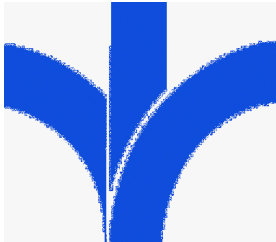


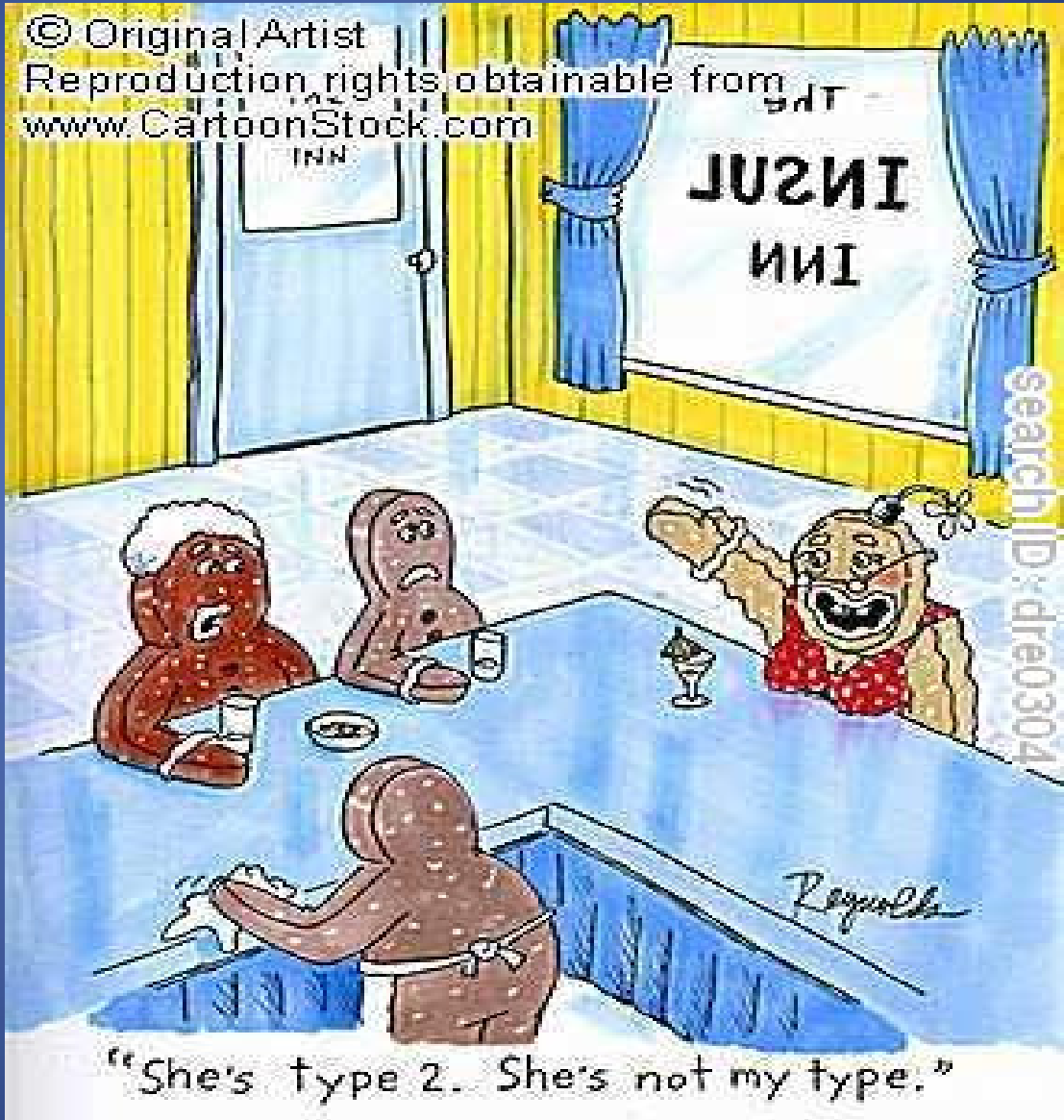
# Renal Disease in Type 2 Diabetes Mellitus

**6th Collaborative DiGP/HSE/UCC Conference**  
25<sup>th</sup> September 2013

Dr. Eoin O'Sullivan  
Consultant Endocrinologist  
Bon Secours Hospital Cork



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# Case

- 69 year old woman with type 2 diabetes x 12 years
- PMHx:
  - OA
  - HTN
  - COPD
- SHx:
  - Ex-smoker
- Medications:
  - Metformin 1g bd
  - Glicazide MR 120mg od
  - Ramipril 10mg od
  - Amlodipine 10mg od
  - Atorvastatin 10mg od
- O/E:
  - BMI 34kg/m<sup>2</sup>
  - BP 145/88



