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LESSONS FROM A SYMPOSIUM ON CARDIOLOGY HELD IN THE COLLEGE ON 30 NOVEMBER AND 1 DECEMBER 1995*

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Most doctors look after patients with cardiac disorders to a major or lesser extent. The 35th St Andrew's Day Festival provided an opportunity for recent advances and difficult problems in heart disease to be presented to a wide audience. The subject matter covered basic scientific matters including molecular biology, ischaemic heart disease, heart failure, disorders of rhythm, and congenital and valvular heart disease and a discussion of established and emerging imaging techniques.

THE ENDOTHELIUM

The last decade has witnessed an explosion of interest in the physiology of the vascular endothelium and in its pathophysiology as this may be related to such common conditions as hypertension, ischaemic heart disease, and chronic heart failure. The endothelium is a large, diffuse 'organ' which occupies the strategic interface between the blood and the rest of the body. Functioning as a barrier, it also plays a central role in the control of vascular tone, the inflammatory response, and the formation and lysis of thrombus.

Endothelium derived relaxing factor (EDRF), identified in 1980, was shown to have as its active part the simple two atom molecule, nitric oxide (NO). In the short term, EDRF optimises cardiovascular efficiency by increasing vascular distensibility, in particular of resistance arterioles, and by amplifying the effect of locally released metabolic vasodilator substances such as adenosine. Longer term effects of EDRF are less well established but it may contribute to the remodelling of arteries, increasingly recognised as a feature of atherosclerosis. In the genesis of atheroma, endothelial dysfunction leads to increased transfer of low-density lipoprotein (LDL) particles into the intima, which provides the opportunity for free radicals to oxidise these particles, which may be followed by their binding to subintimal proteoglycans or their avid uptake by monocyte/macrophages leading to 'foam cell' formation. In addition, oxidised LDL stimulates the local transformation of vascular smooth muscle cells to their synthetic phenotype. In vitro experiments suggested that NO may be protective by scavenging free radicals, inhibiting monocyte adhesion and transfer from the vascular space, and by preventing the altered phenotypic expression of the smooth muscle cell.

In animal studies, cholesterol feeding leads to impaired endothelium-dependent vasodilatation despite an increase in NO production; this is explained by the greatly increased production of superoxide free radical stimulated within the endothelium. This can be overcome by reversing the hypercholesterolaemia or by augmenting the increased NO response by administering supplements of its precursor *L-arginine*. These experiments suggest that a local paradigm for arterial

*A list of speakers and the titles of their papers presented at this symposium is recorded in *Proceedings* Vol. 26 p. 181.

health is the balance between EDRF and free radicals. Other manoeuvres which improve endothelial function include exercise, supplements of anti-oxidant vitamins or marine oils, and pharmacological intervention with oestrogens or inhibitors of the angiotensin converting enzyme (ACE).

Clinical studies which use ultrasound to measure brachial artery dilation in response to hyperaemic flow, showed an impaired responsiveness in hypercholesterolaemia, chronic heart failure, and the syndrome of 'microvascular angina'. This may be adapted to provide a method by which the physician can assess objectively endothelial function at the bedside. The challenge that now presents itself is to establish how to reverse endothelial dysfunction in clinical practice.

MANAGEMENT OF MYOCARDIAL INFARCTION

The optimum immediate management of the patient with acute myocardial infarction (MI) includes relief of pain, transfer to a coronary care unit as soon as possible, and the administration of thrombolytic therapy, aspirin, and beta blockers as soon as practicable, the latter being beneficial whether in the community or in the hospital. Persistent problems still to be tackled are the improvement of the outcome of patients who suffer a cardiac arrest before reaching hospital; those with an initial electrocardiogram not showing ST segment elevation but yet are thought to have suffered an MI; the improvement in the outcome of thrombolytic therapy by additional adjunctive therapy or by primary angioplasty. Furthermore, in patients who present with unstable angina but with definite electrocardiographic changes or who have a history of ischaemic heart disease, the prognosis after discharge from hospital is as poor as for those with proven MI.

Strategies which may help to improve outcome from out-of-hospital cardiac arrest are the availability of ambulances with semi-automatic defibrillators and trained para-medical crews, improved resuscitation skills in the general population, and heightened awareness of the potential for a good outcome after admission to hospital—with up to 50% surviving to hospital discharge.

