laboratories that responded provided measurement of high density lipoprotein cholesterol concentrations and that 70% of these restricted the service.¹ 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.

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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 asthma¹ 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 children² 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.⁴

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.³ 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.

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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.¹ 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*² 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; 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,⁴ again suggesting reduced shedding or a greater role of other precipitating factors in adults.

In contrast with Johnston *et al*³ 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.

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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*,¹ 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.² Also, when infection occurs, response to treatment with antibiotics is generally good.³ Methicillin resistant *S aureus* is not more virulent than methicillin sensitive *S aureus*,⁴ and many strains may be less virulent.² 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.⁴ Such measures have also been shown to have little impact on endemic methicillin resistant *S aureus*.⁵ 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

infection. Indeed, changes in the use of antibiotics have been implicated in exacerbating or even causing the problem of methicillin resistant *S aureus*.

Much remains to be done in evaluating the clinical importance of methicillin resistant *S aureus* and recommended control measures. In the interim, infection control should be based on strictly enforced measures to control hospital infection, encompassing good hygiene practices among staff, thorough cleaning of patients' environment, and a prescribing policy that restricts the use of antibiotics.

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Infection spreads between hospitals

EDITOR,—In response to Georgia J Duckworth's article on infection with methicillin resistant *Staphylococcus aureus*¹ we wish to describe our surveillance programme for the infection and some of the containment procedures that are practised in the Netherlands. In the 1980s hospital epidemics of infection with methicillin resistant *S aureus* were documented in the Netherlands after patients were transferred from foreign hospitals.² Attention was thus drawn to the possibility of spread of the organism between hospitals. In 1989 the National Institute of Public Health and Environmental Protection in Bilthoven set up a nationwide surveillance programme for methicillin resistant *S aureus*. Isolates of the organism from Dutch hospitals were collected for four years (1989-92) along with data on their origin(s), phage types, antibiograms, and propensity for epidemic spread.

A questionnaire was sent to the hospitals to determine the origin of the isolates: a foreign country, the Netherlands, or not known. During this period, 721 isolates were received from 91 hospitals. Of these 721 isolates, 491 from 116 different admissions originated in 26 countries, while 167 seemed to have originated in the Netherlands: these may have been either selected or indigenous strains.³ The origin was unknown or not reported for 63 isolates.

Patients admitted to a Dutch hospital after an admission of more than 24 hours to a hospital abroad were isolated and screened for methicillin resistant *S aureus*. Colonisation or infection, or both, with the organism was usually detected within one week after admission. Isolation was discontinued only after repeated cultures for the organism yielded negative results. Spread of the organism to these patients within the Dutch hospital could therefore be excluded. Despite containment and screening procedures, however, epidemic spread to other patients and staff occurred with some "imported" strains. For example, one phage type designated III-29 originated in France (nine admissions), Spain (three), Portugal (two), Germany (two), and Belgium (one) and caused epidemics after its introduction, being responsible for 79 of the 114 isolates of III-29.

As well as the hygienic and isolation policies discussed by Duckworth, screening for methicillin

resistant *S aureus* in transferred patients has been recommended by the Dutch government since the late 1980s.⁴ Awareness of the possibility of the introduction of the organism is further enhanced by mailings from the Ministry of Health and local infection committees, especially before holiday periods. Furthermore, hospitals are notified of the intended transfer of a patient by the organisations engaged in repatriating patients to the Netherlands.⁵ Good communication between infection control doctors remains warranted when patients positive for methicillin resistant *S aureus* travel between hospitals. In this way the organism has been kept under control in the Netherlands. This is confirmed by a low prevalence of methicillin resistance (0.54% in 27 127 isolates of *S aureus*) found in another surveillance programme conducted by the National Institute of Public Health and Environmental Protection from 1990 to 1992 (A J de Neeling, personal communication).

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Nursing homes act as reservoir

EDITOR,—In her review of methicillin resistant *Staphylococcus aureus* Georgia J Duckworth states that this heterogeneous group of organisms is largely found in hospitals.¹ Her recommendation, and earlier guidance,² is for patients to be discharged early to the community whenever possible. As Duckworth indicates, screening methods used are insensitive, and even if patients are deemed clear of colonisation methicillin resistant *S aureus* may be detected after a few weeks. Persistent, long term carriage of some strains by asymptomatic people living in the community has been reported.³

Many of the patients in British hospitals colonised by methicillin resistant *S aureus* are elderly and will be discharged to residential or nursing homes.⁴ In the United States it has been recognised for several years that nursing homes may serve as reservoirs for the organism in the community.⁵ We observed small outbreaks of the strain EMRSA-15 first in orthopaedic wards and then in wards for care of the elderly in Bradford in the late 1980s and subsequently found the same strain in patients admitted to hospital from the community, particularly from nursing homes. Follow up of contacts of one patient admitted from a nursing home showed six of 43 residents to be colonised by the same strain. We have now observed methicillin resistant *S aureus* in patients admitted from nursing homes to hospitals in Leeds.

At the instigation of one of us (BG) a policy document, *Guidance for the Control of Infection in Private Residential and Nursing Homes*, has been produced by Yorkshire Regional Health Authority. This document provides information and guidance to proprietors and matrons of homes and to officers

of health authorities who register and inspect homes. Because of particular concern about methicillin resistant *S aureus* in these units educational sessions covering this topic have been organised for staff of nursing and residential homes in Leeds.

Although the risk of serious infection with these organisms in residents is low, the reintroduction of methicillin resistant *S aureus* from nursing and residential homes to acute hospitals is a continuing problem in some areas of Britain. The potential threat of this should be emphasised in guidance documents.

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Author's reply

EDITOR,—I believe that Parukutty Nair and John Henderson are incorrect in several factual matters and that their comments are misplaced in the light of current experience. The recommendations in my review are based on those of the combined working party of the Hospital Infection Society and the British Society for Antimicrobial Chemotherapy, which was asked to advise on the growing problem of epidemic methicillin resistant *Staphylococcus aureus* on two separate occasions^{1,2} and is convening again to address the issue of methicillin resistant *S aureus* in the community.

Screening will detect colonised patients, but true infections are an important part of the problem and may be serious.^{3,4} In 11 years' experience of over 1000 patients with an epidemic strain of methicillin resistant *S aureus* (EMRSA-1) at a London teaching hospital, I found that three quarters of the isolates were from patients with infections. The response to antibiotics depends on the infection. Glycopeptides may not be successful in the treatment of endocarditis or meningitis due to methicillin resistant *S aureus*, even in combination with other agents.

The statement that methicillin resistant *S aureus* is not more virulent than methicillin sensitive strains is meaningless as this depends on the strains being compared. Methicillin resistant strains can be as virulent as methicillin sensitive strains.⁵

Multiresistance in *S aureus* tends to be more important than that in *Pseudomonas aeruginosa* because *S aureus* can also be spread through the air. In an outbreak due to multiresistant *P aeruginosa* screening may be required. There is debate about appropriate control measures for enterococci resistant to vancomycin.

Spread is probably unlikely with nasal colonisation alone, while the reverse is true if eczema becomes colonised. Sporadic infections are probably endogenous, but person to person transmission occurs in an outbreak.

Clearance of methicillin resistant *S aureus* is difficult if there is a persistent wound or abnormal skin. Apparent relapses may reflect lack of clearance, subsequent exposure to antibiotics, or reacquisition.

Elimination of carriage with systemic antibiotics is not routinely recommended but is sometimes