Diagnosis and management of maturity onset diabetes of the young (MODY)

Gaya Thanabalasingham,1,2 Katharine R Owen1,2

Maturity onset diabetes of the young (MODY) comprises a heterogeneous group of monogenic disorders characterised by β cell dysfunction. It is estimated to be the underlying cause of diabetes in 1-2% of patients diagnosed with diabetes, but prevalence estimates will not be accurate until large population screening studies are performed.1 It is important to distinguish MODY from type 1 and type 2 diabetes because optimal treatments are different. Furthermore, first degree relatives have a 50% probability of inheriting the same mutation, which confers a greater than 95% lifetime risk of developing diabetes.2 Distinguishing people who have rare forms of diabetes such as MODY from those with type 1 or type 2 diabetes is a diagnostic challenge because clinical features are similar. In this review we discuss when the general physician might suspect MODY and how to identify which patients with diabetes should be offered genetic testing. We focus on the recognition of the common forms of MODY in people diagnosed with diabetes in the age range 10-45 years, drawing mainly on evidence from small trials and cross sectional and observational studies. Other causes of monogenic diabetes, including neonatal diabetes, are beyond the scope of this review.

What is MODY and who gets it?

Case reports in the 1970s described a familial form of non-insulin dependent diabetes that presented before the age of 25 years.3 The molecular genetic basis of MODY was recognised in the 1990s,4,5 and diagnostic genetic testing for common subtypes followed rapidly. Mutations in the genes encoding the enzyme glucokinase (GCK) and the nuclear transcription factors hepatocyte nuclear factor 1α (HNF1α) and hepatocyte nuclear factor 4α (HNF4α) are the most common causes of MODY, and in the United Kingdom they represent 32%, 52%, and 10% of MODY cases, respectively.6 The prevalence of MODY subtypes differs across countries: GCK mutations are more commonly diagnosed in countries where glucose testing of asymptomatic people is routine (such as France, Spain, and Italy), whereas in countries where random blood glucose tests are seldom done HNF1α-MODY is more commonly diagnosed.7,8,9,10

To date, mutations in 10 different genes have been associated with a MODY phenotype (table 1).11,12 On the basis of referrals to the UK diagnostic testing centre, the minimum UK population prevalence of all MODY subtypes is estimated as 68-108 cases per million.7 This figure is comparable with population based cross sectional studies in Oxfordshire, UK, and Nord-Trondelag, Norway, which estimated minimum prevalences for HNF1A-MODY of 84 and 63 cases per million respectively.13,14,15 Although cases of MODY have been described in most ethnic groups, only 0.5% of people referred for MODY testing in the UK were of Asian origin.16 This low referral rate may reflect poor uptake of genetic testing by Asian patients, or that Asian patients, even with clinical features suggestive of MODY, are more readily assumed to have type 2 diabetes.

How does MODY present clinically?

Patients with MODY typically display one or more of the following features: a strong family history of diabetes (of any type), onset of diabetes in the second to fifth decade, insulin independence (although insulin may be needed for optimal control), absence of features of insulin resistance, and absence of β cell autoimmunity. The specific genetic subtype of MODY determines the clinical presentation, prognosis, and treatment response.
The recognition of MODY is challenging because of its relatively low prevalence and the overlap in presentation and clinical features between patients with MODY and those with other subtypes of diabetes. Table 2 summarises the similarities and differences between common MODY subtypes and type 1 and type 2 diabetes. The box lists the features to consider when assessing the cause of diabetes.

Mutations within the GCK gene
Patients with GCK-MODY have a raised threshold for the initiation of glucose stimulated insulin secretion. This leads to lifelong, mild, stable hyperglycaemia, with fasting plasma glucose values of 5.5-8 mmol/L. A large observational study showed that patients with GCK-MODY have a low rise in blood sugar after a glucose challenge, and that their glycaemic haemoglobin (HbA1c) is normally below 8%. Patients are generally asymptomatic, and hyperglycaemia is commonly discovered during routine screening—for example, in pregnancy. Thus GCK-MODY can be diagnosed at any age. Evidence from observational studies (including a study of 95 people with GCK-MODY who were exposed to hyperglycaemia for an average of 50 years) suggests that these patients do not develop diabetes related microvascular complications. No large studies have assessed long term macrovascular outcomes, but patients with GCK mutations seem to have normal cardiovascular risk profiles.

