REMARKS

ON

TESTS FOR ALBUMEN IN THE URINE,
NEW AND OLD.

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

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

In a paper on the above subject in the recently published *Manchester Medical Chronicle*, Dr. William Roberts, referring to the fact that the urine in health contains various forms of albuminoid matter, expresses his belief that the new tests for albumen which have recently been brought into prominence, especially picric acid, tungstate of soda, potassio-mercuric iodide, and the acidulated brine-test, "produce frequently in the urines of perfectly healthy persons a reaction which is undistinguishable from the reaction which indicates disease or abnormality." This point was put to the proof by the examination of the urine of thirty-one healthy persons—students, candidates for insurance, and others, who exhibited no signs of disordered health, and in whose urine heat and nitric acid gave no indication of albumen.

Dr. Roberts, of course, needs not to be reminded that albumen, in greater or less abundance, and for long periods of time, may be unquestionably present in the urine of persons who exhibit no signs of disordered health. If this were not so, albuminuria would not be so frequently unsuspected and overlooked as it is.

Dr. Roberts proceeds to state that "the acidulated brine-test gave a reaction in eleven cases, picric acid in fourteen, the tungstate test in twenty-eight, and the mercuric iodide in twenty-nine cases."

Deferring for the present what I have to say of picric acid, I should have expected, from observations which I have quite recently made, that the other three tests would give a slight but appreciable reaction in every specimen of normal urine. It is a fact that all normal urine contains a small but variable proportion of mucus.

Now, mucus is precipitated by dilute acetic acid and mineral acids. (See the article *Mucus*, in *Watts's Dictionary of Chemistry*, vol. iii, p. 1059-60.) It is also precipitated, as Dr. Oliver has shown (*Bedside Urinary Testing*, p. 37), by citric acid. The addition of a small quantity of acetic or citric acid to normal urine gradually renders it slightly but decidedly turbid, by coagulating the mucus; and Dr. Roberts mentions the fact that, when nitric acid is added to albuminous urine, "the albumen is thrown down just above the line of junction of the two liquids, while the mucus is brought into view toward the upper part of the column of urine, where it gradually forms a diffused haze, quite distinct from the opalescent haze at the line of junction."

To this I may add that, when nitric acid is placed at the bottom of a column of normal urine, a diffused haze of coagulated mucus may commonly, after a time, be seen near the upper part of the column.

Seeing then that mucus is precipitated by both mineral and vegetable acids, we are at no loss to understand that any test containing one or other of these agents should give a reaction with normal urine. The acidulated brine contains hydrochloric acid, the tungstate of soda and potassio-mercuric iodide require the addition of either citric or acetic acid before they act as albumen-precipitants; and they one and all, by the reaction with mucus, slowly cause, in most, if not all, normal urines, a cloudiness more decided than that which results from the action of the acids alone. With picric acid, however, the case is entirely different. In the form of a saturated aqueous solution, and uncombined with any other agent, it is a most delicate albumen-precipitant, but it gives no precipitate in normal urine unless an acid, such as citric or acetic acid, be added to it. This can readily be proved by the following experiment. Take about a drachm of freshly passed normal urine, and add an equal bulk of picric acid solution. The yellow mixture will remain quite clear, unless, as sometimes though rarely happens, some turbidity results from a deposit of urates, which would be at once removed by heat. Now add a few drops of dilute acetic or citric acid, and the mixture will, in a minute or two, become hazy from precipitated mucus, the haziness occurring much more slowly than the immediate opalescence, which results from the presence of a slight trace of albumen, but, like that, being unchanged by heat.

Another experiment consists in adding acetic or citric acid to normal urine, then, after waiting a minute or two to complete the coagulation of the mucus, passing the urine through a filter and adding picric acid to the filtrate; when the mixture will remain quite free from turbidity.

