

Preventing Dialysis in Diabetes

Microalbumin, BP and more!

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Classical Natural History

- ▶ Normal for 10 years
- ▶ Microalbuminuria for 5 years
 - ...with elevated blood pressure
- ▶ Proteinuria for 3-5 years
 - ...with rising serum creatinine
- ▶ End-stage renal failure
 - ...renal replacement therapy
 - ...death due to vascular event (MI or stroke)

Burden of Nephropathy

- ▶ Affected 40% people with Type 1 diabetes
 - ...and 30% of those with Type 2 diabetes
- ▶ Leading cause of death <50y in Type 1 diabetes
- ▶ Leading cause of ESRD in many countries
 - ...commonest reason to start dialysis in USA!
- ▶ Huge burden of morbidity for patients
- ▶ Huge financial burden for healthcare systems

Natural History 2011

- ▶ Normal for 10 years (or even more)
- ▶ Microalbuminuria detected
 - ...ACEI or ARB started early
 - ...BP brought to target (130/70 or lower!)
- ▶ ...microalbuminuria stabilised/abolished
- ▶ ...minimal decline in renal function
- ▶ **END OF STORY!**

Microalbuminuria

- ▶ Best detector of early possible problem
 - Nephropathy in Type 1 diabetes
 - Vascular and/or renal disease in Type 2 DM
- ▶ First morning samples, when well, best
 - Exercise (and illness) can elevate microalbumin
- ▶ Day-to-day variation ++
 - Always confirm with a second (or third) sample
- ▶ Albumin:creatinine ratio preferred

Microalbuminuria Screening

- ▶ Annual assessment sufficient if normal
 - Repeat sample if abnormal
- ▶ 4-6 monthly testing if proven abnormal
 - ...aiming to optimise BP control
- ▶ Should stabilise if BP control good
 - Reversal to normal levels possible
 - Consider other diagnoses if not stabilised

Microalbuminuria Intervention

- ▶ Improve glycaemic control
 - Still of benefit at this stage (kidneys and more!)
- ▶ Vigorous BP management
 - ACEI first-line (ARB if not tolerated)
 - Add other drugs as required to achieve target
 - Target 130/70 or lower to stabilise microalbumin
- ▶ Manage other CVS risk factors (esp T2DM)
- ▶ If rising despite achieving BP targets – refer!
- ▶ Identical approach if overt proteinuria

ACEI and ARB

- ▶ Greater effect on proteinuria than BP reduction would predict
- ▶ Probably due to effects on intra-glomerular pressure
 - ?also anti-inflammatory/anti-proliferative?
- ▶ Usually only part of a 2-4 drug regimen
- ▶ Not without problems
 - Hyperkalaemia
 - Reno-vascular disease

Choosing Your Medicine!

- ▶ Different evidence levels for individual medicines
 - ...but clear evidence of 'class effects'
- ▶ Use evidence to guide your choice of medicine class
 - ...then use the cheapest medicine(s) in the class
- ▶ Save expensive medicines for failures
 - ...or add a second/third cheap medicine

