has persisted. When a large amount of fluid was drunk it was excreted too slowly and the specific gravity of the urine failed to fall as low as it should have done, indicating abnormal glomerular filtration. Neither did water deprivation raise the specific gravity to the levels which ought to have been reached—an indication of impaired tubular absorption.

The transient albuminuria in this case was almost certainly due to sulphanilamide poisoning: it coincided with the discovery of crystals and red cells in the urine and heralded the appearance of agranulocytosis. (Incidentally this emphasizes once again the danger of uncontrolled application of sulphanilamide powder to ulcers; the response of the severe leucopenia to massive doses of pentnucleotide is also worthy of notice.) If the albuminuria had been due to the effects of the original injury, as was presumably the case in the second patient, it should have been evident when the blood urea was at its maximum. During the post-traumatic period neither patient passed red cells in excess, no casts were found, and spectroscopic examination for haemoglobin and muscle pigments was negative.

The kidneys of the second patient were examined post mortem and were similar to those already described (Darmady *et al.*, 1944), the pathological lesions being comparable to those of the crush syndrome and largely confined to the tubules. In addition a few sulphanilamide crystals were present. The changes were certainly insufficient to explain urea retention on the purely mechanical basis of tubular obstruction, and the glomeruli were comparatively healthy. The blood urea does not rise in nephrosis in which pathological changes are confined to the tubules. It therefore seems more likely that the cause of renal failure and of the damage to the tubules is anoxia resulting from vasoconstriction of the renal arteries during the stage of shock, aggravated by blood loss, a fall in blood pressure, and dehydration. This supposition is favoured by the demonstration of similar alterations in the tubules after temporary clamping of the renal vessels (McEnery *et al.*, 1927) and by the theory propounded by Maegraith and Findlay (1944) that peripheral vascular atony with redistribution of renal blood flow explains the suppression of urine in blackwater fever. The action of myotoxin may be accounted for in a similar manner. Oedema of the kidneys and rupture of some of the renal capillaries occur during the anoxic period, and may be responsible for the slow recovery of renal function after the systemic blood pressure has risen to normal.

It has not yet been decided how these cases should be treated. Arguing on purely theoretical grounds, which may be fallacious, the best hope of improvement should lie in the early restoration of an adequate blood flow to the kidneys. Caffeine is said to dilate the renal vessels, and although its effectiveness in these cases is doubtful it can certainly be administered in full doses without harm. Giving oxygen in high concentrations might also be of value, but there has been considerable disagreement about its success in the treatment of shock (*vide* annotation in the *British Medical Journal*, 1942). It would seem particularly important to raise the pressure, volume, and oxygen-carrying capacity of the blood to normal levels, and this can only be achieved by the continuous administration of carefully matched blood, and then with difficulty. Black and Smith (1941) have demonstrated that blood is much more effective than plasma in promoting the excretion of urea when azotaemia develops after haematemeses. Fluids should certainly be provided in abundance, but because these patients tend to develop subcutaneous and pulmonary oedema it should be given by mouth or by rectum and not intravenously.

Summary

Two further cases of traumatic uraemia are reported. It appears that the condition may be relatively common in modern warfare, especially when severe damage to a limb involves large blood vessels. Evidence is given that urea manufacture from tissue protein is increased in the early stages of the illness, and reasons are advanced in support of the view that urea retention is due to renal anoxia. It is suggested that blood transfusion should be the most important factor in treatment. During the recovery phase diuresis is pronounced and the usual renal function tests may show no abnormality. Simpler tests have revealed kidney impairment in one of the cases described.

One patient had severe leucopenia as a result of sulphanilamide poisoning, and responded rapidly to injections of pentnucleotide.

I am indebted to my surgical colleagues for permission to quote their cases, and to Dr. J. L. Edwards for the histological report.

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THE CEPHALIN-CHOLESTEROL FLOCCULATION REACTION AS A TEST OF HEPATIC FUNCTION

BY

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The cephalin-cholesterol flocculation reaction was first introduced by Hanger (1939) as a test of hepatic efficiency. It is recognized that many of the liver function tests in common use fail to detect early or mild liver damage; positive results are often found only in the advanced stages of the disease when clinical symptoms are already manifest. The cephalin-cholesterol flocculation test has been shown by several American workers (Hanger, 1939; Pohle and Stewart, 1941; Rosenberg, 1941; Nadler and Butler, 1942; Mateer *et al.*, 1942; Yardumian and Weisband, 1943) to be an extremely sensitive test in the early detection of hepatic insufficiency. The test was found to be of considerable value in prognosis in cases of acute infective hepatitis; the persistence of a strongly positive reaction indicates severe liver damage. A further important claim was its value in the differentiation of jaundice due to parenchymatous disease of the liver from that due to obstruction of the biliary passages. It therefore promises more diagnostic help than certain of the earlier tests, in which similar results are obtained in all types of liver disease.