Mutations within HNF1A and HNF4A genes
Patients with HNF1A-MODY and HNF4A-MODY are typically normoglycaemic in childhood but have a progressive defect of insulin secretion, with diabetes usually diagnosed in the second to fifth decades. Treatment requirements usually increase over their lifetime, and they are vulnerable to the microvascular and macrovascular complications associated with diabetes. Tight glycaemic control and management of other cardiovascular risk factors are essential aspects of these patients’ long term care.

How is the condition diagnosed?
Diagnostic genetic testing for MODY, by direct sequencing of the genes, is widely available. The sequencing technique used in the UK diagnostic testing centre has greater than 99% sensitivity to detect a heterozygous base substitution. Genetic testing should be performed after informed consent, with the implications of both a positive or negative result discussed with the patient. Predictive and diagnostic genetic testing for MODY was welcome to most adults, but less satisfactory to adolescents, despite previous counselling. General practitioners may prefer to refer patients to the local diabetes or clinical genetics team to discuss MODY genetic testing rather than to organise testing themselves. In general, we recommend genetic counselling before predictive genetic testing (when the person does not have diabetes), especially for children. Offer diagnostic genetic testing to relatives of patients with MODY who have diabetes. Do not assume that all family members will have MODY, because different types of diabetes can occur within the same family.

Why is diagnosis often delayed?
Currently, testing for MODY is largely opportunistic. The UK diagnostic testing centre recently reported an average delay of 13 years from diagnosis of diabetes to establishing a definitive genetic diagnosis in patients with MODY, and it reported considerable variation in referral rates for MODY testing across the UK. It also estimated that more than 80% of MODY cases in the UK are currently undetected/low

<table>
<thead>
<tr>
<th>Gene</th>
<th>Relative prevalence</th>
<th>Other clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>HNF1A</td>
<td>Common (30-70% of MODY)</td>
<td>Low renal threshold for glycosuria; marked sensitivity to sulfonylureas</td>
</tr>
<tr>
<td>HNF4A</td>
<td>5-10% of MODY</td>
<td>Normal renal threshold; marked sensitivity to sulfonylureas; neonatal hyperinsulinaemia and hyperglycaemia with associated macrosomia; low concentrations of high density lipoprotein/high concentrations of low density lipoprotein</td>
</tr>
<tr>
<td>GCK</td>
<td>Common (30-70% of MODY)</td>
<td>Mild fasting hyperglycaemia throughout life; often detected during screening; small incremental glucose rise after carbohydrate load</td>
</tr>
<tr>
<td>HNF1B</td>
<td>5-10% of MODY</td>
<td>Malformations of the genitourinary tract (especially renal cysts and other renal developmental abnormalities); pancreatic atrophy; exocrine insufficient</td>
</tr>
<tr>
<td>IPF1</td>
<td>Very rare</td>
<td>Pancreatic agenesis in homozygotes/compound heterozygotes</td>
</tr>
<tr>
<td>INS</td>
<td>Rare; &lt;1% of MODY</td>
<td>More usually associated with neonatal diabetes</td>
</tr>
<tr>
<td>CEL</td>
<td>Very rare: fewer than 5 families reported</td>
<td>Exocrine pancreatic dysfunction</td>
</tr>
<tr>
<td>NEUROD1</td>
<td>Very rare: fewer than 5 families reported</td>
<td></td>
</tr>
<tr>
<td>KCNJ11</td>
<td>Rare; &lt;1% of MODY</td>
<td>More usually associated with neonatal diabetes; sulfonylurea responsive</td>
</tr>
<tr>
<td>ABCG8</td>
<td>Rare; &lt;1% of MODY</td>
<td>More usually associated with neonatal diabetes; sulfonylurea responsive</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gene</th>
<th>Relative prevalence</th>
<th>Other clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>HNF1A</td>
<td>Common (30-70% of MODY)</td>
<td>Low renal threshold for glycosuria; marked sensitivity to sulfonylureas</td>
</tr>
<tr>
<td>HNF4A</td>
<td>5-10% of MODY</td>
<td>Normal renal threshold; marked sensitivity to sulfonylureas; neonatal hyperinsulinaemia and hyperglycaemia with associated macrosomia; low concentrations of high density lipoprotein/high concentrations of low density lipoprotein</td>
</tr>
<tr>
<td>GCK</td>
<td>Common (30-70% of MODY)</td>
<td>Mild fasting hyperglycaemia throughout life; often detected during screening; small incremental glucose rise after carbohydrate load</td>
</tr>
<tr>
<td>HNF1B</td>
<td>5-10% of MODY</td>
<td>Malformations of the genitourinary tract (especially renal cysts and other renal developmental abnormalities); pancreatic atrophy; exocrine insufficient</td>
</tr>
<tr>
<td>IPF1</td>
<td>Very rare</td>
<td>Pancreatic agenesis in homozygotes/compound heterozygotes</td>
</tr>
<tr>
<td>INS</td>
<td>Rare; &lt;1% of MODY</td>
<td>More usually associated with neonatal diabetes</td>
</tr>
<tr>
<td>CEL</td>
<td>Very rare: fewer than 5 families reported</td>
<td>Exocrine pancreatic dysfunction</td>
</tr>
<tr>
<td>NEUROD1</td>
<td>Very rare: fewer than 5 families reported</td>
<td></td>
</tr>
<tr>
<td>KCNJ11</td>
<td>Rare; &lt;1% of MODY</td>
<td>More usually associated with neonatal diabetes; sulfonylurea responsive</td>
</tr>
<tr>
<td>ABCG8</td>
<td>Rare; &lt;1% of MODY</td>
<td>More usually associated with neonatal diabetes; sulfonylurea responsive</td>
</tr>
</tbody>
</table>

