CLINICAL LECTURE ON VARIOUS MODES OF TESTING FOR ALBUMEN IN THE URINE.

By GEORGE JOHNSON, M.D., F.R.S.,

Professor of Clinical Medicine, and Senior Physician to King's College Hospital.

I PROPOSE to describe, demonstrate, and critically review the various modes of testing for albumen in the urine in the light of recent knowledge and research.

The two tests for albumen which have hitherto been most generally used are heat and nitric acid. I pour into a test-tube a column of urine about two inches in height, and place it over a spirit-lamp. Before the liquid reaches the boiling point, the albumen begins to coagulate; and the more abundant the albumen, the lower is the temperature at which coagulation commences. When the urine is highly albuminous, as the heating proceeds and coagulation commences, the tube must be continually and briskly shaken, to prevent the sudden expulsion of the partially coagulated liquid by the steam generated beneath a dense film on the surface. Now observe that, when albuminous urine is alkaline, heat alone will not show the presence of albumen. I take some of this albuminous urine, and before applying heat, I add a drop or two of liquor potassæ. You see that, when boiled, it remains clear; the potash has combined with the albumen, and the resulting albuminate of potash is not coagulable by heat; but if now I add a few drops of strong nitric acid, coagulation at once takes place.

Again, some specimens of urine, when boiled, give a precipitate which has the appearance of albumen, though none is present. The non-albuminous urines which are thus acted on by heat are usually neutral or alkaline, and the turbidity is due to the precipitation of phosphates. To a specimen of normal urine I add a drop or two of liquor potassæ, and, when heated over the lamp, you see that it becomes turbid.

This phosphatic turbidity is easily distinguished from an albuminous coagulum by the addition of a drop or two of nitric acid, or even of acetic acid, or citric acid solution, which dissolves the phosphates while coagulated albumen remains undissolved.

You see, then, that if heat alone were relied upon as a test for albumen, it might mislead in two opposite directions: (1) by not detecting albumen in alkaline urines, and (2) by giving a delusive phosphatic precipitate in non-albuminous urine.

Nitric acid has long been known and employed as a valuable test for albumen. To this clear specimen of urine, I add a few drops of strong nitric acid, and an abundant coagulum of albumen is immediately formed. In most cases, nitric acid alone is a sufficient test for the presence of albumen in the urine, but there are some exceptional conditions, and some sources of fallacy, which I now proceed to point out.

Here is a specimen of albuminous urine which, as you see, is highly turbid with urates. As I warm it over the lamp, it first becomes clear by the solution of the urates, and then, by the further application of heat, the albumen coagulates, and renders the urine milky. Such a specimen requires to be cleared by heat before nitric acid can be satisfactorily used as a test; although, as you see, a slight excess of nitric acid added to the turbid urine decomposes and dissolves the urates, and precipitates the albumen.

It sometimes happens that, when nitric acid is added to highly acid urine, it causes a turbid deposit of urates, which might be mistaken for an albuminous coagulum. The distinction is readily made by the application of heat, which dissolves the urates, but not the albuminous precipitate.

In the urine of patients who are taking copaiba, nitric acid, acting on the resin, causes a slight milkiness, which has sometimes been mistaken for albumen. Such urines have a peculiar resinous odour; although acid, they are not coagulated by heat, nor, as I shall presently show you, by picric acid, which is a most delicate test for albumen.

When an excess of nitric acid is added to a highly concentrated urine, it sometimes happens that a copious crystallisation of nitrate of urea gradually occurs. This slowly formed crystalline deposit could scarcely be mistaken for an amorphous coagulum of albumen.

