Letters to the Editor

Table 1 Comparison of chlamydia culture and enzyme immunoassay using rectal swabs

Enzyme immunoassay	Culture			
	Positive	Negative	Contaminated	Total
Positive	1	16	1	18
Equivocal	0	1	0	1
Negative	0	2	2	4
Total	1	19	3	23

lated on to two coverslips. After 48 hours incubation coverslips were stained with Giemsa and examined for inclusions. Enzyme immunoassay was performed according to the manufacturer's instructions (IDEIA, Boot's Celltech).

A total of 23 rectal swabs have now been examined. As can be seen in the table, 17 of 23 gave clear positives with the enzyme immunoassay, but only one of these specimens was positive by culture. Urethral swabs were received in parallel with the rectal swabs, which gave discrepant results, and all 16 gave negative culture results. It was clear from these results that the enzyme immunoassay was producing false positive results with rectal swabs. This conclusion was supported by the finding that 15 of 16 swabs taken from randomly selected faeces submitted to the Public Health Laboratory also gave strong positive results in the enzyme immunoassay.

In view of the very strong positive results obtained with faeces and rectal swabs a bacterial antigen cross reacting with the anti-chlamydial monoclonal antibody seemed unlikely. The organisms listed in table 2, however, were tested in the enzyme immunoassay by making heavy suspensions in chlamydia transport medium. All gave negative results in the enzyme immunoassay, including the strain of *Acinetobacter calcoaceticus* var *anitratus*. This organism has been reported³ to give positive results with another enzyme immunoassay for chlamydia (Chlamydiazyme, Abbot Laboratories).

We proceeded to investigate whether protein A of staphylococci could reproduce the effect. Suspensions of six strains were tested.

Four of the five *Staphylococcus aureus* strains gave positive results, whereas the *S. epidermidis* strain was negative. Positive results were also produced by a preparation of protein A. It seems unlikely, however, to be the explanation for false positives with faeces and rectal swabs, as when serial dilutions of *S. aureus* were tested it was established that an inoculum of 10^3 organisms/ml was required to produce positive results. This is clearly far larger than the likely numbers of *S. aureus* in either faeces or rectal swabs.

We have therefore been unable to identify the precise mechanism of the false positive results, but it would seem likely that it entails a non-specific binding to mouse immunoglobulin, as in our studies prior absorption of faeces with mouse serum gave a two fold reduction in reading in the enzyme immunoassays, compared with absorption in transport medium.

We have shown that this kit is quite unsuitable for examining rectal swabs, although in fairness the manufacturer's instructions indicate that it is designed for examining genital specimens only. We consider, however, that this problem should be investigated further to ensure that it cannot produce occasional false positive results, with genital specimens. Even if false positive results were uncommon, they would assume importance if the kit were used to screen populations, such as antenatal clinics, which may have a low prevalence of true positive results, rather than the high incidence in the populations examined in reported studies.

T RIORDAN

DA ELLIS

PI MATTHEWS

SF RATCLIFFE

Central Serology Laboratory,
Withington Hospital,
West Didsbury,
Manchester M20 8LR

References

- 1 Anonymous. Chlamydia in women: a case for more action? [Editorial] *Lancet* 1986;i: 892-4.

- 2 Pugh SF, Slack RCB, Caul EO, Paul ID, Appleton PN, Gatley S. Enzyme amplified immunoassay: a novel technique applied to direct detection of *Chlamydia trachomatis* in clinical specimens. *J Clin Pathol* 1985;38: 1139-41.

- 3 Saikku P, Puolakkainen M, Nissinen A. Cross-reactivity between chlamydiazyme and *Acinetobacter* strains. *N Engl J Med* 1986;314:922.

Human parvovirus associated with erythroblastopenia in iron deficiency anaemia

Anderson *et al*¹ have shown that human parvovirus (HPV) is responsible for aplastic crises in patients with chronic haemolytic anaemia. We report an HPV-aplastic crisis, with rapidly worsening anaemia in a patient without an underlying haemolytic anaemia.

