Matters arising

Clinitec 200 as a screening test for bacteriuria

We recently carried out an evaluation of the Ames Clinitec 200 similar to that of Doran and Kensit[1] on 774 consecutive urine specimens received by our laboratory. In our study we compared the multiple reagent strip tests for blood, protein, nitrite and leucocyte esterase read by the Clinitec 200 with our standard method of urine culture, Bacteruritest strips (Mast laboratories) inoculated on to CLED agar plates and incubated overnight in air at 37°C. For the purpose of this study, one or more positive reagent strip tests and any culture of $>10^5$ bacteria/ml in pure or predominant growth were taken as positive results. We did not test our specimens for the presence of antimicrobial substances. Our results are set out in the table.

Table *Summary of results*

	No (%) of positive strips	*No (%) of negative strips*	*Total (%)*
Positive culture	221 (29)	7 (1)	228 (29)
Negative culture	272 (35)	274 (35)	546 (71)
Total	493 (64)	281 (36)	774 (100)

In our hands the Clinitec 200 had a sensitivity of 97% but a disappointing specificity of only 50% (predictive value for positive result 45% and for negative result 98%). Even so, our results were somewhat more encouraging than those of Doran and Kensit. The reagent strip test responsible for most of the false positive results in our study was that for blood followed in equal second place by protein and leucocyte esterase. There were few false positive nitrite tests. We have therefore decided not to introduce the Clinitec 200 into our laboratory as a screening method for bacteriuria.

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Designation of "HPV" for human parvovirus

In a recent letter in this Journal a case of aplastic anaemia arising after infection with the human parvovirus B19 was discussed.[1] We comment on the use of the designation "HPV" for this (or any other) human parvovirus, which we feel is unfortunate.

"HPV" has been the denominator for the human papilloma viruses for many years and is therefore not appropriate for the human parvoviruses. The fact that B19 fits nicely into the list of human papilloma viruses (6, 11, 16, 18, (B)19 . . .) makes strictness in the nomenclature even more urgent.

It has been internationally recommended and agreed that the human parvovirus B19 should either be designated as such, or as "B19 virus".[2,3] We should like to advise all authors to do so to avoid unnecessary confusion.

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Automated measurement of plasma viscosity by capillary viscometer

The findings reported in the recent paper by Cooke and Stuart[1] are broadly similar to those reported by us in an independent evaluation on behalf of the NHS procurement directorate. We, too, found that the recommended shutdown procedure did not prevent the build-up of protein within the sampling valve, inner syringe, and tubing. It was our experience, however, that a full disinfection procedure is required, and this entails using the "fast prime" function to pump hypochlorite through the rinse line. This operation is described in the manufacturer's reference manual and should be done at least once a week. It was also necessary to remove the sample valve to facilitate thorough cleaning.

We also reported on the high incidence of "data scatter" messages when the viscosity was greater than 3·5 mPascals a second. Because no result is displayed with this message, a previously unsuspected hyperviscosity syndrome may be missed.

We compared the cost of using the Viscometer II with a conventional disposable ESR system. The cost of 100 samples a day, including consumables, labour, capital depreciation and servicing for the viscometer was £16·55 and for the ESR £15·75. The advantages of automated viscometry and its "user compatibility" justify the small extra cost.

Our full report is available from the DHSS Project Officer, M Fuller, 14 Russell Square, London WC1B 5EP.

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Shedding of oocysts of Cryptosporidium in immunocompetent patients

The paper by Shepherd *et al* provides some useful data on the shedding of oocysts by immunocompetent patients with cryptosporidiosis.[1] Our own studies in north Wales, over more than five years, and numerous other recent reports and reviews also show *Cryptosporidium* to be one of the commoner enteric pathogens, particularly among children.[1,2] Several of these studies have shown that oocyst shedding patterns vary considerably among patients. Some of the statements made by Shepherd *et al*, supported in some cases by reference to outdated papers, need to be clarified.

