

Exit of Sulfanilic Acid and pAmino Hippuric Acid from Ventricular Fluid of the Dogfish

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Studies reported last year showed that Sulfanilic Acid (SA), given by repeated intramuscular injections for 100 hours, failed to enter Ventricular cerebrospinal Fluid (VF) to an extent greater than 20% of the plasma concentration. The half-time to achieve this 20% ratio was about 10 hours. ParaAminoHippurate, (PAH) on the other hand, approached a VF plasma ratio of 100% with a $t_{1/2}$ of about 50 hours. The relative exclusion of a compound indicates that some sort of active process is occurring to prevent the attainment of diffusion equilibrium. This year the exit rates of different concentrations of SA and PAH from the VF of the isolated perfused dogfish were determined. The dogfish was anesthetized with barbital. Fresh sea water ran into each spiracle via plastic tubing, perfused the gills and drained out the gill slits. The cranium was opened and 50-150 micro liters of drug solution at pH 7.4-7.8 were injected into the ventricular cavity with gentle barbotage. VF was then sampled at 30 sec. 15, 45, and 105 minutes and the concentration of SA or PAH was determined. At least 3 animals were used for each point in time with each drug concentration.

After 2.5 mg. of PAH, the exit half time was 110 min., after 2.5 mg. SA it was 85 min. When 0.2 mg. of drug was injected the half time's were 90 and 70 min. respectively. In a few experiments 3.0 mg Penicillin plus either 0.1 mg. PAH or SA was injected. Penicillin might be expected to compete with SA or PAH for a stereospecific transport system operating so as to remove drug from VF. Preliminary results indicated that the rate of disappearance of PAH and SA decreased by the penicillin.

These results do not exclude the possibility that SA and PAH might be removed from ventricular CSF by some stereospecific transport mechanism. Some mechanism, active in the broadest sense, must be operative since the exit rates are so much more rapid than the net entry rates.

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Permeability of the Blood-Cerebrospinal Fluid Barrier in the Dogfish to Sulfanilic Acid and pAminoHippurate

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Basic to the current hypotheses describing the blood-cerebrospinal fluid barrier is the supposition that this barrier is lipoidal in nature and is permeable to undissociated drug, but is impermeable to dissociated drug. This notion would be strengthened if it could be shown that a totally dis-