The value of the cephalin-cholesterol flocculation test of hepatic function has not yet been conclusively established in this country. It falls into the category of empirical procedures rather than a definite test of any known hepatic function. The exact mechanism of the test is poorly understood (Hanger, 1939). It is relatively inexpensive to carry out; few reagents are required, and it is more easily performed than other tests in common use. The object of this paper is to present results of this test in hepatic and biliary disease; no attempt is made to explain the mechanism of the reaction.

Method

The method employed was that described by Hanger (1939). First, enough cephalin was obtained by extraction from sheep's brain to last for about one year. Sheep's brains (two or three) were dehydrated by three extractions with acetone, and the dry powdered tissue was three times extracted with ether. The ether extracts were concentrated and the crude cephalin was precipitated by the addition of four volumes of absolute alcohol. The resulting precipitate was dissolved in the minimum amount of ether; the accompanying cerebroside impurities were precipitated by chilling to 5° C. and removed by centrifugation. The supernatant ether solution was again precipitated with four volumes of absolute alcohol, chilled, and the precipitate filtered, washed with alcohol and acetone, and desiccated. The cephalin preparation is a brown powdery material. Hanger (1939) suggested that freshly prepared cephalin was too sensitive and that it should be ripened for some months before use.

A stock solution was then prepared by adding 300 mg. of cholesterol and 100 mg. of cephalin to 8 c.cm. of ether. This stock solution, well stoppered, was kept in a refrigerator at 0 to 5° C. In order to prepare the emulsion 35 c.cm. of distilled water was heated to 65–70° C., and 1 c.cm. of the stock

solution was slowly added, with frequent stirring. The emulsion was heated to boiling-point and allowed to simmer until the volume was reduced to 30 c.cm. This was cooled to room temperature, and 1 c.cm. of the emulsion was added to a centrifuge tube containing 0.2 c.cm. of the patient's serum and 4 c.cm. of freshly prepared 0.85% sodium chloride. The centrifuge tube was stoppered, shaken, and left at room temperature. After 24 hours note was made of the presence of flocculation, which was designated "zero" to "4-plus." The serum should be used immediately or else kept in an ice-box for not longer than 6 hours. The final reading should be made in 24 hours, as normal sera may cause positive flocculation in 48 hours (Clay and Moore, 1942).

Previous workers (Pohle and Stewart, 1941; Clay and Moore, 1942) showed that the test was positive in a small percentage of normal individuals and in those suffering from various systemic disorders. It therefore appeared necessary, in assessing the value of this test, to examine the sera of such individuals as well as the sera of those with definite hepatic disease. Accordingly the test was applied to the sera of three different groups: (1) Healthy individuals attending as blood donors. (2) Patients suffering from a variety of systemic diseases without clinical evidence of hepatic disease. (3) Patients suffering from hepatic or biliary disease.

Results

(1) Sera of Normal Individuals

The test was applied to 100 individuals attending as blood donors who were regarded as healthy. Only one of the 100 sera examined gave a positive reaction (4-plus) after 24 hours. This patient had a history strongly suggestive of a mild attack of infective hepatitis a few weeks previously; the serum gave an indirect van den Bergh reaction of 0.9 mg. per 100 c.cm. This case can therefore be excluded from the controls because there was evidence of hepatic disease; in 99 normal persons the test was negative.

(2) Sera of Those Suffering from a Variety of Systemic Disorders

This group includes 164 patients; 123 were in the wards, and 41 attended as out-patients on account of rheumatoid arthritis. The results are shown in Table I.

TABLE I.—*The Cephalin-Cholesterol Flocculation Test in Various Non-hepatic Diseases*

System Involved	No. of Cases	No. with Flocculation
Cardiovascular	14	0
Haemopoietic	17	4
Respiratory	17	4
Alimentary	29	2
Renal	8	1
Nervous	8	0
Endocrine	13	0
Bones and joints	58	2
Total	164	13

Table I shows clearly that flocculation may occur in those suffering from conditions not primarily hepatic. Positive reactions were encountered in 13 patients (7.7%), and details of these are shown in Table II.