A 28 year old woman presented with a seven day history of abdominal pain, headache, and fever (39°C). She had had iron deficiency anaemia (haemoglobin concentration = 10 g/dl, mean cell volume = 56 fl) for many months and showed non-compliance with iron treatment. Examination showed that there were no signs, apart from pallor and an ejection systolic murmur. Liver, spleen, and lymph nodes were not enlarged. Her haemoglobin concentration was 7 g/dl, her mean cell volume 69 fl, reticulocyte count $5 \times 10^9/l$, white cell count $1.5 \times 10^9/l$, and platelet count $130 \times 10^9/l$. Her bone marrow was hypocellular, with erythroid aplasia (1%), absence of megakaryocytes, normal granulocyte maturation, and 2% giant cells (diameter $100 \mu m^3$) with blue cytoplasm. Her total bilirubin concentration was $10 \mu mol/l$ and serum iron $7 \mu mol/l$. Her serum was negative for HPV antigen, but recent HPV infection was suggested by the presence of specific IgM in radioimmunoassay. Other infections excluded were hepatitis A and B, infectious mononucleosis, and cytomegalovirus. A search for an underlying haemolytic anaemia (blood film, study of osmotic resistance, in vitro autohaemolysis, haemoglobin electrophoresis, erythrocyte enzymatic tests, direct Coombs' test) was negative. She was given three units of packed red cells, after which her haemoglobin rose to 11.3 g/dl. The fever disappeared within two days, and the thrombocytopenia and neutropenia spontaneously resolved with five days by which time the reticulocyte count was high ($250 \times 10^9/l$). A second bone marrow smear showed normoblastic erythroid hyperplasia (34%), the presence of megakaryocytes, and the disappearance of the giant cells seen on the first bone marrow smear.

Table 2 List of faecal organisms tested by enzyme immunoassays

<i>Acinetobacter calcoaceticus</i> var <i>anitratus</i>
<i>Bacteroides fragilis</i>
<i>Bacteroides melanogenicus</i>
<i>Bacteroides ovatus</i>
<i>Escherichia coli</i>
<i>Fusobacterium fusiforme</i>
<i>Klebsiella aerogenes</i>
<i>Salmonella typhimurium</i>

In a healthy subject HPV infection can induce a transient arrest of erythropoiesis, which does not lead to clinical symptoms because the normal erythrocyte life span exceeds that of any effect of HPV on marrow. In patients with haemolytic anaemias the haemoglobin concentration drops greatly with HPV infection, because the red blood cell life span is shortened.² In our case the apparent HPV aplastic crisis was similar to those in previous reports,³ but erythroblastopenia associated with HPV in non-haemolytic anaemia has not been reported as far as we know. It seems that the reticulocytopenia induced by HPV infection can thus worsen a pre-existing anaemia. Our bone marrow findings also showed that HPV, besides its known erythroblastopenic effect, can cause a moderate and transitory decrease in the platelet count, secondary to a hypoplastic effect on the megakaryocytes. Our patient did not have any erythema arthralgia, or vascular purpura, all of which may be seen in HPV infection.⁴⁻⁶

We suggest that when a patient with a haemolytic or any other type of anaemia, presents with a rapid and unexplained fall in peripheral blood haemoglobin concentration compared with steady state values, it seems logical to look for HPV infection.

JJ LEFRERE*

H BOURGEOIS†

*Centre national de transfusion sanguine,
6 rue Cabanel,
75015, Paris,
France,

†Centre hospitalier,
Evreux, 27000,
France.

References

- 1 Anderson MJ, Davis LR, Hodgson J, *et al*. Occurrence of infection with a parvovirus-like agent in children with sickle anaemia during a two-year period. *J Clin Pathol* 1982;35:744-9.
- 2 Lefrère JJ, Couroucé AM, Soulier JP. Le parvovirus B 19. *Nouv Presse Med* 1986;15:703-7.
- 3 Lefrère JJ, Couroucé AM, Girot R, Bertrand Y, Soulier JP. Six cases of hereditary spherocytosis revealed by human parvovirus infection. *Br J Haematol* 1986;62:653-8.
- 4 Anderson MJ, Jones SE, Fischer-Hoch SP, *et al*. Human parvovirus, the cause of erythema infectiosum (fifth disease)? *Lancet* 1983;i:1378.
- 5 Reid DM, Reid TMS, Brown T, Rennie JAN, Eastmond CJ. Human parvovirus associated arthritis: a clinical and laboratory description. *Lancet* 1985;1:422-5.
- 6 Lefrère JJ, Couroucé AM, Muller JY, Clark M, Soulier JP. Human Parvovirus and purpura. *Lancet* 1985;ii:730.

