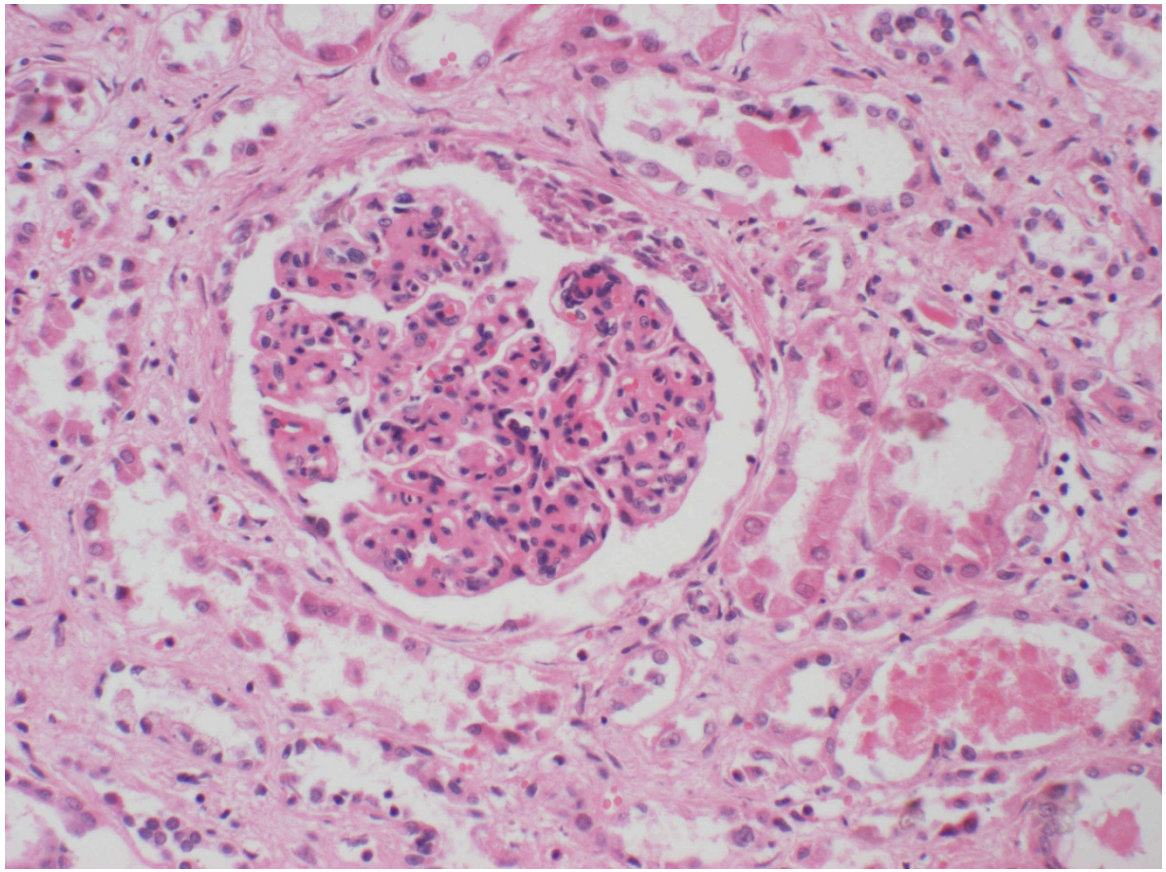