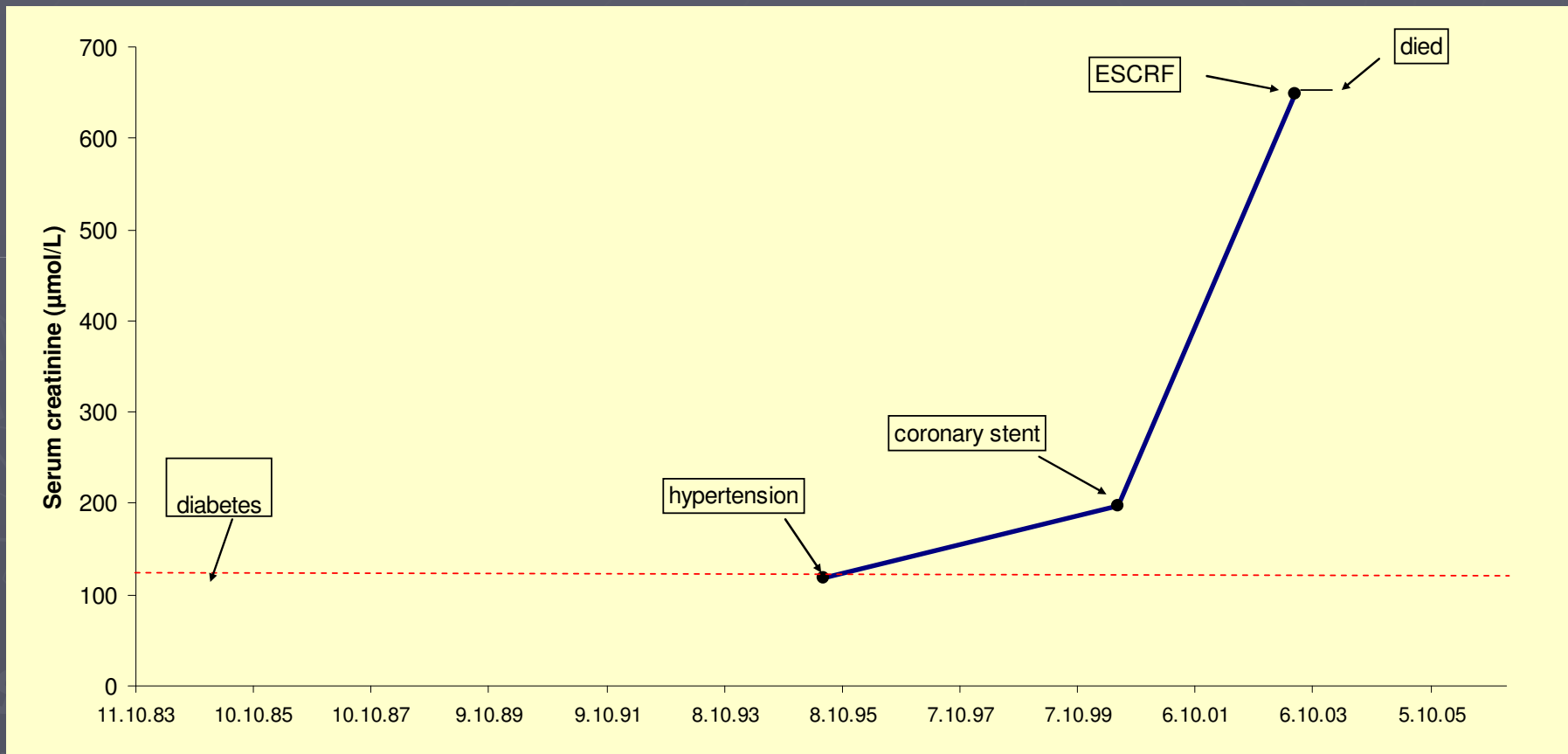
Impact of Intervention

- ▶ Once proteinuria present -
 - No intervention - GFR falls by 1ml/min/month
 - ESRD in ~7 years
 - With intervention - GFR falls by 0.1ml/min/month
 - ESRD in ~70 years
 - Effectively solves the problem of ESRD!

