IMMUNOLOGICAL FUNCTION OF THYMUS AND BURSA OF FABRICIUS

Thymus Lesions in an Auto-immune Disease of Mice

A STRAIN of mice, *NZB/BL*, has been shown by Bielschowsky *et al.*[1] to develop a hæmolytic anæmia of auto-immune type, usually around 6–7 months of age. Through their co-operation we have had this strain of mice available for investigation during the past two years and have fully confirmed their findings. As judged by the occurrence of a positive direct Coombs test on the red cells, the condition can be transferred to young isologous mice by transfer of splenic cells from an older animal showing the typical signs but not from similar numbers of cells from mice in the pre-symptomatic stage[2].

It is well known that in about 70 per cent of human cases of myasthenia gravis the thymus contains numerous lymph follicles with typical germinal centres[3] and that in a significant proportion of early cases thymectomy cures or greatly alleviates the disease. Simpson[4] and Strauss *et al.*[5] have considered the condition a manifestation of auto-immune disease. We have, therefore, recently examined thymus sections from most of the mice of the *NZB/BL* strain being killed for transfer experiments or for other reasons. More than half have shown appearances which we interpret as lymph follicles with germinal centres and which have a close resemblance to the histological findings in typical human cases of myasthenia gravis (Fig. 1).

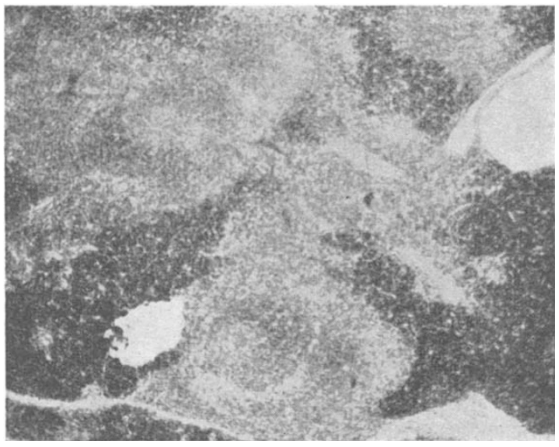

Fig. 1. Section of thymus showing two lymph follicles with germinal centres in the medulla. (× *c.* 66)

Many of the mice in the series were killed routinely when moribund, and in these there was severe involution of the thymus from age and stress, usually with complete atrophy of the cortex. Some of these showed an excess of lymphoid cells in the medulla; but the most striking feature was that in all mice more than 9 months of age in which the thymus cortex was still clearly shown, lymph follicles in the medulla were present. The usual appearance was of a complex area showing two or more germinal centres with incomplete surrounding crescents of mature small lymphocytes. It was characteristic to see small areas or cords of close-packed small lymphocytes, presumably representing over-filled intrathymic lymphatic channels.

These findings will be more fully described and their significance discussed in another publication. Here we wish merely to consider them briefly in relation to recent work[6] which suggests that the thymus is an essential primary source of stem cells for the development of immunologically competent cells in spleen and lymph nodes. It has been claimed[7] that auto-immune disease is a manifestation of the activity of 'forbidden clones' of cells unresponsive to the normal homeostatic controls which prevent the development of cells reactive against body constituents. If the site of origin of such forbidden clones is the thymus, they might well be expected to show their forbidden quality by proliferation as a germinal centre in a region where such activity never normally takes place.

We are also interested in the possible analogy between the condition manifested in our strain *NZB/BL* as auto-immune disease and the emergence of lymphoid leukæmia in mice of the high-leukæmia strain *AKR*. In the latter the first appearance of the forbidden (malignant) clone is almost regularly in the thymus and the incidence of leukæmia is greatly reduced by thymectomy at an early age.

Active experimental work based on these ideas and analogies is in progress.

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Dissociation of Immunological Responsiveness in Fowls with a Hormonally Arrested Development of Lymphoid Tissues

In recent months there has been evidence of an increasing interest among immunologists in the role of the thymus in the development of immunological functions. Several workers[1–3] have independently expressed the view that precursors of immunologically competent cells arise wholly or mainly in the thymus, moving out during the first weeks of life to colonize other lymphoid organs such as spleen and lymph nodes, where they become available for the various types of immunological function.

Experimental evidence supporting this view has been presented by Miller[2], in showing that thymectomy of one-day mice allowed them to accept