PAROXYSMAL HÆMOGLOBINURIA: DESCRIPTION OF A CASE AND OF OBSERVATIONS BEARING UPON THE CAUSATION OF THE HÆMOGLOBINURIA.

By Thomas R. Fraser, M.D., F.R.S., Professor of Materia Medica and of Clinical Medicine in the University of Edinburgh.

The existence of haemoglobin in the urine, unassociated with red corpuscles, entire or disintegrated, was not recognised until 1854, but since that time many cases have been recorded. A consideration of these cases has led to their subdivision into three groups. In one of these groups the hæmoglobinuria is a mere symptom or accident of some more general disease, such as scurvy, purpura, scarlet fever, typhus and other zymotic fevers, septicemia and malaria; the group being accordingly termed the Symptomatic Group. In the second group, the Toxic, the hæmoglobinuria occurs as a result of the absorption of a recognised poison, and it is known to be produced by arsenetted hydrogen, chlorate of potash, pyrogallic acid, and certain snake venoms. In the third group, it occurs without any such recognised concomitants or causes, and then becomes Essential Hæmoglobinuria; or, because it is associated with other well-marked symptoms, Paroxysmal Hæmoglobinuria; or, because of its intermitting character, Intermittent or Periodical Hæmoglobinuria; or, again, because exposure to cold is a usual antecedent to the paroxysm, Hæmoglobinuria a frigore, or Winter Hæmoglobinuria.

While the production of hæmoglobinuria appears to be satisfactorily explained in the first and second groups, and admits, indeed, from the etiological standpoint, of both being equally placed in the one group of Toxic Hæmoglobinuria, it is much more difficult to account for the phenomena of the third group. The designation Paroxysmal, as it merely implies that a group of
symptoms, one of which is the appearance of hemoglobin in the urine, together constitutes a paroxysm, in no way indicates the productive cause; nor is this revealed by the terms Essential and Intermittent or Periodical. The other two designations of this group imply that the hemoglobinuria, and no doubt also the other phenomena of the paroxysm, may be produced by exposure to cold. Little consideration, however, is required to show that this exposure cannot in itself be a cause of hemoglobinuria; but that, at the most, it is effective only because of pre-existing abnormalities, or is merely the starting-point of subsequent changes leading to the effective cause. This, indeed, is so obvious that other explanations have been adopted, in which the essential cause has been assumed to be a transitory congestion of renal capillaries, or abnormal sensitiveness to cold on the part of certain of the red blood corpuscles, whose condition has therefore been described as one of undue fragility or vulnerability.

Since Dressier, in 1854, directed attention to the main phenomena of the most remarkable of the forms of hemoglobinuria, the Paroxysmal, cases have been recorded by George Harley, Gull, Murchison, Pavy, Roberts, and Warburton Begbie, in this country; by Kobert, Kuessner, and Lichttheim, in Germany; by Murri, in Italy; and by Clément, Lépine, and Mesnet, in France; and many other physicians have since published full descriptions of cases.1

No useful purpose, therefore, would be served by the mere recording of an additional case, unless in connection with it facts could be made known which might assist in the solution of the mystery, still unsolved, of the cause of this affection. It is with this object that the following case and the observations made in connection with it are described.

J. M., æt. 42, came under my care in June 1895, with the statement that he suffered from general weakness, and from occasional attacks of sickness, pain in the legs and shivering, followed by the voiding of "black" urine.

The following further information was obtained:—His parents are alive and in good health. He is the eldest of three brothers, who are alive and healthy; and of his five sisters, one died of scarlet fever, and another of phthisis when 21 years of age. His occupation is that of a draper, which he has followed in Glasgow until 1887, and subsequently, during the five years from 1887 to 1892, in Ontario, Chicago, and other parts of the Lake District of North America. He then returned to this country, and has been employed as a collector of rents, but only irregularly, as the state of his health has often prevented him from doing any work. His food has been abundant and of good quality, and his surroundings have been favourable, except that at times he

1 For synoptical references to the literature of hemoglobinuria, see the papers of J. Wickham Legg, St. Barth. Hosp. Rep., London, 1874, vol. x. p. 71; Mesnet, Arch. gén. de med., Paris, May 1881, p. 513; and F. Chvostek, "Ueber das Wesen der Paroxysmalen Hämoglobinurie," Leipzig und Wien, 1894.
experienced much cold when in America. He has always been moderate in the use of alcoholic beverages. Until he went to America, his health has been good. He has never suffered from any pulmonary affection, or from ague, fever, or syphilis; and the latter exemption is confirmed by his statement that his wife has not had any miscarriages, and that he has had four healthy children. For many years, dating previously to his residence in America, he has suffered frequently from bilious attacks, accompanied with pain in the epigastrium, muscae volitantes, and nausea, but not with vomiting; and during them, the skin often became slightly jaundiced. He does not think that these attacks have now any special relationship to the hemoglobinuric paroxysms.

The illness from which he at present suffers originated suddenly, in November 1889, while he was in America. On a very cold afternoon, the ground being covered with snow, he was driving in a sleigh a short distance from Ontario, and while his companion transacted business in several houses, he remained in the sleigh exposed to cold. Although warmly clad, after being out for about two hours, he felt very cold, his hands, feet, and even his tongue became “numbed,” nausea was experienced, pains occurred in the extremities and back, and, as he began to shiver violently, he drove home. On arrival at his house, he tried to regain warmth by sitting close to a stove and drinking hot gruel, but without success; he therefore found it necessary to go to bed, where he covered himself with extra bedclothes. The pain soon disappeared, profuse sweating followed, and he became unduly hot. On now emptying his bladder, he found that his urine was “very deep red, nearly black in colour.” A little pain was experienced in the urethra during the voiding of this dark urine. Some little time afterwards, the sweating and feeling of general heat ceased, and he noticed that the urine afterwards passed had no unusual appearance. He remained in bed for two days, and then returned to work, feeling well but rather weak.

A similar paroxism occurred seven days afterwards, which also followed exposure to cold; and from this time until he came under observation—six years—he has had numerous other paroxysms, which usually came on an hour or two hours after exposure to cold, and especially when the weather was foggy. He volunteered the statements that an attack has almost never occurred during the night; that he is able to prevent attacks, even in the most inclement weather, by remaining in bed all day; and that they are now induced by slighter exposures than were formerly required.