Table 1 | Clinical features associated with mutations in genes that cause maturity onset diabetes of the young (MODY)

<table>
<thead>
<tr>
<th>Gene</th>
<th>Relative prevalence</th>
<th>Other clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>HNF1A</td>
<td>Common (30-70% of MODY)</td>
<td>Low renal threshold for glycosuria; marked sensitivity to sulfonylureas</td>
</tr>
<tr>
<td>HNF4A</td>
<td>5-10% of MODY</td>
<td>Normal renal threshold; marked sensitivity to sulfonylureas; neonatal hyperinsulinaemia and hyperglycaemia with associated macrosomia; low concentrations of high density lipoprotein/high concentrations of low density lipoprotein</td>
</tr>
<tr>
<td>GCK</td>
<td>Common (30-70% of MODY)</td>
<td>Mild fasting hyperglycaemia throughout life; often detected during screening; small incremental glucose rise after carbohydrate load</td>
</tr>
<tr>
<td>HNF1B</td>
<td>5-10% of MODY</td>
<td>Malformations of the genitourinary tract (especially renal cysts and other renal developmental abnormalities); pancreatic atrophy; exocrine insufficient</td>
</tr>
<tr>
<td>IPF1</td>
<td>Very rare</td>
<td>Pancreatic agenesis in homozygotes/compound heterozygotes</td>
</tr>
<tr>
<td>INS</td>
<td>Rare; &lt;1% of MODY</td>
<td>More usually associated with neonatal diabetes</td>
</tr>
<tr>
<td>CEL</td>
<td>Very rare: fewer than 5 families reported</td>
<td>Exocrine pancreatic dysfunction</td>
</tr>
<tr>
<td>NEUROD1</td>
<td>Very rare: fewer than 5 families reported</td>
<td></td>
</tr>
<tr>
<td>KCNJ11</td>
<td>Rare; &lt;1% of MODY</td>
<td>More usually associated with neonatal diabetes; sulfonylurea responsive</td>
</tr>
<tr>
<td>ABCG8</td>
<td>Rare; &lt;1% of MODY</td>
<td>More usually associated with neonatal diabetes; sulfonylurea responsive</td>
</tr>
</tbody>
</table>
FEATURES TO CONSIDER WHEN ASSESSING THE CAUSE OF YOUNG ONSET DIABETES

History
- Duration and severity of symptoms
- History of obesity, hypertension, or dyslipidaemia (suggests metabolic syndrome)
- History of pancreatic disease
- Family history of diabetes, noting the age of diagnosis and treatment in relatives (it is helpful to draw a family tree)
- Family history or personal history of early onset deafness (associated with mitochondrial diabetes) and renal cystic disease (associated with HNF1B mutations)
- Personal history or family history of neonatal diabetes or neonatal hypoglycaemia

Clinical features
- Signs of insulin resistance, such as acanthosis nigricans, abnormal fat distribution (lipodystrophy), central obesity, and dyslipidaemia
- Signs suggesting other endocrine disorders (such as Cushing’s disease or acromegaly)

Investigations
- Measurement of autoantibodies to β cells (antibodies to glutamic acid decarboxylase and islet cells)
- Measurement of C peptide in patients taking insulin—serial measurements may be helpful biomarkers for specific types of maturity onset diabetes of the young, such as high sensitivity C reactive protein (currently mainly a research tool, but likely to enter clinical use in near future)

Genetic testing
- Genetic testing is too expensive for indiscriminate use in MODY. Knowledge and experience of MODY is limited outside of specialist diabetes centres; a diagnosis of MODY is therefore rarely considered in most patients with diabetes who are managed in primary care.

