haemagglutinin content may serve as an indication that other collateral changes—that is, increase in antibodies and opsonins—are also occurring in the same blood serum.

Further, pus cells from a wound in a patient whose blood serum contains haemagglutinins frequently contain ingested red corpuscles. The pus cells in the presence of the iso-haemagglutinins (or the opsonins if these are separate bodies) tend to become auto-haemagglutinative and ingest their own red cells. Pus cells from wounds in patients whose blood serum contains no haemagglutinin do not phagocytose their own red cells.

It is probable that the red cell destruction and anaemia which accompany systemic infection in certain cases are associated with a blood serum and liquor puris of a haemagglutinative character.

In connexion with this inquiry, I wish to acknowledge kind help from my colleagues in military hospitals and from Dr. Mackarell, pathologist to the Leicester Royal Infirmary. The figures in the special plate are reproduced from photographs.

REFERENCES.

¹ BRITISH MEDICAL JOURNAL, June 3rd, 1916, December 23rd, 1916, and February 3rd, 1917. ² See also Dean, *Proc. Roy. Soc.*, 1905, B, 76, p. 506; and *Proc. Roy. Soc.*, 1907, B, 79, p. 399. ³ See Keith, *Proc. Roy. Soc.*, 1906, 77, p. 537. ⁴ BRITISH MEDICAL JOURNAL, February 3rd, 1917. ⁵ See Keith, *Proc. Roy. Soc.*, 1906, 77, p. 546; and Barratt, *Proc. Roy. Soc.*, 1905, 76, p. 624.

ON WAR NEPHRITIS AND SOME CIRCUMSTANCES INCIDENTAL THERETO.

BY

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It was not until fully eight months after the commencement of the war that nephritis loomed large in the sickness returns of soldiers. In the case of the German army the outbreak occurred a few months later. The fact that the winter campaign had been got over and the spring and early summer months had come was advanced by some physicians as a reason why exposure to cold could not have been the cause of the disease. The malady has fallen upon our troops in France and Flanders with unequal incidence and with unequal severity. Occasionally the number of men from one convoy admitted for nephritis under the care of my colleague Dr. Dagger and myself has equalled 40 per cent. of the total, while on other occasions there would be only 10 per cent. or less. It is sometimes said that the number of cases of nephritis among our soldiers at the front has not been larger than that occurring among the civil population. I can hardly subscribe to this opinion, and I base my dissent upon experience of admissions into the Royal Victoria Infirmary, Newcastle, extending over three decades. In the summer of 1915 few of the cases of nephritis admitted into the Northumberland War Hospital presented acute symptoms. This might be explained partly by the fact that the severer and more acute cases had been retained in hospitals on the Continent. Beyond albuminuria and complaints of headache and backache, there were few physical signs and symptoms. Oedema, with us, has been an infrequent physical sign compared with the experience of Colonel J. Michell Clarke,¹ who found it in fifty-seven out of seventy-four patients. It was during my first visit to France in September, 1915, that I saw in the stationary hospitals there cases of nephritis with acute symptoms, including dropsy and uraemia.

War nephritis, to give it the name by which it is generally known, differs from ordinary nephritis in that there is a greater tendency for blood, and blood in fairly large quantity, to appear in the urine, for the specific gravity in many cases to be well maintained, for the urine to be not so scanty, the blood pressure to be lower, also for the malady to be attended by fewer cardio-vascular changes, and to be followed by fewer complications than are found in ordinary nephritis.

We have had no deaths from war nephritis in the Northumberland War Hospital. Hurst² states that death in this malady is extremely rare, not more than 3 or 4 per 1,000 patients, and that when death takes place it is usually through uraemia. A low death-rate has also been noted in the Italian army. On the other hand, and as illustrating the absence of uniform experience, three of Colonel Michell

Clarke's 68 patients died. A fair percentage of our patients at the Northumberland War Hospital have recovered, but in men over 30 years of age albuminuria has frequently persisted, the urine has become pale and watery, and its specific gravity has decreased. Many of these men have become the subjects of chronic kidney disease. In a considerable number of the younger men recovery has only been apparent, for albuminuria after having been absent for days or weeks has returned, without any exaggeration of the symptoms, other than fresh complaint of backache and the presence of blood in the urine. The length of time required for the disappearance of the albuminuria varies—it may be three weeks or it may be as many months, but the longer it persists the more likely are the kidneys to become the seat of chronic and permanent structural changes. While error in diet is a cause of recrudescence of symptoms, muscular exercise—for example, tennis playing and too long walks—may also conduce to their return.