According to the patient’s description, a typical attack of moderate severity may be divided into three stages of nearly equal duration. After exposure to cold, the first stage is ushered in by slight pains in the soles of the feet, and by involuntary yawns and stretching movements of the body. At nearly the same time, a feeling of sickness is experienced, which, though very distressing, never leads to vomiting or even retching. The appetite fails, but great thirst is experienced, which he generally slakes by drinking hot or cold water or tea. With these symptoms, there are severe pains in both arms and legs, passing from the latter
upwards to the trunk; the fingers and toes become cold and livid, and the nose icy cold. A dull pain in the lumbar region, from which he has nearly constantly suffered since the first paroxysm, now becomes severe and assumes a sharp and throbbing character. The tongue feels numbed, and the sensibility of the limbs is blunted, but sight and hearing remain unaffected. He also feels cold all over the body. In the second stage, all of these symptoms are present, but in addition there is shivering. During these two stages the patient can only with difficulty make water, which is generally clear and light in colour in the first stage, but dark in the second. The feeling of coldness causes him to go to bed or to attempt to obtain warmth from a stove or open fire. The third stage commences with abrupt changes in the previous symptoms. The sense of coldness gives place to one of warmth, which sometimes becomes an oppressive hotness; the thirst and pain in the limbs disappear, and profuse perspiration occurs; and the severe lumbar pain ceases, but a diffuse pain is now felt in the hypogastric region, which the patient attributes to distension of the bladder. He now freely passes dark crimson urine in large quantities. When the feeling of hotness or feverishness passes away, he feels nearly well, though weak, and the urine subsequently voided is of a light and normal colour.

The attacks differ much in duration, for they may last only one hour, or so long as six or seven hours. In the milder attacks, the second stage is not well defined, as there may be no marked shivering. In every attack, however, there is a sense of great coldness followed by a sense of warmth, a dry skin succeeded by sweating and nausea, and pains in the legs and back followed by the voiding of "black" urine. While in America, and also since, he was treated with quinine in large doses, but without benefit.

On his return to this country, in the summer of 1892, he had several relatively mild paroxysms, but in the following winter they occurred more frequently and were more severe. In the following summer and winter they recurred with much the same variations; until in the summer of 1895, while he was occupied as a steward on board a passenger steamer running between Glasgow and New York, the attacks recurred three and sometimes four times a week, and compelled him to give up all work. He was treated in Glasgow Infirmary on three occasions, in 1895, but without much benefit, the paroxysms continuing to follow any exposure to cold. In June of that year, he was admitted into the Royal Infirmary of Edinburgh.

State on admission.—The patient is a well-developed man, 5 ft. 8½ in. in height, and 10 st. 11 lbs. in weight, his weight before the first paroxysm having been 13 st. 11 lbs. The surface temperature is subnormal, from 97° to 97°5 F., and the skin is soft and slightly moist. As has been stated, he suffers a little from indigestion, and during the last five or six years, usually three times in each week, he has noticed that he has been
slightly jaundiced during the morning and forenoon. The tongue is
tremulous, there is no undue thirst except during paroxysms, the appetite
is good, but after food he is occasionally slightly sick and troubled with
heartburn. The bowels are rather constipated. The spleen is not
enlarged, and the other abdominal contents are healthy, except that the
liver is slightly and uniformly enlarged, measuring 6\(\frac{1}{2}\) in. in the mam-
mary line. There is no evidence of respiratory disorder; the thorax is
well developed, the expansion good and symmetrical, and physical
examination does not reveal any evidence of disease. The only sub-
jective symptoms in connection with the circulation are slight dyspnoea
and palpitation on exertion. The præcordia, however, bulges slightly,
and there is visible pulsation, synchronous with the apex beat, in the
episternal fossa, and this pulsation extends in the direction of the sub-
clavian artery. The apex beat is diffuse, and may be felt two inches below
and half an inch to the right of the nipple in the fifth interspace, the
maximum impact occurring one inch below and half an inch to the right
of the nipple. The area of cardiac dulness is enlarged, especially in the
vertical direction, the upper border being found by percussion in the
third interspace, and the left border about one inch to the left of the
second interspace, the right border one inch to the right of the sternum in
the mammary line, at the level of the fifth rib. The heart's sounds, how-
ever, are healthy, excepting that the second sound is accentuated in the
aortic and pulmonary areas. The pulse is slow, being often 52 in the
minute, and it occasionally shows a slight irregularity. The arterial
expansion is of considerable size and well sustained, and the walls of
the artery are not thickened. There are no glandular enlargements.
The blood contains 4,000,000 of red cells, and 80 per cent. of
hæmoglobin.

Since the occurrence of the first hæmoglobinuric paroxysm, a nearly
constant sensation of dull and deep-seated, but not severe, pain has been
felt in the back over the kidneys, which, however, becomes more painful
during paroxysms. Micturition is normal. The amount of urine is
about 40 oz. in the twenty-four hours; the specific gravity varies from
1014 to 1020; the urine is acid, straw-coloured, and faintly cloudy,
and it deposits a slight mucous sediment, but it does not contain albumin,
sugar, bile pigments, or excess of phosphates. These healthy charac-
teristics are, however, greatly modified when a paroxysm occurs, as will
afterwards be stated. There are no symptoms of disease of the nervous
system; sensibility, motility, the reflexes, cerebration, and the special
senses being entirely normal; nor is there any evidence of vasomotor
or trophic disturbance. On the admission of the patient, therefore, his
condition was apparently that of good health. Soon afterwards, however,
we had ample and frequent opportunities of confirming the history of the
remarkable symptoms of illness from which he had so frequently
suffered during the last six years.

Two days after his admission into the hospital, on the 8th of June,
he took a cold bath at 9 a.m. Immediately after getting out of the
bath, he felt sick and giddy, and at once went to bed. The giddiness
disappeared, but shivering set in at 10 a.m.; his fingers and feet became
cold and blanched, and the nails blue; thirst was experienced, while
the pain in the back became more severe. Shivering ceased at 10.40 a.m.,
and the patient soon afterwards felt warm. At 1 p.m. sweating began, and soon became profuse, and continued until 5 p.m., when the patient again felt quite well, although weak. His temperature, which soon after the bath was 97°-4 F., rose to 101°-4 F. at 1 p.m., and then fell, until at 2 p.m. it was 99°-4, at 3 p.m. 98°-2, and at 4 p.m. 97°-6. During this time the pulse-rate varied from 60 to 70 per minute. Urine passed at twelve o'clock was port-wine in colour, and acid in reaction, and it deposited a considerable reddish sediment, in which no blood corpuscles or crystalline matter could be found, but only amorphous urates, aggregations of yellow granules, with here and there a doubtful tube cast. On chemical examination, haemoglobin and albumin were found to be abundantly present. Urine passed at 1.30 p.m. was of a Madeira-wine colour, and slightly hazy, and a small mucous-like sediment was deposited, in which only amorphous urates and a few granule groups were found; and this urine also gave, with ordinary tests, evidence of the presence of haemoglobin and of a small quantity of albumin. Urine passed at 4.20 p.m. was of a pale straw colour, and free from albumin and haemoglobin; and these substances were absent also from the urine passed during the next twenty-four hours, and indeed until the second paroxysm that occurred after his admission.

