

laboratories that responded provided measurement of high density lipoprotein cholesterol concentrations and that 70% of these restricted the service.<sup>1</sup> The computer program used by our chemical pathology laboratory was introduced in an attempt to rationalise the provision of analyses of high density lipoprotein cholesterol, which had previously been restricted to named consultants. As a direct result of this the number of assays of serum high density lipoprotein cholesterol has increased more than 10-fold.

The upper and lower limits for measurement, 6.5 mmol/l and 7.8 mmol/l, were chosen for the computer program after review of the available guidelines. This was thought to be the range in which knowledge of the serum high density lipoprotein and low density lipoprotein cholesterol concentrations would help clinicians to decide whether a patient required specialist referral or drug treatment, or both. We accept that with this current upper limit a small proportion of patients with a raised high density lipoprotein cholesterol concentration may not be identified if measurement of the concentration is not requested by the treating physician, as was initially the case with the patient described. Consequently the upper limit is currently under review.

We accept that the savings made in long term drug costs if patients such as the one we reported on are identified far outweigh the cost of measuring the high density lipoprotein cholesterol concentration. However, the cost of the assay, which is not insignificant, must currently be borne by the laboratory, and in the present financial climate we have to consider the cost implications of any change in the service that we provide.

JANE PATMORE  
SEAN COYLE

Department of Clinical Pathology,  
St James's University Hospital,  
Leeds LS9 7TF

1 Laker MF, Reckless JPD, Betteridge DJ, Durrington PN, Miller JP, Nicholls DP, *et al*. Laboratory facilities for investigating lipid disorders in the United Kingdom: results of the British Hyperlipidaemia Association survey. *J Clin Pathol* 1992; 45:102-5.

## Respiratory viruses and asthma

### Importance of infection underestimated

EDITOR.—The study by Karl G Nicholson and colleagues showing that upper respiratory tract viral infections were associated with 44% of exacerbations of asthma<sup>1</sup> gives a surprisingly low result in view of recent evidence. Beasley *et al* showed viruses to be associated with 36% of severe exacerbations using cell culture methods and serology, which as Nicholson and colleagues point out, are five times less sensitive than the polymerase chain reaction they used. Johnston *et al* showed upper respiratory tract viruses to be associated with 78% of asthma exacerbations in children<sup>2</sup> and also a time course correlation between viral isolation rates in children and hospital admission rates for asthma in all ages, thus suggesting viruses as the major precipitating factor for attacks in adults.<sup>4</sup>

The low isolation rate for viruses in asthma in the study by Nicholson and colleagues can perhaps be explained by their wide definition of an asthma exacerbation. Symptoms are notoriously unreliable as indicators of asthma severity.<sup>3</sup> Variations in peak flow are the most reliable indicators of asthma. The guidelines of the British Thoracic Society define an exacerbation as a peak flow less than 60% of predicted values, which for an average 30 year old man is a drop of 240 l/min. Nicholson and colleagues define an exacerbation as a change in mean peak flow of greater than 50 l/min. This will clearly lead to an overestimate of the number of exacerbations and hence an underestimate of the number associated with upper respiratory tract viruses.

A further problem is that patients were not asked to report drops in peak flow. As patients are poor perceivers of the severity of their asthma, reduced peak flow may precede the onset of symptoms by many days. Samples were taken only when changes in symptoms were reported, which is likely to be some time after the onset of the exacerbation in many cases, thus reducing the likelihood of isolating viruses.

A confounding factor is that Nicholson and colleagues may have missed several genuine exacerbations. The detailed list of symptoms sought did not include night time symptoms, yet for many asthmatic subjects such symptoms are the most sensitive indication of an attack. Patients were asked about cough, but it was not included as suggestive of asthma, although for many asthmatic subjects it is the predominant symptom of an attack and for some the only symptom.

Finally, there was a time delay between sample taking and storage of up to 12 hours. RNA is naturally degraded in the environment by ubiquitous RNAses and so the low isolation rate could reflect delay.

JONATHAN CORNE  
NICHOLAS CHANARIN

University of Medicine,  
Southampton General Hospital,  
Southampton SO9 4XY

- Nicholson KG, Kent J, Ireland DC. Respiratory viruses and exacerbations of asthma in adults. *BMJ* 1993;307:982-6. (16 October.)
- Beasley R, Coleman ED, Hermon Y, Holst PE, O'Donnell TVO, Tobias M. Viral respiratory tract infection and exacerbations of asthma in adult patients. *Thorax* 1988;43:679-83.
- Johnston SL, Pattermore PK, Sanderson G, Smith S, Lampe F, Josephs S, *et al*. Role of virus infections in exacerbations in children with recurrent wheeze or cough. *Thorax* 1993;48: 1055.
- Johnston S, Campbell M, Pattermore P, Smith S, Sanderson G, Myint S, *et al*. Association of virus infections with hospital admissions for asthma: a time trend analysis. *Thorax* 1993;48: 1055.
- Kendrick AH, Higgs CMB, Whitfield MJ, Laszlo G. Accuracy of perception of severity of asthma: patients treated in general practice. *BMJ* 1993;307:422-4.