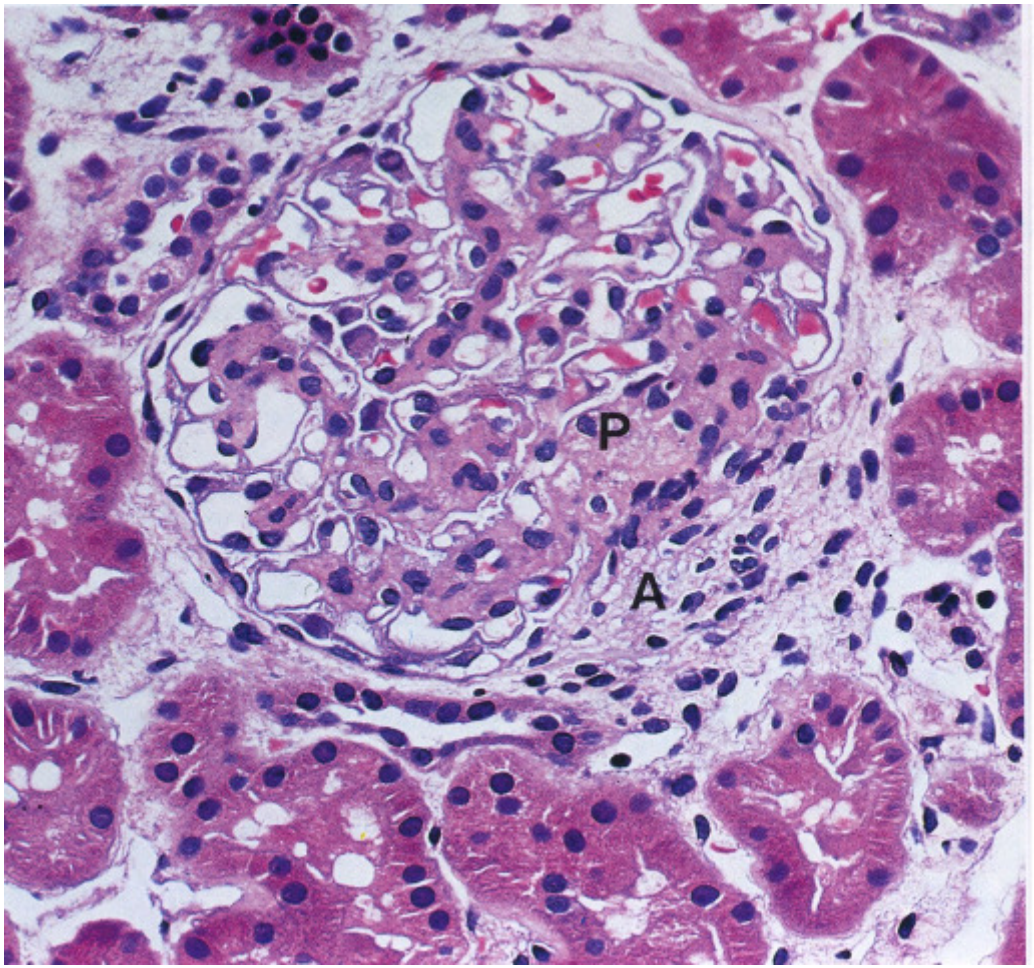
3. Diabetic nephropathy