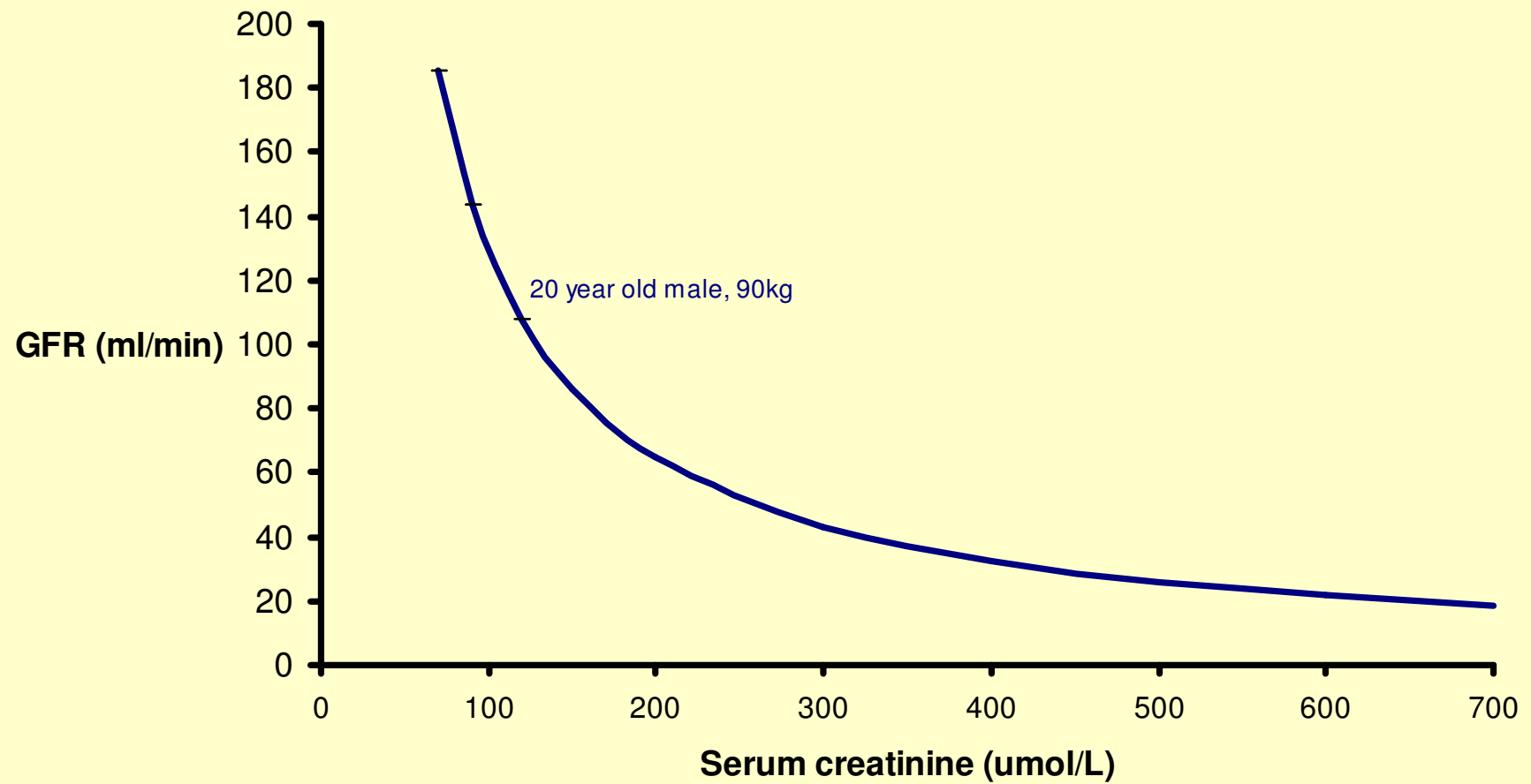
Case History

- ▶ 54 year old male – previously well
 - October 1983 – T2DM – creatinine 100 $\mu\text{mol/l}$
 - 1995 – hypertension – creatinine 125 $\mu\text{mol/l}$
 - 2001 – PTCA/stent – creatinine 187 $\mu\text{mol/l}$
 - 2002 – lethargy – creatinine 689 $\mu\text{mol/l}$
 - Commenced dialysis
 - Died 8 months later from acute MI
 - ...it was all so sudden!!

