rapid haematological recovery with peripheral blood stem cells has reduced the mortality associated with autografting to 2%. This allows the use of high dose chemotherapy and total body irradiation in conditions in which the risk of a bone marrow autograft was considered to be too high and extension of the age limit for autografting to beyond 70.

The impact of autografts of peripheral blood stem cells has so far been seen in haematological malignancies such as non-Hodgkin's lymphoma, Hodgkin's disease, acute and chronic leukaemia, and multiple myeloma.¹⁰ Their use will increase dramatically, however, in the treatment of solid tumours, and they have already been used in neuroblastoma and cancers of the breast, ovary, testis, and lung. Peters *et al* have shown a greater than 30% improvement in survival for selected high risk patients with breast cancer compared with survival after conventional chemotherapy.¹¹ These findings require confirmation in large multicentre studies, two of which are planned for Britain.

Use of repeated infusions of smaller doses of peripheral blood stem cells to support minor escalation of chemotherapy in outpatients may have an even greater impact on reducing the morbidity of chemotherapy for cancer.¹² In this context, unprocessed whole blood collected after administration of haemopoietic growth factors alone or with chemotherapy may contain sufficient peripheral blood stem cells to provide an alternative to relatively costly apheresis. Finally, allogeneic bone marrow transplantation may also benefit from this approach, with the donor being spared a general anaesthetic and the recipient's blood count possibly recovering more quickly.^{13 14}

This new found ability to collect haemopoietic stem cells will have other benefits. The CD34 marker enables their specific selection into a very small volume by one of several commercially available devices. CD34 positive progenitors are ideal targets for gene therapy techniques and the perfect starting point for the effective removal of contaminating tumour cells. For both applications the small volume facilitates handling and reduces costs.¹⁵⁻¹⁷ In addition, the development of reliable in vitro methods to amplify CD34 positive cells before transplantation will soon be possible and may eliminate pancytopenia after chemotherapy.

The cost effectiveness of haemopoietic stem cell transplants, whatever their source, is an important concern. Who will pay for these advances? The cost of an autograft for Hodgkin's disease has almost halved in two years because peripheral blood stem cells rather than bone marrow are used, and the total number of procedures has risen. Worldwide, the use of autografts continues to rise steeply.¹ Transplant centres will

need to reassure purchasers that patients are included in formal clinical trials whenever possible and that transplants of peripheral bone stem cells will not be used to intensify palliative chemotherapy for incurable patients. Despite these concerns such autografts may transform the prognosis for women with poor risk breast cancer and a significant number of patients with lymphoma and myeloma. In the next decade CD34 expansion techniques will eliminate neutropenia and thrombocytopenia, enabling all but a handful of the most intensive anti-cancer regimens to move to the outpatient clinic.

TESSA L HOLYOAKE

Senior registrar and

Leukaemia Research Fund research fellow

IAN M FRANKLIN

Consultant haematologist

Royal Infirmary, Glasgow

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Toxocara canis and human health

Greater awareness needed of its ill effects

Soil sampling shows widespread contamination of the environment, particularly parks and playgrounds, with the eggs of *Toxocara canis*, the dog roundworm.^{1 2} Human toxocariasis occurs after ingestion of infective eggs of *T canis* and migration of larvae, particularly to liver, lungs, muscle, and brain. It accounts for considerable preventable childhood illness and blindness and is often associated with pica and poor hygiene. Although the clinical features vary, three syndromes are recognised: toxocaral visceral larva migrans, ocular larva migrans, and covert toxocariasis.

Toxocaral visceral larva migrans is characterised by fever, malaise, cough and bronchospasm, abdominal pain, and occasionally failure to thrive. Hepatosplenomegaly, lymphadenitis, and bronchopulmonary signs predominate. Severe infection may cause myocarditis or respiratory failure. Focal or generalised seizures may occur. Epilepsy is associated with positive findings on serological testing for toxocara, but pica is also commoner in patients with epilepsy. Contradictory reports relate toxocara to long term defects in cognitive function. Visceral larva migrans is usually, but not invariably,

associated with pronounced IgE hypergammaglobulinaemia, eosinophilia, and increased concentrations of blood group A and B isohaemagglutinins. The findings of antibodies to toxocaral excretory and secretory products on enzyme linked immunosorbent assay has aided diagnosis and given greater credence to studies of seroprevalence.

