apparent as judged by clearances of creatinine, PAH, and total solute. Thus, the renal response to vagotomy was typical for increased ADH activity(7). Decreased osmolality of the plasma was present throughout the experiments; thus, stimulation of "osmoreceptors" was not a factor. It is unlikely that changes in activity of renal nerves, in activity of sub-cardiac efferent vagal fibers, or in respiration were responsible for the renal response to cervical vagotomy; antidiuresis occurred after cervical vagal section in animals with a denervated kidney, with vagi severed below the heart, or during continuous pump respiration.

Reports on bioassay of blood or plasma from non-hydrated dogs indicate increased antidiuretic activity after vagotomy(8,9). Present results agree with these findings and demonstrate their functional significance. Both types of investigation support the hypothesis of vagal control of ADH secretion.

Summary. 1. Prolonged inhibition of water diuresis occurred after bilateral cervical vagotomy in anesthetized dogs. 2. The urine became hypertonic to plasma, and the decline in urine flow was due solely to increased tubular reabsorption of solute-free water. 3. Glomerular filtration rate, renal plasma flow, and solute excretion did not change significantly.

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Effects of Adenosine Triphosphate on Ethionine-Induced Resorption.* (29223)

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Ethionine administration to the pregnant rat has been shown to produce a marked increase in fetal resorption(1). In an attempt to determine the role of ethionine in the initiation of the death and subsequent resorption of the fetus, studies from our laboratory have shown that ethionine is incorporated into the amino acid pool and into the proteins of the rat fetus and placenta and is associated with a fluctuation in methionine content of these tissues(2). However, these same studies indicate that the fetus may persist, apparently normally, with ethionine present in its proteins.

In recent studies on the mechanism of ethionine inhibition of protein synthesis, it has been shown that ethionine administration leads to a rapid fall in concentration of ATP in the liver, that this effect is counteracted by injection of ATP, and that administration of ATP to ethionine-treated rats counteracts the inhibitory effect of ethionine upon leucine incorporation into liver ribosomes(3).

The present study was undertaken to determine whether ATP administration would in a similar manner reverse the ethionine-induced resorption of the rat litter.

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TABLE I. Effects of Ethionine and ATP Administration on Pregnant Rat.

Treatment	No. of mothers		% fetuses resorbed		No. maternal deaths	
	E*	S†	E	S	E	S
300 mg ATP (1×)	18	7	97	20	0	0
300 mg ATP + 300 mg ATP (24 hr)	13	7	100	5	6	0
150 mg ATP + 150 mg ATP (6 hr)	12	8	90	20	1	0
Ethionine control	15	—	69	—	2	—
Saline control	—	8	—	4	—	0

* 300 mg ethionine in conjunction with treatment indicated.
† 0.85% saline in conjunction with treatment indicated.

Materials and methods. A single injection of 300 mg DL-ethionine (Nutritional Biochemicals) was administered on day 9 of pregnancy. Adenosine 5′-triphosphate (Sigma Chemical Co.), administered intraperitoneally or subcutaneously, was given in a single injection of 300 mg at the same time as the ethionine, in 2-300 mg injections 24 hours apart on days 9 and 10 of pregnancy, or in 2-150 mg injections administered 6 hours apart on day 9 of pregnancy. When 2 injections of ATP were administered, the first was always given at the same time as the single injection of ethionine. Both compounds were administered in 0.85% saline. Control animals received equal volumes of saline in place of ethionine and/or ATP. All rats were weighed daily, subjected to a laparotomy on day 12 of pregnancy, and autopsied on day 15 of pregnancy.

Results and discussion. The results (Table I) show that ethionine markedly increased the rate of resorption, bearing out previous work that has shown day 9 of pregnancy to be highly sensitive to the effects of ethionine (2). ATP alone appeared to induce a slight, but variable, increase in resorption. ATP, administered either subcutaneously or intraperitoneally, with ethionine, enhanced the ethionine-induced resorption of the litter and increased the toxic effect upon the mother. In all rats which resorbed completely, the resorption was advanced or complete by the time of laparotomy on day 12.

