is not directed against HL-A antigens but has specificity for epithelial cells. A further indication of this specificity is the finding that the sera failed to react with tissue culture hepatocytes and fibroblasts.

The pathogenesis of the GVH reaction is unknown; but the observation that patients with this disease have an antibody directed to epithelial cells suggests several mechanisms for this reaction. The antibody we are detecting may be directed against minor histocompatibility antigens that are expressed only as epidermal specific antigens not detected by the usual HL-A matching techniques. Boyse *et al.* have presented data suggesting similar antigens in mice[8]. Alternately, it may be that damage initially produced in the skin by the GVH reaction exposes hidden epidermal antigens and these then provoke the formation of "autoantibodies" against epithelial cells. A third possibility is that impaired immune function in the grafted recipient predisposes to certain viral infections, and that alteration of epidermal cell surface antigens induced by virus, or cross-reactivity between viral and epidermal antigens accounts for the antibody detected in these patients. Further investigation of these and other possibilities may provide information about the importance of tissue specific non-HL-A antigens and antibodies in the processes of graft rejection and in the pathophysiology of the GVH reaction.

We thank Dr E. S. Henderson, Medicine Branch, and Dr R. G. Graw, Human Tumor Cell Biology Branch, National Cancer Institute, for the opportunity to study sera from their patients. Miss B. A. Plocinik performed cytotoxicity assays.

C. B. MERRITT
D. L. MANN
G. N. ROGENTINE, JUN.

Immunology Branch,
National Cancer Institute,
National Institutes of Health,
Bethesda,
Maryland 20014

Received December 31, 1970; revised March 15, 1971.

[1] DeVries, M. J., *Exp. Hematol.*, **20**, 112 (1970).
[2] Streilein, J. W., and Billingham, R. E., *J. Exp. Med.*, **132**, 163 (1970).
[3] Billingham, R. E., and Streilein, J. W., *Arch. Dermatol.*, **98**, 528 (1968).
[4] Graw, jun., R. G., Brown, J. A., Yankee, R. A., Leventhal, B. G., Whang-Peng, J., Rogentine, jun., G. N., and Henderson, E. S., *Blood* (in the press).
[5] Graw, jun., R. G., Brown, J. A., Yankee, R. A., Weiderlite, L. W., Leventhal, B. G., Whang-Peng, J., Rogentine, jun., G. N., and Henderson, E. S., *Exp. Hematol.*, **20**, 35 (1970).
[6] Graw, jun., R. G., Rogentine, jun., G. N., Yankee, R. A., Whang-Peng, J., Herzig, G. P., Halterman, R. H., Kruger, G., Berard, C., and Henderson, E. S., *Lancet*, ii, 1053 (1970).
[7] Rogentine, jun., G. N., and Plocinik, B. A., *Transplantation*, **5**, 1923 (1967).
[8] Boyse, E. A., Lance, E. M., Carswell, E. A., Cooper, S., and Old, L. J., *Nature*, **227**, 901 (1970).

Teratocytes as a Means of Resistance to Cellular Defence Reactions

I HAVE suggested that teratocytes, the giant cells which develop from the trophamnion of many parasitoid Hymenoptera, serve as a means of resistance to the defence reactions of insect hosts[1]. These cells are relatively small when they dissociate from the embryonic membrane, but as they become distributed in the blood of the host they expand to as much as 3,000 times their original volume. Their growth is achieved by the absorption of nutrients from the host's blood and I suggested that the consequent depletion of materials in the haemolymph would impede or inhibit haematopoiesis and prevent an effective haemocytic reaction to the young parasitoid.

Evidence supporting the hypothesis has been obtained in the course of experiments designed for another purpose. Eggs and larvae of the ichneumon wasp *Nemeritis canescens*, which does not produce teratocytes, were implanted in caterpillars of *Eucosma hohenwartiana* collected out of doors from heads of knapweed, *Centaurea nigra*. In healthy caterpillars the parasitoid was promptly killed by cellular defence reactions. Against all expectation, one larva of *Nemeritis* was found feeding and developing without encapsulation when it was 5 days old. The caterpillar containing this individual, however, was also infected by a braconid parasitoid, and its blood contained numerous teratocytes about 50 μm in diameter. In two caterpillars infected by wild parasitoids which had not produced teratocytes, the *Nemeritis* was encapsulated as it was in healthy hosts.

Three more examples of this phenomenon have recently been observed in caterpillars of *Chilo phragmitellus* collected from reeds at Wicken Fen. When eggs of *Nemeritis* were implanted in healthy caterpillars of this species, they were encapsulated, melanized and killed; only two hatched, and the larvae were then promptly destroyed in the same way. Three caterpillars in which eggs were implanted turned out to be already parasitized by gregarious braconids, probably *Apanteles ferrugineus*, which had produced many teratocytes. From these three hosts, and from them only, larvae of *Nemeritis* 5 days old were retrieved alive, feeding and apparently developing normally, without any trace of a haemocytic defence reaction.

These observations show that teratocytes are indeed a means of resistance to the cellular defence reactions of insects, and that the protection they afford is not restricted to the species of parasitoid that produces them but extends to other species. Since their action is not specific, attrition of the host is most likely to be the mechanism by which teratocytes have their protective effect.

I thank Mr J. A. Lade for help with the collection of caterpillars.

GEORGE SALT

Department of Zoology,
University of Cambridge

Received April 13, 1971.

[1] Salt, G., *Biol. Rev.*, **43**, 200 (1968).

Cellular Basis for Immunologic Memory

AFTER exposure to an antigen resulting in a primary immune response, experimental animals and human subjects possess the ability to react specifically and in accelerated fashion to a second exposure to the same antigen. This immunological memory presumably involves specific cells, but it is not known whether it involves generation of an increased number of cells or increased synthetic (or some other) ability in individual cells. Nobody has yet identified a cell which was generated by a previous contact with a specific antigen. Lymphocytes present in the circulation of rats have been shown to carry memory[1], and recent work has established that many such cells are thymus-derived and important in many aspects of the immune response[2,3]. Because they are long lived and constantly re-circulating throughout the peripheral lymphoid organs, thymus-derived cells make ideal candidates for the carriage of memory. Indeed, memory can be diminished by killing cells in this sub-population[4].

Exposure to an antigen results in a burst of mitosis in the lymphoid organs, and at least initially many of the cells in mitosis are thymus-derived[5]. Moreover, these cells respond