Is it type 2 or type 1 diabetes?

Practice nurse F Kavanagh

DSNs: F Spear, J Guest, B Wright

GPs: Dr N Cowap, Dr M Khalid

Consultants: Dr S George, Dr P Pusalkar, Dr A Pokrajac

Case 1

- 46 year old male
- Diagnosed with diabetes 5y ago, BMI 39 kg/m2
- Started on metformin - very good control
- HbA1c 6.3%
- No complications
- Family history of type 2 diabetes (father, sister)

Case 1 – progression

- 3 years ago developed a chest infection and was admitted to the hospital with diabetic ketoacidosis
- Managed in intensive care unit
- Discharged on basal/bolus insulin
- Autoantibodies requested during hospital admission

Case 1 conclusion

- Reviewed in the diabetes clinic
- BBG 5-8mmol/l, no swings
- Significant weight gain
- Insulin slowly tapered off and stopped
- GAD and islet cell antibody negative – **T2DM**
- HbA1c has remained 6.5% off insulin and on metformin
- Some weight loss after stopping insulin
- Continues to monitor blood sugars, although not frequently and in particular when unwell

Case 2

- 48 year old male, Dx T2DM age 40
- started on gliclazide and metformin in primary care
- BMI 26 kg/m2 at the time of diagnosis
- Non-compliant to medications and poor attendance with GP
- Poor glycaemic control - HbA1c consistently >11%
- Early complications – neuropathy, retinopathy needing laser treatment
- Did not monitor blood sugars at home

Case 2 progression

- Referred to foot clinic due to foot ulceration in heels (related to footwear)
- O/E - Absence of all modalities of sensation in feet, superficial heel ulcers
- On further enquiry – symptomatic for several months with thirst, polyurea and some weight loss
- Advised to start testing blood sugars, reluctant to start insulin, started taking OHAs regularly
- GAD and pancreatic islet cell antibodies requested

Case 2 ctd

- GAD positive, Islet antibody negative
- Started on insulin
- Weight gain within days and started feeling better
- Diagnosis revised!! - **LADA**

Case 3

Dx 11 yrs, presented ‘well with modest BG’
Presumed Type 1 diabetes
Basal Bolus regime 0.6u/kg/day

Now aged 14 yrs
HbA1c 54mmol/mol (7.1%)
Ht 1.6, Wt 50kg

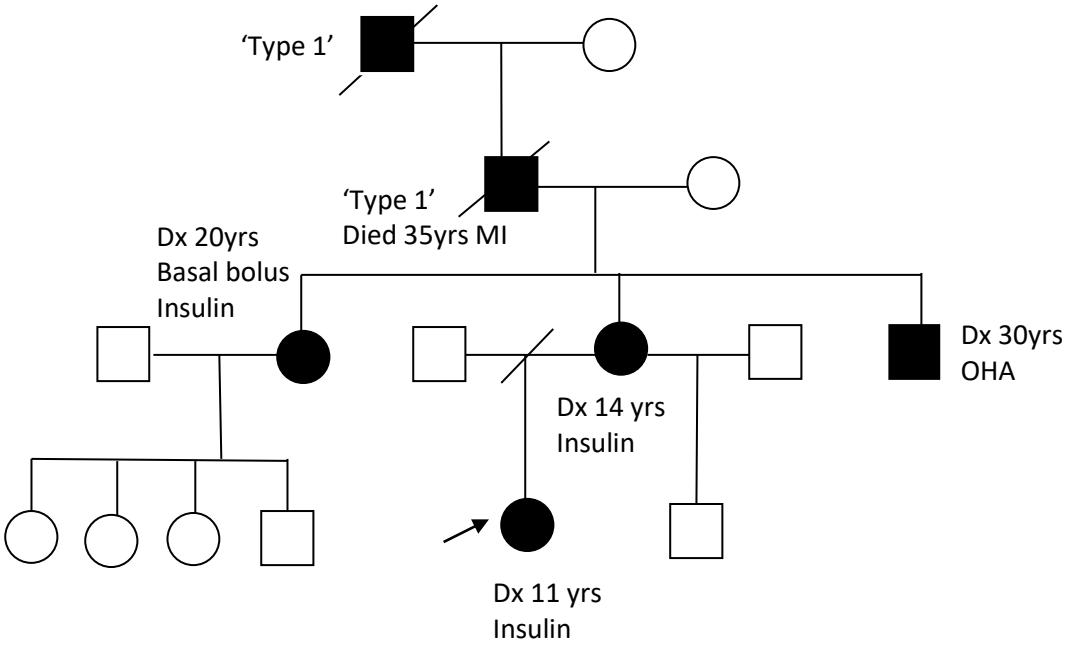
What’s the diagnosis ?

