CARDIOLOGY IN THE 21ST CENTURY*

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INTRODUCTION

This two day symposium was attended by more than 200 delegates and covered a range of topics from molecular genetics to more practical aspects of cardiology.

SUDDEN CARDIAC DEATH IN THE COMMUNITY

Out-of-hospital cardiac arrest: whom do we save and what is the outcome?

Of the 137,000 deaths from coronary disease per annum, approximately 50% die before reaching hospital. In a significant proportion of the deaths, this is the first presentation of coronary artery disease. Relatively little is known about the exact cause of these deaths or how to predict those patients at highest risk of sudden death. In a recent review of the 320 people suffering an out-of-hospital cardiac arrest (OHCA) in the Edinburgh area, only 80 reached hospital alive and of these, only 40 were discharged from hospital. This represents a 12% survival rate! Possible areas for improvement include early recognition of cardiac arrest, by-stander cardiopulmonary resuscitation (CPR), reduced response time of the emergency services, early defibrillation (where appropriate) and early transfer to hospital.

To treat appropriately patients suffering an OHCA, predictors of outcome would help. In another study, several factors were associated with an improved outcome. Cardiopulmonary resuscitation by a trained operator significantly improved outcome when compared to CPR by an untrained person or family member: from 30 to 60%. Outcome was further improved when CPR was performed by trained ambulance personnel to above 70%, possibly due to the early use of defibrillation. The clinical state of the patient also predicted outcome: self-ventilation was a good prognostic factor as was an initial presenting cardiac rhythm of ventricular tachycardia (VT) or ventricular fibrillation (VF) rather than electromechanical dissociation (EMD) or asystole. In addition, neurological status on admission as assessed by the Glasgow Coma Scale (GCS) correlated with survival.[1]

The majority of survivors admitted to hospital die before discharge from sequelae of ischaemic brain injury rather than cardiac failure. Indeed, cardiac status is a poor indicator of outcome in these patients. In a follow-on study of OHCA patients, cognitive dysfunction was assessed at least six months after discharge. Over 95% were discharged to their own home while the others were discharged to further-care institutions. Thirty-five patients were compared with a control group made up of patients who suffered a myocardial infarction with no cardiac arrest. In the controls, cognitive function was within normal limits; in 40% of patients with an OHCA significant memory impairment was observed. This was chronic, persisting at three year follow-up and it appears to be due to generalised brain atrophy (associated with a general reduction in brain mass) rather than due to damage to specific areas of the brain in OHCA patients.

Currently, no other specific tests will predict survival. However, two plasma markers of neuronal damage have been proposed as possible candidates; neuron specific enolase (NSE), which despite its name is also found in red blood cells, and plasma S-100, which are both elevated following significant brain injury. In 143 OHCA patients studied prospectively at 24–48 hours and 72–96 hours, plasma concentration of these markers were correlated to outcome. Neuron specific enolase was shown not to be specific as marked overlap was noted between survivors and non-survivors. However, detection of plasma S-100 over a certain concentration predicted a mortality of 100%. Plasma S-100 concentrations also relate to significant memory deficit in the survivors. However, this plasma concentration was three times higher than previously quoted and clearly more research in this area is needed. In the future, the development of plasma markers alongside clinical details may allow more appropriate triage and treatment for those suffering an OHCA as well as counselling relatives about the likely outcome.

Interactive debate – the best way to reduce sudden death in the community

The most common and potentially treatable abnormal cardiac rhythm resulting in cardiac arrest is VF, with early defibrillation resulting in a better outcome for the patient. The use of implantable cardioverter defibrillators (ICDs) in patients at high risk of sudden cardiac death was approved recently by the National Institute for Clinical Excellence (NICE) for patients in England and Wales. This decision is somewhat controversial as the absolute benefits of ICDs are not clear and the debate is hampered by a lack of robust clinical outcome studies. Previously, ICDs required epicardial plates and a thoracotomy for their placement. New devices can be fitted in a manner similar to pacemakers with a reduction in operative mortality. In addition, newer ICDs can be interrogated and store the rhythm history. Such devices are expensive and benefit from their use has not been clearly demonstrated.