TABLE II.—*The Disease and Degree of Flocculation in Cases with a Positive Reaction*

Case	Disease	Degree of Flocculation
1	Pernicious anaemia	++
2	Iron-deficiency anaemia	++++
3	Malaria	++++
4	"	++++
5	Lung cancer	+
6	Pleurisy with effusion	++++
7	Diaphragmatic pleurisy	+
8	Asthma	++
9	Diabetic coma	+++
10	Cancer of stomach (liver not involved) ..	+
11*	Nephritis and haemolytic anaemia due to sulphonamide therapy ..	++
12	Rheumatoid arthritis	++++
13	"	++++

Table II shows that the patients who had positive reactions suffered from very varied conditions; in 10 cases the reaction was strongly positive, whereas in 3 the degree of flocculation was slight. In most instances it is difficult to explain why posi-

tive reactions were obtained; in Cases 9 (diabetic coma) and 11 (nephritis with jaundice) it is not improbable that it should have been positive. Further liver function tests were carried out in many of the patients (Nos. 1, 2, 3, 4, 10, 11, 12, and 13), but revealed no evidence of hepatic inefficiency. Most patients were dismissed when the primary disease was cured without repetition of the test, but in Cases 1, 2, and 3 the reaction became negative before dismissal. In Cases 12 and 13 the test was carried out on numerous occasions and positive reactions were always obtained. Repeated biochemical investigations failed to show any evidence of hepatic disease in these two patients, and the cause for the positive flocculation could not be explained.

(3) Sera of Those with Hepatic or Biliary Disease

The majority of patients in this group were suffering from hepatitis—the test being performed either during the acute course of illness or in convalescence—or from biliary obstruction. A small number of patients suffering from cirrhosis or cancer of the liver are included because of the variable results of the test so far reported in these conditions. Lastly, the results obtained in 12 patients who developed jaundice during the course of arsenical treatment for syphilis are included in order that some light may be shed on the nature of the jaundice.

(a) *Infective Hepatitis*.—The sera of 38 patients suffering from infective hepatitis were studied. Twenty-six came under observation early in the course of the disease, and in several cases readings were obtained during the illness; in 12 other patients the test was performed after recovery from an acute attack, such patients reporting in convalescence.

TABLE III.—*Cephalin-Cholesterol Flocculation Test in Acute Infective Hepatitis*

Degree of flocculation ..	0	+	++	+++	++++
No. of cases	—	7	2	1	16

TABLE IV.—*Cephalin-Cholesterol Flocculation Test during the Course of Infective Hepatitis*

Case	Date	Degree of Flocculation	Case	Date	Degree of Flocculation
1	25/8/43	+++	15	18/2/44	++++
2	13/9/43	++++		15/3/44	++++
	21/9/43	++++		27/3/44	++++
	22/11/43	—	16	29/3/44	++++
3	13/9/43	+	17	26/5/44	++++
	21/9/43	+	18	16/6/44	+
4	21/9/43	++++		27/6/44	++
	24/9/43	+		7/8/44	++++
5	22/9/43	+	19	14/6/44	++++
6	12/10/43	++		16/6/44	++++
	16/11/43	—		19/6/44	++++
7	11/12/43	++++	20	22/6/44	++++
	12/12/43	++++		27/6/44	++++
8	25/2/44	++++	21	6/7/44	++
	28/2/44	++++		8/7/44	+++
				11/7/44	+
9	2/3/44	++++	22	6/7/44	+
	4/3/44	++		8/7/44	+
				11/7/44	—
10	8/3/44	+		20/7/44	—
	10/3/44	+		24/7/44	—
	23/3/44	—		27/7/44	—
				31/7/44	—
11	15/3/44	++++	23	17/7/44	++++
	21/3/44	++++		24/7/44	++++
	19/4/44	—		27/7/44	++++
12	13/4/44	+		31/7/44	+++
	18/7/44	—	24	2/8/44	++++
13	2/5/44	++++		5/8/44	++++
	5/5/44	++++		11/8/44	++++
	9/5/44	++++		15/8/44	+++
	15/5/44	++++		21/8/44	+++
	30/5/44	—	25	4/8/44	++++
14	26/8/43	+		8/8/44	++++
	21/4/44	++		10/8/44	+++
	7/6/44	+		14/8/44	—
	6/7/44	+		17/8/44	—
	24/7/44	++++		21/8/44	—
			26	15/8/44	+++
				21/8/44	++++

From my experience the test is of definite value, even although its mechanism is not understood.

I wish to thank Prof. J. W. McNee for his helpful advice and criticism, and Dr. J. B. Rennie for the results of other liver function tests in the cases under review.

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EMPLOYMENT OF THE POST-NATAL WOMAN

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It seemed proper that, as a sequel to our article on "Employment of Pregnant Women in Industry" (*Journal*, 1944, **1**, 108), we should follow these cases up and show how the women return to work after their confinements. We have done this in the 90 cases of the original article, and 40 others, up to 17 months after delivery.

