enough to be well embedded with epoxy resin. After embedding the pieces of specimen, it was not difficult to trim off the calcified bone trabeculae and cut thin sections for TEM. Moreover, three-dimensional structure of the marrow specimen could also be studied by observing the cryofractured planes with the scanning electron microscope.

The role of electron microscopy in the field of human marrow aspiration cytology has been well established. Using the technique described in this report, electron microscopy can now be extended to histology of human marrow biopsy specimens.

We thank Professor Ryuichi Kikawada for his constant interest and encouragement. The technical assistance of Mr Shichiro Miyazawa and his colleagues is gratefully acknowledged.

References

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Letters to the Editor

Photographic recording of the ESR

In the article “An automated method for recording the Westergren erythrocyte sedimentation rate,”1 King, et al describe a method of recording the ESR photographically. The principle is not new and photography was used for this purpose many years ago. In the collection of old and obsolete medical laboratory instruments housed at Colchester and under the aegis of the Joint Working Party of the R C Path and the IMLS is an instrument (photograph) on which is stamped: “The Lee Sedimentometer, 1760/15, AL Hawkins Ltd, London W1.” It consists of a holder for a sedimentation tube, to one side of which is a frosted glass window and a source of light. On the other side is a long, narrow, rectangular tube, completely enclosed except for a long slit in the far wall. Beyond this slit and the wall is a clockwork movement, wound by a key in a light-proof container. This carries an old-type photographic plate slowly across the slit presumably in an hour, thus recording the ESR as the cells fall and

The Lee Sedimentometer
light reaches the plate. It is quite an ingenious device. I am not sure how old it is but I think it could have been made before the First World War. I have no information on it and would be pleased to hear from anyone who could enlighten me on the instrument, its date, its inventor Lee or the manufacturing or supplying firm of AL Hawkins Ltd, London. Another machine "The Sedigraph" made by a Swiss firm after the Second World War acted in a similar fashion with rather more sophistication. One of these instruments is also in the collection.

The collection of old instruments now numbers about 1000 items which, it is hoped, will form a valuable asset in the new Medical Department of the Science Museum. If anyone has such instruments or apparatus that are no longer required I should be glad if they would get in touch with me.

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Reference


False positive latex tests for cryptococcal antigen in cerebrospinal fluid

The detection of cryptococcal polysaccharide antigen in CSF or serum is an essential part of the laboratory diagnosis of cryptococcosis with a positive result having diagnostic, prognostic, and therapeutic value. The latex test for cryptococcal antigen detection was originally described by Bloomfield et al1 and either the original test or a subsequent modification, using sensitised charcoal particles,2 are widely used.

This report emphasises the occurrence, significance and subsequent elimination of false positive latex tests for cryptococcal antigen in cerebrospinal fluid (CSF), and their association with the presence of rheumatoid factor.

METHODS AND PATIENTS

The technique used in our laboratory for detecting cryptococcal antigen has been described elsewhere3 and is essentially a modification of the original method.1 The organism used to sensitise rabbits by intravenous route for the production of specific antiglobulin is a serotype A strain of Cryptococcus neoformans. Sera, but not CSF causing agglutination of sensitised latex particles are treated with 0.01 M dithiothreitol (DTT) and the test is repeated. However we have recently noted a number of false-positive CSF cryptococcal latex tests (LA) (Table). When CSF was pretreated with 0.01 M dithiothreitol (DTT) all three positive tests became negative however this procedure had no effect on eight culture proven positive CSF samples. In addition two patients (2 and 3) had similar false-positive LA titres in serum, 1/5 and 1/25 respectively, which were also eliminated by pretreatment with DTT. In all these patients rheumatoid factor (Eosin latex test, Difco, Michigan) was present in CSF as well as serum.

DISCUSSION

False-positive4 5 as well as false-negative6 LA tests for cryptococcal antigen have been described previously. Bennett and Bailey,7 for instance, reported that 9.5% of 252 specimens of serum and cerebrospinal fluid from patients with presumed cryptococcosis showed false-positive responses. In the majority of cases these reactions were seen in serum samples. However, they noted that certain patients with low titre CSF latex tests had negative complement fixation tests for cryptococcal antigen. It has been suggested that rheumatoid factor (RF) or similar substances are responsible and their activity can be eliminated by dithiothreitol (DTT).7 The latter substance splits IgM molecules of RF and prevents the subsequent agglutination of globulin-sensitised particles. Dolan8 has also reported false-positive reactions in serum (2.8%) and CSF (1.4%). The sera gave positive reactions using particles coated with non-immune rabbit globulin.

Both IgG and IgM rheumatoid factors have been demonstrated in CSF in the rare complication of rheumatoid disease, pachymeningitis,9 probably as a result of local synthesis. Alternatively serum RF may diffuse through inflamed meninges,10 Sarcoidosis, lymphoma and systemic lupus erythematosus, which have all been associated with cryptococcosis, may involve the meninges. They are also amongst a group of disorders which may have low titres of serum RF10 and it is not inconceivable that the latter may cross the blood-brain barrier under certain circumstances. Hence we are reporting these cases to emphasise the occurrence of false-positive cryptococcal LA tests in CSF as well as serum which can be removed with DTT and which may be associated with the presence of rheumatoid factor. We suggest that where it is not routine practice already, CSF samples as well as serum positive for cryptococcal antigen by latex test should be treated routinely with DTT.

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References


Results of latex tests for cryptococcal antigen

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
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<td>LA*</td>
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<td>30</td>
<td>M</td>
<td>Rheumatoid arthritis</td>
<td>1/10</td>
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</table>

* Latex agglutination test for cryptococcal antigen.
† Latex test for cryptococcal antigen pretreated with dithiothreitol.