that high molecular weight neutrophil chemotactic activity is derived from mast cells, and increases in plasma histamine with exercise may originate from circulating basophils.[6 12] Furthermore, sodium cromoglycate has several pharmacological effects other than mast cell stabilisation which may be relevant to its protective effect in exercise induced asthma.[13]

Several factors should be taken into account when assessing and treating patients, and especially children, with exercise induced bronchoconstriction.[14] Asthmatics are often in poor physical condition and even small amounts of exercise may produce disproportionate hyperventilation and therefore bronchoconstriction. Nevertheless, they need regular physical activities to maintain their fitness and help them through difficult periods. Children with asthma are commonly exempted from physical exercise at school and they may avoid sports or exercise in their leisure time.[15]

These attitudes need to be reversed, and local activity groups are being or have been set up to encourage physical training and group activities. At least 70 such groups are operating in Britain and have proved a great success. As well as encouraging asthmatic children to be more competitive and sociable they promote the prophylactic use of drugs and the gradual build up of muscle strength. The groups' physical activities include a warming up period followed by games and organised physical training programmes. Several studies have shown definite psychological and social benefit from such programmes.[15] The gains include an increase in aerobic fitness; an improvement in breathing mechanics, posture, body mass, cardiac output, muscle strength, and endurance; and also reductions in the frequency and severity of asthma attacks, absenteeism from school, and requirements for medication. Most training programmes are designed to require submaximal exercise, falling short of inducing exercise induced bronchoconstriction.[16] One recent study, however, has shown that a distance running programme can be safely undertaken by asthmatic children—but with benefit only in relation to physical fitness and not in resting pulmonary function, exercise induced bronchoconstriction, or ventilatory muscle strength.[17]

Plainly the image of bronchial asthma is now changing—a fact reflected in the large number of asthmatic people who have achieved outstanding successes in a variety of international sports. How gratifying it is that these sporting celebrities have been so ready to allow their condition to be widely publicised for the benefit of others.

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Antibiotic resistance in Serratia marcescens

The Gram negative bacillus now called *Serratia marcescens* and classified as a member of the Enterobacteriaceae was formerly known by a variety of names, including *Chromobacterium prodigiosum.* The bacillus is ubiquitous, and it characteristically produces a red pigment, prodigiosin. There are reports of it being responsible for the discoloration of food,[1] and romantic stories from the middle ages of communion bread mystically dripping blood are explained by its growth on a starchy substrate incubated in moist conditions at ambient temperatures.[2] For many years bacteriologists considered *Ser marcescens* to be non-pathogenic and used it as a biological marker because of its easily recognised red colonies. Studies in man were carried out as late as 1960, all apparently without ill effect. In one notable British study *Ser marcescens* was isolated from the blood of nearly half of the patients whose gums had been painted with a culture of the organism before dental extraction.[3]

In hospitals the organism is now regarded as an important pathogen, a reputation which started in the 1950s when infections due to serratia were first reported.[4] Most of the strains that cause infection fail to form pigment, so their colourless colonies are difficult to distinguish from those of other coliform organisms.[5] They are usually identified by a series of biochemical tests which were not routinely performed before the introduction of commercially prepared kits (such as the API 20 E system). Isolates of *Ser marcescens* may have been reported as "paracolon bacilli," and possibly many infections went unrecognised.[6] Although this may be true, two reports from Glasgow Royal Infirmary, separated by a decade, suggest that serratia infections are on the increase in Britain.[7 8]

A genuine increase is not surprising because the organism causes opportunistic infections in patients ill from some other cause and further predisposed to infection by recent treatment with antimicrobial drugs (often cephalosporins) to which

serratia are resistant.[9] The typical patient is recovering from an operation in an intensive care unit[10] and has an indwelling urinary catheter[11] and an endotracheal tube.[12] The number of patients like this has increased in recent years and they may develop life threatening infections with *Ser marcescens* such as septicaemia,[11] endocarditis,[13] and meningitis[14] as well as infections of wounds[6] and of the respiratory[12] and urinary tracts.[15] The range of infection caused by serratia is thus wide.[16]