With regard to nitric acid as a test for albumen, I have yet to show you certain facts which require attention. To this specimen of highly albuminous urine I add a single drop of strong nitric acid. You see that it forms a white coagulum, which, on shaking the tube, is redissolved; a second drop may be added with the same result, while the further addition of acid causes a permanent precipitate. Now, note this fact, that, when a drop or two of nitric acid has caused a coagulum which has been redissolved, the subsequent application of heat will not precipitate the albumen. The explanation is, that a nitrate of albumen has been formed which is not coagulable by heat, but readily by an excess of the acid. Albumen is a neutral substance, which is capable of combining, on the one hand, with alkalies as we have before seen; and, on the other, with acids; and, in both instances, to form compounds not coagulable by heat.

As a drop or two of nitric acid will prevent the coagulation of albumen by heat, so a great excess of nitric acid added to cold urine will either redissolve the coagulum which first forms, or, if rapidly poured in, entirely prevent coagulation, the mixture remaining quite clear.

Nitric acid, carefully added to cold urine, is one of the most delicate tests for a slight trace of albumen in the urine. For this purpose, a few drops of the acid may be placed at the bottom of a test-tube, and the urine slowly poured into the sloping tube, so as to rest on the surface of the acid; or, the urine being first placed in the tube, a few drops of the heavy acid are allowed to fall through the urine to the bottom. The opalescent albuminous coagulum appears at the junction of the two liquids.

In picric acid, we have a more delicate test for minute traces of albumen than either heat or nitric acid, or than both these tests combined. Picric acid may be used in the form of a saturated aqueous solution, or in the form of crystals or powder. An ounce of water at 60° retains in solution 5.3 grains of the dry acid. A saturated aqueous solution may, therefore, be made by dissolving the powder in boiling distilled or rain water, in the proportion of six or seven grains to the ounce. A portion of the acid will crystallise out on cooling, leaving a transparent yellow supernatant liquid.

I now show you that this solution, being added to an equal volume of urine, in a test-tube, immediately coagulates the albumen. The coagulum is made more dense by the subsequent application of heat. The coagulated picrate of albumen is soluble in strong alkalies. If, therefore, the albuminous urine were highly alkaline, it might be necessary to acidulate it with a vegetable or a mineral acid, before adding the picric solution; but, in my very numerous testings with picric acid, I have not once found it necessary to add another acid. The picric acid solution is itself sufficiently acid to dissolve the phosphatic sediment which results from boiling a neutral or alkaline specimen of urine.

When the albumen is very copious, a few drops of picric acid cause cloudiness, which disappears on shaking, like the cloudiness caused by a drop or two of nitric acid. A further addition of the solution causes a permanent coagulation. A small amount of picric acid solution does not prevent the subsequent coagulation of the albumen by heat, and an albuminous precipitate by picric acid is not soluble by an excess of the acid. In these two respects, picric acid differs advantageously from nitric acid.

To detect a very minute trace of albumen, I adopt the method which I will now show you. Into a test-tube six inches long I pour a four-inch column of urine; then, holding the tube in a slanting position, I gently pour an inch of the picric acid solution on the surface of the urine, where, in consequence of its low specific gravity (1.003), it mixes only with the upper layer of the urine; and, as far as the yellow colour of the picric solution extends, the coagulated albumen renders the liquid turbid, thus contrasting with the transparent unstained urine below. Bear in mind that, for the action of the test, there must be an actual mixture, and not a mere surface-contact, of the two liquids. When, in consequence of the scantiness of the albumen, the turbidity is very slight, the application of heat to the upper part of the turbid column is found to increase the turbidity. If, then, the tube be placed in a stand, the coagulated albumen will gradually subside, and, in the course of an hour or so, forms a delicate horizontal film at the junction of the coloured and the unstained stratum of urine; the yellow liquid above, and the unstained urine below, being quite free from turbidity. Any previous turbidity in the urine interferes with the detection of a minute trace of albumen. The turbidity which is due to lithates may be removed by heat, and that caused by mucus by a previous filtration of the urine to be tested. I have proved, by numerous observations, that picric acid, applied in this way, is a more delicate and trustworthy test than nitric acid added to cold urine.