### Authors' reply

EDITOR.—We acknowledge that the diagnostic rate for viruses during exacerbations was lower than expected on the basis of symptoms and commented on its possible relation to (a) virus shedding, (b) the fact that swabs were not tested for antigens by immunological techniques, and (c) the fact that we used complement fixation tests for some pathogens.<sup>1</sup> We believe that viruses are more important than our data illustrate, but not for reasons posed by Jonathan Corne and Nicholas Chanarin.

Beasley *et al*<sup>2</sup> associated viruses with 10 out of 28 (36%) "severe" exacerbations, but in only 18 out of 178 (10%) episodes overall. We identified viruses in 44% (27/61) of severe and 54% (51/95) of less severe episodes—that is, five times as many as Beasley *et al* overall. Beasley *et al* associated viruses with only 16% (30/182) of clinical respiratory tract infections, whereas we identified them in 57% (111/196).

The comparison of virus identification rates in children and adults is erroneous. A study of 2227 acute respiratory illnesses showed a progressive fall in isolations from 31.3% in children aged 0-4 years to 15.8% in adults of 40 and over;<sup>3</sup> Monto *et al* reasoned that the fall was related to decreased shedding secondary to previous infections. A review of viruses as precipitants of wheeze showed pathogens to occur 2.4 times more frequently in children,<sup>4</sup> again suggesting reduced shedding or a greater role of other precipitating factors in adults.

In contrast with Johnston *et al*<sup>5</sup> we used a validated rhinovirus seminested reverse transcriptase polymerase chain reaction that did not identify rhinoviruses in asymptomatic controls. Johnston *et al* used a picornavirus polymerase

chain reaction, which identifies rhinoviruses and other picornaviruses; their polymerase chain reaction was less specific, having a 12% positivity rate among asymptomatic controls.

Rhinoviruses are comparatively thermostable. We transported nasopharyngeal specimens on ice and stored them at -70°C within several hours of collection. We have found no benefit from adding RNase inhibitors to clinical specimens during collection and have amplified sequences from cDNAs of viruses in clinical specimens transported by post.

The mean decrease in peak flow was calculated from measurements throughout the week after onset of symptoms. We were concerned that our objective definition of an exacerbation would actually underestimate their number—those identified seem to be clinically important as half of the cases led to consultations with a general practitioner. Interestingly, we identified viruses with slightly greater frequency (54%) during less severe exacerbations. Thus to focus on exacerbations only as defined in the guidelines of the British Thoracic Society would in our view provide an incomplete picture of the role of viruses.

KARL G NICHOLSON  
JULIE KENT  
DEBORAH C IRELAND

Department of Microbiology,  
University of Leicester School of Medicine,  
Leicester LE1 9HN

- Nicholson KG, Kent J, Ireland DC. Respiratory viruses and exacerbations of asthma in adults. *BMJ* 1993;307:982-6. (16 October.)
- Beasley R, Coleman ED, Hermon Y, Holst PE, O'Donnell TVO, Tobias M. Viral respiratory tract infection and exacerbations of asthma in adult patients. *Thorax* 1988;43:679-83.
- Monto AS, Sullivan KM. Acute respiratory illness in the community. Frequency of illness and the agents involved. *Epidemiol Infect* 1993;110:145-60.
- Pattermore PK, Johnston SL, Bardin PG. Viruses as precipitants of asthma symptoms. I. Epidemiology. *Clin Exp Allergy* 1992;22:325-36.
- Johnston SL, Pattermore PK, Sanderson G, Smith S, Lampe F, Josephs S, *et al*. Role of virus infections in exacerbations in children with recurrent wheeze or cough. *Thorax* 1993;48: 1055.

## Methicillin resistant staphylococcal infection

### Clinical importance remains unevaluated

EDITOR.—Though Georgia J Duckworth's article is a factually correct account about methicillin resistant *Staphylococcus aureus*,<sup>1</sup> we do not agree with her recommendations.

Firstly, the clinical importance of methicillin resistant *S aureus* has not been adequately documented as reports have tended to be of epidemics of carriage rather than infection.<sup>2</sup> Also, when infection occurs, response to treatment with antibiotics is generally good.<sup>3</sup> Methicillin resistant *S aureus* is not more virulent than methicillin sensitive *S aureus*,<sup>3</sup> and many strains may be less virulent.<sup>2</sup> Even when virulence is clinically important, multiple resistance in *S aureus* is no more important than that in other organisms, such as *Pseudomonas* or *Enterococcus* spp, which are often difficult to treat. There are no recommendations that these organisms should be screened for or eliminated.

We do not know the importance of carriage in causing outbreaks of infection as information on infections (as opposed to carriage) is lacking. Evidence suggests that total elimination of methicillin resistant *S aureus* may not be possible even with rigorous intervention measures.<sup>4</sup> Such measures have also been shown to have little impact on endemic methicillin resistant *S aureus*.<sup>5</sup> Finally, use of topical and systemic antibiotics to eliminate carriage is likely to cause additional bacterial resistance, thus further reducing the drugs available for use in clinically important