culosis were therefore detected by this form of screening.

In the case of the other tests, a carrier of non-toxicogenic diphtheria and a carrier of typhoid were detected by screening during the past five years in Newcastle. Detailed information was not, however, kept on the origin and outcome of these infections. It is thought not to be worth while taking throat swabs from asymptomatic children who have been in a tropical country for eight weeks or more, and routine screening may not even avert rare cases of toxicogenic diphtheria (N Noah, personal communication, 1988).

Varying periods of between eight weeks and six months abroad appear to be chosen as conveying a higher risk of contracting one of the target infectious diseases. Alternatively, tests are sometimes applied only to children coming to Britain for the first time. Why should a particular period be chosen? The influencing factors seem to be (a) the usual length of package holidays (under four weeks) and (b) the time needed to contract tuberculosis. Typhoid and diphtheria could be contracted on a very short holiday, but at least several weeks of exposure would be required for tuberculosis. An arbitrary decision must therefore be taken on the length of the period of risk. We suggest eight weeks because it is hallowed by usage and there seems to be no strong rationale for change.

The possible adverse effects of screening children on their return from overseas are that it stigmatises children from ethnic minorities as unhealthy or unhygienic and keeps them away from school at an important period of settling in.

CONCLUSIONS

Our review of screening for infections in children entering Britain from overseas shows that there is a wide variation in screening policies around the country with no national consensus. Screening for tuberculosis is, however, supported by many authorities, is widely

practised, and is probably effective, being mainly of value to the child screened. On the other hand, screening for diphtheria, typhoid, and salmonella is hard to justify and is probably not effective. There is therefore a strong case for rationalising screening, concentrating on the detection of tuberculosis. We should also ensure that advice on prevention of disease is readily available to families before they travel abroad.

We have initiated the following procedure in Newcastle, which we recommend as a national policy. This guidance applies to children entering the education system after spending over eight weeks in a tropical country (Asia, the Far East, Africa, and south America).

(1) The school nurse will interview the family before the child starts school and review the child's health followed by a Heaf test and BCG if this is negative. Some children, however, will have already started school and the family will therefore be interviewed as soon as possible.

(2) The child will normally start school as soon as the interview has been done, provided no symptoms of serious infection have been found—for example, severe sore throat, fever, chronic cough, loss of weight.

(3) The child will be referred to the school doctor at the nurse's discretion or if immunisation is required. If required information will be given on how to register with a general practitioner.

(4) A record will be kept of each interview.

We thank Professor Norman Noah for his comments.

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Lesson of the Week

Invasive aspergillosis in immunosuppressed patients: potential hazard of hospital building work

A G Dewhurst, M J Cooper, S M Khan, A P Pallett, J R E Dathan

Aspergillus fumigatus is an important pathogen acquired from contaminated air.¹ Invasive aspergillosis is increasingly recognised in immunocompromised patients in haematology, oncology, or transplant units. The disease is often difficult to diagnose² and carries a high mortality if untreated,^{1,4} and treatment itself may be hazardous.⁵ The problem may not be widely appreciated by clinicians managing patients receiving immunosuppressive treatment for other diseases. Furthermore, there is a well recognised association between demolition and construction work and outbreaks of invasive aspergillosis.^{4,6,8}

We report on three patients who developed invasive aspergillosis while receiving immunosuppressive therapy for systemic vasculitides at the same time as demolition work was occurring on the hospital site. All three patients died. In two of them invasive aspergillosis was the cause of death and in the third it was a contributory factor.

Case reports

CASE 1

A 73 year old woman developed breathlessness

and was found to have pulmonary oedema, which improved with diuretics. She had a history of hypertension and ischaemic heart disease. Investigations showed the following concentrations: urea 27 mmol/l (normal 3-6.5), creatinine 584 µmol/l (60-125), and haemoglobin 138 g/l. The erythrocyte sedimentation rate was 55 mm in the first hour. A midstream specimen of urine contained no casts or red blood cells, and a 24 hour urine collection contained 0.92 g of protein (<0.3 g). An intravenous urogram showed an absent left kidney with a right kidney of normal size which concentrated poorly. Serum complement and immunoglobulin concentrations were normal and blood cultures were sterile. Acute glomerulonephritis was diagnosed. The patient declined renal biopsy. She improved with conservative management and was discharged home two weeks later with a serum creatinine concentration of 191 µmol/l.

She presented again five months later with increasing breathlessness. A chest x ray film showed bilateral pleural effusions with patchy basal consolidation. Serum creatinine concentration was 294 µmol/l, haemoglobin concentration 93 g/l, and erythrocyte sedimentation rate 105 mm in the first hour. A pleural

Department of Medicine,
Royal South Hampshire
Hospital, Southampton
SO9 4PE

A G Dewhurst, MRCP, senior
registrar
M J Cooper, MRCP, registrar
J R E Dathan, FRCP,
consultant physician

Southampton General
Hospital, Southampton
S M Khan, MB, registrar in
pathology
A P Pallett, MRCPATH,
consultant microbiologist

Correspondence to:
Dr A G Dewhurst, St
Richard's Hospital,
Chichester, West Sussex.

