importance in determining the extent to which the molecule is actively transported, since uracil, 5-methyluracil (thymine), 5-fluorouracil and 5-bromouracil are all transported across the intestinal epithelium to a similar extent. On the other hand, since the hydrogen, fluorine and bromine atoms and the methyl group have Van der Waals radii of a similar magnitude (1·2–2·0 Å.)[8], it is possible that a considerably larger substituent would interfere with transport of the molecule. Investigations are now being made to determine the structural characteristics of pyrimidines which are required for active transport.

The results of this work suggest that anti-metabolites may not only compete with normal substrates for metabolic processes within the cell, but may also compete with these substrates for transport into the cell.

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Changes of Quantity of Flavin in the Brain after Peripheral Administration of Flavins

It has been reported from our laboratory[1] that flavins produce a change in the electroencephalogram, and that the effect produced by chlorpromazine is partly reversed by flavin adenine dinucleotide. These results suggest that the flavins act on the brain *in situ*. In an attempt to discover the mechanism of action of flavins, their penetration of the blood–brain barrier was examined by determining the amount of flavin in the rat brain after peripheral injection of flavins.

Flavin adenine dinucleotide was prepared by the method of Yagi *et al.*[2]. Flavin mononucleotide and riboflavin were purified chromatographically from commercial samples. Albino rats weighing about 100 gm. were used for the experiment. Fifty animals, 10 days after feeding under the same conditions, were divided into five groups, each group consisting of 10 animals. The animals of the first group were used as control, and injected with water intra-abdominally. Each animal of three groups was injected intra-abdominally with 20 mgm./kgm. (calculated as riboflavin) of flavin adenine dinucleotide, flavin mononucleotide, or riboflavin aqueous solution respectively. The animals of the fifth group were injected with 50 mgm./kgm. of an aqueous solution of riboflavin. One hour after the injection, a blood sample was collected from the carotid artery, and then the animal was killed by decapitation. The quantity of flavin in the brain was measured by the lumiflavin fluorescence method described by Yagi[3], and that in the blood sample was measured by the micro-method for riboflavin in blood described by Yagi *et al.*[4].

Table 1. Quantity of Flavin (calculated as Riboflavin) in Rat Brain after the Injection of Flavins (μgm./gm. of Wet Tissue)

	Means of population (n = 10), (α = 0·01)
Controls	3·32 ± 0·35
After the injection of:	
Flavin adenine dinucleotide (20 mgm./kgm.)	3·75 ± 0·69
Flavin mononucleotide (20 mgm./kgm.)	3·73 ± 0·85
Riboflavin (20 mgm./kgm.)	5·18 ± 0·74
Riboflavin (50 mgm./kgm.)	7·37 ± 0·87

The quantities of flavin in the brain after the injection of flavins are shown in Table 1. The variances in the normal cases were rather small, and the values were in good agreement with the earlier results[5]. After the injection of flavin adenine dinucleotide, the increase of flavin in the brain was significant by the t-test with $\alpha = 0{\cdot}1$. In the case of flavin mononucleotide, the increase was significant with $\alpha = 0{\cdot}2$. However, after the administration of 20 mgm./kgm. of riboflavin, flavin in the brain increased, the difference being significant even with $\alpha = 0{\cdot}01$. After the injection of 50 mgm./kgm. of riboflavin, further increase of flavin was observed.

The increases of flavins in blood at 1 hr. after the administration to each animal of 20 mgm./kgm. of flavin were almost equal for the three types of flavins, being less than 1 μgm./ml. of blood. Since the brain contains 0·024 ml. of blood per gm. on the average[6], the increase of flavins due to the blood content of the tissue was about 0·02 μgm./gm. The corrected amounts found by subtracting the values due to the blood from that of the tissue gave a similar result.

It seems, therefore, that the increase of flavin in the brain was due to the penetration of injected flavins from the blood into the brain tissue. It is considered that the flavins penetrate the blood–brain barrier, and that riboflavin can cross this barrier more easily than flavin mononucleotide or flavin adenine dinucleotide.

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Reversible Block of Axonal Conduction by Curare after Treatment with Cobra Venom and a Detergent

The recent experiments of Abbott, Hill and Howarth[1] have revealed that the remarkably high initial heat produced in nerve fibres coincides roughly with electrical activity. This finding re-emphasizes the necessity of explaining electrical activity on a chemical basis. Nachmansohn's theory[2] attributes the change of conductance which initiates the ion movements to the reaction of acetylcholine with a receptor protein. One of the main objections to this theory is the lack of effect of acetylcholine and curare on axons in contrast to their powerful action at junctions. This failure was attributed to the existence of structural barriers for lipid-insoluble quaternary ammonium