proliferation of endothelial cells and formation of solid sprouts. Finally, tube morphogenesis restructures the sprouts into a lumen lined by endothelial cells (Folkman 1995).

1.6.1.1 Prevascular phase of tumorigenesis (the "Angiogenic Switch")

Tumor cells have an absolute requirement for a persistent supply of new blood vessels to nourish their growth and to facilitate metastasis (Folkman 1995). The angiogenic cascade leading to tumor vascularization can be subdivided into two general phases, the prevascular phase referred to as the "angiogenic switch" and the vascular phase (Pepper *et al.*, 1995). The transformation of tumor cells to an angiogenic phenotype is a key event in the progression to malignant disease (for suggested reading, see (Hanahan *et al.*, 1996)). In the absence of a supporting vasculature, the rate of diffusion of nutrients and wastes from surrounding tissues limits tumor growth to that of approximately 1–2 mm in diameter (Campbell *et al.*, 1998). However, once the switch to an angiogenic phenotype has occurred, avascular tumors then can acquire their own blood supply to support a rapid rate of growth.

1.6.1.2 The vascular phase of tumorigenesis

Once tumor cells undergo the transformation to an angiogenic phenotype, these malignant cells in turn induce phenotypical changes in endothelial cells, as well as other cell types (Jackson *et al.*, 1997, Norrby 1997), to initiate the process of neovascularization (Polverini 1996). Normally, endothelial cells are quiescent, with turnover rates measured in months to years. However, when enticed by tumors, endothelial cells switch to an angiogenic phenotype with turnover rates of 50–200 times that of normal endothelial tissues (Derbyshire and Thorpe 1997). This dramatic activation of endothelial cells arises from a shift in the balance of angiogenic inducers and inhibitors in favor of angiogenesis.