



Hayes B¹

¹Patan Academy of Health Sciences

A 16 years male presents with feeling tired and lethargic with weight loss of 10 kg despite a good appetite.

What are Differential Diagnoses?

There are many causes of weight loss with decreased appetite but weight loss with good appetite points to some specific causes particularly:

- Diabetes Mellitus
- Hyperthyroidism
- Malabsorption syndrome

Further information

- Random blood glucose (RBG) was 300 mg/dl and no ketones in urine.
- This confirmed diagnosis of Diabetes
- Rest of examinations were normal

KEY CLINICAL QUESTIONS

How can I know what type of diabetes? What are the implications for treatment? Especially, how do I know if and when to start insulin?

CORRESPONDENCE

Dr. Bruce Hayes
Professor
Department of General Practice and Emergency Medicine
Patan Academy of Health Sciences
Email: blhayes@cms.org.au

SOME KEY POINTS

- All young people (including obese) who present with symptoms and/or biochemical derangements compatible with diabetes should be managed acutely to avoid delayed diagnosis of Type 1 diabetes¹
- Type 1 diabetes remains the commonest form of newly diagnosed in young: How to differentiate from Type 2?
- “Accelerator hypothesis” – proposes Type 1 and 2 are the same disorder of insulin resistance set against different genetic backgrounds.¹
- Clinical distinction between Type 1 and 2 is not always clear – DKA can occur in Type 2 and Type 1 can have pathophysiologic features of Type 2. When doubt, Antibody testing is recommended – if positive then Type 1 but this is not available here²
- See Table 1 for more details in differentiating Type 1 and 2 in young people¹

	TYPE 1 Diabetes Mellitus	TYPE 2 Diabetes Mellitus
AGE Range	Any age – often young	More often in peri and post-pubertal youth
Ethnic Distribution	All groups	More common in Chinese, Indian and Hispanic
Gender	M=F	F>M
Symptom duration	Days or weeks	Weeks or months – slower onset and may be asymptomatic
Obesity	Same as general population	More common > 80%
Family History	Present in 3-5%	Present in 75-100%
Acanthosis Nigricans	Unusual	Common
Insulin Concentration	Usually low	Usually high
Ketosis at presentation	More likely but can be absent	Less likely but can be present
Islet Autoimmunity (Antibodies)	Usually present	Generally absent

Table 1: Type 1 and 2 diabetes mellitus

OTHER EVIDENCE

- UpToDate suggests insulin should be started in any catabolic patient (weight loss and dehydration) or with evidence of ketosis²

In this patient in view of his catabolic state even without ketosis, he would probably be best started on insulin and followed as Type 1 is most likely.

CURRENT CLASSIFICATION of DIABETES MELLITUS²

- ▶ **Type 1 Diabetes /LADA** - β -cell destruction (Genetic and Environmental factors -?Viral) leading to an absolute insulin deficiency
 - Immune-mediated diabetes (common- 90%)
 - GAD – glutamic acid decarboxylase Abs; ICA – Islet cell Abs; IAA – Insulin Abs;
 - Idiopathic diabetes.

LADA (Latent Autoimmune Diabetes of the Adult)³

- ▶ Milder form of Type 1 (often avoid ketosis because have enough B cell function)
- ▶ B cell mass declines and become insulin dependent
- ▶ Suggested that up to 10-15% of previously diagnosed “Type 2” have this
- ▶ Should suspect this in < 50 years, acute symptoms, BMI < 25, personal/family history of Autoimmune disease
- ▶ Detected by using antibody tests (99% specific)
- ▶ There does seem to be an indication that sulphonylureas should not be a first line treatment for antibody positive type 2 diabetes. There is no significant evidence for or against other lines of treatment of LADA.⁴(Cochrane 2007)
- ▶ **Type 2 Diabetes** -May range from predominantly insulin resistance to predominantly an insulin secretory defect leading to a relative insulin deficiency; genetic and environmental factors (particularly low birth weight and obesity).

