diabetes has a marked sensitivity to sulphonylureas, to the extent that patients can have improved diabetes control with a switch from insulin treatment to sulphonylurea therapy if the mutation is identified. Patients with MODY due to heterozygous glucokinase mutations often do not require insulin treatment at all and may be able to come off treatment altogether.

Permanent neonatal diabetes is a non-autoimmune condition that usually presents before the age of 18 months. It can be caused by monogenic mutations in the KCNJ11 and ABCC8 genes that encode constituents of the β-cell KATP channel. Detection of these mutations allows clinicians to offer treatment with sulphonylureas, which act directly on the KATP channel in an attempt to overcome the clinical effects of the mutation. This allows a more readily administered oral treatment with improved disease control in neonates.[2,3]

The specialty of diabetes has had the good fortune to be able to provide concrete examples of how detection of genetic mutations might influence drug choice in small subgroups of patients; it must be hoped that the application of pharmacogenetics will become more widespread within all areas of medicine to allow improved patient care in the near future.

AUGUSTIN BROOKS
Specialist trainee (ST5)
diabetes and endocrinology
Royal Devon and Exeter Hospital

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Should thrombolysis have a greater role in the management of pulmonary embolism?

Editor – We read with interest the review article by Jenkins *et al* exploring the question of thrombolysis in acute pulmonary embolism, particularly considering the subgroup of patients with right ventricular strain but no haemodynamic compromise (*Clin Med* October 2009 pp 431–5).

They acknowledge the technical problems associated in some patients in obtaining good quality transthoracic echocardiographic images, however this review article, the studies upon which it is based[1–6] and the British Thoracic Society[7] guidelines on pulmonary embolism management do not discuss some of the major limitations of transthoracic echocardiography in the evaluation of right ventricular size and function and estimations of pulmonary artery pressure. This may be part of the reason why the studies investigating thrombolysis in this subgroup of patients have been inconclusive.

Anatomically, the right ventricle has a very complex geometrical shape.[8] Physiologically, its mechanism of contraction is also complicated and not fully understood, with longitudinal and circumferential motion occurring. This makes assessment of its size and function using two-dimensional (2D) and M mode echocardiography less reliable than that of the left ventricle. In our experience, cases of severe right ventricular dilation or systolic functional impairment are usually reliably identified on 2D and M mode imaging, but more borderline cases are more difficult to assess accurately. However, one author had experience last year of a case of an acute ventricular septal defect (VSD) opening following myocardial infarction. Echocardiography allowed excellent images of the right ventricle to be obtained in multiple views and did not suggest any right ventricular dilatation. The patient was severely haemodynamically compromised and underwent emergency surgery on the same day during which a massively dilated right ventricle was found, so large that the surgeon was unable to close the chest following the surgery. We suspect that this was missed by the echocardiogram because 2D views were probably obtained that were off axis to the 3D direction in which the ventricle had dilated.

Measurements of the pulmonary artery pressure can also be misleading if the echocardiographer is not vigilant in their technique. The most common way to evaluate this variable utilises the presence of a tricuspid regurgitation (TR) jet found in over 90% of the population.[9] If performed correctly, the maximum velocity of this jet added to the right atrial pressure (calculated from the size and amount of collapse during inspiration of the inferior vena cava on echocardiography) gives a reliable estimate of the pulmonary artery pressure. The maximum velocity is calculated by placing a line of continuous wave Doppler through the TR jet. The equation used to calculate the maximal velocity of flow assumes that the line of continuous wave Doppler is placed by the echocardiographer absolutely parallel to the flow of the jet. Any misalignment will result in an underestimation of the pulmonary artery pressure. We were interested to find that in one study discussed in Jenkins *et al*'s review, the maximum TR velocity was assessed using the subcostal echocardiographic window.[1] In many of the patients that we have assessed over many thousands of studies, it is uncommon for this view to allow parallel intercept with the TR jet, and hence it is likely that this study underestimated this variable.

Most of the studies discussed in the review regarding the role of echocardiography in right heart assessment were performed many years ago and used a variety of differing techniques to assess this structure, making direct comparisons difficult. Echocardiographic equipment has improved substantially since many of these studies were published, leading to much improved image quality. There are also numerous more modalities available that allow the right ventricle to be more accurately assessed.[10] These include 3D echocardiography, tissue Doppler and strain imaging. However, these modalities will not be routinely used in most non-research centres as yet.

In summary, we would ask general physicians to be aware of the limitations of

right ventricular and pulmonary artery pressure assessment by echocardiography. These limitations may partially explain the conflicting data regarding thrombolysis in su-bmassive pulmonary embolism.

DANIEL M SADO
Specialist registrar in cardiology
KIM GREAVES
Consultant in cardiology and honorary senior lecturer
Department of Cardiology, Poole Hospital NHS Foundation Trust, Poole

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In response

We welcome these comments. Our view is that the role of thrombolysis in sub-massive pulmonary embolism (PE) requires definitive investigation – testing its use against the outcomes of mortality, risk of recurrent PE and benefit on long-term pulmonary and pulmonary vascular function. Assessment of right heart strain seems intuitively to be the arbiter for definition of sub-massive PE and modern echocardiographic techniques are best placed to quantify this in the acute medical setting.

PAUL JENKINS
Professor of medicine
University of Western Australia and Joondalup Health Campus
PETER JENKINS
CT1, Whittington Hospital, London

In the December 2009 issue of *Clinical Medicine*, there was an error in Brady and Main's letter, 'Aciclovir neurotoxicity is an important side effect of therapy in patients with renal impairment', page 630.

The following paragraph:

'They describe aciclovir therapy as essentially safe, highlighting the potential risk of crystal nephropathy. This potentially life threatening complication is well recognised in nephrology, but not widely publicised, as it is often only evident in the presence of renal impairment. Recognition has implications for all physicians given the prevalence of chronic kidney disease and acute kidney injury. Such concerns might explain five patients not receiving full dose aciclovir in their study.'

should have read:

'They describe aciclovir therapy as essentially safe, highlighting the potential risk of crystal nephropathy. However, this is a condition most nephrologists will never see, as opposed to aciclovir induced neurotoxicity. This potentially life threatening complication is well recognised in nephrology, but not widely publicised, as it is often only evident in the presence of renal impairment. Recognition has implications for all physicians given the prevalence of chronic kidney disease and acute kidney injury. Such concerns might explain five patients not receiving full dose aciclovir in their study.'