This was induced on the 17th of June, by the patient exposing himself, at 6 p.m., to the open air in an outside balcony attached to the ward. Although the evening was a warm one, and although he stayed in the balcony for only five minutes, nausea and shivering set in within ten minutes after his return to the ward, and were succeeded by the same symptoms as those which occurred on the 8th of June, including the passage of urine containing haemoglobin and albumin. This paroxysm lasted until 12.45 A.M., or about six and a half hours. On the 28th of June, another paroxysm, having essentially the same characteristics, was again unintentionally induced.

On the 14th of July the patient returned to Glasgow, but he re-entered the Edinburgh Infirmary on the 8th of August 1895. While in Glasgow he had experienced seven paroxysms, all of which had followed and had apparently been induced by relatively slight exposures during rainy weather. After this second admission to the Edinburgh Royal Infirmary, he took special care to avoid exposing himself to cold. Still, on the 25th of August, while in the ward, an incomplete paroxysm was accidentally produced, in which he suffered only from symptoms characterising the earlier stages of a complete paroxysm, such as pain in the feet and legs and nausea, which continued for about an hour, but did not proceed so far as shivering and haemoglobinuria.

On the 1st of September, a second paroxysm, not however so incomplete, followed a slight exposure to cold in the ward, at 7.30 A.M. At 8 A.M., pain occurred in the feet, and was soon followed by nausea. No definite shivering occurred, although at 9.30 A.M. he perspired slightly and continued to do so for nearly three hours, before which time the temperature had risen to 101°-4 F. All these symptoms disappeared abruptly at 12.15 P.M.,
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and were not followed by the sense of exhaustion which was generally experienced. Urine passed during this mild paroxysm was, however, of a Madeira-wine colour, and contained hæmoglobin.

The patient left the Infirmary on the 15th of September 1895, but, before he did so, several paroxysms were purposely induced, in which attempts were made to determine on which of the several changes from the normal, characterising a paroxysm, the hæmoglobinuria was dependent. Further reference will be made to these attempts in a subsequent part of the paper.

The patient was readmitted to the Infirmary for the third time on the 2nd of October, and remained until the 22nd of November 1895. As on this occasion, also, care was taken to prevent cold, only a few paroxysms occurred. The patient, indeed, was for the most part confined to bed, and the only four paroxysms which he had followed the slight exposure resulting from his getting out of bed for a short time in the early morning. Each of them was incomplete and of short duration, but in each hæmoglobin appeared in the urine. Thus, on the 7th of October, after being up for half an hour, he felt sick, and at 6.30 A.M. the fingers and toes were cold but not blue. At 7.30 these symptoms had entirely disappeared, and yet urine voided at 8.30 A.M.—the first urine voided in the paroxysm—was of a dark red colour, hazy, neutral in reaction, with a specific gravity of 1021, and it gave a marked hæmoglobin reaction with the guaiac and ozonic ether test. Microscopic examination of the sediment showed small pigment masses, yellow granules, bladder cells, and spermatozoa, but no crystals, red or white blood corpuscles, or tube casts.

The general health of the patient improved, and he gained 5 lbs. in weight. Considering himself able to resume work, he returned to Glasgow. The history of the former years, however, repeated itself, exposures to cold were invariably followed by hæmoglobinuric paroxysms, and he was thereby prevented from following any occupation. He accordingly returned to the Edinburgh Infirmary on the 6th of January 1897. His general physical condition was not found to be obviously deteriorated. The weight was 11 stones 4 lbs.; the small pulsatile tumour, above and immediately external to the right sterno-clavicular articulation, was still present; the pulse was of fair tension, but continued to exhibit an occasional irregularity; and the heart, lungs, and other organs were healthy, and there was no obvious anaemia. An examination of the blood, made on the 8th of January 1897, gave the following results:

| Blood Parameter       | Value       |
|-----------------------|-------------|
| Red corpuscles        | 3,700,000   |
| White corpuscles      | 40,000      |
| Hæmoglobin            | 44%         |
| Blood plates          | 640,000     |
| Specific gravity      | 1054        |
The red corpuscles were well shaped and uniform in size, and they grouped themselves into normal rouleaux.

With the patient's willing acquiescence, several paroxysms were purposely induced, during the several times in which he was in hospital, in order that the phenomena might be more fully observed. So long as the exciting cause was the same, the resulting symptoms were found to repeat themselves with remarkable exactitude. The exciting cause usually selected was the contact for a defined period of time of a defined area of the skin with cold water of known temperature. Before the contact with cold water was made, the normal condition of the patient was recorded, especially in regard to the body temperature, pulse and respiration, and to the composition and characteristics of the urine and blood; and, after cold had been applied, frequent records were made of the changes that occurred. In each of these observations it was necessary to secure the co-operation of several observers. The recording of the general symptoms and the taking of sphygmographic tracings were entrusted to the resident physicians on duty at the time when a paroxysm was induced, who, in succession, were Drs. Briggs, Bowes, and Bannerman. The examination of the urine was undertaken by Mr. Ballantyne, and that of the blood by Mr. Bashford, occasionally assisted by Mr. Cooper and Mr. Murray, each of whom, as clinical clerks, had already had much experience in the special work that was undertaken. As the greater number of the detailed observations were made during the fourth period of the patient's residence in the Royal Infirmary—from 6th January to 14th April 1897—the larger share of the work fell upon Dr. Bannerman, and Messrs. Ballantyne and Bashford, and much credit is due to them for the accuracy with which they performed the special duties entrusted to them.

**OBSERVATIONS SHOWING THE EFFECTS OF COLD ONLY.**

Observation 1.—In the following Observation, made on the 16th of January 1897, the patient's legs, from the feet to the tubercle of each tibia, were immersed for a period of ten minutes in water of the temperature of 45° F. On the 14th and 15th of January the patient had been kept in bed, and the axillary temperature, pulse, and respiration-rate had been recorded every two hours until the immersion in cold water was made on the forenoon of the 16th. The urine of each twenty-four hours was, as a matter of routine, collected and examined during the whole time that the patient was in the Infirmary. On the morning of the 16th, immediately before the patient's legs were immersed in cold water, between 9.30 and 10.15 a.m., a pulse tracing was taken (Fig. 1), and the blood was examined.

