clude, therefore, that ingested NTA does not increase toxicity or teratogenicity of ingested methylmercury hydroxide in rats.

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Hexosaminidase-A and Hexosaminidase-B: Studies in Tay-Sachs' and Sandhoff's Disease

HUMAN tissues contain two isozymes of β-D-N-acetyl-hexosaminidase[1]. Hexosaminidase-A (hex-A) is thermolabile and moves toward the anode on electrophoresis at *p*H 6.0, and hexosaminidase-B (hex-B) is relatively thermostable and moves toward the cathode. In Tay-Sachs' disease, which is found predominantly in Jewish populations, hex-A is absent but hex-B activity is increased[2–5]. In Sandhoff's disease, a variant of Tay-Sachs' disease, found mostly in non-Jewish populations, both enzyme activities are missing[3,6]. Thus, while it is apparent that there is a genetic relationship between hex-A and hex-B, the nature of this relationship has remained obscure. It has been suggested that hex-A may be derived from hex-B by the addition of neuraminic acid residues[1,7].

We have now purified human placental hex-B to homogeneity and hex-A to a very high state of purity. Antibody production against hex-A and hex-B has made possible further knowledge of the relationship between these two enzymes and the diseases which occur in their absence. Our studies of the purified enzymes and the antibodies produced against them resulted in the following three findings, which must be taken into account in any genetic and biochemical model explaining the relationship between these disorders.

First, although incubating purified hex-A with *Clostridium perfringens* neuraminidase at 37° resulted in the formation of a new, thermostable band resembling hex-B in electrophoretic mobility, the same band was also formed at the same rate in the absence of neuraminidase. Either in the absence or presence of neuraminidase only 5 or 6% of hex-A was converted to the more cathodic enzyme.

Second, as previously reported[8,9], antiserum produced against hex-B reacted with both hex-B and hex-A. Similarly, antibody produced against hex-A reacted with both hex-B and hex-A. We have made a specific anti-hex-A antiserum by treating serum produced against hex-A with purified hex-B. The converse, however, is not true. Treatment of anti-hex-B serum with hex-A resulted in absorption of all antibody activity.

Third, immunoelectrophoresis against anti-hex-B (which reacts both against hex-A and hex-B) gave two distinct arcs with normal liver and with liver from a patient with Sandhoff's disease. These arcs corresponded to the position of hex-A and hex-B activity. Only one arc corresponding to hex-B was found with liver from two patients with Tay-Sachs' disease. After elution of non-precipitated proteins from the immunoelectrophoresis slides, the arcs formed with normal liver or the purified enzymes stain for hexosaminidase activity using 4-methylumbelliferone-β-D-N-acetyl-glucosamine substrate. In Tay-Sachs' liver, the single hex-B arc also stained for enzyme activity, but the arcs formed against liver from Sandhoff's disease were, of course, devoid of enzymatic activity.

Table 1 Immunoelectrophoresis of Hexosaminidase A and B from Normal Tay-Sachs' and Sandhoff's Disease Liver Samples

Liver sample	Before treatment with antiserum		After treatment with antiserum and elution			
	Enzyme activity corresponding to mobility of:		Arc corresponding to mobility of:		Arc stained for enzyme activity corresponding to mobility of:	
	Hex-A	Hex-B	Hex-A	Hex-B	Hex-A	Hex-B
Normal	+	+	+	+	+	+
Tay-Sachs'	0	+	0	+	0	+
Sandhoff's	0	0	+	+	0	0

Our findings are compatible with several models, but it seems unlikely that hex-B is merely the aneuraminyl derivative of hex-A. It seems more probable that hex-A and hex-B share a common subunit. Sandhoff's disease would result from a mutation of the active site of the common subunit and Tay-Sachs' disease from a mutation affecting a subunit present only in hex-A. Thus, hex-A may contain two different subunits $(\alpha\beta)_n$ while hex-B has only one of these subunits $(\beta\beta)_n$. This would explain the cross reactivity of antiserum produced against these two forms of enzyme, and the fact that a specific anti-A serum but not a specific anti-B serum can be produced. It also explains the increased amount of hex-B which is found in Tay-Sachs' disease, since uncombined β subunits would be available.

Details of these studies will be published elsewhere.

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Another View of Neutral Alleles in Natural Populations

JOHNSON[1] has suggested that the relationship observed between the actual and effective numbers of alleles in certain natural populations is not consistent with the selectively neutral allele model of Kimura and Crow[2]. We show here, however, that the data from a large number of natural populations are in fact compatible with this model.

If N is the effective size of a population, u the neutral mutation rate at a locus, n_a the actual number of alleles at the locus