Support for the importance of the 'open artery' hypothesis has been provided by the accelerated tissue plasminogen activator (t-PA) regime given in the GUSTO trial, but so far adjunctive anti-thrombins, other than heparin have been associated with an increased risk of intracerebral haemorrhage. In clinical practice prescribing of both aspirin and thrombolytic agents has increased satisfactorily; in contrast the use of beta adrenoceptor blockade, either via the intravenous or oral route, has been disappointing. Primary angioplasty will never be available to the majority of patients for logistical reasons, and as yet, although initial reports are encouraging, more controlled trials are necessary.

Following the acute phase, the importance of maintaining therapy with aspirin and beta blockade is well established. Controversy remains as to whether all patients or only selected groups would benefit from an ACE inhibitor. Certainly, those patients with clinical or radiographic signs of heart failure, or with impaired left ventricular systolic function shown on echocardiography or radionuclide ventriculography, will gain the most but there is evidence to support a strategy of treating all patients at least in the short term.

The Scandinavian 'simvastatin' survival study has provided very strong evidence for lowering the total plasma cholesterol concentration below 5.2 mmol/L in all patients with ischaemic heart disease, resulting in a significant reduction in

both morbidity and mortality. However, not all therapies have been proven to be beneficial, and as yet there is no good reason to recommend the routine prescription of calcium antagonists following MI.

Amidst this therapeutic flurry it is crucial to remember the lifestyle changes which the patient should make to improve their prognosis and the most vital of these is to stop smoking. Dietary modification should be aimed at an increased consumption of oily fish, olive or rapeseed oils, fresh fruit and vegetables. Increased exercise and the participation in cardiac rehabilitation classes are also important to effect a complete recovery.

Aspects of imaging in ischaemic heart disease

Coronary angiography—Who needs it? Coronary angiography is a safe technique and is the only one presently available capable of displaying the anatomy of the coronary arteries. It has applications in 3 main groups of patients, those with angina, acute MI, or recent MI.

Cardiologists are in considerable disagreement as to which patients with stable angina should undergo angiography; in the UK very few of these patients are referred for any form of assessment. The best indication for coronary angiography in this group is the presence of symptoms refractory to medical therapy; other good indications are an early positive exercise stress test or evidence of profound asymptomatic ischaemia. These guidelines also apply to patients with unstable angina, where there is little to support a strategy of routine angiography.

If cardiogenic shock is present following MI this is an indication for immediate angiography because of the potential for improving prognosis with early revascularisation. Other groups who should be considered for investigation are those who are ineligible for thrombolytic therapy or who have continuing ischaemia. At a later stage, those with easily induced ischaemia or significantly impaired left ventricular systolic function may also benefit.

Intracoronary ultrasound

The development of catheters with a 1 mm diameter which house within them a rotating ultrasound transducer has made possible the reconstruction of tomographic images from within the coronary artery. At present its main clinical use is to define better vessels with an ambiguous appearance at conventional angiography; this enables a more accurate assessment of the results of coronary interventions and also the identification of intracoronary thrombus with more confidence than previously. The technique should also facilitate a greater understanding of the pathogenesis of atherosclerosis, the acute coronary syndromes and the mechanisms of re-stenosis.

Detecting hibernating myocardium

The suggestion of a 'hibernating' myocardium was first mooted by the observation that left ventricular ejection fraction can be improved after surgical myocardial revascularisation; the concept is of a metabolically active or viable myocardium which does not contract normally because of chronic ischaemia. This is an important clinical problem because there are patients who may derive benefit from revascularisation and who may be falsely regarded as being at increased risk from surgery because of the apparent impairment of ventricular contraction. The most reliable technique for detecting metabolically active but

functionally compromised myocardium is positron emission tomography (PET) using radio-labelled metabolic tracers, but it is only available in one or two centres in the UK. Other more widely available techniques which may provide useful information on viability include single photon emission computed tomography (SPECT) using a variety of tracers, and dobutamine stress echocardiography.

Chronic heart failure

Epidemiology. The diagnosis of heart failure should only be made in patients who demonstrate both symptoms of the condition and objective evidence of heart disease compatible with it. This automatically leads to the recognition of another important group of patients those with asymptomatic left ventricular dysfunction.

