Cryosupernatant in replacement therapy

possible that some clinically useful replacement could be provided if several units of cryosupernatant plasma were transfused. Clearly, cryoprecipitate would be required to rectify a major deficiency state.

From the data presented above cryoprecipitate supernatant appears to have a therapeutic potential that is currently not fully exploited. This may be of particular importance in areas where shortages of all forms of plasma proteins for transfusion restrict the quality of medical care.

We thank Dr J Giddings, Department of Haematology, University Hospital of Wales, Cardiff, for kindly donating the rabbit antihuman fibronectin.

References


Requests for reprints to: Dr JAF Napier, Welsh Regional Transfusion Centre, Rhydrafar, St Fagans, Cardiff, CF5 6XF, Wales.

Letters to the Editor

Columnar epithelial lined oesophagus (CELO) or Barrett's oesophagus: mucin histochemistry, dysplasia, and invasive adenocarcinoma

We were interested to read the recent article 1 which discussed the incidence and significance of type IIB intestinal metaplasia in biopsies from a series of symptomatic patients with columnar epithelial lined oesophagus (CELO). We have recently studied the mucosal appearances and mucin histochemistry in three patients with endoscopic and histological confirmation of CELO who also had dysplasia. Our findings, together with those of Peuchmaur et al 2 and those of Smith et al 3 in another recent study, strongly support a sequence of dysplasia, in situ carcinoma, invasive carcinoma in patients with CELO.

The clinical and pathological features of our three patients are summarised in the Table. Their ages and symptoms are similar to those of patients in other series, 4 and in all three patients the endoscopic appearances were non-specific. The entire mucosal surfaces of the two partial oesophagectomy specimens were embedded and examined histologically. Dysplasia in the positive biopsies and resection specimens was graded according to a standard classification, 5 which has also been used in other studies. 6,7 The mucin histochemistry was shown and classified as originally applied to CELO. 1,8

There was no evidence of invasive adenocarcinoma in any of the histological material examined from these patients. Analysis of the constituent mucin histochemistry showed type IIB intestinal metaplasia (sulphomucins in columnar cells) in all three patients. Although our findings may not be particularly surprising, we believe that they illustrate several points of interest with regard to CELO. Peuchmaur et al 2 suggest that type IIB intestinal metaplasia in CELO may represent a premalignant lesion. This is based on the observed high incidence of type IIB metaplasia in CELO, the recognised association between this type of metaplasia and adenocarcinoma of the stomach, and also the recently established premalignant character of CELO. The association between type IIB intestinal metaplasia and high grade dysplasia (including in situ carcinoma) is confirmed in our three patients (Table).

Clinical and pathological features of three patients with columnar epithelial lined oesophagus (CELO)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Symptoms (Duration)</th>
<th>Positive biopsy</th>
<th>Previous biopsy</th>
<th>Oesophagectomy Type of</th>
<th>CELO</th>
<th>Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>66</td>
<td>Dysphagia (2 years)</td>
<td>High grade dysplasia (in situ carcinoma)</td>
<td>Inflammatory (and ulcers)</td>
<td>Multiple inflammatory ulcers</td>
<td>IIB</td>
<td>Well, 4 months after operation</td>
</tr>
<tr>
<td>2</td>
<td>Male</td>
<td>69</td>
<td>Reflux (2 years)</td>
<td>High grade dysplasia (in situ carcinoma)</td>
<td>Inflammatory</td>
<td>Multifocal high and low grade dysplasia</td>
<td>IIB</td>
<td>Died 14 days after operation Necropsy showed bronchopneumonia; no evidence of carcinoma</td>
</tr>
<tr>
<td>3</td>
<td>Female</td>
<td>78</td>
<td>Dysphagia (4 years)</td>
<td>High grade dysplasia</td>
<td>No</td>
<td>Medically unfit for surgery</td>
<td>IIB</td>
<td>On a semi-solid diet; otherwise well</td>
</tr>
</tbody>
</table>


Requests for reprints to: Dr JAF Napier, Welsh Regional Transfusion Centre, Rhydrafar, St Fagans, Cardiff, CF5 6XF, Wales.
Peuchmair et al. also comment that dysplasia is rarely found in CELO; conversely, dysplasia is commonly associated with invasive adenocarcinoma arising in CELO. This subject has recently been discussed by Smith et al. They found dysplasia in all the resection specimens from a series of 26 patients who had invasive carcinoma arising in CELO. Low grade dysplasia was found in only three of the 26 resection specimens and Peuchmair et al. suggest that type IIB intestinal metaplasia could be regarded as a form of low grade dysplasia. We believe that our three cases provide further evidence, supporting that of other studies, for a sequence of reflux, CELO, low grade dysplasia (type IIB intestinal metaplasia), high grade dysplasia (including in situ carcinoma), invasive adenocarcinoma for the following reasons: (a) the association between low and high grade dysplasia in patients 1 and 2; (b) the association between type IIB intestinal metaplasia and high grade dysplasia in all three patients; (c) the absence of invasive adenocarcinoma in all three patients (although in patient 3 we base this assumption on biopsy material alone).