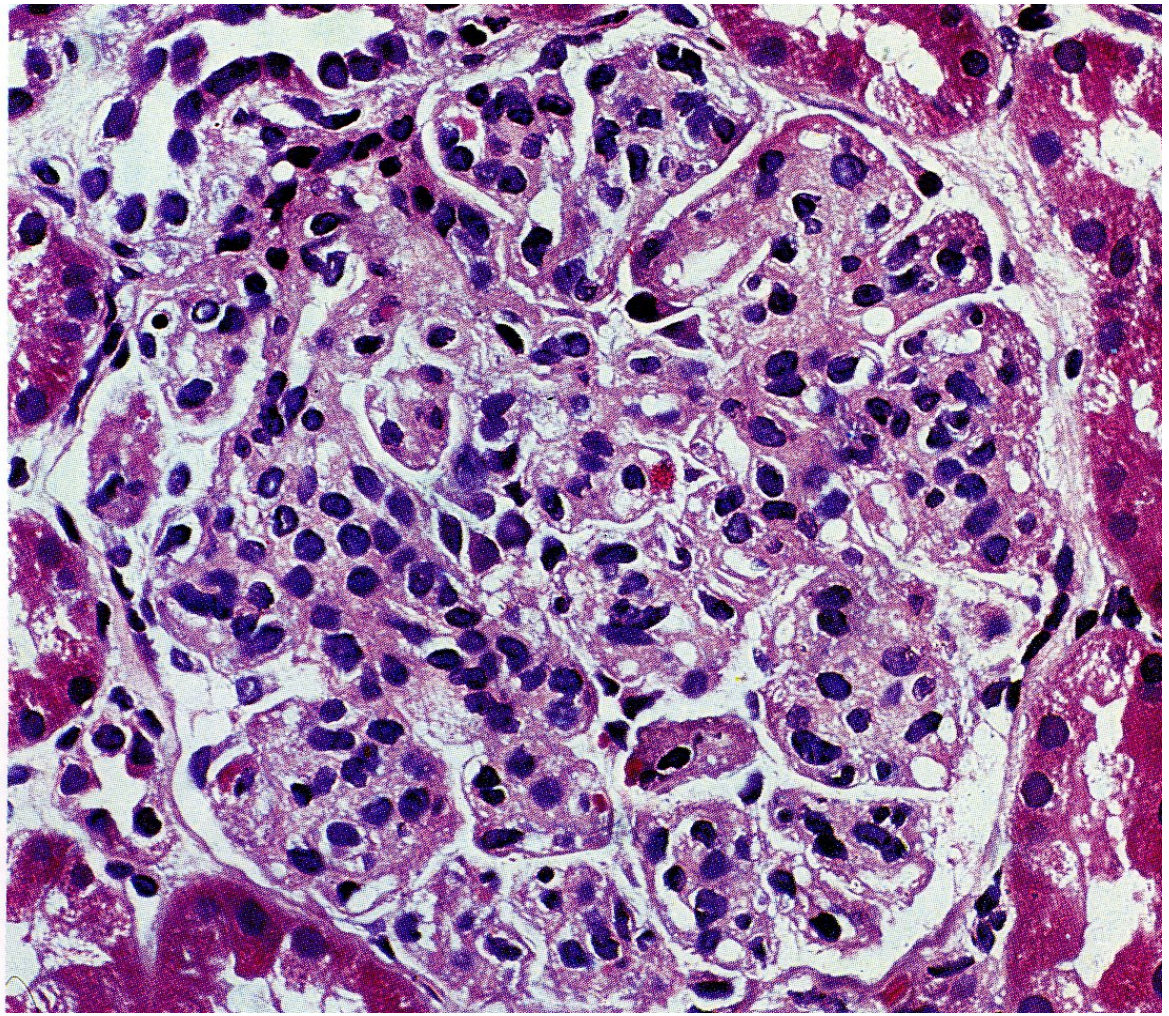
What the renal corpuscle should look like!