Blinded, placebo-controlled trials are difficult to undertake when comparing ICDs with drug therapy but several active control trials have demonstrated benefits in terms of decreased mortality.[2-6] Differing rates of drug usage in the ICD group may explain some of the relative benefits as anti-arrythmic therapies which were shown to be worse than placebo in some studies.[7,8] In addition, the benefit of ICDs is uncertain in patients with mild to moderate left ventricular (LV) dysfunction.[5] In those with severe LV

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dysfunction whose short life expectancy may not justify the use of such expensive ICDs. Many of the trials on ICDs were conducted before the widespread acceptance of the usefulness of ACE-I and beta-blockade. Whether it is appropriate to extrapolate these data to today's population is questionable. Indeed, much of the difference in ICD trials may be explained by a higher use of beta-blockade in ICD patients.

Currently, NICE guidelines suggest usage which will result in the avoidance of one death per ten patients treated for three years (27% reduction in total mortality) and their use in selected patients following cardiac arrest, VT with syncope and VT with poor ejection fraction (EF). They should be avoided in patients with New York Heart Association (NYHA) grade IV heart failure as their life expectancy does not justify the cost.

An alternative approach to secondary prevention is to target a larger population with less expensive but effective preventative therapies. In Scotland, 3,400 per million population deaths occur each year; the current usage of ICD is eight/million Scottish population and therefore the impact that ICD will have on the overall cardiovascular mortality in Scotland will be small.

Many pharmacological interventions reduce mortality in patients with cardiac disease: beta-blockers ~35% mortality reduction;[9-13] ACE-I ~20% mortality reduction;[14-16] spironolactone ~30% mortality reduction;[17] ramipril ~26% mortality reduction;[18] HMG-CoA reductase therapy up to 40%.[19] Medical utilisation of these medications is very low[20, 21] and thus there appears to be a 'failure of mundane medicine'. The most common cause of death in cardiac patients is sudden cardiac death and most people who die of a sudden cardiac death will not have seen a cardiologist. Therefore at the current level of cardiology service provision, simple 'mundane medicine', if widely implemented at the primary care level, will deliver the largest benefit to those who need it.

THE AORTA AND AORTIC VALVE – NEW SOLUTIONS FOR OLD PROBLEMS

Big-time surgery does not mean big-time scars

Aortic dissection (AD) is associated with a high mortality: 50% will die as a result of rupture, a further 30% will die in the following five years from a variety of causes. Most cases of AD result from medial degeneration, and many others result from intramural haematoma. Two novel 'non-surgical' therapies were devised for this condition and its complications: endoluminal stenting of the aorta and fenestration of the flap in acute limb or organ ischaemia. Endoluminal stenting involves the placement of a stent via the femoral artery into the aorta. The aims are to exclude aortic leaks, alleviate branch vessel occlusion and restore a uniluminal aorta, thus reducing the risk of the late complication of aneurysm. Fenestration of the endoluminal flap is used to alleviate branch vessel occlusion following AD and acute limb or organ ischaemia which requires urgent treatment. If appropriate, fenestration of the flap can be performed transcutaneously via the femoral artery, remembering that the strongest pulse will be supplied by the false lumen and felt in the leg. Fenestration should be performed early while the flap is thin, and while reduction of the false lumen is possible.

Although there are no randomised controlled trials of these techniques, hundreds of these procedures have now been performed and the complication rate is low. Randomised trials are difficult to perform as the number of cases is small, therefore recruitment is difficult; a recent study demonstrated that endoluminal stent placement in acute aortic dissection was a safe and effective treatment. Compared to surgery, mortality and morbidity were reduced from 33 and 42% to 0 and 0% respectively.[22] In addition, paraplegia secondary to spinal artery thrombosis was less common, probably because cross-clamping of the aorta is not required. With these techniques, a risk of femoral artery rupture exists but this can usually be repaired easily using a smaller femoral stent. The applicability of this technique in Scotland is yet to be seen, as only 30–40% of cases at presentation are deemed suitable for this treatment. Proximity to a specialist centre is also important as this technique often has cardiovascularly unstable patients.

The natural history of aortic sclerosis

Degenerative aortic sclerosis (AScl) has often been considered as a benign degeneration condition associated with ageing. More than 48% of the population over the age of 85 will have evidence of AScl, however only two to eight per cent will have aortic stenosis (AS). It is unclear whether AScl is a result of the normal ageing process[23,24] and whether there are modifiable risk factors that will alter disease progression.

