliminating from the blood, as well as by relieving the affected organ. Acting upon the skin also, is of the utmost importance in such cases. The use of pilocarpine, of hot vapour baths and hot air baths, as well as of milder diaphoretic medicines, often give relief. Hot poulticing over the loins, and sometimes the local abstraction of blood from that region, also prove serviceable. Under such treatment a large proportion of these cases improves; but, although improvement is obtained, the albuminuria frequently tends to linger, and many attempts have been made to overcome that tendency. Among the remedies which have been praised are, tannic acid, tannate of sodium, iron, arbutin, ergot, belladonna, and hydrochlorate of rosaniline (fuchsin). I have tried very carefully a number of these medicines in some cases of the kind, determining daily the amount of urine, the amount of urea, and the amount of albumen. I have long ceased to have faith in tannic acid, and do not now use it, except in combination with sodium, which has been found useful by Saundby and other careful observers. My own experience of it is not large, but, so far as it goes, it indicates that in this form of albuminuria it produces no effect either upon the discharge of albumen, the amount of water passed, or the amount of urea.

Iron is so distinctly beneficial to the blood, that it is often employed; and in at least one case, which I have watched very carefully, there was no doubt that, although the amount of urine and of urea remained unchanged, the albumen diminished. Arbutin, the active principle of uva ursi, has proved in my hands absolutely inefficacious, the urine remaining unaffected in every particular. Ergot suggests itself

as likely to prove useful by contracting the blood-vessels; but it has failed in my hands to influence in cases of this kind either the total amount of urine, or the urea, or albumen. Many years ago I thought that I obtained good results from belladonna in some cases; but my recent experience, with careful testing of the urine, has scarcely confirmed the very favourable impression. I have pushed the medicine until dryness of the mouth resulted, without seeing more than a slight diminution of albumen. The hydrochlorate of rosaniline, if carefully and perseveringly used, has appeared in some of my cases to be distinctly useful; and in two patients with whom I tried it, determining daily the amount of urine, urea, and albumen, I was able within seven days to satisfy myself of a distinct degree of diminution. I have failed to get decided benefit from iodide of potassium in this respect, and its depressing effect is, of course, to be dreaded; but it is possible that it may be useful in certain chronic conditions, where the process is passing into interstitial contraction.

In the treatment of these acute cases, apart from the question of the albuminuria, there are two sets of urgent symptoms which often endanger life—uræmia and dropsy. For acute uræmia the best treatment is to act freely upon the skin, injecting pilocarpin subcutaneously, applying hot vapour or hot air baths, while keeping the convulsions in check by chloroform, chloral, or bromides. In such cases it is also well to act upon the bowels by means of elaterium, jalap, or other quickly acting hydragogue cathartic, and, as soon as possible, to give digitalis, and adopt other remedies for relieving the kidneys. Blood-letting from the lumbar region I have seen sometimes indicated, and occasionally useful. Venesection is occasionally helpful in extreme cases, particularly those in which pregnancy coexists with the renal inflammation.

Dropsy is best met by diuretics, purgatives, and diaphoretics ; but very often, when these fail, life may be saved by mechanical means. Drawing off a quantity of fluid from the pleura or from the abdomen often saves the patient ; and I have known one, tapped again and again, saved not only from the immediate danger, but actually restored to health.

In cirrhosis of the kidney, no medicine is as yet known to have the power of altering or controlling the essential morbid process. All that we can hope to do is to improve the patient's general condition by relieving certain symptoms. It is true that a great authority, the late Professor Bartels of Kiel,[123] thought that iodide of potassium was able in some measure to control the morbid process, and, partly out of respect to his opinion, I sometimes use this method of treatment, but it has not proved serviceable in my cases. For the relief of the albuminuria I have tried carefully the effects of belladonna, hydrochlorate of rosaniline, and iron, with entirely negative results. Nitro-glycerine, which has been praised by some, has been followed in my hands, in at least one well-marked case, by a slight increase in the amount of albumen, while the urine and urea remained unchanged. In one case the use of ergot was followed by a diminution in the amount of albumen, without change in the urine or urea ; and I have, on at least one occasion, tried the effect of full doses of digitalis in a case of this kind, in which I thought it was not contra-indicated, and I found no alteration in the quantity of urine or of albumen. On the other hand, much relief from headache may be obtained by the use of iron, of quinine, of chloride of ammonium, also of bromides, belladonna, cannabis indica, and caffeine. The excessive vascular tension may be diminished by the iodide of potassium, by nitro-glycerine, and by other nitrites. The anæmia is sometimes improved by iron, and, still more, by

combinations of iron with quinine, strychnine, and arsenic. Nutrient remedies—various preparations of malt, cod-liver oil, and such-like—are of service in improving the general tone of the patient, and retarding the inevitable decay. The uræmic symptoms are generally to be treated as in the inflammatory cases; but as in this disease they are more frequently due to organic changes in the brain, they are, on the whole, less amenable to treatment.

