

What goes Wrong in T2DM

Nemanja Stojanović FRCP

We will talk about

- Diabetes
- Type 1 DM
- Type 2 DM
- Complications

Diabetes Diagnosis

- Fasting plasma glucose ≥ 7 mmol/l
- Random/ 2h after the OGTT glucose of ≥ 11.1 mmol/l
- Do not diagnose it on glucometer!
- Diagnosis carries implications: for the patient, family, driving, life and health insurance

What is Diabetes?

- Group of metabolic disorders characterized by inappropriately high sugar that leads to chronic damage to:
 - Small blood vessels (microvascular complications)
 - Nerves (neuropathy)
 - Large blood vessels (macrovascular

Some Vocabulary

- HbA1c- Glycated Haemoglobin: reflects 3 months of glucose control
- Cholesterol
- HDL: good cholesterol
- LDL: bad cholesterol

Types of Diabetes..

- Type 1 Diabetes Mellitus
- Type 2 Diabetes Mellitus
- Gestational Diabetes Mellitus
- ADA lists 58 other subtypes of DM
- There is also Diabetes Insipidus!

Type I DM

- Usually starts before the age of 30
- Associated with weight loss, occasionally dramatic
- Excessive thirst, passing a lot of urine
- Can not survive without insulin: there is insulin deficiency

T2DM

- Affects middle aged/elderly
- Obese
- Lifestyle: sedentary
- Ethnic & genetic



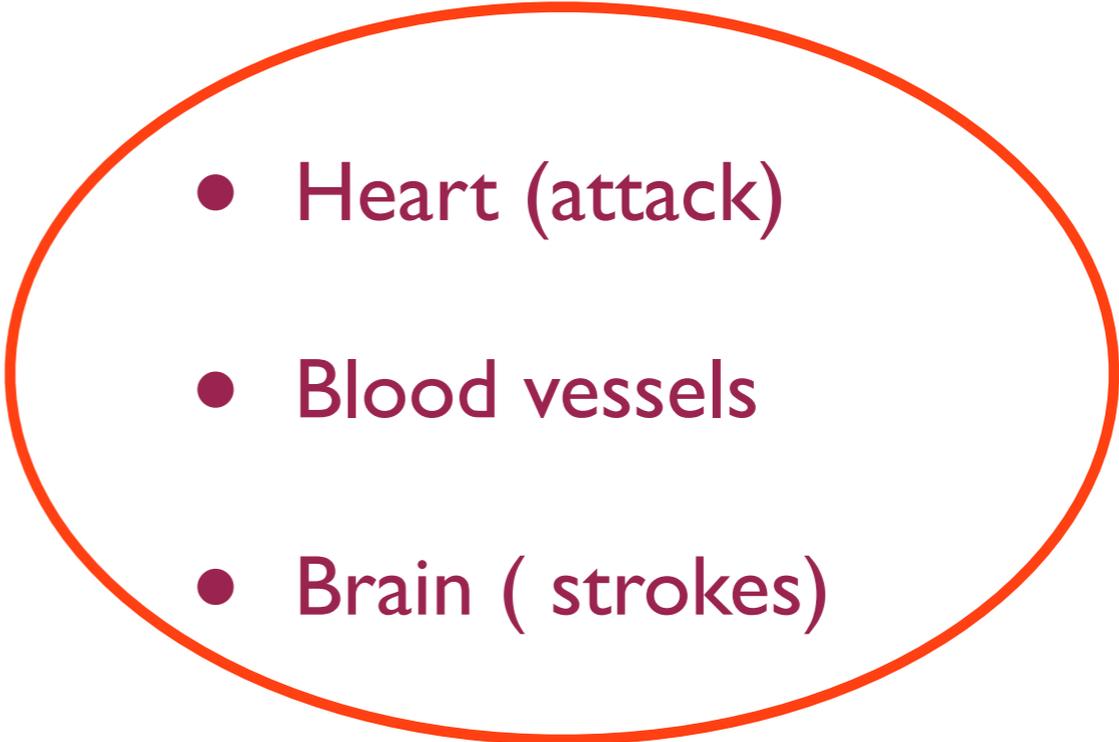
T2DM

- Onset usually insidious
- A person can have it for years without realizing it
- CVD marker (equivalent of having had a heart attack)
- Body is resistant to insulin
- Treatment: sugar, blood pressure,

T2DM: some statistics...

- More people in Africa have T2DM than HIV
- USA 24 million have DM; 51 million have prediabetes
- 50% of newly diagnosed diabetics have evidence of complications
- UK: 2.9 million diagnosed; 800,000 people have DM but are undiagnosed!

