

is formed by cells in the lymphoid organs and reacting with antigen, it is conceivable that under the influence of locally formed chemotactic factors certain types of cells would then migrate from the organ.

It was found that shortly after rabbits had been injected intravenously with 5  $\mu$ g of somatic polysaccharide, a reduction in thymic cellularity began which, with time, became more pronounced until at day 5 (the interval of peak antibody response and maximum number of PFC in blood and in spleen) this organ then was, for all practical purposes, depleted of lymphocytes (LANDY et al.<sup>13</sup>). Thereafter the cells gradually reappeared and by day 20 the thymus was once again found to be a fully cellular apparently normal organ. Since the loss of thymic cellularity coincided with the progressive increase in the number of antibody-forming cells in spleen and in blood, the possibility of a temporal relationship between these two events was considered, i.e. that the cells escaping from the thymus accounted in part for the number of antibody-forming cells in blood measured by localized hemolysis. However, subsequent experiments on thymectomized adult rabbits showed that such animals were capable of responding to the polysaccharide stimulus with the usual number of PFC in both spleen and blood (LANDY and SANDERSON<sup>14</sup>).

The recent work of GOWANS on thoracic duct lymphocytes and the many investigations based on labelling with tritiated thymidine (FLOREY and GOWANS<sup>15</sup>), have shown that lymphocytes are capable of extensive migration via lymph, blood and lymphoid organs. The present work emphasizes that cells actually engaged in synthesis of antibody are capable of similar mobility; once in the circulation these cells could be transported to even the most distant sites. As regards the immunological properties attributed to lymphocytes, these have generally been considered to be capabilities *other* than the production of humoral antibody. Thoracic duct cells are commonly viewed as being a 'pure' population of lymphocytes; accordingly studies on the hyperimmunized rabbits have been extended to include cells from this source (HULLIGER and SORKIN<sup>4</sup>). Antibody production was found in thoracic duct cells of some of these animals and in addition pyroninophilic cells were demonstrated in significant numbers (as compared to controls). However, since pyroninophilic cells were sometimes encountered in thoracic duct lymph in our control animals these findings do not necessarily constitute evidence that lymphocytes per se can produce antibody.

The demonstration of immunologically active cells in sites other than those traditionally associated with the process of antibody synthesis should now perhaps be viewed with greater caution. The knowledge that cells producing antibody come into the circulation raises from a possibility to a certainty that at least some of these cells would reach and lodge in sites not generally associated with the process of antibody production. Thus the

detection of antibody-producing cells by immunofluorescence, incorporation of labelled amino acid into immunoglobulin, autoradiography or by localized hemolysis need not be interpreted as evidence that this activity had actually arisen in locations not ordinarily associated with antibody production. For example, we have reported the finding of antibody-producing cells in thymus (LANDY et al.<sup>13</sup>) after a single intravenous injection of antigen. Furthermore, very considerable numbers of PFC have been found in the liver of rabbits given a single intravenous injection of polysaccharide (SANDERSON and LANDY<sup>16</sup>). One could of course believe that cells in these organs had been directly stimulated, but it seems to us more reasonable to consider the alternative probability that in the thymus there had occurred an infiltration of antibody-forming cells from other sites, and in the liver, because of the relatively enormous blood flow through this organ, antibody-forming cells in the circulation had somehow been trapped or occluded in this organ and local proliferation may have occurred. In this connection may be mentioned studies which suggest that antibody production within the liver (in response to ovalbumin and pneumococcal polysaccharide) is usually correlated with the presence of 'invading' cells forming scattered periportal granulomata leading to the conclusion that hepatic parenchymal cells do not synthesize antibody (HUMPHREY and WHITE<sup>3</sup>). In view of the findings presented here the detection of antibody-producing cells in unfamiliar locations might best be viewed in terms of the transport mechanism provided by the circulation and that additional evidence be sought before concluding that antibody production had been initiated in non-lymphoid tissues<sup>17</sup>.

*Zusammenfassung.* Zirkulierende Blutleukocyten produzieren Antikörper nach mehrmaliger Injektion von Protein-Antigen oder einmaliger Verabreichung von Endotoxin. Ursprung und Bestimmungsort dieser Zellen werden diskutiert.

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<sup>13</sup> M. LANDY, R. P. SANDERSON, M. T. BERNSTEIN, and E. M. LERNER, *Science* 147, 1591 (1965).

<sup>14</sup> M. LANDY and R. P. SANDERSON, unpublished observations.

<sup>15</sup> H. W. FLOREY and J. L. GOWANS, in *General Pathology* (Ed., H. W. FLOREY; Lloyd-Luke Ltd., London 1962), p. 128.

<sup>16</sup> R. P. SANDERSON and M. LANDY, unpublished observations.

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## CORRIGENDUM

G. W. BARNES, M. A. SULLIVAN, E. H. BEUTNER, and E. WITEBSKY: *In vitro and in vivo Interaction of Nuclear Antibodies with Corresponding Antigens*, *Experientia* 21, fasc. 8, p. 485 (1965). The legend for the one and only Figure of the paper reads correctly as follows: 'Direct immunofluorescent staining of S.L.E. (PAT) liver smear with anti-human conjugate.  $\times 500$ . Upper: Conjugate neutralized with human  $\gamma$ -globulin (Cohn Fr. II). Negative reaction. Lower: Active conjugate. Note nuclear and

cytoplasmic staining.' The text-lines (p. 486) referring to this Figure read correctly as follows: 'A few of the stained cells in liver films, in addition showed a distinct nuclear reaction (Figure, lower).' and 'The serologic specificity of the immunofluorescent reaction was confirmed by negative results obtained with similar slides treated with  $\gamma$ -globulin-neutralized conjugate (Figure, upper).' The footnote of Table II reads correctly as follows 'd Tested at an earlier date.'