Using this technique, chloroform extracts of urine that contain no barbiturates have been examined. It was found that the developed color showed a maxima of 5600 and 5750 AU, for copper sulfate treated[6] and untreated urine, respectively. We have found that such extracts contain chromogenic substances[9] which may possibly be of acidic character. Inasmuch as these factors produce similar absorption spectra, and can give artifactual excretion values, results obtained using the cobalt acetate and isopropylamine test in the study of barbiturate excretion in urine must be considered cautiously and accepted with reservation.

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Variations in Concentration of Certain Electrolytes of Blood Serum During Induced Hyperpyrexia.

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The remarkable constancy of the potassium content of the blood under pathologic conditions has been long recognized, but recent studies have brought forth evidence that this constancy may be disturbed greatly in cases of shock of various kinds. However, no uniformity of opinion has emerged from studies of the potassium fluctuations in shock. Different workers have reported different changes in the potassium content of the blood in cases of induced shock, and a variety of conclusions as to the role which such variations play has been drawn. The question whether variations in the blood potassium may be the primary cause of shock, and whether terminal shock may actually result from potassium poisoning caused by release of potassium from intracellular spaces has remained unanswered.[1-3] Furthermore, the theory that changes in the blood potassium level are not the cause of shock, but that such changes are incidental to alterations in blood volume has not been substantiated.

The present work was undertaken to ascertain what variations in the potassium level take place during shock caused by induced hyperpyrexia. This report includes experiments on patients who were

1 Scudder, J., Zwemer, R. L., and Truszkowski, R., *Surgery*, 1937, **1**, 74.

2 Scudder, J., Zwemer, R. L., and Whipple, A. O., *Ann. Surg.*, 1938, **107**, 161.

3 Bisgard, J. D., McIntyre, A. R., and Osheroff, W., *Surgery*, 1938, **4**, 528.

undergoing treatment in the Burdick fever cabinet, and on others who were being treated by induced malaria shock.

In order to ascertain whether changes in the degree of hydration of the blood might affect the potassium level, a hematocrit determination was made on each sample of blood taken from the patient. Since variations in the concentration of one inorganic constituent of the blood might reasonably be expected to produce alterations in that of others, also, sodium and calcium determinations were made concurrently with the potassium and hematocrit studies. In addition, blood sugar estimations were made during progression of the induced shock.

Methods. The sodium content was determined by Salit's[4] triple acetate method, and that of potassium by the method of Truszkowski and Zwemer,[5] as modified by Harris.[6] The concentration of calcium was determined by the Clark-Collip modification of the Kramer-Tisdall method.[7] Blood sugar determinations were made by the micro method of Gibson.[8] Hematocrit readings were obtained by centrifuging 4-5 ml of fluorinated blood in a graduated centrifuge tube for 20 minutes, and rechecking after an additional 5 minutes of centrifugation.

In order to study the variations in blood serum potassium in induced hyperpyrexia, and to correlate such variations with changes in blood concentration, three determinations were made on each patient studied.

A. Fever Therapy. The first blood sample was drawn from each patient at the end of a 12-hour fast, and immediately before an intravenous injection of about 1500 ml of 5% glucose in physiologic saline. The intravenous injection was followed by induced hyperpyrexia in a Burdick fever therapy cabinet. At the height of the fever, which usually occurred about 4 to 5 hours after treatment was begun, a second sample was taken. After treatment was discontinued, and the patient's temperature had returned to normal, a third sample was taken.

All blood samples were withdrawn in amounts of approximately 30 ml from a forearm vein. About 4 ml of blood were immediately placed in a graduated, 15 ml centrifuge tube containing sufficient NaF to prevent clotting, and centrifuged at once for 20 minutes. A reading of total volume and cell volume was then taken, and the tube

4 Salit, B. W., *J. Biol. Chem.*, 1932, **96**, 659.

5 Truszkowski, R., and Zwemer, R. L., *Biochem. J.*, 1937, **30**, 1345.

6 Harris, J. E., personal communication.

7 Clark, E. P., and Collip, J. B., *J. Biol. Chem.*, 1925, **63**, 461.

8 Gibson, R. B., PROC. SOC. EXP. BIOL. AND MED., 1930, **27**, 480.

was then centrifuged an additional 5 minutes to check for variations.

The remaining portion of the sample was placed in a small bottle, and defibrinated by means of a paper clip. A 0.2 ml portion of this was used for a sugar determination, and the remainder was immediately centrifuged. The serum was pipetted off at once, and stored in the refrigerator until all three samples had been thus treated. When all 3 serum specimens were available, the protein-free filtrate was immediately obtained for the potassium determinations. Therefore, the amount of time during which the cells were in contact with the serum never exceeded 15 minutes.

During the course of the treatment, the patient received fluids, in the form of water and cracked ice, in an amount sufficient to control thirst and prevent excessive dehydration from loss of body fluids. Saline tablets were also administered occasionally. No food was taken until after the final blood sample was drawn.

B. Malaria Shock Therapy. Parallel studies were made on patients undergoing malarial shock treatment. In these cases the plan was to ascertain what variations in the blood serum occurred during the chill caused by the treatment. The patient's history was studied in the hope of anticipating the probable time of occurrence of the chill. A blood sample was drawn when there were indications of an impending chill, but before the temperature had risen above normal. The progress of the fever was followed, and, when it was at its height, a second sample was taken. A third sample was obtained after the temperature had returned to normal. The general procedure of handling the samples was the same as in the fever therapy cases.