I have alluded to the fact that in war nephritis there are fewer symptoms and cardio-vascular signs than in the usual forms of nephritis with which we are familiar; hence the comparative absence of well-marked hypertrophy of the left ventricle of the heart and of loud accentuation of the second sound over the aorta. The short duration of the illness may partly, but it cannot altogether, explain the comparative infrequency of cardiac hypertrophy, and of thickened arteries.

I have not been able to ascertain how far the previous occupation of the soldier plays any part in the development and course of the malady. On the Italian front it has been observed that men whose previous occupations exposed them to hardships and who were intemperate have suffered from nephritis in larger numbers than men engaged in more protected occupations and who are of temperate habits.

Some of the soldiers were slightly anaemic, but they seldom exhibited the well known features of patients suffering from Bright's disease. I have not found any well marked reduction in the number of red blood corpuscles, nor any increase or decrease of leucocytes, nor has basophilia been a feature of the blood examinations. Of the presence of eosinophile corpuscles in the urine and their excess in the blood as described by Bernhardt I have no experience. A positive Wassermann reaction was not obtained in a series of 13 of my cases. McKenzie Wallis obtained a positive reaction in 18 out of 56 patients. Since other physicians have secured the reaction, and seen relief follow antisyphilitic treatment, it is possible that syphilis is more than an incident in some forms of war nephritis. The blood pressure has varied from 70 to 130 mm. Hg; in only a small percentage did it rise to or over 180. Some of the soldiers were admitted into the hospital not for kidney trouble at all, but for trench fever, P.U.O., or on account of having been gassed.

SYMPTOMS.

The disease usually commences with a feeling of malaise, pains, especially in the limbs and back, headache, and occasionally sickness with oedema of face and feet. Among German soldiers the disease is said to be ushered in with cough, worst at night, and with shortness of breath, attended by oedema of face, and by thirst and scanty secretion of urine. Our own men, too, suffer at the onset from bronchitis and dyspnoea. By the time the patients have reached the North of England dropsy, if ever present, has usually disappeared. Anasarca we never see. In none of our patients has vision been affected, nor have there been uraemic convulsions. One patient developed acute pulmonary oedema, and, after a serious illness, made a good recovery from the lung trouble, but albuminuria still persisted. It would be interesting to know what the experience of the R.A.M.D. is in regard to the future of the men who have been treated for nephritis, who recovered and were, in the early months of the war, again sent back to the front. Since in a fairly large percentage of patients who have been suffering from nephritis relapses occur, no case should be regarded as cured until, after several months have passed, it is found that, on full diet and after muscular exercise, albumin does not reappear in the urine.

ETIOLOGY.

The causation of war nephritis is obscure. Although the urine and the blood of my patients have on several occasions been examined bacteriologically, in none of them

was a specific micro-organism found to explain the illness. The *Bacillus coli* was found in several of the urines; and while the presence therein of this organism would suggest an intestinal origin of the nephritis, I can hardly regard this as the cause, especially as the patients did not give a history of diarrhoea or of intestinal disturbance.

M. Sacquepée³ draws attention to the fact that cultures from the blood and from emulsions of kidney and spleen in nephritis contained a polymorphous bacterium and cocci bacilli of two kinds, one short and the other long. These organisms, when injected into guinea-pigs and mice, caused oedema and haemorrhagic lesions in the internal organs similar to those found in the patient who had died from nephritis, and from whose blood the cultures were obtained. The fact that until now no specific micro-organism has been found in the blood and urine of our soldiers suffering from nephritis is no proof, of course, that the malady is not of an infectious origin, for after all—so far, at any rate, as the urine is concerned—micro-organisms may fail to pass through the renal barrier, and yet their toxins be capable of doing a considerable amount of damage.

Exposure.