The incidence and prevalence of heart failure increases with advancing age. The diagnosis is associated with a 50% increased mortality over the next 5 years and for patients with New York Heart Association (NYHA) grade IV symptoms the one year mortality is 50%. Recent data from the WHO MONICA study in Glasgow showed that amongst the population aged 26–75 years the prevalence of heart failure was 3%, and the prevalence of asymptomatic left ventricular dysfunction was 5%. Over the age of 65 years, echocardiography detected a left ventricular ejection fraction of less than 35% in 15% of men and 13% of women. However, a number of methodological problems remain to be addressed, including the validity and reproducibility of echocardiographic techniques, strict definitions of what is abnormal left ventricular function, and improved description of subjects who are said to be asymptomatic.

The importance of chronic heart failure to the community is emphasised by economic data. The annual UK expenditure on heart failure is greater than £360 million, which represents 1.2% of the total health budget. In a single year the average UK district general hospital will have 500 inpatients and 10,000 outpatient episodes where the principal diagnosis is heart failure.

The phenomenon of diastolic heart failure, where left ventricular filling is impaired, is generating much interest. As yet no good epidemiological data exists and the concept is even more confounded by methodological difficulties with definition and detection.

Improving management

Clinical trials have contributed enormously to improving the outlook for patients with chronic heart failure but application of the results of these trials to clinical practice remains a major challenge. Principal areas of difficulty are a failure to make the diagnosis, often because of under-investigation, and failure to treat adequately, particularly failure to prescribe ACE inhibitors appropriately. Many patients with heart failure are elderly, but if there is a perception that additional investigations and appropriate drug therapy are not justified, such a position is impossible to defend. A broad spectrum of physicians manage heart failure, from community care to tertiary referral centre and this leads inevitably to different approaches. There is certainly a place for increasing the availability of specialist cardiological advice and perhaps also for specialist nurse practitioners in heart failure. A well-recognised shortage of cardiac ultrasound facilities exists in the UK and needs to be addressed. More information is required on the success of

treatments in elderly patients to develop appropriate local protocols for the management and referral of patients.

Current and future therapies

The ACE inhibitors have been the single most important recent advance in the treatment of heart failure but diuretics still remain the cornerstone of treatment. For ACE inhibitors it remains to be resolved whether the doses used in clinical trials, which tend to be higher than those used in practice, are actually essential to obtain full benefit of this therapy. SOLVD studies and others have suggested that patients prescribed aspirin and ACE inhibitors jointly may not achieve the expected benefit, possibly because of the effect of aspirin on inhibiting vasodilatory prostaglandins and kinins. The most intriguing question surrounding the ACE inhibitors is whether they are able to provide protection against subsequent myocardial infarction as suggested in the SAVE and SOLVD studies, possibly through an effect of enhancing endogenous fibrinolysis. A recent suggestion was that the addition of aldosterone antagonists to ACE inhibitors may lead to additional diuresis, and improvement in neuroendocrine response and clinical features.

Although the mechanism of benefit of digoxin for patients in sinus rhythm remains obscure, two drug withdrawal trials suggest that at least a third of patients derive clinical benefit from it. Placebo-controlled mortality trials are also under way.

Counter-intuitive evidence for two therapies has recently been provided. Although the calcium antagonists in general confer an adverse influence on prognosis in heart failure, the Praise trial with amlodipine in patients with moderate to severe symptoms suggested an improved mortality in those with non-ischaemic disease and no adverse effect in those with ischaemic heart disease; this may have particular importance for the large number of heart failure patients with active angina. In a similar patient population the vasodilating beta-adrenoceptor antagonist 'carvedilol' was shown to improve outcome signifiantly over a 6 month period, adding to the body of evidence that when beta blockade is tolerated it improves outcome in heart failure.

Newer therapies not yet shown to improve outcome in heart failure but with favourable haemodynamic and neuroendocrine effects include angiotensin antagonists, endothelin antagonists, and inhibitors of the neutral endopeptidase that breaks down atrial natriuretic peptide.