Diabetic Glomerulosclerosis
Proliferation of mesangial cells and acellular mesangial tissues.



Diabetic Glomerulosclerosis
Mesangial and endothelial cell proliferation

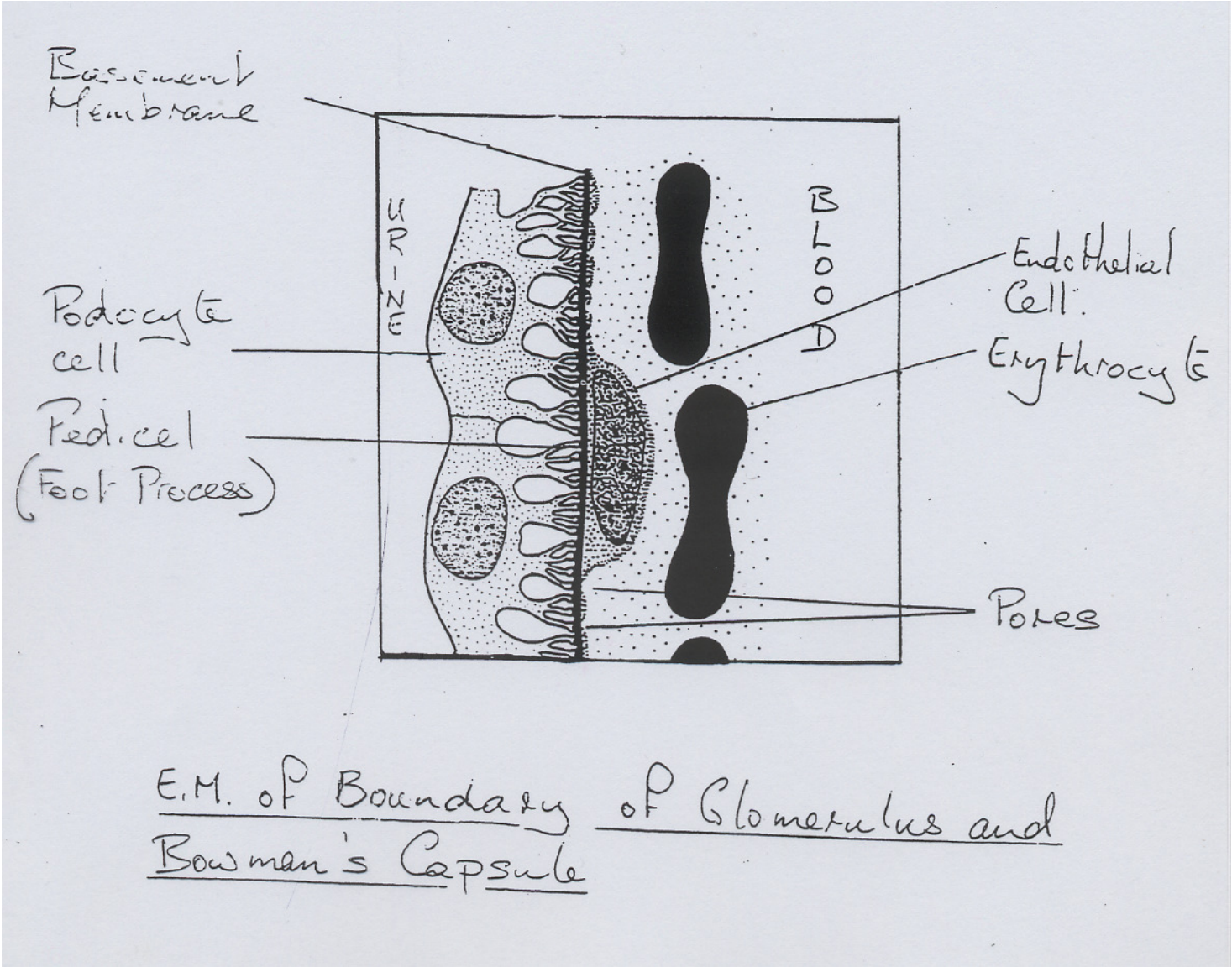


Diabetic Nephropathy and Albuminuria.

1. Hyperfiltration
2. Microalbuminuria (albuminuria 30-300mg/day)
3. Overt nephropathy (albuminuria >300mg/day)
   - Relentless decline in renal function (untreated 1ml/min/month)
     - Hypertension
     - Increase in CVD
4. End stage renal failure

What histological and physiological changes occur?

- Glomerulosclerosis
- People with diabetes have increased predisposition to renal infections (more glucose in urine) and papillary necrosis
- Arterial hypertension – leads to formation of hyaline layer in afferent arterioles – narrows lumen – increase BP.



E.M. of Boundary of Glomerulus and Bowman's Capsule

Podocyte injury

- It is likely that damage to the glomerular capillaries and the podocyte lead to glomerulosclerosis.

Micro-vascular disease

- Many people with diabetes develop both retinopathy and nephropathy
- Similar damage has been reported in both the retinal capillaries and the glomerular capillaries.
- Damage to the glomerular fenestrations and podocytes reduces glomerular filtration and allows protein to appear in the urine
- Reduced GFR and proteinurea are signs of nephropathy

Nephropathy and CV complcations

- Hypertension and proteinuria lead to progressive loss of functional renal tissue, and ultimately end stage renal failure.
- Collins et al. (2005) argue most people with chronic renal disease die of CV complications because the nephropathy exacerbates other CV conditions.
- **As kidney fails, BP is increased in an attempt to maintain GFR.**

Albumin in urine

- Macroalbuminuria
- Over 300 mg/litre of urine

  (0ver 300 mg excreted per day)

- Micoabuminuria
- Under 300 mg/litre or urine

  (between 30 and 300 mg excreted per day)

Overt nephropathy

Part of annual check up

- Within the NHS an assessment of microabuminuria has been introduced as part of the annual check up for all patients who do not prove positive for proteinuria with a 'dipstick’

Screening for albuminuria

- Most convenient test is ACR
- Early morning urine preferred
- Normal range is:
  - <2.5 mg/mmol (male)
  - <3.5 mg/mmol (female)
- Exclude UTI, fever, heavy exertion
- If normal repeat at 1 year

