change in GFR has taken place than can be accounted for by normal day-to-day variation.

References


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Commentary

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Morris et al.,1 and Davies et al.,2 present almost identical data, but come to seemingly opposed conclusions about the value of plasma creatinine (Pcr) as an estimate of glomerular filtration rate (GFR) in children. The underlying principles need to be considered.

There is no single test that encompasses all aspects of renal function, but the glomerular filtration rate commands the greatest attention for it determines the filtered load presented to the renal tubules and thus the flexibility of the renal response to homeostatic requirements and, in the long run, decline in GFR is the principal functional abnormality underlying chronic renal failure.

The GFR has somehow to be viewed in relation to the child's size, and convention decrees that body surface area (SA) is the most appropriate reference standard as GFR/SA is constant over age 2 years, although McCance and Widdowson3 made a strong case for total body water, this being the domain over which the kidney exercises its homeostatic function. Tanner4 is required reading on the problem of per-weight and per-surface area standards, and describes situations 'where investigators had drawn positive conclusions not justified by their data, had been confused by a seemingly uninterpretable phenomenon in their data, had proposed a less effective and more biased normal standard in preference to a more effective and less biased one, had reduced a correlation between two physiological functions from a very high to a median value, and had invented a new clinical syndrome.' It does not inspire confidence that the best method of estimating SA in young children views them as an assembly of cylinders and spheres.5

The clearance of inulin remains the definitive estimate of GFR but is technically demanding; creatinine clearance exceeds GFR due to tubular secretion and is in any case a nuisance as timed urine collections are required. The clearance of 51-chromium edetic acid (51Cr-EDTA) is virtually equal to that of inulin, and a reasonable and convenient estimate of GFR can be obtained from the rate of fall of plasma concentration after intravenous injection. However, analysis of the plasma disappearance on a single compartmental model leads to an overestimate of GFR owing to the fact that the extracellular fluid is not an ideal 'well-stirred pool,' and there is delay in equilibration, necessitating what is known in the trade as the 'Chantler fudge factor.'6 It is therefore somewhat hazardous to assess other methods of estimating GFR by comparing them with the plasma clearance of 51Cr-EDTA.

Transformation of the clearance equation thus:

\[ P_{cr} = \frac{U_c V}{C_c} \]

indicates that the plasma creatinine concentration (Pcr) is directly proportional to creatinine excretion (UcV, and hence production) and inversely proportional to creatinine clearance (Cc, and hence GFR), and thus GFR should be predictable from Pcr if UcV is defined. However, creatinine production bears a complicated relationship to height (Ht) and weight (Wt).7 Theoretical arguments8 and empirical analysis9 indicated that GFR/SA correlated best...
with \( \text{Ht/P}_{\text{cr}} \). The theoretical arguments are rather tenuous, and the relationship between \( \text{Ht/P}_{\text{cr}}, \text{GFR} \), and SA are best analysed empirically.

In the two preceding papers both groups observed a better prediction of \( \text{GFR/SA} \) from \( \text{Ht/P}_{\text{cr}} \) if the GFR was reduced than if it was in the normal range: in part this arises from less accurate plasma creatinine determinations at lower concentrations with a greater proportional contribution from non-creatinine chromogens (even with the more specific reaction rate analysis), in part it is due to greater errors in GFR estimation from the plasma disappearance of \(^{51}\text{Cr-EDTA} \) at high clearances, and in part from the habit of looking at life from a linear rather than a logarithmic viewpoint, although in fact an error in estimate of GFR of 5 ml/min is much more significant if the true GFR is 15 ml/min than if it is 150 ml/min.

Davies et al.\(^6\) are concerned that the relationship between \( \text{GFR/SA} \) and \( \text{Ht/P}_{\text{cr}} \) is not linear, and that the correlation is not significant at all if analysis is confined to cases with GFR >90 ml/min per 1.73 m\(^2\) SA. The correlation coefficient will however inevitably be reduced if the analysis is restricted to only a segment of the population, but they do have a point: it might be better to undertake a multiple regression analysis of the relationship between the absolute value of GFR on the one hand and \( \text{Ht, Wt}, \text{and P}_{\text{cr}} \) on the other without getting caught up in the spurious calculations of surface area. Morris et al.\(^1\) robustly eschew any statistical hesitations and point out that if \( \text{Ht/P}_{\text{cr}} \) (cm/\( \mu \)mol) is <1.5 then GFR can be confidently predicted to be normal, whereas if >2.1, GFR will be abnormal; approximately the same conclusion can be inferred from Fig. 1 of Davies et al.\(^6\).

Thus the greater convenience of the plasma creatinine concentration as an estimate of GFR is purchased at the expense of some loss of the precision of more rigorous clearance methods, but remains much superior to the plasma urea concentration which, with its pronounced dependence on metabolic and nutritional factors, should now be abandoned as a test of renal function. The relationship between \( \text{Ht/P}_{\text{cr}} \) and \( \text{GFR/SA} \) will be distorted if there are abnormalities of muscle bulk—for example with emaciation—and remains to be analysed in the neonatal period and around puberty. The paediatrician needs to familiarise himself with the normal ranges of plasma creatinine concentration in childhood (Table),\(^10\)\(^11\) and to ensure that his chemical pathology laboratory is devoting adequate resources to an accurate and specific creatinine method.

## References


### Table 1 Plasma creatinine concentration (\( \mu \)mol/l) in healthy children

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Girls Mean ±2 SD</th>
<th>Boys Mean ±2 SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>31 22–40</td>
<td>36 18–54</td>
</tr>
<tr>
<td>3</td>
<td>37 23–51</td>
<td>40 21–59</td>
</tr>
<tr>
<td>5</td>
<td>40 21–59</td>
<td>44 25–63</td>
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<td>47 26–68</td>
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<td>9</td>
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<tr>
<td>13</td>
<td>55 33–80</td>
<td>60 30–90</td>
</tr>
<tr>
<td>15</td>
<td>59 20–98</td>
<td>67 23–97</td>
</tr>
</tbody>
</table>

Method: Technicon N-11 autoanalyser

Data from Schwartz et al.\(^9\)