

The suppurative cases require support, and, as soon as we are reasonably sure of their character, surgical interference, the admirable outcome of which was seen in the cases of Caspersohn,<sup>1</sup> of Williams and Shield,<sup>2</sup> of Alexieef,<sup>3</sup> of Mason,<sup>4</sup> of Osler and Halsted,<sup>5</sup> of Mark and Maurice H. Richardson.<sup>6</sup> Among the perforation cases I know of only one recovery without operation, the case of Salzman,<sup>7</sup> which discharged through the abdominal wall. An operation alone promises success, and how well it may succeed is proved by the results of Williams and Shield and one of the cases of Osler and Halsted.

THE SIGNIFICANCE OF ALBUMOSURIA IN MEDICAL PRACTICE;  
SUGGESTED BY A FATAL CASE OF ALBUMOSURIC MYXŒ-  
DEMA TREATED WITH THYROID EXTRACT.<sup>8</sup>

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THE following case of myxœdema is reported more particularly for the purpose of calling especial attention to the presence of a symptom which, with but a single exception, so far as I am aware, has hitherto been unrecorded in this disease except as a mere statement of fact in the *Practice of Medicine*, by Wood and Fitz. The patient therein referred to was seen by me in consultation with Dr. M. L. Chamberlain, of Boston, to whom I am indebted for permission to give the following account and for information concerning the progress of the malady.

The case is of further interest, if not importance, in showing that the prognosis of myxœdema still may be grave despite the immediate and repeated benefit so generally resulting from the use of thyroid preparations.

I first saw Mrs. — November 17, 1895. She was fifty-three years of age, and had lived the greater part of her life in Vermont. The last two years had been spent in California. She never had been pregnant.

As a girl she suffered considerably from discomfort referred to the stomach, in the region of which there would be a sense of distention for a day or two at a time. Cramps would occur suddenly, and tenderness along the spine was complained of. With these exceptions she en-

<sup>1</sup> Festschr. f. Fr. von Esmsch, 1893, p. 455, Kiel and Leipzig.

<sup>2</sup> Lancet, March 2, 1896.

<sup>3</sup> Journ. Nitskaya Med., 1896, No. 4. Quoted in THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, Oct., 1897, p. 466.

<sup>4</sup> Trans. Assoc. American Physicians, 1897.

<sup>6</sup> Ibid.

<sup>5</sup> Boston Med. and Surg. Journ., December, 1897.

<sup>7</sup> Med. Corresp. Würtemb. Arztl. Vereln., 1870, xl, 84.

<sup>8</sup> Read at the annual meeting of the Association of American Physicians, Washington, D.C., May 3, 1898.

joyed good health throughout the greater part of her life, recalling to mind solely an operation for anal fistula when she was about forty-seven years old.

At the age of forty-nine, while in Vermont, she observed a gradual loss of flesh, strength, and color. A year later, when tired, would feel a gripping sensation in the back of the neck and a pain between the shoulders. These discomforts were noticeable especially on going down hill. There was also a temporary stiffness of the joints in the morning. At this time the eyelids were slightly swollen and an increased flow of saliva began, a symptom which has continued since, and persists at present.

In the following year, 1893, while in California, the joints again became appreciably stiff, and she felt a sense of numbness in the right heel, in the knees immediately above and below the joint, and in the fingers of the right hand. In 1894 the stiffness diminished somewhat, but the numbness persisted. In the fall of this year the teeth were troublesome and, despite the care of a dentist, became painful, and since have remained in this state. An upper canine tooth is said to have extended into the bone one-fourth of an inch. There was a metallic taste in the mouth, and she became unable to masticate resistant food, being obliged to live upon soft articles of diet. Walking now caused so much fatigue that she was obliged to give up active exercise. The gripping at the back of the neck and the pain between the shoulders continued to be annoying at times, and she suffered also from wakefulness.

In January, 1895, superficial swellings first were noticed. They appeared as an enlargement of the back of the neck, a lump beneath the jaw, hypertrophy of the tongue, and, later, indurations in the legs and arms. At first the swellings would vary temporarily in size, and that in the neck would lessen somewhat under the influence of fomentations; but later the enlargement remained constant. The voice was now changed, and the increased flow of saliva became a more or less constant drooling. In the course of a few months, in consequence of a loose molar tooth, the jaws were prevented from closing. The tooth was extracted, but the jaw and the neighboring portion of the tongue became sore and, finally, a fragment of dead bone was removed.

