



Dr Rick Cutfield

Physician, Diabetologist and
Endocrinologist

Mercy Specialist Centre

Diabetes Case Studies - Concurrent Breakout Session Repeated

Friday, 10 June 2011

Start 2:00pm

Start 4:00pm

Duration: 60mins

Duration: 60mins

Sovereign

Sovereign



Diabetes Case Studies from the clinic

Dr Rick Cutfield

Physician and Endocrinologist
Waitemata District Health Board
Mercy Specialist Centre





Case 1:

48 year old Mrs DM:

- BMI = 35
- HbA1c = 64 mmol/mol
- Type 2 diabetes 5 years
- On Metformin 500mg t.d.s.

N.B.: HbA1c 64 = 8%

Remember:

9%	=	75 mmol/mol
8%	=	64 mmol/mol
7%	=	53 mmol/mol

Metformin Points

- 
- a) How do you prescribe Metformin?
How often and maximum dose?
 - b) What if egfr is down to 36/ml/min?
Do you stop Metformin?
 - c) Metformin causes hypoglycaemia. **T / F**
 - d) Metformin affects B12 levels ? **T / F**
 - e) Metformin may reduce cancer risk in
Mrs DM **T / F**
 - f) Metformin will reduce C/V risk in a
patient like Mrs DM **T / F**

What is next drug of choice to reach glycaemic target of 53 (7%)

a) Sulphonylureas (NOT GLIBENCLAMIDE)

Pro

- Known for years
- Can ↓ glucose levels effectively in most people
- Cheap
- Given twice daily

Con

- Slight ↑ weight
- Hypoglycaemia
- May only work for 2-5 years



What is next drug of choice to reach glycaemic target of 53 (7%)

b) TZDs (Thiazolidinedione) Pioglitazone

Pro

- ↓ glucose in insulin resistant patients
- Once daily
- ↓ fat in liver
- ↓ T.G. levels
- No hypoglycaemia given alone or with Metformin

Con

- ↑ risk of Fracture (2x)
- Weight gain ++
- Fluid retention in some
- Rarely heart failure
- Takes 4-6 weeks to work

What is next drug of choice to reach glycaemic target of 53 (7%)

c) Incretins

1. DPP 4 inhibitors, ↑ GLP Levels e.g. Sitagliptin

Pro

- ↑ Insulin release after meals. ↓ Glucagon
- 100mg once daily
- Weight neutral
- NO hypoglycaemia
- Ideal for elderly Type 2, or those at risk of hypos

Con

- These are new oral agents not funded currently (\$100 / month)
- Not a powerful agent

What is next drug of choice to reach glycaemic target of 53 (7%)

c) Incretins

2. GLP Analogues, e.g. Exanatide

Pro

- S.C. injection B.D.
- Weight loss an advantage
- An option for those overweight wealthier Type 2 patients instead of insulin
- May decrease BP slightly

Con

- Expensive (over \$200 / month)
- Nausea (often temporary)

N.B.: New once/week analogue soon to be released in U.S.

What is next treatment of choice to reach glycaemic target of 53 (7%)

d) Bariatric Surgery

A real option

- Which operation best?
- What ages?
- What B.M.I. to include?
- Public vs Private
- Long Term Benefits vs Long Term side effects



**If your patient is not at TARGET
after maximising oral agents**

**HOW DO YOU
START INSULIN**



Insulin in Type 2 Diabetes

- Keep it safe
- Keep it simple
- Introduce concept early
- Explain concept of B cell failure
- Discuss barriers

BUT DO NOT DELAY

if patient adhering to programme but
not reaching TARGET.





If fasting glucose elevated start NPH at bedtime, .e.g. Protophane or Humulin N.

N.B: We are currently not funded to use insulin Glargine in this setting in Type 2 Diabetes (unlike US/Europe)



DOSE

- Try 8-12u and titrate dose by 1-2 units every 4 days to reach fasting glucose target of 6 mmol/L
- Teach patient to do this but arrange f/up after 1 week
- May use B.D. NPH Insulin or pre-mixed insulin depending on results of capillary glucose

Case 2:

65 year old with tiredness and diabetes for 3 years on Gliclazide 120 mg b.d.

- BMI 33
- HbA1c 8.1%
- Cholesterol 6.1 - LDL 3.4 - TG 3.2 - HDL 1.0
- Bili 14 - GGT 78 - AST 89 - ALT 110 - AlkPO4 110
- Testosterone 10.2 ↓
- Ferritin 420 ↑ (iron saturation normal)
- eGFR 42. S.Creatinine 140

These findings are most consistent with:

- Chronic Hep C
- Haemachromatosis
- Alcohol abuse
- Hepatic steatosis
- Sulphonylurea sensitivity.



