

the apparent carbon dioxide production is significantly reduced. An example of such a calculation is given in Table II.

Glucose was added to the spinal fluid to bring the concentration to approximately 0.2%. All experiments were run in duplicate. No specimens of spinal fluid were used which contained enough protein to give a visible precipitate with 20% trichloroacetic acid.

The results of the comparison of the oxygen consumption, Q_{O_2} , and carbon dioxide production, Q_{CO_2} , of liver slices in 9 experiments are given in Table III.

It may be concluded from these experiments that the metabolism of rat liver in the synthetic medium herein used is not significantly different from that observed in cerebro-spinal fluid, when care is taken to make the composition of the synthetic medium approximately equal to that of the spinal fluid.

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Possible Rôle of Glutathione as a Detoxifying Agent.

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Aside from the probable rôle which glutathione plays in oxidative mechanisms, the suggestion has been advanced that it may be of importance as a detoxifying agent.¹ It is, to say the least, extremely suggestive that this polypeptide consists of 3 amino acids, each one of which is known to act as a detoxifying agent.

It occurred to us that experimental evidence for or against such a hypothesis might be gathered by injecting a substance which is known to form a detoxified product with one of the amino acids of the glutathione molecule, and then determining the glutathione content of the blood. We proceeded on the hypothesis that such an injection would be followed by a mobilization of the glutathione in order to furnish the required amino acid for detoxifying purposes.

Waelsch,² using tribromoethanol and phenylacetic acid, claims to have obtained a decrease in the glutathione of the blood.

The substances we selected for subcutaneous injection were benzoic acid and bromobenzene. The former is known to combine

¹ Harrow, B., and Sherwin, C. P., *Annual Rev. Biochem.*, 1935, **4**, 263.

² Waelsch, H., *Arch. Exp. Path. Pharm.*, 1933, **169**, 625.

with glycocoll and the latter with cysteine; and both these amino acids are found in the glutathione molecule.

Rabbits weighing about 2 kilos were used. Two gm. of benzoic acid (as the sodium salt) and an equivalent (molar) amount of bromobenzene were subcutaneously injected. The experiments were carried out with rabbits which had been fed, and also with rabbits which had been starved for 24 hours.

Blood was withdrawn for glutathione estimation, which was carried out according to Woodward and Fry.³ The highest value within 3 hours after the injection was taken. We, of course, realize, as have others, that this method of glutathione determination has its shortcomings. For one thing, it is not specific for glutathione. For another thing, with small quantities of blood, extraordinary precautions have to be taken to avoid serious errors. However, we do believe that the figures can be taken as worthy of consideration in a *comparative* sense. [Our values for reduced glutathione for 34 normal fed rabbits ranged from 28 to 47 mg. %, with an average value of 33.0 mg. %. This agrees well with the findings of other workers (see, for example, Parker and Kracke⁴), who report an average value of 34.5 mg. % of reduced glutathione for a series of 24 normal rabbits.]

TABLE I.
Effect on Blood Glutathione (GSH) of Injected Benzoic Acid and Bromobenzene.

		No. Rabbits		Av. % Increase		Range	
		Control	Injected	Control	Injected	Control	Injected
Benzoic Acid (as sodium benzoate)	Fed	22	22	0.0	-0.6	-9.0 to 3.4	-8.5 to 10.5
	Starved	13	20	-0.6	20.9	-3.1 to 1.8	8.1 to 33.4
Bromobenzene	Fed	30	30	-0.3	3.8	-6.0 to 3.9	-9.9 to 14.4
	Starved	25	29	0.5	9.3	-12.0 to 5.4	3.3 to 23.0

The condensed results are represented in Table I. The figures are given in percentage increases (or decreases).

It can be stated that, in so far as animals which have been fed are concerned, the results are practically negative. But with the animals which had been starved, the results are suggestive, especially in the case of benzoic acid; for here it can be seen that there is a definite increase in the glutathione of the blood.

³ Woodward, G. E., and Fry, E. G., *J. Biol. Chem.*, 1932, **97**, 465.

⁴ Parker, F. P., and Kracke, R. R., *Am. J. Clin. Path.*, 1936, **6**, 41.

Conclusions. 1. The injection of benzoic acid into rabbits which have been starved for 24 hours causes an increase of glutathione in the blood. 2. Using bromobenzene, the results, though less striking, are suggestive that this detoxication process is accompanied by a definite increase of glutathione in the blood.

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Hormones in Urine of a Normal Non-Pregnant Woman.*

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The gonadotropic and estrogenic hormone content of 24-hour urine specimens from normal women has been studied at weekly intervals.^{1, 2} More recently the daily urinary excretion of hormones has been determined³⁻⁸ with results which have demonstrated a point not shown in weekly assays, namely, that the gradual rises and falls in estrin excretion curves are sudden in their occurrence and are confined to certain days. If hourly examinations could be made perhaps still sharper peaks might be found. Cohen, *et al.*,⁹ reported their observations pertaining to the combined and free state of estrin in the urine of pregnant women at the onset of labor. Is there sudden freeing and combining of estrogenic substances associated with events of the menstrual cycle? My report, developed from the study of the urine excreted by one woman during one menstrual cycle, suggests that ovulation and menstruation are possibly associated with changes in the chemical state of estrin. Gonad-

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¹ Frank, R. T., *The Female Sex Hormone*, 1929, Charles C. Thomas, Springfield, Ill.

² Frank, R. T., and Salmon, U. J., *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **32**, 1237.

³ Gustavson, R. G., and Green, D. F., *J. Biol. Chem.*, 1934, **105**, xxxiv.

⁴ Smith, G. V. S., and Smith, O. W., *Am. J. Physiol.*, 1935, **112**, 340.

⁵ Gustavson, R. G., Wood, T., and Hays, E., *J. Biol. Chem.*, 1936, **114**, xlvi.

⁶ Smith, G. V. S., and Smith, O. W., *New England J. Med.*, 1936, **215**, 908.

⁷ Gustavson, R. G., Hays, E. E., and Wood, T. R., *Proc. Am. Soc. Biol. Chemists*, 1937, **31**, xlii.

⁸ Yerby, L. D., *PROC. SOC. EXP. BIOL. AND MED.*, 1937, **36**, 496.

⁹ Cohen, S. L., McMaster, B. A., Marrian, G. F., and Watson, M., *Lancet*, 1935, **1**, 674.