What other information would be helpful ?

GAD and IA2 negative

UCPCR 1.73 nmol/mmol
(<0.2nmol/mmol)

Case 3



Mum, Emma, Dx 14 yrs
Now 34 yrs, BMI 20
Presumed Type 1 treated with insulin from diagnosis
Basal bolus regime
1.3u/kg/day
HbA1c 96 mmols/mol

UCPCR 3.75 nmol
(20yrs post diagnosis)

GAD and IA2 negative

***HNF1A* MODY confirmed**

Case 3: Impact of diagnosis

Georgia: Stopped Insulin
On Gliclazide 20mg od
HBGM within target range,
HbA1c awaited

Mum: Due to change to Gliclazide but now pregnant so has remained on Insulin. Will transfer post delivery

Mum's siblings currently undergoing genetic testing also

What to look out for

- Low/normal BMI
- Young onset
- Recent/sudden weight loss
- Absence of insulin resistance phenotype
- Syndromic features
- Strong family history – Type 2, autoimmune disease
- Ethnicity

Autoantibodies and type 1 diabetes

- Commonly checked are GAD, IA, IA-2 antibodies
- Positive in about 80-90% of patients with type 1 diabetes and in <1% of normal subjects
- Negative antibodies do not rule out type 1 diabetes
- Widely used at presentation and sometimes later in the course

C-peptide

- Measure of endogenous insulin secretion
- Can be helpful to differentiate between type 1 and type 2 DM (Cut off 0.2 nmol/mmol)
- Fasting/non-fasting C-peptide generally used in clinical practice rather than stimulated C-peptide
- Some limitations to testing and should be interpreted with caution

- C-peptide gives a measure of patient's current status ie does the patient produce endogenous insulin now?
- Autoantibodies are of prognostic value ie will thay continue to produce endogenous insulin in the future?

LADA

- Late autoimmune diabetes of the adult
- Abs positive (one or more) + DM over 40 y of age
- Prevalence - 10% of T2DM
- Slow progression to beta-cell failure
  - 1 Ab +ve up to 12 years
  - 2 or more Abs +ve within 5 years