The simplest method of comparing the two tests, as regards their relative delicacy, is to dilute a specimen of albuminous urine until one or the other test fails to act; and it will be found that the picric acid solution shows the presence of albumen in a specimen diluted much beyond the point at which the nitric acid fails to give any indication of its presence. The picric acid often gives an immediate albuminous opalescence in urine, when nitric acid only slowly, after an interval of some minutes, gives a similar, but perhaps a doubtful, indication. I shall presently have something to say on the practical value of a test for minute traces of albumen.

Here let me remark that the albuminous opalescence with picric acid, which always occurs immediately, if at all, and which is increased by heat, may readily be distinguished from the coarse granular particles of urate of soda which, after a delay of some minutes, sometimes result from the acidity of the picric solution. The granular masses of urates, often mixed with crystals of free uric acid, quickly fall to the bottom of the test-tube, and carry with them so much of the picric colouring matter that, when placed under the microscope, they are so opaque as to appear almost black.

It very rarely happens that the picric solution causes an immediate turbidity in non-albuminous urine caused by the precipitation of urates. I have met with this result in only three or four specimens out of some hundreds. This turbidity, like the similar turbidity sometimes caused by nitric acid, is readily distinguished from albumen by its speedy and complete disappearance when heat is applied.

It has been objected to picric acid as a test that it gives with peptones a precipitate not distinguishable from albumen. To this statement, I reply, first, that the precipitate with peptones is most easily distinguished from that with albumen by its ready solubility when heated. I have here a peptonised solution of mutton-fibre; the addition of picric acid solution causes a copious yellow precipitate, which, as you see, is entirely dissolved over the spirit-lamp before the liquid reaches the boiling point. The distinction, then, between picrate of albumen and picrate of peptone is sufficiently easy. In fact, there is no known substance, occurring in either normal or abnormal urine, except albumen, which gives a precipitate with picric acid insoluble by the subsequent application of heat.

Precipitated peptones resemble a sediment of urates in the fact that both are dissolved by heat, but they are readily distinguished by the microscope, which shows the urates to be composed of large granules of urate of soda and uric acid crystals. Freshly precipitated peptones appear under the microscope quite homogeneous and free from solid particles; but when, after being dissolved by heat, they are reprecipitated on cooling, they contain exceedingly minute granules, which are incessantly dancing about with the so-called "Brownian movement."

The question arises, Do peptones occur in the urine? It has been asserted that they do under certain rare conditions, and that they may be detected by the rose-red colour produced at the junction of the two liquids, when the urine is gently poured on the surface of Fehling's solution previously introduced into the test-tube. I have met with some few specimens of highly albuminous urine which have given a rose-red colour with Fehling's solution; but after the coagulation of the albumen by heat, and its separation by filtration, the filtrate either gave no precipitate with picric acid or a slight cloudiness not dissolved by heat; the cloudiness, therefore, was due to previously uncoagulated albumen and not to peptones. I conclude that Fehling's solution is not a trustworthy test for peptones; and since, in some hundreds of specimens of urine, picric acid has afforded no indication of peptones by giving a precipitate soluble by heat, I infer that their occurrence in the urine must be very rare. That picric acid is a much more delicate test for peptones than Fehling's is shown by the fact that the addition of artificially prepared peptones to normal urine, in amount sufficient to give a copious precipitate with picric acid, affords only a slight colour-indication with Fehling's solution.

Dr. J. Frank Nicholson, writing to the *Lancet* (November 10th, 1883, p. 835, mentions the fact that, in the urine of patients taking large doses of quinine, he got with picric acid copious opalescence, which was cleared by heat. Most of the vegetable alkaloids, such as morphia, atropine, etc., are precipitated by picric acid and by the potassio-mercuric iodide; but quinine is the only one which is likely to be taken in sufficient doses to render the urine opalescent with either of these tests, and then the complete clearance by heat at once distinguishes it from an albuminous precipitate.

