Typing diabetes mellitus

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ADA classification

1. Type 1 diabetes (β-cell destruction, leading to absolute insulin deficiency)
    1. Immune mediated
    2. Idiopathic
2. Type 2 diabetes (from insulin resistance with relative insulin deficiency to predominantly secretory defect with insulin resistance)
3. Others specific diabetes
    1. Genetic defects of β-cell function
    2. Genetic defects in insulin action
    3. Diseases of the exocrine pancreas
    4. Endocrinopathies (acromegaly, cushing's syndrome, hyperthyroidism, …)
    5. Drugs- or chemical-induced
    6. Infections (congenital rubella, cytomegalovirus, …)
    7. Uncommon forms of immune-mediated diabetes
    8. Other genetic syndromes sometimes associated with diabetes
4. Gestational diabetes mellitus (GDM)

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Useful parameters for classification of a diabetes

- Familial history
- Personal history and co-existing diseases
- History of the diabetes mellitus
- History of treatment of the DM
- Clinical examination: *weight, BMI, waist circumference*
- Biology: *glycaemia at admission, HbA_1C, C-peptide, ketosis, lipids, antibodies*
- HOMA test: *β function, insulin sensitivity, hyperbolic product*
- Anti GAD, IA2 antibodies, other Abs
- Evolution

Clinical case 1 Ms. AV, 39 yrs

- Personal history : -
- Familial history: -
- Treatment : -
- History of the DM :

  Symptoms ++ since 1 month

  Weight loss 10 kg

  Visual problems (accomodation) +

  Fatigue ++

Ms. AV, 39 yrs

- Clinical examination:

  56 kg, 1m73, BMI **18.7** kg/m²

- Biology :

Glycaemia	mg/dl	304
HbA_1C	%	15
ketonuria		++
c-peptide	pmol/ml	0.15
Cholesterol total	mg/dl	230
LDL-cholesterol	mg/dl	**169**
HDL-cholesterol	mg/dl	39
Triglycerides	mg/dl	110
Ab TPO, Tg		-

Ms. AV, 39 yrs

- HOMA Test :

		0′	5′	10′
Glucose	mg/dl	**267**	**262**	**260**
Insulin	µU/ml	3	4	3

β Cell function : 8.3 %
Sensitivity : 122 %
Hyperbolic product : 10 %

Antibodies : **GAD + (87.6 U/ml), IA2 + (2.93 U/ml)**

→ Type 1 diabetes

Clinical case 2 Mr. HO, 41 yrs

- Personal history :
  Hypertension
- Familial history :
  diabetes in the mother's family
- Treatment :
  Aldactazine
- History of the DM :
  Symptoms ++ since 6 months
  Weight loss 4 kg
  Visual problems (accomodation) +
  Fatigue ++

Mr. HO, 41 yrs

- Clinical examination :

  87 kg, 1m74, BMI **28.7** kg/m², waist **104** cm

- Biology :

Glycaemia	mg/dl	**367**
HbA_1C	%	10.8
ketonuria		+
c-peptide	pmol/ml	0.56
Cholesterol total	mg/dl	195
LDL-cholesterol	mg/dl	156
HDL-cholesterol	mg/dl	39
Triglycerides	mg/dl	349
Ab TPO, Tg		-

Mr. HO, 41 yrs

- HOMA Test :

		0′	5′	10′
Glucose	mg/dl	**212**	**214**	**212**
Insulin	µU/ml	11	12	10

β Cell function : 33 %
Sensitivity : 38 %
B x S : 13 %

Antibodies : **GAD -, IA2 -**
→ Type 2 diabetes (insulinopenic)

Clinical case 3 Mr. OP, 28 yrs

- Personal history : -
- Familial history : -
- Treatment : -
- History of the DM :

  Symptoms ++ since 2 months

  Weight loss 12 kg

  But previous weight gain of 30 kg in 6 years

Mr. OP, 28 yrs

- Clinical examination :

  94 kg (- 12kg), 1m86, BMI **27.2** kg/m², Tour de taille **104** cm

- Biology :

Glycaemia	mg/dl	322
HbA_1C	%	12.6
ketonuria		+++
c-peptide	pmol/ml	0.17
Cholesterol total	mg/dl	142
LDL-cholesterol	mg/dl	64
HDL-cholesterol	mg/dl	34
Triglycerides	mg/dl	220

Mr. OP, 28 yrs

- HOMA Test :