▶ **Other Specific Types**

A. Genetic defects in Beta Cell Function/Insulin secretion

Maturity Onset Diabetes of the Young (MODY)

- Rare (< 5% Type 2)
- Six genetic loci on different chromosomes have been identified to date.
- Glucokinase related MODY(MODY 2) is common but in India HNF-4 alfa.
- Usually Nonketotic /Nonobese/non insulin dependent
- Often in successive generations - autosomal dominant
- Present in under 25 year olds
- Hyperglycaemia is due to impaired glucose induced secretion of insulin
- Few microvascular complications and responds well to diet and oral hypoglycaemics
- Clinical course is similar to Idiopathic Type 2

B. Genetic defects in Insulin Action

1. Type A insulin resistance
2. Leprechaunism
3. Rabson-Mendenhall syndrome
4. Lipoatrophic diabetes
5. Others

C. Diseases of the Exocrine Pancreas

- Acquired causes include Pancreatitis, Trauma, infection, pancreatectomy, and pancreatic carcinoma;
- Fibrocalculous pancreatopathy – abdominal pain, steatorrhoea and diabetes;
- Cystic fibrosis and Hemochromatosis;
- Occult Ca pancreas

D. Endocrinopathies

E. Drug or Chemical Induced - glucocorticoids, phenytoin, thiazides, interferons and Intravenous pentamidine

F. Infections – viral

G. Uncommon Immune forms

H. H. Genetic Syndromes with Diabetes e.g. Down's, Turner's

▶ **Gestational Diabetes**

QUIZ on CLASSIFICATION.

CASE 1

20 year old gentleman was diagnosed to have diabetes on pre employment check up. He was born of non consanguineous marriage and his mother and his maternal grand father were having diabetes. His BMI was 21 kg/m². BP =120/80 mm Hg. What is the Probable Type?

Answer

He has MODY – fits features of

Young person (< 25 years old), Nonketotic and Nonobese with strong FH (Often in successive generations - autosomal dominant)

CASE 2

39 yr old male was diagnosed to have diabetes. Glycemic control for first one year achieved with Oral Hypoglycaemics. He now presents with polyuria and weight loss in previous 4 months. No recurrent abdominal pain/steatorrhea. His BMI is 20 kg/m². Urine ketones are negative. What type of diabetes?

Answer

It is likely he actually has LADA (perhaps misdiagnosed as Type 2 Diabetes) - suspect this in < 50 years, acute symptoms with BMI < 25. He now requires insulin and if could be tested, it is likely he will be antibody positive.

CASE 3

36 year old male who had his blood glucose levels checked since he had a family history of diabetes. His BMI was 31 kg/m² and his fasting plasma glucose(FPG) was 118 mg%, 2hr PPBG was 155 mg%. What is the Probable Type?

Answer

He has Impaired Glucose Tolerance (IGT) and needs follow up to assess progression and good lifestyle (diet and exercise) advice.

Remember DIAGNOSTIC Classification. American Diabetes Association ⁴

- **Normal** — Fasting plasma glucose (FPG) <100 mg/dL (5.6 mmol/L). NOTE - The 1997 criteria had been <110 mg/dL (6.1 mmol/L) and European Diabetes Epidemiology Group (EDEG) issued a position statement in 2006 recommending that the original cut-off point for IFG (110 mg/dL or 6.1 mmol/L) be retained

Diabetes Unlikely. If high risk – retest yearly, if risk-3 yearly (General pop – start screening at 65, If Risk factors –start at 50)

- Categories of increased risk for diabetes
 - Impaired fasting glucose (IFG)— FPG ≥100 to 125 mg/dL (5.6 to 6.9 mmol/L).
 - Impaired glucose tolerance (IGT)— 2-h PG (75 g OGTT) ≥140 to 199 mg/dl (7.8 to 11.0 mmol/L).
 - A1C— 5.7 to 6.4 percent (the International Expert Committee recommended 6.0 to 6.4 percent)

NOTE - European Diabetes Epidemiology Group (EDEG) also recommend that the term "non-diabetic hyperglycemia" be used in preference to "impaired fasting glucose."

- Diabetes mellitus — A1C ≥6.5 percent, FPG ≥126 mg/dL (7.0 mmol/L), 2-h PG ≥200 mg/dL (11.1 mmol/L); random PG >200 mg/dL (11.1 mmol/L) in the presence of symptoms

NOTE - In 2009, an International Expert Committee recommended using a hemoglobin A1C (A1C) value of ≥6.5 percent to diagnose diabetes, and the ADA affirmed the decision

NOTE - Any one of these criteria must be repeated on subsequent testing.

- A1C, FPG and 2-h PG are used to diagnose lesser degrees of impaired glucose regulation. There is currently no consensus on using one in preference to the other. While the 2-h PG is a more sensitive test in most populations, A1C and FPG are more convenient.

REFERENCES

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