![Fig. 1.](image_url)

*Fig. 1.*—16th January 1897, 9.50 a.m.—
Pulse 66, resp. 20 per minute.
10.30 A.M.—The patient's legs were immersed in water of 45° F., for a period of ten minutes. Towards the end of the immersion he complained of a sick feeling, the pulse-rate had risen from the previous rate of 66 per minute to 120 per minute, the pulse was of low tension, and the temperature had fallen to 97° F. (see Fig. 1a). At the end of the ten
minutes he returned to bed shivering all over the body, and soon the pulse-rate became slower, and the tension higher.

10.45 a.m.—The pulse is of high tension, and of the rate of 66 per minute (Fig. 2). The patient voided 6 drms. of urine, which, on examination, was found not to contain haemoglobin, or any other abnormal constituent (see Table of Urine Examinations No. 1).

10.50 a.m.—The patient feels less nauseated and altogether better.

10.52 a.m.—Pulse is of high tension, and at the rate of 48 per minute (Fig 3), and the shivering or general tremors are less.

11 a.m.—The patient feels the hands and feet cold, and the teeth are chattering.

11.6 a.m.—The whole body is shaking, and more sickness and chilliness are felt.

11.10 a.m.—Blood was taken for examination; half a drm. of urine voided with some difficulty, and is of a claret-red colour, and contains haemoglobin and albumin.

11.19 a.m.—The fingers are white, waxy-looking, and slightly blue at the nails. The shivering movements have become coarse.

11.33 a.m.—Cold felt all over the body. Patient has much shivering, and feels sick.

11.35 a.m.—Stretching movements, the whole body being at the same time continuously shaking. Pulse 80 per minute, and of high tension (Fig. 4). Respirations 24 per minute, laboured and noisy.

11.38 a.m.—The patient is very cold all over the body, shaking is very marked. 1½ drms. of very dark red urine passed easily, in which both haemoglobin and albumin were found to be present.

11.41 a.m.—Shivering is not continuous; it intermits for five to ten seconds, and then occurs for twenty or thirty seconds. Each attack of shivering begins rather gradually in the body and extremities, and becomes more severe until all parts of the body are shaking, and then declines, tremors of the lower jaw marking the termination. During a shivering attack, the patient stretches himself, raises the body on his arms, and is restless, with the eyebrows contracted.

11.45 a.m.—Again feels sick. There is slight dull pain in the back, legs, and feet; intermittencies in the shivering are more irregular; the respirations are 30 per minute, irregular and laboured; and the axillary temperature is 97°6 F.

11.49 a.m.—There is numbness of the hands, which feel cold, and the patient is restless and irritable.
11.52 a.m.—He feels rather better, respiration is 26 per minute.
11.55 a.m.—He is thirsty, and drank a tumblerful of cold water.
12 Noon.—The temperature is 100°6 F.; the respirations are 26, and the pulse-rate 66 per minute, and of high tension (Fig. 5). Patient is still shivering.

12.10 p.m.—The shivering has almost ceased, and the nausea is much less; still he describes a sick feeling, which extends from the stomach to the throat. Pain continues in the back and legs, and the latter feel tired. The patient is less restless.

12.15 p.m.—While the shivering has ceased, the patient still feels cold. Pulse 66, respiration 20 per minute; 1 oz. of very dark urine passed, containing much hæmoglobin and albumin.

12.20 p.m.—Patient is again thirsty, and drank a tumblerful of cold water. The hands are not so white, and the patient feels less cold.

12.25 p.m.—The pain in the back and legs has become less severe, very slight shiverings occur every few minutes, nausea is still marked.

12.30 p.m.—Patient feels slightly warmer, and the axillary temperature is 101° F. There is no shivering, the pain in the back and legs remains much the same as five minutes ago.

12.35 p.m.—Shivering has recurred in the arms; the hands and other parts of the body feel cold; and nausea and tired sensations are again experienced. The pulse is still of high tension, and its rate is 62 per minute (Fig. 6).

12.40 p.m.—Shivering has ceased, but the feeling of nausea is very distressing.

12.45 p.m.—Still experiences pain in the back and legs, feels warmer, axillary temperature 101° F.

12.50 p.m.—Is again thirsty, and drank a third tumblerful of cold water. Nausea remains in a distressing form; 1 oz. of dark red urine passed (see Urine Table No. I.), containing much less hæmoglobin and albumin than the urine of 12.15 p.m.

12.55 p.m.—Condition as to nausea and pain is unchanged, patient feels warmer.

1 p.m.—Nausea and pain as much as before. The feet and hands are still cold; temperature 101°8 F.; respirations 28 per minute; pulse 72 per minute, and of lower tension.

1.5 p.m.—The feet, hands, and nose feel warm; again drank a tumblerful of water.

1.10 p.m.—While the pains remain as before, the nausea is lessened, and the pulse tension is still lower (Fig. 7).
1.15 p.m.—6 drms. of dark urine passed, containing less haemoglobin and albumin than the urine of 12.50 p.m.

1.25 p.m.—There is only slight nausea, and the pains are less severe. Patient feels warm, and the skin of the trunk is slightly moist.

1.30 p.m.—Patient feels more comfortable. Pulse tension is low, axillary temperature 100°-3 F., and the respirations 26 in the minute.

1.35 and 1.40 p.m.—Nausea is again distressing.

1.45 p.m.—Nausea is less, pains are only slight, and there is now obvious sweating over the body. 14 drms. of clear red urine passed, containing less haemoglobin and albumin than the urine of 1.15 p.m.

2 p.m.—Pains have almost disappeared, but nausea is still present. Sensations are felt as of waves of heat and cold passing over the body. Temperature is 101° F., and the pulse of low tension, and at the rate of 76 per minute (Fig. 8).

2.15 p.m.—Patient feels hot all over. There is no pain, and but little nausea. The patient was able to take some chicken and pudding for dinner. 12 drms. of clear red urine passed, containing less haemoglobin and albumin than the urine of 1.45 p.m.

2.30 p.m.—Temperature 101° F., pulse 68 per minute, and of higher tension (Fig. 9).

3 p.m. (4½ hours after immersion of the legs).—The sensation of nausea has almost entirely disappeared, but patient feels weak, with a tired sensation in the legs, and there is slight perspiration.

3.15 p.m.—13 drms. of clear red urine passed, containing less haemoglobin and albumin than the urine of 2.15 p.m.

3.30 p.m.—The nausea has finally disappeared; free perspiration continues, the forehead being covered with beads of sweat; the pulse-rate is 70 per minute, with a moderately high tension (Fig. 10); and the temperature has fallen to 99°-8 F.