Old therapies not to be forgotten include the vasodilator hydralazine, the long-acting nitrates, and anticoagulation with warfarin to prevent embolic complications. In patients with ischaemic heart disease and significantly impaired left ventricular systolic function there is strong evidence for an improvement in prognosis with surgical revascularisation.

Palpitations

A palpitation is the abnormal awareness of the heart beat. The patient with a tachyarrhythmia may present with palpitations or with symptoms of dyspnoea, chest pain, or syncope/presyncope. Features to be elicited from the history which may aid diagnosis include preciptants, mode of onset or offset, rate and regularity, and an association with polyuria. In all cases a past history of heart disease of certain familial cardiac conditions, and a detailed drug and alcohol

history should be taken. A 12 lead electrocardiogram is mandatory and one during the bouts of tachycardia is particularly helpful. Other tests which may be helpful include ambulatory electrocardiography, treadmill exercise testing, echocardiography and electrophysiological cardiac studies.

In the management of paroxysmal atrio-ventricular nodal re-entry tachycardia which is the commonest form of regular supraventricular tachycardia, the first line of therapy is vagal manoeuvres. In the absence of evidence of ventricular pre-excitation, digoxin should be tried first, closely followed by beta adrenoceptor blockade or verapamil. If these fail, or if pre-excitation via an accessory pathway is suspected, then an electrophysiological study with the possibility of radio frequency ablation should be considered ahead of more conventional class I or class III anti-arrhythmic agents.

In the prophylactic treatment of paroxysmal atrial fibrillation, care needs to be exercised in the use of these class I and class III drugs because of their pro-arrhythmic potential. An alternative strategy in patients with sino-atrial disease is a permanent atrial pacemaker which significantly reduces the incidence of atrial fibrillation.

Broad complex tachycardias are more of a conundrum; accurate diagnosis should help to identify future prognosis and need for prophylaxis. Well documented electrocardiographic criteria can be used if a 12 lead electrocardiogram is obtained and the response to full dose adenosine is useful. The most likely diagnosis is ventricular tachycardia, particularly with a history of ischaemic heart disease. Sustained ventricular tachycardia (of >30 seconds duration) outside the setting of acute myocardial infarction carries a poor prognosis. These patients should be considered for specialist referral and assessment for significant coronary artery disease with a view to an electrophysiological study and an automatic implantable cardioverter defibrillator (AICD). If significant coronary artery disease is present then the patient should undergo surgical revascularisation. If at electrophysiological study, it is impossible to stimulate ventricular tachycardia or if an inducible tachycardia is effectively suppressed with drug therapy, that indicates a good prognosis. If effective, beta adrenoceptor blockade is the preferred drug therapy followed by drugs with class III anti-arrhythmic activity. Class I drugs have proved disappointing in clinical trials because of increased morbidity and mortality, probably attributable to their pro-arrhythmic potential. The use of the AICD in selected patients is likely to increase.

Syncope

The patient with syncope is difficult to treat and even after extensive investigation the cause will remain obscure in up to 20%. A good history is often the best guide, preferably with eye witness accounts; the patient should be encouraged to keep a diary. The story is not always straightforward, and an example of this is the profound bradycardia which often accompanies a temporal lobe seizure and which will respond much more successfully to carbamazepine than to a pacemaker. The hypersensitive carotid sinus syndrome is very common in the elderly; it may therefore be coincidental to the cause of syncope; the diagnosis is suggested by either a ventricular pause of 3 seconds or a fall in systolic blood pressure of >50 mm Hg on massage of either carotid sinus. The malignant vasovagal syndrome is a common cause of syncope in those with no other evidence of heart disease and is caused by abnormal activation of the Bezold–

Jarisch reflex causing bradycardia and vasodilatation. As compared with true cardiac syncope, patients take a longer period to recover from episodes because of the associated autonomic upset. Symptoms are often not abolished by a pacemaker but paradoxically are improved by beta adrenoceptor blockade, disopyramide, or theophylline. The diagnosis may be made using head-up tilt testing which provokes either bradycardia, hypotension or both.

The vast majority of ambulatory electrocardiograms performed in the investigation of syncope do not show any significant arrhythmia. However, if a patient has evidence of structural or ischaemic heart disease then the probability of a significant arrhythmia as the cause of syncope is over 75%, and if an arrhythmia is not detected by ambulatory monitoring or exercise stress testing, a formal electophysiological study should be considered.