Waxy disease is also, in its essential nature, little amenable to the action of medicines; but in syphilitic cases, the iodide of potassium or of starch, and in all cases the syrup of the iodide of iron, may possibly be useful. The albuminuria has remained unaffected under treatment with belladonna and hydrochlorate of rosaniline. I have seen it distinctly increase while ergot was being given, and slightly under nitro-glycerine, neither of these producing any effect upon the amount of urine or of urea. Iron, in the form of tincture of perchloride, I have seen followed by a slight diminution of the daily discharge of albumen. Cod-liver oil, various malt preparations, and a liberal diet, are indicated in this disease.

In the mixed forms of organic renal disease the treatment must be determined according to the preponderating element. In all of them, whether combined or not, the choice of climate is of much importance. When it is possible, these patients should avoid cold and damp districts. It is well for them to winter in the South of Europe, in Algiers, or in Egypt; and practitioners in high altitudes, such as Davos, find that renal cases should not try treatment there. The only exception to this rule is afforded by purely waxy cases which have resulted from chronic phthisis, and in which the advantage to be derived in respect of the pulmonary disease tells favourably upon the kidney also.

Before leaving the treatment of the organic renal conditions, I shall say a word or two regarding the treatment of some of the leading complications. In gastric catarrh, careful regulation of diet, feeding the patient upon milk, soup, or peptonised preparations, and giving them in small quantities, frequently is the first indication. The use of bismuth, or of that substance with a very small dose of rhubarb, and of alkali with occasionally, if the liver be specially affected, a little grey powder, podophyllin, or other cholagogue, is constantly of service. Counter-irritation over the stomach and liver should also be employed.

Constipation and diarrhœa demand no special comment, only it is to be noted that when the latter occurs in waxy cases, opiates in enemata, or suppositories may be safely employed, while they are, of course, eminently dangerous in cirrhotic or inflammatory cases.

The anæmia, which is so constant a symptom, demands the use of iron, as I have already shown, and very often it will be found that chalybeates, in combination with bitter tonics, are of value also in the way of improving digestion.

The condition of the heart and the circulation often calls for very careful management. Frequently iodide of potassium, nitro-glycerine, and other nitrites are indicated for their action in the way of relieving excessive arterial tension; and, on the other hand, digitalis, strophanthus, and caffeine, are helpful when the muscular fibre of the heart threatens to fail, and arterial tension is consequently falling. Such tonics as nux vomica, quinine, iron, arsenic, and their combinations, also help to give tone to the weakened muscular fibre of the heart.

No complication is more alarming than pericarditis, for it often ushers in the fatal result, but in such cases recovery may take place. The application of leeches over the præcordia has appeared to me of real service in some cases. You

have lately seen an instance of this in the Paton Ward: a patient, who was suffering from severe subacute inflammation of the kidneys with great dropsy, who was passing only about twenty ounces of urine per diem, complained of pain in the chest. Examination showed that this was due to pericarditis, and the most marked to-and-fro friction rapidly developed. Six leeches were applied over the præcordia; no further effusion took place into the pericardium, and within three days the friction disappeared. It may be worth while to remind you that the dropsy was so severe, and was interfering to such an extent with respiration, that it was necessary to tap the pleura even while the pericarditis was going on. One hundred and four ounces of fluid were withdrawn, and the heart showed no sign of disturbance during the process. You will not often see so satisfactory a termination of acute pericarditis in this disease, especially when attended by such a complication.

The affections of the bronchial tubes, and of the trachea and larynx, require little special notice, excepting in so far as they may render the use of pilocarpine hazardous, and may increase the tendency to œdema glottidis. You will remember that I have seen tracheotomy suddenly rendered necessary from this cause.

For the relief of acute and chronic œdema of lung, counter-irritation and dry-cupping are among our best remedies. Much good also comes from the use of cardiac tonics acting as diuretics, and at the same time improving the pulmonary circulation. The ordinary expectorant and antispasmodic remedies must not be neglected.