I have shown you that picric acid is a most delicate and trustworthy test for albumen in the urine; and if you ask whether there

is any practical advantage to be gained by the employment of so sensitive a test, I reply that, unquestionably, there is. For instance, during the convalescence from acute nephritis with albuminuria, whether the result of scarlet fever, of exposure to cold, or of the other well-known exciting causes, it is of vital importance to be assured that the urine is entirely free from albumen before the patient is allowed to pass from medical supervision and to return to his usual habits. For the want of such exact and careful observation, it too often happens that, in these essentially curable cases, the recovery is incomplete; a trace of albumen remains, but unattended by any signs of functional disorder, until, it may be many years afterwards, the patient presents himself with some of the many distressing symptoms and unequivocal physical signs in the urine, the heart, the arteries, the eyes, and various other tissues, of advanced and incurable degeneration of the kidneys.

And here let me warn you to avoid the not uncommon mistake of testing for albumen only a specimen of urine passed before breakfast. It frequently happens that, while the urine which is passed after resting in bed and before breakfast is quite free from albumen, that which is secreted after food and exercise contains albumen in abundance. It is, therefore, obvious that, if a morning specimen alone were tested, a patient might be considered and pronounced convalescent while disease of a dangerous tendency was still present. It is always desirable to have for testing both a night and a morning sample of urine; the former showing the effect of food, exercise, and low temperature, the latter of abstinence, rest, and warmth.

It will very commonly be found that the amount of albumen in the urine secreted after food and exercise is twice as great as that passed after some hours of abstinence and rest in bed.

The erect posture alone has sometimes a remarkable influence. In one of my patients lately, a youth recovering from acute albuminuria, it was found at one period that, although no albumen appeared after his breakfast, so long as he remained in bed, soon after he assumed the erect posture, whether before or after breakfast, although he remained in the same warm room, a trace of albumen was found in the urine. The only probable explanation of this is that the erect posture caused some congestion of the kidneys, and consequent escape of albumen by the gravitation of blood into their weakened and relaxed vessels.

There is yet another class of cases in the investigation of which it is of practical importance to employ a delicate and trustworthy test for albumen. I refer to that common form of Bright's disease in which the small red granular, or so-called cirrhotic, kidney is found after death. In this class of cases, the amount of albumen is often small, and is no index or measure of the gravity of the disease; indeed, more than one recent observer has asserted that an entire absence of albumen is of common occurrence in this form of disease. This statement, however, is not in accordance with my experience. The cases of this disease that have come under my observation have been very numerous, and I am constantly meeting with fresh examples; and, when the existence of the disease has been unequivocally established by other signs and symptoms, I have very rarely found that a careful testing of the urine at different periods of the day has failed to detect albumen. The idea that the urine is often free from albumen in these cases must, I think, have resulted from carelessness or want of skill in testing.

One method of testing which is in common use is very likely to mislead; I refer to the practice of adding acetic acid to the urine before boiling. The result often is that, albumen not being coagulable by an excess of the acid, an acetate of albumen is formed, which, like the nitrate of albumen before mentioned, is not coagulable by heat; the albumen, therefore, remains in solution, and is not detected.

I cannot too emphatically insist upon the fact that the smallest trace of albumen in the urine, whether with or without the appearance of renal tube-casts, is always abnormal and pathological. Not long since, during a discussion at the Clinical Society, it was suggested by one speaker that an amount of albumen so minute as to require for its detection any test more delicate than heat and nitric acid should be looked upon as physiological. I scarcely need say that such a distinction would be purely artificial, and not in accordance with facts.

I said just now that picric acid, as a test for albumen, may be used in the form of powder or crystals. In this form, it may conveniently be carried in the pocket for bed-side use. In my pocket urinary test-case, which was made for me by Hawksley, 357, Oxford Street, the powdered acid is contained in a small bottle. It may be carried in paper, or in a small box in the waistcoat-pocket. Unlike

nitric acid, which I now never carry about with me, it is perfectly harmless, even if it escape from the bottle.