A permanent pacemaker should never be implanted on empirical grounds alone—it may take weeks of monitoring to discover ventricular tachycardia as the cause of a patient's syncope. The aims of a permanent pacemaker are to protect from the consequences of an arrhythmia, usually a bradycardia, from sudden death or accidental injury and to achieve optimum exercise tolerance. Modern pacemakers may be single or dual chamber, and may include rate-responsiveness to improve exercise capacity. The guiding principles are that the ventricle should be paced if there is actual or threatened atrio-ventricular block; the atrium should be paced unless there is atrial tachyarrhythmia or atria paralysis; rate-responsiveness is desirable if the chronotropic competence of the sinus node is in doubt. The most physiological system is a dual chamber rate-responsive pacemaker which preserves atrio-ventricular synchrony and a chronotropic response. The main disadvantage of the simple single chamber ventricular pacing system is loss of the contribution of atrial filling during ventricular diastole, and the possibility of worsening the situation by retrograde ventriculo-atrial conduction leading to the 'pacemaker syndrome'.

Structural heart disease

Atrial septal defect in adults. The incidence of patent foramen ovale (PFO) decreases with age, but in young adults probe patency may be present in up to 25%. The possibility of paradoxical embolism, particularly in young stroke victims, has led to studies showing echocardiographic evidence of PFO in over half such patients. Patients with atrial septal defects are at greater risk of atrial arrhythmias, pulmonary hypertension, right ventricular impairment, and Eisenmenger's syndrome. Mitral valve prolapse is associated in 20% of patients and left ventricular dysfunction in some.

Developments in imaging such as transoesophageal echocardiography and reconstructional 3-dimensional cardiac ultrasound have led to improved detection without the need to resort to cardiac catheterisation. Interventional cardiologists have developed catheter techniques for closing defects of a limited size, which are currently under evaluation. The benefits of closure of a PFO identified in adulthood are controversial, although most cardiologists would advocate repair if there is any evidence of symptoms, pulmonary hypertension or ventricular compromise. The natural history of an atrial septal defect from early studies is a 90% mortality by 60 years of age.

Valvular heart disease

Enhancing quality and duration of life in valvular heart disease requires careful assessment of the patient to time any intervention in such a way that preservation of valvular and myocardial performance is maximised.

Aortic stenosis is a particularly difficult condition because of the non-linear progression in valve dysfunction, which makes single assessments of its severity unreliable predictors of prognosis. Once left ventricular compromise sets in then prognosis is poor. The best indications for surgery are ventricular dysfunction or the presence of symptoms. Too great an importance should not be placed on objective measurements of transvalvular gradient, whilst remembering the incidence of sudden cardiac death in severe stenosis. Elderly patients with aortic stenosis are a difficult group in whom to make the diagnosis and to manage. They predominantly have calcific degeneration of a valve with 3 cusps and the presence of a characteristic murmur in this group is of poor positive predictive value. The limited availability of cardiac ultrasound is unfortunate because these patients require an accurate assessment of the severity of stenosis by a thorough and comprehensive echocardiographic interrogation rather than a cursory measurement of Doppler flows. For elderly patients who are symptomatic the 3 year survival is 25%, whilst the operative mortality for valve replacement is about 15%. Stratification of risk pre-operatively is improved by taking account of the patient's functional status, the degree of left ventricular impairment and the coexistence of significant coronary artery disease, cerebrovascular disease, impaired renal function, or airways disease. Although many elderly patients with symptoms might benefit from aortic valve replacement, in most countries there are inadequate resources to provide for this. An alternative is percutaneous aortic balloon valvuloplasty, but this carries a higher mortality than surgery; an improvement in symptoms is seen in less than one quarter of patients.

Valvular heart disease during pregnancy may be difficult to manage, as may establishing the diagnosis in the first instance. Aortic stenosis is predominantly due to a congenital bicuspid valve and usually can be managed by bed rest and control of blood pressure. If symptoms develop then balloon valvotomy or urgent caesarean section followed by valve replacement should be considered. The most common rheumatic valvular lesion in pregnancy is mitral stenosis; the most important part of its management is ensuring adequate control of heart rate with beta blockade and the use of only small doses of diuretic. If significant deterioration occurs, balloon valvuloplasty or closed surgical valvotomy can be considered. In the woman with severe mitral stenosis who wishes to become pregnant a mechanical prosthesis is the preferred option, despite the need for careful anticoagulation during pregnancy, because of the poor short and long term performance of mitral prostheses. Regurgitant valvular lesions are usually well tolerated in pregnancy with small doses of diuretic, digoxin and vasodilator therapy with hydralazine.

