The situation in London clearly requires action. The data, however, suggest different approaches to those taken in New York City (table 1). New entrant screening deserves greater attention, and a heightened awareness of tuberculosis in primary care could complement the current system. The tuberculin skin test has a poor specificity and sensitivity and we should investigate newer methods of diagnosing those patients with latent tuberculosis who have a high probability of progressing to disease. We should maintain our vigilance to prevent active transmission by treating those with infectious, smear positive pulmonary tuberculosis rapidly and effectively. This can be complemented with well targeted contact tracing. Selective DOT is a part of this programme, but we would emphasise that each patient should be treated as an individual and treatment should be tailored to his or her needs.

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References

Guidelines on prevention of venous thromboembolism during long haul flights

The guidelines drawn up on prevention of venous thromboembolism and long haul flights should be welcomed, though seen in the light of incomplete evidence. We would like to draw attention to several points. Scurr et al looked prospectively at a group aged over 50 years undergoing long haul travel from which anyone with recognised risk factors was excluded, putting such individuals into a low risk group for venous thromboembolism. Twelve of 116 people who were randomised to the “no stocking” group were diagnosed with symptomatic calf deep vein thrombosis after their long haul travel. None of the group randomised to wear compression stockings developed deep vein thrombosis. Even if we take this surprising finding at face value, we are left with the
question: what is the clinical significance of asymptomatic calf deep vein thrombosis in a low risk population? It is far from clear in such a low risk group that we need to treat such events, which weakens any guideline aimed at prevention. Unlike a postoperative patient, the traveler is mobile before and after flight as well as potentially during it.

Furthermore, considering the uncertainty of the evidence, it would be wise to advise passengers of potential side effects from our recommendations. Unofficial thrombophlebitis occurred in four individuals (3%) wearing compression stockings in the study by Scurr et al, indicating some morbidity with their use. As far as we are aware, no study has looked at the preventative effect of long socks or support tights recommended for low risk passengers. It is also a shame that no study has included compression stockings in the study by Scurr et al.

It is also a shame that no study has evaluated the non-invasive measures of mobility and promote the use of support tights or long socks. Until further evidence emerges, can we reasonably entertain the use of such stockings? It is also a shame that no study has raised.

In the passenger with a moderate to high risk of venous thromboembolism, the recommendations are for compression stockings and aspirin or anticoagulation. This is based on extrapolation from studies of postoperative patients, but it is not clear that passengers fall into the same category. While it may be prudent to make unsubstantiated guidelines for high risk individuals, are we really going to recommend pre-flight aspirin and use of compression stockings for every individual on chronic replacement therapy and the oral contraceptive pill? What will be the morbidity associated with aspirin use?

While we await further studies to answer our questions, we agree that all at risk patients should be strongly recommended to take lifestyle measures. This information should be dispensed by airlines and public health. There is no evidence for the use of knee socks in any group, and this recommendation should be dropped. Patients with low to moderate risk factors should be advised that compression stockings have reduced the risk of thromboembolism in other situations, but that superficial thrombophlebitis can occur as a side effect. Any further intervention with aspirin or low molecular weight heparin can be offered to moderate to high risk individuals only on the basis that direct evidence is lacking and side effects are possible.

Finally, when making the recommendations, patients should be warned that case studies and few anecdotal reports of an increased risk of thromboembolism in long distance travel, not just long haul flights.¹

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References

Author’s reply
We appreciate the interest expressed by Drs Campbell and Rayner in the BTS’s flight to fly guidelines and welcome their valuable comments. We would like to clarify the issues they raised.

Firstly, we agree that the clinical significance of asymptomatic calf deep vein thrombosis in a low risk population is as yet unclear, and for this reason we avoided didactic advice while awaiting further evidence. Our recommendations were that physicians may wish to recommend low dose aspirin or non-elasticated long socks in patients at increased risk of venous thromboembolism. The physician’s decision will depend on individual circumstances, including patient preference.

Secondly, we refer to the guidelines recommendation by Scurr and Rayner raising the issue of superficial thrombophlebitis, which developed in 3% of passengers who wore below knee elastic compression stockings. The significance of this result, as indicated by the confidence intervals, is unclear, and our recommendations did not include such stockings. Rather, we suggested the possible use of non-elasticated long socks which are less likely to compress varicose veins in the knee region.

Thirdly, we agree that further studies are required to examine the effects of lifestyle measures such as mobility and hydration, and our guidelines recommended further research into this area. With regard to the possible morbidity associated with a single tablet of low dose aspirin, we consider that this is likely to be very small.

Finally, regarding passengers on oral contraception, we have made it clear that the risk is not equal with all forms of contraception, and physicians and passengers will have to make their own decisions in the light of available evidence and individual circumstances.

The process of producing these guidelines has highlighted the fact that there are a considerable number of unknowns regarding flying with respiratory disease, and more research is clearly required.

