haps be achieved in man by applying such compounds to mucous membranes.

Summary and Conclusions. Various steroid hormones, especially D.C.A. and progesterone produce deep anesthesia in rats and mice if injected into the peritoneum whence they can be rapidly absorbed. After recovery from the anesthesia such animals show no ill effects. Partially hepatectomized rats are much more sensitive to the anesthetic effect of the steroids than intact controls. This probably indicates that the liver plays an important rôle in the detoxification of these compounds. Males are less sensitive than females of the same size.

11908

Availability of Sodium Pyruvate for Human Brain Oxidations.*

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We have previously described a method for the study of the availability of various substrates for human brain metabolism *in vivo*.[1] In the absence of glucose during therapeutic insulin shock it has been shown that the metabolism of the brain is diminished. This is indicated by an extremely low oxygen uptake of the brain[2, 3] in association with characteristic changes of the cortical brain potentials[4] and the onset of clinical coma. Intravenous administration of glucose rouses the patient and restores the normal arterio-venous oxygen difference.[5] In previous publications we have reported that as little as 4 g of glucose administered intravenously invariably roused the patients from coma and approximately doubled the oxygen uptake of the brain.[6] Ethyl alcohol had no effect on the clinical

* Aided by a grant from the Havelock Ellis Fund for Psychiatric Research.

1 Wortis, J., and Goldfarb, W., *Science*, 1940, **91**, 270.

2 Damashek, W., Myerson, A., and Stephenson, C., *Arch. Neur. and Psychiat.*, 1935, **33**, 1.

3 Himwich, H. E., Bowman, K. M., Wortis, J., and Fazekas, J. F., *J. Nerv. and Ment. Dis.*, 1939, **89**, 273.

4 Hoagland, H., Cameron, D. E., and Rubin, M. A., *Am. J. Psychiat.*, 1937, **94**, 183.

5 Himwich, H. E., Frostig, J. P., Fazekas, J. F., and Hadidian, Z., *Am. J. Psychiat.*, 1939, **96**, 371.

state or the oxygen uptake of the brain,[7] while racemic sodium lactate resulted in only a slight increase in the oxygen uptake of the brain, and had no effect on the comatose state of the patients.[8] In this report we are presenting evidence on the availability of sodium pyruvate for brain oxidations.

Experimental. The method has been previously described.[6] The cerebral metabolism was estimated from the arterio-venous differences of O_2, CO_2, and glucose. Duplicate analyses of blood gas determinations checked within 0.2 vol. %. The velocity of circulation in the peripheral vascular system was estimated with the method of Robb and Weiss.[9] In 9 experiments the metabolism of the brain was estimated after the patients were in deep hypoglycemic coma, and again 15 minutes after the administration of various amounts of sodium pyruvate. The data from these experiments are presented in Table I. Patients 1 and 6 roused slightly after administration of the pyruvate, but soon lapsed into coma again. The remaining patients did not rouse. The doses varied from 4 to 8 g of pyruvate, and are indicated in the table. In 4 additional patients 15 g of sodium pyruvate were administered, and in none of these cases did the patient rouse from the comatose state. The average oxygen uptake during coma was 2.9 volumes %, and after the pyruvate was 4.08 volumes %. Statistical analyses of these averages reveal that the difference was barely significant. It is interesting to note that this increase closely

TABLE I.
Effect of Sodium Pyruvate Administered Intravenously on Cerebral Metabolism of Schizophrenic Patients in Insulin Coma.

Exp. No.	Dose of pyruvate, g	Volume % oxygen art.	ven.	diff.	Circ. time, sec.
1	4.0	19.5	15.1	4.4	15
2	6.7	19.9	15.0	4.9	
3	8.0	20.9	16.9	4.0	12
4	8.0	19.1	16.0	3.1	10
5	8.0	23.2	21.6	1.6	12
6	8.0	20.0	14.6	5.4	11
7	8.0	19.5	15.2	4.3	10
8	8.0	19.6	16.1	3.5	9
9	8.0	20.8	15.3	5.5	10
	Avg	20.26	16.20	4.08 ± 1.10	11.1
Avg of 60 cases in insulin coma		19.6	16.7	2.90 ± 1.49	11.8

Difference ± St. Deviation = 1.18 ± 0.418.

[6] Wortis, J., and Goldfarb, W., PROC. SOC. EXP. BIOL. AND MED., 1940, **44**, 382.
[7] Goldfarb, W., and Wortis, J., *Quart. J. Studies in Alcohol*, 1940, **1**, 268.
[8] Wortis, J., and Goldfarb, W., *Am. J. Physiol.*, 1940, **129**, 502.
[9] Robb, G. P., and Weiss, S., *Am. Heart J.*, 1932-3, **8**, 650.

approximates the increase previously observed after lactate administration.

The estimation of brain metabolism in these experiments was based on the differences between the concentrations of various substances in the arterial and venous blood. This method is subject to error if the blood flow varies, and other investigators have suggested that changes in blood flow can account for the changes observed. In collaboration with Himwich, *et al.*,[10] we have confirmed the observations of Loman and Myerson[11] that in the absence of convulsions there is no appreciable change of the brain blood flow during insulin coma. During the course of this research we also observed that the administration of glucose, lactate and pyruvate did not affect the blood flow of the brain of patients during insulin coma. It therefore appears probable that the changes observed in the arterio-venous oxygen difference of the brain indicates that there is a corresponding increase of the brain metabolism after the administration of sodium pyruvate, but this increase is not sufficient to rouse patients from coma. These results are not in agreement with the effects of pyruvate on the metabolism of isolated brain tissue in the Warburg apparatus. The possibility remains, however, that the oxidations *in vitro* occur at a diminished rate[12] and may be maintained by the oxidation of pyruvate, while the oxidation of pyruvate *in vivo* is too slow to supply sufficient energy for brain metabolism during insulin hypoglycemia.

Summary and Conclusions. The availability of sodium pyruvate for brain oxidations in hypoglycemic insulin coma was studied in human patients. In 2 of 14 experiments with various amounts of pyruvate the patients roused slightly from coma, and in the remaining 12 there was no change observed in the clinical state. In 9 patients the oxygen uptake of the brain was observed, and there was a small, though statistically significant, rise. These results are in striking contrast to those observed with glucose, and indicate that the oxidation of pyruvate by the brain is not sufficient to adequately support cerebral functions.

[10] Himwich, H. E., Bowman, K. M., Daly, C., Fazekas, J. F., Wortis, J., and Goldfarb, W., PROC. SOC. EXP. BIOL. AND MED., 1940, **45**, 468.

[11] Loman, J., and Myerson, A., *Am. J. Psychiat.*, 1936, **92**, 791.

[12] Gerard, R. W., *Ann. Rev. Biochem.*, 1937, **6**, 419.