A comparison of 13 guinea pig and human anti-tissue transglutaminase antibody ELISA kits

R C W Wong, R J Wilson, R H Steele, G Radford-Smith, S Adelstein

ORIGINAL ARTICLE

Aims: Tissue transglutaminase (tTG) is a major autoantigen recognised by IgA anti-endomysial antibodies (IgA EMA). Enzyme linked immunosorbent assays (ELISA) for IgA anti-tissue transglutaminase antibodies (IgA tTG) have therefore been developed as an alternative serological screening test to IgA EMA for coeliac disease (CD). The use of human tTG (h-tTG), as opposed to guinea pig liver tTG (gpl-tTG), in these assays has been reported to produce superior results. This study compared 13 commercial IgA tTG ELISA kits to ascertain their performance characteristics in the diagnosis of CD in patients with biopsy confirmed disease compared with controls. All patients and controls were adults aged 21 years or older.

Methods: Sera from the following groups of patients were tested in each kit: (1) 49 patients with CD confirmed on small bowel biopsies (all IgA EMA positive); (2) 34 patients with small bowel biopsies that were not consistent with CD; and (3) 30 patients with biopsy confirmed inflammatory bowel disease. All controls were negative for IgA EMA and were not IgA deficient. Sensitivities and specificities were determined using both the manufacturers’ recommended cut off points and receiver operating characteristic (ROC) analysis derived decision thresholds. The area under the curve (AUC) for each ROC plot was also calculated and compared between kits.

Results: In general, the h-tTG based IgA tTG ELISA kits demonstrated superior performance (especially specificity) compared with the gpl-tTG based kits, although 100% sensitivity and specificity (comparable to the IgA EMA assay) was obtained in only one recombinant h-tTG based kit.

Conclusions: The use of h-tTG in IgA tTG ELISA kits is generally, but not universally, associated with superior performance. Factors other than antigen source are important in determining kit performance.

Although many studies have concluded that the IgA tTG assay has comparable performance to the IgA EMA IIF assay, several have described false negative IgA tTG results in subjects with IgA EMA positive untreated CD, 4 10–16 18–19 22 24 26 28–30 32 33 36 38 and false positive IgA tTG results in the absence of IgA EMA and CD. 7 9 12–13 18 19 20–22 24 25 28–30 31 32 34 38 However, most of these studies used gpl-tTG, which has only about 81% homology with h-tTG. 10 In contrast, the use of h-tTG has been reported to be associated with fewer false negative and false positive results, and an overall performance closely comparable or equal to the “gold standard” IgA EMA IIF assay. 11–15 21 24 29 30 33 34 48 However, because none of these studies has compared gpl-tTG based ELISAs with two or more h-tTG-based ELISAs, it is unclear whether the use of h-tTG alone results in superior performance to the gpl-tTG-based assays.

We compared 13 commercial IgA tTG ELISA kits, seven gpl-tTG based and six h-tTG based (four recombinant h-tTG), in 49 IgA EMA positive adult patients with CD and 64 adult disease controls to establish the sensitivity and specificity of each
Comparison of anti-tTG ELISA kits