Anticoagulation with warfarin—some problems and pitfalls

For patients with rheumatic mitral valve disease and atrial fibrillation the benefit of chronic anticoagulation is beyond dispute. Similarly, for the recipients of a mechanical valve prosthesis, warfarin is essential, though the more modern tilting disc or bileaflet valves do not require the same intensity of anticoagulation as the ball and cage variety. Aortic prostheses in particular may not require warfarin but patients with bioprosthetic valves will require anticoagulation in the presence of co-existing conditions such as atrial fibrillation, left atrial thrombus or impaired

left ventricular function. If a patient should suffer an embolic event then adding aspirin or increasing the target international normalised ratio (INR) range are to be considered.

Anticoagulation in patients with non-rheumatic atrial fibrillation is now of interest. This is prevalent in about 5% of the population over the age of 70 years with an annual risk of stroke of about 5%. Clinical trials suggest that this risk can be reduced to 1·5% with warfarin but this is associated with an excess risk of haemorrhage. The dilemma is to translate the information obtained in clinical trials to an individual who may be different to the study population, who has an inherent risk of haemorrhage, and whose ability to comply with therapy or with accurate monitoring of INR may be far from perfect. An alternative is to use aspirin, less effective at preventing embolic events but with a far lower risk of major haemorrhage. In general, patients with a greater risk of stroke, including those with a previous stroke, rheumatic heart disease, hypertension, heart failure and the elderly with lone atrial fibrillation, stand to benefit most from carefully controlled, long term anticoagulation.

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PRIORITIES IN HEALTH CARE OF ELDERLY PEOPLE: CONFLICTING IMAGES, CONFLICT OF INTEREST?★

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When discussing priorities in health policies for the elderly it is important to assess to what degree these policies are based on and shaped by popular misconceptions or fashionable ideas and ideologies. In fact, it may be argued that such assessment should be part of any kind of policy making. In this paper we address the issue of policy priorities in health care of elderly people. We observe that there has been a fundamental shift from a 'positive' to a 'negative' image of the elderly. This shift has been influential in recent social and health policies.

CHANGING IMAGES

In our view, there are four competing images about the elderly. The first is the traditional 'biblical image'. This image depicts the elderly as keepers of moral values; as heads of extended families, and as a source of knowledge and experience. This image is also reflected in the fifth Commandment: honour thy father and mother. Another biblical reference is Moses' Council of the seventy Elderly.

The second one is the 'policy image'. In this, the elderly are the object of government welfare and social security policies. The dominant view here is the equating of the elderly to poor and dependent persons.

Thirdly, there is the 'new modern image'. This depicts the elderly as a large group of healthy, self-assured and spending citizens. This image is reflected in the new publications for the elderly, with advertisements for cruise ship travelling, fashion, private home care and other services.

And finally, we see the 'new negative image'. In this, the elderly are seen as a group of self-centred, spending and, above all, costly segment of the population. They are perceived as the 'greedy geezers'.[1] This image has also entered our thinking about health care policies.

The last few decades have witnessed some remarkable shifts in societal ideas and ideologies regarding the elderly. These have also brought importants shifts in images. The traditional biblical one has virtually disappeared and been replaced partly by the policy image, partly by the new modern image. Recently, there has been a further shift towards the new negative image.[2,3] These shifts have led to conflicting interests between generations. The conflicts may be ethical, economic or political, perceived or not perceived, and within or outside health care. Some of the conflicts outside health care are particularly relevant as they may affect the shaping of health care policies. A few examples of such conflicts are as follows.

Almost all member countries of the Organisation for Economic Cooperation

★Based on a Sydney Watson Smith Lecture, presented by Dr Els Borst-Eilers at the Symposium on *Ethical and Economic Conflicts in a Changing Health Service* held in the College on 1 February 1996.

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