produce interferon and other biologically active products which, as a result of non-specific stimulation, may contribute to the overall pattern of the cellular immune response in the recipient. It should be noted that transfer factor seems to be exceedingly potent; the amount of factor required to confer systemic skin reactivity on a normal recipient is the extract of only 0.1 ml of packed leukocytes. Reactivity to the other antigens to which the donor was sensitive, such as *Candida*, mumps, streptococcal and other antigens, is transferred simultaneously. But transfer of the capacity for antibody formation does not occur.

The clinical use of transfer factor is based on the view that depressed cell-mediated immunity is of pathogenic importance in various disease states and that, by reversing the deficiency, transfer factor can ameliorate the disease process. This has been tested in severe infections caused by mycobacteria, fungi and viruses, particularly in patients with defective lymphocyte responsiveness either *in vivo* or *in vitro*. On the same basis it has been possible to correct certain primary immunodeficiency states in some patients exhibiting selective depression of lymphocyte function.

Patients suffering from a number of infectious diseases, including mucocutaneous candidiasis, coccodioidomycosis, leprosy and a number of viral infections, have been treated with transfer factor. The patients responded to treatment with transfer factor obtained from donors in whom skin tests to the particular antigen were strongly positive. Successful outcome has been reported in a few patients with generalised vaccinia, herpes zoster, neonatal herpes virus infection, measles "giant-cell" pneumonia and subacute sclerosing panencephalitis.

Spitler and colleagues (*Clin. Immunobiol.*, edit by Bach, F. H., and Good, R. A., Academic Press, 1974, p. 153) treated a number of patients with verruca vulgaris, an example of a chronic viral infection, with transfer factor pooled from normal donors presumed to have immunity to this virus. Clinical improvement occurred in only one patient after several months of therapy so that the improvment may be quite unrelated to the use of transfer factor. A note of caution was added recently by Stevens and his associates (*Clin. exp. Immun.*, **21**, 520; 1975). Dialysed transfer factor, prepared from the leukocytes of a donor whose warts had undergone spontaneous regression, was used in the treatment of a child with Wiskott–Aldrich syndrome, a congenital immune deficiency. The child then had a spontaneous regression at multiple areas with warts. A similar relationship was observed in a pilot study in four otherwise healthy patients. But a randomised double-blind study of thirty patients failed to confirm a causal relationship between therapy with transfer factor and wart regressions.

Attention has also been directed recently to persistent infection with hepatitis B virus. Kohler and his colleagues (*Clin. Immun. Immunopathol.*, **2**, 465; 1974) treated a healthy persistent carrier of hepatitis B surface antigen with lymphocytes from an individual who had recovered eight months previously from hepatitis B. Within 24 h there was an increase in the titre of antigen and of serum aspartate transaminase levels, an indication of liver damage. It was suggested that the recipient's liver cells were transiently injured by a cell-mediated immune response, which was insufficient to terminate the infection. Transfer factor prepared from the same donor had no effect on the patient's liver function tests. The biological activity of this material, however, was not evaluated and it may have been inactive. Another patient, an infant who acquired hepatitis from her mother at birth, was given transfer factor prepared from the mother's lymphocytes. On two occasions the preparation caused a prompt, moderate increase in both the antigen and transaminase levels. Subsequently, the liver function tests became normal and the titre of hepatitis B surface antigen was reduced by 95%. It is generally considered that cell-mediated immunity is important in terminating hepatitis B infection. Temporary falls in the levels of hepatitis B antigen have also been reported after the use of transfer factor in a few patients with antigen-positive chronic active hepatitis. Jain and his colleagues reported at the meeting of the British Society of Gastroenterology held in Oxford in September, 1975, the results of treating three patients with "specific" transfer factor prepared from subjects recently recovered from hepatitis B infection. One patient with chronic active hepatitis, and cirrhosis associated with antigenaemia showed no response to transfer factor prepared from a normal blood donor but "specific" transfer factor increased the number of T lymphocytes; a second similar patient also showed no response to "normal" transfer factor but "specific" transfer factor increased transiently the serum aspartate transaminase levels suggesting stimulation of cell-mediated immunity with a resulting hepatitic reaction. The third patient suffered from antigen-positive active chronic hepatitis complicated by primary liver cancer; he was receiving corticosteroid therapy and did not respond to transfer factor. It was concluded that although there was no alteration in the serum titres of hepatitis B surface antigen further trials wtih transfer factor seem justified.

Finally, Bullock *et al.* (*New Engl. J. Med.*, **287**, 1053; 1972) pointed out that there is a risk of transfer factor exciting generalised hypersensitivity reactions to disseminated microbial or other antigens and that, paradoxically,

Earthquakes without precursors?

from Peter J. Smith

SOME shallow earthquakes are known to be preceded by significant decreases in P and S wave velocities (V_p and V_s) and the seismic velocity ratio V_p/V_s. One of the problems in using these effects as a basis for earthquake prediction, however, is that not all shallow shocks appear to give such warning. Reasons proposed so far for the lack of premonitory effects in certain cases range from failure to measure V_p and V_s at the appropriate times to possible variations of the V_p, V_s and V_p/V_s decreases when measured in different directions with respect to the trend of elongated cracks in the surrounding rock. But two new experiments carried out by Wang *et al.* (*Geophys. Res. Lett.*, **2**, 309; 1975) now suggest that the apparent presence or absence of precursory phenomena may depend not simply on observational arrangements but on something much more fundamental.

In the first experiment, a block of dry 'Westerly' granite with an imposed normal load was subjected to an increasing shear load until fracturing occurred. Both V_p and V_s for waves travelling normal to the shear plane decreased before rupture, and dilation took place in the same direction. V_p/V_s decreased from a 'normal' value of 1.7 to 1.4 in line with previous field and laboratory observations. In the second experiment, the granite block was first sliced in half and then subjected to normal and shear stresses to give stick-slip motion. But no V_p and V_s changes were observed either before or during sliding, and there was no dilation against the normal pressure.

Wang and his colleagues conclude from this that there must be appreciable variations in the faulting process leading to shallow earthquakes. The degree to which V_p and V_s decrease will then depend on the extent to which faulting is associated with dilation and fracturing. The implication is that prediction based on precursory seismic wave velocity variations will not be possible even for all shallow earthquakes.