ferred to nitrocellulose filters and hybridised with a nick-translated Jh probe, which was kindly provided by Dr TH Rabbitts (Cambridge). A unique rearranged band could be detected on autoradiography.

Immunofluorescence studies in our patient indicated that lambda light chains were produced. Because monoclonal immunoglobulin seems to be present in the cytoplasm of plasma cells in nearly all patients studied by immunocytochemical methods,³ the most likely mechanisms to explain non-secretory myeloma could be a defective secretory system of the cell, or an abnormal immunoglobulin structure which is not capable of being transmitted further along the secretory pathway.

In our patient detection of heavy gene rearrangement suggests that the failure of heavy chain expression could result from dysfunctionally rearranged genes, or because of the presence of an abnormal mRNA.

Among light chains producing non-secretory myeloma, a preponderance of kappa type has been pointed out, so the lambda type is rare and to the best of our knowledge only two such patients have been described previously.^{4,5}

Although it has been reported that non-secretory myeloma has a better prognosis than secretory myeloma,^{2,3} our patient died quickly. We attribute the poor response to chemotherapy and short survival to diagnosis at an advanced stage, even in an initial leukaemic phase which is very unusual.¹

G SORIANO

S BURNET

J SOLER

C GUANYABENS

C GUARNER

*Servei d'Hematologia,
Escola de Patologia Digestiva,
Hospital de la Santa Creu i Sant Pau,
Barcelona, Spain*

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Matters arising

Screening for bacteriuria

Doran and Kensit recently reported the results of a study on screening for bacteriuria using a dipstick read by Clinitek 200.¹

We recently conducted a similar study on 1000 consecutive urine specimens randomly submitted to this laboratory. The same four tests—namely, leucocyte esterase, nitrite test, blood, and protein on the Ames 10SG strips—were used and read by Clinitek 200. All urines were tested in parallel with the methods normally used for enumeration of leucocytes by microscopical examination and quantitative culture for bacteria. At this time Kova slides with grids (ICL Scientific) were used to detect pyuria defined as the presence of at least 10 white cells per cubic mm. Semiquantitative bacterial counts were made by impression of bacteriuritest strips (MAST Laboratories) on to MacConkey agar, and inoculation of urine using a 0.05 ml calibrated loop on to horse blood agar and incubated for 18-24 hours at 37°C before examination for discrete colonies.

Culture was defined as negative if less than 10⁵ organisms/ml and positive if 10⁵ organisms/ml or greater, in either pure or mixed cultures. Urines with borderline counts of 10⁴-10⁵ organisms/ml were not assessed.

A positive dipstick result was defined as one or more positive reactions with tests for leucocyte esterase, nitrite, blood and protein. A negative result was one in which all four tests were negative.

We used the formulae of Galen and Gambino² to obtain statistical results.

For the dipstick screening method, sensitivity was 80.4% and specificity 97.8%. Predictive values for a positive result were 83.7% and for a negative result 97.2% when all four tests were used in combination. The overall false negative rate was 1%.

For our largely asymptomatic population, these figures suggest that the method could be used as a routine screen, and we suggest that those urines that prove negative for the four dipstick tests need not be examined further for leucocytes and bacteria unless specifically requested by the clinician in the case of problem patients. Consequently our workload would be reduced by 36%. Similar conclusions were reached by Boreland and Stoker³ and Lowe.⁴

We found that the urine screening procedure was not applicable to all patients. The level of bacteriuria must be modified in

some cases as small numbers of bacteria can be associated with urinary tract infection and have been reported.⁵ Therefore, all urines from symptomatic patients and specimens of suprapubic aspiration and catheter urine would be cultured and microscopy performed without screening.

We agree with the comments made by the authors that, used as a screening method, the dipstick is more expensive than microscopy and culture (£0.14 as opposed to about £0.90 per specimen) and we found no savings in technician time.

We found that the incorporation of 10 biochemical tests in the one dipstick was excessive for investigations in this department and feel that a strip adapted to bacteriological screening using the four variables of leucocyte esterase, nitrate, blood and protein read by Clinitek 200 would be more cost effective as a urine screening procedure.

BA BARKER

JG RATCLIFFE

*Public Health Laboratory,
Fazakerly Hospital,
Lower Lane,
Liverpool L9 7AL*

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False negative results with benzodiazepine screening test

The recently updated ACP Broadsheet by Widdop is an excellent commentary on a range of simple tests to detect poisoning.¹ The author mentions benzodiazepines as currently the most common cause of drug induced coma and names immunoassay and TLC, following hydrolysis with acid and heat, as routine screening procedures. For completeness, we would like to emphasise that, while indeed, 1,4-benzodiazepines are detectable using either assay procedure, the

relatively new but fashionable 1,5-benzodiazepine, clobazam is not. The TLC procedure relies on the hydrolysis of benzodiazepines or their metabolites to aminobenzophenones which are detected by their yellow colour, fluorescence characteristics and, in the case of primary aminobenzophenones, the formation of an azo dye. Whereas the 1,4-benzodiazepines readily undergo cleavage to the corresponding open-ringed benzophenone, no such similar reaction occurs with clobazam or its pharmacologically similar metabolite, N-desmethyloclobazam.