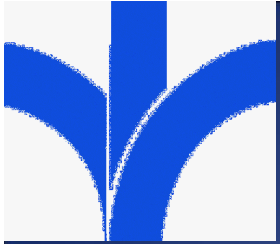
# Case

- HbA1c 59mmol/mol
- Fasting total and LDL cholesterol 3.9 and 1.4
- Serum creatinine 120umol/l
- Spot urinary albumin to creatinine ratio (ACR)  
22 (<3.5)



# Issues

- HbA1c
  - Targets in this patient
  - Suitability of metformin
- BP
  - ? Sufficient control
  - ? Correct agents
- Renal impairment
  - ? Severity
  - ? Action to be taken



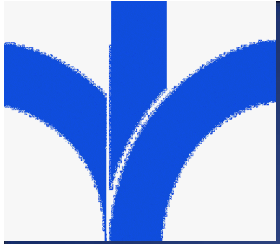
# What next for renal dysfunction?

- Calculate eGFR
- Add another agent to improve glycaemic control
- Add another agent to improve BP control
- Stop metformin
- Refer to endocrinology/nephrology



# Topics

- Definition and classification of chronic kidney disease (CKD) using eGFR
- Microalbuminuria – uses, pitfalls and significance
- Metformin in CKD
- Management issues in diabetic CKD
  - Blood pressure control
  - Glycaemic control



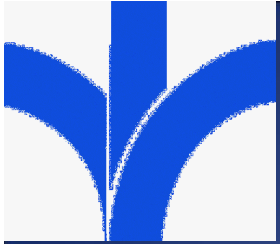
# CKD and eGFR





# Definition of CKD

- Calculation of eGFR
  - MDRD (Age, gender, creatinine, ethnicity)
  - CKD-EPI (Age, gender, creatinine, ethnicity)
  - Cockcroft Gault (Age, gender, creatinine, weight)
- MDRD eGFR for 69 year old woman with creatinine 120 $\mu$ mol/l
- 41ml/min



# MDRD issues

- 90% of individuals' actual GFR will be within 30% of **e**GFR
- 20% fall likely significant
- Ethnicity
- Tends to underestimate normal or near-normal renal function
  - >60ml/min sometimes reported
- Does not include weight (cf Cockcroft Gault)



# Stages of CKD

GFR (mL/min per  
1.73 m<sup>2</sup> body  
surface area)

Stage	Description	
1	Kidney damage* with normal or increased GFR	≥90
2	Kidney damage* with mildly decreased GFR	60–89
3	Moderately decreased GFR	30–59
4	Severely decreased GFR	15–29
5	ESKD	<15 or dialysis

GFR = glomerular filtration rate

\*Kidney damage defined as abnormalities on pathologic, urine, blood, or imaging tests.

ADA. VI. Prevention, Management of Complications. *Diabetes Care* 2013;36(suppl 1):S35-S36; Table 12.



# Management of CKD in Diabetes

## GFR

## Recommended

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All patients

Yearly measurement of creatinine, urinary albumin excretion, potassium

45-60

Referral to nephrology if possibility for nondiabetic kidney disease exists

Consider dose adjustment of medications

Monitor eGFR every 6 months

Monitor electrolytes, bicarbonate, hemoglobin, calcium, phosphorus, parathyroid hormone at least yearly

Assure vitamin D sufficiency

Consider bone density testing

Referral for dietary counselling



# Management of CKD in Diabetes

GFR

Recommended

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30-44

Monitor eGFR every 3 months

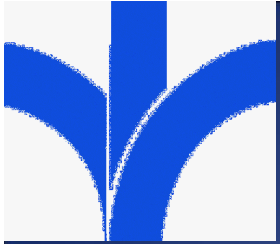
Monitor electrolytes, bicarbonate, calcium, phosphorus, parathyroid hormone, hemoglobin, albumin

weight every 3–6 months

Consider need for dose adjustment of medications

<30

Referral to nephrologist

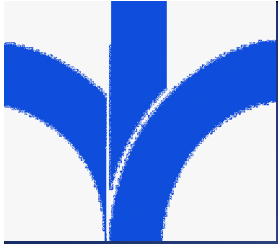


Is the renal impairment due to  
diabetes?