Table 1

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Source of tTG</th>
<th>Calcium activated</th>
<th>Serum dilution</th>
<th>Conjugate</th>
<th>Substrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>AESKULISA/Aesku.Lab Diagnostica (Wendelsheim, Germany)</td>
<td>Recombinant human</td>
<td>NS</td>
<td>1/100</td>
<td>30, 15</td>
<td>HRP antihuman IgA</td>
</tr>
<tr>
<td>The Binding Site (Birmingham, UK)</td>
<td>Guinea pig liver</td>
<td>Yes</td>
<td>1/100</td>
<td>30, 30</td>
<td>Rabbit HRP antihuman IgA</td>
</tr>
<tr>
<td>Eurospital S.p.A (Trieste, Italy)</td>
<td>Guinea pig liver</td>
<td>NS</td>
<td>1/25</td>
<td>60, 30</td>
<td>Sheep HRP antihuman IgA</td>
</tr>
<tr>
<td>Genesis Diagnostics (Littleport, UK)</td>
<td>Guinea pig liver</td>
<td>Yes</td>
<td>1/100</td>
<td>30, 30</td>
<td>Rabbit HRP antihuman IgA</td>
</tr>
<tr>
<td>Immunopharmacology Research Diagnostics (Catania, Italy)</td>
<td>Guinea pig liver</td>
<td>NS</td>
<td>1/100</td>
<td>30, 30</td>
<td>HRP antihuman IgA†</td>
</tr>
<tr>
<td>QUANTA Lite/Inova (Diagnostics Inc, San Diego, California, USA)</td>
<td>Guinea pig liver</td>
<td>NS</td>
<td>1/100</td>
<td>30, 30</td>
<td>Goat HRP antihuman IgA</td>
</tr>
<tr>
<td>Orgentec Diagnostika GmbH (Mainz, Germany)</td>
<td>Purified human NS</td>
<td>1/100</td>
<td>30, 15</td>
<td>Rabbit HRP antihuman IgA</td>
<td>TMB</td>
</tr>
<tr>
<td>Varelisa/Pharmacia &amp; Upjohn Diagnostics GmbH &amp; Co (Freiburg, Germany)</td>
<td>Recombinant human</td>
<td>NS</td>
<td>1/100</td>
<td>30, 30</td>
<td>HRP antihuman IgA</td>
</tr>
</tbody>
</table>

†In the manufacturer’s kit insert, alkaline phosphatase was mentioned under “Principle”, but HRP was mentioned under “Reagent supplied.”


tTG, tissue transglutaminase.

IgA tTG ELISA kit details

IgA EMA IIF assay

The IgA EMA assay was performed by IIF using cryostat sections of monkey oesophagus (The Binding Site, Birmingham, UK), as described previously at a screening dilution of 1/4. All slides were viewed by two independent observers and a positive or negative result was determined by consensus.

IgA tTG ELISA

The manufacturer’s instructions (table 1) were followed for all 13 IgA tTG ELISA kits. All specimens were tested in duplicate.

Bovine serum albumin and gelatin coated ELISA plates

To investigate the possibility of IgA anti-bovine serum albumin (BSA) antibodies producing false positive IgA tTG results, ELISA plates (Costar, Corning Inc, New York, USA) were coated with 250 µl of 5% BSA (Sigma Chemical Co, St Louis, Missouri, USA) or 1% gelatin (Bio-Rad, Hercules, California, USA). Serum diluted 1/100 in Tween/phosphate buffered saline was incubated for one hour at room temperature. After three washes, horseradish peroxidase (HRP) labelled goat antihuman IgA (Sigma Labs, Melbourne, Australia), at a dilution of 1/500, was added and the plates were incubated for one hour (room temperature). ABTS (2,2′-azino-bis-3-ethylbenzthiazolin-6-sulphonic acid) substrate (Medical Innovations, Sydney, Australia) was added for 15 minutes, and absorbances read at 405 nm.

Cut off values

Both the manufacturers’ recommended cut off values and decision thresholds determined by receiver operating characteristic (ROC) plots (see below) were used to calculate the sensitivity and specificity of each assay/kits. The IBD controls
were not used in the calculation of specificity because some had not undergone small bowel biopsy to exclude CD.

**ROC plot analysis**

ROC plot analysis was performed on each kit using the Accuroc software package (Accumetric Corporation, McGill University Health Centre, Montreal, Quebec, Canada) to determine a decision threshold and area under curve (AUC) estimation. The IBD controls were not included in the ROC analysis because some had not undergone small bowel biopsy to exclude CD. The AUC was calculated using the trapezoid rule. Comparisons between the AUCs of each kit were performed by the non-parametric method for correlated samples, as previously described by DeLong et al.

**RESULTS**

The IgA tTG values of the patients with CD and the non-CD and IBD controls measured with the 13 kits are shown in fig 1 (gpl-tTG based kits) and fig 2 (h-tTG based kits) with corresponding ROC curves and AUC estimations. The numbers of sera from patients with CD, and the non-CD and IBD controls that were positive in each assay, using both the manufacturers' and ROC analysis derived decision thresholds, are shown in table 2 (gpl-tTG based kits) and table 3 (h-tTG based kits), with corresponding sensitivities and specificities. Table 4 shows the AUC comparisons between kits, with a significant difference denoted by a p value of < 0.05.