Most of the men attribute their illness to exposure to wet and cold in the trenches and dug-outs. It is difficult for any one who has visited the trenches, as on three occasions I have, and seen the soldiers in cold, damp, and snowy weather lying in their wet clothes, to exclude altogether exposure to wet and cold as a direct or indirect cause of the malady. It is an interesting point, therefore, as to how far we are to regard the nephritis we are discussing as an incident of trench warfare and of campaigning in the open. As a consequence of the routine four days spent in the trenches and of exposure to wet and cold we can readily understand the rheumatism and muscular pains the soldiers complain of. Is there any reason why the conditions which give rise to the joint and muscular pains should not in some instances operate upon a larger area of the body so as to include the kidneys as well? The vessels of these organs are extremely sensitive to external changes of temperature. Nephritis is apt to follow chilling and wetting of the lower extremities; hence its frequent occurrence in men employed in making drains. It occurred, too, with great frequency in the German soldiers when they slept on the bare pavement without a covering of straw, and it ceased when they slept on wood. Nephritis also occurred in the Italian army when, during the month of May, one blanket was withdrawn, and it disappeared on the blanket being restored and warmer clothing supplied.

Colonel Manella, sanitary director of one of the Italian army corps, has drawn attention to the fact that in his area there are nephrogenous zones where nephritis is met with in greater proportion than in other areas. A fact equally interesting is that in these Alpine regions few cases of nephritis occur at high altitudes where the air is cold and dry compared with lower altitudes where the air is damp and cold.

Professor Luigi Devoto of Milan, in an article on acute nephritis among troops at the front,⁴ attaches considerable importance to the influence of damp and cold. In one sector of the front, at an altitude of 1,250–2,600 metres, out of 1,200 soldiers the following cases of nephritis occurred:

1916.					1916.				
June	...	...	...	5	December	...	...	...	7
July	...	...	...	10					
August	...	...	...	11					
September	...	...	...	13	January	...	...	...	7
October	...	...	...	19	February	...	...	...	0
November	...	...	...	5	March	...	...	...	1

The largest number of cases occurred in the autumn.

Antecedent Nephritis.

In many of the men affected there may have been a latent nephritis, ready to be lit up on slight provocation; but in a large number of my patients, especially the younger men, interrogation failed to reveal the existence of previous kidney trouble as evidenced by oedema, headache, back-ache, vomiting, and scanty urine. On the other hand, it is a possibility which should not be ignored, although the absence of hypertrophy of the left ventricle and high blood pressure point in a negative direction.

Postural albuminuria also must not be lost sight of. Reher and Lauer, who examined the urine of Swiss

soldiers who belonged to the 34th Battalion Mounted Infantry, found albumin in the urine of a large percentage of the soldiers who had remained many hours in an erect position during extremely cold weather.

Haematuria.

Haematuria is a frequent sign. It may disappear and return on the slightest provocation. Its return has in some of my cases been associated with large quantities of oxalates in the urine. Nonnenbruch of Wurzburg⁵ states that 50 per cent. of the patients admitted into his hospital had haematuria. My experience is that it is only about 20 per cent., but this varies. It may be that the haematuria is simply the bleeding which occurs in chronic interstitial nephritis, also that in many instances the kidney disease of the soldiers is the result of an old infection, such as scarlet fever or diphtheria. It is impossible to say to what extent the patient in every instance was in good health previous to joining the colours. In the case of some of the men over 40 years of age there was probably latent kidney disease or renal inadequacy. Taking twenty-eight of my patients at random, I find that there were nine cases of nephritis in men between the ages of 30 and 35, seven between 35 and 40, six between 40 and 45, three between 25 and 30, and two between 40 and 45. There is no unanimity of pathological opinion as to the nature of the nephritis. The character of the urine suggests that it is parenchymatous, while the pain in the loins and the recurring haematuria, the blood being frequently in large quantity, indicate an enlarged and swollen kidney, the pain in the back being due to stretching of the capsule.

Professor H. Ziemann and Dr. Oehring of Saarburg⁶ found that of 2,011 patients admitted into their hospital 2.93 per cent. were suffering from war nephritis, and that of these 1.4 per cent. were the subjects of nephritis in an acute form, 0.145 per cent. of chronic nephritis, 0.78 per cent. of temporary albuminuria, and 0.34 per cent. of albuminuria of greater persistence; 0.24 per cent. suffered from albuminuria with complications.

Lead in the Urine.

