Heterogeneity among Indians, Pakistanis, and Bangladeshis is key to racial inequities

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When is an emergency department not an emergency department?

Editor—Recently, a young couple, equipped with backpacks and bedrolls, walked into our local accident and emergency department at about 11 pm, climbed into sleeping bags, and set their alarm clock. Early next morning, roused by their alarm, the couple rolled up their bags and left. What was the explanation for this behaviour? It was not careful preparation for attending a department in which the waiting time can often be eight hours or more. The young couple, who lived in Surrey, had booked a holiday that started with a morning flight from Stansted Airport. Rather than get up at 4 am to get from Surrey to Stansted, they had worked out that it would be easier to spend the night nearer to the airport, and that our emergency department would be the safest (and cheapest) place in which to do this.

This curious but true story may raise a laugh, but it also raises a far more serious problem: that of the current abuse and misuse of emergency services. Initiatives involving patient education or NHS Direct are having minimal impact in stopping the public using emergency departments inappropriately.1 Departments are still overrun by patients with conditions that can be treated in primary care, with the result that waiting times remain lengthy and staff are subject to abuse by tired and tetchy people.

Is it time to invert the knowledge pyramid and put experienced doctors back into primary decision making roles? An emergency consultant, in partnership with an experienced nurse, could effectively triage (and weed out) patients at the first point of contact. Only patients with a genuine emergency would gain access.

Finally, in this era of rebranding, where accountants become days of the week, steel firms morph into male voice choirs, and the president of Turkmenistan renames the months of the year after himself and his mother, we should perhaps follow the American example and rename emergency departments emergency rooms. Then put a large legend on the door defining emergency for each patient about to pass through it: “An unforeseen occurrence or combination of circumstances that is potentially dangerous and calls for immediate action.”

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Focus on emergency departments to reduce delays in thrombolysis

Editor—Qasim et al reported the safety and efficacy of nurse initiated thrombolysis in patients with acute myocardial infarction.1 The stepwise improvement in thrombolysis times over the three phases is impressive and a credit to the medical and nursing staff of the coronary care unit. We hope that phase 4 will continue to show improvement, enabling the 2003 national service framework targets to be met.

The emergency department gets merely a cursory mention in the context of reasons and causes of delays in treatment. It seemed not to be deemed important in streamlining the management of patients with acute myocardial infarction. Yet during phase 1 it was one of the “two main reasons” for delays identified.

Phase 2 does not address this problem. Patients with suspected acute myocardial infarction in the emergency department were transferred to the coronary care unit for further assessment by a nurse. Presumably the patient had already seen a doctor in the department? Why not initiate treatment there? The coronary care nurse still had to call the on call medical team to see the patient; this was identified as a source of delay.

Phase 5 improved on this with nurse initiated thrombolysis, yet the patients coming from the emergency department had already been assessed. The diagnosis of a barn door myocardial infarction is based on the first electrocardiogram; if this is taken in the emergency department why not treat the patient there? The coronary care nurse repeats the electrocardiography, which again represents an unnecessary delay.

In our department we have a protocol for the prompt assessment and treatment of patients who attend with acute myocardial infarction. All patients with chest pain are triaged as red, have electrocardiography, and are considered immediately for thrombolysis by the medical staff in the department. Since all staff are fully aware of the protocol and the urgency with which acute myocardial infarction needs to be treated, the operation runs smoothly. Our results are frequently audited to identify and minimise delays and inappropriate thrombolysis. In the six months before April 2002 we gave thrombolysis in 92 barn door myocardial infarctions, 92% within 30 minutes and 85% within 20 minutes.

We believe that an emergency department is the most appropriate place for patients with myocardial infarction to be assessed and treated. Our methods have proved that with training of staff and audit of data the national framework targets are achievable, with patients benefiting the most.

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Probiotics and antibiotic associated diarrhoea

Lactulose is effective

Editor—D’Souza et al evaluated potential agents for the prevention of antibiotic associated diarrhoea, whose full spectrum of activity is immense both in the community and in hospital.1 In particular, the antitherapeutic default selection of Clostridium difficile...
with resultant colitis is associated with a considerable morbidity and mortality.