The recombinant h-tTG based Varelisa (Pharmacia & Upjohn Diagnostics, GmbH & Co, Freiburg, Germany) and
purified erythrocyte h-tTG based QUANTA Lite (Inova Diagnostic Inc, San Diego, California, USA) kits performed best, with sensitivities of 100% and 98%, specificities of 100% and 100% (using the manufacturers’ cut off values), and AUC estimations of 1.000 and 1.000, respectively (fig 2; table 3).

Of the seven gpl-tTG based kits (fig 1; table 2), the QUANTA Lite kit performed best, with 86% sensitivity and 100% specificity using the manufacturer’s cut off value of 20 arbitrary units/ml, and an AUC of 0.987. Applying the ROC analysis derived decision threshold of 14.1 arbitrary units/ml improved sensitivity to 92% but reduced specificity to 97%.

Figure 2 IgA anti-tissue transglutaminase (tTG) antibody values of the patients with coeliac disease (CD), and the non-CD (SBX) and inflammatory bowel disease (IBD) controls in the six human tTG based enzyme linked immunosorbent assay (ELISA) kits, with corresponding receiver operating characteristic (ROC) curves and area under curve (AUC) estimations. The solid lines represent the manufacturers’ recommended cut off values and the broken lines represent the ROC plot analysis derived decision thresholds. (A) AESKULISA (Aesku.Lab), (B) The Binding Site, (C) Eurospital, (D) QUANTA Lite (Inova), (E) Orgentec, (F) Varelisa (Pharmacia & Upjohn).

<table>
<thead>
<tr>
<th>Table 2</th>
<th>IgA EMA and IgA tTG results in patients with CD and controls using the manufacturers’ cut off points and ROC plot analysis derived decision thresholds for the seven guinea pig liver tTG based ELISA kits</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assay type/Manufacturer</strong></td>
<td><strong>Manufacturer’s cut off point</strong></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>IgA EMA IIF/The Binding Site</td>
<td>1/4</td>
</tr>
<tr>
<td>Guinea pig liver tTG based ELISA/The Binding Site</td>
<td>4 U/ml</td>
</tr>
<tr>
<td>Guinea pig liver tTG based ELISA/Eurospital</td>
<td>5 AU</td>
</tr>
<tr>
<td>Guinea pig liver tTG based ELISA/Genesis Diagnostics</td>
<td>10 U/ml</td>
</tr>
<tr>
<td>Guinea pig liver tTG based ELISA/ImmuLisa</td>
<td>20 EU/ml</td>
</tr>
<tr>
<td>Guinea pig liver tTG based ELISA/Immunopharmacology Research Diagnostics</td>
<td>25 AU</td>
</tr>
<tr>
<td>Guinea pig liver tTG based ELISA/QUANTA Lite</td>
<td>20 units/ml</td>
</tr>
<tr>
<td>Guinea pig liver tTG based ELISA/Medizyme</td>
<td>25 U/ml</td>
</tr>
</tbody>
</table>

Results equal to or greater than the cut off/threshold were considered positive. Specificity was calculated using only the non-CD controls (see text). AU, arbitrary units; CD, coeliac disease; ELISA, enzyme linked immunosorbent assay; IBD, inflammatory bowel disease; IgA EMA, IgA anti-endomysial antibody; IgA tTG, IgA anti-tissue transglutaminase antibody; IIF, indirect immunofluorescence; NA, not applicable; tTG, tissue transglutaminase; ROC, receiver operating characteristic.
To exclude the possibility that some reactions to tTG were really reactions to blocking agents used in the ELISA kits, anti-BSA and antigelatin antibodies were determined (data not shown). Sera from one IBD control and two patients with CD reacted significantly on the BSA coated ELISA plates, suggesting the presence of IgA anti-BSA antibodies. However, none of the non-CD controls reacted significantly on the BSA coated plates, and no sera reacted on the gelatin coated plates.