4 p.m.—5 oz. of clear light red urine passed, containing less haemoglobin and albumin than the urine of 3.15 p.m.

4.50, 5.20, and 5.50 p.m.—Pulse tracings were taken which showed a reduction of tension, gradually proceeding until it had become decidedly low (Figs. 11, 12, and 13).

5.55 p.m.—2½ oz. of clear straw-coloured urine passed, in which only traces of haemoglobin and albumin could be found.

6 p.m.—The low tension of the pulse is being recovered from, until at 7 p.m. it had become nearly normal.
7 p.m.—6½ oz. of clear straw-coloured urine passed, containing a mere trace of haemoglobin and albumin.

8 p.m.—The only symptom is exhaustion; the pulse-rate is 60 per minute, and the tension good; and perspiration has ceased (Fig. 14).

8.15 p.m.—7 oz. of clear urine of a pale straw colour passed, still containing traces of haemoglobin and albumin.

10 p.m.—The patient is free from all symptoms, but still feels tired, and this tired feeling remained until the following day.

On the 17th of January the urine was entirely free from haemoglobin and albumin, the temperature was subnormal, and the pulse was at the rate of 86 per minute, with a somewhat low tension.

Urine.—The chief facts connected with the urine are recorded in the annexed table (see Urine Table No. 1), and several of them have already been stated in the protocol of this paroxysm. The presence of haemoglobin was detected not only by the guaiac and ozonio-ether test, but also by spectroscopic examinations, which were made for me by so skilled an observer as Dr. Milroy, one of the Assistants in the Physiological Department of the University. The claret-red urine passed at 11.10 A.M., and also the very dark port-wine coloured urine passed at 12.15 P.M., contained only oxyhaemoglobin and no methaemoglobin. The double bands between D and E, with one band touching D, were displayed; sulphide of ammonium and Stokes’ solution added to the urine gave the band of reduced haemoglobin; but no other bands appeared in the spectroscopic field. In the sixteen hours between 10 A.M. on the 16th of January and 2 A.M. on the 17th of January, 62 oz. of urine were passed. Assuming that the excretion of urine was continued at the same rate during the remaining eight hours, this would give a total amount of 90 oz. of urine for the twenty-four hours of the day in which the haemoglobinuric paroxysm was induced. On the following day, 60 oz. of urine were passed, containing 480 grs. of urea.

Blood.—The blood was examined in regard to the characters of its formed constituents in an ordinary field, the specific gravity was
Urine Table No. 1.—Paroxysm of 16th January 1897.

| Date       | Quantity of Urine | Characters of Urine | Characters of Deposit | Reaction | Sp. Gr | Urea | Albumin | Glucose | Blood | Bile Pigments | Quantity of Haemoglobin |
|------------|-------------------|---------------------|-----------------------|----------|--------|------|---------|---------|-------|---------------|-------------------------|
| Total urine from 10 A.M. 15th Jan. to 10 A.M. 16th Jan. | 70 oz. | Amber, turbid. | White, flaky mucus. Microsc.—Round, granular cells. | Acid. | 1018 | Grs. p. oz. 8 (560 grs. in 24 hours) | Absent. | Absent. | Absent. | Absent. |
| 16th Jan.—10.50 A.M. | 6 drms. | Straw, cloudy. | Scanty, white. Microsc.—Round, granular cells. | " | 1016 | 6 | " | " | " | " | " |
| 11.10 , | 1½ drms. | Red (claret-coloured), cloudy. | Microsc.—Many round cells, epithelial cells, squames, and filaments. | " | ... | Present, large amount. | " | Present. | " | Present. |
| 11.38 , | 1½ drms. | Very dark red (port colour). | Moderate in amount, reddish black. Microsc.—(1) Numerous dark elongated bodies without envelopes, containing blood pigment and leucocytes; (2) round cells, discrete and in groups; (3) epithelial cells from urinary tract. | " | ... | 7 | 17.5 | " | " | " | 11 per cent. |
| 12.15 p.m. | 1 oz. | Very dark red (port colour). | Dark, reddish black, and flocculent. Microsc.—1, 2, and 3, as at 11.38. | " | ... | 8 | 19.6875 | " | " | 2 | 12 |
| 12.49 , | 1 oz. | Dark red. | Do. do. | " | ... | 6 | 7.65625 | " | " | " | 3 |
| 1.15 , | 6 drms. | " | Do. do. | " | ... | 5.5 | 4.375 | " | " | " | 2 |
| Time  | Volume | Colour       | Description                                                                 | Micro. | Leucocytes | Cast | Other Observations |
|-------|--------|--------------|-----------------------------------------------------------------------------|--------|------------|------|-------------------|
| 1.45  | 14 drms. | Red, clear. | Red, partly flocculent, partly granular. Microsc.—1, 2, and 3, as at 11.38. | 4      | 3.28125    |      |                   |
| 2.15  | 12 drms. | Red, clear. | Light red, flocculent. Microsc.—1, 2, and 3, as at 11.38.                   | 4.5    | 2.1875     |      |                   |
| 3.15  | 13 drms. | Red, clear. | White, scanty. Microsc.—1, 2, and 3, as at 11.38.                           | 5      | 1.91775    |      |                   |
| 4     | 5 oz.   | Light red, clear. | Faint, white cloud. Microsc.—A few epithelial cells.             |        |            |      |                   |
| 4.50  | 9.5     | Light red, clear. | Do. do. Microsc.—A few epithelial cells.                           | 1004   | 4.5        | 1.09375 |                   |
| 5.55  | 11.5    | Straw colour, clear. | None. Microsc.—A few epithelial cells.                               | 1004   | 2.5        | 0.21875 | Present, small.   |
| 7     | 6.5     | Straw colour. | Abundant, flaky mucus. Microsc.—Round, granular cells.                  | 1011   | 7          |       | Present, small.   |
| 8.15  | 7       | Light straw. | Do. do. Microsc.—Leucocytes a few bodies like (1) at 11.38 A.M.            | 1007   | 3.5        | 0.109375 | Trace.           |
| 17th January | | Straw, clear. | Mucus. Microsc.—Leucocytes a few bodies like (1) at 11.38 A.M.            | 1010   | 4          |       | Doubtful trace    |

1 Spectrum of oxyhaemoglobin only; no evidence of methaemoglobin.

2 Do. Both specimens of urine (11.10 A.M. and 12.15 P.M.) showed the double band of oxyhaemoglobin (between D and E, with one band touching D); when reduced by ammonium sulphide or by Stokes' solution only the band of reduced haemoglobin appeared.
determined, and an estimation made of the haemoglobin and of the number of red and white corpuscles and blood plates. This was done immediately before the immersion in cold water; on four separate occasions during the paroxysm, namely, at 11.38 A.M., 12.15 P.M., 2.30 P.M., and 4.15 P.M.; and also at 11 A.M. on the following day. No material departures from health were observed, with the single exception that the blood plates were increased in number, and reached the maximum increase attained on the day of the observation, soon after the time when the urine contained the largest quantity of haemoglobin; but on the following day, at 11 A.M., the number of blood plates was greatly in excess of the largest number found during the paroxysm. No observable diminution occurred in the amount of haemoglobin.

