

EXCRETION OF 5-S-CYSTEINYLDOPA IN THE URINE OF HEALTHY SUBJECTS

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Abstract. Seventy-six Caucasians, 30 men and 46 women, were investigated for the 24-hour excretion of 5-S-cysteinyldopa in the urine during the months of September to November, 1973. No subject had had strong sun exposure for \pm at least 4 weeks prior. A preliminary finding of a variation of 5-S-cysteinyldopa with season necessitated this precaution. The excretion varied between 9.0 and 242 μ g/24 hours. The mean value in men was 100 μ g/24 hours and in women 77.8 μ g/24 hours. Subjects with white hair had lower values than those with pigmented hair, but there was no other difference between the excreted amounts in subjects with differing hair colour. There was no variation with age when the subjects with white hair were excluded. No variation with weight or body surface was found. Excretion of dopa and dopamine determined together did not correlate with the excretion of 5-S-cysteinyldopa.

Key words: Cysteinyldopa; Amino acids, sulfur; Amino acids, diamino; Amino acids, dicarboxylic

It has recently been demonstrated that 5-S-cysteinyldopa is excreted in the urine of healthy subjects (1). This amino acid was first found in the tumour tissue of a human melanoma (4), and was also demonstrated in large amounts in the urine of patients with melanoma metastases (5). Increased urinary excretion of 5-S-cysteinyldopa seems to be an early and sensitive sign of melanoma metastases and determination of 5-S-cysteinyldopa has now become a routine investigation in the follow-up of patients with treated melanoma at our hospital.

The 5-S-cysteinyldopa urinary excretion reflects the pigment metabolism of the normal and pathological melanocytes. There are probably a number of factors which determine the excretion of 5-S-cysteinyldopa. Definition of such factors is in progress. In the meantime we have thought it of value to report the normal 24-hour values for 5-S-cysteinyldopa in the urine.

MATERIAL AND METHODS

Seventy-six Caucasian subjects between 18 and 91 years of age were investigated; 30 were males and 46 were females. All were living in or near Lund, Sweden. Any strong sun exposure that could have produced erythema antedated the investigation by at least 4 weeks, since we have preliminary observations indicating that 5-S-cysteinyldopa excretion varies with season and sun exposure. Some of the subjects in the higher age groups were taking medicines, e.g. for previous cardiac complaints and for hypertension, but all others were apparently healthy and without medication. Many subjects were excluded because fluorimetry of the urine revealed drugs or drug metabolites which could interfere with the determination of 5-S-cysteinyldopa. Salicylic acid, glutethimid, L-dopa and α -metyldopa were such drugs. The hair colour, weight and height of the subjects were recorded.

Urine was collected for 24 hours in the months of September to November, 1973. The urine was kept in plastic bottles containing 50 ml acetic acid and 1 g sodium metabisulphite. 5-S-cysteinyldopa was determined fluorimetrically according to a recently described method (6). Determination of dopa and dopamine was also performed (3).

RESULTS

The excretion of 5-S-cysteinyldopa varied between 9.0 and 242 μ g/24 hours (Fig. 1). The mean value of all subjects was 86.7 μ g/24 hours. It was higher in men than in women, 100 and 77.8 μ g/24 hours, respectively. The amount of 5-S-cysteinyldopa was not correlated with body weight or body surface as calculated from weight and height.

When 5-S-cysteinyldopa was related to the hair color of the subjects it was evident that those with white hair had lower excretion than those with pigmented hair. There was no statistically significant difference between subjects with red, blonde or dark hair (Fig. 2).

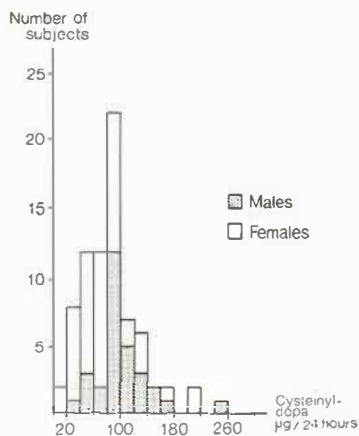


Fig. 1. 24-hour excretion of cysteinyl-dopa in the urine of healthy subjects, 30 men and 46 women.