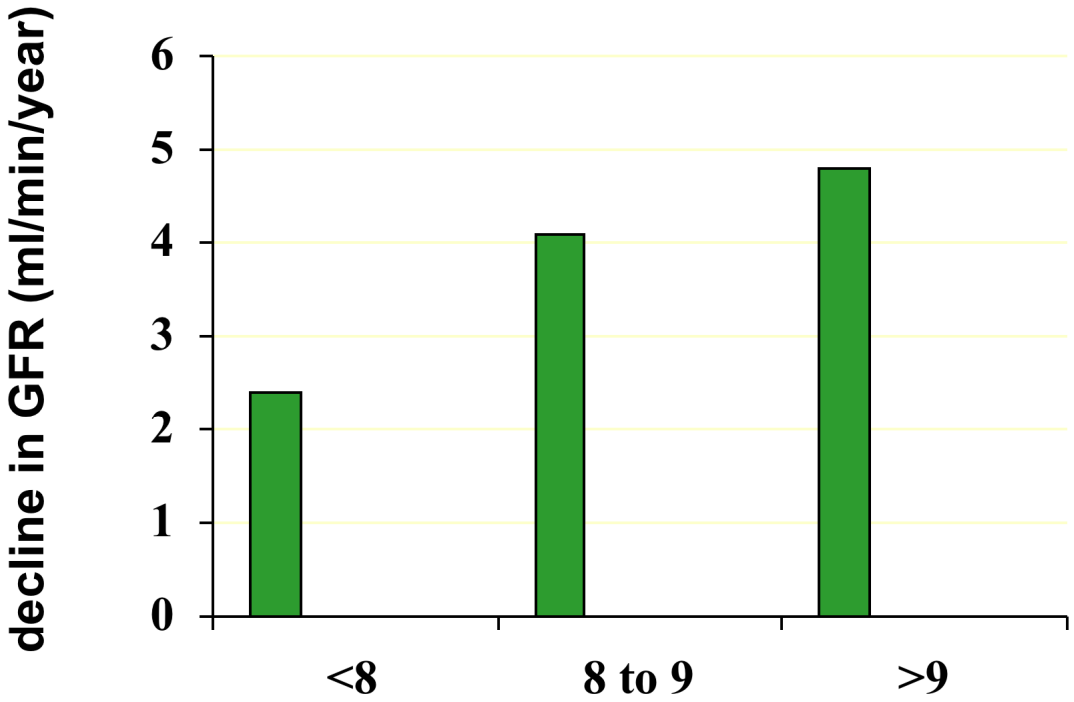
Stages of Kidney disease related to GFR

- Stage 1: Normal GFR > 90 ml/min
- Stage 2: Early CKD GFR 60-89 ml/min
- Stage 3: Moderate CKD GFR 30-59 ml/min
- Stage 4: Severe CKD GFR 15-29 ml/min
- Stage 5: End-stage renal disease GFR below 15ml/min

What can be done?

- Prevent people developing type 2 DM (targeting high risk groups – lifestyle modification)
- Prevent diabetic patients developing microalbuminuria
- Prevent microalbuminuric patients developing overt nephropathy
- Slow progression of diabetic nephropathy
- Cardiovascular risk factor management

Glycosylated Haemoglobin and Control



Mulec NDT 1998

Diabetic Nephropathy: Cardiovascular Disease

- Cardiovascular disease is the commonest cause of death in people with diabetes
- The presence of proteinuria increases the risk substantially
- Up to 70% of deaths in patients with diabetic nephropathy – vascular disease

Cardiovascular Protection

- Glycaemic control
  - UKPDS – intensive (HbA1c 7.0%) vs conventional (HbA1c 7.9%)
  - For each 1% reduction in HbA1c – 21% reduction in deaths related to DM
    - 12% reduction in any endpoint related to diabetes
    - 25% reduction in microvascular disease
  - Metformin offered greater protection

