TRANSPORT FUNCTIONS OF THE BLOOD-RETINAL BARRIER SYSTEM
AND THE MICRO-ENVIRONMENT OF THE RETINA

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1. Introduction

As we shall see, the blood-retinal barrier system consists of at least three topographically, morphologically and functionally distinct components. Experimental approaches to the demonstration and definition of ocular transport processes across various regions of this barrier system are manifold, and in most cases no single approach can prove the existence of transport. Yet, it appears that with the exception of dissolved gases, virtually all normal solutes and drugs enter into or are removed from the intraocular fluids (IOFs), including the extracellular fluids (ECFs) of the retina, by facilitated or active transport processes across the blood-aqueous and blood-retinal barriers. A complete review of this field is clearly beyond the scope of this article. We shall, therefore, focus on principles rather than details, and will present data and references which are illustrative rather than inclusive.

2. Sites of Passive Exchanges and Transport Processes

The blood-retinal barrier (BRB) is generally regarded as consisting of two components, the endothelium of retinal blood vessels ("inner barrier") and the retinal pigment(ed) epithelium ("outer barrier"). This is, however, an oversimplification. There are no diffusional barriers between the extracellular fluid (ECF) of the retina and the adjacent vitreous (89), nor does the vitreous body itself significantly hinder the diffusion of most solutes (77). Hence, there are free diffusional exchanges between the posterior chamber and retinal ECF, and the epithelia of the ciliary processes.
(see Section 2a), which serve as the barrier between the posterior chamber and blood, must also be regarded as part of the BRB system.

2a. Ciliary processes. Before the advent of electron microscopy and modern techniques of analytical chemistry, the ciliary processes and their secretion, the aqueous humor, were assumed to be very similar to the choroid plexus and its secretion, the cerebrospinal fluid (CSF; 44). Sometimes even a direct analogy between these two systems was advocated (104). However, information developed over the past decades indicates that these systems are not analogous on either physiological or morphological grounds.

The chemical composition of aqueous is, in fact, grossly different from that of CSF (16, 22). This is not surprising if we consider that aqueous humor has a dual function; it not only provides a suitable chemical environment for the avascular ectodermal tissues, the lens, cornea and trabecular meshwork (16), but also contributes to the chemical composition of retinal ECF.

Modern techniques capable of distinguishing cellular orientation and revealing different types of intercellular junctions also show that the ciliary processes are morphologically unique among secretory tissues, and are clearly different from the choroid plexus. While the choroid plexus is covered with a single layer of epithelium, the ciliary processes have two distinct epithelial cell layers in a unique apex-to-apex orientation. This orientation need not be regarded as a morphological oddity if these cell layers are considered to be two separate simple cuboidal epithelia. The deep layer should clearly be called the ciliary epithelium. However, the surface ("non-pigmented") layer whose basement lamina covers a connective tissue compartment, the posterior chamber, is more accurately regarded as the epithelium of the posterior chamber. The two cell layers, which appear to form a secretory unit, will be referred to here as the ciliary epithelia rather than epithelium. The "non-pigmented epithelial layer" by itself will be referred to as the epithelium of the posterior chamber and the pigmented layer as the epithelium of the ciliary stroma.

The transport functions of the ciliary processes, which were originally deduced from observed differences between the chemical composition of aqueous humor and plasma dialysate (44), were demonstrated by in vitro "Ussing chamber" (33, 65) and accumulation studies (5, 55). A better understanding of the scope of these transport functions was achieved by analysis of aqueous humor collected from the posterior chamber, which more closely approximates the composition of freshly secreted fluid (67), and by more detailed studies on the concentration gradients of solutes in the whole IOF system (20, 16). Literature on the transport functions of the ciliary processes (66), the mechanism of fluid production (36), and the chemical composition of the freshly secreted fluid (67, 16)