"Amino Acids of the 21st Century" (8)
—THE ROLE REQUIREMENT AND FUTURE POSSIBILITIES FOR AROMATIC AMINO ACIDS (AAA) FOR A HEALTHY HUMAN BODY—

The aromatic amino acids, phenylalanine tryptophan and tyrosine are constituents of protein. In addition tyrosine is the precursor of the catecholamines, melanin and thyroid hormone (Figure 1) and tryptophan a precursor of the neurotransmitter serotonin (Figure 2). Quantitatively the amounts needed for catecholamine and thyroid hormone synthesis and for serotonin synthesis are small and hence dietary requirements are primarily to meet the needs for protein synthesis. Phenylalanine is irreversibly converted to tyrosine in the liver and kidney. Provided that there is no limitation in this conversion, dietary aromatic amino acid needs can all be provided as phenylalanine (which we have termed "maximum phenylalanine requirement"). Excess dietary tyrosine will limit the need for dietary phenylalanine to meet the needs for protein synthesis. Therefore by supplying an excess of tyrosine it is possible to determine the "minimum obligatory phenylalanine requirement". The concept of a maximum and minimum phenylalanine requirement is analogous to the concept of the maximum and minimum (in the presence of an excess of cysteine) requirements for methionine that we have reported recently. In vitro studies in mammalian liver have shown that, in the presence of an excess of exogenous tyrosine, tyrosine derived from phenylalanine hydroxylation is channeled within the hepatocyte directly to oxidation.

Fig. 1: PATHWAYS OF PHENYLALANINE AND TYROSINE METABOLISM

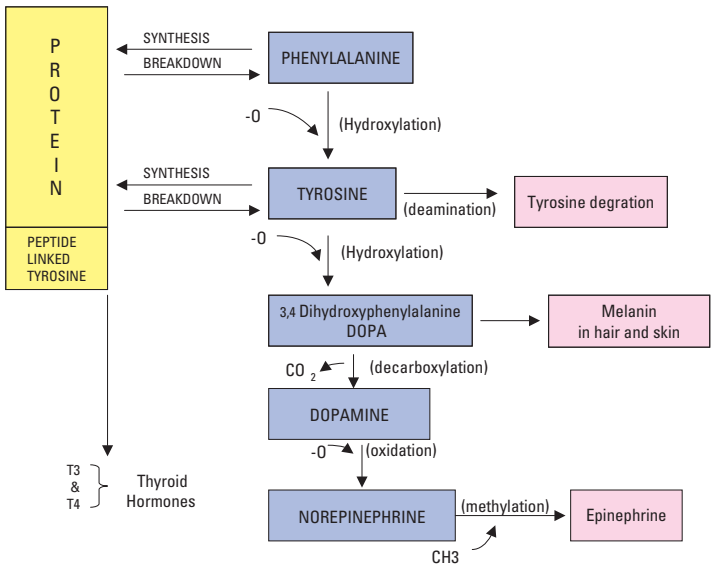
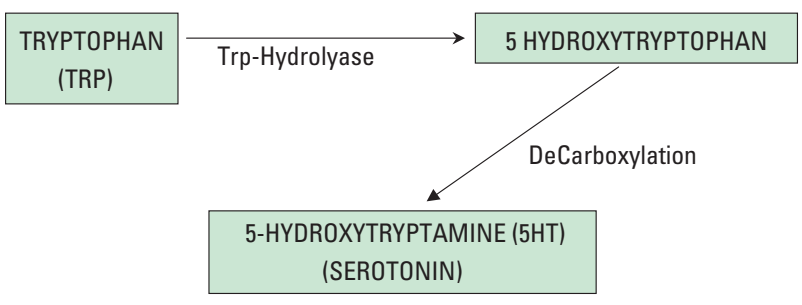


Fig. 2: CONVERSION OF TRYPTOPHAN TO SEROTONIN (5 HYDROXY – TRYPTAMINE)



