

How Do Lymphocytes Mediate?

It may be felt by some readers that the subject treated in Bergstrand's review in this issue is very basal and perhaps too detailed to justify publication in *Allergy*. Such a feeling, however, is not entirely justified. The lymphocyte is the essential cell of the immune system because it enables the organism specifically to recognize, digest, and respond to environmental macromolecular information. The lymphocytes constitute a heterogeneous cell population, which on the basis of functional and/or morphological criteria can be subdivided into several subclasses (B-cells, T-cells, T-helper cells, T-suppressor cells, T- and B-memory cells, T-killer cells, K-cells, T-effector lymphocytes). The T-effector lymphocytes are responsible for the immunologically specific initiation of type IV (delayed type) inflammatory reactions, and this inflammatory response plays a decisive pathogenetic role in several conditions, e.g. contact dermatitis, drug hypersensitivities, autoimmune diseases, bacterial, parasitic, and viral infections, etc. Although the activity pattern of lymphocytes has been biologically well illustrated in experiments *in vivo* and *in vitro*, we are only just beginning to comprehend the biochemical details of lymphocyte activity. Bergstrand reviews knowledge of a comparatively restricted field of lymphocyte biology: How do lymphocyte products control the migration of other cells? The subject is essential for the explanation of immune inflammatory processes, especially lymphocyte-mediated inflammation. The complicated combined effects and interactions of cells in the inflammatory process are sometimes specifically started by and always influenced by the lymphocytes. We now possess a comprehensive, detailed, although somewhat

hazy picture of the action of lymphocytes and their mediators. This picture, however, is mainly perceived through observations of cell activity and cellular interactions *in vitro*, whereas an *in vivo* significance of these *in vitro* phenomena is assumed by analogy, and has so far little experimental basis. A necessary future step in the research process: Explanation of cellular function and behaviour at the biochemical level, is only beginning to emerge. Activated lymphocytes have an effect on surrounding cells in cultures and in the tissues. This effect is caused by biochemical compounds (lymphokines) that are produced and secreted by the activated lymphocytes. The lymphokines are becoming increasingly recognized as biological mediators of fundamental significance in the immunological response. The many *in vitro* systems that have been used to explore lymphokines have created correspondingly numerous terms, each indicating a biological activity as observed in the *in vitro* cell culture systems used. The 30-50 lymphokines thus described are doubtless to some extent identical chemical compounds, which are observed under different experimental circumstances. On the other hand, a number of different lymphokines, each with its own individual role and activity, is clearly in existence.

If we want therapeutically to modify and adjust type IV immune inflammatory reactions, we need precise knowledge of the biochemical details as well as techniques in order to analyse and follow the associated biological developments. Drug treatment of conditions in which functional or structural tissue damage is caused by immunologically induced inflammation is still conducted somewhat in the dark. However, the specific

immunological reaction and its inflammatory consequences can not be therapeutically modified on a rational basis without mapping out the biochemical interactions which the drug is supposed to change. In his review Bergstrand confronts us with the complexity of one specific side of lymphocyte biology, and however sophisticated the experiments, observations and interpretations, we find ourselves at a rather primitive stage when we want to apply this information to clinical problems. Biochemistry has not really entered the field and facilitated analytical possibilities. However, this development is within reach.

Methods for registering lymphokine activity are already in use in human clinical investigations, and the future availability of better methods for lymphocyte monitoring may be closer than we think.

Direct biochemical detection of lymphokines would certainly be a powerful instrument in future clinical investigations of diseases with immunological and allergological pathogenesis. Development has been known before to exceed expectations, especially in the field of lymphocyte research.

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