A Red Herring in the Detection of Bence-Jones protein

In about 20% of patients with myelomatosis there is no circulating paraprotein, and the demonstration of Bence-Jones proteinuria becomes a crucial part of the diagnostic process (Hobbs, 1971). The following case illustrates the importance of using adequate technical methods.

A woman aged 55, who had been on steroids for asthma for many years, presented with a two-year history of back pain, and pathological fractures of the femur and two thoracic vertebrae. There was radiological evidence of focal osteolytic bone disease and of generalized osteoporosis. She had proteinuria, and was thought to have multiple myelomatosis possibly with renal amyloidosis.

The total plasma protein concentration was 5.6 g/100 ml and albumin 3.0 g/100 ml. Electrophoresis of the plasma proteins showed no evidence of a paraprotein band. The γ-globulin was decreased, and the immunoglobulin concentrations were IgG 450 mg/100 ml, IgA 121 mg/100 ml, and IgM 70 mg/100 ml. A bone marrow biopsy showed no abnormality of the plasma cells or lymphocytes.

A concentrated dark-brown early-morning urine specimen contained protein. The heat test for Bence-Jones protein (Jones, 1847) was carried out at pH 4.9 under the conditions of ionic strength recommended by Putnam, Easley, Lynn, Ritchie, and Phelps (1959). A moderate precipitate had appeared after heating at 56° for 15 minutes, indicating the presence of Bence-Jones protein. When the urine was boiled the density of the precipitate increased, but no precipitate reappeared when the hot filtrate was allowed to cool. The stained urine protein electrophoresis strip showed a generalized proteinuria, together with a sharp 'paraprotein' band in the slow α1 position.

Since a normal bone marrow biopsy does not exclude the presence of myelomatosis, the evidence at this stage was thought to indicate that the patient had a dedifferentiated myeloma producing only light polypeptide chains, and that the protein behaved in an anomalous fashion in the heat test. However, no paraprotein could be detected when the urine was examined by immunoelectrophoresis. Antiserum to κ and λ-light polypeptide chains showed the presence of normal immunoglobulins only. When the electrophoretic separation of the urinary proteins on cellulose acetate membrane was examined before staining, the 'paraprotein' band was seen to be a faint reddish-brown, and staining with a peroxidase stain, o-tolidine/hydrogen peroxide, showed that this was a haem protein.

The patient died of a pulmonary embolism shortly after these investigations were completed, and postmortem examination (Dr D. G. F. Harriman) showed numerous deposits of a reticulum cell sarcoma.

The many variations of the heat test for Bence-Jones protein are unsatisfactory as screening procedures because of a failure rate of up to 33% (Hobbs, 1966). False positives may be given by a high concentration of γ-globulins, or, as shown here, by haemoglobin. The insolubility of haemoglobin at 57° at pH 5.28 is, in fact, the basis of a method for separating it from carboxyhaemoglobin (Whitehead and Worthington, 1961). The most sensitive methods for the detection of Bence-Jones proteinuria are electrophoresis of the concentrated urine followed by immunoelectrophoresis (Hobbs, 1966).

It is important to bear in mind that mild haemoglobinuria can both give a positive heat test and appear as a 'paraprotein' band on simple electrophoresis.

I am grateful to Professor B. E. C. Nordin for permission to publish the case report of this patient who was under his care.

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The Circulating Platelet

Platelets are a hot topic these days and many monographs and symposia have recently been devoted to them. Of the three new volumes on the subject which have arrived on my desk during the last month, the present expensive production has perhaps the most enticing title. But do not be misled: the emphasis on in-vivo observations which it implies is hardly borne out by the contents, which consist of 16 review articles by distinguished research workers on different aspects of platelet structure and function, most of them largely based on the results on in-vitro experiments. Although ostensibly intended for a wider readership, this is really a book for platelet specialists: they will be pleased to possess it as a fitting memorial to Dr Shirley Johnson, whose untimely death is widely regretted. The book cannot be recommended to those without much previous knowledge of the subject, who will find it difficult to appraise many of the chapters—several of which are highly controversial.