**Temperature.**—The effect of the immersion in cold water upon the temperature was a very marked one. When the patient was in his usual state of health, the temperature was generally slightly subnormal, and its ordinary variations are fairly represented in the chart in which the temperature has been recorded every two hours during the day preceding the paroxysm of the 16th of January (see Temperature Chart, Fig. 1a). The immediate effect of the immersion was to lower the temperature. About twenty minutes after the immersion had been completed, the temperature began to rise rapidly, and the maximum escape of haemoglobin in the urine corresponded with the time when the temperature was highest. It is important, however, to observe that the urine passed at 11.10 A.M. already contained haemoglobin, although even at 11.30 A.M. the temperature was still below the normal, being only 97.6° F.

**Circulation.**—The rate of the pulse was not much modified. A comparison of the rate on the 15th with that on the 16th (see Temperature Chart, Fig. 1a) merely shows a slightly higher average on the latter date; but although the temperature rose to 101.8° F., the quickest pulse-rate was not more than 80 per minute. On the other hand, a very marked change was produced in the blood-tension. The effect of the immersion in cold water was quickly and strongly to raise the tension, and a high pulse tension accompanied the largest outflow of haemoglobin. The tension soon afterwards fell, but haemoglobin continued to be eliminated in the urine while the tension was much below the normal. The latter fact may, however, only imply that haemoglobin separated from the blood corpuscles during the state of high vascular tension continued to pass from the blood serum into the urine after the high tension had disappeared.

In the Observation next described the conditions were the same, excepting that, in order to obtain more definite information regarding the changes in the amount and chemical composition of the urine, the urine passed on the day before the Observation and on the day succeeding it was each collected in three separate portions, representing the urine of eight hours, and each of these portions was measured and separately examined with regard to its general characters, deposits, and chemical composition. Irrespective of this, however, the urines voided shortly before, during, and after the paroxysm were separately examined.

**Observation 2.**—On the morning of the 7th of February 1897 the patient’s legs were immersed for ten minutes to the level of the tubercles

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of the tibia, in cold water of 45° F. The axillary temperature was 97°.6 F. Immediately before immersion the pulse had assumed the unusual rate of 90 per minute, probably because of some excitement on the part of the patient, but the tension was low (Fig. 15). The immersion was begun at 10.30 A.M.; at 10.37 A.M. the pulse was slightly dicrotic, and its rate 116 per minute; at 10.38 it was distinctly dicrotic, and at the rate of 140 per minute; at 10.39 the tension was slightly higher and the rate 103, and the patient felt a choking sensation; at 10.40 the tension was somewhat high and the rate 90 per minute, and the patient now experienced a sensation of nausea, with pain in the lumbar region.

After immersion, the patient at once returned to bed, slight shivering commenced, and there was some arching of the back (Fig. 16). 10.50 A.M.—Another pulse tracing was taken, showing much increase of blood tension (Fig. 17); and two minutes afterwards 5½ oz. of slightly cloudy, pale, straw-coloured urine was passed, which did not contain either hemoglobin or albumin (see Urine Table No. 2).

1 In all the pulse tracings of this Observation, the paper was travelling at an unduly slow, but uniform, rate.
11.5 A.M.—The pulse is of high tension, and its rate 72 per minute (Fig. 18a).

11.15 A.M.—2½ drms. of dark port-wine coloured urine voided, containing both haemoglobin and albumin, and the temperature is only slightly above normal (see Temperature Chart, Fig. 18 on preceding page). The patient is also shivering a little. He feels his fingers cold, and they look blanched; the back is less arched, and there is pain in the lumbar region.

11.30 A.M.—Patient is shaking all over, feeling sick and disposed to vomit, and thirsty, and the fingers are waxy-looking, with the nails cyanosed.

11.40 A.M.—The general shaking is so violent that a pulse tracing could not be taken, but this was accomplished at 11.45 A.M., and showed that the tension was still high (Fig. 19), the rate being 74 per minute.

12 noon.—Shivering is much less, but pain in the back and coldness in the fingers are still present.

12.30 P.M.—The patient is in much the same state, but the shivering has ceased.

12.40 P.M.—15 drms. of very dark port-wine coloured urine passed, containing the maximum quantity of haemoglobin and albumin present in any sample of this paroxysm. The temperature has now attained its maximum of 102°-2 F.

1.30 P.M.—A pulse tracing showed that the pulse tension had become low (Fig. 20). The temperature is 101°-4 F.

1.45 P.M.—3½ oz. of cloudy, very dark, brownish-red urine voided, in which there is much albumin, but a smaller quantity of haemoglobin than in the urine of 12.40 P.M. On microscopic examination of the blood, well-formed rouleaux are seen, and the individual corpuscles appear to present no abnormal character.

2.30 P.M.—The skin has become moist, the temperature has fallen to 101° F. (see Temperature Chart, Fig. 18), and a pulse tracing shows the tension to be moderately low (Fig. 21).

3.15 P.M.—1½ oz. of dark, brownish-red urine passed, containing less haemoglobin and albumin than the urine of 1.45 P.M. (see Urine Table No. 2), and the temperature is 100°-5 F. (see Temperature Chart, Fig. 18).
3.30 p.m.—There is still pain in the back, and moderate sweating, and although the nausea has disappeared the patient feels no desire for food.

4.15 p.m.—The patient is sweating profusely and feeling tired, and the temperature is 100°-2 F.

4.45 p.m.—8½ oz. of cloudy, reddish-brown urine voided, containing only a very little haemoglobin and albumin. The pulse tension has now become higher (Fig. 22), and the pulse has nearly regained the characters it had possessed immediately before the legs had been immersed in water.

6.20 and 8 p.m.—Urine is again voided, now containing only traces of haemoglobin and albumin, and on the latter occasion being amber-coloured, with only a very faint reddish tinge. All other symptoms have disappeared, and only a tired feeling remains.

9.30 p.m.—The urine is straw-coloured and free from haemoglobin, but a very slight trace, almost doubtful, of albumin remained in it for twenty-four hours longer.