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Endotoxin: does it have a role in prevention of lung cancer

The paper by Drs Douwes, Pearce and Heederik provides an interesting overview of how endotoxin may interact in atopy and asthma. It discusses issues as to whether endotoxin plays a role in prevention of atopy and asthma or may, in fact, be a contributor to these respiratory diseases. However, readers should be aware that there is another important issue, although controversial, related to endotoxin and the lung—that is, does endotoxin exposure in some occupational groups result in reduced lung cancer rates?²

There have been a number of reports³ suggesting that endotoxin exposure, mostly in organic dusts, results in reduced lung cancer rates. This reduced lung cancer rate was first identified in textile workers¹ and later in agricultural¹ and other groups¹ exposed to endotoxin. Experimental studies³ have supported epidemiological findings and clinical trial.¹² have been undertaken to evaluate this agent and the effectiveness of its immunomediators in cancer treatments. Although the concept of a beneficial effect from occupational exposure is novel, it is of interest in at least one other occupational epidemiological investigation of reduced lung cancer rates for a potentially better recognised anticancer agent (selenium).¹³ Most investigations disagree with any beneficial effect from occupational exposure and attribute these findings to various forms of selection bias (healthy worker effect) and lower rates of smokers in study populations (compared with controls).

Certainly exposure to organic dusts and endotoxin does not occur without risk. There are numerous reports of the detrimental outcomes associated with such exposures. However, when various forms of bias are evaluated, there appears to be in some studies an inability to explain the reduced lung cancer rates.¹¹

It is encouraged that scientists accept the concept that there is an alternative view for lower lung cancer rates in some study populations. Even though this challenges prevailing thought and conventional thinking, we must remember that tradition dies hard and the birth of a new idea requires a creative and innovative spirit.¹⁰

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References
High incidence of cystic fibrosis in children born in Italy to Albanian immigrants

The incidence of cystic fibrosis (CF) can vary significantly among different racial groups; within white populations it has been reported to vary from 1/3419 in the USA to 1/2500 in Italy. According to Lewis, the highest incidence that can be reliably expected in white populations is 1/2500, although a value as high as 1/936 has been reported in a well-defined community.

Italy and other European countries have experienced a heavy influx of immigrants from the former Yugoslavia in the last 10 years following political and economic upheaval in that country. Although precise numbers are not available, since 1989 some tens of thousands of Albanian immigrants have settled in Italy, a region of Central Italy populated by 3.5 million people in an area of 23 000 sq km. There are no data on the incidence of CF in Albanians, so we have calculated the incidence of CF in newborn infants of the Albanian community residing in Tuscany.

We analysed the records for the period from 1 July 1991 to 31 December 2001 contained in the Tuscany regional neonatal screening programme for CF which was carried out using the immunoreactive trypsin assay with lactase meconium complementary test, and which covered 99.99% of the newborns born in the region. During the observation period 275 520 newborn infants were screened for CF in Tuscany. On the basis of the information contained in the forms completed at birth by the obstetricians in the maternity wards or at home and checked by the CF Regional Centre, 1803 children were born to both ethnic Albanian parents during this period. The number of Albanian newborns was not constant over the years of the study, but it has grown steadily from 15 in 1991 to 474 in 2001.

During the observation period four cases of CF were diagnosed (by two positive sweat tests) among children born to both Albanian parents (incidence 1/450 (95% confidence intervals (95%CI) 1/176 to 1/1653)) and 60 cases were diagnosed among the 273 717 non-Albanian newborn infants in the region (incidence 1/2381 (95% CI 1/1354 to 1/3577); point estimate ratio 10.12 (95% CI 2.67 to 27.28); p=0.0009). The four Albanian infants with CF were born to parents who were unrelated and who came from different geographical areas of Albania.

To define the incidence of CF correctly it is important that the study is based on a well defined, large population belonging to a precise geographical area and that it covers a sufficiently long period of time. We are confident that we have analysed an entire population of immigrants in a well-defined geographical zone over a period of 10 years. The CF cases were diagnosed using an appropriate screening programme with good sensitivity.

We are not aware of any factor that could account for the increased incidence of CF in the population studied. There is no evidence to suggest the selection of CFTR mutation carriers among Albanian immigrants to our region. We did not note any selection bias in the cases we observed based on parental or geographical provenance of immigrants from Albania, since couples were unrelated and came from different regions of the country. The suggestion that more Albanian newborns with CF emigrated because of the knowledge of being a carrier or because of a prenatal diagnosis can be excluded both on the basis of patients’ annamnesis and considering the poor status of the Albanian health system.

Available publications on Albanian emigration following the political and social upheaval of the early 1990s do not provide any information relating to migratory patterns based on certain geographical zones, familial origins, or cultural level, and show a weak correlation between intention to emigrate and income.