In testing with the powder, about one third of a grain, equal in bulk to a peppercorn, may be shaken up in a test-tube, with a column of urine about one inch in height. As the powder dissolves, the urine becomes turbid with coagulated albumen. The object is to add as much of the powder as the urine will dissolve, and no more. In the absence of a test-tube, the powder may be stirred up with the urine in a wine-glass. The solution of the picric acid in the urine, and the coagulation of the albumen, are quickened by heating the tube over a spirit-lamp or candle, or by immersing the tube or glass in hot water.

The dry picric acid should be used in the form of fine powder, not in crystals. One of my correspondents was perplexed by finding that crystals of the acid dropped into a highly albuminous urine became surrounded by a film of coagulated albumen, and, becoming caked together, formed a dense precipitate. This can never occur if the fine powder be shaken up with the urine.

Another convenient mode of using the powder at the bedside is to add twenty or thirty minims of water to the peppercorn bulk of the acid in a tube, and quicken the solution by the application of heat; an equal bulk of urine is then gradually added to the hot saturated solution, when albumen, if present, is at once detected. It has been objected to the picric acid solution that it stains the fingers; but this stain, unlike the yellow stain caused by nitric acid, which penetrates into the skin, and remains for several days, is merely a surface-stain, and is immediately and completely removed by washing with soap and water.

Dr. George Oliver has devoted much time and labour to a comparison of the various tests for albumen, and also to the preparation of test-papers for bedside use. His observations agree with my own, that the three most delicate liquid tests for albumen are solutions of potassium-mercuric iodide, picric acid, and tungstate of soda. He finds "these three albumen-precipitants of equal keenness;" but I have found the tungstate of soda decidedly inferior to the other two. In the form of paper-test, Dr. Oliver states that picric acid is "the weakest of the series" (*Lancet*, Jan. 27th and Feb. 8th, 1883). The explanation of this result is that, in consequence of the comparative insolubility of picric acid, the small slips of paper dried after immersion in a saturated solution do not retain sufficient of the acid to render them a satisfactory means of testing. But there is no need for picric acid papers. The main advantage of the test-papers consists in their ready portability; but this advantage is shared equally by the picric acid powder, which, moreover, possesses these advantages over any forms of test-papers, that it requires no elaborate preparation or the addition of any other agent, that it is therefore cheaper and more simple, that it affords a more ready and trustworthy indication of the amount of albumen, and, lastly, as I shall show you in a future lecture, that, in combination with caustic potash, it forms an admirable qualitative and quantitative test for sugar.

INSANITY IN FRANCE.—One of the most striking features of modern French life is the rapid increase of insanity; the number of cases of which, and especially those induced by alcoholism, is becoming larger each year. During 1882 there were 13,434 admissions into the asylums, of which 10,184 were new cases, the total number under treatment in the year being 58,760, of which about 27,000 were men and 31,000 women, showing that females are the most liable to the disease. That they are less influenced by treatment is shown by the fact that the average duration of treatment for men is 276 days, while for women it is 295 days. The following statistics represent the character of the brain-diseases, and the average time that each class requires for supervision in the asylums:—Simple insanity, 33,629 patients, average time 287 days; softening of brain and paralysis, 8,665, average time 250 days; senile dementia, 4,495, average time 289 days; idiots and *crétins*, 5,377, average time 298 days. The latter, therefore, appears to be the most intractable form. In all France there are only 61 public and 42 private asylums, of which nine are for men only, and 14 for women only, the remainder being for both sexes. No fewer than 34 departments have no establishment whatever for the care and treatment of the insane.

