up water to the extracellular compartment only by a reduction of its mass of protoplasm.

Summary. 1. The volume of sulfocyanide available water of cats is definitely increased after hemorrhage. 2. The chloride concentration of serum water was found to be decreased in all experiments save one. 3. The total water and sulfocyanide available water content of cardiac muscle, pancreas, pylorus, duodenum, colon, skin and liver (chloride available water) was increased after hemorrhage. No significant differences were found in the case of skeletal muscle (gastrocnemius and diaphragm). 4. The significance of the above findings is discussed.

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A Simple Method for Prolonging Therapeutic Insulin Coma.*

JOSEPH WORTIS AND IRVIN M. KORR. (Introduced by Homer W. Smith.)

From Bellevue Psychiatric Hospital and New York University College of Medicine, New York City.

In the treatment of psychoses, insulin coma[1] (or the period of unconsciousness) is generally not allowed to persist beyond an hour or an hour and a half. In cases inadvertently allowed to linger in coma beyond that period, an irreversible insulin coma[2] frequently follows that can no longer be relieved by intravenous glucose. This dangerous and sometimes fatal complication has, however, directed the attention of several investigators to the important fact that patients who survive several hours or days of this relatively irreversible coma often show dramatic psychiatric improvement on awakening. Kraulis[3] attempted to utilize this phenomenon for therapeutic ends by prolonging insulin coma with periodic small glucose feedings sufficient to sustain the patient but not sufficient to rouse him. The difficulties in the clinical management of these sporadic feedings, however, and the frequent presence of gastric retention[2] (which

* This work was aided by the Havelock Ellis Fund for Psychiatric Research.

1 Sakel, Manfred, *Insulin Shock Treatment of Schizophrenia*, Nervous and Mental Disease Monograph No. 62, New York, 1937.

2 Wortis, Joseph, and Lambert, R. H., *Am. J. Psychiatry*, 1939, **96**, 335.

3 Kraulis, W., *Schweiz. Arch. f. Neur. u. Psychiat.*, Erganzungsheft, 1937, **39**, 219.

Kraulis did not suspect) made this mode of treatment too dangerous for clinical application.

It can be assumed that the cerebral injury which ensues in accidentally protracted coma is due to the diminution of brain metabolism (by withdrawal of substrate) below levels adequate for cell maintenance over long periods of time. In our cases (30 experiments on 10 subjects), we have succeeded in prolonging hypoglycemia as long as 21 hours and coma as long as 18 hours, without mishap, by sustaining brain metabolism above this dangerous level, but still below levels which support consciousness and other associated cerebral functions. This has been achieved by administering infusions of 5% glucose in physiological saline (Sterisol) intravenously at controlled rates. Inasmuch as large doses of insulin exert their hypoglycemic effect for many hours after administration,[4] one need only maintain the blood glucose at a moderately high level (*e.g.,* 35 mg per 100 ml) to prolong coma for many hours. When the insulin effect begins to subside, a fresh intramuscular injection of insulin can be administered. We have found that a variation in infusion rate between 3 and 10 ml per minute (0.15 to 0.5 g of glucose per minute) is generally sufficient to maintain both the sugar level and the state of consciousness at a uniform level. The adjustment of the blood sugar level by regulation of the speed of flow has proven to be surprisingly simple and reliable. Rapid bedside sugar determinations[5] together with clinical observations govern the adjustment of the rate of infusion. Arousal with the injection of 25 g of glucose by vein has been prompt and complete. The patients are then allowed to eat and drink and are carefully watched for late shock.

In these early experiments we have established the practice of rousing the patients for a minute or two, 2 or 3 times during each treatment, in order to assure ourselves of the continued reversibility of the coma. This is done merely by accelerating the infusion for a short period of time. Upon slowing the infusion once more, the subjects quickly revert to the comatose state. Under the conditions of our experiments, the transition from complete unconsciousness to the state in which the patient can answer questions, and *vice versa,* can be regulated by varying the blood sugar by as little as 2-5 mg %. We have found that the critical level for coma is generally around 40 mg %. Progressive lowering of the blood sugar below these concentrations causes deepening coma with the typical changes in level of neurological integration noted in ordinary coma.

[4] Greeley, Paul O., *Am. J. Physiol.,* 1940, **129**, 17.

[5] Hawkins, J. A., and Van Slyke, D. D., *J. Biol. Chem.,* 1929, **81**, 459.

The method thus provides a unique opportunity for the systematic study of physiological and psychological functions at different levels of neurological integration.

These moderately prolonged comas administered at intervals of several days have resulted in improvement in patients whose psychoses were resistant to the ordinary full course of insulin treatment. The therapeutic value of the procedure must, however, await more extended study. We are gradually increasing the duration of coma in successive trials. Further modifications in the technique may become necessary. Since numerous cases of accidentally induced protracted coma have amply demonstrated its therapeutic effectiveness,[1] we hope that a single prolonged coma of one or more days, of the controlled type described above, may prove to be the equivalent of long periods of ordinary treatment. At any rate, it can be reasonably anticipated that this modification of the so-called insulin shock treatment will shorten its duration, simplify its management and still further extend its range of usefulness.

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Presence of Estrogenic Hormone(s) in Testicular Material.

BERT CUNNINGHAM, JOSEPHINE MAY, AND SETH GORDON.

From the Zoology Department, Duke University.

Although a number of studies have been made on male urine to determine the presence or absence of estrogens, comparatively few have been made upon testes. This is rather surprising in the light of the work of Zondek[1] who reported enormous quantities of estrogenic substance (more recently identified as alpha-estradiol and estrone by Beall[2]) in the testes of the stallion.

Zondek,[1] while more often credited with the report on the stallion testes, examined also the bull testes. Perhaps because of the relatively minute amounts (less than 0.1%) found in the latter as compared to the former it was not thought to be worth recording in the later literature. Zondek assumed that "the mass production and excretion of the estrogenic hormones in the testes is a peculiarity of the equines."

1 Zondek, B., *Nature*, 1934, **133**, 209.

2 Beall, D., *Bioch. J.*, 1940, **34**, 1293.