Discussion

The final session culminated in a discussion chaired by Professor John McMurray, which centred on three questions based on the key themes and topics presented during the two day meeting.

**Are renin-angiotensin system modulators effective in reducing cardiovascular mortality and morbidity solely due to their effect on blood pressure, or can their efficacy be attributed to additional benefits?**

There was a general agreement that, although the primary goal remains effective blood pressure lowering, there must be other additional mechanisms responsible for the impressive efficacy of renin-angiotensin system modulators. Dr Meredith pointed out that STOP-Hypertension-2 showed a selective benefit associated with angiotensin converting enzyme (ACE) inhibitors in terms of incidence of myocardial infarction and frequency of heart failure. In addition, a review of data from the Glasgow blood pressure clinic reveals a benefit associated with ACE inhibitors which is independent of blood pressure lowering. However, if blood pressure is lowered sufficiently, the difference between treatments becomes less apparent.

Professor Swedberg acknowledged that ACE inhibitors and β blockers are doing more than was anticipated when they were first introduced. In addition, the full potential of spironolactone is only just being realised. Similarly, Professor Shepherd observed that when a new drug is introduced, it is often expected that it will do only what it was originally designed to do. He added that it is frequently forgotten that within the framework of a drug's pharmacology there are elements that have not been taken in to account such as the presence of a side chain. Instead of trying to attribute all the benefits of an agent to a single mechanism it is often necessary to consider other possibilities.

Professor Hobbs highlighted the fact that in GISSI-3 50% of the benefit of lisinopril was achieved within the first 24 hours of treatment. This is an acute effect which cannot be explained solely by blood pressure lowering. The panel concluded that there are compelling data that the benefits associated with RAS modulators are the result of more than blood pressure lowering. However, this should not minimise the importance of effective blood pressure control.

**AT, receptor blockers demonstrate both efficacy and placebo-like tolerability. Does this mean that side effects are now unacceptable in antihypertensive treatment?**

It was generally felt that the clinical situation is more complex than simply choosing a treatment based on tolerability alone. For example, Dr Meredith pointed out that it should still be possible to improve the efficacy of antihypertensive treatment, as a threshold has not yet been reached in terms of clinical efficacy.

Professor Swedberg explained, the majority of patients will need more than one drug to control their blood pressure. The greater the number of drugs that are used, the more important it is that agents are truly once daily. Tolerability and drug interactions will also become key issues. Professor Swedberg highlighted that a problem with the current antihypertensive therapeutic approach is that blood pressure is only a marker of disease. If a measurement of actual vessel disease could be made, it would provide a more accurate indication of a drug's efficacy. He agreed that using various combinations of agents provides a number of future treatment possibilities.

**What single breakthrough (medical, political or social) will have the biggest impact on reducing cardiovascular mortality and morbidity in the next century?**

The panel felt that information technology will change the future of medicine. Professor Hobbs emphasised the importance of the increasing use of computers at the point of physician–patient consultation, providing physicians with patient specific information as well as evaluating the doctor's performance. By the judicious use of this technology, clinical targets are more likely to be reached and improved efficacy achieved.

Professor Shepherd concluded that the reason the panel was reluctant to agree on a single therapy as the optimal treatment for hypertension was because patients comprise a wide spectrum of individuals with different risk factors, different symptoms, and different responses to treatment. It is important for physicians to have a choice of agents that takes into account the treatment benefits, costs, and side effect profile in an individual patient. It would clearly not be a good policy if all of yesterday's drugs were swept away when a new drug appears.