Can diagnosis of MODY be improved?
- Genetic testing is too expensive for indiscriminate use in all patients with diabetes. In 2008 best practice guidelines were produced for the diagnosis of MODY secondary to mutations in the GCK, HNF1A, and HNF4A genes.10 These guidelines recommend genetic testing for people who match specific clinical criteria: diabetes presenting before the age of 25 years, a strong family history of diabetes, and evidence of insulin independence. The extent of underdiagnosis described above suggests that genetic testing is not routinely offered to patients meeting these testing criteria. Furthermore, more than half of patients with confirmed mutations identified in European countries do not meet these clinical criteria for referral, so even adherence to current guidelines will continue to miss a large proportion of patients with MODY.9 11

Which patients diagnosed with type 1 diabetes should be referred for genetic testing?
- Patients with MODY who present at a young age may be misdiagnosed as having type 1 diabetes and inappropriately treated with insulin.
- In type 1 diabetes, autoimmune destruction of the β cells results in complete insulin deficiency within three to five years of diagnosis (the “honeymoon period”), whereas some β cell function is maintained in MODY.12-15 Consider MODY in patients with evidence of continued endogenous insulin secretion (for example, persistent C peptide production, low insulin dose (<0.5 units/kg/day), and no tendency to ketoacidosis when insulin is omitted) three to five years after diagnosis with apparent type 1 diabetes.

A PATIENT’S PERSPECTIVE

I was diagnosed with type 1 diabetes in 2003 at the age of 18. It was a surreal experience because, although I have a strong family history of diabetes, I never expected to be diagnosed myself. After diagnosis I did all that I could to adjust to having to take insulin each day but found this very hard, especially given how much exercise I did and all the associated complications for balanced control. At one point, I needed eight injections a day to help support my rugby training. I have learnt to live with diabetes for the past eight years but it has not been easy. My re-diagnosis this year with maturity onset diabetes of the young (MODY) has completely changed my lifestyle. I currently take just 40 mg of oral gliclazide each day and have been able to exercise regularly with no problems. My recent glycated haemoglobin results show that with this pill I still have good glucose control. I no longer have to worry about carrying around and administering insulin, and I have had no hypoglycaemic events since taking the pill. Although I have received excellent care in this transition period and am thankful that it is working, it is not easy to live with the memory of the hardships of taking insulin for eight years because of the misdiagnosis. It is frustrating that the lack of awareness about MODY among health professionals led to this option for diagnosis never being considered.

4 Explanations for this variation include financial restraints on accessing genetic testing and differences in local clinical expertise in MODY. Knowledge and experience of MODY is limited outside of specialist diabetes centres; a diagnosis of MODY is therefore rarely considered in most patients with diabetes who are managed in primary care.

Can diagnosis of MODY be improved?
- Genetic testing is too expensive for indiscriminate use in all patients with diabetes. In 2008 best practice guidelines were produced for the diagnosis of MODY secondary to mutations in the GCK, HNF1A, and HNF4A genes.10 These guidelines recommend genetic testing for people who match specific clinical criteria: diabetes presenting before the age of 25 years, a strong family history of diabetes, and evidence of insulin independence. The extent of underdiagnosis described above suggests that genetic testing is not routinely offered to patients meeting these testing criteria. Furthermore, more than half of patients with confirmed mutations identified in European countries do not meet these clinical criteria for referral, so even adherence to current guidelines will continue to miss a large proportion of patients with MODY.9 11

Which patients diagnosed with type 1 diabetes should be referred for genetic testing?
- Patients with MODY who present at a young age may be misdiagnosed as having type 1 diabetes and inappropriately treated with insulin.
- In type 1 diabetes, autoimmune destruction of the β cells results in complete insulin deficiency within three to five years of diagnosis (the “honeymoon period”), whereas some β cell function is maintained in MODY.12-15 Consider MODY in patients with evidence of continued endogenous insulin secretion (for example, persistent C peptide production, low insulin dose (<0.5 units/kg/day), and no tendency to ketoacidosis when insulin is omitted) three to five years after diagnosis with apparent type 1 diabetes.