Next step would include:

- a) Lifestyle change for 6-12 months.
- b) Add Metformin.
- c) Add Pioglitazone.
- d) Increase Gliclazide.
- e) Check Haemachromatosis gene.
- f) Liver ultrasound.

Teaching Points:

- Hepatic steatohepatitis is very common in insulin resistant states. ALT & GGT reflect liver fat and insulin resistance, and predict diabetes.
- Hepatic steatohepatitis can occasionally lead to fibrosis/cirrhosis.
- Haemachromatosis is associated with diabetes and testosterone deficiency, and while not rare is a much less common cause of abnormal LFT in diabetes.
- Glitazones not contraindicated unless significant fibrosis/cirrhosis and may be helpful in reducing liver fat.
- Hep C is associated with ↑ incidence of diabetes.
- Metformin is safe with mild-moderate liver function abnormalities. Lactic acidosis is very rare and safe to use if eGFR is over 30.



Case 3:

A woman aged 42 with Type 1 Diabetes for 8 years has a history of recent severe daytime and nocturnal hypoglycaemia and mild weight loss.

Which is least likely ?:

- a) She should have diet / exercise reviewed.
- b) She should have a screen for celiac disease.
- c) She should have Addison's disease ruled out.
- d) She likely has renal impairment reducing insulin clearance.
- e) Insulin Glargine and Determir have been demonstrated to reduce nocturnal hypoglycaemia and would be useful here.

Treatment Issues with Hypoglycaemia:

- Types of insulin:
 - Rapid acting analogues
 - most should benefit
 - Long acting analogues
 - most should benefit – espec noct. hypos. [Lantus, Determir]
- Timing of insulin. NPH at bed not dinner; Glargine AM or PM or B.D.



Treatment Issues with Hypoglycaemia:

- Severe hypoglycaemia with Sulphonylureas may be prolonged especially with glibenclamide. Consider admission for 24 hours for IV glucose $\pm$ somatostatin.
- Meals, exercise, alcohol, age.
- If SMBG doesn't reveal answer; search for nocturnal hypos. Sometimes use continuous glucose monitoring.
- Consider Addison's, celiac disease in T1DM. Consider renal failure. Reduce medication.
- Prevention of hypoglycaemia for 2-3 weeks can improve hypoglycaemic awareness.



Case 4:

Mr L.G.:

- Aged 75 with PHX of I.H.D.
- Diabetes 15 years

On:

- | | | |
|------------------|---|---------------|
| – Novorapid 8u | } | Pre-breakfast |
| – Protophane 18u | | |
| – Novorapid 10u | } | Pre-dinner |
| – Protophane 14u | | |

C/O Nocturnal hypos

What to do next?



**Are nocturnal hypos
of concern in
patients with I.H.D.?**

Reduce Nocturnal Hypos by:

- Adding supper ?
- Move Protophane to bed $\pm$ reduce dose
- Consider Insulin Glargine – replace NPH using 20% lower dose



i.e.:	Glargine	24u	breakfast
	Novorapid	6u-8u	breakfast
	Novorapid	8u-10u	dinner

Case 5:

48 year old man with type 2 diabetes.

- HbA1c 8.8% - BP 130/84
- Urine microalbumin 48mg/l ACR 3.2
- S. Creatinine 112



Case 5: continued

Which would you do?

- a) Add ACE inhibitor.
- b) Add Angiotensin 2 antagonist.
- c) Repeat microalbumin after attempt at improved glycaemic control.
- d) Do nothing as ACR is normal.
- e) Check MSU.



Case 5: continued

If microalbuminuria persists, but BP settles to 130/80 should he be on:

- Ace inhibitor?
- Statin?
- Aspirin?
- All of above?



Microalbuminuria:

- Persistent albumin excretion 30-300mg/day.
If > 300mg/d overt proteinuria.
 - $ACR \geq 2.5(m) \geq 3.5(f)$.
 - Marker of diabetic nephropathy.
 - Marker of endothelial dysfunction.
 - Associated with $\uparrow$ C/V mortality.
 - May be present at diagnosis and reflect underlying C/V disease.
- Transient microalbuminuria.
 - Fever; exercise; heart failure.
 - Poor glycaemic control.

