

Part IV

Single Complexity: The Spleen

The spleen in both man and rodents is the largest filter of blood in the body. This filtering function is coupled to the three main activities of the spleen: removal of aging red blood cells, participation in innate immunity, and promoting various forms of adaptive immune responses against blood-borne pathogens. These functions are attributed to three main tissue regions within the organ. Of these, the red pulp filters blood and removes senescent erythrocytes and other effete blood cells; the white pulp and marginal zone represent the lymphoid region of the spleen, and consist of B- and T-lymphocyte-rich lymphoid compartments. Their function to establish adaptive immune responses is based on a highly efficient and dynamic co-operation between its cellular constituents, including both migratory hemopoietic cells and sessile stromal elements.

Of the peripheral lymphoid organs, first the spleen developed during evolution in vertebrates. The presence of spleen in vertebrate classes lacking lymph nodes (from fish through birds) also indicates that, for the overwhelming majority of animals in the biosphere with adaptive immunity, the spleen (along with mucosal lymphoid structures of various degrees of complexity) is sufficient for providing appropriate systemic protection against pathogens. Surprisingly, its main organization scheme has remained largely the same throughout the phylogeny – it is a single organ containing two strikingly different domains, which form during divergent developmental pathways. Generally, its erythro-myelopoietic red pulp part evolves earlier during embryogenesis, and subsequent specification directs the formation of the white pulp, comprised overwhelmingly of lymphoid cells and, to a lesser extent, dendritic cells and macrophages. During evolution the variations in size, shape and position of spleen become more restricted as the animal approaches the class of mammals where, nevertheless, significant differences exist between various species. This chapter summarizes the main structural and ontogenic characteristics of spleen in various vertebrate classes, and provides a detailed analysis of the developmental properties of spleen in mouse and man. These include both the formation of spleen as a whole organ and its different compartments. Importantly, although several common morphogenic regulators involved in the formation of lymph nodes and Peyer's patches (such as various members of the lymphotoxin/tumor necrosis family and their downstream signaling components) also participate in the organogenesis of spleen, crucial differences exist between the development

of spleen and other peripheral lymphoid organs, including the transcriptional regulation of spleen as a solitary organ and lymph nodes. Finally, the role of organ development and proper splenic tissue compartmentalization in the maintenance of both local and systemic immunological responsiveness will be described in this part.