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Review

Max D. Cooper and the delineation of two lymphoid lineages in the adaptive immune system

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ABSTRACT

This article outlines the fundamental contribution of Max D. Cooper to the analysis of the role of the thymus and of the bursa of Fabricius in the development of immunologic competence both before and after birth, placing a new scientific paradigm in the definition of the ontogeny of the lymphoid tissues.

1. Biographic notes

Max D. Cooper (Fig. 1) attended medical school at "Tulane University" and received doctoral degree in 1957. After a year spent at the University of San Francisco, Cooper worked to establish the dual nature of the immune system with Robert A. Good as postdoctoral fellow and Assistant Professor at the University of Minnesota from 1963 until 1967. He was the appointed Associate Professor at the University of Alabama at Birmingham (UAB) where he remained for the next 41 years, as Professor of Immunology at the Departments of Pediatrics, Medicine, Microbiology and Pathology. In 1974, while on sabbatical at the University College in London, he worked with Martin Raff and John Owen to identify the bone marrow and fetal liver precursors of B cells.

He has received the Sandoz Prize in Immunology, American College of Physicians Science Award, AAI Lifetime Achievement Award, Avery-Landsteiner Prize, and the Robert Koch Award.

2. The role of the bursa of Fabricius and of the thymus in the definition of two patterns of lymphocyte lineages

The bursa of Fabricius and the thymus are the central lymphoid organs in the chicken essential for the ontogenetic development of the adaptive immunity. In the chicken embryo, the thymus is the first lymphoid organ to develop. The epithelial component is evident before the ninth day of incubation, and the thymus is a fully developed lymphoid organ by the twelfth day of incubation. Between the twelfth and the fourteenth day, budding of the epithelial fold of the bursa is observed, and on the fourteenth day the lymphoid structures begin to develop by direct transformation of epithelial cells to lymphoid cells (Fig. 2).

The functional dissociation within/of the chicken immune system was firstly suggested by Szenberg and Warner in 1962 [1]. In 1956, Bruce Glick and co-workers [2] demonstrated that the bursa plays an important role in antibody production, showing that antibody responses are suppressed in the majority of bursectomized chickens.

In 1958, Francis A.P. Miller [3] discovered the role of thymus-derived cells in cellular immunity. In 1960, Metcalf [4] studied the peripheral blood lymphocyte levels and histology of the lymphoid tissues in mice thymectomized between 4 and 6 weeks of age and demonstrated that there was a slow progressive fall in circulating lymphocytes to a maximum of 30–40% below normal values.

Observations on the changes in the lymphoid organs after bursectomy and thymectomy in chickens have indicated the possible

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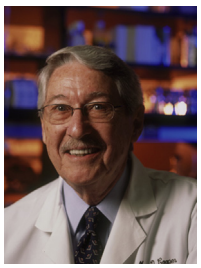

Fig. 1. A port trait of Max D. Cooper.

existence of two almost completely separate lymphocytopoietic systems (Fig. 3). The earliest scientific contribution of Max Cooper defined the basis of adaptive immunity. In 1964, as postdoctoral fellow in the laboratory of Robert Good, he discovered the dual origin of lymphoid cells in the chicken. Earlier removal of the thymus and of the bursa was needed to clarify their respective roles in immune system development.

As Robert A. Good has written: "Max Cooper, then an allergist-pediatrician, had just come to our laboratory to begin his immunology post doctorate fellowship training. He decided to revisit in laboratory studies the roles played by the thymus and bursa on lymphoid development in the chicken. Removal of the thymus from X-irradiated, newly hatched chickens, removal of the bursa of Fabricius from similarly sublethally irradiated newly hatched chickens, or removal of both thymus and bursa from such newly hatched chickens each produced very different results. Removal of the thymus so early in life prevented the development of lymphocytes in the blood and in the dense aggregates of lymphocytes in the white pulp of chicken spleen, leaving the germinal center and plasma cell development impressively intact" [5].

