sodium measurement. When direct potentiometric methods are used, the presence of hyperviscosity does not significantly influence the sodium value. With measurements using flame photometry and indirect potentiometry, pseudohyponatremia occurs. With indirect potentiometric measurements, a correction factor which can be used is 2 mmol/1 decrease in serum sodium for every centistoke increase in serum viscosity. This is linear, at least in our study to a serum viscosity of approximately 20 centistokes. With flame photometric measurements of serum sodium, no such correction factor can be meaningfully applied. For example, one patient with a serum viscosity of five centistokes had almost the same decrease in serum sodium as the patient with a viscosity of 15 centistokes.

It is essential that every laboratory report indicate the technique used for measuring serum sodium. Moreover, the clinician should also be aware of the methodology in use especially when different techniques are in use in the same laboratory.

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References


Tripeptidylcarboxypeptidase activity of angiotensin I converting enzyme in human serum

Angiotensin I converting enzyme (ACE) is considered as a dipeptidylcarboxypeptidase (EC 3.4.15.1). Two of us, however, were able to demonstrate that in hag lung and kidney, ACE also acts as a tripeptidylcarboxypeptidase. The possibility of enzymatic release of C-terminal peptides of substrates having a proline group in the penultimate position has never been shown in human serum but may induce new insights in the generation and deactivation of some vasoactive peptides—for example, des-Arg9-bradykinin.

With benzoyl-glycyl-l-seryl-l-prolyl-l-phenylalanine as a substrate we were able to demonstrate that human serum also contains this tripeptidylcarboxypeptidase activity. When examining normal human sera (n = 27) with a high resolution chromatography-assisted technique, a normal range of 13 μmol/min/l (SD ± 4) liberated benzoyl-glycine was shown. The tripeptidylcarboxypeptidase activity could be completely inhibited by 1 μmol/l captopril. Sera of four patients with active sarcoidosis were also examined. Since different studies have confirmed that active sarcoidosis is reflected in a high dipeptidylcarboxypeptidase activity of ACE, we thought it would be interesting to measure the tripeptidylcarboxypeptidase activity in four cases of active sarcoidosis with increased dipeptidylcarboxypeptidase activity of ACE, there was also significant increase in tripeptidylcarboxypeptidase activity (mean 27 μmol/min/l). Although the increase of ACE activity in sarcoidosis and other pathological conditions could still have been due to an isoenzyme, the results we obtained did not support this hypothesis.

This is the first observation in which the existence of a tripeptidylcarboxypeptidase activity of ACE in human serum is demonstrated under normal and pathological conditions. Therefore we would like to suggest the reconsideration of the trivial name of ACE.

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Assessing bone marrowcellularity

I was very interested in the recent report by Dr Al-Adhadh and Dr Cavill on the assessment of cellularity in bone marrow fragments. Some four years ago, I and my colleague, Mr W Slidders had shown the close correlation (r = 0·98) between our point-counting method and results from the Quantimet 720. In this paper, we devised a method to overcome the non-random distribution of fragments because of their different rates of sedimentation during fixation and processing.

Al-Adhadh and Cavill obtained a coefficient of variation (CV) between 8·2 and 34·7%. These authors felt that their result reflected the more likely level of reproducibility of the point-counting method than our CV of 2·6%. However, the crucial difference is that the method of
Al-Adhadh and Cavill was totally different from ours. They made no attempt to compensate for the non-random distribution of the fragments during fixation and processing. Indeed, the reason we devised a special method of sampling was because similar results to those of Al-Adhadh and Cavill were obtained without our method.

I agree with Al-Adhadh and Cavill that a wide range of marrow cellularity can be associated with any particular level of haemoglobin concentration in the peripheral blood. However, these authors' range of cellularity for normal Marrows (40–60%) is very narrow and may reflect the fact that only 10 subjects were studied. I have studied 25 such subjects (mean Hb ± SD = 14.6 ± 1.7 g/dl; mean WBC ± SD = 8.2 ± 2.1 × 10^9/l; mean platelets ± SD = 250 ± 50 × 10^9/l) and I have found a range for normal marrows of 30–70%. This result is consistent with those of Dunnill et al. who obtained a range of 20–70% in 95 subjects and Schroder and Tongaard. who found a range of 30–80% in 52 subjects.

