5.1 Introduction

In addition to protection from pathogenic invaders by systemic innate and adaptive immune defence mechanisms, bodily surfaces enjoy a privileged position by harbouring the so-called local immune system. The local immune system provides a first wall of defence at possible entrance sites of pathogens, such as the skin and surface exposed mucosa, e.g. of the eyes, the gastrointestinal and the respiratory tract. These locations, with dense accumulation of mononuclear cells, which in most instances also contain numerous germinal centers, are designated as the mucosa-associated lymphoid system (MALT) [1, 2].

The most prominent members of the MALT are the gut-associated lymphoid tissue (GALT) and the bronchial-associated lymphoid tissue (BALT). The importance and potency of the local immune system is, e.g., reflected by the fact that its daily production of immunoglobulins, notably secretory IgA (sIgA), by far exceeds that of the systemic immune system. Interestingly, interconnections between sites of local immunity exist that, e.g., lead to production of specific IgA antibodies in the lung after oral application of a given antigen [3]. One explanation of this phenomenon, albeit still hypothetical, is that antigens are transported from one site of the local immunity to another by migrating dendritic cells (DCs) that recognize certain common “addresses” within this system represented by specific adhesion molecules or a combination of these.
In addition to surfaces exposed to the outer environment, the local immune system also extends to internal, more secluded surfaces, e.g. the mucosa of the gall bladder. Taking into account the fact that the inner surface of the vascular system is, of course, constantly exposed to potentially harmful exogenous and endogenous material, the discovery of mononuclear cell accumulations in the intima of healthy vessels presented in this Chapter was rather logical and consistent with this biological design. It was, however, nevertheless unexpected and surprising that in the age of molecular biology new findings can still be made by conventional histological and immunohistological methods. This is even more startling if one takes into account the fact that accumulation of mononuclear cells, mainly lymphoid cells, in the adventitia and in the perivascular space have been known for a long time [4, 5]. This latter issue is being dealt with in Chap. 4.

Compared to MALT, the accumulation of mononuclear cells in the vascular intima, which lacks dense lymphoid follicles as well as germinal centers, is much less massive. Nonetheless, on the assumption that the presence of these cells in the intima represents a local immunosurveillance system, we coined the term vascular-associated lymphoid tissue (VALT) for these aggregates [6].

A more pronounced appearance of the VALT, similar to the MALT, would, of course, have caught the interest of vascular research much earlier. In hindsight, in the light of subsequent findings, it may now be appropriate to semantically subsume the perivascular and the intimal vascular lymphoid accumulation under the designation of a common VALT, a notion that in the meantime has also been adopted by other groups [7–9]. In this connection, an interesting phenomenon should be mentioned: supply of oxygen and nutrients to the vascular wall of vessels up to a certain diameter is provided by passive diffusion from the lumen, on one side, and the vessels of the adventitia, on the other. Above a certain thickness of the vessel wall, this task is accomplished by the vasa vasorum. In a classical paper, the group of Glagov [10] showed that 29 muscular layers of the media – that can be easily discriminated by counting the interstitial bands of elastic fibres – is the threshold for the formation of vasa vasorum. In our laboratory, we have meticulously reassessed and verified this assumption.

5.2 The Vascular-Associated Lymphoid Tissue (VALT)

The interest of our group in the pathogenesis of autoimmune diseases in general and atherosclerosis in particular has always been and still is focussed on the very earliest, clinically still unapparent stages of the disease. Our first paper on the immunology of atherosclerosis therefore reported results of an immunohistochemical study of atherosclerotic lesions from young (<35 years) vs. old (>65 years) subjects. This study clearly showed that lymphoid cells rather than macrophages or vascular smooth muscle cells (VSMCs) are the first inflammatory cells that infiltrate the intima [11]. In more advanced lesions, macrophages and VSMCs then by far exceed lymphocytes (Fig. 5.1). In the course of these studies, we also had access to a small number of arteries of babies and infants, at an age long before the