At the time of my first visit Mrs. — was unable to walk, on account of muscular stiffness. There was no evidence of mental impairment, nor had such been observed by her friends. Her face was pale, moderately swollen, and expressionless from partial effacement of wrinkles and furrows. In sharp contrast was the elevation of the eyebrows and wrinkling of the forehead from apparent tension of the occipito-frontalis muscle. The upper eyelids were relatively normal, but the lower lids were somewhat puffy. The lips were slightly thickened and everted, the surface roughened. Especially conspicuous was the greatly enlarged and resistant tongue, filling the partially opened mouth. The dorsum of the tongue was dry, although the flow of saliva was constant. The submaxillary region was prominent, presenting the appearance of a double chin, and both submaxillary salivary glands were greatly swollen and dense. The back of the neck was smooth and much swollen, like that of a very obese person, but was dense and resistant to the touch. It measured from sixteen and one-half to seventeen and one-half inches in circumference. The hands and feet were cold. The skin covering the back of the hands was thickened, coarsely wrinkled, the surface being rough and of a dirty-

yellowish tint, the whole appearance suggesting that of a fowl's claw. The skin covering the front of the chest and abdomen was normal, but that of the forearms, legs, feet, back, and buttocks was pale, dry, smooth, tightly drawn, not displaceable from the subjacent structure in consequence of the resistance of the subcutaneous tissue. The anterior wall of the vagina was smooth, thickened, and dense like the abnormal portion of the skin. There were no supraclavicular swellings. The hair was coarse and dry, but the nails were normal in appearance. The thyroid gland was not palpable. Nothing abnormal was found on auscultation and percussion of the chest and on palpation of the abdomen. The temperature was 98.4° F. The examination of the blood by Dr. R. C. Cabot showed 5,030,000 red corpuscles, 11,600 leucocytes, and 35 per cent. of hæmoglobin. The differential count gave 74 per cent. of polynuclear leucocytes and 23 per cent. of lymphocytes.

On the addition of nitric acid to the urine a dense, white precipitate was formed, occupying nearly one-half the volume of urine. The precipitate was dissolved when the specimen was boiled, but reappeared on cooling. When the urine in a test-tube was boiled it became opaque until the boiling-point was reached. It then became clear, and thus remained until the liquid was cool, when a white precipitate formed. Under the microscope a few red blood-corpuscles and an occasional hyaline and granular cast were seen.

The dissolving of the nitric acid precipitate by heat and the formation of a white precipitate when the boiled urine was cooled led me to suspect the presence of albumose, and Prof. E. S. Wood was asked to test further for this substance. He informed me that after boiling and filtering the urine to free it from albumin the clear filtrate, when acidulated with acetic acid and heated gently, became opaque, but the opacity disappeared on boiling, and a white precipitate formed when the fluid was cooled. Acetic acid and ferrocyanide of potassium gave a precipitate which dissolved when the mixture was boiled, and reappeared as the temperature fell. The biuret reaction was positive.

Professor Wood analyzed the urine from this patient repeatedly during a period of six weeks. A trace of albumin was present usually, but albumose was found constantly, by estimate varying from  $\frac{1}{2}$  per cent. to  $\frac{1}{4}$  per cent. December 10, 1895, a quantitative determination was made and showed 0.93 per cent. of albumose. The per cent. of urea on this day was 3.63, and the total quantity 18.66 grammes.

The diagnosis of myxœdema was made, and the treatment with thyroid extract begun, the five-grain tabloids of Burroughs, Wellcome & Co. being used. The dose of five grains on the first day was increased by one tabloid daily, but on the third day there was a sense of præcordial oppression, and the pulse became quickened. The dose then was diminished to one or two tabloids daily for a week, when it again was raised to three five-grain tabloids in each twenty-four hours.

I saw Mrs. — a second time December 10, 1895, a little more than three weeks after my first visit. The change in her appearance had greatly improved, although previous to the use of the thyroid extract her condition was steadily deteriorating. At the end of the first week of thyroid treatment the œdema suddenly left the eyelids, but a watery œdema, pitting on pressure, appeared and persisted in the feet. The flow of saliva diminished, the swollen tongue became smaller, and the

pain in the shoulders was less disturbing. In the third week of treatment the swelling of the neck and of the submaxillary glands was noticeably lessened, and the expression of the face became more mobile. The weight at the beginning of the thyroid treatment was one hundred and twenty-five and one-half pounds, and there had been a loss of about three pounds each week. The quantity of urea eliminated increased from eleven to sixteen grammes. The appetite was unaffected, but the pallor and debility were greater than when first seen. The pulse varied between 83 and 107 beats per minute, and the temperature remained in the vicinity of 99.7° F.

It was considered desirable to continue the use of the thyroid extract under careful supervision, that cardiac weakness might not prove a source of danger. The especial discomforts produced by it were fleeting pains in the muscles or in one joint or another, precordial constriction, and a choking sensation, all more likely to occur at night when the greatest quantity of the thyroid preparation had been taken within a limited number of hours.