Diabetes: Target Organs

- Eye
 - Kidney
 - Nerves
 - Foot
 - Erectile Dysfunction
- 
- Heart (attack)
 - Blood vessels
 - Brain (strokes)
- Skin can also be affected

T2DM and CVD: baseline predictors

- LDL cholesterol
- Low HDL cholesterol
- HbA1c
- Systolic blood pressure
- Cigarette smoking

Turner RC et al UKPDS (23).*BMJ* 316:823–828, 1998

Treating T2DM

- Treating glucose (sugar): first line treatment is diet and exercise
- Cholesterol
- Blood Pressure

UKPDS: Tight Glycaemic Control 10 years on

**SU ±
Insulin**

Endpoint

**Metformin vs
Control**

9%

Any DM Endpoint

✓

24%

Microvascular Disease

17%

DM related death

✓

15%

Myocardial Infarction

✓

13%

Death: Any Cause

✓



N Engl J Med 2008 0: NEJMoa0806470

Treating Cholesterol



2.8 mmol/l



5.0 mmol/l

3.3 mmol/l

Values/ Targets

- Cholesterol 4mmol/l
- HDL: good cholesterol 1mmol/l men;
1.1mmol/l women
- LDL: bad cholesterol < 2mmol/l or <
2.6mmol/l ADA

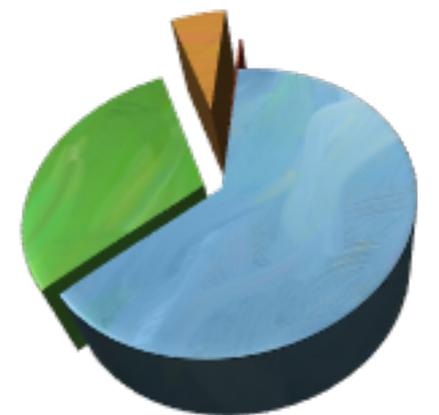
Treating Lipids...

	Diabetic		Non Diabetic	
	n	CHD	n	CHD
Secondary prevention				
4S	483	-42%	3237	-32%
CARE	586	-25%	3104	-25%
LIPID	782	-19%	8232	-25%
HPS	2981	-14%	11405	-33%

FIELD vs CARDS

- Fenofibrate
- Patients: 9795
- 2131 previous CVS event
- Cholesterol 3.0-6.5 mmol/l

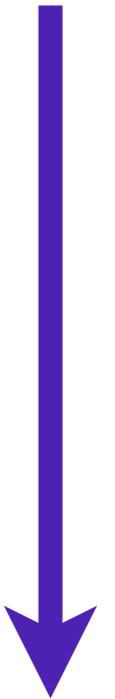
- Atorvastatin
- Patients: 2838
- At least one complication
- LDL < 4.14 mmol/l



FIELD vs CARDS

- CVD morality NS (p=0.16)
- Non fatal MI 24% in FF group (p=0.01)
- Total CVD events reduced from 13.9 to 12.5% p=0.04
- Microvascular disease significant improvement

- Acute CHD 36%
- CVG (revascularisation) 31 %
- CVA 48 %
- NNT 27/event



What We Eat ... Past & Present

	Natural human diet	Modern Human Diet
K ⁺	> 150mmol/ day	100- 400mmol/ day
Na ⁺	20- 40 mmol/ day	30- 70mmol/ day
K / Na ratio	3-10:1	< 0.4

- Na^+ intake of 50-100 mmol/l necessary but not sufficient for development of hypertension
- Median urinary Na excretion is ~ 170mmol/ day (9.9g NaCl)
- 50g ham ~ 32mmol Na^+ and 1.4mmol K^+

CDC Diabetes Cost Effectiveness Group

- Markov Model: Predominantly Macrovascular Disease
- Achieving BP 144/ 86 mm Hg

- Also
 - Cholesterol treatment: Pravastatin
 - Glycaemic control: Diet, followed by OHA's ± Night time insulin

JAMA 2002, 287: 2542- 50

CDC Diabetes Cost Effectiveness Group

- Reducing Cholesterol
- Improving Glycaemic Control
- Improves health outcomes

- Treating BP: Reduces cost and improves

JAMA 2002, 287: 2542- 50

Dietary Changes

- Chimpanzees 98.4% genome identical to human
- Fed 15g NaCl /day
 - Systolic BP up by 33mmHg
 - Diastolic BP up by 10mmHg
- Withdrawal of NaCl in diet reversed the BP changes...

Denton D. Nat Med: 1995: 1009- 16

Nephropathy

- 35-50% with Type 1 after 20 years of disease
- 15- 20% Type 2 patients

Nephropathy: aetiology

- HbA1c >7–8%
- Genetic factors
- Hypertension
- Inflammation
- Altered vascular permeability
- Hyperlipidaemia
- Excessive protein intake

Nephropathy

- Generally speaking bad news
- Herald of:
 - impending CV disease and possible dialysis in T1DM
 - Forthcoming CVD and other vascular complications in T2DM

Complications: Neuropathy

DPN: associated Factors

- Degree of hyperglycaemia
- Hypertension
- Hyperlipidemia
- Duration of Diabetes
- Height

Scale of the Problem

- 50% will have neuropathy after 25 years of DM
- T2DM: 10% will have it neuropathy at diagnosis
- Up to 26% will have painful neuropathy (PDN): symptoms vary from mild

Foot Amputations

Ipswich 1995-2005

- General population reduced from 7.4 to 2.8/ 100,000
- Diabetic population:
 - Total amputations fell from 53.2 to 16/ 10,000
 - Major amputations fell from 36.4 to 6.7/

Complications: Retinopathy

We have discussed

- T1DM
- T2DM
- Complications

In Conclusion

- Prevention is better than cure
- Diet and exercise
- There are conditions that are associated with DM and should be recognized!