

# Systemic Disease Affecting The Kidney

# Diseases Causing ....

- ▶ Nephrotic syndrome
- ▶ Acute glomerulonephritis  
(acute nephritic syndrome)
- ▶ Rapidly progressive glomerulonephritis (RPGN)
- ▶ Asymptomatic haematuria, proteinuria or both

# Systemic Diseases Causing Nephrotic Syndrome

## ► With bland urinary sediment

Diabetic nephropathy

Amyloidosis

## ► With active urinary sediment

SLE

Henoch-Schonlein syndrome (HSP)

Cryoglobulinaemia

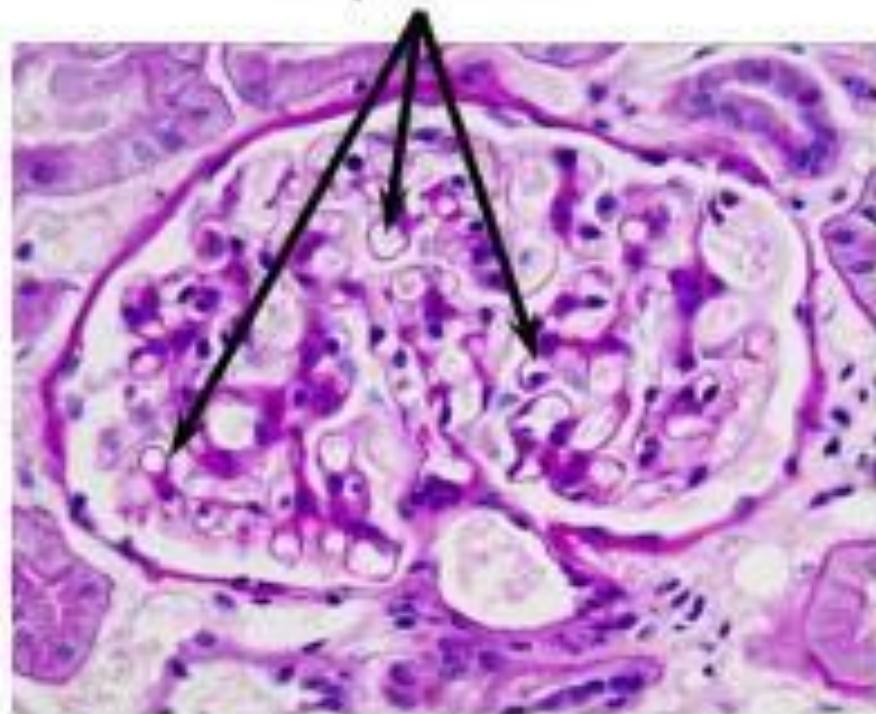
# Diabetic Nephropathy - Epidemiology

- ▶ Most common cause of ESKD world-wide
- ▶ Manifests 15-25 yrs after diagnosis of DM
- ▶ Type I → affects 25-35% of patients  
Type II → affects 20-40% of patients
- ▶ Onset & course can be altered by various interventions, sp if instituted early

# Diabetic Nephropathy - Pathophysiology

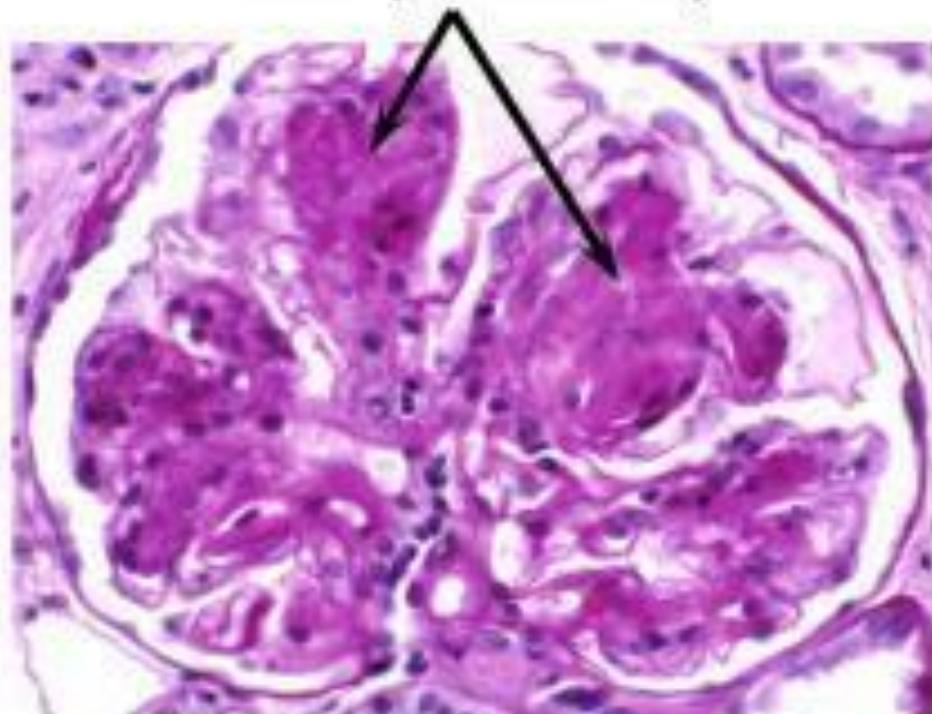
- ▶ Initially **Microalbuminuria** - urinary albumin which is undetected by dipstick testing
- ▶ Progress to intermittent albuminuria → persistent proteinuria
- ▶ LM – diffuse glomerulosclerosis  
nodular glomerulosclerosis (Kimmelstiel-Wilson lesion)