Monogenic Diabetes or MODY

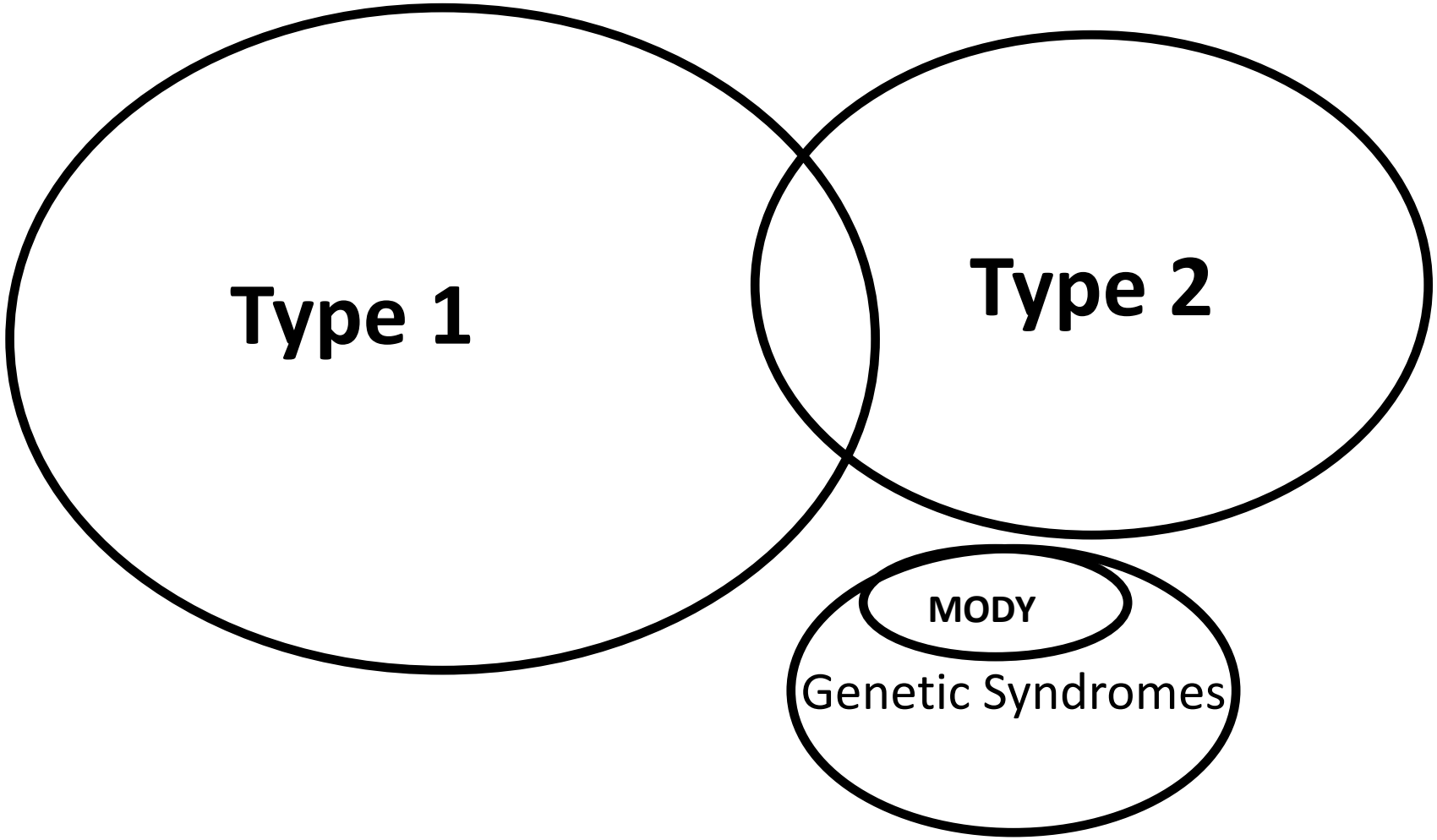
- Prevalence is about 1%
- Early onset diabetes
- Single gene defects
- 6-7 different mutations identified so far
- Autosomal dominant
- All children with affected parent with MODY have a 50% chance of inheriting gene