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I have tested many hundred specimens of normal urine with picric acid, and I confidently assert that in such specimens, no precipitate or haziness occurs when unmixed picric acid is used as the test-agent; and it may be that the different results with this test obtained by Dr. Roberts are due to his having added acetic or citric acid to the picric acid in his experiments. The only precipitates other than albuminous which may result from picric acid, employed alone, are urates, which rarely occur, except when the mixture is allowed to stand for some time; peptones, which I have met with only twice in as many years; and vegetable alkaloids, such as quinine, when large doses are being taken. These all differ from an albuminous precipitate in the fact that they are readily and completely redissolved by heat, while they may be distinguished from each other by the microscope. (See the author's lectures on *Albumen and Sugar Testing*, p. 11, Smith, Elder and Co.)

It appears, therefore, from very numerous and careful observations, that albumen is the only substance found in the urine which gives with picric acid a precipitate insoluble by heat.

The difference, then, between picric acid and the other new tests for albumen is this—that picric acid, unmixed with other reagents, while it is a most sensitive and trustworthy test for albumen, gives no reaction with mucus. On the other hand, the potassio-mercuric iodide, tungstate of soda, and brine, do not precipitate albumen, unless when combined with an acid; and this combination gives a reaction with mucus, which is not distinguishable from a minute trace of albumen.

I have been in the habit of using the potassio-mercuric iodide only as a check upon the picric acid test, when small quantities of albumen only were present, and, until lately, had not thought of applying it to normal urine. I now find, however, that this test-liquid, when acidulated—as it must be, to act at all—gives a distinct opalescence in most, if not all, normal urines. I find, too, that after the mucus has been removed from normal urine by its coagulation with acetic or citric acid, and subsequent filtration, the addition of the potassio-mercuric iodide to the filtrate causes a decided opalescence, which is probably due to the precipitation of some substance other than mucus in the urine.

In testing urines which contain a mere trace of albumen, it is important to remove any turbidity that would interfere with the process. Urates would be removed by heat, suspended mucus and other particles by filtration. The addition of the picric acid solution to a turbid specimen might give a fallacious appearance of coagulated albumen, when, in fact, there is nothing more than some increased opacity, due to the yellow staining of the suspended particles.

Picric acid is itself sufficiently acid, when added in excess, to dissolve and clear a phosphatic turbidity. In the rare case of the urine being so highly alkaline as to prevent the coagulation of the albumen by an excess of picric acid, the plan is to add sufficient citric or acetic acid to neutralise the alkali, then to filter, and add the picric acid to the filtrate.

It appears, then, that picric acid as a test for albumen is more free from fallacy than any other, not even excepting heat and nitric acid, which Dr. Roberts expresses his determination to fall back upon. Of course, in a doubtful case, no one would neglect to apply more than one test. That picric acid is a more sensitive test than heat and nitric acid is easily proved by taking a highly albuminous specimen and gradually diluting it up to the point where—though these tests fail to detect it—picric acid still gives a distinct reaction.

The main advantages of picric acid as a test for albumen are the following. It instantly detects a small amount of albumen which nitric acid would indicate only slowly or not at all; while, on the one hand, an insufficient addition of the test does not, as is the case with nitric acid, prevent the subsequent coagulation by heat; neither, on the other hand, does an excess of picric acid redissolve the precipitate, as does an excess of nitric acid. For bedside urinary testing, the portability of the innocuous powder is a great convenience. The fact that, with caustic potash, it is an infallible qualitative and quantitative test for sugar, may be said to more than double its value as an urinary test. For bedside use, Mr. Hawksley, 357, Oxford Street, makes a waistcoat-pocket test-case, consisting of a test-tube four inches long, in which are packed two smaller tubes, one containing picric acid powder, the other grain-lumps of caustic potash, and also a small spirit lamp. These are enclosed in a metal case, not much larger than a pencil-case.

Another small case contains a nipple-pipette, which, amongst other uses, is convenient for conveying urine from the vessel to the test-tube.

The picric acid which is used for sugar-testing should be purified by recrystallisation. The commercial samples usually give a red colour when boiled with liquor potassæ; and I lately saw an impure sample which not only gave this red colour, but the liquid was rendered

turbid by fine granules. The impurity was removed by solution and recrystallisation. A simple test of the purity of picric acid for chemical purposes is to boil a mixture of one volume of the saturated solution with half its volume of liquor potasse. The resulting liquid should be quite pellucid, and of a pale lemon yellow colour, with no red tinge.