Alteration of the faecal flora is attractive as a low risk means of preventing or, possibly, treating *C difficile* and associated infections. Induced disequilibrium of the colonic flora can be achieved either through supplemental probiotic loading or by therapeutic manipulation. Faecal flora can be manipulated through the use of lactulose, a synthetic disaccharide that is predominantly used as an osmotic laxative. It is neither absorbed nor metabolised in the upper gastrointestinal tract but is degraded by the bacterial flora of the proximal colon to organic acids. These acidify the proximal colon and result in a dose dependent catharsis.

Lactulose has several additional properties, including an antiendotoxin effect and alteration of faecal floral patterns. This quantitative alteration in faecal floral patterns, with an increase in faecal *Lactobacillus acidophilus* and a reduction in both coliforms and bac terioerys, has been confirmed in our own unpublished work. A qualitative alteration in bacterial pathogenicity may result with lactulose as an alternative substrate.

Additional historical evidence shows effective treatment of shigellosis and salmonellosis with lactulose. Several risk and host factors have been recognised, and identification of people at high risk of antibiotic associated diarrhoea could facilitate targeted pretreatment with lactulose or con-joint treatment with lactulose and antibi-otics. An effective means of gaining rapid benefit might be through combining lactulose with a probiotic such as *L acidophilus*.

Additionally, in people who have developed antibiotic associated diarrhoea, lactulose induced manipulation of the faecal flora may prove to be an effective means of treating the infective cause of the diarrhoea, although clinicians may not easily be convinced to treat diarrhoea with *C difficile*, and infections are most commonly seen in elderly people.

Only four of the studies analysed included elderly patients (Gotz, Surawicz, McFarland, and Lewis), and in only four studies were any analyses for *C difficile* done (Orhage (normal volunteers, no cases seen), Surawicz, McFarland, Lewis). Either on their own or combining the results of these studies shows no benefit from probiotics (odds ratio 0.71, 95% confidence interval 0.29 to 1.76) (figure)

There are several rigorous systematic reviews on the subject of probiotics and diarrhoea, but the temptation to perform a meta-analysis has been resisted because of the lack of comparability of different probiotic organisms. D’Souza et al recognise this limitation when postulating the different mechanisms of action for the yeast and bacterial probiotics.

The author’s principal inclusion criterion was the occurrence of diarrhoea, defined as two or more loose motions per day for at least two days. Of the studies analysed only three met this criterion (Surawicz, McFarland, and Vanderhoof).

There was an error in table 1, instead of no cases of diarrhoea (Gotz et al) three cases (8.3%) occurred in the active group. In the study by Orrhage et al only half the volunteers who received active treatment were included, those not included had a higher incidence of diarrhoea. It is not clear why the prospective double blind placebo controlled study by Borgia was excluded; yet a trial by Orrhage was included that was principally a bacteriological study in healthy adults.

Furthermore, a trial by Colombel et al was excluded for being single blinded, although it was a double blind placebo controlled trial. Five studies were not analysed on an intention to treat basis (Surawicz, Tankaow, Vanderhoof, Gotz, Adam). The study by Adam et al had the biggest impact on the analysis yet is the most suspect of all the trials, with only 19.4% of recruited cases being analysed, the remaining being excluded because of protocol violations.

Probiotics are not without risk, with over 11 case reports of *Salmonella bouardi* septicaemia in the literature. Uncritical reading of this meta-analysis is misleading and risks injudicious use of possibly ineffective, potentially hazardous treatments. It may also distract from proved interventions such as modification of antibiotic policies.

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**Authors’ reply**

**Ennour**—We agree with Battle et al that the use of probiotics remains but one method of manipulating faecal flora as a means of controlling antibiotic induced diarrhoea. Using lactulose is an interesting idea, although altering bacterial flora by introducing an organism that can colonise the bowel as well as modify the proliferation of other organisms seems easier. Probiotics also have an antiendotoxin effect with an added benefit of stimulating an immunoglobulin response in the gut wall.

Furthermore, the use of lactulose is limited by lack of knowledge on the optimum dose at which it can have an effect on gut flora while not causing diarrhoea.

We agree that *Clostridium difficile* accounts for only 10-25% of cases of antibiotic associated diarrhoea. It accounts, however, for the most cases of colitis that occur and remains treatable once diagnosed. Our recommendations on the use of probiotics were not specific to elderly people—we did point out that a trial was needed in this age group.

