Detection of cobalamin deficiency using the urinary methylenonic acid test by gas chromatography mass spectrometry

In their recent paper Chanarin et al. state that urinary methylenonic acid (MMA) concentrations are not an early sign for the detection of cobalamin (Cbl) deficiency. They base their opinion on a study that used gas chromatography as a means to quantify urinary MMA. Methodology using gas chromatography only lacks the specificity and sensitivity to accurately differentiate slightly increased concentrations of urinary MMA from normal amounts of urinary MMA.

Gas chromatography of urinary MMA by gas chromatography mass spectrometry (GC/MS) is a highly sensitive and specific test for detecting Cbl deficiency.1-3 Norman et al.4 identified 54 consecutive inpatients with Cbl deficiency using the urinary MMA assay by GC/MS and 20% had a normal hematocrit at diagnosis. In a prospective clinical evaluation of the urinary MMA test by GC/MS Matched inpatients with obvious Cbl deficiency and Cbl deficient patients. They determined the assay to have a sensitivity of 100% and a specificity of 99%. Specker et al.5 used the urinary MMA assay to detect Cbl deficiency in a non-anemic strict vegetarian population. More recently, the high sensitivity of the assay was demonstrated by identifying Cbl deficient non-anemic persons over the age of 65 of whom 40% had serum Cbl concentrations in the normal range.6

False negative results have not been reported for the urinary MMA assay by GC/MS.7 It should be noted, however, that a "gold standard" test for Cbl deficiency does not exist because neither the Schilling test nor the serum total Cbl assay is a functional test. The serum MMA assay lacks specificity because the test can give falsely high values in patients with renal insufficiency or intravascular volume depletion. The urinary MMA test by GC/MS is normalised to urinary creatinine, and falsely high urinary MMA concentrations have not been reported in patients with renal insufficiency or intravascular volume depletion. Thus the urinary MMA test by GC/MS detects early Cbl deficiency, can routinely identify non-anemic Cbl deficiency and is perhaps the "gold standard" for identifying true functional Cbl tissue deficiency.

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Acanthamoeba keratitis

The case report on Acanthamoeba keratitis1 and subsequent response2 require elaboration.

Acanthamoeba is a ubiquitous free-living protozoan which occurs in a wide range of environmental niches including domestic tap water. Inhalation of the organism or its penetration into open wounds can lead to development of granulomatous amoebic encephalitis, or chronic systemic nervous system infection with a prolonged clinical course which in some circumstances may prove fatal.3 Acanthamoeba has been cultured from the nasopharynx of normal, healthy subjects and there are a significant number of people with antibody against the organism. Acanthamoeba keratitis was first recorded in 1974. More recently, this condition has become recognized as a major cause of keratitis.4-9 Presentations are from pre-existing contact lens wearers, increasingly with so-called "disposable" contact lenses, where these have been immersed in inappropriate disinfecting systems.1 For example, commercially available chlorine systems will fail to kill Acanthamoeba cysts if the latter are present in the reusable contact lens storage case.4 The condition is more frequently detected in young immunocompetent persons who wear contact lenses for cosmetic purposes. People who wear contact lenses for近距离 vision have poor compliance with contact lens disinfection regimens. In one study, about 7% of contact lens cases contained viable cysts of Acanthamoeba.10 The incidence of Acanthamoeba keratitis in contact lens wearers in the USA is of the order of 1:250,000.11

Recognition of early ocular disease in contact lens wearers due to Acanthamoeba is all important. In clinical practice and in research, the lack of sensitivity and specificity of other tests means that it is often necessary to proceed on the basis of a compatible clinical history and positive results of available diagnostic tests. The most common of these is a positive immunoassay test for Acanthamoeba antibodies.12 The usefulness of this test is limited by false positive results which have been reported in contact lens wearers with other forms of keratitis.13

Factors affecting the maintenance dose of warfarin

James et al.14 have confirmed the observations of others that early treatment with warfarin is safer than treatment with warfarin for younger patients to achieve the same intensity of anticoagulation.1,2 They suggest that the age dependency of dose should perhaps be taken into account in judging initial dose. We have already studied this question1 and have demonstrated that if a flexible induction dose regimen such as that of Pfenning et al.15 is used elderly patients can safely be started on the same initial dose as other patients. Should a fixed dosage schedule be used this might not necessarily be so.

References


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Electron microscopy is often regarded by those who are not well versed in the ultrastructural approach as the ultimate method of diagnosis on a tissue sample. It is therefore salutary to read in the introduction that useful ultrastructural information can be obtained in only 1–5% of samples received in a teaching hospital laboratory. The figure is even less if tumours are excluded. Why then do we need such a weighty (3-25 kg; 7-15 lb) tome? It is needed because it fills a gap in general ultrastructural teaching (Ghadiially) and the ultrastructural appearance of tumours (Henderson, Papadimitriou and Coleman), and is welcome for that reason.

The editors have gathered a variety of experts who have written concisely or extensively and have illustrated sparingly or profusely. As a consequence the coverage is unequal. For example, in vitro fertilisation has 40 references and 31 figures, while the eye has 426 references, eight tables, and only two figures, clearly inadequate for an atlas of ultrastructure. Other chapters are more even.

There are chapters on technique, scanning electron microscopy, general cell pathology, stromal pathology, viruses, infectious agents, parasites, tumour-like disorders, immune responses, respiratory tract disorders, digestive system (746 references; only 21 figures, liver, endocrine system, kidney, breast, CNS, PNS, muscle, bones, joints, lymphoid system (with light microscopy immunohistochemistry included in the text but not illustrated), and blood and bone marrow. I found the chapter on storage disorders disappointing because this is one area where electron microscopy is most helpful and uses many different tissues for diagnosis. The coverage could have been more extensive. The chapter on skin is an invaluable source of reference.

The choice of sizes of illustrations is very variable and many pages are nearly half empty. The quality of the illustrations is generally good. References are up to 1990.

As a working atlas and text this book should be available to all those involved in diagnostic electron microscopy, especially if they read the introductory short chapter.


This monograph is a compilation of the proceedings of the first seminar on renal involvement in systemic vasculitis held in Vimercate, Italy, in September 1990. It comprises a series of chapters of variable length and quality, somewhat haphazardly arranged. It would be far better if the editors had tried harder to establish some sort of continuity. The book largely documents our current lack of understanding of the basis of systemic vasculitis with renal involvement.

Several papers deal with observations on the emboli found in one of the lesions which react with anti-neutrophilic cytoplasmic antigens (ANCA) confirming that c ANCA antibodies tend to be found in Wegener's granulomatosis and p ANCA antibodies in microscopic polyarteritis nodosa, but there is no clear message as to whether they are primary in the cause of the vasculitis or merely an epiphenomenon which is, perhaps, more likely.

The aim of the text is said to be to identify more effective therapeutic schedules for patients patients with various forms of vasculitis and, given the relative lack of scientific clarity in this area, it is fortunate that the empirical regimens used continue to improve the prognosis for patients with the vasculitic syndromes.

If you want to read what we don't know about vasculitis this is the book for you.

From the pathologist's point of view Systemic Vasculitis edited by Andrew and Jack Chung and published by Igaku Shoin, New York, 1992 is, in my opinion, much more user friendly.


This book aims to highlight recent advances in the diagnosis of gynecological pathology.
Factors affecting the maintenance dose of warfarin.

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