Preparations of iron, arsenic, manganese, strychnine, digitalis, and nitroglycerin were given from time to time as the indications for their use were apparent. On account of the progressive weakness of the patient, despite the early improvement in the surface manifestations, the thyroid preparations were discontinued from time to time.

At a third visit, February 25, 1896, Dr. C. F. Folsom also saw the patient. At this time, although the expression was brighter, she was pale, weak, and emaciated. The especial improvement was in the condition of the skin, which was smooth, moist, and free from the yellow discoloration so marked at the outset. The hands were warm, the hair was moist and less bristling, but the brawny induration of the back of the neck and the swelling of the tongue and submaxillary glands had not materially diminished in the previous two months. It was decided to continue the use of the thyroid, and from seven to nine grains were daily given for a week, during which time the pulse was about 100 and the temperature varied from 99.3° to 100.4° F. A sudden severe attack of precordial pain then occurred, and the use of the thyroid was discontinued for four weeks. During this time the pulse fell to the normal and became stronger, the salivation lessened, the weight increased somewhat, but the tongue felt as if it was somewhat enlarged. The thyroid extract was then given in one-grain doses, and, for greater convenience in supervision and care, Mrs. — entered the Boston City Hospital, where she came under the charge of Dr. Folsom, to whom I am indebted for the report of her further progress.

She was admitted to the hospital April 18, 1896. The circumference of the neck then was fifteen inches, the tongue was about four inches wide and one inch thick. The head could not be bent backward, nor could the chest be touched with the chin. The hands and feet were cold, the skin was smooth, and the hair moist. The blood examination showed 84 per cent. hæmoglobin, 4,532,000 red corpuscles, and 10,500 leucocytes. The patient received one grain of thyroid extract daily, but she gradually became weaker, took little nourishment, decidedly failed on April 26, and died early on the following day. There was no autopsy.

There having been some difference of opinion among the physicians who saw this patient as to the exact nature of the disease, the reasons

for the diagnosis of myxœdema may be summarized. There were present "the firm swelling of the skin, not pitting on pressure, inelastic, adherent to the parts beneath, and not affected by gravitation; the dryness and roughness of the skin, tending, with the swelling, to obliterate all lines of expression; the imperfect nutrition of the hairs . . . the local tumefaction of the skin and subcutaneous tissue noticed in various parts of the body . . . an affection of the teeth homologous with that of the hairs just mentioned; the remarkable physiognomy; the slow . . . monotonous voice . . . and elimination or apparent absence of the thyroid gland." These are among the characteristics of myxœdema described in the *Report of the Committee of the Clinical Society of London*, 1888 vol. xxi., Supplement, p. 178. The mental impairment and subnormal temperature alone are lacking to complete the picture. But mental disturbances were absent in twenty-seven out of forty-six cases tabulated by the committee.<sup>1</sup> The temperature was normal in eight cases, and in a few was 99.6 F., or even higher, though never above 100° F. The swelling in the back of the neck was duplicated in Dr. Ord's case, No. 87, in which there was a "swelling at the back of the neck over trapezius, so that he cannot bear to wear a collar." Salivation was present in three of the committee's cases, and the submaxillary gland of Hale White's cases<sup>2</sup> showed marked changes. A large, swollen tongue was noted in fifty-two cases.

If the correspondence in clinical characteristics is not considered as sufficient for the confirmation of the diagnosis, additional evidence is furnished by the effects of the treatment with the thyroid extract. According to Murray<sup>3</sup> there are rise in temperature, disappearance of swelling, loss of weight, a soft, smooth, moist condition of the skin, growth of the hair, improvement in the mental condition, and increase in the elimination of urea. Her temperature became somewhat higher, and the previously cold hands were warm. The swelling diminished, there was a loss of weight, the skin became soft, smooth, and moist, and the elimination of the urea increased. A growth of hair was not conspicuous, since there was no tendency to alopecia, but a considerable improvement in its nutrition was apparent from the return of its normal characteristics.

The failure of the thyroid treatment to accomplish more marked relief is in striking contrast to the almost constant benefit derived from its use in the treatment of myxœdema. Mitchell Clarke,<sup>4</sup> however, reports two cases in which thyroid treatment proved unsuccessful, and Macpherson,<sup>5</sup> although causing improvement by thyroid grafting, did

<sup>1</sup> Report of the Committee of the Clinical Society of London, 1888, vol. xxi., Supplement, p. 14.

<sup>2</sup> Op. cit., p. 41.

<sup>3</sup> Twentieth Century Practice, 1895, vol. iv. p. 712.

<sup>4</sup> British Medical Journal, 1892, vol. ii. p. 451.