On the other hand, in the mind of Cooper: "The plan was to compare the immunological status of the different experimental groups, after they recovered from the effects of surgery and irradiation" [6]. He specified that: "I devised an alternative strategy that would combine posthatching thymectomy or bursectomy together with whole body irradiation to destroy cells that might have seeded earlier from the thymus and bursa or that could have

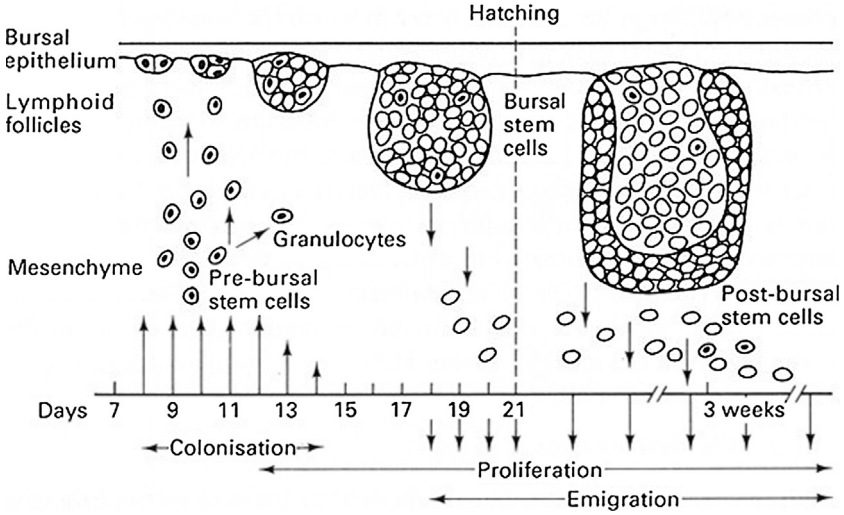

Fig. 2. Time-course of the morphogenesis of lymphoid follicles in the bursa of Fabricius.

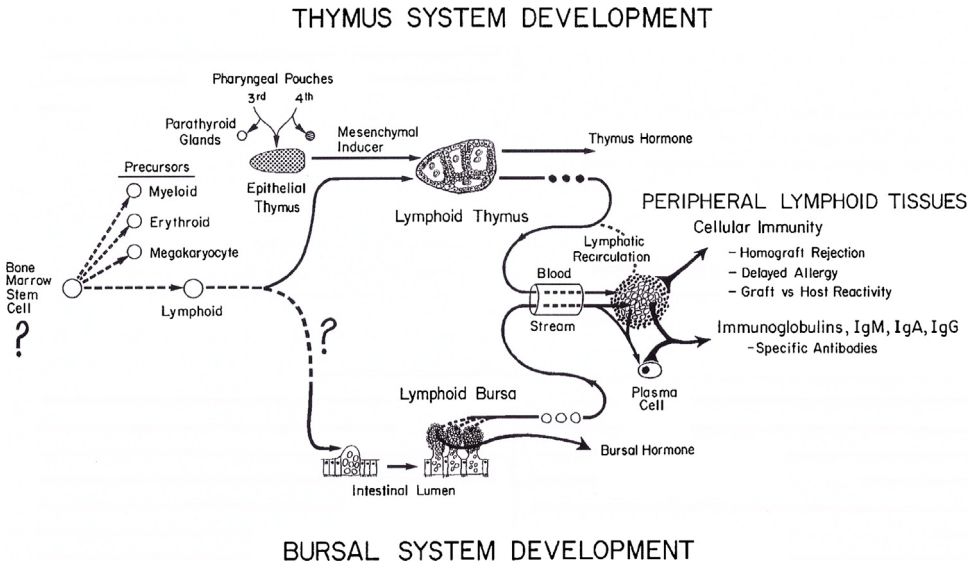

Fig. 3. An original model of Max D. Cooper concerning the different development of thymus and bursal systems. Reproduced from Ref. [17].