Discussion. Our analyses showed that there was no uniform variation in the blood potassium level during the course of treatment, which indicates that an increase in the potassium content of the blood is not a factor in the shock caused by hyperpyrexia. Contrariwise, the results suggest that the blood potassium level may vary directly with the degree of hydration of the blood. No significant changes in Na or Ca concentration occurred as a result of fever treatment, and the blood sugar curves followed no regular pattern.

The hematocrit determinations showed that the degree of hydration of the blood was maintained within narrow limits during the fever therapy treatments. This was accomplished by the intravenous administration of fluids before treatment, together with the oral administration of water and saline tablets. There were no indications of severe shock.

Summary. In 15 cases of induced hyperpyrexia, there were no changes in the potassium content of the blood which would indicate

TABLE I.
Variations of Electrolytes of Blood Serum in Hyperthermia.

Case	Treatment No.	Temperature variations (rectal)		Hematocrit % cell volume			Blood Sugar Mg%			Potassium Mg%			Sodium Mg%			Calcium Mg%		
		(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)
1	3	105.6	100.4	x	41.5	33.3	114	109	109	16.7	22.6	22.6	314.7	319.8	319.8	10.7	10.7	10.6
2	10	102.5	100.0	41.0	36.1	34.9	91	100	80	18.2	22.5	22.2	321.2	349.7	342.1	9.7	10.2	10.2
3	1	105.8	99.4	31.8	35.5	40.0	157	120	122	22.0	20.4	18.9	351.3	348.2	348.2	10.0	10.0	9.9
4	9	105.8	101.0	36.3	37.1	36.27	78	94	126	18.2	17.9	19.1	314	322	325	11.5	11.9	11.1
3	3	105.8	99.2	33.3	32.4	34.22	147	107	90	21.1	20.4	20.8	322.5	322.5	322.5	9.7	10.5	10.3
1	6	105.6	100.8	33.3	33.3	33.3	x	98	81	18.5	19.8	20.4	319.9	322.5	322.5	10.4	10.9	11.5
3	7	104.5	99.6	32.9	31.0	31.0	133	112	109	19.2	20.2	20.8	322.5	325.1	317.3	12.0	11.2	11.7
5	1	103.4	100.0	41.8	46.8	45.3	116	96	85	16.3	17.5	16.7	327.9	353.8	334.5	9.2	10.7	10.7
6	*7	104.0	100.0	42.3	40.6	41.5	85	109	189	18.0	21.1	19.2	336.3	333.4	325.2	10.3	10.6	9.7
7	1	104.0	100.6	22.0	22.0	21.8	157	68	96	x	x	x	300.3	300.3	300.3	8.5	8.4	8.3
8	1	104.6	100.4	33.3	31.7	32.4	165	100	110	x	x	x	348.1	348.1	339.2	9.0	9.2	9.2
8	3	104.4	100.0	28.9	29.3	34.6	131	84	100	18.0	18.0	17.4	—	—	—	—	—	—
7	3	104.0	100.8	12.2	16.3	14.3	—	—	—	21.3	22.2	20.8	—	—	—	—	—	—
9		105.8	100.0	36.4	36.4	39.3	100	129	105	21.7	21.3	20.0	345.1	345.1	342.1	9.7	9.7	9.8
10		104.8	100.0	29.0	29.1	28.0	120	104	94	19.3	19.0	20.3	x	314.7	322.5	10.3	10.3	9.9

*No intravenous injection preceding treatment. Final sample taken 20 minutes following an intravenous injection of 1000 ml of 5% glucose in saline (physiologic).

(1) Normal conditions before treatment; (2) Height of fever; (3) Return to normal.

— Determination not made.

x Duplicate values not satisfactory.

Patients, 1-8, Burdick fever cabinet therapy.

Patients 9-10, Malaria shock therapy.

that an increase in the amount of potassium is a factor in shock. The blood potassium level tends to vary directly with the degree of hydration of the blood. There were no significant changes in the Na, Ca, or blood sugar levels, produced by this condition.

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Toxic Substance in Extracts of Postpartum Rabbit Uterus.*

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In a previous communication it was demonstrated that saline extracts of postpartum rabbit uterus were highly toxic after intravenous injection in the same species.[1] Death occurred with the characteristic symptoms of histamine shock and the activity of the extracts was destroyed by the enzyme histaminase.[2] It was tentatively concluded that the active material was histamine or a histamine-like substance.

In order to determine whether the effects of this "histamine-like substance" on the guinea pig ileum were identical with those of histamine, uterine extracts were subjected to acid hydrolysis, the hydrolysates neutralized and assayed on an isolated strip of guinea pig ileum, according to the method of Barsoum and Gaddum, and the responses compared to those of histamine.[3]

Extracts so treated assayed between 2.2 and 3.2 γ histamine per cc. This is approximately the histamine content of normal rabbit tissues, and would be by no means sufficient to cause death in the amounts injected.[4] It was possible, moreover, to recover between 70 and 80% of histamine dichloride added to saline extracts of rabbit uterus and of various guinea pig tissues in quantities between 10 and 60 γ per cc and treated in the same manner (Table I). The failure to recover toxic quantities of histamine from uterine extracts led to the conclusion that some substance other than histamine is responsible for the toxic activity of the extracts.

It was considered possible that the active substance was protein-

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1 Krichesky, B., and Pollock, W., *Science*, 1940, **91**, 410.

2 Krichesky, B., and Pollock, W., *Am. J. Physiol.*, 1940, in press.

3 Barsoum, G. E., and Gaddum, J. H., *J. Physiol.*, 1935, **85**, 1.

4 Best, C. H., and McHenry, E. A., *Physiol. Rev.*, 1931, **11**, 371.