The brief description of the biology of the parasite given in their report is supported by

reference to other papers and reflects the confusion existing at the time of their publication. More recently published work, particularly by Current *et al*, has largely established the classification and life-cycle, although some areas of uncertainty remain.[1,3] Although it is true to say that most infections in man and in livestock mammals are with a single species, probably *Cryptosporidium parvum*, the parasite is no longer regarded as a single species genus, there being at least four distinct named species.[3] Shepherd *et al* refer to "sporocysts" and to "so called oocysts". The sporogenous developmental stages share some features of both oocysts and of sporocysts of other coccidia. The stage excreted in the stool, however, should correctly be referred to as an oocyst.[3]

Other studies on oocyst excretion were briefly reviewed and a claim made to this being the largest series (49 subjects) reported so far. Other excretion studies not cited include the first such detailed report on 33 patients in Liverpool,[4] on 50 patients in Finland,[5] and on 91 patients in north Wales.[2] Some of the differences in findings referred to by Shepherd *et al* probably result from the effects of statistically small sample sizes, variable sampling patterns, and to variations in laboratory methodology. Attention is drawn by Shepherd *et al* to the continuation of excretion of oocysts after diarrhoea has stopped. Lack of correlation between diarrhoea and occyst excretion in some patients has been noted previously.[4] The finding of a continuation of symptoms beyond the last direct smear positions for oocysts is not uncommon and may be attributable to several possible factors, including continuing infection with intermittent or low level oocyst excretion, post-infective or residual damage to the intestinal mucosa, or extra-intestinal infection. The statement that "oocysts had cleared completely", which presumably refers to direct (unconcentrated) faecal smears, needs to be qualified. The modified Ziehl–Neelsen stain is not as sensitive as some other staining methods such as phenol-auramine. Concentration by an appropriate method or immunofluorescence, which are not mentioned, may continue to detect oocysts after Ziehl–Neelsen stained direct smears have become negative. The importance of symptoms other than diarrhoea is now well recognised. Although excretors without diarrhoea may provide a reservoir of infection, however, it may be argued that diarrhoea is the most important symptom in relation to the potential for transmission.

There is little reliable evidence on the incubation period and numerous confounding factors hinder attempts to arrive at an estimate in most cases, because of the complex epidemiology of the infection. The review paper cited to support speculation on the effect of age on the incubation period refers to experimental animals and not to patients. There is no evidence that the incubation period in man, as opposed to animals, is directly influenced by the age of the subject. The reasons for the apparent age dependency of susceptibility to infection in some animals but not in man are not yet clear. The differences in age specific incidence in man are probably related to exposure and hence to immune state. This may not be the case in some animals species as the phenomenon of decreasing susceptibility with increasing age has been detected experimentally in previously unexposed young gnotobiotic or specific pathogen free animals (Dr KW Angus, personal communication).

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Nucleolar organising regions in cervical squamous pathology

The variation in nucleolar organising regions (NORs) stained by a silver technique was investigated on the following types of squamous cervical tissue: normal, atrophy, chronic cervicitis, squamous metaplasia, papilloma virus infection (HPV), cervical intraepithelial neoplasia grades I-III, and invasive squamous carcinoma (table 1). Our findings did not agree with those of Rowlands, who performed a similar, though less extensive, study of AgNOR's in cervical intraepithelial neoplastic tissue.[1]

Table 1 *Mean AgNOR count in the various types of tissue studied*

Group	*Mean AgNOR count*
Normal	1·31
Atrophic	1·09
Chronic cervicitis	1·47
Immature squamous metaplasia	1·80
Koilocytosis only	1·54
CIN I	1·65
CIN II	2·10
CIN III	2·36
Invasive squamous carcinoma	2·46

Unlike Dr Rowlands, who found a significant difference in AgNOR counts between normal, CIN I, and II biopsy specimens compared with those showing CIN III, we did not. In our study there was a gradual increase in AgNOR counts with increasing severity of CIN, but there was an overlap between each group, with a significant difference observed only between normal biopsy specimens and those showing CIN III.

In the nine groups of cervical tissue samples studied, 10 biopsy specimens from each group were examined with an extra five biopsy specimens in the invasive carcinoma group. We used the same standardised silver staining method for NORs as Dr Rowlands had used, but our counting procedure was different. Counts were made only on the basal cells in all groups except those showing CIN or invasive carcinoma; for these counts were made on the full thickness of the epithelium occupied by morphologically abnormal cells. All cases were counted by one observer and then two cases from each group were recounted by the same and a different observer. The AgNORs in 200 cells were counted in each case. This method of counting gave a lower mean AgNOR count in normal biopsy specimens and those showing CIN of all grades than was observed in the published study.[1] While counting AgNORs in CIN, we observed occasional pockets of increased counts, reflecting increased activity.

Scheff's test was applied to the results which showed significant differences among the groups (table 2).

Our study showed that the use of AgNOR counts in cervical (squamous) pathology is of limited value and gives no extra information over that gained by morphological examination of conventional, haematoxylin and eosin stained sections.