Aortic sclerosis can be diagnosed by echocardiography as an irregular thickening of the valve leaflets with a variable degree of calcification; it affects bicuspid aortic valves earlier in life than structurally normal valves. Structural changes in AScl are characteristic with thickening of the valve on the aortic side. This lesion is usually confined to the superficial layer of the valve structure and contains macrophages with inflammatory markers such as apo B, LDL and LPa.[25] In addition, osteopontin, a protein that promotes calcium deposition, co-localises with macrophages. T lymphocytes and oxidised lipids are also present but there are no smooth muscle cells. Aetiology of AScl is unclear, but it appears that both mechanical and low shear stress may be involved as illustrated by a more rapid progression of AScl in bicuspid valves and by the fact that the non-coronary aortic cusp is most often affected in valves with three cusps. Other co-factors which are related to progression of disease include age, gender, lipid status, blood pressure and smoking. Thus, both similarities and differences exist between the process of AScl and atherosclerosis.[23]

The majority of cases of AScl will not result in significant flow obstruction across the valve, but this is a progressive disease. Therefore flow obstruction (AS) should be looked for in these patients,[26] and the development of a flow obstruction across the valve should be monitored, although it is unclear how often this should be done. Currently available prospective studies involve small numbers of patients.[26-9] In general, patients with asymptomatic AS have a low event rate of <1% per year, and progression is slow although there is a wide variation. Symptoms, such as chest pain, breathlessness or syncope, confer a much increased risk and such patients need prompt assessment for valve replacement.[30] The timing of valve replacement is often a difficult decision. The risks of surgery and the limited 'life time' of a prosthetic valve, along with the risks of co-incidental requirement for anticoagulation must be weighed against the risk of sudden death and left ventricular damage. As progression may be slow and the annual event rate in

asymptomatic patients is low, surgery is generally delayed where possible, although local waiting lists may dictate the timing of referral.

Aortic sclerosis is then not a completely benign condition and should no longer be regarded as a reassuring diagnosis as, regardless of progression of AS, patients with AScl are at increased risk of death from cardiovascular and other causes.[31] As AScl is a progressive disease interest has increased in risk factors modification and clinical trials are ongoing.

PRACTICAL MANAGEMENT ISSUES IN ATRIAL FIBRILLATION

Optimal anti-thrombotic management of atrial fibrillation

Atrial fibrillation (AF) is a common condition with a significant co-morbidity secondary to embolic events which may be preventable. A two- to five-fold increase in mortality occurs in patients with AF compared with sinus rhythm.[32] It affects 0·5% of the population aged 50–59 years; this rises to nine per cent in the 80–9 years age group. Thus, as the population continues to age so also the prevalence of AF increases. Atrial fibrillation significantly contributes to mortality as it causes a reduction in cardiac output of approximately ten per cent, thus causing, or worsening, symptomatic heart failure. The causes of AF and appropriate investigations were reviewed recently.[33] Choices of anticoagulation were discussed, with aspirin and warfarin being the most common agents used. New agents such as clopidigrel may become more popular as the results of ongoing clinical trials become available.

UNDERSTANDING CORONARY ATHEROSCLEROSIS-1

New insights into the biology of the atheromatous plaque

The central pathogenic event in the acute coronary syndrome is rupture of an atheromatous plaque consisting of a highly thrombogenic, lipid-rich centre covered by a fibrin-rich cap. Thus, the integrity of the cap is of vital importance in plaque stability and preventing coronary artery occlusion. Several key events occur in the development of an atheromatous plaque and the vascular smooth muscle cell (SMC) appears to be central to plaque stability. In brief, injury to the vessel wall leads to monocyte migration, cytokines are released which can change SMCs to form the fibrous cap over the plaque.[34, 35] Recently, distinct genes were shown to determine the action of the SMC. Phosphorylation of these genes may result in the SMC in the fibrous plaque to have slower growth rate, and they undergo the process of apoptosis (programmed cell death) more easily. In the unstable fibrous plaque, macrophages are found at the site of plaque rupture. They are thus implicated in plaque stability, which appears to be a balance between inflammation and repair. Many other factors may be involved in this process including interferon gamma, interleukin-1, serum amyloid A, ICAM-1, TNF alpha, stromelysin[36] and other matrix metalloproteinases produced by inflammatory cells.[37]

Many studies demonstrated regression of plaque size as a good outcome from an intervention. However, this may not be so important, as the smaller haemodynamically insignificant plaques are more likely to rupture and cause an acute coronary syndrome than larger plaques which are more stable. HMG-CoA reductase inhibitors (statins) which may act by stabilising plaque were shown to improve outcome.