## Less likely if...

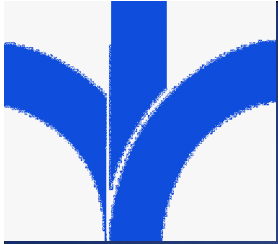
- There is no significant or progressive retinopathy
- Blood pressure is particularly high or resistant to treatment
- The person previously had a documented normal ACR and develops heavy proteinuria (ACR > 100 mg/mmol)
- Significant haematuria is present
- Glomerular filtration rate has worsened rapidly
- The person is systemically ill



# Microalbuminuria

Definition, issues and controversies





## True or False

Microalbuminuria differs from proteinuria in that it refers to small-sized albumin being excreted than large-sized albumin excreted in proteinuria

False

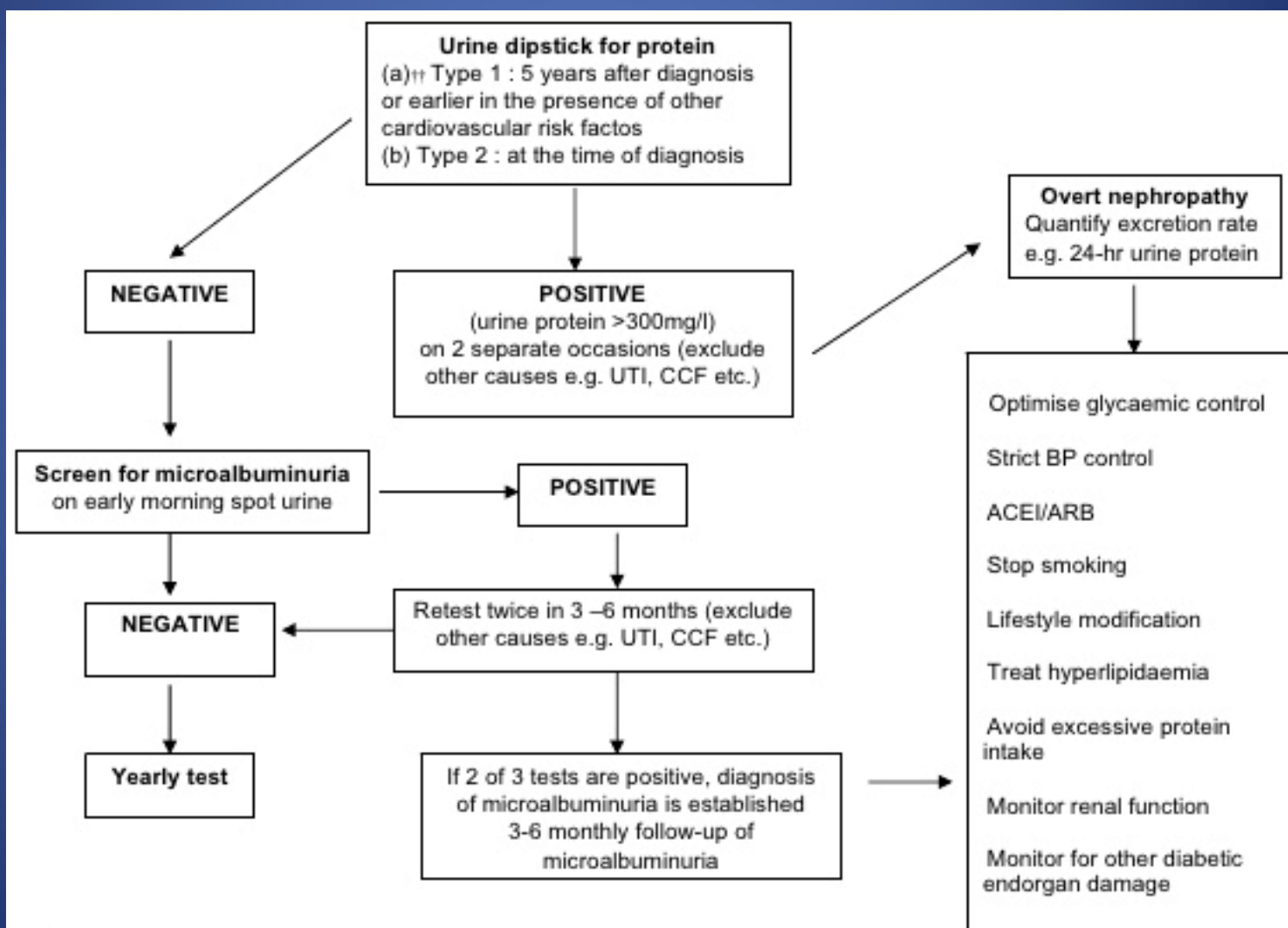


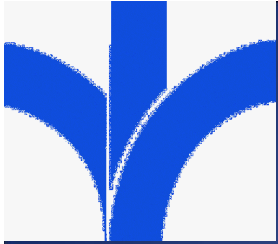
# More definitions...