Urine.—The details of the examinations of the urine are stated in the annexed tables (Urine Tables Nos. 2 and 3). It will be observed that the first urine passed after the immersion had been commenced, that obtained at 10.52 a.m., or twelve minutes after the commencement of immersion, was free from haemoglobin and albumin. At this time the pulse was already of high tension (Fig. 17). The next urine was obtained twenty-three minutes afterwards, and it contained both haemoglobin and albumin. The largest quantities of these substances were present in the two subsequently voided urines—that passed at 12.50, or two hours and ten minutes, and at 1.45 p.m., or three hours and fifteen minutes, after the commencement of the immersion. The quantities then gradually fell until haemoglobin and albumin had practically disappeared at 9.30 p.m., or eleven hours after the commencement of the immersion. The albumin was chiefly in the form of serum albumin. This was inferred from an examination made of the very dark port-wine coloured urine of 12.40 p.m., in which serum albumin was abundant, along with a little albumose, but without peptone or free globulin. The total quantity of urine passed from 10 a.m. on the 6th of February, the day preceding the paroxysm, to 10 a.m. on the 7th, was 70 oz.; from 10 a.m. on the 7th (day of the paroxysm) to 10 a.m. on the 8th, it was 98½ oz.; and from 10 a.m. on the 8th (day following paroxysm) until 10 a.m. on the 9th, it was 54½ oz. (see Urine Table No. 3). This appears to show that a paroxysm does not hinder the elimination of urine, in so far as its total bulk in the twenty-four hours is concerned. A comparison of the figures recording the elimination of urine during the eight hours of the paroxysm (10 a.m. to 6 p.m.), and during the eight hours immediately following it (6 p.m. to 2 a.m.), shows, however, that while in the former period there is only a moderate elimination, in the latter period the elimination is an excessively large one. An examination of the total urea of the twenty-four
| Date               | Quantity of Urine | Characters of Urine          | Characters of Deposit | Reaction | Sp. Gr. | Urea. | Albumin. | Blood. | Bile. | Quantity of Hemoglobin |
|-------------------|-------------------|-----------------------------|-----------------------|----------|--------|-------|----------|--------|------|------------------------|
| 6th February—10 A.M.—6 P.M. | 1897 | 31 oz. Clear, straw colour. | Mucous. *Microsc.*—A few epithelial cells. | Acid. | 1018 | 5·75 | 178·25 | None. | ... | Absent. None.          |
| 6 P.M.—2 A.M. | 17 "" | Do. | Mucous. *Microsc.*—Numerous cells. | "" | 1022 | 9 | 153 | Do. | ... | "" |
| 7th February—2 A.M.—10 A.M. | 22 "" | Do. | Mucous. *Microsc.*—A few epithelial cells and leucocytes. | "" | 1014 | 5·5 | 121 | Do. | ... | "" |
| 10.52 "" | 5¼ "" | Pale, straw colour, slight cloud. | Mucous. *Microsc.*—Cells and leucocytes. | Slightly acid. | 1010 | 3·75 | 20·625 | Do. | ... | "" |
| 11.15 "" | 2¼ drs. Deep port colour. | *Microsc.*—Numerous leucocytes and cylindrical aggregations, without envelopes, containing blood pigment. | "" | ... | 4 | 1·25 | 4·68 | Present. | ... | 8½ per cent. |
| 12.40 P.M. | 15 "" | Very dark port colour. | *Microsc.*—Do., and also fragments of the latter. | "" | 1017 | 4 | 7·5 | 10·593 | "" | ... | 11½ |
| 1.45 "" | 3¼ oz. Very dark, brownish-red, black, cloudy. | Brownish, flocculent. *Microsc.*—Brownish, flocculent. | "" | 1012 | 3·25 | 12·2 | 7·062 | "" | ... | 4½ |
| 3.15 "" | 1¼ "" | Dark, brownish-red. | Brownish, flocculent. *Microsc.*—Fragments of cylinders, a few cells and leucocytes. | Acid. | 1013 | 5·5 | 8·25 | 4·375 | "" | ... | 3 "" |
| Time          | Quantity  | Description | Microscopy | Specific Gravity |比重 | Leucocytes | Cylinders |
|--------------|-----------|-------------|------------|-----------------|-----|------------|-----------|
| 4.45 p.m.    | 8 1/2 oz. | Reddish-brown, cloudy. Brownish, flocculent. | Microc. — Brownish, flocculent. | 1005 | 3 | 25.5 | 1.09375 | Present | ... | iths as light as Gowers' standard; 0.025 per cent. |
| 6.20         | 7 1/2     | Light reddish-brown, cloudy. Brownish, flocculent. | Microc. — Brownish, flocculent, but leucocytes numerous. | 1004 | 3.5 | 26.25 | 0.4375 | ... | 0.147 per cent. |
| 8            | 11        | Amber, slightly smoky, faint reddish tinge. Small, mucous, brownish. | Microc. — Leucocytes and a few cylinders. | 1008 | 4 | 44 | 0.164 | Trace. | ... | Trace. |
| 9.30         | 11 1/2    | Straw colour. Small, mucous, brownish. | Microc. — Leucocytes and a few cylinders. | 1008 | 3 | 34.5 | Trace. | Faint trace. | ... | None. |
| 8th February—12.30 a.m. | 21     | Straw colour, clear. Mucous. | Microc. — Numerous leucocytes, but no cylinders. | 1010 | 4 | 84 | Trace. | Very faint trace. | ... | " |
| 2 a.m.—10 a.m. | 26      | Do. Mucous. | Microc. — Numerous leucocytes, but no cylinders. | 1011 | 5.5 | 143 | Absent. | ... | " |
| 10 a.m.—6 p.m. | 24      | Straw colour, slight cloud. Mucous. | Microc. — Leucocytes and epithelial cells, fragments of cylinders. | 1010 | 6 | 144 | " | " | ... | " |
| 6 p.m.—2 a.m. | 20      | Do. Mucous. | Microc. — Leucocytes and epithelial cells, fragments of cylinders. | 1015 | 7.5 | 150 | " | " | ... | " |
| 9th February—2 a.m.—10 a.m. | 10 1/2 | Do. Mucous. | Microc. — Leucocytes, but no fragments of cylinders. | 1018 | 7.75 | 81.4 | " | " | ... | " |
Urine Table No. 3.—Paroxysm of 7th February 1897.—Showing the Amounts of Urea and Urine excreted every Two, Four, Eight, and Twenty-four Hours.

