Asymptomatic microscopical haematuria

SIR.—Because most studies of asymptomatic microhaematuria have dealt with referred populations, we read with interest the recent study by Dr Carolyn D Ritchie and others (8 March, p 861) on the importance of occult microhaematuria found at screening. Before fully investigating all patients with microhaematuria, as suggested in the article and accompanying leading article (p 645) we should consider several features of the article. Firstly, the population studied was not necessarily asymptomatic when it presented for health screening. Asymptomatic patients may have a lower prevalence of serious disease. Secondly, mid-stream analyses of urine were performed, and the application of the recommendations to routinely collected specimens is uncertain. Thirdly, many of the diseases found were not necessarily serious and the patients may not necessarily have benefited from their screening test. Finally, the presence of proteinuria and pyuria was not determined. Often the presence of these abnormalities leads to further testing in higher risk patients, leaving lower risk patients with isolated asymptomatic microhaematuria.

To establish the use of the analysis of urine for blood as a screening test for serious urological disease a controlled study is needed to assess aspects of sensitivity and specificity. Asymptomatic microhaematuria has not yet been proved to have a high positive predictive value for serious urological disease in a truly asymptomatic unselected population of patients.

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Increase in bronchopulmonary infection due to *Branhamella catarrhalis*

SIR.—Like Dr D T McLeod and colleagues (26 April, p 1103) we also report *Branhamella catarrhalis* when isolated from sputum in significant numbers and have noted an increase in β lactamase producing isolates. However, we are less convinced of its pathogenicity in most patients. To elucidate this further we have also just completed a six month prospective survey of bronchopulmonary infections due to this micro-organism.

From October 1985 to March 1986 *B. catarrhalis* was isolated as the predominant organism from the sputum of 56 hospital inpatients (32 men and 24 women). All except two: a 27 year old renal transplant recipient and a 24 year old with bronchiectasis were aged 50 or more (mean 70.5, range 50-90). Most patients were smokers or ex-smokers (41) and/or had chronic pulmonary disease: chronic bronchitis and emphysema (17), congestive cardiac failure (5), asthma (4), and bronchial carcinoma (3). In addition, 4 patients had diseases associated with generalised immunosuppression: acute leukaemia (2), renal transplantation, and myelodysplastic syndrome. *B. catarrhalis* was the sole pathogen isolated in 45 patients and was mixed with *Haemophilus influenzae* in nine, *Staphylococcus aureus* in one, and *Streptococcus pneumoniae* in one.

The incidence of β lactamase production was higher than that recorded in Edinburgh, 49 isolates (88%) being positive. This may reflect the different patient population studied (exclusively inpatients); interestingly, all seven β lactamase negative strains were isolated from specimens taken within five days of admission (mean, 2.0 days). β Lactamase positive strains were isolated at a mean of 11.8 days, range 0-59. All isolates were otherwise sensitive to erythromycin or amoxycillin and clavulanic acid (Augmentin) and all but one to co-trimoxazole.

In this hospital ampicillin or amoxycillin and co-trimoxazole are the agents of first choice for treating

bronchopulmonary infection.¹ Of 18 patients receiving amoxycillin, only four required a change of therapy after the report of β lactamase producing *B. catarrhalis*. Overall, about 10% of patients in our survey had genuine infection as judged by laboratory and clinical findings, and all such patients had a recognised predisposition.

Dr McLeod and colleagues suggest that the widespread use of ampicillin class antibiotics in the community has produced an ecological niche in the oropharyngeal flora which β lactamase producing *B. catarrhalis* has exploited. Our finding of β lactamase negative strains only in recently admitted patients who had not received prior antibiotics may support this. Whether this in turn enables this species to play an increasing part in bronchopulmonary infection or whether it is just identified more often because of increased interest is open to question.

The rise in β lactamase production of this organism since it was first noted in 1977^{2,3} has indeed been dramatic. The consequence of this on other closely related species in the orthopharynx remains to be seen.

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Biosynthesis of thromboxane in patients with systemic sclerosis and Raynaud's phenomenon

SIR.—We read with interest the paper by Dr I A G Reilly and others (19 April, p 1037) reporting increased thromboxane production in patients with systemic sclerosis and Raynaud's phenomenon, since it supports our own work,¹ not cited by the authors.

Apart from showing enhanced platelet reactivity in response to adrenaline, we found significantly raised plasma concentrations of β thromboglobulin but not of platelet factor 4.¹ In contrast, Dr Reilly and colleagues found that β thromboglobulin and platelet factor 4 were similarly raised, suggesting that the platelets had been activated in vitro, an artefact which in our experience can be avoided by taking appropriate precautions during blood collection and processing.

Their finding that a further significant increase in urinary 2,3 dinor thromboxane B₂ occurred after a brief period of central cooling is difficult to interpret without obtaining some idea of how much thromboxane A₂ release from the platelets this represents. Moreover, careful evaluation of renal function has to be undertaken when using urine to monitor changes in the concentration of constituents in the blood.²

We could not show any significant increase in platelet reactivity in the blood after a short period of local cooling in patients with Raynaud's phenomenon, although we found increased release of thromboxane A₂ during aggregation of platelets in platelet-rich plasma from patients with Raynaud's phenomenon.¹ The finding of a trend towards increased concentrations of the urinary metabolite of prostaglandin I₂, albeit non-significant, also supports an earlier report of raised plasma levels of 6-keto prostaglandin F_{1 α} in patients with systemic sclerosis and Raynaud's phenomenon.³

Finally, there are some inconsistencies in the

statistical analysis used by Dr Reilly and others, who while selecting non-parametric methods to "avoid making assumptions about the distribution of the variables," nevertheless inexplicably report their results as means and standard deviations rather than as medians and ranges as recommended by the *BMJ*.⁴

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Bleeding from peptic ulcers and use of non-steroidal anti-inflammatory drugs

SIR.—We are concerned that the *BMJ* should continue to publish articles such as that by Dr J D O'Brien and W R Burnham (7 December, p 1610). While it is never possible to correct for the faults of a retrospective analysis of data this paper is a classic example of the ascertainment and interpretative errors to which such studies are prone.

The authors do not indicate that their patient population of 460 subjects is comprehensive and includes all subjects from the catchment area with upper gastrointestinal haemorrhage or whether the hospital attracts an appreciable visiting or itinerant population. However, even if we assume that these are minor potential sources of error, the restriction of the analysis to 204 patients out of 460 subjects with gastrointestinal haemorrhage is quite unacceptable for any meaningful analysis.

In how many of the remaining 256 subjects can peptic ulcer be confidently excluded? How many of these 256 subjects were also taking non-steroidal anti-inflammatory drugs, and was the ratio of prescriptions of individual non-steroidal anti-inflammatory drugs the same as or different from that reported in the 204 patients? This would be of major importance as bleeding associated with these drugs is much more likely to be secondary to gastritis than to a peptic ulcer, as implied by the authors.¹

Have the authors made any efforts to analyse the percentage of patients with peptic ulceration without haemorrhage who were also taking non-steroidal anti-inflammatory drugs and did the distribution of drugs in these subjects differ from that in the patients described?

An even more fundamental problem is apparent. The relationship between non-steroidal anti-inflammatory drugs and gastrointestinal haemorrhage is generally considered as given but the link is doubtful and very difficult to prove.² The link between ingestion of non-steroidal anti-inflammatory drugs and peptic ulcer is even more tenuous and if it exists relates only to gastric ulcers and certainly not to duodenal ulcers.³ In the current study the failure to distinguish the site of ulceration makes any conclusions about causation tenuous.