Setting aside the influence of exposure to wet and cold as a possible cause of the type of nephritis we are discussing, other causes may be in operation—for example, infection and the influence of poisons, organic and inorganic. C. Powell White found lead in the urine of four soldiers suffering from kidney disease, and tin also in the urine of one of the men. Mackenzie Wallis did not find any trace of lead in the urine of his patients. Mr. T. M. Clague, analytical chemist, Newcastle-upon-Tyne, has made for me analyses of the urine of several of the sick soldiers under my care in the Northumberland War Hospital. The urines were those of men of different convoys, and the results are as follow:

Of five samples of urine of different patients two contained lead; of eight samples five contained lead; of five samples of urine one contained lead, and of three samples one contained lead.

Several single samples were, in addition, examined and found to be free from lead—others showed mere traces of the metal.

In twenty-nine samples of urine of soldiers in the Northumberland War Hospital lead was found nine times, or in something like 43 per cent.

This is a large percentage of cases with lead in the urine. Care was taken to eliminate the possibility of drugs having been taken, such as bismuth for example.

These observations raise the question, How did lead get into the system? Powell White found that a salt solution boiled in a meat tin extracted both lead and tin. At my request, Mr. Clague submitted the meat which the soldiers are receiving at the front—namely, bully beef and Maconachie—to analysis; he found traces of lead in the meat, but the amount was so infinitesimal that it raised doubts as to whether this could be the source of the metal in the urine of nephritic soldiers. I then had metallic scrapings of the interior of the pans in which the food is cooked at the front tested, but no lead was found therein; the metal present was mostly calcium. One possible source still remained, and that was the drinking water, and as this was frequently delivered to the soldier in cleansed petrol tins, we tried the effect of various kinds of water, sterilized and non-sterilized, chlorinated and not, upon the tins, but without obtaining lead.

The etiology of war nephritis is still obscure. I have not dealt with such a possible cause as the combined

influence of overwork, fatigue, and the physical discomfort of life at the front.

Recent findings have led me to give some attention to the possible effects of bullet and shrapnel retained in the body. In the urine of a young corporal with a bullet in his right thigh we found lead; in that of a sergeant shot through the arm and chest, and with the metal retained in the chest, lead was also found; in the urine of a soldier with pieces of shrapnel in knee and shoulder a small quantity of lead was found; while in the urine of a young lieutenant, mortally wounded, with shrapnel in his pelvis, lead was found. It is only right to add that in the urine of other soldiers with shrapnel retained in the body no lead was found, and that in the urine of one patient similarly circumstanced lead was on one occasion absent, while a fortnight after it was present. Although in cases where lead was found in the urine albumin was not present in every instance, yet in other instances there seemed to be a distinct connexion between the albuminuria and the retained shrapnel, as the following indicates:

I was asked by one of my surgical colleagues to see a young soldier with a piece of shrapnel in the front of the uppermost part of the left thigh. The patient was extremely ill. He had albuminuria, with recurring haematuria; the wound in the thigh kept closing and opening every now and then, attended by rises of temperature. The surgeon took the view that the wound would not heal on account of the condition of the patient's kidneys, which he thought antedated the receipt of the wound. My opinion was that the presence of the shrapnel in the body was the cause of the kidney trouble, and that if the shrapnel was removed the kidney trouble would cease. The patient was transferred to my own ward, where, by external applications aided by natural processes, the shrapnel gradually came nearer the surface, and could be readily felt under the skin. As the patient was too ill to be given a general anaesthetic, local anaesthesia was employed and the shrapnel removed by the surgeon. From the date upon which the shrapnel was removed the temperature gradually fell to the normal, the wound closed, the albuminuria entirely and permanently disappeared, and the patient made a good recovery.

It has been the practice of surgeons during this war where pieces of projectile have become embedded in the tissues, are not readily accessible, are not pressing upon nerves or upon important organs, and where there is neither haemorrhage nor excessive suppuration, to leave the metal in the body undisturbed. There is always the possibility of the piece of shrapnel or bullet becoming encysted and remaining as an inoffensive foreign body. Yet, now and again, it has happened that some of these metal carriers whose wounds have healed have been observed to become anaemic, to be suffering from disorders of the intestinal and nervous system and to have become the subjects of albuminuria. Since in their urine lead is frequently found, it is clear that resorption of the metal must be taking place. It goes without saying that pieces of shrapnel are more likely to cause plumbism than portions of shell. All depends upon the type of metal, the organ or tissues in which it is embedded, and whether there is or is not suppuration. In all cases, therefore, where pieces of shrapnel are retained in the body it would be well to have the patient's urine examined for lead.