Response to SU in some MODY types

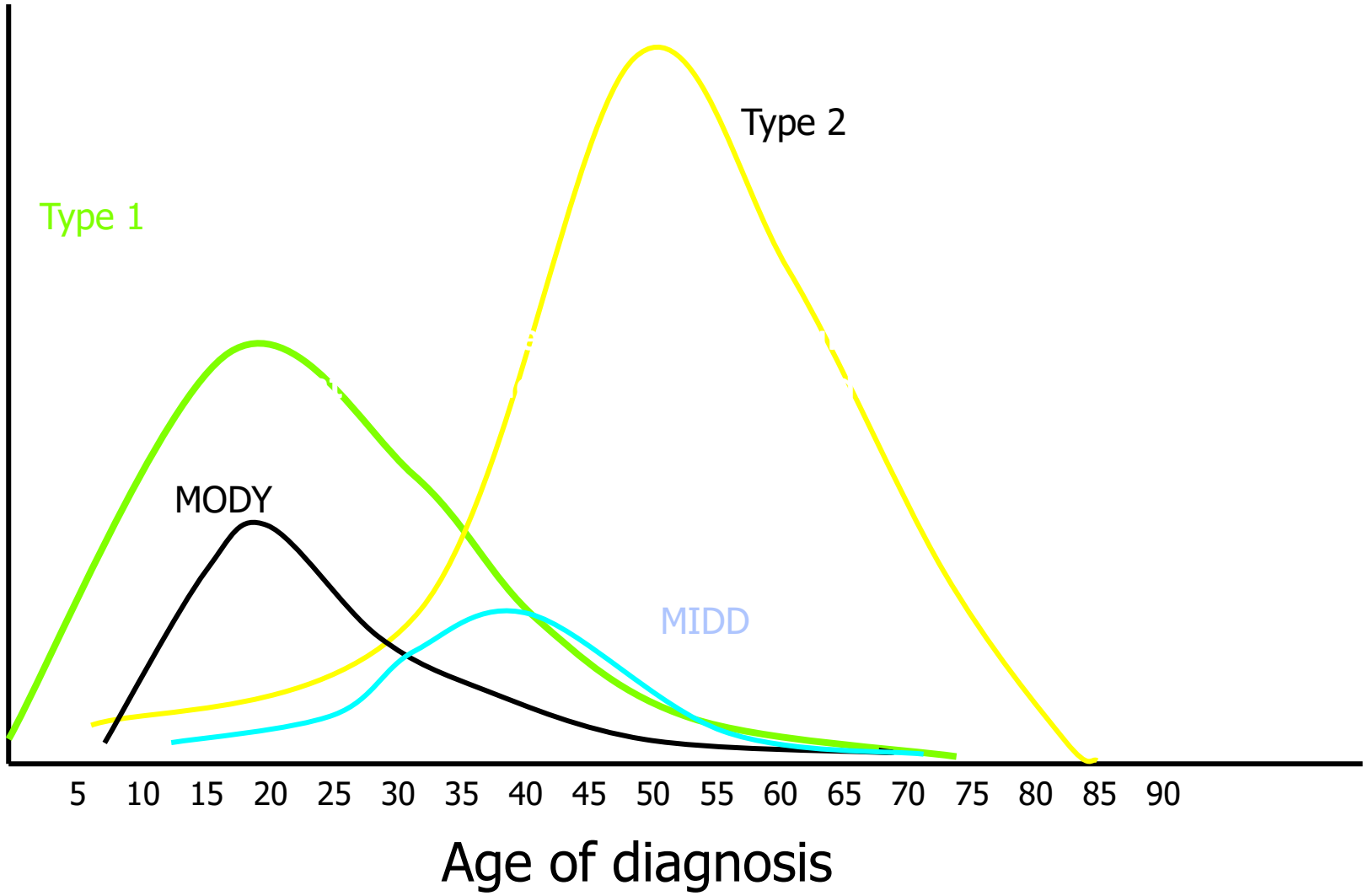
- Quite dramatic response to SUs as compared to patients with type 2
- Stopping insulin a reality in many of these patients
- 8 patients on with type 1 on insulin since diagnosis, 75% had insulin >25 years, HbA1c average 8.6%

