Preliminary evidence has been obtained, *in vitro*, using dialysis and two-phase solvent partition techniques, for the formation of a complex between the phosphatido-peptide fraction and benzomethamine.

In previous studies it had been shown that intestinal mucus, and polysaccharides extracted from mucus, inhibited the absorption of quaternary ammonium compounds.[1, 2] While the role of phosphatido-peptide in the mechanism of absorption has not been established, this is the *first* evidence that intestinal absorption of a quaternary ammonium compound can be enhanced by material extracted from intestinal tissue.

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Effect of injected estradiol on the uptake of α-amino*iso*butyric acid by tissues of the ovariectomized rat

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ESTROGEN treatment produces an elevation of free amino acids in the rat uterus.[1] The accumulation of an amino acid that is not metabolized to any appreciable extent, α-amino*iso*butyric acid (AIB), is also enhanced by estrogens; thus, a few years ago, Noall and coworkers[2] reported a three-fold increase, on a wet-weight basis, in uterine AIB 20 hr after a single subcutaneous injection of estradiol. This report follows the uptake by the uterus and other tissues of AIB, after estrogen treatment, and extends the previous observations which were limited to one time period.

METHODS

Long–Evans female rats, three weeks of age, were injected intraperitoneally with 1·25 μc (0·25 μmoles) of AIB-1-C^{14}. At intervals of from 0 to 30 hr before sacrifice, groups of 4 rats were anesthetized with ether and given intravenous injections of 0·1 μg of estradiol in 0·1 ml of saline, or of saline alone for controls. The rats were sacrificed under ether anesthesia 20 hr after the injections of AIB, in order that our data could be compared with that of Noall *et al.*[2] Blood was taken from the heart, the uteri were removed and blotted, and portions of muscle, from the hamstring mass, and of liver were obtained.

The 4 blood samples from each group of rats were pooled. After clot formation, an aliquot of serum was mixed with 75% ethanol to precipitate protein; the supernatant fraction was saved for the measurement of radioactivity. The other tissue samples were pooled in tared all-glass homogenizers. They were weighed (to 0·1 mg) before and after drying at 75 °C for 24 hr and then were homogenized in 75% ethanol. The radioactivity in the supernatant fraction was measured in a liquid scintillation counter. Each vial contained 10 ml of dioxane, in which were dissolved 0·9 g of naphthalene, 70 mg of 2:5-diphenyloxazole, 0·5 mg of *p*-bis[2-(5-phenyloxazolyl)]-benzene, and 0·15 ml of the supernatant material.

Radioactivity for each tissue was calculated on the basis of counts/min/mg of dry weight. For serum, the activity was expressed as counts/min/μl of serum. The accumulation of AIB-1-C^{14} by each tissue was then presented as a ratio, tissue to serum activity. By chromatography of the tissue extracts (butanol/acetic acid) all radioactive material was identified as α-aminoisobutyric acid.

RESULTS AND DISCUSSION

The time course of the accumulation of AIB by the uterus is presented in Fig. 1. The ratio of uterine to serum radioactivity is plotted against time after an intravenous injection of 0·1 μg of estradiol. After estrogen administration, uterine activity increased from a control ratio of 27 to a peak of 66 at 12 hr; a rapid decline to near control levels by 20 hr followed.