Sign 116

9	**Management of kidney disease in diabetes**
	9.3 SCREENING FOR KIDNEY DISEASE IN DIABETES
B	ACR should be used to screen for diabetic kidney disease.
C	Young people with diabetes should have ACR tested annually from the age of 12 years.
	9.5 PREVENTION AND TREATMENT OF KIDNEY DISEASE IN DIABETES
A	Intensive glycaemic control in people with type 1 and 2 diabetes should be maintained to reduce th risk of developing diabetic kidney disease.
A*	Reducing proteinuria should be a treatment target regardless of baseline urinary protein excretion However, patients with higher degrees of proteinuria benefit more. There should be no lower targe as the greater the reduction from baseline urinary protein excretion, the greater the effect on slowing the rate of loss of GFR.
A*	In people with diabetes and kidney disease, blood pressure should be reduced to the lowest achievable level to slow the rate of decline of glomerular filtration rate and reduce proteinuria.
A*	People with type 1 diabetes and microalbuminuria should be treated with an ACE inhibitor irrespective of blood pressure.
A*	People with type 2 diabetes and microalbuminuria should be treated with an ACE inhibitor or an ARB irrespective of blood pressure.
A*	ACE inhibitors and/or ARBs should be used as agents of choice in patients with chronic kidney disease and proteinuria *(≥0.5 g/day, approximately equivalent to a protein/creatinine ratio of 50 mg/mmol)* to reduce the rate of progression of chronic kidney disease.
A	Dietary protein restrictions (*<0.8 g/kg/day*) are not recommended in patients with early stages of chronic kidney disease (*stages 1-3*).
B	People with diabetes and microalbuminuria should be treated with a multifactorial intervention approach.
	9.6 MANAGEMENT OF COMPLICATIONS
D	Patients with diabetes and CKD stage 3-5 should have their haemoglobin checked at least annually
A	Erythropoiesis stimulating agents should be considered in all patients with anaemia of chronic kidney disease, including those with diabetic kidney disease.
D	Individuals with diabetes and mild to moderate CKD should be managed in a setting that can provide appropriate investigation, monitoring and intensive clinical management.

Conclusions for diabetic nephropathy

- Diabetic nephropathy is common
  - Renal aspect
  - Cardiovascular aspect

- These patients are high risk individuals

Conclusions for diabetic nephropathy (continued)

- Patients with diabetes – must identify microalbuminuria early - SCREEN urine
- When there are early warning signs of high risk individuals - advocate
  - Good glycaemic control
  - Control BP
  - Use of ACE inhibitors
  - Encourage healthy lifestyle – diet, exercise, stop smoking

Conclusions for diabetic nephropathy (continued)

- Diabetic renal disease – overt nephropathy
  - Intensively manage BP, lipids, glycaemic control, stop smoking
  - Use of ACE inhibitors and ARBs
  - Promote healthy lifestyle – exercise and healthy eating
  - Sodium restriction (urinary <150mmol/day)
  - Consider protein restriction

4. Skin disorders

Acanthrosis nigrans

in *diabetes mellitus*

High levels of insulin cause the skin to become discolored and velvety in texture, a condition called acanthrosis nigricans. This is common in people with darker skin who have type 2 diabetes, including African Americans, Native Americans, and people of Hispanic origin. Acanthrosis nigricans "is a thickening and a darkening of the skin, typically around the neck, in the underarms, and in the groin," adds Einhorn. "It's quite a specific indicator of insulin resistance --. It is definitely a warning sign---"

5. Depression

- Many people with diabetes suffer additionally because of depression.
- Depression appears to increase the risk of developing severe complications

Lin et al. (2010), *Diabetes Care.*

6. Pregnancy related complications

St. Vincent Declaration

‘Achieve pregnancy outcome in the diabetic woman that approximates that of the non-diabetic woman’

Have We Succeeded?

- Congenital malformation rate 4-10 fold higher.
- Perinatal mortality rate 4-7 fold higher.
- Stillbirth 5 times more common.
- Babies 3 times more likely to die in the first 3 months of life.
- Maternal Mortality Rate 0.1-0.5% compared to 0.01% for a non-diabetic mother

Diabetes should be regarded as teratogenic

With thanks to Andy Gallagher

Diabetes and pregnancy

Basic potential problems if mother has diabetes:

- Maternal blood has high glucose level therefore foetus will grow too fast and hence macrosomia.

- If baby is delivered after receiving high glucose levels via the placenta, (s)he is faced with a sudden drop in glucose in his/her body.

What should be done.

1. Pre-pregnancy counselling

- Discussion of risks and proposed management strategy
- Diet & lifestyle advice
- Smoking cessation
- Assessment and management of diabetes complications
- Good glycaemic control
- BP control
- Folic acid to be taken

What should be done

2. Management during pregnancy

- Regular check-ups – every two weeks until 30 weeks then weekly
- Fundoscopy each trimester
- Ultrasound 18-20 weeks
- Plan labour

7. Erectile Dysfunction

(with thanks to John MacCoid)

Be proactive when a man presents with ED. Use comments such as , many men with diabetes discover they experience problems with having an erection. If you ever experience that problem let me know as there are a number of avenues we can explore.