Our findings that ATP did not reverse ethionine-induced resorption, in contrast to findings that ATP can reverse ethionine effects in the liver(3), may be explained on the basis of the differences in time factors in the 2 experiments. The studies on the liver generally terminated 5 hours after injection of ethionine and/or ATP, while our first observations on the effects of ethionine and/or ATP upon pregnancy were made 48-72 hours after injection of the compounds.

Addition of adenine has been shown to maintain the ATP level of the liver of ethionine-treated rats for at least 3 hours after injection(3). Longer time studies have not been reported. Our previous work has shown that ethionine is present in the free amino acid pool of the fetus and amniotic fluid in substantial amounts 24 hours after injection (2). Therefore, injected ATP may remain in the tissues and fluids of the body long enough to reverse ethionine effects for a short time but the concentration does not remain high enough to counteract the levels of ethionine present up to 24 hours after injection.

Since we have found that the days of pregnancy after day 9 are much less sensitive to the effects of ethionine(2), we had hoped that our periods of injection of ATP would be sufficient to protect the pregnancy. Since this was not the case, it may be that the placenta is presenting a barrier to the passage of adenine or ATP or may be inactivating the ATP in some manner.

The fate of injected ATP is open to question since Bishop *et al*(4) found none in human plasma and suggested that little ATP crosses cell membranes. Its administration has been shown to enhance the teratogenic effect of cortisone in pregnant mice(5).

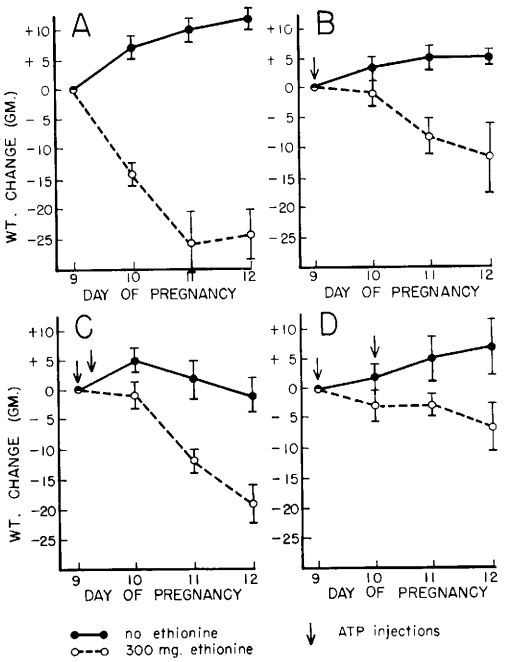

FIG. 1. Weight change in pregnant rats following injection of ethionine and/or ATP on day 9 of pregnancy. A, no ATP; B, single injection of 300 mg ATP; C, two 150 mg injections of ATP at 6 hr interval; D, two 300 mg injections of ATP at 24 hr interval. Mean ± standard deviation of mean.

Therefore, the observations to date on the effects of ATP or its metabolic products on pregnancy may indicate that the fetal and placental tissues handle or react to ATP in a manner different than other maternal tissues.

Further injections of ATP and ethionine will not be of value until we have determined the effects of ethionine and ATP on the cellular concentration of ATP within the fetus and placenta. These studies are now in progress.

The animals receiving ATP along with ethionine did not demonstrate the weight loss characteristic of ethionine treatment (Fig. 1). Since these animals showed greater resorption than those receiving ethionine only, this substantiates previous observations(6) that degree of weight loss associated with ethionine treatment cannot be correlated with degree of resorption. It may also be an indication that addition of ATP with ethionine may be of benefit to the maternal tissues and not affect or affect adversely the fetal tissues.

Summary. Administration of ATP with ethionine enhanced, rather than counteracted, the ethionine-induced resorption of the rat litter. ATP decreased the maternal weight loss caused by ethionine, thereby indicating a lack of correlation between maternal and fetal effects of the compounds.

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Correlation Between Kidney Muramidase* Activity and Plasma Iron Removal in Rats with Walker-256 Carcinosarcoma.† (29224)

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Muramidase activity in kidneys of rats with transplanted tumors is increased 2 to 12 times(1,2,3). Suu *et al*(4,5) found a similar large increase in kidney muramidase activity in irradiation chimeras. The highest level of enzyme activity was found in bone marrow, spleen and kidney. Because the

* Name for Lysozyme (E.C.3.2.1.17) recommended by Commission on Enzymes of International Union of Biochemistry.

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