Microalbuminuria in Type I Diabetes:

- Strict glycaemic, lipid control, aspirin.
- If BP > 130/80 – ACE.
- If BP < 130/80 – treat with ACE If ↑ in albumin excretion.
- Use ARB if intol of ACE, but not both.
- Do not treat normotensive patients with normal microalbumin with ACE-I.

Microalbuminuria in Type 2 Diabetes:

- ACE or ARB if:
 - Microalbuminuria.
 - BP > 130/80.
- Aggressive combined approach with statin, aspirin, tight glycaemic control and BP control (Steno 2) reduces mortality by ½.



Case 6:

Mrs D.G.:

- T2 diabetes
- HbA1c 7.2%
- microalbumin level of 68
- ACR of 8.4.
- She is on maximum ACE inhibitor plus Metformin.
- BP is 140/90

NEXT ?

Would you add?

- A_2 antagonist, e.g. Cozaar
- Thiazide
- Calcium antagonist
- β Blocker
- α Blocker
- Frusemide



Would you add STATIN?

If LDL cholesterol 2.5

Y / N

Would you add Aspirin?

Y / N





If C/O muscle pains on
Simvastatin 40mg/d.

What do you do?

- 
- Check CK
(can have myalgia 2° statin without CK rise)
 - Consider:
 - Reducing dose
 - Changing statin, e.g. Lipitor, Crestor
 - Review indication for treatment
 - Consider:
 - Ezetemide
 - Fibrate (evidence for ↓ in microalbuminuria retinopathy)
 - Nicotinic Acid (or Tredaptive)

Case 7:

69 year old smoker; type 2 diabetes on:

- Metformin 850 mg b.d.
- Gliclazide 80mg b.d.
- Accupril 10 mg b.d.
- Bezalip 400 mg plus Simvastatin 40mg
- O/E BP 130/85 BMI 32

- Femoral bruit with no foot pulses.
- Creatinine 0.18 (creatinine 0.14 1 year ago)
eGFR 32ml/min.
- Urine microalbumin 54 mg/l – MSU 10 rbc.
- ACR 4.3 – HbA1c 7.5%.
- Cholesterol 4.3 – LDL 3.1 - HDL 1.0 - TG 2.1.



Case 7: Continued

Next best step is:

- a) Stop Bezalip.
- b) Order MRI renal arteries.
- c) Stop accupril.
- d) Increase Metformin to improve HbA1c.



Teaching Points:

- Renal artery stenosis is common in Type 2 diabetes but usually does not need intervention. MRI of Renal Artery may be best test if BP troublesome.
- ACE inhibitor can be continued unless creatinine rises 30% soon after initiation.
- Fibrates should be avoided if abnormal creatinine. Consider use with fasting TG over 3 mmol/l if egfR > 60.
- Proteinuria is almost always present if significantly elevated creatinine is due to diabetic renal disease.

Teaching Points: continued

- Diabetic nephropathy can be associated with some microscopic haematuria.
- If significant haematuria; urine casts; no proteinuria; no retinopathy think of non-diabetic cause of renal failure, especially if diabetes of very short duration.

NB: In patients with T2DM and proteinuria up to 20% have non-diabetic causes of nephropathy. Only 60% of diabetic nephropathy in T2DM have significant retinopathy.

Teaching Points: continued

- If creatinine $\uparrow$ in diabetes always check if recent use of contrast media; diuretics, NSAID; Fibrates.
- Patient with renal disease and diabetes, esp smokers, esp with femoral bruits WILL have coronary disease. look for subtle symptoms, e.g. SOB, minimal chest discomfort, diaphoresis and plan ex ECG.
- Aggressive C.V. management:
 - Statin - aim LDL < 2.0
 - Aspirin
 - BP to $< 130/80$ but not less than 120/80.



Case 8:

19 year old female presents ↑ with fasting hyperglycaemia. A repeat fasting glucose is 7.2mmol/l. She has BMI 23 and a family history of diabetes in mother and grandmother.

Which of the following tests would you find the most clinically useful:

- a) Islet Cell and GAD Ab.
- b) Serum Insulin.
- c) Thyroid function test.
- d) HNF-1 α check for MODY3 diabetes .
- e) HbA1c.

Case 8:

Indeed she could have:

- Early autoimmune “Type I” diabetes
- Monogenic Diabetes – autosomal dominant MODY3 due to HNF 1 α mutation



Case 9: 64 year old presents with:

- Glucose 15.3
- HbA1c 9.2%
- O/E Enlarged liver
- Ferritin 4000
- ↑ Iron saturation
- Positive Gene for haemachromatosis.