The supposed error in table 1 relates to the percentage free of diarrhoea in the active and placebo groups in the study by Gotz et al. Our analysis was performed by using the numbers as mentioned (8.3% in the active group v 21% in the placebo group); the table highlighted the numbers in the groups when other treatment limits to include diarrhoea were excluded.

The study by Borgia et al was excluded because it primarily studied effects on body weight. The study by Colombel et al did not provide enough information on the number of cases of diarrhoea alone (diarrhoea was grouped as a side effect along with nausea, vomiting and abdominal pain). We are critical of these exclusions and yet for including studies analysed on a “per protocol” basis, an acceptable scientifically rigorous procedure.

We acknowledge the risks posed by probiotics, but most complications occurred in immunosuppressed individuals and people with other life threatening illnesses. This was mentioned in our paper, and we would leave it to clinicians to decide the individual suitability of patients to receive probiotics.

Our proposals about these agents seek not to replace antibiotic and infection control policies but to supplement them. A
Metronidazole is used for antibiotic associated diarrhoea in pregnancy in UK

**Entroor—Barbut and Meynard quote US guidance when recommending vancomycin as first line treatment for antibiotic associated diarrhoea in pregnancy.**

In the United Kingdom guidance issued by the medicines information centres and the National Teratology Information Service recommends metronidazole rather than oral vancomycin after a careful risk assessment of each drug.

Vancomycin is poorly absorbed from normal, intact gastrointestinal mucosa, but an inflammatory bowel process can result in increased absorption of the oral product. In patients with pseudomembranous colitis vancomycin may occasionally reach therapeutic concentrations in serum, which can be associated with diarrhoea in pregnancy. In the United Kingdom is to use metronidazole 400 mg thrice daily in preference to oral vancomycin. It is used in the dosing schedule (continuous or pulsed therapy) recommended locally by microbiology department and for the shortest time to clear the infection.

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Heterogeneity among Indians, Pakistanis, and Bangladeshis is key to racial inequities

**Entroor—Feder et al recently confirmed and extended observations pointing to inequity in the invasive management of coronary disease.**

The inequity in invasive management is not due to physician bias or socioeconomic status and emphasise as explanations patients’ understanding of risks and benefits, and barriers in the healthcare system after placement on a waiting list.

Similar observations in the United States have led to intense debate, particularly on the potential role of race. In my overview I also wrote that even if patients’ preferences are partly responsible for the disparities, race will not be wholly exonerated.

Within the data of Feder et al are buried interpretations and conclusions.

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**Letters**

multipronged approach should facilitate a reduction in the occurrence of antibiotic associated diarrhoea.

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5 Colombel JF, Cortot A, Neuf C, Ramond C, Yogaert with oral metronidazole during the first trimester. A recent prospective controlled study of 228 women exposed to metronida- zole in pregnancy, 80% of whom were exposed in the first trimester, confirmed these findings.

The long term postnatal effects of intrauterine exposure to metronidazole, if any, have yet to be determined. However, data from a 20 year ongoing study give no indication of an increased incidence of malignancies after metronidazole treatment.

Given the wide experience of metronida- zole in pregnancy and the theoretical risks and less experience of using vancomy- cin in pregnancy, the advice in the United Kingdom is to use metronidazole 400 mg thrice daily in preference to oral vancomycin. It is used in the dosing schedule (continuous or pulsed therapy) recommended locally by microbiology department and for the shortest time to clear the infection.

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5 Barbut F, Meynard J. Why should you avoid metronidazole? BMJ 2002;324:1345-6. (6 June.)

Sex differences in occupation may affect height associations

**Entroor—Power et al use data from the national child development study to show that height is related to both social position and social mobility. They also try to measure the effect of changes in social structure on inequalities in height by comparing two simple summary measures of the relation of height to social class at age 7 (1965) and at age 33 (1991), separately for men and women. They describe the**
differences in the social class distributions at age 7 and 33 as changes in social structure between 1965 and 1991 for parents and offspring at a comparable age in the life span.

For the men this is a fair comparison, but it is potentially misleading for the women. For both men and women social class at age 7 is defined by the occupation of their father. Comparing women's occupations at 33 with their father's at roughly the same age is more complex as the comparison is confounded with sex differences in occupation. These differences affect the social class distribution and hence the measures of social inequalities.