		0′	5′	10′
Glucose	mg/dl	**277**	**274**	**275**
Insulin	µU/ml	4	4	4

β cell function : 9.8 %
Sensitivity : 86.4 %
B X S : **8.5** %

Antibodies : **GAD + (16 U/ml), IA2 + (4.4 U/ml)**

→ **type 1 diabetes**

Clinical case 4 Mrs. AM, 55 yrs

- Personal history :
  Hypothyroidism
- Familial history : -
- Treatment :
  L-T4
- History of the DM :
  June 2005 : mycosis, no weight loss (58 kg, 1m55), Glycaemia 200 mg/dl, HbA_1C 10.5 %, R/ Metformin $\Rightarrow$ 6.5 %
  August 2006 : HbA_1C 8.8 %, R/ + Gliclazide
  June 2007 : HbA1c 8.1%

Mrs. AM, 55 yrs

- Clinical examination :

  59 kg, 1m55, BMI 24.5 kg/m²

- Biology :

Glycaemia	mg/dl	128
HbA_1C	%	8.1
Insulin	µU/ml	< 3
c-peptide	pmol/ml	0.41
Cholesterol total	mg/dl	217
LDL-cholesterol	mg/dl	159
HDL-cholesterol	mg/dl	44
Triglycerides	mg/dl	69
Ab TPO, Tg		+

Mrs. AM, 55 yrs

- Test HOMA:

		0′	5′	10′
Glucose	mg/dl	128	129	128
Insulin	µU/ml	3	< 3	3

β cell function : 27.9 %
Sensitivity: 197.8 %
B X S : **55** %

Antibodies : **GAD + (38.2 U/ml)**

→ **Type 1 diabetes « slow onset » or LADA**

Clinical case 5 Mr. NK, 62 yrs

- Personal history :
  Biliary pancreatitis in 2006 (R/ sphincterotomy)
  Hypertension
  Hypercholesterolemia
- Familial history : -
- Treatment :
  Creon 5/day, Simvastatin 20mg, Nexiam 20mg
- History of the DM :
  Symptoms -
  Weight : stable

Mr. NK, 62 yrs

- Clinical examination :

  56 kg, 1m61, BMI **21.6** kg/m², waist 80 cm

- Biology :

Glycaemia	mg/dl	300
HbA_1C	%	**8.9**
ketonuria		-
c-peptide	pmol/ml	0.57
Cholesterol total	mg/dl	179
LDL-cholesterol	mg/dl	106
HDL-cholesterol	mg/dl	63
Triglycerides	mg/dl	50

Mr. NK, 62 yrs

- Test HOMA:

		0′	5′	10′
Glucose	mg/dl	**190**	**189**	**188**
Insuline	µU/ml	3	3	3

β Cell function : 13 %
Sensitivity : 180 %
B x S : **23.4** %

- Abdomen CT Scan: atrophy of the corpus and tail of the pancreas, pseudo-cysts, calcifications

→ **Diabetes secondary to chronic pancreatitis**

Clinical case 6 Mrs. MG, 54 yrs

- 54 year-old woman sent for

  - muscle weakness and fatigue
  - Polyuria-polydipsia
  - fasting glycaemia 273 mg/dl

Mrs. MG, 54 yrs

- Personal history

  - Peripheral arteritis R/plavix
  - Recurrent mycosis of the GI tract
  - Sideropenic anemia (gastritis)
  - Rectal ulcers (analgesics)
  - Auto-immune hypothyroidism R/thyroxine
  - Hypercholesterolaemia
  - Chronic renal insufficiency < benign nephroangio-sclerosis
  - Chronic sinusitis since 2000

Mrs. MG, 54 yrs

Treatment:

- Plavix
- L-thyroxine 125 µg
- Adalat 5mg
- Pravasine 10 mg
- Befact, Folavit
- Movicol

1/ Confirm diabetes mellitus:

- fasting glucose - OGTT if glucose < 150
- HOMA Test
- HbA1c

HOMA Test

	0′	5′	10′
Glucose (mg/dl)	155	156	161
Insulin (μU/ml)	12	13	11

- Sensitivity : 40 %
- ß-cell function : 57 %
- B x S = 23 %

Mrs. MG, 54 yrs

HbA_{1c} : 8,3 % (3-6)

2/ Etiology of diabetes ?

Mrs. MG, 54 yrs

- Type 1 ? No
  - Clinically no argument
  - Homa test : quite good ß-cell function
  - Antibodies: anti GAD65 (-), IA2 (-)
  - (Auto immune thyroiditis)

- Type 2 ?
  - No familial history
  - No overweight, no metabolic syndrome
  - But <u>insulin resistance</u>

Other specific diabetes ?