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aspirate had a protein concentration of 45 g/l, was sterile, and contained no malignant cells. Serum neutrophil cytoplasm antibody was weakly positive. A diagnosis of probable Wegener's granulomatosis was made, and she was treated with oral prednisolone and cyclophosphamide. Over the next four weeks she improved, but three months later she developed frontal headaches, deteriorating vision in her right eye, a right retinal artery occlusion, and a right sixth nerve palsy over a few days despite receiving high dose steroid therapy. The erythrocyte sedimentation rate was 39 mm in the first hour. A temporal artery biopsy and computed tomography of the brain showed nothing abnormal. Over the next two days her condition deteriorated and she died.

At necropsy the lungs showed evidence of bronchopneumonia with abscess formation with abundant fungal hyphae typical of aspergillus species (fig 1). There was invasion of blood vessels and the brain contained multiple right sided aspergillus abscesses, including one of 5 cm diameter in the right frontal lobe (fig 2). Death was due to disseminated aspergillosis.

FIG 1—*Aspergillus* hyphae in lung abscess

FIG 2—Cerebral aspergilloma

CASE 2

A 73 year old woman developed a swollen calf, and a diagnosis of a deep vein thrombosis was made, for which she was anticoagulated with warfarin. Full blood count and liver and renal function were all normal.

One month later she had recurrent epistaxes. Investigations showed a haemoglobin concentration of 78 g/l, with normochromic and normocytic red cells, platelet count $54\,000 \times 10^9/l$, white cell count $6600 \times 10^9/l$, erythrocyte sedimentation rate 70 mm in the first hour, prothrombin time 1.6 (normal 1.1-1.2), serum creatinine concentration 508 $\mu\text{mol/l}$, urea concentration 30 mmol/l, 24 hour urinary protein 1.2 g, serum haptoglobins absent, Coombs test negative, and autoimmune profile normal. Abdominal

ultrasonography showed normal kidneys with no evidence of obstruction, and a bone marrow aspirate showed reduced erythropoiesis but no diagnostic changes.

The cause of her renal failure and haemolytic anaemia was not clear, and renal biopsy was not possible because of the clotting abnormalities. Her renal function improved with conservative treatment, including withdrawal of the warfarin, and one month later she was discharged with a creatinine concentration of 300 $\mu\text{mol/l}$ and a haemoglobin concentration of 81 g/l.

Two months later she developed cardiac failure and hepatosplenomegaly. Her haemoglobin concentration was 72 g/l, erythrocyte sedimentation rate 40 mm in the first hour, creatinine concentration 330 $\mu\text{mol/l}$, and liver function normal. In view of the multisystem nature of her disorder she was treated with intravenous methylprednisolone 1 g daily for three days and prednisolone 60 mg daily. One week later she developed a fever and blood cultures yielded viridans streptococcus. A cardiac ultrasound examination showed a thickened aortic valve but vegetations were not seen, and she was treated with benzylpenicillin and netilmicin.

Over the next three weeks she gradually improved but then became intermittently drowsy and confused. An electroencephalogram showed occasional generalised slow activity but no epileptiform activity. Computed tomography of the brain showed mild generalised cerebral atrophy with patchy attenuation in the white matter of the frontal lobes but no mass lesion. She continued to deteriorate, developed gastrointestinal bleeding, and died.

At necropsy there was an aspergillus lung abscess with vascular invasion. Death was due to bleeding oesophageal varices from micronodular cirrhosis with portal hypertension.

CASE 3

A 58 year old woman had a six month history of malaise, night sweats, and breathlessness, and examination showed signs of mitral regurgitation. Haemoglobin concentration was 90 g/l (normochromic), erythrocyte sedimentation rate 100 mm in the first hour, alkaline phosphatase activity 450 IU/l (normal 1-300), urea concentration 11 mmol/l, creatinine concentration 114 $\mu\text{mol/l}$, proteinuria 0.85 g/24 h, and blood cultures sterile. Bone marrow biopsy showed reactive changes only, and liver biopsy was normal.

One month later she was admitted with progressive breathlessness and signs of congestive cardiac failure. An echocardiogram showed reasonable left ventricular function and mild mitral regurgitation but no vegetations. Serum creatinine concentration was 360 $\mu\text{mol/l}$. She was treated with diuretics, vasodilators, and 40 mg of prednisolone daily. Her renal function continued to deteriorate and she was transferred to this hospital, where she underwent a renal biopsy. This showed evidence of a vasculitis of medium sized arteries consistent with polyarteritis nodosa. She received 1 g of intravenous methylprednisolone on three occasions and cyclophosphamide 2 mg/kg daily when she subsequently developed haemolytic anaemia.

