LETTERS TO THE EDITOR

Scope
Heart welcomes letters commenting on papers published in the journal in the previous six months. Topics not related to papers published earlier in the journal may be introduced as a letter: letters reporting original data may be sent for peer review.

Presentation
Letters should be:
- initially submitted by fax +44 171 388 0323 or e-mail 100536.2733@compuserve.com (where practicable). Always follow this up by posting the paper copy to us
- not more than 600 words and six references in length
- typed in double spacing (fax copies and paper copy only)
- signed by all authors.

They may contain short tables or a small figure.

Is aspirin safe in heart failure? More data

SIR,—We recently reviewed the evidence for an interaction between aspirin and ACE inhibitors on mortality in heart failure.[1] At that time the data from SOLVD (studies of left ventricular dysfunction), the most alarming evidence of an interaction, had been presented but not published. The data have now been published in abstract form (table).[2] The authors suggest that the data support a beneficial effect of aspirin in heart failure, though the administration of aspirin was not randomised. The arguments suggesting the reverse were presented by us in our review.[1]

Careful scrutiny of the SOLVD data suggest that the lowest mortality in both the treatment and prevention arms of SOLVD was among patients taking placebo and aspirin (B1 and D1 in the table). Assertion that aspirin is beneficial, based on these data, would logically lead one to withdraw the ACE inhibitor, at least if it were being given to reduce mortality rather than to improve symptoms. This would be flying in the face of the data from properly constructed randomised controlled trials. If one accepts that enalapril is effective, based on a properly randomised comparison, then it is evident that the addition of aspirin is of little or no benefit in patients with heart failure (comparison of C1 and C2 in table). However, the possible loss of benefit with aspirin (comparison of C1 with D1; P = 0·002) remains worrying. About 12% of patients in the SOLVD prevention trial and 16% in the SOLVD treatment trial were taking warfarin. The higher percentage use in the treatment arm reflects the higher proportion of atrial fibrillation and the likely association between severity of heart failure and use of warfarin. Patients taking warfarin are less likely to receive aspirin. Thus the higher mortality in the aspirin non-users may reflect the fact that they were a sicker population.

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1 Cleland JGF, Bulpitt CJ, Falk RH, Findlay IN, Oakley CM, Murray G, *et al.* Is aspirin safe for patients with heart failure? *Br Heart J* 1995;74:215–9.
2 Al-Khadra AS, Salem DN, Rand WM, Udelson JE, Smith JJ, Konstam MA. Effect of anti-platelet agents on survival in patients with left ventricular systolic dysfunction (abstract). *Circulation* 1995;92:I-665–6.

Interaction of enalapril and antiplatelet agents on mortality (%) in SOLVD

	Prevention		*Treatment*	
	Enalapril	*Placebo*	*Enalapril*	*Placebo*
APA+	(A1) 12·7%	(B1) 12·5%	(C1) 34·8%	(D1) 30·7%
APA–	(A2) 17·4%	(B2) 19·3%	(C2) 35·2%	(D2) 44·3%

APA, antiplatelet agent.

New directions in anticoagulant and antiplatelet treatment

SIR,—Simoons and Deckers comprehensively surveyed the therapeutic potential of inhibiting platelet activation and aggregation (*Br Heart J* 1995;74:337–40). They did not consider the importance of passivation (inactivation) of platelets once haemostasis or limited thrombosis has occurred. Haemostasis requires platelet activation, adhesion, and aggregation to plug the damaged vessel. This process is often assisted by high shear and involves von Willebrand factor. Once haemostasis is achieved it is self-evident that the intensely attractive deposited platelets must be inactivated; otherwise platelet deposition on the haemostatic plug will continue and lead to progressive platelet deposition, namely a platelet thrombus. Thus platelet inactivation or passivation[1–3] may be clinically as important as the inhibition of activation. The mechanism of inactivation is not fully understood, though in an in vitro system aspirin potentiated the passivation of originally highly attractive platelets.[4] In an artificial system some normal people show "rebleeding", indicating passivation of an haemostatic plug. Others show reproducible and persistent activation of the platelets. It remains to be shown if there is an increased risk of thrombosis in the latter group. This approach deserves further study.[5]

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1 Kinlough-Rathbone RL, Packam MA, Mustard JF. Vessel injury, platelet adherence and platelet survival. *Arteriosclerosis* 1983;3:529–46.
2 Heynen HFG, Molero ML, de Groot PG, Nieuwenhuis HK, Sixma JJ. Absence of ligands bound to glycoprotein IIb/IIIa on the exposed surface of a thrombus may limit thrombus growth in flowing blood. *J Clin Invest* 1994;94:1098–112.
3 O'Brien JR. Platelet activation at high and low shear is followed by inactivation: the clinical relevance. *Platelets* 1995;6:242–3.
4 O'Brien JR, Etherington MD. Another antithrombotic action of aspirin. *Thromb Res* 1995 (in press).
5 Reilly JT, Toh CH. Shear stress and platelet function: a therapeutic challenge? *Lancet* 1995;346:196–7.

Atrial thrombi occurring during sinus rhythm in cardiac amyloidosis: evidence for atrial electromechanical dissociation

SIR,—Dubrey and colleagues reported on a series of patients with cardiac amyloidosis, atrial thrombi, and evidence of atrial electromechanical dissociation. They suggested that systemic anticoagulation may be indicated when atrial systolic function is impaired.[1] Plehn *et al* described a similar case presenting with systemic embolisation and again recommended anticoagulation for atrial failure in amyloidosis.[2]

It is perhaps worth noting that atrial dysfunction may be the first manifestation of previously unrecognised amyloid heart disease and that atrial systolic failure can precede clinically detectable ventricular involvement.

We have reported a case of apparent isolated atrial cardiomyopathy complicated by systemic embolisation.[3,4] Diagnostic evaluation at presentation showed dilated, akinetic atria with normal ventricular function. Endomyocardial, rectal, and skeletal muscle biopsies performed at this time did not show any histological evidence of amyloidosis. The patient progressed over several years to ventricular dysfunction and died in congestive heart failure. Necropsy was not performed but ventricular biopsies had been obtained some months previously during an elective operation to replace the tricuspid valve. These showed systemic amyloidosis.

Cardiac amyloidosis should be considered in the differential diagnosis of patients presenting with atrial systolic failure: systemic anticoagulation seems to be indicated in these cases.

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1 Dubrey S, Pollak A, Skinner M, Falk RH. Atrial thrombi occurring during sinus rhythm in cardiac amyloidosis: evidence for atrial electromechanical dissociation. *Br Heart J* 1995;74:541–4.
2 Plehn JF, Southworth J, Cornwell GGI. Atrial systolic failure in primary amyloidosis. *N Engl J Med* 1992;327:1570–3.
3 Stables RH, Bailey C, Ormerod OJM. Idiopathic familial atrial cardiomyopathy with diffuse conduction block. *Q J Med* 1989;71:325–32.
4 Stables RH, Ormerod OJM. Atrial systolic failure in cardiac amyloidosis. *Q J Med* 1993;86:465–6.