  HNF 1alpha
- Transferred to gliclazide (40-160 mg/day)
- 75% reduced their HbA1c at 3months mean 0.85%

Young-adult diabetes (15-30yrs)



Diabetes in Young Adults (15-30 years)



Glucokinase and Transcription factor diabetes rather than "MODY"

MODY

Glucokinase mutations

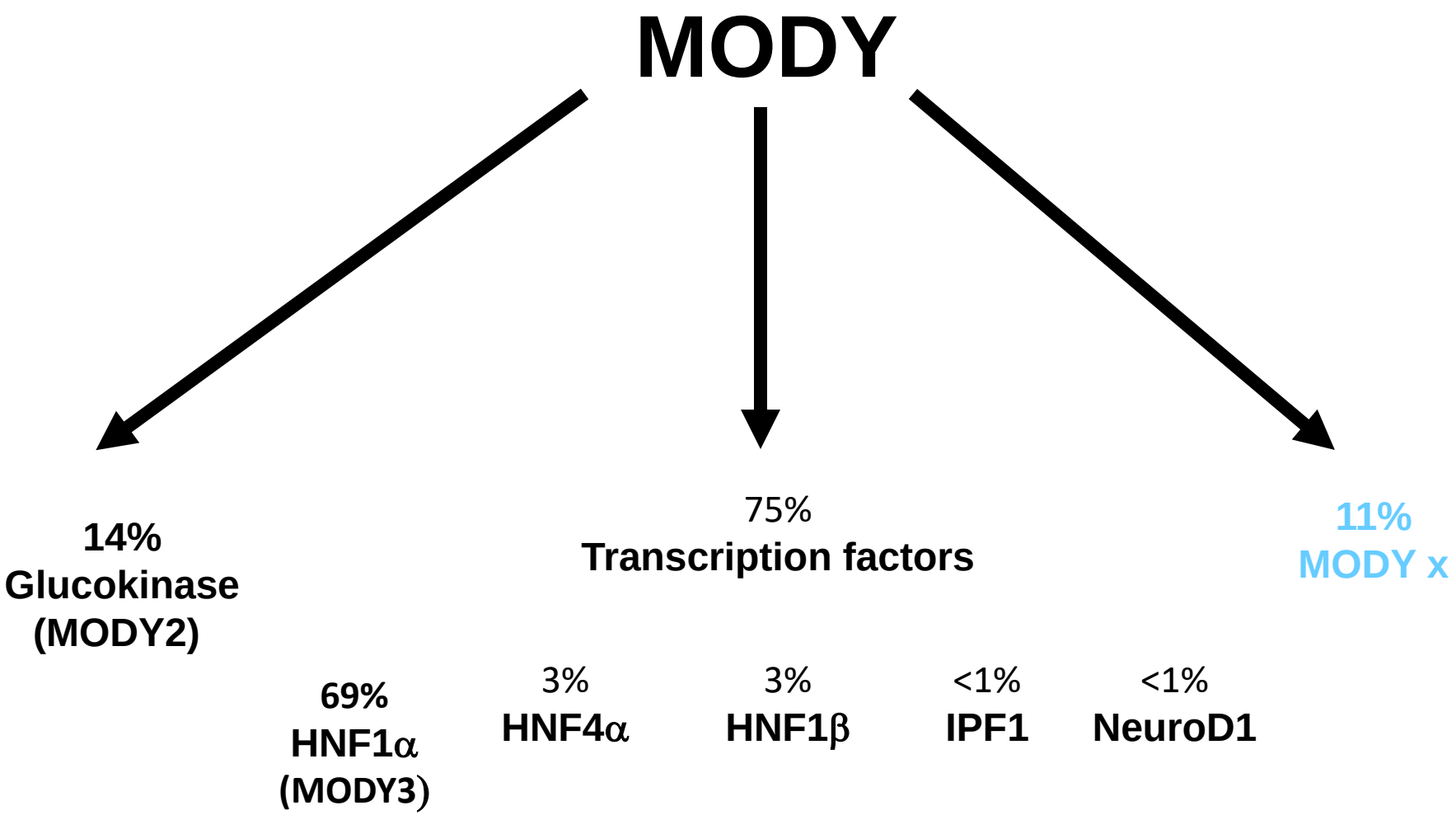
Transcription factor mutations

(HNF-1α, HNF-1β, HNF-4α)

Onset at birth
Stable hyperglycaemia
Diet treatment
Complications rare

Adolescence/young adult onset
Progressive hyperglycaemia
1/3 diet, 1/3 OHA, 1/3 Insulin
Complications frequent

The Genetic Causes of MODY



Frayling, et al Diabetes 2001

Diagnostic criteria for MODY

- Early-onset diabetes
- Not insulin dependent diabetes
- Autosomal dominant inheritance

Caused by a single gene defect altering beta-cell function

Diagnosis of diabetes before 25 years in at least 1 & ideally 2 family members

Off insulin treatment or measurable C-peptide at least 3 (ideally 5) years after diagnosis

Must be diabetes in one parent (2 generations) and ideally a grandparent or child (3 generations)

HNF1α (MODY3)

Commonest cause of MODY
May be misdiagnosed as type 1

Typically develop 12-30 yr
FPG maybe normal initially
Large rise (>5mmol/l) in OGTT
Worsening glycaemia with age

Low renal threshold (glycosuria)
Not obese (usually)

Parents and grandparents
usually diabetic

Young adult diabetes diagnosis

NOT on a single clinical criteria
or a single investigation

multi - facetted approach needed

	MODY	Type 2	Type1
Non insulin dependent	**Yes**	**Yes**	**No**
Parents affected	**1**	**1-2**	**0-1**
Age of onset < 25yr	**Yes**	**unusual**	**Yes**

MODY diagnostic criteria **do not** separate well from early-onset Type 2

	MODY	Type 2	Type1
Non insulin dependent	**Yes**	**Yes**	**No**
Parents affected	**1**	**1-2**	**0-1**
Age of onset < 25yr	**Yes**	**unusual**	**Yes**
Obesity	**+/-**	**+ + +**	**+/-**
Acanthosis Nigricans	**-**	**+ +**	**-**
Racial groups (Type 2 prevalence)	**low**	**high**	**low**

Take home messages

- **Be safe – young pt with osmotic symptoms best treated with insulin until proven otherwise BUT>>>>**
- **Think about BMI, how bad is glucose, are there any ketones when you see patient**
- **Always take a family history- include ages at diagnosis, other disorders that ‘ run through the family’ may be relevant**
- **Early follow up to consider response to treatment and refer to secondary care if you think there is a suspicion of something out of the ordinary**
- **Be inquisitive – stopping insulin makes a lot of difference to life style, driving, wt…**
- **Think of implications for offspring in case it is MODY**