To determine the effects of treatment on human coronary plaques *in vivo* better anatomical imaging of coronary artery plaques is required. Coronary angiography can only give information on luminal contours while intra-vascular ultrasound can give detail of plaques structure. Other techniques such as magnetic resonance imaging (MRI)/ magnetic resonance angiography (MRA)[38] and positron emission tomography (PET) scanning are currently under development.

Childhood origins of atheroma

Symptomatic coronary artery disease becomes more prevalent with age, however the origin of the lesion clearly occurs much earlier. Studies on aortas in fetuses aborted from women with hypercholesterolaemia demonstrated aortic fatty streaks – the precursor to atheroma. Interestingly, these appear to resolve in some fetuses in the third trimester when the fetus takes over its own cholesterol metabolism, suggesting reversibility. Alarmingly, 37% of people in their twenties will have coronary artery lesions, rising to 85% in the fifties. Indeed, in one series of 3,000 autopsies with an average age of 22 years, 75% had evidence of coronary atherosclerosis!

While there are many factors which can increase coronary plaque number and instability, such as smoking[39] and hypercholesterolaemia,[40] it would appear that the origins of the atheromatous plaque occur before these risk factors are present, and long before any intervention is currently advised. Perhaps risk factors should be targeted in primary prevention at a much earlier age and the aim should be event-free life prolongation rather than relative risk-reduction.

UNDERSTANDING CORONARY ATHEROSCLEROSIS-2

Primary prevention – getting the timing right

The role of primary prevention is complex and involves many issues. It is known from large-scale randomised placebo-controlled trials that statin therapy will reduce cardiovascular risk by ~30%. The benefit is rapid, being present at six months and maximal at two years. Reduction in the incidence of stroke also occurs resulting in a combined relative reduction in mortality of 50%. Classically the assessment of whom to treat can be based on a risk-benefit relationship. Statin therapy is relatively risk-free and the benefits appear large, thus making the decision to treat more complicated and dependent on factors such as numbers needed to treat, percentage of the population to treat and cost-effectiveness.

Currently, the guidelines suggest treating a 30% ten year cardiovascular risk which translates into eight per cent of the population, a cost of £8,100 per life-year gained and 25% of the current drug budget! If the data from the West of Scotland Primary Prevention Study (WOSCOPS) trial[41] were to be implicated in practice, patients with a risk of 15% over ten years would receive treatment resulting in 24% of the population being treated costing £12,500 per life-year saved, costing 90% of the current drug budget! Clearly this is not financially practical at present, however as drugs come 'off patent' and their cost decreases, then perhaps current guidelines should be reassessed.[42, 43]

Secondary prevention – keeping the atherosclerotic plaques stable

The recently published Joint British Recommendation highlight specific targets for reducing cardiovascular risk.[44] These included smoking cessation, weight control, reduced fat intake, and targets of BP <140/85, cholesterol is <5·0

mmol/l. If cholesterol >6·0 mmol/l, statin therapy is advised, however, if 5·0–6·0 mmol/l then dietary advice is recommended and there should be repeat measurement at follow-up. Other therapies include aspirin, beta-blockers and ACE-I where appropriate. Despite clear guidelines, the utilisation of therapies is low. In a recent study in 15 European countries, secondary prevention was evaluated in patients who had had a MI, angiography, coronary bypass grafting or angina. Patients were reviewed on average 1·4 years after the event: 20% of patients still smoked, 33% were obese (BMI >30), 50% had a BP>140/90, 60% had a cholesterol >5 mmol/l, 84% were on antiplatelet therapy, 66% were on beta-blockers, 63% were on statin therapy and 43% on an ACE-I.[21] Similar numbers are seen in the UK[20] and there clearly is much work to be done to improve these poor results.

Reducing the burden of CHD in Scotland

Deaths from CHD have fallen since the late 1970s and cancer is now the highest killer; the reasons for this are unclear. Despite this reduction, Scotland still has one of the highest rates of mortality and morbidity from CHD in the western world. Mortality data are generally crude and a fall in deaths could be due to either a reduction in incidence or a reduction in case fatality. One reason for a fall in cardiovascular deaths may be a reduction in risk factors: in general, there has been a reduction in systolic blood pressure, total cholesterol and smoking over the last ten years. However, there has been an increase in BMI in both men and women. The reasons for reduction in risk factors are complex and while there is evidence that general public health measures can modify behaviour to a small degree this does not necessarily translate into a reduction in mortality.[45]

In terms of public health strategies, in general, fiscal control is the most effective. This was clearly demonstrated in California, US when there was a successful public anti-smoking campaign sponsored by the local government in 1989. In 1993 funding was stopped and, following increased tobacco industry advertising, tobacco usage increased to pre-campaign levels. Thus, while we are aware of the impact of risk factor modification, implementation of lifestyle changes may require more dramatic fiscal interventions than are presently in place.