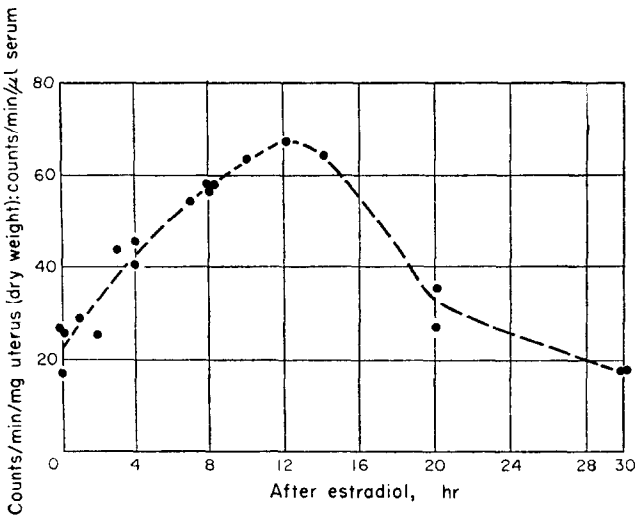

FIG. 1. The accumulation of AIB in the immature rat uterus as a function of time after the intravenous injection of estradiol (0·1 μg). Each point represents the pooled tissues of 4 animals. All animals received intraperitoneal injections of AIB (1·25 μC) 20 hr before sacrifice.

Studies *in vitro* by Noall,[3] using surviving uterine segments, led to similar conclusions concerning the rapid induction of this estrogen effect. The data are particularly interesting in that the onset of the accelerated transport of AIB coincides with an increased rate of incorporation of amino acids into protein.[4, 5]

The effect on the uterus far exceeds that on any other tissue studied. Table 1 presents data for the levels of AIB in liver and muscle (relative to serum levels, which did not change). There was no

TABLE 1. MEAN AIB RATIOS (TISSUE : SERUM) FOR RAT LIVER AND MUSCLE, WITH AND WITHOUT THE INTRAVENOUS INJECTION OF 0·1 μg OF ESTRADIOL

	Control No estradiol	Experimental 4–30 hr after estradiol
Liver	(12) 17·2 ± 0·9	(52) 20·5 ± 1·1
Muscle	(12) 17·8 ± 0·7	(52) 11·1 ± 0·7

Tissue dry weights were used. All animals were given intraperitoneal injections of AIB (1·25 μC) 20 hours before sacrifice. The number of animals is given within parentheses. Data are expressed with their standard errors. For liver, the difference between control and experimental means is not significant. The difference between control and experimental groups for muscle is significant ($P < 0{\cdot}001$).

significant increase in liver to serum AIB ratios ($P > 0.05$); however, a significant decrease in muscle: serum AIB ($P < 0.001$) occurred.

Whether the uptake of α-amino*iso*butyric acid serves as a satisfactory model for the transport of all amino acids is unknown. It has recently been observed that its distribution is similar to that of glycine.[6] In any event, we have described a very early estrogen effect on the accumulation of this α-amino acid which corresponds in time with changes in distribution and metabolic fate of natural amino acids. Although this effect of estrogen is most pronounced in the uterus, there is a perceptible shift in the distribution of AIB in muscle in a direction opposite to that observed for the uterus.

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Potentiation of the carcinostatic action of azauridine by chloramphenicol*

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CHLORAMPHENICOL, a well-established antibiotic agent in the chemotherapy of bacterial infections, has also been shown to depress hematopoiesis in man.[1, 2]

This toxic effect upon bone marrow function led to further investigation of the possible utility of chloramphenicol as a carcinostatic agent in the treatment of experimental[3, 4, 5] and human neoplasms.[6] Although ineffective as a carcinostatic agent *in vivo*, chloramphenicol inhibits the growth of mammalian cells in culture.[7]

Observations made during the course of treatment with 6-azauridine (the ribonucleoside of 6-azauracil)[8] of three patients with leukemia,† suggested that potentiation of its action by chloramphenicol might have occurred when the antibiotic agent was given for the treatment of intercurrent bacterial infections. Preliminary studies of combinations of these compounds in the chemotherapy of an experimental neoplasm in mice have confirmed this impression and the results are presented in this communication.

METHODS

Male DBF_1 hybrid mice, 6–8 weeks old and weighing 19–24 g, were used in all experiments. All animals were fed powdered Purina Lab Chow, with and without chloramphenicol‡ added in concentrations ranging from 0·5 to 2·0 per cent. Azauridine§ was added to the drinking water of

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