<sup>5</sup> Edinburgh Medical Journal, 1892, vol. xxxvii. p. 1021.

not remove the myxœdematous condition. Byron Bramwell<sup>1</sup> gives an account of two fatal cases of myxœdemn during or shortly after thyroid treatment. In each instance the death was sudden.

I am indebted to my colleague, Dr. E. G. Cutler, for the following summary of a fatal case under his charge.

"A patient in whom I made the clinical diagnosis of myxœdema had gradually over a period of a year and a half come into the following condition: The skin of the face, neck, shoulders, hands, arms, legs, and feet was pale and a little glossy, rather dry, much distended by a subcutaneous growth which did not pit and apparently was not fat. The wrinkles in the face were obliterated, the hair on the head had become sparse and dry, the hands and feet were much wrinkled, and the skin and nails coarse and rough. Speech was slow and peculiar. The mental condition was variable: at times the patient was rather inclined to be talkative, but the range of subjects was limited; at other times the patient would be quiet for hours and rather somnolent. Frequently there was mild delirium at night, with occasional hallucinations of sight. The patellar reflex was absent. The pulse was slow, the surface cool, and the temperature in the mouth 98° F., though no complaint of cold was made. The urine was free from albumin. The thyroid could not be made out. Toward the end there was marked tendency to somnolence. Thyroid tablets, five grains each, were given up to nine a day for two months, beginning with small dose, but with little effect. Death was sudden and apparently due to asyæope."

The novel feature of my case was the albumosuria, which continued throughout the progress of the disease from the time it first was observed. Occasional or slight traces of albumin were noticed in twenty out of ninety cases, and in one a large quantity, in the series tabulated by the London Clinical Society's Committee,<sup>2</sup> in which mention was made of this condition, and in twenty-one out of one hundred and twelve cases collected by Hun and Prudden.<sup>3</sup> Murray<sup>4</sup> states that "mucin" has not been found in the urine of human myxœdema, but refers<sup>5</sup> to Halliburton's discovery of an abundance of "mucia" in the urine of a sheep that developed myxœdema two years after the thyroid was removed by Horsley. Buzdyan,<sup>6</sup> however, found traces of mucin, but no albumin, in the urine of a patient examined by him. The only instance of myxœdema in which I have found mention of the occurrence of albumosuria is the patient of von Jaksch.<sup>7</sup> The case was one of typical Basedow's disease in which there were present a swelling of the legs, regarded as myxœdematous, and an albumosuria observed during a period of six months.

As is well known, this term is applied to the presence in the urine

<sup>1</sup> Edinburgh Hosp. Rep., 1895, vol. III, p. 116.

<sup>2</sup> Op. cit., p. 21.

<sup>3</sup> THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1888, vol. xcvi, p. 1.

<sup>4</sup> Loc. cit., p. 722.

<sup>5</sup> Loc. cit., p. 726.

<sup>6</sup> Wien. Klin. Wochenschr., 1891, Band IV, p. 510.

<sup>7</sup> Prag. med. Wochenschr., 1892, Band xvii, p. 602.

of a peculiar substance first observed by Beace Jones<sup>1</sup> in 1845. As described by him, "It gave no precipitate with an excess of nitric acid unless left to stand, or unless heated and left to cool, when it became solid. This solid redissolved by heat and again formed on cooling. Continued boiling with strong nitric acid evolved but little gas, and did not quickly hinder this reaction. Hydrochloric acid gave the same solid precipitate, soluble by heat. Strong acetic acid gave only a slight precipitate, which redissolved by heat. Caustic potash and sulphate of copper gave a splendid bright-blue, clear liquid, passing over, when heated, to a claret color, . . . coagulated firmly with heat, very perfectly with a drop or two of acetic acid."

According to Maly<sup>2</sup> the product of the gastric digestion of albuminous substances was designated albumose by Mialbe in 1846, but subsequently Lehmann named it peptone. Meissner and his pupils, in a series of articles published between 1847 and 1853, assumed the existence of a number of products of digestion intermediate between albumin and peptone, to which the terms parapeptone, metapeptone, dyspeptone,  $\alpha$ ,  $\beta$ , and  $\gamma$  peptone were applied. In 1869 Kühn received from Stokvis a specimen of urine which presented reactions similar to those observed by Beace Jones, and Kühn regarded the substances as identical. In the same year Gerhardt<sup>3</sup> sought in the urine for other albuminous substances than serum albumin, and discovered a variety, called by him "lactat," which resembled in its characteristics one of the peptones described by Meissner. He found it in a number of diseases, and observed that it was to be met with in persons whose temperature, frequently or constantly, was in the vicinity of 104° F. Senator<sup>4</sup> later observed in the urine easily distinguishable quantities of what he regarded as peptone. He recognized that this substance might have been produced in albuminous urine by the process of boiling used in its isolation, but suggested that it may have been present in the freshly voided urine. In support of this view he referred to Gerhardt's discovery of a substance resembling peptone in urine in which no evidence of ordinary albumin was to be obtained. Leick,<sup>5</sup> however, states that, although boiling may produce albumose from albumin, such a result does not necessarily follow, since numerous specimens of albuminous urine were so treated without the formation of albumose. Even in experiments on isolated albumin the quantity so transformed was too small to be significant. It was recognized also by Senator as possible for the albumin or albuminous urine, on its passage from the kidneys to the bladder and during its retention in this viscous, in part to be con-

<sup>1</sup> Philosoph. Trans. Royal Soc. London, 1848, Pt. 1, p. 55.

