Furberg goes over the top on calcium channel antagonists

In March 1995, Dr Bruce Psaty (University of Washington, Seattle, USA) shook the world of cardiology when he presented a case control study at a meeting in San Antonio in which it was claimed to show that, compared with other agents, calcium channel antagonists (CCAs) are associated with a higher risk of heart attack when used to treat hypertension. The matter has been debated in the literature ever since, and one of the main critics of CCA safety has been Curt Furberg, Professor of Public Health, Bowman Gray School of Medicine, Winston-Salem, NC, USA. Consequently, one of the hottest items at the *45th Annual Scientific Session of the American College of Cardiology*, held in Orlando in March 1996, was a debate on this topic between Professor Furberg and Dr Robert Roberts (Baylor College of Medicine, Houston, TX, USA).

An audience of about 3,000 attendees assembled for the start of the debate at 8.30 am, probably helped by the rumour that Furberg was going to present some fresh information. The initial sessions in which Furberg presented his thesis and Roberts attempted to demolish it were relatively uneventful and revisited information published in the literature in the previous 12 months. Briefly, Furberg maintains that there are no good long-term safety data on CCAs and he sees them as, at best, third-line treatments and, if indicated, he believes verapamil may be better than dihydropyridines such as nifedipine. He also slated what he saw as an unhealthy relationship between doctors and the pharmaceutical industry, citing the latter's sponsorship activities in areas such as research and conferences. Roberts countered these claims, suggesting that case-control studies were the lowest form of epidemiological tool, usually only useful to generate and test hypotheses. He cited a number of distinguished cardiologists who have criticized the Psaty study and some, such as Dr Franz Messerli (Ochsner Medical Clinic, New Orleans, LO, USA) have even found methodological errors in the way in which it was performed.

However, it was only when Furberg was given a few minutes to reply to these criticisms that he really pulled out the stops. He showed a slide which described how calcium was involved in a number of physiological and pathological processes, such as apoptosis, and suggested that CCAs may produce adverse effects in diseases where calcium plays an important role, such as cancer, AIDS and Parkinson's disease. None of these claims was supported with evidence, and it was hard to decide what the audience thought of it. Cardiologists tend to be fairly polite, and no questions were allowed from the floor. However, it is hard not to believe that pharmacologists would have had a field day if they had been unleashed.

One thing is certain – the debate will continue, but Furberg has done his case a lot of harm unless he can quickly produce supporting evidence.

David B. Jack

Cystic fibrosis: new strategies for drug therapy

It has been more than six years since the discovery of the genetic defect that causes cystic fibrosis (CF); the defect is located on a gene that encodes a membrane protein now known as the CF transmembrane conductance regulator (CFTR). This key protein is a chloride channel that regulates the flow of water and salt across epithelial tissues and thus controls the degree of hydration of bodily secretions. Its discovery provided an explanation for the presence of poorly hydrated airway mucus and associated life-threatening bacterial infections of the lung that are characteristic of the disease. Many different genetic defects have now been discovered on the same gene, each of which alters the function of CFTR to a different degree. This heterogeneity of genetic defects presumably accounts for the wide diversity in the severity of CF.

Consequently, many scientists and clinicians considered gene therapy to be the most promising solution to the most common genetic disease of the Caucasian population. It was anticipated that reengineered adenoviruses would be the ideal vector to deliver the wild-type CFTR gene to the airways of CF patients. The new gene would reverse the susceptibility of CF patients to lung infections irrespective of the position of the gene defect on CFTR. So far the promise is unfulfilled, and in the past two years, clinical trials have exposed fundamental problems with the adenoviral vector. In some cases, the vector caused an unexpected inflammatory reaction, but the major problem is the lack of efficiency of infection. Airway cells appear much more resistant to adenoviral infection than anyone ever expected, making it impossible to deliver sufficient amounts of the wild-type gene.