- No sign of pancreatitis - Imaging (-)

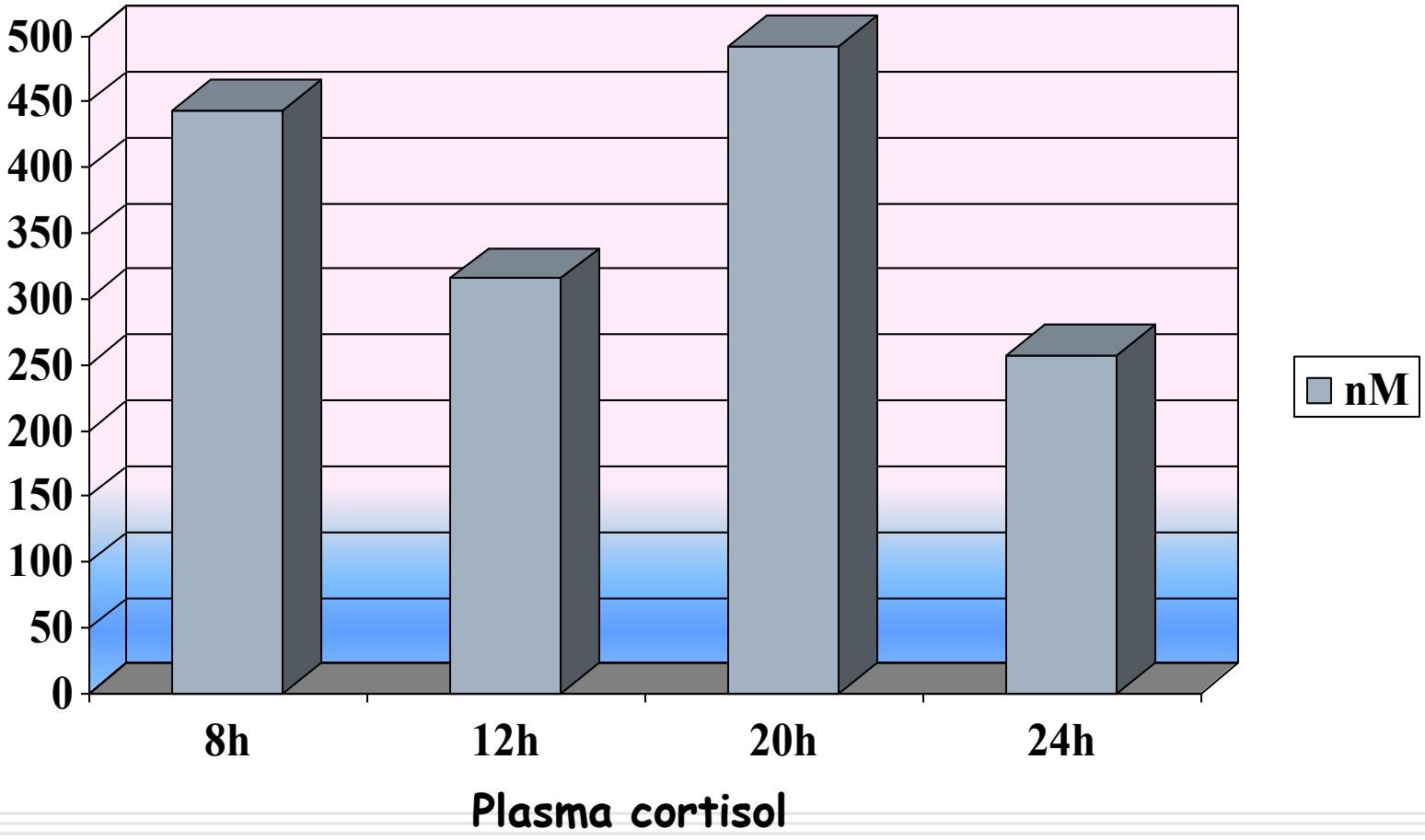
- ***Other signs and symptoms***
  - Weight gain 10 Kg in 1 yr , HTA
  - Moon face, easy bruising of the skin, ecchymoses .. (Plavix ?)
  - Mycosis and gastritis
  - General weakness
  - Leucocytosis (neutrophilic) observed since months

→ diagnosis ?

Cushing's syndrome

- What would you ask to confirm CS ?
  - 24 h – Urinary free cortisol (< 100 µg)
  - Dexamethasone suppression test (1 mg overnight or Liddle's test over 2 days)
  - Cortisol rhythm (+ ACTH)
  - If available: midnight salivary cortisol

Cortisol rhythm



ACTH low 3-10 pg/ml (20-60)

Mrs. MG, 54 yrs

- 24 h UFC : 147 µg (nl < 100)

- Low dose dexamethasone suppression test (4 x 0,5 mg 2 days) : no suppression !

Cortisol	355nM	(< 140 nmol/L)
ACTH	4 pg/ml	(< 20 pg/ml)
24 h UFC	247 µg	(< 25 µg)

→ **CONFIRMED CUSHING'S SYNDROME**

Cushing syndrome

- What would you ask to search for aetiology ?