<sup>2</sup> Herrman's Handb. d. Physiol., 1831, Band v. S. 94.

<sup>3</sup> Deutsches Arch. f. klin. Med., 1869, Band v. S. 212.

<sup>4</sup> Arch. f. path. Anat., etc., 1874, Band ix. S. 476.

<sup>5</sup> Deutsche med. Wochenschr., 1896, Band xxii. S. 22.

verted into peptone, in accordance with the statement of Eichwald, that fluid albumin in contact with animal tissues at the temperature of the body is readily transformed into peptone. Eichwald found this substance in the urine of nephritis, and Ohermüller, in 1873, in that of scarlet fever and Asiatic cholera. Gowers<sup>1</sup> a few years later noticed its presence in a patient who previously had suffered from glycosuria.

About this time Kühne gave the term hemialhumose to this substance, which was considered to correspond with the  $\alpha$ -peptone of Meissner, and Schmidt-Mülheim<sup>2</sup> designated it propeptone. Its properties were studied also by Salkowski.<sup>3</sup> All these observers recognized the resemblance between this so-called peptone, hemialhumose, or propeptone, and the substance discovered by Bence Jones. The methods employed for the recognition of the "peptone" were faulty, especially from the difficulty of wholly removing the albumin often associated, and from the frequent, if not constant, presence of "mucin," which also was precipitated by the alcohol used in isolating the substance, and which gave rise to reactions similar to those attributed to the peptone. Hofmeister<sup>4</sup> consequently devised a method for the isolation of the so-called peptone which should free it from these sources of error. This method and the improvement subsequently made by Salkowski served as the basis of numerous contributions to the study of what has been designated "peptonuria."

The researches of Kühne and of Kühne and Chittenden<sup>5</sup> led to the use of the term albumosuria as a substitute for propeptonuria. According to these investigators alhumose, hemialhumose, or propeptone was a mixture of four ulhumoses which were designated protalhumose, deuteroalhumose, heteroalhumose, and dysalhumose. Each varied slightly from the others, especially with reference to the degree of solubility in water and in behavior toward solutions of sodium chloride, being either soluble or insoluble in dilute solutions and precipitated by concentrated solutions alone or in the presence of an acid according to the variety of alhumose concerned. When in solution they were not precipitated by heat alone, but if precipitated by acids or salts were redissolved at a boiling temperature and were precipitated when the solution was cooled. According to Huppert, Mathes, and Rosin they become opaque at temperatures of 150°-152° F., and clot at 166°-178° F. They were precipitated by nitric acid and by acetic acid, by magnesium sulphate, concentrated solutions of sodium chloride, and of ammonium sulphate in an acid, alkaline, or neutral solution, and gave the biuret reaction.

<sup>1</sup> Lancet, 1878, vol. II. p. 3.

<sup>2</sup> Arch. f. Physiol., 1880, S. 33.

<sup>3</sup> Arch. f. path. Anat., 1880, Band lxxxi. S. 552.

<sup>4</sup> Ztschr. f. Physiol. Chem., 1880, Band iv. S. 253.

<sup>5</sup> Ztschr. f. Biol., 1883, Band xix. S. 159, 219; 1884, Band xx. S. 11.



Like albumin, they were precipitated by nitric acid, ferrocyanide of potassium and acetic acid, sodium chloride and acetic acid, and ammonium sulphate, but they were not coagulated on boiling. They resembled peptones in being soluble at a boiling temperature, precipitating as the fluid became cool, and in giving the biuret reaction. They differed from peptone, according to Kühne,<sup>1</sup> in being precipitated by ammonium sulphate.

The search for albumose then became instituted, and the term albumosuria soon replaced that of propeptonuria, although for a long time it was considered to be a different condition from peptonuria.