AROMATIC AMINO ACID REQUIREMENTS

Amino acid requirements should be determined by feeding graded levels of the test amino acid across a range of intakes which includes the "predicted mean requirement level". In the recently published Dietary Reference Intakes for the Macronutrients it was agreed that the isotope oxidation methods are currently the preferred method to determine amino acid requirements. Further, it was agreed that the indicator amino acid oxidation (IAAO) model was the best approach. Earlier we determined the minimum phenylalanine requirement in the presence of an excess of tyrosine in adults to be 9 $mg.kg^{-1}.d^{-1}$. Since total aromatic amino acid requirements were not known we and others have conducted studies in adults using IAAO in which the only source of aromatic amino acids was phenylalanine. Consistent results have been obtained with an average maximal phenylalanine need (which covers the needs for phenylalanine plus tyrosine) of 42 $mg.kg^{-1}.d^{-1}$.

We have conducted similar studies using IAAO in children and to our surprise discovered that 6-10 year old children are unable to meet all of their tyrosine needs via phenylalanine hydroxylation. Hence amino acid based diets for this age group must contain tyrosine.

We have also determined tryptophan requirements using IAAO to be 4.0 $mg.kg^{-1}.d^{-1}$. To the present no parallel studies have been conducted in children. Recent reports on amino acid requirements in childhood have applied the factorial approach. This assumes that the maintenance requirement for amino acids is the same in children as it is in adults and indeed we have shown that to be the case for the branched chained amino acids and for the sulphur amino acids. To the maintenance value is added that required for growth. Aromatic amino acid requirement estimates are summarized in Table 1.

Table 1: Summary of the average aromatic amino acid requirements for healthy subjects

Age (y)	Phenylalanine* ($mg.kg^{-1}.d^{-1}$)	Tryptophan
0.5	76	9.5
1-2	57	6.4
2-10	47	4.8
10-14	47	4.8
14-18	45	4.5
> 18	42	4.0

* Sum of phenylalanine plus tyrosine (see text)

THE SPARING OF PHENYLALANINE BY TYROSINE

As mentioned above the minimum phenylalanine requirement has been defined as being 9.1 $mg.kg^{-1}.d^{-1}$. From the three studies of the maximum phenylalanine requirement which range from 38 to 48 $mg.kg^{-1}.d^{-1}$, the proportion of the total aromatic amino acid requirement that can be met by tyrosine ranges between 76 and 81%. In a separate study in which phenylalanine was set at the minimum phenylalanine intake of 9 $mg.kg^{-1}.d^{-1}$, protein synthesis was optimized at a mean tyrosine intake of 6 $mg.kg^{-1}.d^{-1}$. This suggests that for optimal protein synthesis that the optimal dietary ratio of phenylalanine and tyrosine in mass units is 60:40. It is of interest to note that this ratio is similar to that seen in human tissue.

PHENYLALANINE AND TYROSINE NEEDS IN PATIENTS WITH PHENYLKETONURIA (PKU)

Until recently the only estimates of phenylalanine requirements were clinical based in changes in plasma phenylalanine in response to alteration in dietary phenylalanine. We modified the IAAO model so that it was minimally invasive and could be used in children basically by sampling urine and breath. Using this technique in children with Phenylketonuria we shown them to have a mean phenylalanine requirements of 14 $mg.kg^{-1}.d^{-1}$ and a mean tyrosine requirement of 19 $mg.kg^{-1}.d^{-1}$ for a total mean aromatic amino acid requirement of 33 $mg.kg^{-1}.d^{-1}$. These estimates are for optimal protein synthesis and growth. It had earlier been suggested that patients with PKU might require higher intakes of tyrosine in order to optimize neurotransmitter function. However studies of mental functioning following supplementation of graded higher does of tyrosine showed no benefit and hence the tyrosine estimates for optimal protein synthesis of 19 $mg.kg^{-1}.d^{-1}$, appear reasonable.

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