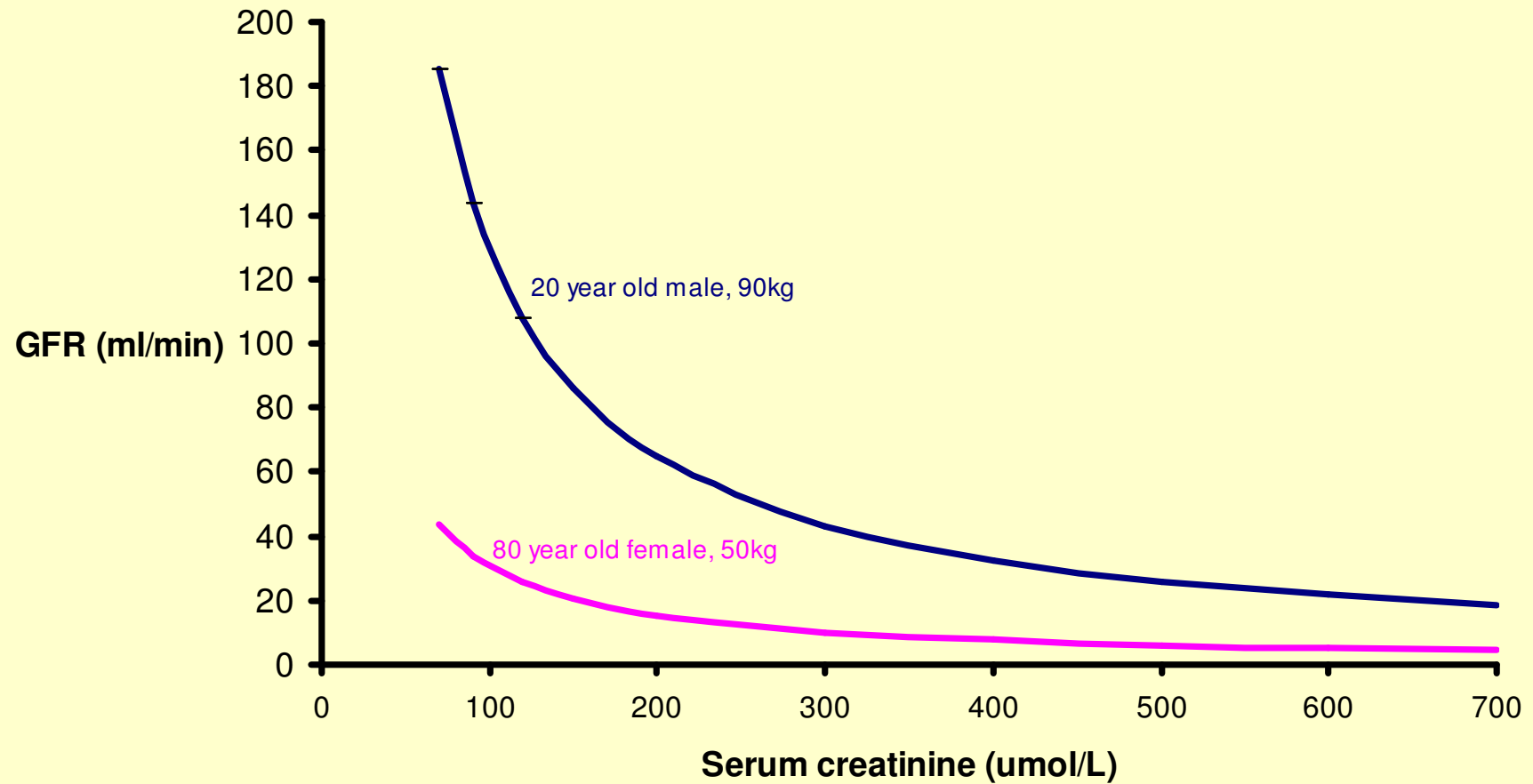
Serum Creatinine v Time



Serum Creatinine v GFR



Serum Creatinine v GFR

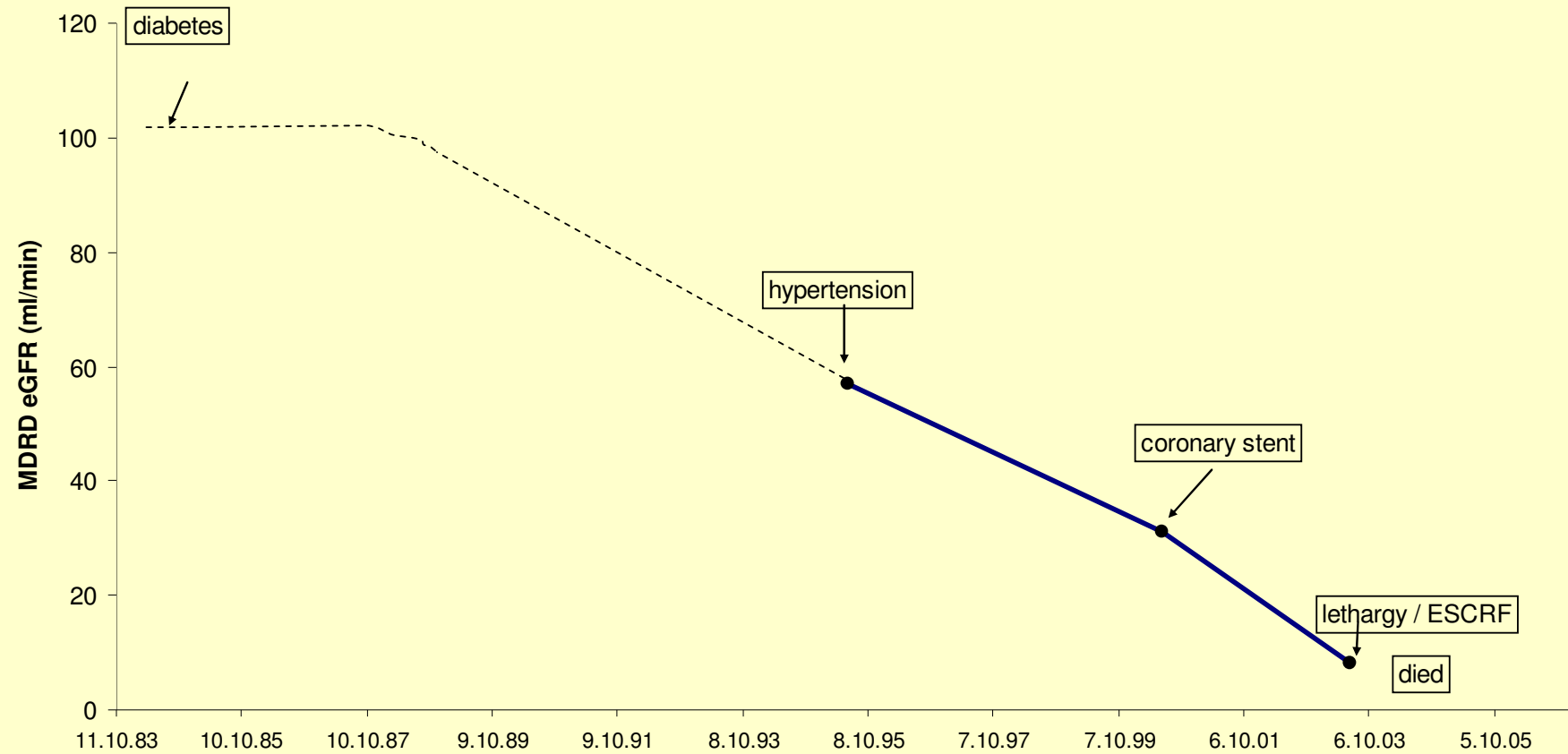


The MDRD 4-Variable Formula

$$\text{eGFR} = 186.3 \times \text{SCr}^{-1.154} \times \text{age}^{-0.203} \\ \times 0.742 \text{ (if female)} \times 1.212 \text{ (if black)}$$

Does NOT take account of body weight or muscle mass

eGFR v Time



eGFR Benefits (...but)

- ▶ Can detect loss of renal function early
 - ...and permit earlier intervention
- ▶ Should avoid 'surprise' severe disease
 - ...too late for useful preventive intervention
- ▶ Takes account of effects of age
- ▶ Easily calculated from readily available data
- ▶ **BUT**
- ▶ Not suitable for drug dosage adjustment
 - Needs calculated creatinine clearance

eGFR

- ▶ Pay attention to results and to **TRENDS**
- ▶ Remember non-diabetic renal disease
 - Obstruction
 - Reno-vascular disease
 - Haematuria/no albuminuria warning signs
- ▶ Remember that ACEI/ARB may reduce eGFR by up to 15% when first started
 - ...but clear long-term benefits
- ▶ Remember limitations

Conclusions

- ▶ Microalbuminuria is still the best early predictor of renal problems
 - Treat it aggressively and save lives!
- ▶ Monitor eGFR and pay attention to trends
 - Refer patients early if continuing decline
- ▶ Interventions are safe and highly effective
- ▶ Screening and interventions are cheap
 - Highly cost-effective use of resources
 - Highly effective way to improve patient health

Always Follow the Guideline!