The distinction made between albumoses and peptones, based upon the insolubility of the former in ammonium sulphate, was opposed by the observation of Neumeister<sup>2</sup> that this agent does not precipitate entirely all the albumoses, especially deuteroalbumose. Stadelmann in 1894 concluded that peptone as distinguished from albumose never occurred in fresh urine, although it might be found in stale albuminous urine from the action of bacteria upon the albumin. Von Noorden and Senator<sup>3</sup> accepted this view, and maintained that both peptonuria and propeptonuria were albumosuria. According to Senator, if a part of the urine which gives a positive reaction to Salkowski's test, and, therefore, is considered to contain peptone, is slightly acidified and treated with ammonium sulphate in excess and filtered, there will be no biuret reaction in the filtrate, indicating the absence of Kühne's peptone, which should be soluble in the ammonium sulphate.

Albumose was found not only in the gastric contents during the digestion of albumin, but also in artificial peptone preparations and by Fleischer<sup>4</sup> in normal bone-marrow. The discovery of its presence in semen is generally attributed to Posner,<sup>5</sup> but this observer and others who have written upon the subject, with the exception of Kahler,<sup>6</sup> have overlooked the fact that Beace Jones,<sup>7</sup> the discoverer of albumose, found it not only in the urine and in pus, but also "in the secretion from the vesiculæ seminales." Virchow<sup>8</sup> recognized in the bone-marrow of osteomalacia a substance which he considered to resemble that described by Beace Jones. Salkowski<sup>9</sup> sought successfully for it in the liver and spleen of leukæmia and in the liver of acute yellow atrophy. Miura<sup>10</sup> observed it in the liver, heart, and kidneys of phosphorus poisoning produced experimentally, and in the organs of a case of puerperal

<sup>1</sup> See article by Wenz: *Ztschr. f. Biol.*, 1886, Band xxii. S. 1.

<sup>2</sup> *Ztschr. f. Biol.*, 1888, Band xxiv. S. 267.

<sup>3</sup> *Deutsche med. Wochenschrift*, 1895, Band xxi. S. 217.

<sup>4</sup> *Arch. f. path. Anat.*, etc., 1880, Band lxxx. S. 482.

<sup>5</sup> *Berlin klin. Wochenschrift*, Band xxv. S. 417.

<sup>6</sup> *Prag. med. Wochenschrift*, 1889, Band xiv. S. 33.

<sup>7</sup> *Arch. f. path. Anat.*, etc., 1852, Band iv. S. 309.

<sup>8</sup> *Loc. cit.*, 1880, Band lxxxi. S. 166; 1882, Band lxxxviii. S. 394.

<sup>10</sup> *Loc. cit.*, 1885, Band ci. S. 316.

<sup>8</sup> *Loc. cit.*

fever. Schültzen and Riess<sup>1</sup> previously had found albumose in the urine of phosphorus poisoning. Fischel<sup>2</sup> stated that albumosuria was present almost constantly during the involution of the puerperal uterus, and Kottwitz<sup>3</sup> when there was a macerated foetus.

Albumosuria has been produced experimentally by Lassar<sup>4</sup> by rubbing petroleum into the skin of animals. Plosz and Gyergai<sup>5</sup> and Hofmeister<sup>6</sup> caused it by the injection of peptone into the veins, and Jitta<sup>7</sup> by the subcutaneous injection of glycerin. Rosenheim<sup>8</sup> states that he has seen albumosuria follow the ingestion of large quantities of albumose in a case of severe intestinal disturbance.

The clinical importance of albumosuria has been made a matter of study by many observers whose results in the main agree. Although published under the titles of peptonuria, propeptonuria, or albumosuria, the method used for the purpose of determining the presence of the albumose was that of Hofmeister, or, in more recent years, by this method as modified by Salkowski.<sup>9</sup> The chief advantages of the modification are gain in time and the use of a much smaller quantity of urine.

The urine to be tested must first be freed from any albumin present by acidifying from 30 to 50 c.c. with acetic acid, adding an equal quantity of saturated solution of common salt, boiling, and filtering. The albumins and albumoses are precipitated, but the latter are redissolved at the boiling temperature. The filtered fluid containing the albumose in solution is to be placed with a few drops of hydrochloric acid in a beaker, and then a solution of phosphotungstic acid is to be added while precipitation continues. The precipitate is to be consolidated by gentle heat into a coherent or powdery substance. The supernatant fluid is to be poured off, and the precipitate, washed with water, is to be dissolved in a solution of soda (specific gravity 1.16), which is to be added drop by drop until a blue or a colorless solution results. The solution, if blue, is to be decolorized by heat, and a few drops of a 1 per cent. solution of sulphate of copper are to be added to the soda solution, when a red or violet color, the biuret reaction, results if albumose is present.

Recently Salkowski<sup>10</sup> has called attention to a possible source of error. He has found that urobilin, which is precipitated by phosphotungstic acid, gives also the biuret reaction, and that consequently a specimen

<sup>1</sup> Ann. d. Char-krankenh. zu Berlin, 1869, Band xv. S. 1.