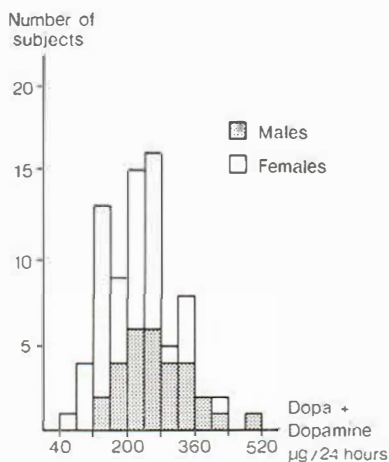


Fig. 3. 24-hour excretion of dopa and dopamine in the urine of healthy subjects, 30 men and 46 women.

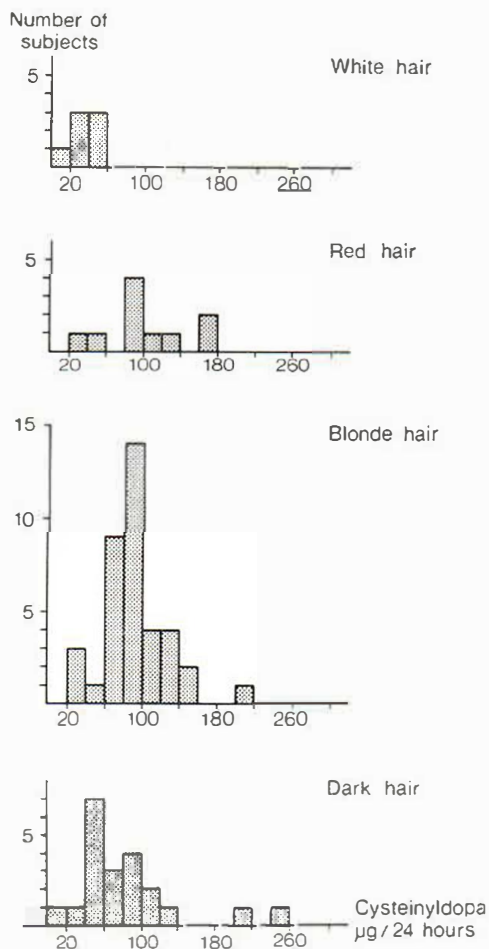


Fig. 2. 24-hour excretion of cysteinyl-dopa in the urine of subjects with differing hair color.

When the subjects with white hair were excluded, no correlation of 5-S-cysteinyl-dopa excretion with age was found. It should be noted, however, that only adults were investigated.

The sum of dopa and dopamine excretion is given in Fig. 3. There was no correlation between dopa/dopamine amounts and 5-S-cysteinyl-dopa excretion.

DISCUSSION

There was a wide range of variation in the urinary excretion of 5-S-cysteinyl-dopa. The values observed did not show a Gaussian distribution. It seems likely that several factors may be of importance in determining the excretion of 5-S-cysteinyl-dopa in the individual. The higher values observed in men may be due to a higher number of anagen hairs in this sex. The direct effect of sex hormones on the excretion of 5-S-cysteinyl-dopa, however, is not known and it is possible that the sex difference may represent a direct hormonal effect on pigment metabolism.

It has been found that the summer excretion of 5-S-cysteinyl-dopa is much higher than the winter excretion (2). This is probably related to solar exposure, but it is not known to what extent time lag after exposure influences the excretion. The importance of the complexion of the subject in this regard is also unknown. In our study no standardization of sun exposure was made, except that strong exposure did not occur for at least 4 weeks before the investigation.

When people with different complexions were compared, no difference in 5-S-cysteinyl-dopa excretion was found, but the occurrence of partially depigmented hair was not taken into consideration. The subjects with white hair only, most of them belonging to the higher age groups, had a lower excretion of 5-S-cysteinyl-dopa. It is reasonable to assume that the number of terminal hairs may be of importance for the 5-S-cysteinyl-dopa excretion, but in this study no assay was made to investigate the importance of this parameter.

No attempt was made to measure surface or volumes of pigmented nevi and lentigines in the subjects, but it can be assumed that the occurrence of pathologic melanocytes could have an influence on 5-S-cysteinyl-dopa excretion.

The absence of any correlation between the excreted amounts of dopa/dopamine and of 5-S-cysteinyl-dopa is not surprising since 5-S-cysteinyl-dopa is probably formed in melanocytes only, whereas dopamine, at least, should reflect in part the activities of the adrenergic nervous system.

Many patients with melanoma have so pronounced an increase in urinary excretion of this amino acid that they are easily differentiated from the normal group. In others the excretion values are less conclusive. For interpretation of the findings in these cases further studies of the effects of physiologic and pathologic pigment metabolism on 5-S-cysteinyl-dopa excretion will be necessary. Meanwhile, the observations in normals reported here will form a basis for our interpretation of findings in suspected malignant cases.

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