PUBLIC BATHS AT SMETHWICK.—At the meeting of the Local Board on Friday, November 9th, a letter from Mr. Tangye was read, stating that, if the Board would establish public baths, the firm of which he is a member would contribute £1,000. The offer was accepted, and a committee appointed to have plans prepared without delay.

A LECTURE ON NETTLE-RASH.

By MCCALL ANDERSON, M.D.,

Professor of Clinical Medicine in the University of Glasgow; Physician to the Western Infirmary, etc.

URTICARIA (URTICA—A NETTLE) NETTLE-RASH—URTICAIRE
—NESSELAUSSCHLAG.

THE symptoms of this disorder are very familiar to most persons, seeing that the rash is identical with that resulting from the sting of the common nettle (*urtica urens*); hence the term nettle-rash. It makes its appearance in the shape of circumscribed elevations, rarely larger than the finger-nail, which are rounded or oval, or which assume the form of segments of circles (pomphi or wheals); and, when the patches are present in their most typical form, the centre of each is pale, while the periphery is red. This eruption is accompanied by itching, burning, or stinging sensations, which are increased by scratching, and are often very distressing; but its most remarkable character—that by means of which it can be distinguished from most other eruptions, and which often enables us to say that a rash is a member of the nettle-rash group, although it does not assume the typical characters of that disease—is the wonderful rapidity with which it appears, and its transient character; for, in a few minutes, it may be fully developed over the greater portion of the body, and within an hour it may all have vanished, although sometimes two or three days elapse before it disappears; it is never followed by desquamation. Its tendency to resolution is indicated by the wheals feeling softer, by the fading of the peripheral redness, and by the subsidence of the irritation. Occasionally, vesicles or bullæ make their appearance upon the patches if the inflammatory action run high, so that the careless observer might mistake the eruption for herpes or pemphigus. And not unfrequently the rash is accompanied by œdema, especially where there is much loose cellular tissue; or œdema may take the place of the eruption—oftenest on the hands and face (*urticaria edematosa*). The extent of the rash is very various; sometimes it is partial, being limited to the hands or face, while at other times the whole surface is more or less involved. Sometimes the patches are distinct from one another, sometimes they are confluent (*U. conferta*). It presents, too, certain peculiarities, according to the region affected. "When it occurs on the face, it generally produces an œdematous swelling, especially of the eyelids and lips; the wheals, however, are less distinct than usual, and the rash for the most part assumes the character of an urticaria rubra, and consists of red lines and striae. The neck is comparatively rarely the seat of this eruption, which is, however, more commonly seen on the chest and back, where, as on the face, it often takes the form of striae, and sometimes of peculiar wavy lines. On the limbs, it is observed less frequently than on the trunk. When nettle-rash affects the neighbourhood of a joint, the skin over the articulation becomes swollen and œdematous. If the hands and feet are attacked by it, the patient often complains merely that they feel as if covered by some woollen substance..... and no particular change in the appearance of the skin of these parts is to be detected. In some cases, however, the fingers and toes become so swollen, that their movements are interfered with." (*On Diseases of the Skin*, by Ferdinand Hebra, M.D., Sydenham Society's translation, vol. i, p. 304.)

The rapidity with which nettle-rash comes out, and its evanescence, have led to much speculation as to its cause. There are some who hold that spasm of the muscular fibres of the skin leads to the development of pomphi; while Liveing is of opinion that they are the result of a spasmodic contraction of the muscular coat of the vessels. The most generally received opinion, however, is, that they are due to an acute inflammatory œdema, having its seat in the papillary layer of the corium; and the reason why the rash is so fleeting is, apparently, that the exudation is thinner and more serous than in the case of most other inflammatory affections, and that the vessels soon recover their tonicity, and absorb the exudation.

Urticaria is usually an acute affection which disappears in a few hours (*U. ephemera*), or at most within a very few days (*U. evanida*), and sometimes it is preceded and accompanied by fever (*U. febrilis*). The presence of febrile disturbance is rather a favourable feature