The table gives the social class breakdown of 33 year old men and women from the samples of anonymised records from the 1991 census. It shows a close match to the social class distributions of the subjects in the national child development study at age 35 in 1991, reinforcing their claim to representativeness. It also shows the differences in social class distributions of men and women.

These differences are particularly noticeable for classes III non-manual and III manual: women are much more likely to be in class III non-manual than III manual, the reverse being true for men. In the national child development study 11% of women are classified as III non-manual and 46% as III manual at age 7, whereas at age 33, 37% are in class III non-manual and 7% in III manual.

These "changes" may be more appropriately attributed to sex differences in occupation than to social mobility. Although there may not be a better 'measure' of social class of origin available for the women, interpretation of changes merits some caution.

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2 Census Microdata Unit, A user's guide to the SRS, Manchester: University of Manchester, CMU, 1999.

Alcohol and death: the New Zealand experience

Editor—As a simple measure of human nature, I suspect the initial impact of the paper by White et al on alcohol consumption and mortality will depend on the age of the reader; as someone in the two unit a week group (by a whisker of course) I was drawn to read the article in more depth.

Although it is clear what the paper adds, it is harder to decide how it affects what we do as health professionals and as part of society. The last comment made by the authors in the discussion is particularly pertinent: "Finally, as most deaths attributable to alcohol at younger ages are due to injuries, a greater focus could be placed on avoiding risky patterns of drinking rather than on reducing average alcohol consumption."

Injuries are a significant cause of death in young adults; even looking at all age death rates given in table 1 in the paper, this category is the third largest cause of death. It would therefore be simplistic to respond to this paper by reviewing recommended alcohol intake alone and ignoring behaviour. Taking drunk driving as an obvious example, I have been interested to see the New Zealand approach to this problem since moving here from the United Kingdom. Until recently, New Zealand had one of the highest per capita death rates for road traffic injuries in the world, and alcohol played a large part in this (between 1987 and 1992, 35-46% of fatally injured drivers tested were over the limit—two thirds to three quarters were tested). Most of these alcohol related deaths were in the age group 15-44 (peak 20-24 years), which reflects the risk findings of the paper.

One of the strategies that has probably helped to reduce this figure (20% of fatally injured drivers in 2000) has been to vary the legal alcohol limit by age. The legal limit under the age of 20 years is 30 mg/100 ml (blood)—this is effectively zero tolerance. Penalties at all ages are high: financially, through suspension, and through potential custodial sentence. With alcohol as the intervention and death as the outcome, one of the key consequences of this paper should be to continue to seek ways of minimising or avoiding the processes that link them together.

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Surveillance of whooping cough should continue

Editor—Crowcroft and Britto's editorial on whooping cough provides little evidence of global resurgence, mentioning only limited outbreaks associated with strains producing variants of pertactin and pertussis toxin and no adverse role associated with variants among British or French isolates. These two components are virulence factors in mice, but antibodies to them correlated poorly with protection of children, and acellular vaccines containing them have been less efficacious than whole cell vaccine.

Of more concern is the reliability of the diagnosis of pertussis in some outbreaks of coughing. Of 23 recently reported cases in Leicestershire, only six had laboratory confirmation, largely on the basis of tests of less certain specificity (polymerase chain reaction and serology) than positive culture. Culture confirmation rates of 80% can be achieved by efficient pernasal swabbing and meticulous laboratorial procedures. Culture negative cases, with a paroxysmal cough of less than three weeks, may well be caused by viruses or other microbes. With genuine pertussis infection the organism has been cultured while coughing persists for up to three months from onset.

The editorial suggests that vaccination may be more effective in preventing disease than infection. But, if the organism cannot be cultured from mild infections in older children and adults, these atypical cases are unlikely to be a serious source of transmission. Moreover, this hypothesis is inconsistent with the elimination of pertussis in countries that have persisted with compulsory vaccination from 3 months of age with whole cell vaccine containing all three agglutinogens.

