can be seen that the ^{14}C-urea activities in the CSF and choroid plexus water spaces equal that of the plasma within 30 minutes, and thereafter their relative activity is greater than that of the plasma. The significance of the value of 1.08 (see table) is not known at present. The brain tissue itself takes up tracer urea from the blood more slowly; however the tissue next to the CSF (labeled "inner" in the table) appears to equilibrate more rapidly than the deep tissue. This is probably the result of diffusion of ^{14}C-urea from the CSF into the adjacent tissue as well as direct uptake of tracer from the blood.

In another group of experiments the uptake of ^{14}C-urea by pieces of choroid plexus tissue incubated at 12-15°C was studied. The entry of tracer urea was exceedingly fast. The ratio of ^{14}C-urea in choroid plexus water to ^{14}C-urea in the medium was greater than one in two minutes and remained constant (ratio = 1.2-1.4) after ten minutes.

From these studies it appears that the transport of urea between blood and CSF is rapid and may be uphill. Urea exchange between blood and brain seems to be slower and not concentrative. Also, these studies and others to be reported in this journal suggest that urea moves freely between CSF and brain. This probably occurs by diffusion.

1968 #14

RELATION OF TRANSPORT COMPETITION TO CARRIER SATURATION IN THE ACTIVE SECRETION OF ORGANIC ACIDS BY THE AGLOMERULAR KIDNEY OF THE GOOSEFISH, *Lophius*

Roy P. Forster, Dartmouth College, Hanover, N. H.

Earlier transport studies on isolated flounder renal tubules showed that maximal transfer rates for various organic acids secreted by a common carrier differ, and that the more slowly transported compounds were relatively the more effective competitive inhibitors (Foster et al., J. Cell. Comp. Physiol. 44:315-18, 1954). These also had the tendency to accumulate intracellularly during transit across proximal tubule cells (Foster, R. P., and S. K. Hong, J. Cell. Comp. Physiol. 51:259-72, 1958). In the aglomerular kidney of *Lophius* the maximal tubular transfer rate (Tm) of p-aminohippurate (PAH) was found to be four times that of iodopyracet (Diodrast). However, when these transport competitors were presented simultaneously in equimolar concentrations with plasma levels of each sufficiently high to saturate the carrier system, the relative excretion rates were reversed with the iodopyracet transfer rate then four times that of PAH. The combined excretion rate was far below Tm_{PAH} alone, and roughly equal to Tm_I (Forster, R. P., and S. K. Hong, J. Gen. Physiol. 45:811-20, 1962). On this basis it appeared that iodopyracet had the higher affinity for the secretory mechanism, and the situation presumably was comparable to that of carrier-mediated transport of different sugars across the erythrocyte membrane under conditions approaching saturation of the transfer mechanism when penetration rates are proportional to K_m, i.e., inversely proportional to affinity for carrier.

The current preliminary studies were undertaken to observe the transport rates of these two organic acids measured separately, and simultaneously as competitors under conditions of equimolar loading, when there is low saturation of carrier at plasma levels less than that needed to achieve Tm values.

Chemical methods and techniques used in handling the fish were similar to those of the

1962 Lophius study except that urine here was obtained directly in chronic preparations by ureteral catheterization in order to shorten the collection periods and more accurately measure urinary volumes. Observations of excretion rates were made with falling plasma concentrations of iodopyracet and PAH subsequent to intramuscular injections of the compounds 3-4 hours before taking the first plasma sample and starting urine collections. In a typical experiment to determine iodopyracet plasma values needed to obtain saturation of the carrier mechanism 40 mg/Kg injection into a 4.2 Kg fish gave a plasma iodopyracet concentration of .04 μmole/ml at the midpoint of a 2.25 hr urine collection period during which the urine flow was 1.5 ml/Kg x hr. The iodopyracet excretion rate in this instance was 5 μmole/Kg x hr. The average Tm_I for three separate determinations on this animal was 6.25 μmole/Kg x hr, which is comparable to average values of 6.05, 5.62, and 5.51 μmole/Kg x hr for 3 fish in the 1962 series. Saturation of the iodopyracet transfer system occurred when plasma concentrations were approximately .02 μmole/ml, and when values fell below this there was a linear decline in excretion rates extrapolating to zero.

Far below saturation of the common carrier iodopyracet was found to be excreted more rapidly than PAH, either when each was presented alone or simultaneously in plasma concentrations lower than those needed to provide maximal transport rates. Thus, both at high saturation of carrier as noted in the 1962 series, and currently with low saturation the behavior of these transport competitors appears to obey Michaelis-Menton kinetics as discussed by Rosenberg and Wilbrandt (Exptl. Cell Research 9:49-67, 1955). Iodopyracet seems to have the higher affinity for the common carrier involved in the rate limiting step of this transcellular secretory process. At low saturation it would be predicted that transfer rates of various competitors would depend on the reciprocal of K_m and hence be proportional to the respective affinities; whereas with high saturation the rates of penetration would be proportional to K_m, i.e., inversely proportional to carrier affinity. The transport characteristics of PAH and iodopyracet at both high and low plasma levels comply with this interpretation.

The technical assistance of Gary Fouty is gratefully acknowledged. The project was supported in part by PHS grant HE-04457 and the Life Insurance Medical Research Fund.

1968 #15

THE ANATOMY, MICRO-ANATOMY, AND ULTRASTRUCTURE OF THE KIDNEY OF THE DOGFISH, Squalus acanthias

A. Masood Ghouse, Bahram Parsa, John W. Boylan, and James C. Brennan, Department of Pathology, Buffalo General Hospital, State University of New York School of Medicine, Buffalo, N. Y.

An increasing interest in kidney function in the spiny dogfish, Squalus acanthias, and the initiation of micropuncture studies in this experimental animal have prompted us to examine the microanatomy of its nephron. This was accomplished by a combined approach using light and electromicroscopy and microdissection.

Microdissection of the nephron of Squalus acanthias is more difficult than in mammalian kidneys because of its greater length, its more intricate coiling and looping, the intermingling of loops of one portion amongst loops of a separate but adjoining portion of the same nephron,