PRENATAL DIAGNOSIS OF β-THALASSEMA MAJOR BY AMNIOTIC FLUID 6-AMINOLAEVULINIC ACID DETERMINATION

Sr,—The reported correlation between raised levels of 6-aminolaevulinic acid (ALA) in amniotic fluid and β-thalassaemia major in the developing fetus appears to offer a less hazardous procedure than fetoscopy and globin chain synthesis for the prenatal diagnosis of this disease.

Applying the reported procedure we collected amniotic fluid from 18 patients, 5 of whom were known to be potential carriers of an affected fetus. On testing for ALA in amniotic fluid by the cited colorimetric method, we found none of the samples to have a raised ALA level. However, 2 of the patients at risk were subsequently shown, by fetoscopy and globin chain separation, to be carrying an affected fetus. Using the more specific and sensitive technique of gas chromatography-mass spectrometry, we developed an ALA assay, and, with controls, we showed that the colorimetric method was satisfactory analytically. However, we did not see the correlation between amniotic fluid ALA levels and β-thalassaemia reported by Phadke et al.

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R. G. COOMBE

AMINOTERMINAL PARATHYROID HORMONE RADIOIMMUNOASSAY TO EVALUATE BONE STATUS IN RENAL FAILURE

Sr,—The clinical and biological significance of determinations of immunoreactive parathyroid hormone (iPTH) in plasma is controversial, particularly in patients in terminal renal failure, in whom the metabolic clearances of the different circulating fragments of PTH are considerably reduced. The aminoterminal fragment is the biologically active part of the molecule and its clearance is less impaired in renal failure than that of the carboxyterminal fragment. Thus assays which detect the aminoterminal iPTH should be more reliable for indicating the magnitude of PTH activity on bone cells.

A sensitive and homologous radioimmunoassay for the aminoterminal determinants of PTH, which differentiates well between euparathyroid and hyperparathyroid sera, has been developed in our laboratory. Using this assay, we have measured plasma iPTH levels in 51 patients (34 men and 17 women, aged from 18 to 71) being treated with chronic haemodialysis and with radiological signs of renal osteodystrophy.

Immunoreactive PTH was detected in all but 5 plasma samples, and the values ranged from 40 to 450 pg/ml. 12 patients had plasma values greater than 450 pg/ml. We have correlated these results with the histomorphometric data obtained for an iliac crest bone biopsy taken at the same time. The extent of the bone resorption surface (BRS) was estimated by counting the percentage of the bone surface occupied by active resorption processes. The extent of the bone formation surface (BFS) was estimated by counting the intersections with surfaces lined with active osteoblasts. Normal values are ≤4% for BRS and ≤8% for BFS.

Significant positive correlations were found between iPTH and BRS (r=0.004) and between iPTH and BFS (r=0.005). All the patients who had plasma iPTH levels above the normal range had BRS and BFS values higher than normal (see figure), a typical pattern.

SIR,—While agreeing with your calling for a re-examination of the conventional 5–10 day course of chemotherapy for acute urinary infections (Jan. 3, p. 26) I was surprised at the omission of the ultra-long-acting drug sulfadoxine from consideration as a single dose therapy. Like the pharmacologically similar agent sulfadiazine, sulfadoxine produced satisfactory cure rates in both acute urinary infections and in asymptomatic bacteruria in pregnancy with a single dose of 2 g. Bacteriuria in pregnancy is recognised as being less susceptible to cure than bacteriuria accompanying the acute dysuria/frequency syndrome—indeed better cure rates were achieved in the former by using 4 g (two 2 g doses 4 days apart) of sulfametopyrazine as opposed to 2 g, or by combining the more usual 2 g dose with a single dose of streptomycin.