The absence of factors which could have biased the results of our study allow us to hypothesise that there is a high incidence of CF in Albanians. For a long time Albania had no external migratory fluctuations and had closed social structures with a high incidence of endogamy, remaining politically and socially isolated from the rest of the world. These factors may have contributed to a high prevalence of carriers of the CFTR gene in the Albanian population.

Our data call attention to the necessity of studying the incidence of CF among Albanians in their own country. While awaiting these results, physicians should give particular attention to the possibility of CF when caring for ethnic Albanian children.

We thank Telethon Foundation, Italy for its grant EC 2000-2001.

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References

Urorinokase in the treatment of childhood empyema

Thomson et al reported the first double blind placebo controlled study of intrapleural urokinase for the treatment of childhood empyema. They found a statistically significant reduction in hospital stay in the treatment group and concluded that “urokinase is a successful adjunct to the management of pneumothoracic empyema”.

The primary management of childhood empyema is controversial with some groups advocating open decortication. However, because of reports of wound infection, air leaks and bleeding in open decortication, there has been an increase in the potential for video assisted thoroscopic surgery (VATS) as primary treatment for childhood empyema. We have recently undertaken VATS in children undergoing primary VATS for empyema between September 2000 and September 2001. The mean (SE) length of stay in hospital was 7.6 (1.2) days, which is comparable to that in the study by Thomson et al (7.4 days).

Importantly, no child went on to open decortication; in Thomson’s study five of 58 patients went on to surgery. This reflects our own experience of a failure rate with urokinase treatment approaching 10%. We have recently undertaken VATS in six children referred to our centre for further management following the failure of urokinase treatment. Five were successful treated with VATS but one proceeded to open decortication. Urorinokase causes the intrapleural loculations to become very adhesive and increases the difficulty of the VATS procedure. Thus, urokinase is likely to increase the chances of a child undergoing open decortication in those who fail medical treatment.

There may be a role for urokinase in early empyema (although this was not specifically studied by Thomson et al), and it is likely that VATS is more useful in stages 2 and 3. We call for studies to examine prospectively the primary treatment of choice in childhood empyema and, to this end, we have recently embarked on a randomised prospective study to compare primary VATS with urokinase and chest drain in childhood empyema.

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References

Authors’ reply

We are pleased that Sit et al are interested in our controlled trial. We do not doubt that...
video assisted thoracoscopic surgery (VATS) will have a role in a limited number of patients with empyema, but do not consider it first line treatment. The major limitation of VATS is that it is highly dependent on the skill of the operator and poor results in some centres were reported at the recent American Thoracic Society meeting. Good paediatric practitioners will be limited to a few major centres in the UK.

One of the strengths of our study was that we obtained excellent results using urokinase in a multicentre trial with very variable previous experience of the technique. Sit and colleagues should note that, of the five patients who had surgery in our study, three were in the control group; the need for surgery in the urokinase group was therefore only 6.6%. Our single centre experience (Oxford) of 69 consecutive patients with empyema treated with urokinase is a median post intervention length of hospital stay of 5 days (range 3–13) with only one patient needing surgical intervention (1.5%). These data should be useful in the power calculations needed before a comparative randomised trial of VATS versus urokinase is commenced.

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BOOK REVIEWS

Childhood Respiratory Infections


When opening a new book, a logical first place to start is the Table of Contents. Here one is immediately struck by the lack of logical order of the chapters. The topics covered suggest they were chosen by the authors to match their interests rather than in a concerted effort to cover subjects of importance or of recent interest in the field. Some newer topics appear to be missing—for example, there is no obvious treatment of metapneumovirus. Some “specialist” areas are covered—for example, “Respiratory infections following haematopoietic stem cell transplantation in children”—whereas others that might be expected such as mycobacterial infections appear to be missing. In fact, most of the important areas in childhood respiratory infections are covered in this book; it is just a challenge to find some of them.

The chapters themselves are generally easy to read and informative. I particularly liked the simple and separate descriptions of the roles of the innate and adaptive immune systems, together with non-immune factors in host defence that were included in the early chapters. The “Key points for clinical practice” included at the end of most chapters are likely to be particularly useful for most readers. The information in the chapters is up to date and strikes a nice balance between providing sufficiently detailed information to satisfy the informed reader and presenting important concepts simply enough to be understandable to the less well informed. The references are extensive and up to date.

Overall, this is an easy to read and informative book that should be of great interest to practising physicians, paediatricians, respiratory trainees, and medical undergraduates.

P D Sly

Clinicians’ Guide to Sleep Medicine


I enjoyed reading this book and wholeheartedly recommend it to anyone (especially respiratory trainees) wishing to acquire a practical up to date understanding of the rapidly developing specialty of sleep medicine. Even those with years of experience in the field are likely to derive benefit and the later sections are relevant to all doctors.

M Chandri
High incidence of cystic fibrosis in children born in Italy to Albanian immigrants

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Thorax 2003 58: 93
doi: 10.1136/thorax.58.1.93

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