PRACTICAL MANAGEMENT ISSUES IN HEART FAILURE

Optimal management of heart failure

The most common cause of heart failure is left ventricular (LV) dysfunction. With the widespread use of echocardiography, LV systolic dysfunction is easily demonstrated and once identified, many therapeutic options exist for its treatment. Neuroendocrine activation is central to the development of heart failure with activation of the sympathetic, renin-angiotensin and endothelin systems. This results in vasoconstriction, tachycardia and inotropic effects on the heart with resulting arrythmias, ischaemia, salt and water retention, hypertrophy, fibrosis and myocyte apoptosis.

Standard therapeutic options for the treatment of heart failure now include ACE-I, diuretics, digoxin and beta-blockers. The evidence for using beta-blockers is increasing and, despite being potentially negatively inotropic, beta-blockers reduce mortality in patients with stable heart failure when they are introduced with a gradual controlled up-titration.[10, 11]

New treatments, such as angiotensin receptor type II antagonists (ATIIRAs), continue to be developed and investigated. Although ATIIRAs have not been licenced for heart failure they are used in hypertension, and clinical trials are ongoing to assess their role in the treatment of heart failure. The first ATIIRA trials in heart failure were evaluation of losartan in the elderly study (ELITE) I[46] and ELITE II.[47] These trials outlined the importance of sample size and power in clinical trials. ELITE I was designed to investigate the safety and tolerability of losartan in the elderly and appeared to demonstrate mortality benefits. This trial was not adequately powered to look at mortality. The results of ELITE II demonstrated no mortality benefit for losartan over captopril and indeed showed a non-significant trend towards a poorer outcome.

At the recent American Heart Association meeting in New Orleans (2000) the valsartan in heart failure (ValHeft) trial was presented: this investigated the effects of adding an ATIIRA to existing best therapy which includes ACE-I, beta-blockers, spironolactone and digoxin. The details of the results are limited at present, but there was no difference in all-cause mortality although a significant reduction in hospital admissions occurred in the valsartan treated group. In addition, a reduction in mortality was shown in the group which were ACE-I intolerant although this only accounted for seven per cent of the trial population. An increase in mortality with valsartan in the beta-blocker treated patients is a cause of some concern and further details are awaited. The candesartan in heart failure – assessment of reduction in mortality and morbidity (CHARM) and the valsartan in acute myocardial infarction (VALIENT) trials are two ongoing trials which involve the use of ATIIRAs in patients with chronic heart failure.

Neurohumoral blockade with endothelin antagonists (ETRAs) is another potential treatment for CHF. Data are currently limited but ETRAs have shown systemic haemodynamic improvements in short-term studies.

Diastolic dysfunction is an under-recognised cause of heart failure: in one series of patients it was reported to account for 30–60% of those diagnosed with heart failure, although the true figure is probably somewhat smaller. It is characterised by a stiff ventricle that demonstrates impaired relaxation and therefore impaired diastolic filling. Diastolic dysfunction responds to therapies used in LV systolic dysfunction. Beta-blockers will reduce heart rate thus increasing diastolic filling time and spironolactone may reduce fibrosis. ACE-inhibitors may also be of use although these may reduce filling pressures. Studies such as the perindopril for elderly people (PEP) study, using an ACE-I, and CHARM, using an ATIIRA, are ongoing to assess the best treatment for diastolic dysfunction.

Morphine has long been used to aid breathlessness in the terminal care setting and in patients with chronic obstructive airways disease. A recent pilot study investigated the effects of morphine in patients with breathlessness secondary to severe heart failure. It demonstrated a reduction in breathlessness with no increase in drowsiness or change in quality-of-life.

Pacing in heart failure is another relatively novel treatment option. Atrial, synchronised, biventricular pacing involves slightly more work to insert than normal pacing: it requires lead placement in the right ventricle, coronary sinus, to pace LV, and a lead in the atria to sense, if in sinus rhythm. In studies of biventricluar pacing, increases occurred in

quality-of-life and six minute walking, but there are no mortality data although studies are ongoing.

CHEST PAIN

Chest pain in casualty: who is it safe to send home?