BRITISH MEDICAL ASSOCIATION.

FIFTY-SECOND ANNUAL MEETING.

PROCEEDINGS OF SECTIONS.

ON THE CAUSATIVE RELATIONS OF PHTHISIS.

Introduction to a Discussion in the Section of Medicine.

By R. DOUGLAS POWELL, M.D., F.R.C.P.,

Physician to the Middlesex Hospital and to the Hospital for Consumption and Diseases of the Chest at Brompton.

I ACCEDED to the flattering invitation to introduce the subject of the etiology of phthisis for discussion to-day, because I thought the present time and occasion peculiarly fitting; for in the light of recent discoveries and active speculation with regard to the real nature of phthisis, all previous observations as to its etiological relations will have to be reconsidered. I venture to think, too, sir, that this is the right place for such a discussion, for the Father of Medicine in this city, Dr. Macnamara, has done much in his time to quicken thought on this matter; and the outcome of his teaching, in the shape of prophylactic measures, would go far to satisfy the requirements suggested by the most modern discoveries for the prevention of this scourge of our race.

The great objects I shall have in view in shaping my own remarks will be to elicit the points calling for further elucidation, and to see how far clinical observation and experimental research are in accord, and whether in any points they clash in such a manner as cannot be met by any mere readjustment in terminology.

Phthisis may be described as synonymous with consumption, namely, a progressive consolidation and decay of the lungs with progressive wasting of the body. And it will be convenient and generally correct to consider the other lesions of phthisis as for the most part of secondary tubercular origin.

The progress of consumption is remittent, or even intermittent, there being with each period of activity fresh destruction of lung, extension of local signs, renewal or exacerbation of local symptoms, and the phenomena of hectic.

What is the lesion of phthisis? Hippocrates seems to have regarded it as a suppuration and ulceration of the lung; and in a sense it has ever since been so regarded, whilst "inflammation," "deposit," "growth," have for centuries been the standards round which have most densely gathered the disputants in the controversial field of tubercular pathology.

Finally, we seem to have come to this pass, that all the lesions of phthisis are stated to be tubercular, but that we have no anatomical criterion of tubercle. The inoculation-experiments of Villemin indicated a new test for tubercle—its power of reproducing its likeness when inoculated into healthy animals; and the further pursuance of experimental inquiry has brought to light a still readier test of tubercle in the wide sense of that term, as including the whole morbid anatomy of phthisis, namely, the bacillus of Koch, a vegetable parasite, by the presence of which these lesions are determined, and to the necessities of which they minister. Hence one's definition of phthisis might now run, that it is a progressive consolidation and decay of the lungs, and progressive wasting of the body due to the presence, growth, and diffusion of a particular micro-organism. And if we accept this definition, the causes of phthisis must be spoken of as those varied conditions favourable to the preservation of this organism, and to its entrance into the human body.

Now, the causes of phthisis may be grouped under the headings climatic, social, industrial, and infective. It is manifestly impossible to enter with any minute detail upon the several reputed causes of phthisis; nor is it necessary, for they have quite recently been very fully considered by Dr. Andrew, in his Lumleian Lectures. I shall attempt little more than to refer to those most interesting to us at the present day.

Much careful search up and down the world has shown that no climate is exempt from phthisis, but that towards the same levels in

altitude and latitude it becomes of rare occurrence, and ceases to be endemic. It most abounds in subtropical and temperate climates, and within the lower ranges of elevation. The only positive climatic influence made out in relation to phthisis (and this only distinctly so for temperate latitudes) is that dependent upon insufficient surface-drainage. "Towns, villages, hamlets, and houses situated at or near undrained localities, on heavy impermeable soils, or on low-lying ground, and whose sites are consequently kept damp, have a much larger number and proportion of cases of consumption than those which are situated on dry or rocky ground, or on light porous soil, where redundant moisture can easily escape." Such was the observation of Gavin Milroy (*Seventh Annual Report of the Registrar-General for Scotland*) in Scotland.