<sup>2</sup> Arch. f. Gynäk., 1884, Band xxiv. S. 400.

<sup>3</sup> Deutsche med. Wochenschrift, 1888, Band xiv. S. 613.

<sup>4</sup> Arch. f. path. Anat., etc., 1889, Band lxxvii. S. 157.

<sup>5</sup> Arch. f. d. ges. Physiol., 1875, Band x. S. 53.

<sup>6</sup> Zeitschr. f. physiol. Chem., Band v. S. 127.

<sup>7</sup> Jahrb. u. d. Fortsch. d. Thier. Chem., 1885, Band xv. S. 474.

<sup>8</sup> Allg. med. Centr., 1897, Band lxi. S. 1132.

<sup>9</sup> Centralblatt f. d. med. Wissensch., 1894, Band xxii. S. 113.

<sup>10</sup> Berlin. klin. Wochenschrift, 1897, Band xxxiv. S. 353.

of urine tested by the Salkowski method may give a 'positive result, but due to urobilin and not to albumose. Urobilin in the urine does not necessarily produce this reaction, but is more likely to in case the spectroscopic examination of the urine gives a well-marked urobilin line. Leick<sup>1</sup> already had suggested a modification of the Salkowski test, having found it necessary to use a stronger soda solution or a larger quantity of the weaker variety. After removing the albumin he added also the neutral lead acetate to the filtrate for the purpose of precipitating "mucin," coloring matter, and any remaining albumin. According to Salkowski, albumose also is precipitated by this reagent, and the negative results of the examination by this method could not exclude the possibility of albumosuria. Fortunately for practical purposes, the question relates to quantity and not to mere presence. Bang<sup>2</sup> also has devised a method for finding albumose in the urine, even in a dilution of 1:4-5000, when urobilin is present in any considerable quantity. A test-tube containing 8 grammes of finely powdered ammonium sulphate in 10 c.c. of urine is to be heated till the former is dissolved. The contents are to be boiled for a minute, centrifuged for another minute, and the clear liquid poured off. The residue, containing albumose, albumin, urobilin, uric acid, and urates, is to be stirred in alcohol (97 per cent.), which dissolves the urobilin and is to be poured off. This residue is boiled with a little water and filtered; the filtrate gives the biuret reaction if albumose is present. The centrifuge may be dispensed with, if the quantity of albumose is considerable, and the following method employed. After boiling some of the albumose adheres to the wall of the tube. The liquid is to be poured out and the adherent residue washed with alcohol to which a little chloroform is to be added if there is presumably much urobilin. The biuret test is to be applied to the filtrate from the residue dissolved in water. The presence of urobilin in the alcoholic extract is shown by a fluorescence when a few drops of a solution of zinc chloride are added. Hæmatoporphyrin may simulate albumose by causing a red color when the alkali of the biuret test is used. Its presence is to be suspected if the alcoholic extract is red and proven by the spectroscope. If, therefore, the alcoholic extract is red the urine should first be treated with barium chloride, which precipitates hæmatoporphyrin.

Maixner,<sup>3</sup> von Jaksch,<sup>4</sup> and Pacanowski<sup>5</sup> examined hundreds of cases of various diseases by Hofmeister's method, and came practically to the same conclusion, that albumosuria was oftenest found in suppurative processes associated with the retention and disintegration of pus,

<sup>1</sup> Loc. cit.

<sup>2</sup> Deutsche med. Wochenschrift, 1898, Band xxiv. S. 17.

<sup>3</sup> Vrtljschr. f. d. prakt. Heilk. Prag., 1879, Band cxlv. S. 75; Ztschr. f. klin. Med., 1881, Band viii. S. 234.

<sup>4</sup> Zeltschr. f. klin. Med., 1883, Band vi. S. 413.

<sup>5</sup> Ibid., 1885, Band ix. S. 429.

in acute infectious diseases, and in affections with more or less extensive destruction of tissues. Köppen<sup>1</sup> observed it in a number of insane persons, especially those who were maniacal or delirious. W. Robitschek,<sup>2</sup> Senator,<sup>3</sup> and Leick,<sup>4</sup> using Salkowski's method, arrived at a similar result. The albumosuria was relatively constant in deep-seated suppuration and in acute fibrinous pneumonia, especially during resolution.

Gerhardt's claim that ordinary or "latent" albuminuria occurred in persistent or frequent elevations of temperature above 104° F., and the statement of Krehl and Matthes<sup>5</sup> that albumosuria was almost constant in fever, are subject to a different interpretation in the light of Salkowski's discovery concerning the reaction of urobilin.

Albumosuria has been found in various chronic affections, as well as in those of an acute nature. Among these chief importance is to be attached to the albumosuria of osteomalacia or of affections regarded as of this nature.