  - High dose dexamethasone suppression test
  - CRH test
  - Imaging (Pituitary MRI – Adrenal CT)
  - (Inferior petrosal sinus sampling?)

MG, 54 yrs

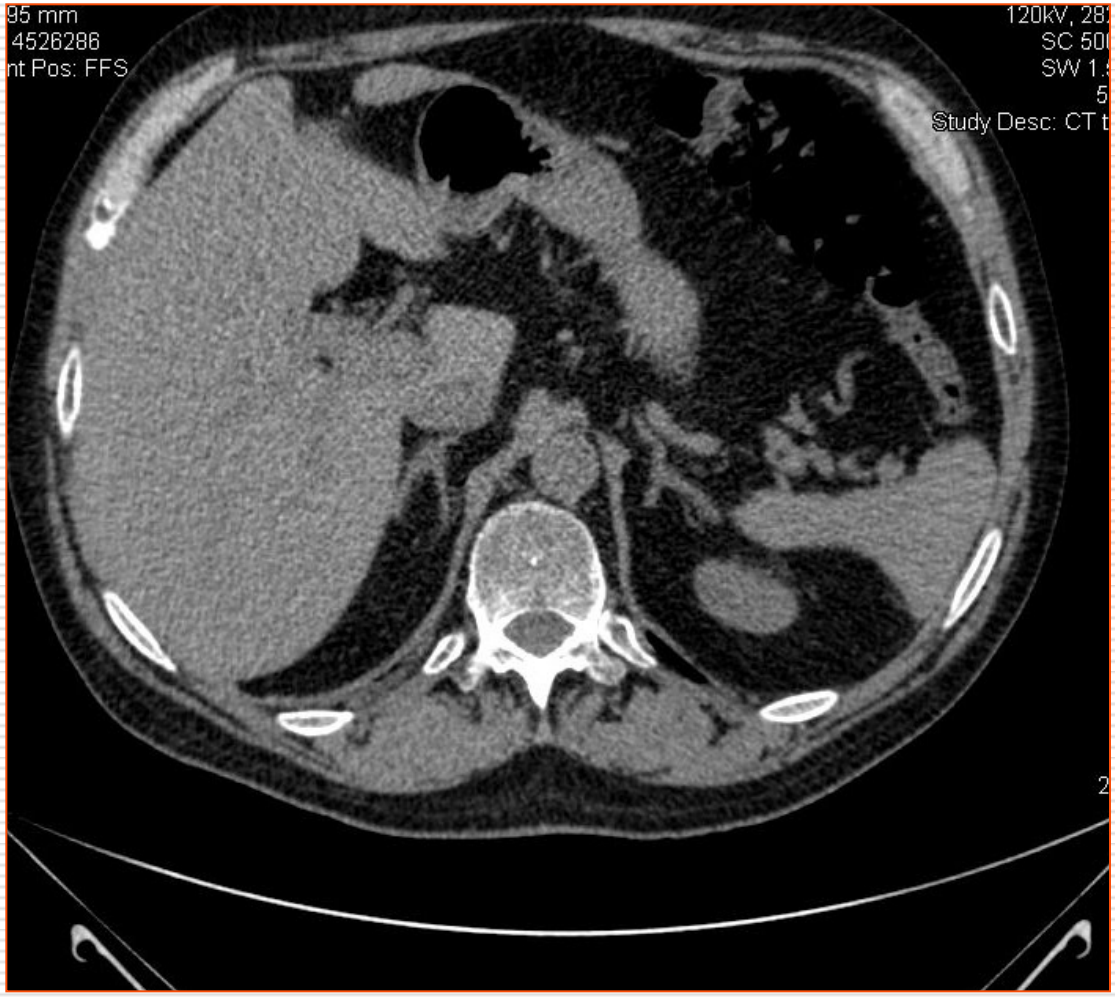
- High dose dexamethasone suppression test (4 x 2 mg 2 days) : no suppression !

  - Cortisol 477 nM
  - ACTH 2 pg/ml
  - 24 h UFC 587 µg

→ **ADRENAL CUSHING ?**

Adrenal CT Scan

No tumor – No hyperplasia



Other diagnosis?

Proven Cushing's syndrome → diabetes

ACTH-independent

with normal adrenal (and pituitary) imaging

… ??

Chronic exogenous glucocorticoid intake

Complaints of chronic sinusitis ...

Daily use of nasal drops of Sofrasolone®

- = prednisolone acetate 2,5 mg/ml – 10 ml (over-the-counter medication !)
- admitted use of 3 to 4 vials per week !
- = 75 - 100 mg prednisolone/week or 10-14 mg/day)
- since 4 years

Conclusion

- Specific diabetes induced by iatrogenic Cushing

- Iatrogenic Cushing due to exogenous abuse of corticoids in nasal drops (Sofrasolone)