Buchanan, in 1867, established the relationship with regard to our home counties between phthisis mortality and wetness of soil, and his observations showed that the mortality in certain localities—for example, Worthing and Salisbury—had considerably diminished since drainage had been effected.¹ The researches of Bowditch, in America, in 1862, pointed to the same conclusion. "Phthisis is invariably present in low and damp countries," says Lancereaux (*Distribution Géographique de la Phthise Pulmonaire*, 1877). On the other hand, the climatic influences unfavourable to the development of phthisis are associated with dryness of soil and rarefaction of the atmosphere. Elevation above the sea-level is regarded by many observers as of the utmost importance in the prevention of phthisis. M. Jourdanet maintains that the disease almost ceases to appear at the half-distance between the sea-level and the snow-line for any given latitude (quoted by Lancereaux, p. 30). It is, again, well pointed out by Walshe that "there exists in each of the earth's zones spots enjoying a more or less complete immunity from phthisis, the exemption of which is inexplicable on any acknowledged meteorological principle" (*Dis. of Lungs*, p. 466). And again: "The real potential conditions of climate, both antagonistic and attractive, with the exception to a certain extent of barometric pressure, remain unrevealed" (p. 467).

Those who, with Dr. Andrew (*Lecture iii, BRITISH MEDICAL JOURNAL*, April 19th, 1884, pp. 751, 755), find a resemblance between phthisis and ague, endeavour to explain the prevalence of the former disease in certain low-lying, ill-drained situations, by the existence there of conditions favourable to the well being of the tubercle-bacillus. As I shall point out presently, however, the bacillus of tubercle can be said to flourish, that is, to grow and multiply, under no conditions of Nature, however favourable, outside the animal body; and, on the other hand, its tenacity of life is so great as to place it apparently beyond the reach of adverse local influences. With regard to high altitudes, we do not yet know how far the scarcity of phthisis is attributable to sparsity of population; how far to climatic influences proper; how far to conditions unfavourable to the activity, or even presence of the bacillus. The answer to these questions may, however, soon be found; for the experiment of massing the population in these regions is being made; the germs are there in increasing abundance; and, whether they will flourish in such localities can be easily proved by inoculation and by culture-experiments there conducted. Cases of active phthisis continue to be active in elevated regions; and it is emphatically stated by Walshe that "tubercular deposition is by no means very uncommon in certain other organs of natives of the highest habitable regions" (p. 465). Amongst these and other more disputed conditions in connection with climate, it cannot escape observation that phthisis is nourished under those influences favourable to the prevalence of catarrhal and inflammatory affections of the air-passages—more especially bronchitis and pleurisy—that is, on cold and damp soils, with variable temperature; and, as we know, at those seasons of the year, the spring and autumn, when these conditions prevail. In high situations, especially in dry situations, catarrhs are much less prevalent, respiratory conditions are more robust and active, and the processes of nutrition go on more vigorously in those to whom such climates are favourable.

An examination of both climatic and industrial conditions predisposing to phthisis, cannot fail to convince any one how largely they are mixed up with conditions that fall under the heading of social relations. Phthisis is essentially a scourge of what we call civilisation.

¹ It has been claimed for the late Mr. Middleton of Salisbury, that he first drew attention to the effect of subsoil drainage in diminishing phthisis-mortality, in his paper read before the British Association at Bath in 1864. Mr. Middleton appears, however, to have regarded the prevalence of phthisis as largely due to "humidity and nastiness of atmosphere produced by the canals and cesspools," and its diminished prevalence to improved drainage and sewerage works. Buchanan pointed out that the lessened death-rate was attributable to the diminished wetness of subsoil—apart from improved sewerage-works—effected by drainage, and to have fairly established this doctrine. (See correspondence in *Lancet*, 1869, and *Salisbury Times*, June 10th, 1884.)