Table 1

	Environment	
	Seawater	Diluted seawater
Urine volume, ml/hr x kg BW	0.38	1.35
GFR, ml/hr x kg BW	1.96	2.56
U/P, inulin	5.2	1.9
P_{osm}, mosmol/L	995	766
U_{osm}, mosmol/L	841	403
U/P_{osm}	0.85	0.53
$[P_u]$, mM/L	348	274
$[U_u]$, mM/L	94	142
U/P_u	0.27	0.52
Urea excretion, mM/hr x kg BW	0.04	0.19
P_u/P_{osm}	0.37	0.35
$[P_{na}]$, meq/L	266	234
$[U_{na}]$, meq/L	281	124
Sodium excretion, meq/hr x kg BW	0.107	0.17

tendant anion, accounted for a decrement in plasma osmolality equal to that accounted for by urea.

In the seawater group total plasma osmolality exceeds 2 x Na + urea by more than 100 mosmols/L. This osmolality gap is due for the most part to TMAO which in *Squalus acanthias* has a plasma concentration of about 74 mM/L (Cohen et al, Am. J. Physiol. 194:229, 1958). In the hypo-osmotic group the osmolality gap is nearly obliterated (see table) indicating that in the dogfish, as in the lemon shark (Goldstein, Am. J. Physiol. 215:1493, 1968) TMAO is preferentially excreted in the adjustment to a dilute environment.

Augmentation of renal excretion of urea, TMAO and salt and the lowered plasma concentration of these constituents were anticipated responses to the hypoosmotic challenge. Of greater interest is the finding that the dogfish nephron is capable of increasing its rate of free water excretion tenfold, a feat approaching the dilutional capacity of the mammalian kidney.

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METABOLIC CONTROL OF PYRIMIDINE SYNTHESIS IN THE OVARY OF *Squalus acanthias*

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Prior studies had demonstrated that dehydrogenase enzymes of the ovary of *Squalus acanthias* were activated by the administration of gonadotropins. In the endocrine tissues of mammals the dehydrogenase enzymes of the pentose phosphate pathway are intimately concerned with steroidogenesis and other aspects of cellular function including cell replication.

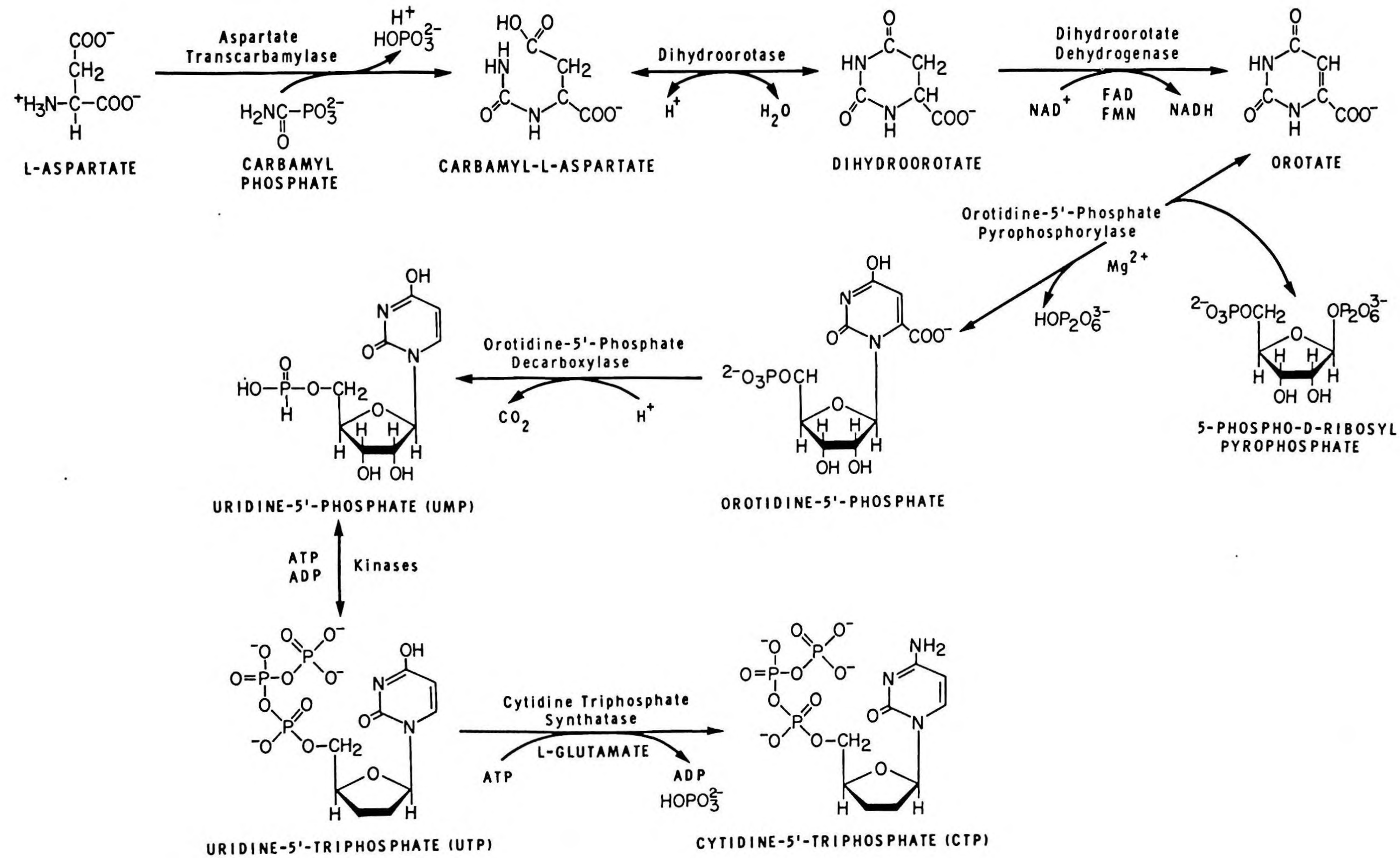
L-ASPARTATE
Aspartate Transcarbamylase
CARBAMYL PHOSPHATE
CARBAMYL-L-ASPARTATE
Dihydroorotase
DIHYDROOROTATE
Dihydroorotate Dehydrogenase
NAD+
FAD
FMN
NADH
OROTATE
Orotidine-5'-Phosphate Pyrophosphorylase
5-PHOSPHO-D-RIBOSYL PYROPHOSPHATE
OROTIDINE-5'-PHOSPHATE
Orotidine-5'-Phosphate Decarboxylase
URIDINE-5'-PHOSPHATE (UMP)
ATP
ADP
Kinases
URIDINE-5'-TRIPHOSPHATE (UTP)
Cytidine Triphosphate Synthatase
L-GLUTAMATE
CYTIDINE-5'-TRIPHOSPHATE (CTP)