**DISCUSSION**

In this comparison of 13 commercial IgA tTG ELISA kits, we found that the human tTG based kits tested generally demonstrated superior performance (especially specificity) to the gpl-tTG based kits (tables 2, 3). However, the use of h-tTG alone was insufficient to confer performance equal to the IgA EMA IIF assay, because only two h-tTG based kits (recombinant h-tTG based Varelisa and purified erythrocyte h-tTG) produced closely comparable results to the IgA EMA IIF assay, because only two h-tTG based kits (recombinant h-tTG based Varelisa and purified erythrocyte h-tTG) produced closely comparable results to the IgA EMA IIF assay, because only two h-tTG based kits (recombinant h-tTG based Varelisa and purified erythrocyte h-tTG) produced closely comparable results to the IgA EMA IIF assay. Furthermore, two of the gpl-tTG based kits (Quanta Lite and Eurospital (Trieste, Italy)) had AUC values really reactions to blocking agents used in the ELISA kits.

**Table 3** IgA EMA and IgA tTG results in patients with CD and controls using manufacturers’ cut off points and ROC plot analysis derived decision thresholds for the six human tTG based ELISA kits.

<table>
<thead>
<tr>
<th>Manufacturer’s cut off point</th>
<th>ROC plot analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cut off</td>
<td>CD (sensitivity) Non-CD controls (specificity)</td>
</tr>
<tr>
<td>IgA EMA IIF/The Binding Site 1/4 49/49 (100%) 0/34 (100%) 0/30 NA NA NA NA</td>
<td></td>
</tr>
<tr>
<td>Human tTG based ELISA/AskuLab 15 U/ml 35/49 (71%) 0/34 (100%) 0/30 4 U/ml 47/49 (96%) 0/34 (100%) 1/30</td>
<td></td>
</tr>
<tr>
<td>Human tTG based ELISA/The Binding Site 4 U/ml 48/49 (98%) 3/34 (91%) 1/30 6 U/ml 47/49 (96%) 1/34 (97%) 0/30</td>
<td></td>
</tr>
<tr>
<td>Human tTG based ELISA/Eurospital 7 AU 47/49 (96%) 4/34 (88%) 0/30 9 AU 47/49 (96%) 1/34 (97%) 0/30</td>
<td></td>
</tr>
<tr>
<td>Human tTG based ELISA/QUANTA Lite 20 U/ml 48/49 (98%) 0/34 (100%) 0/30 16 U/ml 48/49 (98%) 0/34 (100%) 0/30</td>
<td></td>
</tr>
<tr>
<td>Human tTG based ELISA/Orgentec 10 U/ml 49/49 (100%) 5/34 (85%) 1/30 11 U/ml 49/49 (100%) 2/34 (94%) 0/30</td>
<td></td>
</tr>
<tr>
<td>Human tTG based ELISA/Varelisa 5 U/ml 49/49 (100%) 0/34 (100%) 0/30 4 U/ml 49/49 (100%) 0/34 (100%) 0/30</td>
<td></td>
</tr>
</tbody>
</table>

Results greater than or equal to the cut off/threshold are considered positive. Specificity was calculated using only the non-CD controls (see text). AU, arbitrary units; CD, coeliac disease; EMA, enzyme linked immunosorbent assay; IBD, inflammatory bowel disease; IgA EMA, IgA anti-endomysial antibody; IgA tTG, IgA anti-tissue transglutaminase antibody; IIF, indirect immunofluorescence; NA, not applicable; tTG, tissue transglutaminase; ROC, receiver operating characteristic.

**Table 4** Comparisons between AUC estimations.

<table>
<thead>
<tr>
<th>Assay type/Manufacturer</th>
<th>Cut off</th>
<th>CD (sensitivity)</th>
<th>Non-CD controls (specificity)</th>
<th>IBD controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guinea pig liver tTG</td>
<td>0.406</td>
<td>0.908</td>
<td>0.073</td>
<td>0.034 *</td>
</tr>
<tr>
<td>Binding Site</td>
<td>0.049</td>
<td>0.286</td>
<td>0.128</td>
<td>0.166</td>
</tr>
<tr>
<td>Eurospital</td>
<td>0.094</td>
<td>0.115</td>
<td>0.014 *</td>
<td>0.016 *</td>
</tr>
<tr>
<td>Genesis</td>
<td>0.018</td>
<td>0.020 *</td>
<td>0.018</td>
<td>0.026</td>
</tr>
<tr>
<td>Immunco</td>
<td>0.031</td>
<td>0.166</td>
<td>0.026 *</td>
<td>0.013</td>
</tr>
<tr>
<td>Medizyme</td>
<td>0.016</td>
<td>0.066</td>
<td>0.023 *</td>
<td>0.008 *</td>
</tr>
<tr>
<td>Organitec</td>
<td>0.014</td>
<td>0.008</td>
<td>0.023</td>
<td>0.026</td>
</tr>
<tr>
<td>Varelisa</td>
<td>0.198</td>
<td>0.029</td>
<td>0.023 *</td>
<td>0.024</td>
</tr>
<tr>
<td>Asku Lab</td>
<td>0.143</td>
<td>0.026</td>
<td>0.024 *</td>
<td>0.026</td>
</tr>
</tbody>
</table>