Ocular larva migrans was described over 40 years ago after examination of 47 eyes enucleated for retinoblastoma: 23 had larval or hyaline remnants in eosinophilic granulomatous lesions, which were identified subsequently as *T. canis*.^{3,4} It tends to occur in older children and adults, is not strongly associated with contact with puppies, and is rarely accompanied by eosinophilia or a raised IgE concentration. Serum antibodies to toxocara excretory or secretory products are few or absent and may be evident only in vitreous biopsy specimens.⁵

A single larva may cause unilateral blindness, but bilateral signs occur in up to 3% of patients. Presenting symptoms include leucocoria, squint, red eye, and impaired vision. Granulomas are usually situated at the macula or elsewhere in the posterior segment and may include a uveitis, pars planitis, papillitis, chorioretinitis, or endophthalmitis. Visual loss occurs from the effects of acute inflammation in the retina and optic nerve, while chronic disease may cause retinal fibrosis, leading to traction retinal detachment.^{5,6}

Commoner than visceral larva migrans and ocular larva migrans is a toxocaral illness that may be entirely subclinical or have a constellation of features associated with positive results on serological testing—namely, covert toxocariasis. It may be mistaken for any of the transient fevers of childhood. Cough, sleep disturbance, abdominal pain, headaches, and behavioural disturbance may be associated with hepatomegaly, adenitis, wheeze, and fever.⁷

The results of recent research have been reported in the proceedings of a symposium on toxocariasis held by the British Society of Parasitology.⁸ The variability of clinical features in toxocariasis may be related to larval load, different pathways of migration, the amount of toxocaral excretory and secretory products, and differences in the host immune response (this in turn may be influenced by the nature of the primary exposure or even by exposure to other ascarids).

Immune attack is directed at the larval outer coat, which is rendered highly antigenic by the high glycosylation of the toxocaral excretory and secretory products. Shedding of this outer coat means that attack by antibodies or effector cells is evaded.⁹ Furthermore, the carbohydrate moiety resembles the composition and stereochemistry of mammalian blood group epitopes, which may explain the increased concentrations of isohaemagglutinins during toxocariasis and other ascarid infections.⁸ The eosinophilia and increased IgE concentration, which are often appreciable in visceral larva migrans and covert toxocariasis, are due to increased numbers and activity of T cells with a T helper 2 pattern of secretion of cytokines (interleukin 4 and interleukin 5) and a reduction in secretion of T helper 1 lymphocytes. Interleukin 4 amplifies production of IgE, and interleukin 5 facilitates growth differentiation and vascular adhesion of eosinophils.⁸

As the symptoms and signs of various syndromes of toxocariasis result from both acute and chronic inflammatory responses directed at toxocaral excretory and secretory products and not necessarily the larvae, treatment is primarily aimed at the symptoms—for example, bronchodilators, antihistamines, and occasionally systemic steroids. Although anthelmintics are often given, their value is not proved.

Spontaneous resolution of visceral larva migrans and covert toxocariasis will occur if reinfection is avoided, but the structural damage in ocular larva migrans is often irreparable. Removal of retinal fibrotic membranes may restore anatomical integrity, but macular disease will preclude a return of good vision.

Prevention would obviously be preferable, but eradicating *T. canis* is difficult because of the complexity of its life cycle. Adult worms live in the small intestine of dogs and their puppies. Eggs may be shed at a rate of 200 000/day, and take two to five weeks to become infective. Their thick shells confer resistance to cold, environmental change, and sewage processing and they survive many years. After ingestion, the second stage larvae penetrate the bowel and migrate in blood and tissue to the liver and lungs and finally the gut as adult worms. Migrating larvae may remain dormant for several years but become activated in the pregnant and lactating bitch leading to transplacental and transmammary transmission. Postnatally, the mother ingests not only the eggs but immature worms from the puppies' faeces so that the combination of lactating bitch and puppies shed formidable quantities of eggs to the environment. Almost all puppies are infected at or soon after birth.²

The principal reservoir for *T. canis* is the dog (in Britain there are 7.5 million dogs), though the role of urban and rural foxes may be important.¹⁰ Other paratenic (non-definitive) hosts may exist—for example, cattle, pigs, and sheep may be a source of human and canid infection if raw or inadequately cooked meat or offal is ingested. Seroprevalence studies show that 2-3% of adults and 7-14% of schoolchildren have been exposed to *T. canis*. It is pertinent to emphasise that though toxocariasis is linked with dog ownership, half the cases in Britain occur in children with no exposure to dogs or puppies.¹¹

As no satisfactory treatment for larvae migrating to tissue or prevention of transplacental and transmammary transmission of infestation exists, the prevention of toxocariasis must focus on a reduction of the environmental load of *T. canis* eggs. Thus treatment of adult dogs and, especially, early and regular treatment of puppies is essential to kill the worms before they are mature enough to produce eggs.

Children's playgrounds and sandpits should have no access for dogs, particularly strays, or foxes. Dog owners must remove their pets' faeces for disposal. The motivation for such measures depends on education of the public, doctors, veterinarians, local authorities, and politicians to stimulate and maintain awareness of the problem.

M G KERR-MUIR
Consultant ophthalmologist

St Thomas's Hospital,
London SE1 7EH

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