Circadian rhythm of the total hydroxyproline: creatinine ratio in urine


In a recent paper in *Clinical Science* Dr Wharton et al. (1973, 44, 359-365) found a significant correlation of both height and weight velocities with the total hydroxyproline: creatinine ratio (THP:Cr) in random urine samples from twenty-six adolescent boys. The validity of results obtained in random samples of urine is based on previous reports where THP:Cr of 24 h specimens was compared with the results obtained in spot samples from the same period. Howells, Wharton & McCance (1967) observed that the ratios were closely correlated ($r = 0.98; P < 0.001$). Younoszai, Kacic, Dilling & Haworth (1969) found a good correlation for low values, but at higher ratios the spread was greater.

### Table 1. Average circadian rhythm of total hydroxyproline (THP) excretion and THP : creatinine ratio in seventeen normal subjects

<table>
<thead>
<tr>
<th>Period</th>
<th>THP (%) of the mean 24 h value</th>
<th>THP:Cr ratio (mg/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>08.00-12.00 hours</td>
<td>91.9</td>
<td>20.0</td>
</tr>
<tr>
<td>12.00-16.00 hours</td>
<td>83.5</td>
<td>17.2</td>
</tr>
<tr>
<td>16.00-20.00 hours</td>
<td>87.6</td>
<td>17.9</td>
</tr>
<tr>
<td>20.00-24.00 hours</td>
<td>95.6</td>
<td>23.5</td>
</tr>
<tr>
<td>24.00-04.00 hours</td>
<td>119.1</td>
<td>27.2</td>
</tr>
<tr>
<td>04.00-08.00 hours</td>
<td>122.6</td>
<td>28.6</td>
</tr>
<tr>
<td>24 h specimen</td>
<td>100.0</td>
<td>22.4</td>
</tr>
</tbody>
</table>

However, THP excretion in normal adults follows a definite and reproducible circadian rhythm with peak excretion from midnight to 08.00 hours and lowest excretion from 12.00 to 20.00 hours (Mautalen & Casco, 1970). Furthermore, since creatinine excretion is higher during daytime than during the night THP:Cr was found to change significantly throughout the 24 h (Table 1).

Our findings on the circadian rhythm of THP:Cr could be reconciled with the close agreement found by Howells et al. (1967) and Younoszai et al. (1969) between random samples and 24 h specimens if the spot urine samples were mainly collected during the morning. At this time the average THP:Cr of normal subjects was similar to the average THP:Cr of the 24 h collection (Table 1).

Field studies based on the determination of THP:Cr should take into consideration the proved circadian periodicity of such an index in adults. Proper studies should be performed to determine the periodicity of THP:Cr in children. Meanwhile, it is advisable to collect spot
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urine samples at the same hour of the day, as was done by Wharton et al. (1973). The hour of collection should be recorded to permit adequate inter-laboratory comparison, a precaution not taken in the majority of the published studies (Whitehead, 1965; Howells et al., 1967; Crowne, Wharton & McCance, 1969; Younoszai et al., 1969).

References


Author's Reply

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We are grateful to Dr Mautalen for his interest in our paper. We agree with some, but not all, of the points he raises.

Three studies in children have shown a reasonable correlation of THP:Cr in random urines with that in 24 h collections (Howells, Wharton & McCance, 1967; Younoszai, Kacic, Dilling & Haworth, 1969; D. S. McLaren, personal communication). Urines in the first and third papers quoted were collected at differing times during the day (personal communications from authors). Some variation in THP:Cr in sequential urines does occur, however, in children (van Gemund, Vio & Giesberts, 1968; Mohanram, Anasuya, Rao & Srikantia, 1969; our own observations) and more so in adults (Mautalen & Casco, 1970). Hence in 1972 we commented 'for clinical purposes random samples from children are adequate. . . . As a safeguard it is wise to collect more than one sample and to collect always at the same time of the day' (Wharton, Gough, Williams, Kitts & Pennock, 1972). On reflection, it would have been more accurate to have labelled the urine sample as 'single' rather than 'random'. We agree that single samples are preferably collected at the same time each day and this should be stated.

Our study reported in this journal adequately confirms this comment since height and weight velocities correlated well with the THP:Cr in the single urines of the children. The significant coefficients of correlation were empirical observations; their validity in no way depended, as Dr Mautalen suggests, on the relationship of the ratios in 24 h collections to those in random sample.

It seems that for studies in children single timed samples of urine are adequate.