Figure 1.

It was also found that gonadotropins such as follicle stimulating hormone and luteinizing hormone, by stimulating the activity of glucose-6-phosphate dehydrogenase, increase the rate of formation of 5-phospho-D-ribosyl pyrophosphate (5-PRPP) required for the synthesis of pyrimidines and purines. Purine and pyrimidine triphosphates are the components of RNA. It has been proposed that tropic hormone regulation of the genetic potential involves the pentose phosphate pathway with an increase in the rate limiting formation of 5-PRPP (K. W. McKerns, The Gonads, Chapter 6, New York: Appleton-Century-Crofts, 1969).

A study of pyrimidine synthesis was carried out in the 105,000 x g supernatant prepared from homogenates of dogfish ovaries. The mechanism of synthesis of uridine-5'phosphate (UMP) is apparent from Figure 1. Orotate labeled with ^{14}C in the carboxyl position was incubated with the supernatant fraction. The rate of UMP formation was monitored by the rate of formation of $^{14}CO_2$.

The following observations were made: The addition of preformed 5-PRPP greatly stimulated the rate of formation of $^{14}CO_2$ derived from ^{14}C-orotate. This demonstrates that this pathway exists in the dogfish ovary. Furthermore, an increased rate of formation of 5-PRPP was demonstrated when the pentose phosphate pathway was stimulated. This stimulation was accomplished by adding extra glucose-6-phosphate and $NADP^+$, showing that 5-PRPP could be derived from glucose-6-phosphate in the dogfish ovary. Preliminary experiments also indicated that FSH of mammalian origin stimulated glucose-6-phosphate dehydrogenase with the ultimate formation of UMP.

Specificity of the reaction was also demonstrated by the fact that azaorotate markedly inhibited the decarboxylation of orotidine-5'-phosphate and the stimulus due to added 5-PRPP or to the generation of 5-PRPP by activation of the pentose phosphate pathway.

In summary, formation of the purine and pyrimidine triphosphates required in DNA and RNA synthesis occur by pathways previously demonstrated for mammalian systems. The rate-limiting aspect of this synthesis would appear to be the rate of formation of 5-phospho-D-ribosyl pyrophosphate by the pentose phosphate pathway.