Our three patients were symptomatic and did not have invasive adenocarcinoma; however, Smith et al. re-emphasise that many patients with adenocarcinoma in CELO are asymptomatic and present late in the course of their disease. Furthermore, the medical "cure" of reflux symptoms does not equate with cure of reflux. The problems of following up patients with CELO, especially those who are asymptomatic, have been discussed previously. Our three cases emphasise the existence of clinically and endoscopically undetectable in situ malignancy in patients with CELO which may be diagnosed on biopsy or brush cytology and which is potentially curable by surgery. We also re-emphasise the value of mucin histochemistry in the early detection of type IIB intestinal metaplasia because the latter may act as a marker for reflux or mild dysplasia or both in patients with CELO.

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References


Replicated Kem-O-Mat gentamicin EMIT

Although we have stated that the manufacturers recommend duplicate analyses of blank control and clinical specimens for EMIT serum gentamicin assays on the Coulter Kem-O-Mat, we used single analyses in the interests of economy. We now present an assessment of the effect of replication on the results achieved by Kem-O-Mat gentamicin EMIT.

The findings are based on assaying four sera obtained from the United Kingdom National Control of Serum Aminoglycoside Assays programme. The Kem-O-Mat EMIT method was used to assay each specimen four times per run, and in total 20 runs were performed on separate days. A full set of standards was included in each run to construct a calibration curve. The blank control and the high and low control sera were assayed in duplicate on each run. Runs were assessed for acceptability by the standard practice of evaluating the calibration curve and control sera results. No runs were rejected as a result of this assessment.

The contribution made by between batch and within batch random error sources to the total random error of a test result is expressed as follows:

$$S_{TOT} = (S_b^2 + [S_w^2 + (r - 1)])^{1/2}$$

where $S_{TOT}$ is the total variation, $r$ the number of times a specimen is assayed, and $S_w$ and $S_b$ are respectively the intrinsic between batch and within batch random error variance components. The calculation of the $S_w$ and $S_b$ components from our quality control replication study is based on a component of variance analysis, the full details of which are described elsewhere. Krouwer and Rabonowitz discuss the undisturbed state of terminology in this area. We follow their recommendations, which are in line with strict statistical usage. Having established the $S_w$ and $S_b$ of a method it is possible to predict the total random error associated with a reported test value based on any given number of replicated assays (Table).

We found that adhering to the manufacturer's recommendations of replicated test analyses caused negligible increases in the time to process each specimen and technician time per specimen. The financial cost of replication was calculated by including the price of the kit, standards, control specimens, and all disposables but not technician time or capital equipment outlay.

Our results show that a major component of the total random error associated with the Kem-O-Mat gentamicin EMIT method is the between batch error variance component, which is largely a function of calibration errors. Therefore, little is gained in terms of reducing the total var-

<table>
<thead>
<tr>
<th>Specimen number</th>
<th>Cost per laboratory result</th>
</tr>
</thead>
<tbody>
<tr>
<td>662</td>
<td>877</td>
</tr>
<tr>
<td>$S_w$</td>
<td>0.25</td>
</tr>
<tr>
<td>$S_b$</td>
<td>0.13</td>
</tr>
<tr>
<td>$S_{TOT}$ (r = 1)</td>
<td>0.28</td>
</tr>
<tr>
<td>$S_{TOT}$ (r = 2)</td>
<td>0.22</td>
</tr>
<tr>
<td>$x$</td>
<td>1.62</td>
</tr>
<tr>
<td>UK value</td>
<td>1.6</td>
</tr>
</tbody>
</table>

$r$ = see text.

$S_w$ = between batch standard deviation.

$S_b$ = within batch standard deviation.

$S_{TOT}$ = total random error.

$x$ = mean specimen value after 80 analyses.

UK value = reference value given to specimen by the United Kingdom National Control of Serum Aminoglycoside Assays centre.

All values are $\mu g/ml$ of gentamicin.

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