C peptide is co-secreted with insulin from the β cell and can be measured in blood or urine. Urinary C peptide to creatinine ratio can be measured in urine with boracic acid preservative that has been sent by post.27 A case-control study found that this test provided excellent discrimination between 97 patients with MODY and 69 patients with long duration type 1 diabetes.15 However, assessment of C peptide is less useful for distinguishing MODY from type 1 diabetes close to diagnosis, when endogenous insulin production is still present.

At diagnosis of type 1 diabetes, most patients have pancreatic autoantibodies, including antibodies to glutamic acid decarboxylase and to islet cells. Patients with MODY are not thought to have pancreatic autoantibodies, and their absence is often part of the selection strategy for genetic testing. A recent case-control study reported that less than 1% of 508 patients with a confirmed genetic diagnosis of MODY had antibodies to β cells.16 A paediatric survey, however, found that 17% of patients with confirmed MODY mutations had positive antibodies.7 The difference between the studies probably relates to different laboratories and methods of antibody testing used, but the results suggest that the presence of pancreatic antibodies should not preclude genetic testing in cases where there is high clinical suspicion.

Parental history of diabetes is more common in MODY than in type 1 diabetes, although family history alone does not discriminate well between type 1 diabetes and MODY.28

Which patients diagnosed with type 2 diabetes should be referred for genetic testing?
- In contrast to type 2 diabetes, patients with MODY have β cell dysfunction that typically occurs in the absence of insulin resistance. Thus, patients with young onset (<45
ADDITIONAL EDUCATIONAL RESOURCES FOR HEALTHCARE PROFESSIONALS AND PATIENTS

- Diabetes Gene (maintained by the UK diagnostic testing centre in Exeter) (www.diabetesgenes.org)—Provides information on clinical care and research into genetic types of diabetes including maturity onset diabetes of the young (MODY) for patients and professionals
- Diabetes UK (www.diabetes.org.uk/Guide-to-diabetes/Introduction-to-diabetes/What_is_diabetes/mody/)—Information for patients on the different types of diabetes including MODY
- University of Chicago (www.monogenicdiabetes.org/what-is-monogenic-diabetes)—Provides information on different types of diabetes with an underlying genetic cause including MODY
- Diabetes Genes (http://beta.diabetesgenes.org/content/genetic-diabetes-nurses-locations-map)—Locations of regional genetic diabetes nurses in the UK, some associated with specialist MODY clinics, who can offer advice
- International Society for Paediatric and Adolescent Diabetes (ISPAD; http://www.ispad.org/)—Provides clinical details on rare types of diabetes and serves as a repository of stored DNA for research

...and serves as a repository of stored DNA for research associated with specialist MODY clinics, who can offer advice locations-map)—Locations of regional genetic diabetes nurses in the UK, some associated with specialist MODY clinics, who can offer advice

Special case 1: children with hyperglycaemia
As discussed, type 1 diabetes can be distinguished from MODY by examining several disease markers. The initial management will depend on the severity of hyperglycaemia at presentation. MODY is more common than type 1 diabetes in children who have asymptomatic hyperglycaemia; GCK mutations were found in 11-43% of children presenting with incident hyperglycaemia. In children with few or no symptoms we recommend genetic testing (GCK sequencing first) along with serial blood glucose monitoring. In children with more severe hyperglycaemia, it is safer to start insulin treatment and re-evaluate the causes later. This approach should prevent most children with GCK mutations from starting unnecessary treatment with insulin.

Most children with symptomatic hyperglycaemia have type 1 diabetes. However, infants who present with diabetes before 6 months are likely to have a genetic rather than autoimmune basis for their diabetes, and specialist investigation should be instigated.

Special case 2: pregnancy
Women with asymptomatic hyperglycaemia secondary to GCK-MODY may present with gestational diabetes during routine screening in pregnancy. A cross sectional study found GCK-MODY in 12 of 15 white women with gestational diabetes who met four additional criteria—fasting...
hyperglycaemia outside pregnancy, low glucose increment during an oral glucose tolerance test, diet controlled diabetes outside pregnancy, and a family history of diabetes.\textsuperscript{11,13} Other studies suggest that GCK-MODY and HNF1A-MODY explain 2-5\% and around 1\% of gestational diabetes, respectively.\textsuperscript{14-17} Clinical experience of treating patients with MODY in pregnancy is limited, so there is a lack of consensus about treatment between specialist centres. Although many clinicians use insulin routinely, some centres treat women with GCK-MODY with insulin only if fetal monitoring suggests development of macrosomia and treat with glibenclamide in HNF1A/HNF4A-MODY if patients were previously well controlled with sulfonylureas.

