tests of allergy function do not point to any specific disturbance.

Acute brucellosis contracted at work is a compensable condition. Claims for compensation for so-called chronic brucellosis by workers in the meat industry stopped after a study showed that the symptoms it allegedly caused were more common in bus drivers.1 The diagnosis of chronic fatigue syndrome can, in the absence of organic or psychiatric disease, be given to any patient whose symptoms include tiredness. The condition has been well reviewed by Abbrey and Garfinkel,2 who regard it as a modern variety of neurasthenia.

So-called multiple chemical sensitivity, alleged formalin or mercury poisoning, chronic candidiasis and hypoglycaemia are offered as explanations for non-specific symptoms, depending on the circumstances in which they occur. Sufferers find their way to practitioners of clinical ecology who may use a variety of investigative and therapeutic techniques not yet scientifically validated.1

Although some doctors try to give their patients a diagnosis of a culturally approved organic illness by pursuit of possible viral and immunological causes, it is apparent in many cases that psychosocial factors play a dominant role and include dissatisfaction, disappointment and disillusionment with various domestic and occupational conditions. While some sufferers of these conditions continue to work, especially if self-employed, the availability of an alternative source of income in the form of superannuation or disability insurance may contribute to a decision to seek a certificate of unfitness.

The similarity of the clinical pictures of these nebulous entities is more than can be attributed to coincidence; they appear to be part of the one disturbance. Whether it is called neurasthenia, somatisation or a psychosocial disturbance, it does patients no service to foster their belief that they have an illness.

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Gynaecomastia and amlodipine

To the Editor: Gynaecomastia has been well recognised as an uncommon side effect of certain calcium channel blockers, including verapamil, nifedipine and diltiazem. We report a case associating gynaecomastia and the new agent amlodipine.

A 46-year-old man with a 15-year history of hypertension and chronic renal failure secondary to focal glomerulosclerosis developed progressive symptoms of ureaemia in 1993. He has since used continuous ambulatory peritoneal dialysis while awaiting renal transplantation.

He started taking amlodipine (10 mg daily) in late October 1993 for blood pressure control. Subsequently, he noticed increasing symptoms of breast swelling and discomfort. There was no associated galactorrhoa or hepatic dysfunction. Concurrent medications included caltrate, allopurinol and fluocoxacin.

Physical examination revealed bilateral tender nodules of subareolar tissue measuring 3 cm in diameter. No other hepatic or hormonal signs were elicited.

Investigations revealed a mildly elevated alkaline phosphatase level (1151 IU/L; normal range, 36-95 IU/L), hypoalbuminaemia and an elevated creatinine level (908 μmol/L; normal range, 50-120 μmol/L). These results were consistent with measurements obtained before the introduction of amlodipine. Prolactin levels are elevated in some cases of drug-induced gynaecomastia,1 but were not measured in this case.

Rampipril was substituted for amlodipine in January 1994. Symptoms of gynaecomastia were duly noted to subside over the next five days. At review in one month he was symptom free.

This case describes a temporal relationship between amlodipine use and gynaecomastia. Rechallenge is required to fully define this link, but would be ethically inappropriate. Renal failure must be considered a confounding factor in view of its independent association with gynaecomastia. In this case, however, renal failure had been stable on dialysis for two months before the onset of symptoms and the patient had not had previous difficulties with gynaecomastia throughout his long history of renal failure.

Of the calcium channel blocking agents, verapamil has been implicated as most frequently causing gynaecomastia,2 but it has also occurred with nifedipine and diltiazem. No physiological mechanism adequately explains this phenomenon.3 Our case suggests that amlodipine is another calcium channel blocker that can cause gynaecomastia.

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HIV western blot test

To the Editor: As a clinician, I have problems reconciling certain aspects of the HIV western blot (WB) test. The specificity of the HIV WB is widely accepted to exceed 99.5% and a positive WB is regarded as synonymous with HIV infection. WB results are interpreted according to the presence of combinations of particular antigen/antibody bands, but there are a number of different criteria used to define a positive result. For example, in the United States the Food and Drug Administration (FDA) requires the presence of antibodies to the following HIV proteins (p) and glycoproteins (gp): p24, p32 and gp41 or gp120/gp160. The Consortium for Retrovirus Serology Standardization (CRSS) requires an antibody profile to p24 or p32, and gp41 or gp120/gp160. Other North American institutions, for example, the Association of State and Territorial Public Health Laboratories Directors, Department of Defense and Centers

Correspondents

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There should be no more than 6 references. The reference list should not include anything that has not been published or accepted for publication. Reference details must be complete, including: names and initials for up to 4 authors, or 3 authors, et al if there are more than 4; places and dates for conferences and publishers, places and year of publication for their proceedings; publishers, places, year of publication and page numbers for monographs; volume numbers and page numbers for journal articles.
for Disease Control, require any two bands chosen from p24, gp11 and gp120/gp160, while the World Health Organization requires the presence of at least two of gp41, gp120 and gp160. Laboratories also recognize two other categories: WB negative (that is, no bands whatsoever, including no reactivity to bands which do not represent HIV proteins) and WB indeterminate (WBI) (that is, neither positive nor negative). The CRSS defines WBI as "any bands present, but pattern does not meet the criteria for positive".