Such cases have been reported by Bence Jones,<sup>6</sup> Kühne,<sup>7</sup> Kahler,<sup>8</sup> Stokvis and Ribbiak, Matthes,<sup>9</sup> Huppert,<sup>10</sup> and Rosin.<sup>11</sup> According to Kahler, these are not examples of true osteomalacia, but of myelogenous tumors, sarcoma, lymphoma, myeloma, especially of the bones of the thorax. Matthes,<sup>12</sup> in four cases of osteomalacia which probably were of multiple myeloma, isolated from the urine a substance with the characteristics of albumose, but which, when digested for some time, gave rise to a ferrated auclein. Hence the substance was regarded as a nucleo-albuminose arising from the ferrated nucleo-albumin of bone-marrow discovered by Nasse. It was not found in typical puerperal osteomalacia.

Raschkes,<sup>13</sup> on the contrary, states that albumosuria occurs in senile osteomalacia, and Hammer<sup>14</sup> and Marckwald<sup>15</sup> make no mention of the importance of albumosuria in their analyses of the reported cases of multiple sarcoma or of allied affections of the bones.

In most of the diseases in which albumosuria has been found the albumose has been observed, as a rule, for a short time and in small quantity, although in rare instances for a long time and in large quantities. Pacanowski,<sup>16</sup> indeed, subdivided the condition into acute and

<sup>1</sup> Arch. f. Psychiat., 1888-1889, Band xx. S. 825.

<sup>2</sup> Zeitschr. f. klin. Med., 1884, Band xxiv. S. 556.

<sup>3</sup> Deutsche med. Wochenschrift, 1895, Band xxi. S. 217.

<sup>4</sup> Deutsches Archiv f. klin. Med., 1895, Band lvi. S. 501.

<sup>5</sup> Loc. cit.

<sup>6</sup> Prag. med. Wochenschrift, 1889, Band xiv. S. 35.

<sup>7</sup> Verhand. d. Cong. f. innere Med., 1896, Band xiv. S. 476.

<sup>8</sup> Zeitschr. f. physiol. Chem., 1896-97, Band xxii. S. 500.

<sup>9</sup> Berlin. klin. Wochenschrift, 1897, Band xxxiv. S. 48.

<sup>10</sup> Prag. med. Wochenschrift, 1894, Band xix. S. 642.

<sup>11</sup> Archiv f. path. Anat., etc., 1894, Band cxxxvii. S. 280.

<sup>12</sup> Ibid., 1895, Band cxli. S. 128.

<sup>13</sup> Loc. cit.

<sup>14</sup> Loc. cit.

<sup>15</sup> Loc. cit.

<sup>16</sup> Loc. cit.

chronic albumosurin. But his distinction applied solely to the occurrence of the symptoms in acute and in chronic affections. A more practical division is into transitory and persistent albumosuria. Transitory albumosurin is to be found, despite the faulty methods and the opportunities of error, in such a variety of diseases as to have proven of but little practical value except in the diagnosis of acute pneumonia, deep-seated suppuration, including meningitis, and of macerated fœtus. In all of these conditions the ordinary means of diagnosis are usually sufficient, and the leucocyte count affords a most satisfactory aid, and is an efficient substitute for the search for albumose.

Greater value is to be attached to the recognition of persistent albumosuria, the importance of which in practice has become especially suggested of late years in connection with the diagnosis of multiple but latent tumors of the trunk. Such an albumosuria is sometimes nearly a pure form, and is spoken of as primary or typical, better, perhaps, as persistent or excessive. This variety thus far has been observed principally in multiple bone tumors and in myxœdema, and in but few cases of these affections. These observations, however, are so suggestive as to demand general attention.

It has been my fortune in the past two years to have seen two cases of persistent and excessive albumosuria, so generally recognized as an exceedingly rare condition. The first case serves to introduce this communication; the second, now in charge of my colleague, Dr. F. C. Shattuck, to illustrate it. In the latter the presence of albumosuria, and its extreme degree, led to the probable diagnosis of multiple tumors of the bones, and the use of the Röntgen rays showed such changes in the structure of the bones as confirmed this opinion.

The source of the albumose in these cases may prove to be in the bone-marrow, as suspected by Virchow, but chemical analyses to determine this point have yet to be made. It is important also that the subcutaneous tissues in myxœdema should be examined chemically for albumose, since the nature of the infiltrating substance in this disease is still a matter of conjecture, and the presence of albumose in the urine of the two cases suggests a possibility requiring disproof, even if the search give no other information.

Whatever the value of albumosuria may be in diagnosis, its persistent and excessive presence is apparently a sign of grave prognosis, since the cases in which this condition has been found have, almost without exception, proven fatal.