In recent years, the management of patients with abdominal aortic aneurysms has improved with the introduction of screening, the advent of endovascular aneurysm repair and the changing emphasis on the medical management of patients with arterial disease. There has been increasing importance placed on basic science investigations into the cellular and molecular events that drive the aneurysmal process. However, many fundamental questions regarding the pathobiology of abdominal aortic aneurysms remain unanswered. In particular, the molecular processes that underpin aneurysm expansion and rupture are not fully defined. Understanding these events will be crucial in designing medical therapy to retard aneurysm expansion, The promise of pharmacotherapy is particularly applicable to small aneurysms which may be diagnosed in screened populations. Pharmacotherapy for small aneurysms is likely to become a realistic proposition within the next 5–10 years. There is some evidence to suggest that current medical management with anti-hypertensive agents and HMG Co-A reductase inhibitors may retard aneurysm expansion, and encouraging results with low dose doxycycline have been reported. In a recent experimental investigation, Yoshimura et al. demonstrated aneurysm regression for the first time by inhibition of a major signalling pathway. Pharmacotherapy, when available, is likely to have some side effects and targeting patients that will achieve maximum benefit from this therapy is essential.

One of the key steps in improving management of abdominal aortic aneurysms is to identify which patients with small aneurysms will demonstrate rapid expansion. These patients may then be targeted with pharmacotherapy or early endovascular surgery. At present, only the initial size of the aneurysm provides a reliable guide to the likely expansion rate. The identification of serum factors that might predict expansion rate has been a goal of many investigators in recent years. The concentration of various factors within the serum has been reported to be associated with rapid rates of aneurysm expansion. These factors have included osteoprotegerin, t-PA, macrophage migration inhibitory factor, cystatin C and MMP-9. Interestingly most of these serum factors have been involved in the inflammatory and proteolytic pathways that have been implicated in the matrix degradation that characterises mature aneurysm wall.

In this issue of the journal, Halazun et al. report a convincing independent association between homocysteine concentrations and the rate of aneurysm expansion. Of particular note was the finding that elevation of homocysteine levels doubled the expansion rates of aneurysms exceeding 4 cm in diameter. Although the study was of relatively small size, there was a weak correlation between aneurysm expansion rates and plasma homocysteine. This association is biologically plausible. Previous reports have revealed a step wise increase in plasma homocysteine and aortic diameter in subjects with a normal aortic diameter, and in patients with aneurysms. Homocysteine is involved in several inflammatory pathways and may well have an effect on the biology of the aortic wall. The difficulty with interpretation of this study, as with many others, is whether the association is causative. This question will really only be answered by a combination of larger series, experimental results and possibly genotype-phenotype associations.
Nevertheless, the findings reported by Halazun et al. are a significant contribution to the literature surrounding plasma markers and aneurysm expansion. With further larger studies it may be possible to construct a model that incorporates demographic, morphological and biochemical factors that predict the rate of aneurysm expansion. This model would be invaluable in targeting patients for either aggressive pharmacotherapy or early aneurysm repair.

References