Many people with SD still aren't talking to their physician

- 38% of men had never talked to a physician about their SD

- Of those men who had spoken to their physician, 86% initiated the conversation themselves

Where are the women ?

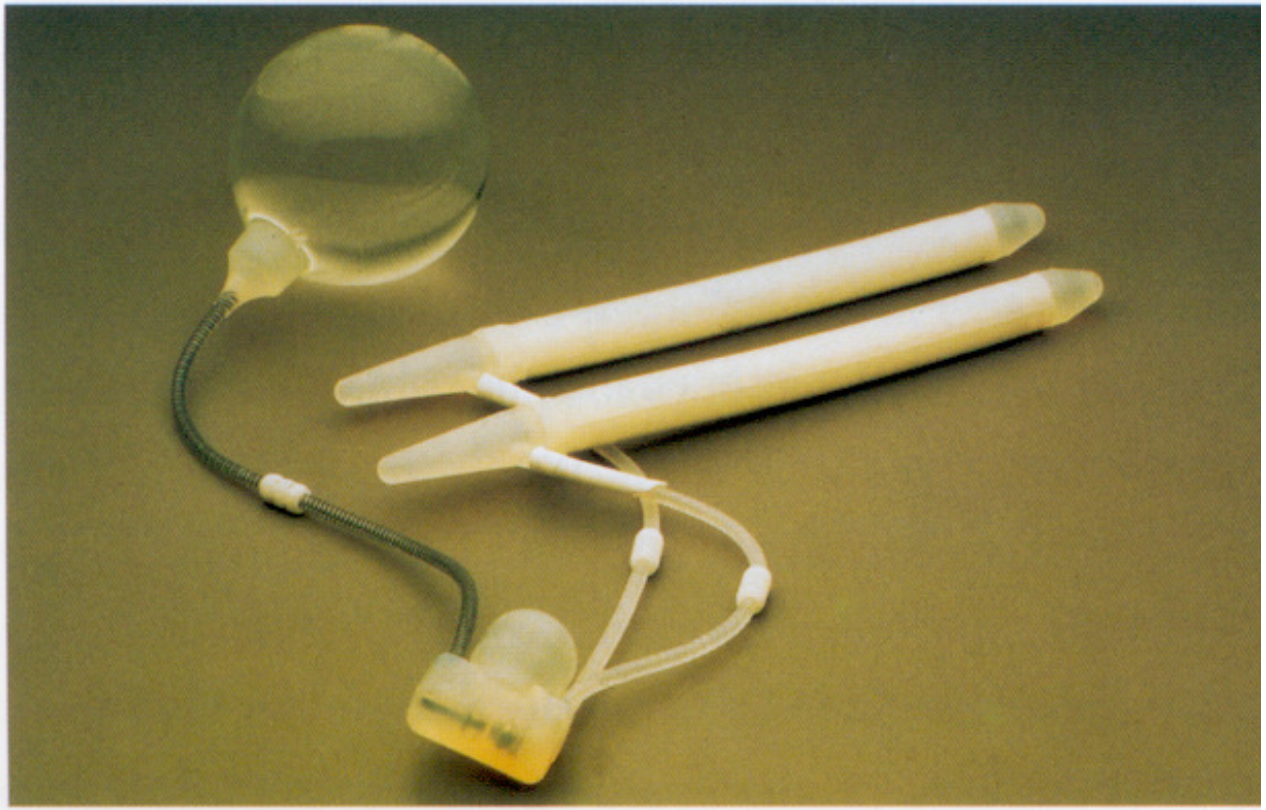
Ipsos Survey 2008.http://www.menshealthnetwork.org/library/EDsurvey2008.pdf

Treatments available

- Oral – Viagra, Cialis, Levitra
- Intra-urethral – Medicated Urethral System for Erection (MUSE)
- Intra-cavernosal – Caverject

The above are the brand names

Vacuum Erection Devices



Inflatable
Penile
Prosthesis

To think about over lunch!

The devil has put a penalty on all things we enjoy in life. Either we suffer in health or we suffer in soul, or we get fat!

- *Albert Einstein (1879 – 1955)*

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Cheers !

Thank you for your attention

Any questions?

Please email me (F.W.Young@gcu.ac.uk) if you do not understand anything or think of something you need to clarify but remember I am part-time.