Return to Work after Confinement

In our last follow-up of the original patients, in Feb., 1944, only 61 of the 90 mothers could be communicated with owing to change of address, evacuation, etc. The striking fact was that only 14 out of the 61 had returned to work at all, and only 4 at the end of four months after delivery. Two returned one month after the baby was born: one of these, a multipara with several children, had to do so for financial reasons, and her own mother looked after the baby. The other had a stillborn child. Two returned at two months: one of these was a single girl whose baby had been adopted; the other had lost her baby at birth. Four returned at three months. One of these had a premature stillbirth, the second arranged for the baby to be looked after by a neighbour, the third had her baby cared for by her mother, and the fourth took her baby to a day nursery. One returned at four months, her baby being cared for at a day nursery. Two returned at five months, their babies being in the care of relatives. One returned at six months, but did not continue, as the baby fretted in her absence. Two returned at ten months, giving no reason.

Thirty-six mothers preferred to stay at home. Fifteen said that they found the housework plus caring for the baby as much as they could manage. Three stayed at home because their husbands wished them to do so. Two said they would not trust their babies to anyone else. Two mothers were evacuated because of the air raids. Two did not feel well enough to return to work. Nine mothers said they would return to work if they had somebody to care for the babies, who were all under 1 year and could not, as a rule, be accepted by local day nurseries. Eight women gave no reasons for not returning to work.

In addition to the original 90 cases we have attempted to follow up 40 other mothers who attended our clinic. Through the difficulties previously noted, we were not able to contact more than 22, and only 4 of these had returned to work. One of them lost her baby at two months and then started work; the second started work at six months, the third—a single girl—at four months, and the fourth at nine months. We analysed the reasons why patients did or did not return to work, and the following is a summary of their replies.

Fifteen stated that, with the care of the baby and housework, they had too much to do. Two said their housework and caring for the baby were as onerous as factory work. One

mother stated that she found the housework and baby even more tiring than factory work when she was pregnant. Eight mothers visited the clinic only for post-natal examination. Of these six were normal, one had a relaxed outlet, and one fairly severe haemorrhoids.

The medical officers of health of five boroughs in which the patients lived gave the following rules as to the permitted age of entry of babies to their day nurseries:

- A. Not under 6 months.
- B. From birth to 5 years. Under 3 months only in very special circumstances.
- C. One year and over.
- D. No minimum age limit, but very young babies accepted only under special circumstances.
- E. Not under 6 months except in special circumstances—i.e., unmarried mother, etc.

There appears to be no uniformity locally, and we infer that this may be general throughout the country, although the Ministry of Health issues general recommendations.

The Position in the United States

In a personal communication to one of us (L. B. B.) Dr. Barbara Hewell, Acting Director, Division of Research in Child Development, U.S. Department of Labor, made some interesting observations on the situation in America which are worth recording. Her Department has suggested that women be granted at least two months' leave ordinarily, and longer if parturition or a post-partum period has been in any way complicated (*Standards for Maternity Care and Employment of Mothers in Industry*, U.S. Department of Labor, July, 1942). As most American employers have little or no experience of female labour there is considerable variation in or complete absence of policies in different industries on the subject of maternity leave. There has been no development, on anything like the national scale we have in Great Britain, of nurseries to care for children under 2 years of age of mothers working in war industries. However, centres have been set up for the group care of children from 2 to 5 years of age and also of school age. Federal funds have been made available to communities up to approximately 60% of the cost. There has been some supervision of these by State, Health, Welfare, and Education Departments in the different States.

"The policy of the Children's Bureau is strongly against the development of group care for children under 2 years of age. They feel that the young infant needs the continuous affection and consistent care of his own mother for his best emotional, physical, and mental development. There is no adequate substitute for a mother's care or for the care of some one person who holds this relationship to the child. Regardless of how good a group centre may be as to plant, hygienic conditions, number and training of staff, there remain the danger of communicable diseases when young babies are in groups, and the strong probability that the care cannot be as individual in type, and may not meet the emotional and developmental needs of the young infant.

The man-power situation in this country has not been so urgent that mothers of young children under 2 are essential in industry. It is realized, of course, that some mothers of young babies must work. When substitute care is necessary, the Children's Bureau advises foster-home care for children under 2, as more likely to meet the needs of the individual child. This type of care—both full-time for dependent or neglected children and day-time for children of working mothers—has been considerably developed in this country. This programme is under the supervision of child-welfare agencies whose trained workers approve the homes and the qualifications of foster-parents to care for children, and who give continuing supervision of the child in the foster home, working with both the employed mother and foster-home mother for the best interests of the child. The foster home should be near the child's home, caring for only a few children, and should duplicate home life as much as possible. The working mother pays the foster mother for this care.

There are scattered day nurseries in local communities where young infants receive care under private agency auspices, but this is not an extensive development. Many mothers, of course, make their own arrangements as to care of the children."

The following quotation from an interesting paper by Dr. Charlotte Silverman (U.S. Department of Labor) gives an account of her investigation of the problem:

"*Post-natal Leave of Absence.*—Most of the establishments that did not actually discharge employees on account of pregnancy stipulated that those who were required to take leave of absence