Generally, an accurate measure of marrow cellularity has limited usefulness, however, it may have an important role in defining hypoplasia. Yet, it still should be remembered that the greatest value of any laboratory test is when it is interpreted with all the available information and not in isolation.

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References

Marrow cellularity and polycythaemia

We read with interest the recent paper by Lucie and Young and would like to make the following comments. The value of assessment of bone marrow cellularity in the diagnosis of polycythaemia vera has been raised by several authors. However, unlike the above paper, there has usually been a reasonable attempt to correlate the bone marrow appearances with other diagnostic criteria—for example, those of Modan and Lillienfeld or those of the Polycythaemia Vera Study Group. Most authors have emphasised the need for red cell volume measurements and normal arterial O2 saturation.

Objective measurement of cellularity in bone marrow sections is also important and has been attempted by some researchers. The application of point counting to marrow aspirate sections presents some problems due to the different rates of sedimentation of marrow fragments during processing and most authors (with the exception of one) have failed to take this into account. This problem does not, of course, arise with iliac crest trephine biopsies. In addition, Lucie and Young rightly state that there is variation in the iliac crest marrow cellularity with respect to age; however, if age (and sex) matched controls are used this can be overcome.

We, in Dundee, have been undertaking a prospective study of bone marrow morphology and morphometry in patients referred for assessment of erythrocytosis and so far have collected comprehensive data on approximately 40 such patients. Below are some preliminary results from 15 subjects (eight with unequivocally primary polycythaemia and seven with polycythaemia secondary to respiratory disease). None of the "secondary" group satisfied any of the diagnostic criteria of Berlin et al.

Bone marrow cellularity in patients (primary polycythaemia; 7 secondary polycythaemia) and age- and sex-matched controls

<table>
<thead>
<tr>
<th>Bone marrow cellularity (%)</th>
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<tbody>
<tr>
<td>Patient</td>
<td>Primary</td>
<td>Secondary</td>
</tr>
<tr>
<td>Bone marrow cellularity (%)</td>
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<td></td>
<td>Trpheine</td>
<td>Aspirate</td>
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<tr>
<td>Primary</td>
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<td></td>
<td>81-6</td>
<td>59-9</td>
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<tr>
<td></td>
<td>83-1</td>
<td>93-1</td>
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<td>85-6</td>
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<td>81-3</td>
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<tr>
<td></td>
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<td>35-5</td>
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<tr>
<td></td>
<td>83-9</td>
<td>53-5</td>
</tr>
<tr>
<td></td>
<td>87-6</td>
<td>61-2</td>
</tr>
<tr>
<td>Secondary</td>
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<td></td>
<td>43-8</td>
<td>50-8</td>
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<tr>
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<td>64-1</td>
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<td>49-8</td>
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<td>77-5</td>
<td>77-5</td>
</tr>
<tr>
<td></td>
<td>73-6</td>
<td>55-4</td>
</tr>
</tbody>
</table>

In some patients a trephine biopsy was not done (ND); in others, there was insufficient (Insuf) marrow aspirate for point-counting.

Bone marrow cellularity was assessed as previously described with age and sex matched controls as before. Results are shown in the Table. There is good correlation between the aspiration and trephine biopsy results (p < 0.05). In four cases (three primary, one secondary), there was insufficient marrow aspirate for a proper assessment of cellularity, and in these cases the trephine result has been used in the calculations. The marrow cellularity is significantly higher in the patients with primary polycythaemia compared with the age and sex matched controls (paired t test, p < 0.001), and the patients with secondary polycythaemia (unpaired t test, p < 0.001). There were no significant statistical differences (paired t test) between the patients with secondary polycythaemia and the age and sex matched controls.

Thus, using a method of assessing marrow cellularity which takes into account different rates of sedimentation of marrow fragments and when patients are selected with strict diagnostic criteria, there is significantly higher marrow cellularity in patients with primary polycythaemia.

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Letters to the Editor


References
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