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D. S. REEVES

HYPERCALCAEMIA IN HOSPITAL PATIENTS

SIR,—Dr Fisken and colleagues (Jan. 24, p. 202) provide interesting data on the symptoms, biochemical investigations, and final diagnoses of patients admitted to Queen Elizabeth Hospital, Birmingham, during 1979 who were found to have significant hypercalcaemia on biochemical "profiling". Two diagnoses accounted for 140 of the 153 patients—namely, malignant disease, which was usually clinically apparent, and hyperparathyroidism. Fisken et al. commented that mental changes were more common in hyperparathyroidism and that muscle weakness was more common in malignant disease. However, differences in the frequency of these symptoms in the two diagnostic groups are not significant (table).

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Malignancy (n=73)</th>
<th>Hyperparathyroidism (n=49)</th>
<th>p (x2 test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexia</td>
<td>64</td>
<td>39</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Constipation</td>
<td>58</td>
<td>20</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Weight loss</td>
<td>64</td>
<td>24</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bone pain</td>
<td>58</td>
<td>45</td>
<td>0.17</td>
</tr>
<tr>
<td>Muscle weakness</td>
<td>36</td>
<td>24</td>
<td>0.19</td>
</tr>
<tr>
<td>Mental changes</td>
<td>33</td>
<td>47</td>
<td>0.12</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>34</td>
<td>35</td>
<td>0.9</td>
</tr>
<tr>
<td>Polydipsia/thirst</td>
<td>43</td>
<td>49</td>
<td>0.6</td>
</tr>
<tr>
<td>Polyuria</td>
<td>29</td>
<td>37</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Malignant disease is not an expected, significantly more common in patients with malignancy, implying that the effects of the malignant process itself and of hypercalcaemia are additive. Although there are many causes of nausea and vomiting other than hypercalcaemia in the later stages of malignant disease, it is clearly important to measure serum calcium should these symptoms appear at any stage of the disease because they, like the other symptoms of hypercalcaemia, commonly respond to medical treatment. Significant hypercalcaemia may be masked by hypoalbuminaemia, both in malignancy and in hyperparathyroidism complicating another disease.

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FALSE POSITIVE ACETYLCHEOLINESTERASE GEL TEST

SIR,—Our one false positive in the qualitative amniotic fluid acetylcholinesterase (ACHE) test for the prenatal diagnosis of neural tube defects (NTD), out of around 1000 samples tested, resembles the two reported by Dr Bead and his colleagues (Feb. 7, p. 129), except that we repeated the amniocentesis, whereupon the second band had disappeared.

Our patient had an amniocentesis at 18 weeks because of a previous NTD; the alpha-fetoprotein (AFP) was normal (1.46 × median), but the gel test gave two clear bands, typical of an NTD, which were shown by the use of inhibitors to be a faster ACHE band and a slow cholinesterase (ChE) band. Our ACHE studies hitherto,6,7 have shown that when the ACHE and AFP findings conflict, it has always been the ACHE which is correct. However, because the scan (Prof. S. Campbell and Dr David Griffin) seemed normal, amniocentesis was repeated 2 weeks after the first. The AFP was again normal (1.6 × median), but there was only a single ChE band, as in normal pregnancies. In addition, there was a very faint cathodic band (one of a number of normal variants occasionally seen) present in both samples, suggesting that they came from the same patient. The pregnancy was regarded as normal and is proceeding to term.

A possible explanation for our finding is that, on the first occasion, the amniocentesis needle caused escape of maternal ACHE from the uterine wall into the liquor. Evidence that this might be comes from creative kinase studies (Dr D. C. Watts and Dr R. Edwards, personal communication) when amniotic fluid levels are occasionally found to be raised and isoenzyme analysis shows that smooth muscle and nerve type isozymes are present. This is avoided if the first few drops of amniotic fluid are discarded. Perhaps the same practice should always be used in amniocentesis to avoid any possible contamination from maternal sources.

We thank Mr C. J. Young for permission to publish details of his patient.

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SYMPTOMS IN PATIENTS WITH HYPERCALCAEMIA