We conclude that TLC of the acid hydrolysate will lead to false negative results when clobazam has been ingested, and laboratories using this methodology for benzodiazepine screening should note this exception.

NR BADCOCK
GD ZOANETTI

Department of Chemical Pathology,
The Adelaide Children's Hospital,
North Adelaide,
South Australia,
5006 Australia

Reference

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Hepatitis B (HBsAg and HBcAg) hepatic markers in HBsAg positive chronic liver disease

Patients without circulating hepatitis B surface antigen (HBsAg) can none the less have positive viral markers in liver tissue. Usually such patients have high serum titres of anti-hepatitis B core (anti-HBc) antibodies. Several explanations for this phenomenon have been suggested, including low HBsAg concentrations undetectable by traditional diagnostic methods and immunocomplex formation with circulating antibodies.

Recently Cuccurullo *et al*¹ showed that 17% of alcoholic patients and 21% of non-alcoholic patients were positive for HBsAg or HBcAg (core antigen) in liver tissue, despite being seronegative for all serum markers of hepatitis B virus. We studied liver markers (HBsAg and HBcAg) on a total of 60 patients with chronic liver disease and seronegative for HBsAg—30 with alcohol-induced hepatic disease and 30 with non-alcohol-induced hepatic disease. In all cases hepatitis serum B virus markers were studied using ELISA techniques (HBsAg, anti-HBs, anti-HBc, HBcAg and anti-HBe), and liver

tissue markers (HBsAg and HBcAg) with immunoperoxidase.

Fourteen patients had anti-HBs associated with anti-HBc; only a single patient was seropositive for anti-HBc alone. The rest were all hepatitis B virus seronegative. None had positive tissue markers for hepatitis B virus (HBsAg, HBcAg).

Our findings suggest that it is highly unlikely that a seronegative patient will display HBsAg or HBcAg in the liver. It is also unlikely that such a patient will have liver disease related to hepatitis B. These findings contradict, to some extent, those of Cuccurullo *et al*,¹ but the difference is unlikely to be due to geographical factors or methodological variables, because our serum HBsAg positive patients showed highly sensitive and specific hepatic markers.

FJS ESCOBAR

JT GILBERT

TC MORALES

Servicio de Digestivo,
Hospital Inversitario,
Granada,
Spain

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Dr Rimbaldi *et al* comment:

Salmerón Escobar *et al* report that none of the 60 patients with chronic liver disease seronegative for HBsAg studied showed positive tissue markers for hepatitis B virus (HBsAg and HBcAg), which is contrary to our previous data.¹ Many authors have reported positive tissue markers for HBsAg or HBcAg in the absence of HBsAg or HBcAg in both alcoholic and non-alcoholic patients. Further observations, conducted in a wider range of cases (n = 164) confirm our previous data (table). In all cases we verified

the specificity of the method as reported elsewhere.¹

In contrast to the findings of the Spanish authors, we maintain that geographical factors could have had a certain effect on the discrepancy found between their data and those of the other authors, ours included. Indeed, only 15 of the 60 hepatic patients (25%) that they studied showed anti-HBs or anti-HBc, or both, in the serum, which probably reflects a low percentage of hepatitis B infection in their population. The spectrum of this infection does, indeed, vary in different parts of Europe—for example, in alcoholics with chronic liver disease the positive percentage oscillates between 10 and 40%; in Northern Europe²⁻³ it is 45% in a French survey⁴ and reaches 75% in an Italian survey.⁵ This most probably reflects varying risks of exposure in different countries.

One could also hypothesise that at least a part of chronic liver disease with HBsAg and HBcAg negative tissue could be the result of infection with the non-A, non-B hepatitis virus.

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Distribution of serum and tissue positivity in alcoholic and non-alcoholic patients

Liver HBsAg or HBcAg, or both	At least one marker	Alcoholics		Non-alcoholics	
		n	(%)	n	(%)
Tissue positive	Serum positive	15/71	(21.12)	15/93	(16.13)
Tissue negative	Serum negative	30/71	(42.25)	28/93	(30.10)
Tissue positive	Serum negative	13/71	(18.30)	20/93	(21.50)
Tissue negative	Serum positive	13/71	(18.30)	30/93	(32.25)