The WBI category poses unexplained dilemmas. Individuals testing positive in one laboratory may be indeterminate in another. Quite reasonably, such individuals may wish to know if they are HIV infected or not. Since the first few years after the discovery of HIV, diagnostic criteria have altered so that, if patients are restested and found to possess the same WB bands, they may no longer be categorized as WB positive. Haemophiliacs tested before 1987, many of whom were reported to be HIV positive but who are very unlikely to develop AIDS, may face these uncertainties.

If we consider the FDA criteria, the presence of a p24 and a gp41 band is considered WBI, while the "addition" of a p32 band is considered WB positive. What is the explanation for the presence of the p24 and gp41 bands in an individual with the indeterminate result? If not because of specific HIV antibodies, then what is the scientific rationale for a positive result when the same p24 and gp41 bands are accompanied by a p32 band? Logically this either is, or is not, due to the presence of specific anti-HIV antibodies in the individual's serum. If due to specific anti-HIV antibodies, what is the scientific rationale for classing the result as "indeterminate" when the same p24 and gp41 bands, accompanied by a p32 band, are considered positive? The same question could also be asked in relation to the 4000 of 1 200 000 healthy military recruits who tested WB negative after two positive results for HIV with enzyme-linked immunosorbent assay (ELISA) screening and the 80 of 1 200 000 who had two positive ELISA results, an initial positive WB result but a negative second WB result.

If the justification for each WB category from a particular institution is dependent on observational data as to the presence of the eventual development of AIDS, then, leaving aside the problem of interinstitutional bias, it is possible to use the WB as a predictor of AIDS when, for example, the CRSS, under the FDA criteria only 54 of 111 AIDS patients were WB positive (49%), while 127 of 1306 low risk individuals (including blood donors) were positive (10%).

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Comment: Turner's letter highlights some of the deficiencies of the western blot test (WB), but these should be placed in the context of 1994.

HIV infection is usually diagnosed by the presence of anti-HIV antibodies in an individual's serum, specifically by the presence of appropriate reactivity in at least two tests which are selected so that nonspecific reactivity is minimised. However, for screening tests to be highly sensitive they are necessarily of lesser specificity (that is, specific and non-specific antibody will be identified). A positive result on screening must be followed by a supplemental test or tests to identify specific antibodies — traditionally, the supplemental test of choice has been the WB.

WBs were developed using viral lysates and in the early days many of the antigen preparations were quite crude. Further, the glycoproteins (envelope proteins) were poorly transferred onto nitrocellulose strips from the electrophoresis gels and often gave relatively poor reactivity. Manufacturers of WBs have addressed these technical deficiencies but, more importantly, testing strategies and quality control procedures have been developed which have led to improved standardisation of blot performance. The WB is not the only test used as a supplemental assay. Positive diagnoses are made on a consensus of results from at least two different tests.

Up to 0.6% of sera from people not infected with HIV will be repeatedly active on screening by enzyme immunoassay. We know from the sera are likely to contain cross-reactive antibody demonstrable on WB and therefore show an indeterminate result. As a screening test WB demonstrates reactivity in a large proportion of sera. As a supplemental test to distinguish true from false positive screening results, the WB, with the application of strict interpretation criteria, is highly specific.

Indeterminate results may be minimised by the use of the highly specific screening tests available and the careful choice of assay sequences used for supplemental testing (the testing strategy). So many assays other than the WB are now available that it is possible to generate strategies using tests employing differing antigens and technologies, thereby minimising indeterminate results. This approach has developed greatly since 1988, when Burke et al. commented on the screening results in US army recruits.

Turner points out that a number of different criteria have been developed to interpret the WB. The number of criteria reflect some of the confusion that occurred in the early days of testing but criteria now are more uniform. The glycoprotein bands (gp41, gp120 and gp160) are critical in interpretation because it has been demonstrated over time and in a large number of blots that the presence of these bands is highly predictive of specific anti-HIV antibody. The inclusion of other bands in the criteria enhances the specificity of interpretation.

The different interpretation criteria have become much closer and the number of samples that have divergent diagnoses are very few. However, indeterminate patterns may vary according to the type of blot, the operator and the conditions. Very few indeterminate blots demonstrate glycoprotein bands and the rare occurrence of these is usually because the screening and supplemental assays used favour the selection of non-specific bands in the glycoprotein area.

Clinical statistics overwhelmingly support the fact that individuals have been exposed to HIV if their sera demonstrate reactivity in sequentially performed anti-HIV tests that have been carefully selected and interpreted with time-trialed criteria. While the WB is not the complete answer to HIV-testing, it is a stalwart in anti-HIV testing strategies.

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