- Microalbuminuria: Dipstick negative proteinuria
- Proteinuria: Dipstick positive proteinuria
- Microalbuminuria
  - $\geq 2.5$ mg/mmol in males\*
  - $\geq 3.5$ mg/mmol in females\*

\*In 2 out of 3 samples

# Screening





## True or False

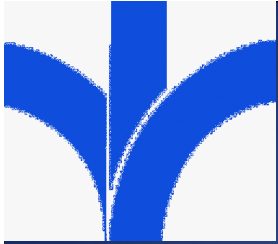
Urinary ACR is commonly elevated at diagnosis of diabetes if significant hyperglycaemia present

True

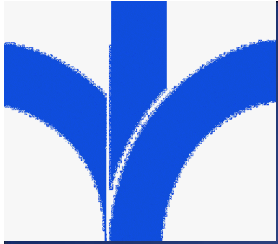


# False positive “microalbuminuria”

- Strenuous exercise
- Menstruation
- Uncontrolled hyperglycaemia
- Uncontrolled hypertension
- UTI
- Sepsis with pyrexia
- CCF



# Metformin and CKD



## True or False

It is exceptionally rare for metformin to cause lactic acidosis in the absence of an underlying predisposing disease

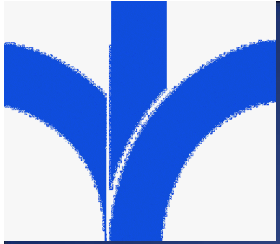
True



# Metformin and CKD

- Guidelines
  - eGFR > 60 ml/min – no dose change
  - eGFR < 30 ml/min – discontinue
  - eGFR 30-45 or 60 ml/min – half dose (500mg bd)
- Often see significant deterioration in glycaemic control following d/c so clinical judgement required



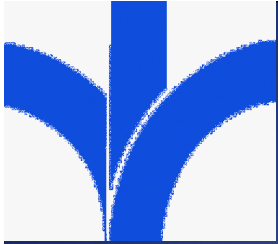


# BP control in diabetic CKD



## What is target BP in T2DM with proteinuric CKD?

- <140/80
- <130/80
- <125/75
  
- <130/80 (probably!)



## True or False

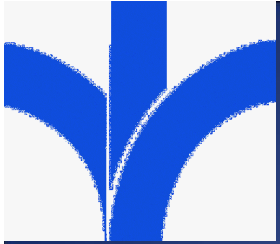
ACE-/ARB therapy should be instigated in normotensive normoalbuminuric patients with T2DM to prevent the onset of microalbuminuria

False

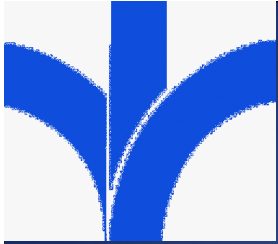


## ACE- or ARB?

- ACE-/ARB is 1<sup>st</sup> line therapy in hypertension in T2DM
- ACE- and ARBs likely equivalent in T2DM
- Combination use may be harmful
- RAAS system blockade slows development of microalbuminuria in hypertensive (but not normotensive) T2DM



# Glycaemic control in diabetic CKD



# True or False

Tight glycaemic control prevents progression to  
ESKD

False



# Glycaemic control in T2DM

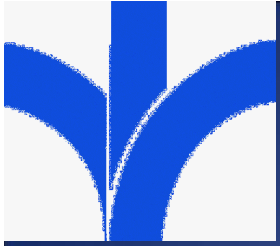
- Tight glycaemic control reduces development and progression of micro- and macro-albuminuria but not development of ESKD or renal deaths
- Possible exception is ADVANCE trial with glicazide but post-hoc analysis, NNT of 445 for 5 years to prevent one case of ESKD, and findings not reproduced elsewhere
- Reasonable to target HbA1c <48 at diagnosis, but as risk of hypoglycaemia and co-existent vascular morbidities emerge, reduce to 53mmol/mol



# Issues

- HbA1c
  - Targets in this patient
  - Suitability of metformin
- BP
  - ? Sufficient control
  - ? Correct agents
- Renal impairment
  - ? Severity
  - ? Action to be taken





# Renal Impairment

- eGFR 41ml/min = Stage 3
- ACR 22 = Microalbuminuria



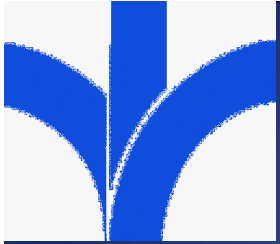
# HbA1c

- Consider reducing metformin
- Subsequent deterioration in glycaemic control may need additional agent
  - ? Consider incretin
- Target HbA1c 53 if can be achieved without hypoglycaemia



# BP

- 145/88 too high and if confirmed on repeat (and no postural symptoms), consider adding diuretic (thiazide vs. frusemide) or beta-blocker
- Remember ACDB, but the main thing is get the BP down!

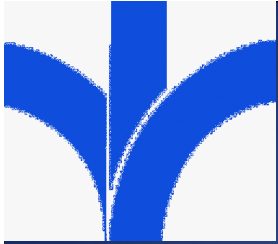


In 2010/2011 in the UK, 25% of individuals with diabetes didn't have urinary ACR measured



# Take home messages

- Classify into CKD stage
- Check urinary ACR (and know how to confirm)
- Optimise BP (and glycaemic) control



Thank you

Questions