Her condition deteriorated. Blood cultures were sterile, but she improved with broad spectrum antibiotics (ceftazidime and metronidazole). Over the next four weeks her clinical state deteriorated on two further occasions with impairment of her conscious level. Computed tomography of the brain showed a few low density areas indicative of previous infarction or ischaemia, and a lumbar puncture was normal. She deteriorated further despite anticoagulants, antibiotics, and diuretics and died. Fungal infection had been

considered, but in view of her impaired renal function amphotericin was not used.

At necropsy a subpleural aspergillus abscess was found in the right lung and two fungal microabscesses in the brain. A healed vasculitis was seen in the kidneys. Death was due to disseminated aspergillosis.

Discussion

We have described three patients who were receiving standard immunosuppressive treatment with high dose corticosteroids and cyclophosphamide for presumed vasculitis. Two died from invasive aspergillosis, and in the third it was an important contributory factor to the patient's death. In all three cases invasive aspergillosis was diagnosed only retrospectively, although the diagnosis was considered in one.

During their hospital admissions from July 1988 to January 1989 they started taking immunosuppressive treatment, and we believe that they first contracted aspergillosis shortly after that. Construction work and demolition of hospital buildings, including the old kitchens, was occurring from June 1988 to March 1989 on a site adjacent to the medical ward where all three were nursed. This ward had no special ventilation system, and many of the windows were ill fitting at the time and could not be closed completely. None of the patients in an oncology ward situated more than 90 metres away (with properly fitting windows) developed aspergillosis, although they also received empirical antifungal treatment when appropriate.

During the 18 months before this outbreak there were no recorded cases of aspergillosis at this hospital and there were none in our unit in the preceding 10 years. At no time was there sustained neutropenia (cell count $<1 \times 10^9/l$) in any of the reported patients, nor was aspergillus isolated from the sputum of any patients. Although we have no conclusive proof that the demolition and construction work was the cause of this outbreak of aspergillosis, we believe that the evidence above is highly suggestive of an association.

The risk of developing infection with aspergillus is directly related to the length of exposure to the organism. Nosocomial infection is well documented and is particularly associated with hospital construction work.^{4-6,8} Independent risk factors for infection are prolonged neutropenia, with the risk increasing exponentially in those in whom neutropenia exceeds 14 days,⁹ and exposure to high dose corticosteroids.^{10,11} The role of antibiotics remains uncertain.^{10,11}

Invasive aspergillosis can be prevented by avoiding exposure to high aspergillus counts. This is achieved by nursing susceptible patients in areas of controlled laminar airflow or where there is high efficiency particulate air (HEPA) filtration. The effectiveness of these measures is well documented¹² and is demonstrated by nosocomial outbreaks of invasive aspergillosis when these measures fail or are inadequate.⁶⁻⁸

Although the empirical use of antibiotics and antifungal agents in immunocompromised hosts is common,^{3,13,14} the role of prophylactic antifungal agents has yet to be established. Some studies suggest that the incidence of aspergillosis and other fungal infections is reduced with prophylactic itraconazole or ketoconazole.¹⁵ Others have suggested that although in vitro activity can be shown, the practical benefit of this is marginal.¹⁶ Empirical antifungal therapy with amphotericin is usually avoided in patients with severe renal failure. The role of itraconazole in such patients is

still being evaluated, but it will probably prove to be a valuable alternative.

Although invasive aspergillosis is well recognised in bone marrow and renal transplant units, discussion with our general medical colleagues has led us to believe that it is not perceived as a great problem in other groups of patients. We recommend increased awareness and vigilance in any patient receiving immunosuppressive agents, including high dose corticosteroids alone, particularly if there is demolition or building work occurring nearby. In these circumstances the use of specialised air filtration systems and empirical (and possibly prophylactic) antifungal agents should be carefully considered. In addition, the airborne concentrations of aspergillus spores should be monitored at frequent intervals both outside and inside the wards.

A further phase of demolition and construction work is due to begin shortly at our hospital. Our clinical practice has changed and aspergillus counts are now being monitored. If the counts are seen to rise patients receiving immunosuppressive therapy will be managed on an alternative site and, if appropriate, prophylactic antifungal agents will be used.

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Correction

Major maxillofacial injuries

Two printer's errors occurred in this article by Mr Iain Hutchison and others (22 September, p 595). The last sentence of the section on management of bleeding refers to ligation of an internal jugular vein and not an external jugular vein as published, and point (8) of the secondary survey refers to the zygoma and not the zygoma.