As lending support to this, Loeper and Verpy⁷ may be quoted. They found lead in the urine of six out of sixteen soldiers in whose body pieces of projectile had been retained. They found it only with shrapnel and not with the debris of shell, also never when the bullet was intact. They found lead to the extent of $\frac{1}{2}$ to 1 mg. per litre of urine; in other words, that more than 1 mg. of lead was being eliminated in twenty-four hours. This is a smaller quantity than is occasionally found in the urine of lead workers, but it is equal in quantity to, or slightly more than, that found in the urine of persons poisoned by food or by drinking water contaminated by lead. When a wounded soldier with shrapnel retained in his body is passing from $\frac{1}{2}$ to 1 mg. of lead daily the kidneys in course of time are almost sure to become affected, for secondary lead compounds are being formed; these are absorbed, and pass on into the circulation. The extent to which this takes place will depend upon the leucocytes and the chemical activity of the tissues. Absorption of shrapnel is slow; lead does not appear in the urine until three to four weeks after a soldier has been wounded. When resorption of the metal is taking place there is a tendency in some instances for the blood pressure to rise, for albumin to appear in the urine, for the red blood cells to decrease in number, and for colic and constipation to be complained of. Since

in one of my own patients albuminuria and suppuration gradually ceased after removal of the shrapnel it would seem as if there had been a causal relation between the condition of the kidneys and retention of the metal in the body. I am not in a position to say whether the presence of shrapnel in the lung is more provocative of plumbism than when the piece of projectile is retained in the body elsewhere.

With the object of testing the solubility of lead bullets generally, and of throwing light upon the fate of shrapnel retained in the body and exposed to the influence of the fluids of the tissues, also to the influence of fat upon metallic lead, I secured the co-operation of Messrs. T. M. Clague and A. J. Watson, analytical chemists of this city, to whose report I invite attention.

EXPERIMENTS ON THE SOLUBILITY OF PLAIN LEAD AND ANTIMONIAL LEAD.

BY

T. MALTBY CLAGUE, Ph.C., and A. J. WATSON, Ph.C.

"CERTAIN clinical observations made by Sir Thomas Oliver suggested the desirability of an examination into the comparative solubilities in the fluids of the human body and in analogous liquids of the modern hardened bullet and the old bullet of pure lead.

"The uncoated shrapnel bullets used by the enemy and allied forces of to-day contain antimony in large amount (10 per cent. and upwards).

"Bullets were placed by us in the blood serum of sheep and macerated for seven days. After burning off, the residue was found to contain lead equivalent to 10 parts per million of the blood serum, but the analytical difficulties of dealing with the blood were great, and for convenience a solution was prepared containing 0.9 per cent. of NaCl and 0.13 per cent. NaHCO₃ to represent blood serum. Shrapnel bullets macerated for four days (heated each day to 35° C. (95° F.) for six hours) yielded in the case of pure lead 260 parts per million, and in the case of antimonial lead 300 parts per million.

"With a view to a more complete conformity to the conditions found in the human body an automatic circulating system was arranged in which an alkaline saline solution circulated through a U tube containing six bullets.

FIG. 1.—Water at 70° C. surrounded the limb of U tube containing the bullets; this caused the solution to circulate; the temperature did not rise above 25° C. to 30° C. After six hours' circulation, 20 c.cm. removed from Woolf bottle at position of least contact (X) contained 5 parts of lead per million of water; after fourteen hours' circulation it contained 7 parts per million. The liquid in the U tube was allowed to digest thirty-six hours in the cold and then removed. Pb content was found equal to 14 per million.

Antimonial Lead Bullet.

Oily Solvents.	Acidity.	Lead Yielded in Parts per Million of Solvent.
Lard	1.0	10
Neatsfoot oil	3.2	200
Suet	0.7	5
Olive oil	1.6	100
Liquid paraffin	0.0	Nil.

Bullets in solvent for six days heated to 35° C. (95° F.) each day for six hours.