

vascular disease, risk factors, interventions, and prognosis, fulfilling criteria for a suitable non-invasive assessment of endothelial function. Furthermore, several groups have targeted this molecule as a means of intervening in the thrombotic process.¹⁶ The next five years will tell if this approach is successful.

The non-invasive approach outlined by Mullen and colleagues has provided invaluable opportunities to dissect the pharmacology of the endothelium. However, by its very nature such an approach is unlikely to provide epidemiological data or even data to compare groups with large numbers of subjects. We submit that plasma markers such as von Willebrand factor and soluble thrombomodulin are likely candidates for providing data of this nature.

ANDREW BLANN
GREGORY LIP

*Haemostasis, Thrombosis and Vascular Biology Unit,
University Department of Medicine,
The City Hospital, Dudley Road,
Birmingham B18 7QH, UK*

- Mullen MJ, Thorne SA, Deanfield JE, Jones CJH. Non-invasive assessment of endothelial function. *Heart* 1997;77:297-8.
- Lip GYH, Blann AD. Von Willebrand factor and its relevance to cardiovascular disease. *Br Heart J* 1995;74:580-3.
- Blann AD, Taberner DA. A reliable marker of endothelial cell dysfunction: does it exist? *Br J Haematol* 1995;90:244-8.
- Badimon L, Badimon JJ, Chesebro JH, Fuster V. von Willebrand factor and cardiovascular disease. *Thromb Haemostas* 1993;70:111-18.
- Greaves M, Pickering C, Knight G, Boulton ALM, Ball J, Ward JD, et al. Changes in the factor VIII complex in diabetic ketoacidosis: evidence of endothelial cell damage? *Diabetologia* 1987;30:160-5.
- Van den Berg M, Boers GHJ, Franken DG, Blom HJ, van Kamp GJ, Jakobs C, et al. Hyperhomocysteinaemia and endothelial dysfunction in young patients with peripheral arterial occlusive disease. *Eur J Clin Invest* 1995;25:176-81.
- Thompson SG, Kienast J, Pyke SDM, Haverkate F. Hemostatic factors and the risk of myocardial infarction or sudden death in patients with angina pectoris. *N Engl J Med* 1995;332:635-41.
- Blann AD, Miller JP, McCollum CN. Von Willebrand factor and soluble E-selectin in the prediction of cardiovascular disease progression in hyperlipidaemia. *Atherosclerosis* 1997;132:151-6.
- Boffa MC. Considering cellular thrombomodulin distribution and its modulating factors

- can facilitate the use of plasma thrombomodulin as a reliable endothelial marker. *Haemostasis* 1996;26(Suppl 4):233-43.
- Blann AD, Amiral J, McCollum CN. Circulating endothelial cell/leucocyte adhesion molecules in ischaemic heart disease. *Br J Haematol* 1996;95:263-5.
 - Seigneur M, Dufourcq P, Gin H, Delafaye C, Amiral J, Pruvost A, Boisseau MR. Plasma thrombomodulin levels increase with the severity of diabetic retinopathy. *Blood Coag Fibrinolys* 1994;5:845-6.
 - Blann AD, Amiral J, McCollum CN. Prognostic value of increased soluble thrombomodulin and increased E-selectin in ischaemic heart disease. *Eur J Haem.* [In press.]
 - Gearing AJH, Newman W. Circulating adhesion molecules in disease. *Immunol Today* 1993;14:506-12.
 - Blann AD, Seigneur M, Steiner M, Boisseau MR, McCollum CN. Circulating endothelial cell markers in peripheral vascular disease: relationship to the location and extent of atherosclerotic disease. *Eur J Clin Invest.* [In press.]
 - Belch JFF, Shaw JW, Kirk G, McLaren M, Robb R, Maple C, Morse P. The white blood cell adhesion molecule E-selectin predicts restenosis in patients with intermittent claudication undergoing percutaneous transluminal angioplasty. *Circulation* 1997;95:2027-31.
 - Ruggeri ZM. Inhibition of platelet vessel wall interaction. Platelet receptors, monoclonal antibodies, and synthetic peptides. *Circulation* 1990;81(Suppl 1):I35-9.

This letter was shown to the authors, who reply as follows:

We read with interest the letter from Drs Blann and Lip regarding the advantages and limitations of plasma markers of endothelial cell function. We share their interest in this area of research and its potential clinical application. We feel, however, that evaluation of nitric oxide mediated arterial physiology in large conduit arteries using the non-invasive techniques described¹ may provide insight into the pathophysiology of vascular disease, be an early marker of endothelial injury, and a means of evaluating interventions early in the natural history of atherogenesis.

The value of these measures in predicting disease development and outcome is not known and is central to current research efforts. Our published data, however, indicate that this technique can be used to study

endothelial function in large groups of subjects from early in childhood, to provide epidemiological data, compare groups of subjects with risk factors, and demonstrate beneficial response to interventions.²⁻⁵

M J MULLEN
M E DEANFIELD
*Great Ormond Street Hospital for
Children NHS Trust,
Great Ormond Street,
London WC1N 3JH, UK*

- Celermajer DS, Sorensen KE, Gooch VM, Spiegelhalter DJ, Miller OI, Sullivan ID, et al. Non-invasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis. *Lancet* 1992;340:1111-15.
- Leeson CPM, Whincup PH, Cook DG, Donald AE, Papacosta O, Lucas A, et al. Flow mediated dilatation in 9-11 year old children: the influence of intrauterine and childhood factors. *Circulation.* [In press.]
- Celermajer DS, Sorensen KE, Bull C, Robinson J, Deanfield JE. Endothelium-dependent dilation in the systemic arteries of asymptomatic subjects relates to coronary risk factors and their interaction. *J Am Coll Cardiol* 1994;24:1468-74.
- Sorensen KE, Celermajer DS, Georgakopoulos D, Hatcher G, Betteridge DJ, Deanfield JE. Impairment of endothelium-dependent dilation is an early event in children with familial hypercholesterolemia and is related to the lipoprotein (a) level. *J Clin Invest* 1994;93:50-5.
- Clarkson P, Adams MR, Powe AJ, Donald AE, McCredie R, Robinson J, et al. Oral L-arginine improves endothelium-dependent dilation in hypercholesterolemic young adults. *J Clin Invest* 1996;97:1989-94.

CORRECTION

Pregnancy and congenital heart disease
C M Oakley Heart 1997;78:12-14.

The first sentence of the section **Atrial septal defects** should have read:

"The only frailty of patients with unrepaired atrial septal defects is intolerance of blood loss that can force left to right shunting, to the sudden detriment of left ventricular and coronary flow."

And not as published. The error is regretted.