**Future strategies for diagnosing MODY**

A cost effective biomarker that could be used to screen all patients with young onset diabetes to pick out those most likely to have MODY would improve rates of diagnosis. Most candidate biomarkers investigated so far have had insufficient sensitivity and specificity to be useful for screening.\textsuperscript{18-20} High sensitivity C reactive protein, which is under transcriptional control by HNF1A, has recently been reported to be significantly lower in patients with HNF1A mutations than in those with other types of diabetes.\textsuperscript{21} This finding has now been replicated in two large European studies of around 1500 patients with MODY.\textsuperscript{22-24} Low concentrations of this protein (<0.25-0.75 mg/L, depending on the assay used) discriminated well between patients with HNF1A-MODY and those with young onset type 2 diabetes, with receiver operator characteristic curve derived C statistics of more than 0.8. Given its wide availability and modest costs, this test could be readily incorporated into diagnostic pathways to facilitate the identification of patients with HNF1A-MODY.

**Conclusion**

Despite the wide availability of molecular genetic testing, identification of patients with MODY remains a challenge for clinicians. An accurate genetic diagnosis of MODY has important clinical implications for individual patients and their relatives. Therefore, clinicians should be aware of the rarer causes of diabetes, particularly MODY, and should not be afraid to challenge existing diabetes diagnostic labels. We propose that a systematic assessment of the underlying cause of diabetes is incorporated into diabetes care plans for patients with diabetes diagnosed between the ages of 10 and 45 years, using a simple diagnostic algorithm such as that outlined in the figure. Otherwise most patients with MODY will continue to be misdiagnosed and forgo the opportunity of individualised care, tailored to the underlying genetic causes.

We thank Amanda Webster, our genetic diabetes specialist nurse, our colleagues at the Oxford Centre for Diabetes, Endocrinology and Metabolism, the molecular genetics team at the Peninsula Medical School, and most importantly the many patients who have increased our knowledge and understanding of monogenic diabetes over the years.

**Contributors:** Both authors are responsible for the conception, design, and structure of this article. GT drafted the article and KRO reviewed and amended it. KRO is guarantor.

**Funding:** KRO is an NHRI funded clinician scientist. GT is an Oxford NHIR Biomedical Research Centre funded clinical research fellow.

**Competing interests:** Both authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

**Provenance and peer review:** Not commissioned; externally peer reviewed.

**Patient consent obtained.**

1 Ledermann HM. Is maturity onset diabetes at young age (MODY) more common in Europe than previously assumed [letter] [see comments] Lancet 1995;345:648.
4 Shields BM, Hicks S, Shepherd MH, Colclough K, Hattersley AT, Ellard S. Maturity-onset diabetes of the young (MODY): how many cases are we missing? Diabetologia 2010;53:2504-8.
15  Besarre RE, Shepherd M, McDonald TJ, Shields BM, Knight BA, Ellard S, et al. Urinary C-peptide creatinine ratio is a practical outpatient tool for identifying hepatic nuclear factor 1-α/hepatocyte nuclear factor 4-a maturity-onset diabetes of the young from long-duration type 1 diabetes. Diabetes Care 2011;34:286-91.

ANSWERS TO ENDGAMES, p 853. For long answers go to the Education channel on bmj.com

PICTURE QUIZ

A 71 year old man with right sided facial droop

1 The echocardiogram shows a large inferolateral left ventricular aneurysm with a large volume of thrombus (figure). The aneurysm is likely to be secondary to the previous myocardial infarction.
2 The stroke is cardioembolic in origin.
3 Other investigations include carotid Doppler ultrasound and a 24 hour Holter ECG.
4 The patient is best managed in a specialist stroke unit with input from cardiologists and cardiothoracic surgeons. Stroke is a common and disabling condition and urgent treatment improves outcome. Left ventricular aneurysms can be managed conservatively with anticoagulation or surgically by aneurysmectomy.

STATISTICAL QUESTION

Statistical tests: matched pairs categorical data

McNemar’s test (answer c) would have been used to compare the proportions of children and drivers who were wearing a seat belt at the time of the crash.

ON EXAMINATION QUESTION

Trauma

Answer A is correct.