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

In their recent paper Chanarin et al 1 state that high urinary methylnsalicylic 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.

Another method of urinary MMA by gas chromatography mass spectrometry (GC/MS) is a highly sensitive and specific test for detecting Cbl deficiency.2,3 Norman et al 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. Martinez et al identified 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 used the urinary MMA assay to detect Cbl deficiency in a non-anaemic strict vegetarian population. More recently, the high sensitivity of the assay was demonstrated by identifying Cbl deficient non-anaemic persons over the age of 65 of whom 40% had serum MMA concentrations in the normal range.3 False negative results have not been reported for the urinary MMA assay by GC/MS.4 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 MMA 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.

Thus the urinary MMA test by GC/MS detects early Cbl deficiency, can routinely identify non-anaemic Cbl deficiency and is perhaps the "gold standard" for identifying true functional Cbl tissue deficiency.

ERIC J NORMAN
Monarch Foundation, 400 Oak Street, Columbus, Ohio 43219

Acanthamoeba keratitis

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

Acanthamoeba is a ubiquitous free-living protozan 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, sinus infections or 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 1974.5 However, this disease is not often diagnosed and practice is limited. Earlier reports suggested an association between keratitis and trauma with a foreign body contaminated with Acanthamoeba. Currently, most presentations are from contact lens wearers, increasingly with so-called "disposable" contact lenses, where these have been immersed in inappropriate disinfecting systems.6 For example, commercially available chlorine solutions will fail to inactivate Acanthamoeba cysts if the latter are present in the reusable contact lens storage case.7 The condition is more frequently detected in young immunocompetent persons who wear contact lenses for cosmetic purposes. Acanthamoeba keratitis is a condition requiring a high index of suspicion for cases with a poor compliance with contact lens disinfection regimens.

In one study, about 7% of contact lens cases contained viable cysts of Acanthamoeba.3 The incidence of Acanthamoeba keratitis in contact lens wearers in the USA is of the order of 1.250,000.8 Recognition of early ocular disease in contact lens wearers due to Acanthamoeba is all important. The condition must be suspected and treated as a purulent or dendritic epitheliopathy and may proceed to stromal invasion. Acanthamoeba keratitis is therefore most often diagnosed initially as herpes simplex keratitis and treated as such with topical agents and possibly corticosteroids. If such treatment fails the next diagnosis is often of fungal infection. Definitive diagnosis of Acanthamoeba keratitis from superficial corneal scrapings may prove inconclusive, because the organism can be present deeper within the stroma. In such circumstances corneal biopsy extending deeper into the stromal abscess is required; excised tissue should then be subjected to light and transmission electron microscope examination and cultured for the presence of viable amoeba.

For routine culture, a non-nutrient agar (1.5%), prepared at least 24 hours in advance, is seeded with heat-killed Escherichia coli or Klebsiella aeruginosa. Corneal scraping or tissue is gently spread across the central area of two separate plates, one to be incubated at 25°C and the other at 33°C. If the specimen is to be forwarded to a reference laboratory, it should be placed in sterile isotonic saline and kept at room temperature before despatch. Often clinical specimens which contain Acanthamoeba, and amoebae which have been subjected to topical chemotherapy or corticosteroids, require supplements to promote growth and development of the amoebae in culture. If necessary, various biochemical or molecular biological methods can be used to provide unequivocal speciation and strain identification of the pathogenic Acanthamoeba.

Medical treatment with combined topical treatment comprising propamidine isethionate plus neomycin at an early stage can be successful.9 If unrecognized, if the infection progresses to a ring abscess when medical treatment is often unsuccessful and a corneal graft, including on occasion, a second graft, is required. Anti-corticosteroid drugs at this stage may result in emergence of temperature sensitive and drug resistant strains of the organism.10 Sensitivity testing of cultured clinical isolates must therefore be performed.


Correspondence

J HAY
DV SEAL
Acanthamoeba Research Laboratory, Glasgow Royal Infirmary, Wolfson Centre, Level 3/1 Taylor Street, Glasgow G4 ONA

CM KIRKNESS
Tennent Institute of Ophthalmology, Western Infirmary, Glasgow G11 6TW

Factors affecting the maintenance dose of warfarin

James et al1 have confirmed the observations of those that even slight differences in the maintenance dose of warfarin between younger patients to achieve the same intensity of anticoagulation.2 They suggest that the age dependency of dose should perhaps be taken into account in judging initial dose. We have already studied this question3 and have demonstrated that if a flexible induction dose regimen such as that of Pernetti et al4 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.

B J BAIN
University of London, St Mary's Hospital Medical School, Department of Haematology, Norfolk Place, Paddington, London W2 1PG

References

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

E J Norman

J Clin Pathol 1993 46: 382
doi: 10.1136/jcp.46.4.382-a

Updated information and services can be found at:
http://jcp.bmj.com/content/46/4/382.1.citation

These include:

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.

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/