**Pseudoleucocytosis and pseudothrombocytosis due to cryoglobulinaemia**

Erroneously high blood counts, measured by the Coulter Model S plus phase IV blood counter, may be caused by artefactual particulate matter, such as platelet clumps, epidermal cells, dust or small air bubbles.\(^1\) Cryoglobulins are immunoglobulins of one or more classes that precipitate on cooling below 37°C to form globules. This phenomenon is most prominent at 4°C, though it occurs to a lesser degree at higher temperatures. Pseudoleucocytosis due to cryoglobulinaemia has long been recognised,\(^2\) but the phenomenon of pseudothrombocytosis due to cryoglobulinaemia has not been previously reported.

**Case report**

A sixty year old West Indian woman presented with menorrhagia in March 1986. A full blood count on a Coulter Counter S plus phase IV showed a haemoglobin concentration of 13·5 g/l, with an increased leucocyte count of 46·9 \times 10^9/l and a platelet count of 464 \times 10^9/l. The red cell count was within normal limits at 5·24 \times 10^{12}/l. Examination of the peripheral blood film and manual white cell and platelet counts did not corroborate the automated results. The peripheral blood film showed small translucent globules dispersed among the red cells. Cryoglobulinaemia was suspected, and the sample was reprocessed at varying temperatures. This showed a progressive increase in the leucocyte and platelet counts when the sample cooled on standing (figure). The plasma viscosity using a Luckham clinical viscometer was 2·9 cPs, at 37°C but was greater than 5 cPs at 4°C. Donath-Lehmann cell counts showed a progressive decrease in the leucocyte and platelet counts when the sample was cooled.

**Leucocyte and platelet counts on whole blood with falling temperature. There is progressive increase in both leucocyte and platelet counts when sample is cooled.**

- • White cell count: ○ ○ ○ platelet count.

Landsteiner and direct Coomb’s tests yielded negative results. The total serum protein concentration was 83 g/l with an albumin concentration of 40 g/l. Electrophoresis showed the presence of a monoclonal band of IgM containing \(^7\) light chains. IgM measured at 37°C was 16·0 g/l, and at 4°C was 10·0 g/l. There was no immune suppression. Urinary Bence-Jones protein reaction was negative. Bone marrow aspirate and a trephine biopsy showed gross infiltration with small lymphoid cells, with some plasmacytic differentiation consistent with Waldenstrom's macroglobulinaemia.

**Table Comparison of cell counts on plasma and serum with falling temperature**

<table>
<thead>
<tr>
<th>Temperature</th>
<th>White cell count (\times 10^9/l)</th>
<th>Platelet count (\times 10^9/l)</th>
<th>Red cell count (\times 10^{12}/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Plasma</td>
<td>Serum</td>
<td>Plasma</td>
</tr>
<tr>
<td>37°C</td>
<td>0·2</td>
<td>0·1</td>
<td>90</td>
</tr>
<tr>
<td>30°C</td>
<td>0·3</td>
<td>0·1</td>
<td>90</td>
</tr>
<tr>
<td>20°C</td>
<td>42·7</td>
<td>0·2</td>
<td>776</td>
</tr>
<tr>
<td>4°C</td>
<td>85·6</td>
<td>58·5</td>
<td>1125</td>
</tr>
</tbody>
</table>

**Discussion**

Cryogoblins form particles of various sizes ranging from 3–24 µm when they precipitate.\(^3\) The Coulter Counter Model S plus phase IV is an electronic blood counter, which operates on the principle of an impedance change being produced by particles passing through a small aperture. It usually measures particles ranging from 2 fl to 450 fl (Instruction Manual, Coulter Model S, 1983.) Our findings showed interference in whole blood counts in the 2 fl and 35 fl regions, the smaller particles being counted as platelets and the larger ones as leucocytes. As expected, the spurious platelet and leucocyte counts were greater in plasma than in serum. Emori et al\(^3\) described a case of pseudo-leucocytosis due to cryoglobulinaemia, in which they attributed the spuriously increased leucocyte count to the particle formation between cryoglobulin and fibrinogen.

Previous reports of pseudoleucocytosis caused by cryoglobulinaemia have been on counts performed on older models of blood counters without the ability to report platelets.\(^2\) With the advent of the Coulter S plus series and the additional availability of automated platelet counts, pseudo-thrombocytosis should now also be detected. Leucocytosis and thrombocytosis, unsubstantiated by examination of a peripheral blood film and manual counts, should raise the suspicion of cryoglobulinaemia.

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Letters to the Editor

References


Some preliminary studies on low incidence of infant botulism in the United Kingdom

Since the first recognition of infant botulism in 19761 over 500 cases have been reported worldwide, more than 95% of which have occurred in the United States. There has been one reported case in the United Kingdom.2 About one third of all cases occurred in babies known to have eaten honey.3 Several surveys4–6 in the United States on the incidence of *Clostridium botulinum* in honey have shown that up to 10% of retail samples (principally American produce) were contaminated with the organism. There have also been reports7,8 of the presence of *C botulinum* in post mortem faecal specimens from infants who had died suddenly and unexpectedly (sudden infant death syndrome, SIDS).

In view of these findings we felt it worth while to investigate the incidence of *C botulinum* in honey, either produced in or imported into this country, and to determine whether any deaths in infants diagnosed as SIDS could be attributed to *C botulinum* intoxication.

Honey samples on sale in the United Kingdom from 16 countries, excluding the United States, were examined for *C botulinum* using a combination of dilution and centrifugation9 and membrane filtration.9 The technique was validated using a naturally contaminated honey sample provided by Dr SS Arnon, Department of Health Services, California, United States, and could detect one *C botulinum* type B spore per 5 g honey. *C botulinum* was not detected in a 20 g portion of 122 samples examined.

Specimens of faeces (n = 97), ileocejunal contents (n = 34), and heart blood (n = 34) from 97 cases of SIDS, and specimens of faeces (n = 27) and serum (n = 7) from 27 cases of suspected infant botulism were examined by standard procedures.1,9 Neither *C botulinum* toxin nor the organism were found in any of the specimens examined.

*C botulinum* has been found in honey only in the United States to date, except for a single case in Canada.3 This may reflect a more common occurrence of the organism in the American environment, although this is difficult to substantiate. Variations in the numbers of spores in the environment have been suggested as a reason why some states in America have a very low incidence of infant botulism.11 It seems unlikely that increased clinical awareness of the disease in the United States would account for the difference in reported international incidence.

One of the many theories concerning some cases of SIDS proposes that the syndrome is a clinical manifestation of infant botulism in its most severe form.12 If this were the case then it is not surprising that none of the specimens examined from the SIDS cases in this study was positive, as infant botulism in this country is extremely rare. The two conditions may not be linked, however, as Swiss workers9 found that 15% of SIDS cases were associated with the presence of *C botulinum* or its toxins, yet Switzerland has a very low incidence of infant botulism. We are continuing the investigation of cases of SIDS in this country for the presence of *C botulinum*.

Although *C botulinum* intoxication is very rare in the United Kingdom, it would seem prudent to avoid potential risk factors, such as feeding honey to infants under 12 months of age12 especially as a good deal of honey is imported into this country.

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References


Bios = life

Alas, I had on two occasions to write to one of your predecessors to remind him that a biopsy after death is, by definition, an impossibility. I note in the paper by Cairns et al all that three references to the impossible have escaped the present editorial eye.

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Reference


Professor Stanin replies:

Dr Penman is correct—and the editor nodded. This is particularly comprehensible for he (GS) performed the necropsy.
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