For dropsical effusion into the pleura, or into the peritoneal cavity, tapping is our best means of treatment. We, of course, try first what can be accomplished by means of diuretics, but I have long been in the habit of giving mechanical relief whenever dropsy is considerable and refuses to yield to

the simpler methods. In the case of the man to whom I have just referred, you observed how rapidly diuresis set in when once the pleural fluid had been removed. His urine rose to 70, 100, 130 ounces, and his anasarca correspondingly subsided.

The nervous complications of a uræmic character have been already mentioned. The hæmorrhagic and embolic processes require no special treatment.

You will occasionally find yourselves in a difficult position when renal disease is associated with pregnancy. It is best to let the friends of the patient know that the combination is always formidable, and sometimes very dangerous. At the same time it must be remembered that a large proportion of the cases pass through the confinement without showing any untoward symptom, and your duty is simply to be watchful and to act with promptitude if serious symptoms manifest themselves. The delivery should be brought on and carried through as quickly as possible, while the uræmic symptoms should be treated on the ordinary principles applicable in such conditions, only it may be remarked that in these cases general blood-letting seems to be of service more frequently than it is in the more ordinary forms.

In febrile albuminuria the indications appear to me to be mainly to favour the action of the bowels and the skin, and to stimulate the kidney by the use of diluent drinks. Perhaps free action of the bowel is useful, if not distinctly contra-indicated; but as the mere albuminuria is generally unimportant when compared with other elements in the case, this subject need not be dwelt upon.

In albuminuria due to heart disease the most strikingly good effects follow the use of appropriate medicines. In the majority of cases the increased backward pressure from

weakness of the cardiac muscle is the cause; and the cardiac tonics—above all, digitalis and strophanthus, but also caffeine, convallaria majalis, and iron with arsenic—prove of service. In the rarer cases, where the albuminuria is due to embolic processes, these remedies are to be avoided; the circulation must be kept as quiet as possible. The discharge is usually transitory. But, as with regard to diet, so with medicine, the treatment of albuminuria in these cases scarcely deserves mention.

In albuminuria with derangement of the digestive system, the treatment has, of course, to be directed to the digestive abnormalities. In the hepatic forms, arsenic and chloride of ammonium have seemed to me specially serviceable.

If suitable cases occurred, I should try gastric sedatives where I found that the ingestion of food was immediately followed by albuminuria. A combination of bismuth with hydrocyanic acid would deserve the first trial. If one found reason to suspect defective action of the pancreatic secretion it would be well to try the liquor pancreaticus or pancreatine, as Dr. Lauder Brunton[108] did in a case which he has most interestingly described in his work on the Disorders of Digestion.

The albuminuria attending upon nervous disease and upon glycosuria does not demand special treatment.

Of the varieties of functional albuminuria, the paroxysmal does not require active medication during the persistence of the attack. If the patient be kept quiet, the action of the skin favoured, and diluent drinks administered, it will spontaneously subside. During the intervals, such drugs as arsenic, quinine, iron, and chloride of ammonium, should

be carefully tried. The dietetic albuminurias are really of the nature of idiosyncracies, and, beyond the obviously indicated attention to diet, I have not found any treatment serviceable, excepting where the chloride of ammonium seemed to check it in one case, and arsenic in some others. There, also, it seemed to be by improving the general condition of the system that the good result was obtained. The remarks which I have already made as to albuminuria with derangement of the digestive system find application here also. In the varieties connected with muscular exercise, I cannot claim to have seen medicines of distinct service. The simple persistent albuminuria has also, in my experience, generally resisted the action of drugs.

Accidental albuminuria is, of course, relieved when we succeed in checking the source of contamination. Astringents which arrest hæmorrhages are thus sometimes of service. The removal of gravel or of calculi by medical or surgical means leads often to the subsidence of pyelitis, of hæmorrhage, or of vesical catarrh. Such remedies as uva ursi, triticum repens, liquor potassæ, hyoscyamus, and copaiba, which diminish inflammation of the urinary tract, are, of course, of great service. I have given a careful trial to arbutin and tannate of sodium in cases of this kind, and have found nothing to record in their praise.

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ERRATA.

Page 9, for "derivations" at foot of page, read "derivatives."
„ 18 and 23, for "Van Noorden," read "Von Noorden."

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