These findings raise the important issue of contaminants in gpl-tTG,24 25 30 which may contain other hepatic proteins.22 23 On sodium dodecyl sulfate-polyacrylamide gel electrophoresis, the gpl-tTG extract (Sigma T5398; Sigma Chemical Co) used in several gpl-tTG based ELISAs5 6 11 13 15 17 19 22 26 28 32 34 38 contains multiple bands in addition to the 82–83 kDa tTG band,24 25 31 which only accounted for about 30% of the total protein.25 30 This may be partially overcome by further purification steps, and should be less of an issue with recombinant h-tTG.24 25 31

However, three of the six h-tTG based kits (two recombinant h-tTG based) evaluated also produced false positive results in the absence of IgA EMA and CD, as previously reported.11 13 14 15 24 27 Therefore, other explanations for false positive results are required.

“**The methods used to extract and purify tissue derived tissue transglutaminase (tTG), produce and process recombinant tTG, and then coat tTG on to ELISA wells may lead to alterations in the tertiary structure of tTG**”

More false positive IgA tTG results were detected in the non-CD controls compared with the IBD controls. A possible explanation may be the presence of IgA anti-BSA antibodies in some of the non-CD control sera, reacting with the BSA used as a blocking agent in some kits.11 However, Lock and colleagues10 did not detect significant IgA anti-BSA antibodies in two disease controls tested, and significant IgA anti-BSA antibodies were not demonstrated in our non-CD controls.

False negative results were found in six of the seven gpl based and five of the six h-tTG based kits in IgA EMA positive patients.
patients with CD (figs 1, 2; tables 2, 3), in agreement with previous reports. 4-10-16 25-26 30-32 14-18 19-23 24-25 28-30 32-34 36-38 30-32 34-36 38 40-46 48 49-52 54-56 58 60 The methods used to extract and purify tissue derived tTG, produce and process recombinant tTG, and then coat tTG on to ELISA wells may lead to alterations in the tertiary structure of tTG. Therefore, conformational epitopes may be lost or formed, with a loss leading to a reduced ability of tTG to bind IgA tTG, thus explaining some of the false negative results. 49-51 Furthermore, the formation of conformational neoepitopes may also result in false positive results (see above).

The function and tertiary structure of tTG is also altered by the presence of ionised calcium. 46 It has been suggested that antibody binding epitopes may be formed or hidden by the presence of ionised calcium in the coating buffer of the IgA tTG ELISA. 46-66 Sulkamen and colleagues' reported that the pretreatment of tTG with calcium ("calcium activation") dramatically improved the separation between CD and non-CD sera in a gpl-tTG based ELISA, and also increased the binding affinity of tTG to CD sera. However, in our study, the two kits in which the use of "calcium activation" of tTG is recorded (Binding Site gpl-tTG kit and Genesis) did not clearly demonstrate superior performance to the other kits. Furthermore, Lock and colleagues' found that the addition of calcium to the coating buffer increased both the signal and background values, and therefore produced no overall improvement in the performance of their in house gpl-tTG based IgA tTG ELISA. Nakachi and colleagues' also reported that the autoantibody binding sites of tTG were formed in a manner that was essentially calcium independent.

Finally, we found that the performances of most of the IgA tTG ELISA kits were significantly improved by adjusting the cut off values/decision thresholds via ROC plot analysis. These discrepancies between the ROC analysis derived decision thresholds and manufacturers' recommended cut off values illustrate the importance of cut off point revalidation by laboratories, using appropriate samples from their referral population.

ACKNOWLEDGEMENTS

We acknowledge K Smithers (Central Sydney Immunology Laboratory, Royal Prince Alfred Hospital) for excellent technical assistance; the Australian distributors of the commercial IgA tTG kits for the generous provision of their kits for assessment in this study; and P Hobson (Department of Immunology, Sullivan Nicolaides Pathology, Brisbane, Australia) for providing some of the sera for the study and performing some of the assays.