He begins weekly venesection & remains on Metformin 850_{mg} bd with gliclazide 40_{mg} bd added

After 16 weeks he has HbA1c of 5.9% with pre-meal glucose tests 6-9 mmol/l on his 2 year old meter.

The low HbA1c most likely represents:

- a) Nocturnal hypoglycaemia 2° gliclazide use and possible cirrhosis of liver.
- b) Iron interference with capillary glucose measurement.
- c) Increased red cell turnover.

Teaching Points:

- ↑ RBC turnover can cause falsely low HbA1c, e.g. Blood loss, haemolysis, venesection.
- HbA1c < 6.5% should prompt a search for hypoglycaemia (especially nocturnal) in those on Insulin or sulphonylurea.



Case 10:

- 28 year old with poorly controlled diabetes HbA1c 12% achieves excellent control after a “rev-up” from her new boyfriend after mild retinopathy discovered.
- Her HbA1c improves to 7.2% over four months, but her repeat eye check shows worsening retinopathy and she c/o burning slightly swollen feet?



Teaching Point:

When glucose control is improved rapidly and especially when HbA1c drops from over 11% quickly to 7%

- Patients can develop a self limiting “neuritis” with severe pain in lower limbs and occasionally over trunk.
- Can be temporary worsening of retinopathy. Usually returns to normal after 12-18 months.



Case 11:

70 year old with diabetes for many years and moderate neuropathy presents with swollen and hot foot. CRP is 7. W.C.C. normal. Afebrile. Xray shows possible fracture and disorganisation of mid-tarsal bones.

What is the clinical problem to rule out, and what other tests to order?

What is probable diagnosis?

Charcot Neuroarthropathy:

- Peripheral neuropathy – insensate foot.
- Increased A-V shunting with ↑ peripheral blood flow and ↓ bone flow.
- Minor mechanical trauma / micro-fractures.
- Unilateral warmth, oedema, redness in foot with minor trauma, with little or no pain.
- Collapse of arch and bony prominence.
- Local osteopenia.
- Differential diagnosis is septic arthritis; gout; other arthritis.
- MRI & serial xray – ortho opinion.
- Avoid weight bearing / offloading cast essential.
- Pamidronate infusion?



Case 12:

72 year old with T2DM with good control:

- HbA1c 7.2%.
- No Retinopathy or significant peripheral neuropathy.
- Develops severe pain in L) thigh with:
 - weight loss
 - thigh wasting
 - weakness of hip flexion
 - loss of knee reflex.





Acute femoral neuropathy (amyotrophy-proximal motor neuropathy)

- Rapid onset.
- Usually reversible in 6-24 months.
- Seldom recurs but can do.
- No relation to other long term complications.
- Often older, T2DM and M > F.
- Severe neuropathic pain and yet mild sensory deficit.
- Cause - ? Perivascular ? Immunological ?

Case 13:

38 year old with Type I Diabetes for 25 years.

C/O:

- Intermittent Diarrhoea
- Dizziness on standing
- Facial sweating after some foods

O/E:

