In vivo observations provide insight into roles of eosinophils and epithelial cells in asthma

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ABSTRACT Observations *in vivo* in patients, supported by guinea-pig *in vivo* data, take centre stage in this perspective. Its objective is to highlight dichotomies between asthma features observed *in vivo* and accepted views involving cell/molecular biology research paradigms. For example, increased bronchial epithelial permeability is now considered a major paradigm and trait of asthma, yet, absorption of inhaled tracers has not been increased *in vivo* in asthma. Such maintained barrier function in exudative asthma reflects *in vivo* asymmetry of the epithelial lining as barrier between outside and inside world of molecules and cells. In desquamatory asthma, maintained epithelial tightness may be explained by *in vivo* demonstrations of exceedingly patchy epithelial loss, prompt creation of plasma-derived provisional barriers, and high-speed epithelial regeneration. Acknowledged protein/peptide secretion by epithelial cells *in vitro* is contrasted here with a dominant, unidirectional movement *in vivo* of plasma-derived proteins/peptides (including antimicrobial peptides) to the surface of an intact epithelial lining. Furthermore, longstanding claims that epithelium-produced adenosine is a mediator of asthma are eroded by observations *in vivo* in asthmatics. Notions concerning activation/fate of mucosal tissue eosinophils illustrate additional distinctions between accepted views and *in vivo* patient observations. Finally, *in vitro*-based paradigms preaching defect epithelial regeneration and increased permeability in pathogenesis of asthma are contrasted with experimental *in vivo* observations of exaggerated epithelial regeneration, which is multipathogenic in its own right. In conclusion, unexpected and challenging *in vivo* observations in recent decades underpin novel insights into mucosal mechanisms in asthma.