Epidemics have been recorded in intensive care[10 11] and neonatal units, and this week Dr Lewis and colleagues report (p 1701) another outbreak in a special care nursery in which five babies became infected, two of whom died. *Ser marcescens* thrives in moist conditions, and investigation of an outbreak may identify a common source of the organism such as saline in plastic bottles,[17] water in ultrasonic nebulisers,[18 19] solutions used for inhalational treatment,[12 20] quaternary ammonium disinfectant solutions (which in one report contaminated the bypass machine used in cardiopulmonary operations),[21] and hand lotions.[22] Despite thorough investigation Dr Lewis and colleagues could find no such point source and they concluded that the reservoir of *Ser marcescens* in the unit was the infants' gastrointestinal tracts. This reservoir has been recognised before in neonates,[23 24] though faecal carriage is rare in adults.[4 25 26] *Ser marcescens* was also found in voided urine samples collected from the babies but these turned out to be merely an indication of colonisation of the gut because suprapubic aspirates were sterile. In adults, however, the infected urinary tract is an important reservoir, especially if the patient has an indwelling catheter.[26–28] Except in those epidemics due to a common source, hand to hand transmission is thought to be the most important mode of spread within a unit[2 26 27]—an assertion supported by the report this week.

Infections due to *Ser marcescens* are difficult to treat because the organism is resistant to a variety of antibiotics including ampicillin and both first and second generation cephalosporins.[16] Nevertheless, it is sensitive to the aminoglycosides as well as to the newer cephalosporins. Netilmicin, a promising new aminoglycoside with a high level of antibacterial activity against multiply resistant strains of *Escherichia coli*, *Klebsiella aerogenes*, and *Enterobacter cloacae*,[29] has good activity against strains of *Ser marcescens* resistant to gentamicin.[30] This drug has found favour in clinical practice because of evidence from studies in animals[31] and in patients[32] which suggests that it is less ototoxic than other aminoglycosides.[33] Paediatricians in particular have been keen to use it for this reason.

Bacteria acquire resistance to aminoglycosides by preventing the drug from reaching its target site in the ribosome. This may be achieved in two ways: firstly, alterations in the cell envelope render the cell impermeable to the drug, and, secondly, the drug itself is modified by so called inactivating enzymes which adenylate, acetylate, or phosphorylate aminoglycoside hydroxyl and amino groups. Drugs modified in this way cannot enter the cell. The former mechanism usually confers low level but clinically important resistance to all aminoglycosides, although one drug may be more affected than another; the second mechanism, which is the more important, is more selective. Enteric bacteria resistant to gentamicin are uncommon in Britain, though resistant strains have posed a major problem in parts of the United States and Europe. Amikacin resists attack by enzymes which degrade other aminoglycosides, and netilmicin is also resistant to some of these enzymes.[34] The netilmicin sensitive gentamicin resistant pattern of resistance in *Ser marcescens* is probably due to acetyltransferase AAC(3)I—an enzyme which inactivates gentamicin but not tobramycin, netilmicin, or amikacin.

It is disappointing, but not surprising, that strains of *Ser marcescens* have now emerged which are resistant to netilmicin and the most important and intriguing finding of Dr Lewis and colleagues is the antibiotic resistance shown by the epidemic strain that they describe. This strain produced acetyltransferase AAC (6′) which conferred resistance not only to netilmicin but also to tobramycin and, to a less extent, amikacin, though the organism remained sensitive to gentamicin. Aminoglycoside resistance in *Ser marcescens* due to inactivating enzymes is commonly mediated by plasmids and is transferable,[8 25 35] but in this instance it was due to mutation and was not transferable. Treatment of infected babies with either gentamicin alone or gentamicin and cefotaxime gave rise to strains that showed increased resistance to gentamicin and the other aminoglycosides in addition to a number of β lactams. This may have been due to elaboration of a variety of chromosomal enzymes and mutation to single and multiple drug resistance, perhaps consequent on genome rearrangement, which is more common in *Ser marcescens* than in other enteric bacteria.[36]

Dr Lewis and colleagues describe a particularly resistant strain of *Ser marcescens* which, given the potential for spread within a closed community containing susceptible hosts, caused an epidemic. Their report is yet another salutary lesson about the adaptability of bacteria. Hospital pathogens such as *Ser marcescens* have mechanisms which enable them to overcome the threat to their survival posed by the ever increasing number of new antibiotics.

