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Session Summary

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One of the key questions in AIDS is whether HIV virus itself can cause gastrointestinal abnormalities, superimposed upon which are the additional difficulties caused by enteric infections. The development of SIV infection in monkeys is therefore a major advance since careful longitudinal studies will allow the evolution of gut disease to be followed and good mechanistic experiments to be carried out. In this regard the work of the group led by Kaup (Göttingen) is especially important since he has shown that macaques can be infected with SIV by nontraumatic rectal inoculation. SIV+ cells underlying the epithelium in macaques are probably macrophages and Smith's (Birmingham) observations that human lamina propria macrophages are readily infected with macrophage-tropic isolates of HIV is important. The cytokine profile of mucosal macrophages infected with SIV or HIV is likely to be a fruitful area of study and deserves further investigation. A major change in perception of HIV in the gut should be from trying to explain disease in terms of loss of T cells but to the effects of HIV-infected macrophages. Progress is already being made in this area since monocytes infected with HIV produce large amounts of TNF- α , IL-

1 β and interferon- α (Schmitz, Berlin). If the same is true in the gut, then the studies of Schulzke (Berlin) who showed that TNF- α alters epithelial barrier function are highly relevant.

It is also important to remember that the gut in normal individuals is in a state of controlled inflammation and MacDonald (London) proposed the activated T cells in normal bowel promote epithelial proliferation by activating mucosal macrophages to secrete TNF- α hereby inducing stromal cells to make KGF, a potent epithelial growth factor. Clearly therefore if mucosal T cells are depleted by SIV or HIV, in the absence of any other confounding variable, mucosal atrophy may follow. Kewenig (Homburg) showed early villous atrophy in the first few weeks after SIV infection in macaques, consistent with this notion. On the other hand, if, later in infection, infected macrophages secrete large amounts of TNF, then this could increase KGF production, leading to crypt hyperplasia as well as impair barrier function. Anti-TNF- α therapy with antibodies is well tolerated in man and it would be worthwhile to determine in a pilot study if it is effective in HIV enteropathy.