R. M. HARDISTY

Blood Disorders in the Elderly
By J. H. Thomas and D. E. B. Powell. (Pp. v + 284; 85 figures; 29 tables. £4.50.) Bristol: John Wright and Sons Ltd. 1971.

The authors of this book disclaim any intention of writing a textbook of haematology and state their aim as bridging the gap between geriatrics and haematology. However, the types of blood disorder found in older people differ very little from those seen in more general haematological practice and the chapter headings in this book cover the whole range of the subject. If a textbook of haematology were truncated so as to exclude references to subjects below the
Letters to the Editor


We have given the authors this opportunity to reply to the criticisms of Hirst and Howorth and King et al.—EDITOR

Abbreviations for Names of Diagnostic Importance

A recent communication (Baron, Moss, Walker, and Wilkinson, 1971) is disturbing inasmuch as the group, although representatives of specified organizations, was acting without the authority of these bodies. In addition, the authors state that although the International Union of Biochemistry (1961, 1965) strongly discouraged the use of abbreviations for enzymes, and that this was still upheld, they nevertheless arbitrarily continue, 'we recommend . . .

The pitfalls of abbreviations have been discussed elsewhere (King, 1969). The system put forward by Baron et al differentiates glutamate dehydrogenase and glutathione reductase as GMD and GTD respectively, but what happens to glyceraldehyde dehydrogenase and glyoxalate reductase? Alcohol dehydrogenase is AD, and presumably adenosine deaminase would be ADS, trypsin is TPS, and triose phosphate isomerase, TPI. It becomes easier to remember and use the trivial name than the abbreviation and it requires little imagination to see what the computer-controlled data processing systems mentioned would do with some of these abbreviations.

A second communication from this group (Moss, Baron, Walker, and Wilkinson, 1971) deals with the 'standardization' of alkaline phosphatase assay and a further report on the standardization of aspartate and alanine transaminase is promised. This raises the problem of how many standardizations the world can expect, since the German Society of Clinical Chemistry (1970) have already published their standard assays for the transaminases, alkaline phosphatase, lactate dehydrogenase, 2-hydroxybutyrate dehydrogenase, creatine kinase, and 'leucine arylamidase'. The situation is even more complicated because the London group state that an 'expert panel' of the International Federation of Clinical Chemists has the same subject under discussion.

Doubtless it is natural progression from the first report which discredits recommendations made by an international representative and authorized body to the later reports which disqualify such proposals before they are even made.

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References


Correction

We regret that the list of references, now set out below, was not printed with the Letter to the Editor, 'A red herring in the detection of Bence Jones protein', by R. B. Payne (J. clin. Path., 25, 183).

References


Book reviews


This booklet could be useful although it is incomplete. There is no mention of the surface plate count and its advantages or the importance of anaerobic counts. There is no section on the isolation of Clostridium welchii (perfringens) which figures highly in both UK and USA statistics for food poisoning.

All the methods given appear in 'Microorganisms in foods' by the International Committee on Microbiological Specifications for Foods.

Many media are available for the isolation and enumeration of coagulase-positive staphylococci so surely a reference method could have been chosen but no information is given.

In the salmonella section there is no guidance on the preparation of samples. The beneficial effect of incubation at 43°C for some liquid enrichment media is not given.

Methods for faecal streptococci, Vibrio parahaemolyticus, and Bacillus cereus are not given, but there is a clear description of the serological identification of the enteropathogenic E. coli.

BETTY C. HOBBS


This book contains the edited proceedings of an applied seminar held under the auspices of the Association of Clinical Scientists in March 1970. The book is divided into four parts: 'General toxicological considerations', 'General methodological considerations', 'Specific toxic agents', and 'Clinicopathologic considerations'. Fifty-five papers are presented over a very wide toxicological field. Papers range from mode of action of poisons, metabolism, toxicity of food additives...