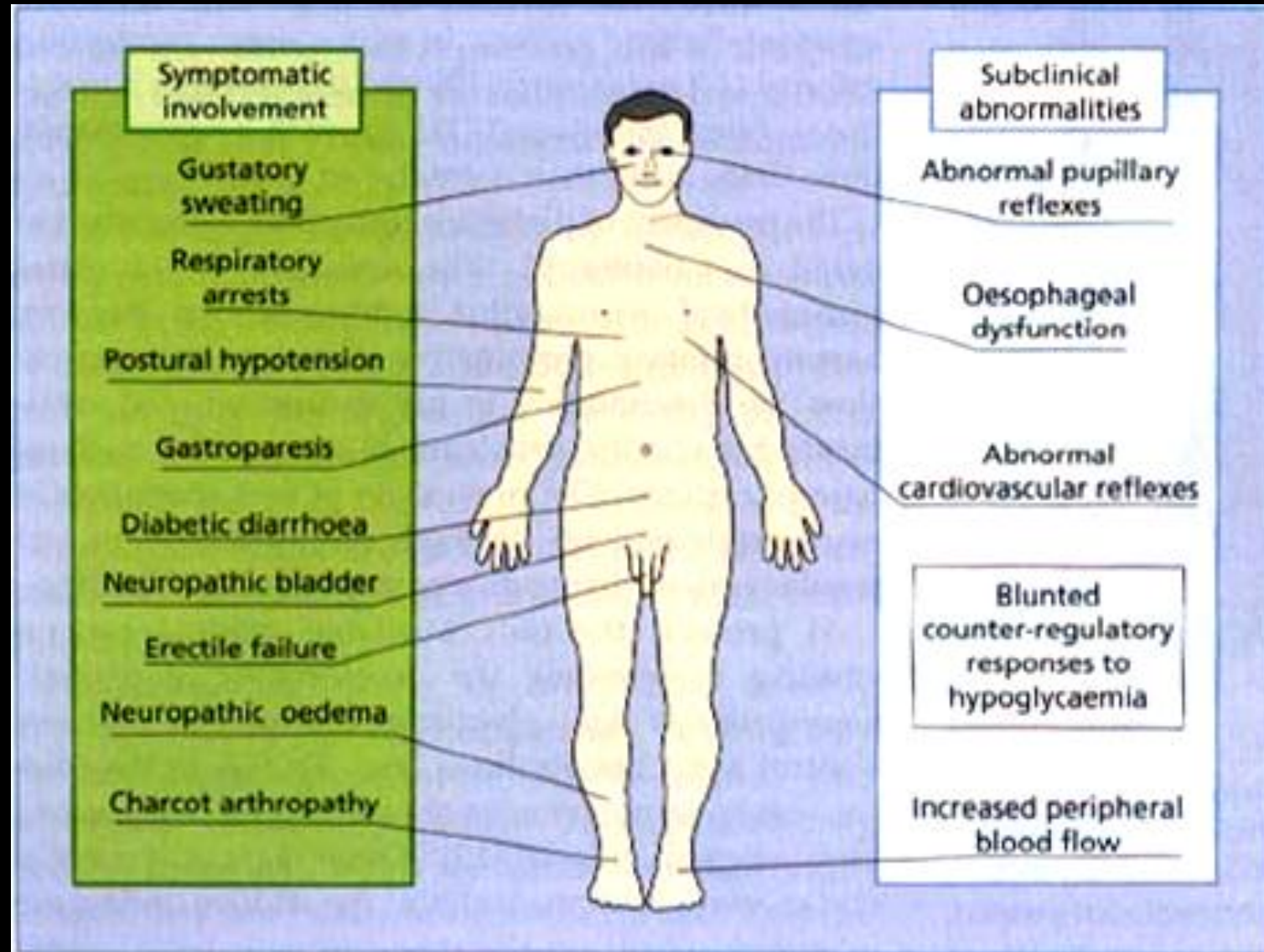
- Pulse 90/min
- BP 130/70 – Lying
- 90/60 – Standing

Investigations:

- Thyroid function normal.
- 9:00am Cortisol 480
- Stool sample:
 - No pathogens
 - No RBC
 - No WCC.
- Celiac Screen negative
- Colonoscopy normal



Clinical & subclinical features of diabetic autonomic neuropathy



Cardiovascular autonomic function tests

	Normal	Abnormal
Heart rate variation during deep breathing • Maximum-minimum (bpm)	> 15	< 10
Heart-rate increase on standing • 15 secs after standing (bpm) • 30 : 15 ratio	> 15 > 1.04	< 12 < 1.00
Heart-rate change during Valsalva • Maximum : minimum ratio	> 1.21	< 1.20
Postural fall in systolic BP • 2 min after standing (mmHg)	< 10	> 30

Note that these tests normally decline with age; the normal values given here generally apply to subjects less than 60 years of age.

Classification of diabetic Neuropathies

Progressive neuropathies	Reversible neuropathies	Pressure palsies
Distal symmetrical polyneuropathy • Predominately sensory • Autonomic involvement common (mostly asymptomatic) • Clinical Motor involvement very rare	Mononeuropathies • Femoral (amyotrophy) • Cranial-nerve palsies (III and VI) • Truncal radiculopathies	Median nerve • Carpal-tunnel syndrome Ulnar nerve
‘Small-fibre’ neuropathy • Autonomic involvement common and usually symptomatic • Gradual onset • No recovery • Associated with increasing duration of diabetes • Associated with other chronic diabetic complications	Acute diffuse painful neuropathy • Stocking distribution • Sudden onset • Spontaneous recovery • No association with duration of diabetes • No association with other chronic diabetic complications	Lateral popliteal nerve (very rare) • More common than in the non-diabetic population • No association with duration of diabetes