Our own experience with British isolates shows that in recent years the annual incidence of culture confirmed cases has been less than half that recorded in 1997, with an appreciable fall in serotype 1.2. Crowcroft and Britto are right to recall the low efficacy of some vaccines in the 1970s and 1980s in Canada and Sweden (and Finland). If the vaccine was deficient in agglutinin 2, serotype 1,2 infection occurred in vaccinated children. If the vaccine was deficient in agglutinin 5, type 1,3 infection occurred, but type 1,2 was found also in non-vaccinated children because of the colonising advantage of this fimbriate serotype.

We therefore support the call for continued surveillance. This should include thorough attempts to obtain culture confirmation of the infection, backed up by carefully controlled serology in clinically suspected, culture negative cases. The pertussis reference laboratory will continue to confirm the identification and serotype of isolates received and provide a serology service for diagnosis and for assay of immune response to vaccination.

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The table gives the social class breakdown of 33 year old men and women from the samples of anonymised records from the 1991 census. It shows a close match to the social class distributions of the subjects in the national child development study at age 35 in 1991, reinforcing their claim to representativeness. It also shows the differences in social class distributions of men and women.

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2 Census Microdata Unit, A user’s guide to the SRS, Manchester: University of Manchester, CMU, 1999.
Bad bugs travel as well as happy holidaysmakers

Editor—Zuckerman's timely article, coming hot on the heels of Getting ahead of the curve, should remind us of the personal risks posed by tropical and imported infections.1 It should also remind us of the even greater risks posed not only to individual patients but also to the population as a whole by the unevenness of availability of quality clinical acumen across the United Kingdom when it comes to diagnosing and managing this category of illness.

Nowhere is this made clearer than by the case of a 78 year old female woman who was admitted to a British district general hospital in December 1997.2 Subsequently she developed thrombocytopenia, melaena, and a haemorrhagic rash. She died without a diagnosis having been made, despite having undergone numerous invasive investigations.

In retrospect, the key factor in this history was that she had returned from Zimbabwe a few days before admission, Zimbabwe has Congo-Crimean haemorrhagic fever, which therefore would—and should—form part of the differential diagnosis in a febrile patient. Congo-Crimean haemorrhagic fever was diagnosed postmortem in this case.

Rare though cases of viral haemorrhagic fever may be, the earliest possible recognition of the possibility is crucial as there is great potential for secondary spread. Congo-Crimean haemorrhagic fever is associated with severe haemorrhagic features—for example, one case in a patient who was resuscitated in a Saudi Arabian emergency unit gave rise to seven secondary cases.3 The possibility of a viral haemorrhagic fever should accordingly result in expert bedside clinical assessment and transfer to a category 4 isolation facility, as well as potentially life saving ribavirin treatment in some cases.

On public and staff safety grounds alone, therefore, the existence of this worrying British case merits widespread recognition. This is becoming especially and increasingly important as tourism to Africa and South America (where the bulk of the most hazardous viral haemorrhagic fevers are encountered) is increasing every year. The new generation of double decker “Super Jumbo” planes are each likely to be able to carry 850 passengers rapidly across vast distances, and it will only take one case of viral haemorrhagic fever in any one of these seats to lead to a major problem.

Coppetts Wood Hospital in London and Newcastle General Hospital in Newcastle upon Tyne are the only centres in the United Kingdom that currently have adequate category 4 facilities for managing not only viral haemorrhagic fevers but also patients potentially infected with highly transmissible biological agents used as weapons, such as smallpox and pneumonic plague. Out of almost 60 million people residing in the United Kingdom, a densely populated country, almost 50 million travel abroad annually so two centres may in time prove to be not enough.

Forewarned is forearmed—we should take travel medicine and international health issues seriously and be prepared.

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Correction
Don't forget syphilis

An editorial error occurred in the second letter of this cluster, by David Goldmeier and Linda Greene (5 October, p 776). The first sentence of the third paragraph should have read: “Although treatment failures with one injection of benzathine penicillin 2 MU in patients with early syphilis and HIV have been described,” the latest guidelines from the US Centers for Disease Control and Prevention continue to advocate this one off injection for HIV coexisting with syphilis.2

[Not, as published: “Although treatment with one injection of benzathine penicillin 2 MU in patients with early syphilis and HIV have been described,” the latest guidelines from the US Centers for Disease Control and Prevention continue to advocate this one off injection for HIV coexisting with syphilis.2]