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Medicine's Booker

Sitting comfortably in their definitive posts, survivors of the publish or perish race may harbour little ambition to do more than rest on their paper laurels, secure in the knowledge that their words are recorded for posterity in journals of repute. But the urge to be seen in print may remain, and some go for the next literary hurdle—writing a medical textbook. Undoubtedly many succeed, for there are an increasingly large number of texts, at an increasingly large price, on most medical topics. The prospective buyer may then be faced with as wide and confusing a choice as the physician leafing through *MIMS* in search of an anti-inflammatory agent. Pharmaceutical companies know that the initial choice of a drug is more likely to be determined by an attractive promotion package than by the results of a placebo controlled double blind crossover trial. Publishers know their market equally well. Promotion may assume a more gentlemanly guise, but the approach is similar, and colour rather than content may influence choice.

There is, therefore, a case for more critically evaluating prospective publications and a drive towards quality rather than quantity. But how can these be achieved? One group of people who are attempting to answer this question and are particularly concerned with the quality of medical textbooks and the special difficulties facing their authors, is the Medical Writers Group. Formed in 1979 (as part of the Society of Authors, itself founded in 1884 to promote the interests of authors), the group has about 120 members, most of whom are medically qualified and all of whom have had "full length" works published. (The criteria for associate membership are less weighty.) One way to stimulate both competition and an appreciation of quality, the group decided, was to award an annual prize for medical writing. Abbott Laboratories Ltd has agreed to fund an annual prize of £1000 for the next three years. The Abbott prize is the first of its kind, although there are some 136 British and Irish literary awards for which a non-medical tome may be entered.

Of the 70 entries, most were medical textbooks, although a few texts were devoted to the other caring professions, and most of the leading medical publishers were represented. The criteria for judging the entries included clarity of expression and aesthetic appeal as well as scholarship. But decisions of this nature are bound to have their subjective elements and, to borrow an expression of one of the judges (Professor Hugh Dudley), at the end of the day "it was very much a gut reaction."

Of the six books shortlisted (p 1729), the winner of this year's Abbott prize was *Occupational Lung Disorders* by W R Parkes, but it was a close run thing.

It is interesting to extrapolate from the effects of winning other literary prizes to the possible benefits of winning the Abbott prize. Over the past few years the publicity surrounding the Booker McConnell prize has increased by leaps and bounds, and few remain ignorant of either the winner or the runners up. As a direct result of this sales soar—for example, *Midnight's Children* by Salman Rushdie initially sold about 4000 copies in hardback; after it won the Booker prize in 1981 it sold 40 000 copies in hardback and about 250 000 copies in paperback, and is still selling well. Given that our medical texts have a more recherché appeal, I still hope that one spin off of winning (or being shortlisted for) the Abbott prize will be increased sales and some prestige for the author(s) and publishers concerned. With luck it might improve the quality of our medical textbooks and deter the literary equivalent of the "me too" drug. In any case it is a step in the right direction.

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More information about the Medical Writers Group is available from its secretary, Philippa MacLiesh, The Society of Authors, 84 Drayton Gardens, London SW10 9SB.

Correction

The lipoproteins: predictors, protectors, and pathogens

We regret that the last line of the 7th paragraph of Professor Barry Lewis's Regular Review leader on "The lipoproteins: predictors, protectors, and pathogens" (22 October, p 1161) was incorrect. It should have read "by, and in part catabolised, in the liver.[16 18 19]" We apologise for this error.