There are 600,000 admissions for chest pain annually, which represents 20% of acute medical admissions. In addition, there are a further 300,000 patients discharged from Accident and Emergency departments. Only two per cent of these patients will have suffered a myocardial infarction. In the US, it is estimated that unnecessary admission of patients with chest pain costs $5 billion per year. It is often difficult to identify which patients are suffering true cardiac pain, and it is therefore essential that an electrocardiograph is performed and adequate cardiac enzymes at an appropriate time after the chest pain. Myoglobin is the earliest maker to rise following myocardial damage but is not specific. Creatinine kinase and troponin are most specific, but must be measured at least 6–12 hours following suspected myocardial damage. Chest pain observation units are of increasing use and may allow for more accurate diagnoses and triage.

Interactive debate – cardiac catheterisation has a vital role in the early management of acute coronary syndromes

The term 'acute coronary syndromes' (ACS) encompasses a variety of clinical conditions including myocardial infarction and unstable angina; the most common pathological feature being acute coronary artery insufficiency. Cardiac catheterisation can be used to radiologically image coronary arteries and to treat coronary artery stenosis with balloon angioplasty or the placement of intraluminal stents (coronary intervention). The aim is to mechanically restore vessel patency and to stabilise ruptured plaques in ACS. However, the value of this procedure in the early management of ACS is controversial and benefit from its use, in all such patients, is not proven.

Rates of coronary intervention in the UK are increasing but still much lower than the rest of Europe. It is an extremely safe procedure, and in 22,000 single vessel procedures only four deaths occurred during elective angiography. Coronary angiography has a defined place in the treatment of stable angina, myocardial infarction and in unstable patients with myocardial ischaemia; its role in all patients with an ACS is more controversial, the alternative being thrombolytic therapy. For patients with persistent symptomatic blocked coronary arteries, the alternative may be coronary artery bypass grafting; coronary intervention has the advantage that it may be offered to patients for whom surgery would be too risky, e.g. those with other significant co-morbidity or with poor ventricular function. In ACS, coronary artery intervention may reduce future MI, need for revascularisation and reduce stroke rate when compared with thrombolysis but no mortality outcome data are available for the procedure. Indeed, although coronary intervention rates in ACS varied dramatically between European countries (8–62% for myocardial infarction) in the recent European network for acute coronary syndrome treatment (ENACT) study, little difference occurred in mortality. This phenomenon is also present in North America where vast differences in coronary intervention rates in Canada and the US (19% vs 50%) do not translate into any difference in case mortality; indeed there is a case fatality odds ratio of 0·8 in favour of

LIST OF SPEAKERS FROM THE 40TH ST ANDREW'S DAY FESTIVAL SYMPOSIUM 'CARDIOLOGY IN THE 21ST CENTURY'.

SPEAKERS	LECTURE
Dr Neil Grubb	Out of hospital arrest; who do we save and what is the outcome?
	Interactive debate: The best way to reduce sudden cardiac death in the community is:
Dr Andrew Rankin	1) treat high risk patients with implantable defibrillators;
Professor Allan Struthers	2) treat the underlying mechanisms with drug therapy.
Professor Tim Buckenham	Big-time surgery does not mean big-time scars.
Dr Catherine Otto	The natural history of aortic sclerosis.
Dr Peter Bloomfield	Case presentations and audience survey.
Professor Gordon Lowe	Optimal antithrombotic management of atrial fibrillation.
Professor Peter Weissberg	New insight into the biology of the atheromatous plaque.
Professor John Deanfield	Childhood origins of atheroma.
Professor Larry Ramsay	Primary prevention – getting the timing right.
Professor David Wood	Secondary prevention – keeping the atherosclerotic plaques stable.
Dr Harry Burns	Reducing the burden of CHD in Scotland.
Dr Nick Boon	Case presentations and audience survey.
Professor Henry Dargie	Optimal management of heart failure.
	Interactive debate: Cardiac catheterisation has a vital role in the early management of acute coronary syndromes.
Dr John Perrins	For
Professor Keith Fox	Against

Canada! One reason for this may be that although 'culprit' lesions may be identified by angiography the majority of unstable plaques which subsequently rupture and cause thrombus are relatively small and diffuse and therefore predicting which plaques are unstable is difficult.

In conclusion, coronary intervention has a role to play in coronary artery disease although its use in ACS remains to be clarified and indeed may change as new pharmacological options, such as glycoprotein IIbIIIa inhibitors, become available.

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