| Date       | Time       | Urea. 2 hrs. | Urine. 2 hrs. | Urea. 4 hrs. | Urine. 4 hrs. | Urea. 8 hrs. | Urine. 8 hrs. | Urea. 24 hrs. | Urine. 24 hrs. |
|------------|------------|--------------|---------------|--------------|---------------|--------------|---------------|---------------|---------------|
| 1897. 6th Feb. | A.M. P.M. 10—6 | ...          | ...           | ...          | ...           | ...          | ...           | 178 1/2       | 31            |
|            | P.M. A.M. 6—2 | ...          | ...           | ...          | ...           | ...          | ...           | 153           | 17            |
|            | A.M. A.M. 2—10| ...          | ...           | ...          | ...           | ...          | ...           | 121           | 22            |
| 7th Feb.   | A.M. N.N. 10—12 | 21 1/2      | 5 1/2         | 41 9/16      | 11 1/2        | 75 5/8       | 21 1/2        |               |               |
|            | N.N. P.M. 12—2 | 19 3/4     | 5 1/2         | 33 3/4       | 10            | 397 1/8      | 98 1/2        |               |               |
|            | P.M. P.M. 2—4 | 8 1/2       | 1 1/2         | 94 3/4       | 30            | 178 1/2      | 51            |               |               |
|            | P.M. P.M. 4—6 | 25 1/2      | 8 1/2         |               |               | 323 3/4      | 98            |               |               |
|            | P.M. P.M. 6—8 | 60 1/2      | 18 1/2        |               |               | 397 1/8      | 98 1/2        |               |               |
|            | P.M. P.M. 8—10| 34 1/2      | 11 1/2        |               |               | 178 1/2      | 51            |               |               |
|            | P.M. N.N. 10—12| 0            | 0             | 8 1/2         | 21            |               |               |               |               |
| 8th Feb.   | A.M. A.M. 12—2| 84           | 21            |               |               |               |               |               |               |
|            | A.M. A.M. 2—10| ...          | ...           | ...          | ...           | 143          | 26            |               |               |
|            | A.M. P.M. 10—6| ...          | ...           | ...          | ...           | 144          | 24            |               |               |
|            | P.M. A.M. 6—2 | ...          | ...           | ...          | ...           | 150          | 20            | 375 3/8       | 54 1/2        |
|            | A.M. A.M. 2—10| ...          | ...           | ...          | ...           | 81 3/8       | 10 1/2        |               |               |

Urea in grains.  Urine in fluid ounces.
| Estimation. | Specific Gravity | Hemoglobin | Red Blood Corpuscles. (C. M. C.) | Red Blood Corpuscles. (E. F. B.) | White Blood Corpuscles. (C. M. C.) | White Blood Corpuscles. (E. F. B.) | Blood Plates. (C. M. C.) | Blood Plates. (E. F. B.) |
|------------|-----------------|------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|--------------------------|--------------------------|
| **7th February**— | | | | | | | | |
| 10 A.M. — *Before* bath; 10.30 to 10.40 A.M., legs immersed in cold water. | 1053 | 50 | 4,100,000 | 4,025,000 | 15,000 | 15,000 | 450,000 | 456,000 |
| 11.5 A.M. — *After* bath, but before appearance of haemoglobin in urine. | 1055 | 50 | 3,533,300 | 3,733,000 | 20,000 | 23,100 | 686,000 | 710,000 |
| 11.45 A.M. — Haemoglobin in urine at 11.15 A.M. | 1056 | 60 | 3,883,300 | 3,645,580 | 21,000 | 21,600 | 530,000 | 520,000 |
| 12.30 P.M. — *Just before* second micturition. | 1056 | 55 | 4,016,000 | 4,200,000 | 20,000 | 18,900 | 600,100 | 460,000 |
| 1.15 P.M. | 1056 | 50 | 4,216,000 | 4,194,000 | 21,000 | 22,000 | 4,250,000 | 4,250,000 |
| 2.30 | 1054 | 50 | 3,708,000 | 3,903,300 | 23,000 | 24,000 | 2,760,000 | 2,410,000 |
| 3.45 | 1054 | 50 | 3,750,000 | 3,883,000 | 17,800 | 17,600 | 1,590,000 | 1,600,000 |
| 5.15 | 1054 | ... | 4,809,000 | 4,879,200 | 18,000 | 17,780 | 1,560,000 | 1,500,000 |
| 7 | 1054 | ... | 4,256,000 | 4,250,000 | 18,700 | 18,200 | 1,210,000 | 1,200,000 |
| **8th February**— | | | | | | | | |
| 1 P.M. | 1054 | 50 | 4,080,000 | 4,180,000 | 18,700 | 18,760 | 500,000 | 500,000 |
hours in which the paroxysm occurred, and of the twenty-four hours preceding and following it, seems to indicate that its total elimination also was not materially affected; for on the day preceding the paroxysm $452\frac{1}{4}$ grs. were eliminated, on the day of the paroxysm $397\frac{1}{6}$ grs., and on the day following the paroxysm $375\frac{3}{6}$ grs. If, however, the output on each of these days during the eight hours between 10 A.M. and 6 P.M. be compared, it is found that on the 6th the quantity of urea was $178\frac{1}{4}$ grs., on the 7th (day of paroxysm) $75\frac{3}{4}$ grs., and on the 8th $144$ grs. During the paroxysm, therefore, urea elimination is much lessened, although the total urea of the twenty-four hours is not diminished to a corresponding extent. This lessening is also shown by the figures representing in the table the urea passed each two and four hours of the day of the paroxysm.

Blood.—In the appended table (see Table of Blood Estimations, No. 1), the state of the blood during, as well as before and after, the paroxysm is recorded. As in the previous Observation, no material changes were observed in the amount of haemoglobin, specific gravity of the blood, or number of the red and white corpuscles; but a similar and striking increase in the number of the blood plates, following the immersion by a considerable interval of time, was again found to occur. In order to avoid errors, the enumeration of the red and white blood corpuscles was made simultaneously, but independently, by two observers. By means of a cupping-glass, some blood was taken from the patient during the paroxysm, at about 3 P.M. It was allowed to coagulate, and on the following day the clear serum was found to have a distinct red colour, approaching that of red-currant jelly, and to contain haemoglobin. By comparison with the standard of Gowers’ haemoglobinometer, the amount of haemoglobin in this serum was estimated to be $2\frac{5}{10}$ per cent. For purposes of comparison, blood serum was similarly obtained from a convalescent patient whose blood was healthy. This serum, on the other hand, was pale yellow in colour, and no indications of haemoglobin could be found in it. The experiment appears definitely to prove that, in paroxysmal haemoglobinuria, haemoglobin is set free in the blood while it is circulating in the blood vessels.

The changes in the temperature (see Temperature Chart, Fig. 18) and circulation were in all important respects the same as in the previous Observation.

(To be continued.)