REFERENCES

New JCP online submission and review system

We are pleased to inform authors and reviewers of the new online submission and review system at JCP. Developed by High-Wire Press (CA, USA), Bench Press is a fully integrated electronic system that utilises the web to allow rapid and efficient submission of manuscripts. It also allows the peer review process to be conducted entirely online. We are one of the first journals in the BMJ Special Journals group to go online in this way. The aim, apart from saving trees, is to speed up the often frustratingly slow process (for both authors and editors) from submission to publication. Many reviewers might appreciate this too.

The system is very easy to use and should be a big improvement on the current peer review process. Full instructions can be found on Bench Press http://submit-jcp.bmjournals.com and JCP online at http://www.jclinpath.com. Please contact Natalie Davies, Project Manager, HYPERLINK mailto:ndavies@bmjgroup.com for any further information.

H Holzel, P van Diest
A comparison of 13 guinea pig and human anti-tissue transglutaminase antibody ELISA kits
R C W Wong, R J Wilson, R H Steele, G Radford-Smith and S Adelstein

doi:

Updated information and services can be found at:
http://jcp.bmj.com/content/55/7/488

These include:

**Supplementary Material**
Supplementary material can be found at:
http://jcp.bmj.com/content/suppl/2002/09/19/55.7.488.DC1

**References**
This article cites 44 articles, 6 of which you can access for free at:
http://jcp.bmj.com/content/55/7/488#BIBL

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Errata**
An erratum has been published regarding this article. Please see next page or:
/content/55/10/800.2.full.pdf

**Topic Collections**
Articles on similar topics can be found in the following collections
- Immunology (including allergy) (1664)
- Clinical diagnostic tests (805)
- Inflammatory bowel disease (40)
- Small intestine (45)

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/
This established classification of the acute erythroleukaemias is based partly on the old FAB criteria and also upon morphological, cytochemical, and immunophenotypical criteria. All bone marrow aspirates demonstrate ≥ 50% erythroid precursors, with erythroid dysplasia. Dysplasia of the granulocytic and megakaryocytic cell lines may or may not be present. The M6a subtype is defined as ≥ 30% blasts of the non-erythroidic component (FAB exclusion criteria); the M6b subtype is defined as ≥ 30% promonoblasts of the erythroidic elements; and the M6c subtype has ≥ 30% blasts and ≥ 30% promonoblasts by the aforementioned exclusion criteria. Because the dysplastic changes may, at times, make definitive characterisation of the blasts as erythroidic versus non-erythroidic difficult, the morphological features must always be confirmed by cytochemical stains, immunohistoch- echemical stains, and/or flow cytometric analysis.

These three separate subtypes must be distinguished from one another to provide useful prognostic information for the clinician and the patient. When treated with the standard myeloid protocol, the M6a and M6c subtypes demonstrate a very high remission rate, whereas most patients with the M6b subtype remain refractory to treatment. Notably, patients with the M6b subtype remain in remission for a significantly shorter time than the M6a group. Mean survival for these subtypes is: M6a, 31.4 (SD, 32) months; M6b, 3.13 (SD, 4.2) months; M6c, 10.5 (SD, 12.7) months.

The malignant clonal cell of origin manifesting as acute erythroleukaemia of any subtype appears to be a multipotential stem cell, which shows varying degrees of erythroidic and granulocytic lineage maturation. Therefore, the three distinct subtypes of acute erythroleukaemia are not three separate diseases, but rather represent a spectrum of the same disease. The poor remission rate and short survival characteristic of this disorder are dependent upon: (1) a high pronormoblast to myeloblast ratio within diagnostic bone marrow aspirates, (2) a high proliferative index, (3) “unfavourable” cytogenetic aberrations, and (4) a high incidence of P-glycoprotein expression (the multidrug resistance phenotype).

F M Mazzella
Medical College of Georgia, Augusta, 30912–3695 Georgia, USA; fmazzella@mail.mcg.edu

H R Schumacher
University of Cincinnati Medical Centre, Cincinnati, 45367 Ohio, USA

References

CORRECTIONS