Evaluation of strategy for testing thyroid function applied to hypothyroidism

In their interesting account of an evaluation of a strategy for thyroid function testing, Corns and Miller¹ illustrate the particular importance of relevant clinical information accompanying requests to the laboratory.

Tests for thyroid function services have been changing rapidly over the past two decades, and in many hospitals the laboratory has had to take the initiative in the selection of appropriate tests for individual patients. Various strategies have been argued recently,^{2,3} with agreement that a cost effective laboratory service can be achieved if there is cooperation between clinician and pathologist.

For 15 months we have been operating a thyroid function strategy based on ideas of Britton *et al*,² but using free thyroxine (Amerlex-M Free T4 RIA kit) as the primary screening test and thyroid stimulating hormone as a discretionary test. The strategy requires a set of decision aiding reference ranges and levels. For detection of hypothyroidism, the relevant values were: euthyroid reference range 9.9-23.7 pmol/l (0.77-1.84 ng/100 ml); a therapeutic reference range for patients receiving thyroxine 12.9-30.8 pmol/l (1.0-2.39 ng/100 ml), and a further decision aiding range 12.3 pmol/l (0.9 ng/100 ml) to select thyroid stimulating hormone in patients presenting with features of hypothyroidism. Thyroid stimulating hormone was also assayed with free thyroxine as the primary investigation, whether or not requested in the following: paediatric cases; patients receiving lithium, amiodarone, or fenclufenac; pregnant patients; those with carcinoma of the thyroid; and goitre with antibodies (we called all these "the problem group").

Continuous review of our results over 12 months showed that:

- (i) 22 cases of thyroid stimulating hormone were not tested because, in the absence of clinical details, the patient had not been allo-

cated to the "problem group." Subsequent testing showed that nine of these patients had raised thyroid stimulating hormone values.

- (ii) Fifty six patients with low free T4 values had normal thyroid stimulating hormone results, and all of these were acutely sick inpatients with no features of thyroid disease.
- (iii) Three patients with repeatedly normal serum free T4 concentrations had consistently raised thyroid stimulating hormone values. They all had clinical features of hypothyroidism. On subsequent testing clinically important titres of antithyroxine antibody were detected in the sera (anti-T3 was also detected in one patient). Reassay of hormone after precipitation of interfering immunoglobulin⁴ gave more accurate free T4 values (table).

We agree that relevant clinical details with requests for thyroid function testing are necessary to the successful management of laboratory testing strategy.

Screening for thyroid disease in acutely ill patients with no suspicion of thyroid disorder seems to be wasteful of essential resources, and the results can be misleading. Accordingly, we requested house doctors not to screen patients during acute illness.

It seems that interfering antihormone antibodies may occur more commonly than originally suspected, and both laboratory staff and clinicians should be alert to this possibility when confronted with anomalous results.

AI POLANSKY
District Laboratory
The General Hospital
South Shields
Tyne and Wear
NE34 0PL

References

- 1 Corns CM, Miller AL. Evaluation of strategy for testing thyroid function applied to hypothyroidism. *J Clin Pathol* 1986;39:293-6.

Table Thyroid function test

Case No	First free T4 (pmol/l)	Thyroid stimulating hormone mu/l	Percentage counts precipitated as antibody	Supernatant free T4 (pmol/l)	Clinical details
1	24.7 (1.92)	> 60	49	3.6 (0.3)	"Puffy face" look
2	11 (0.85)	15.5	11	8.0 (0.62)	myxoedematous
3	10.1 (0.78)	31.9	13	4.5 (0.35)	Gaining weight, enlarged thyroid, Deep voice, slowing up, myeloma

Patients with circulating antithyroxine antibody (values in parentheses given in ng/100 ml.)