### Normal glomerular capillaries



Microscopic photograph of a cross section of a **NORMAL GLOMERULUS** in a kidney biopsy specimen. The small capillaries that filter blood to make urine are open.

### Nodules of glomerular scar (sclerosis)



Microscopic photograph of a cross section of a glomerulus with **NODULAR DIABETIC GLOMERULOSCLEROSIS**. The small capillaries that filter blood are distorted or compressed by the nodular scarring (sclerosis).

# Microalbuminuria

- ▶ Initial sign of DM nephropathy
- ▶ Urinary albumin excretion **30-300 mg/day**

Spot sample **Albumin/Creatinine ratio -**

Male            2 - 20 mg/mmol

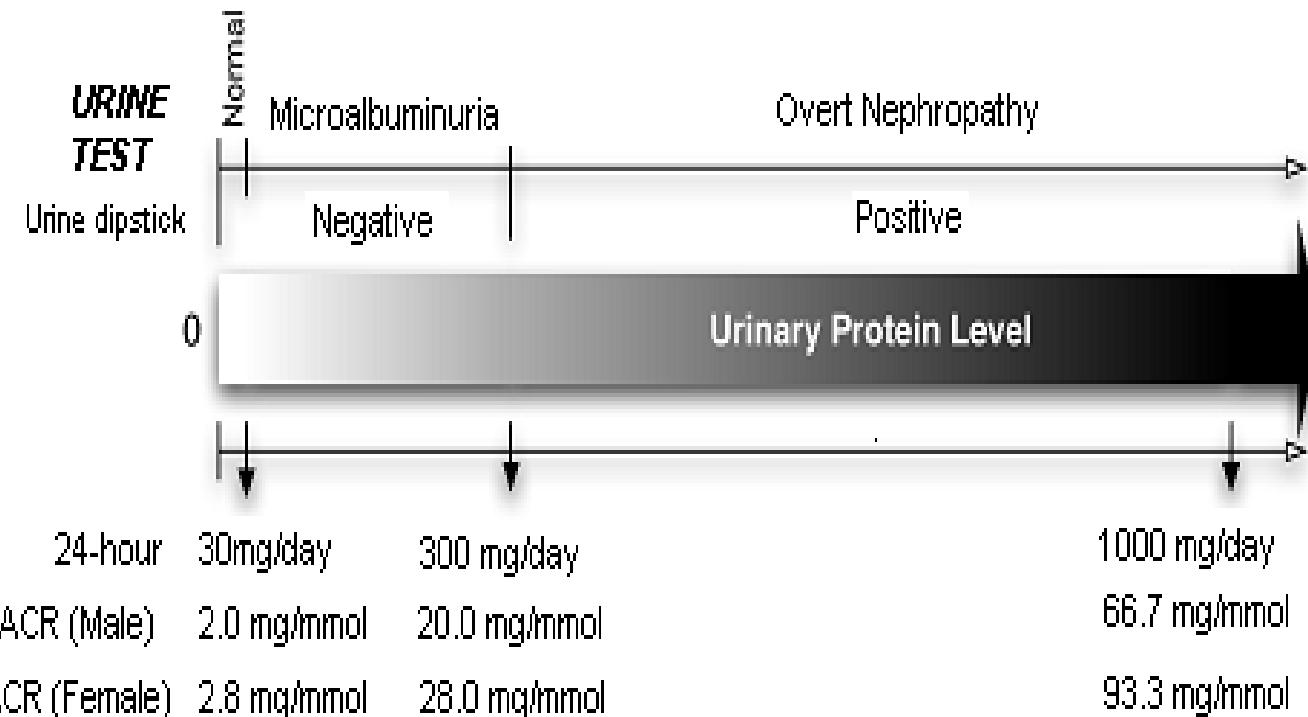
Female        2.8 - 28 mg/mmol

- ▶ Progress to overt nephropathy

# Macroalbuminuria

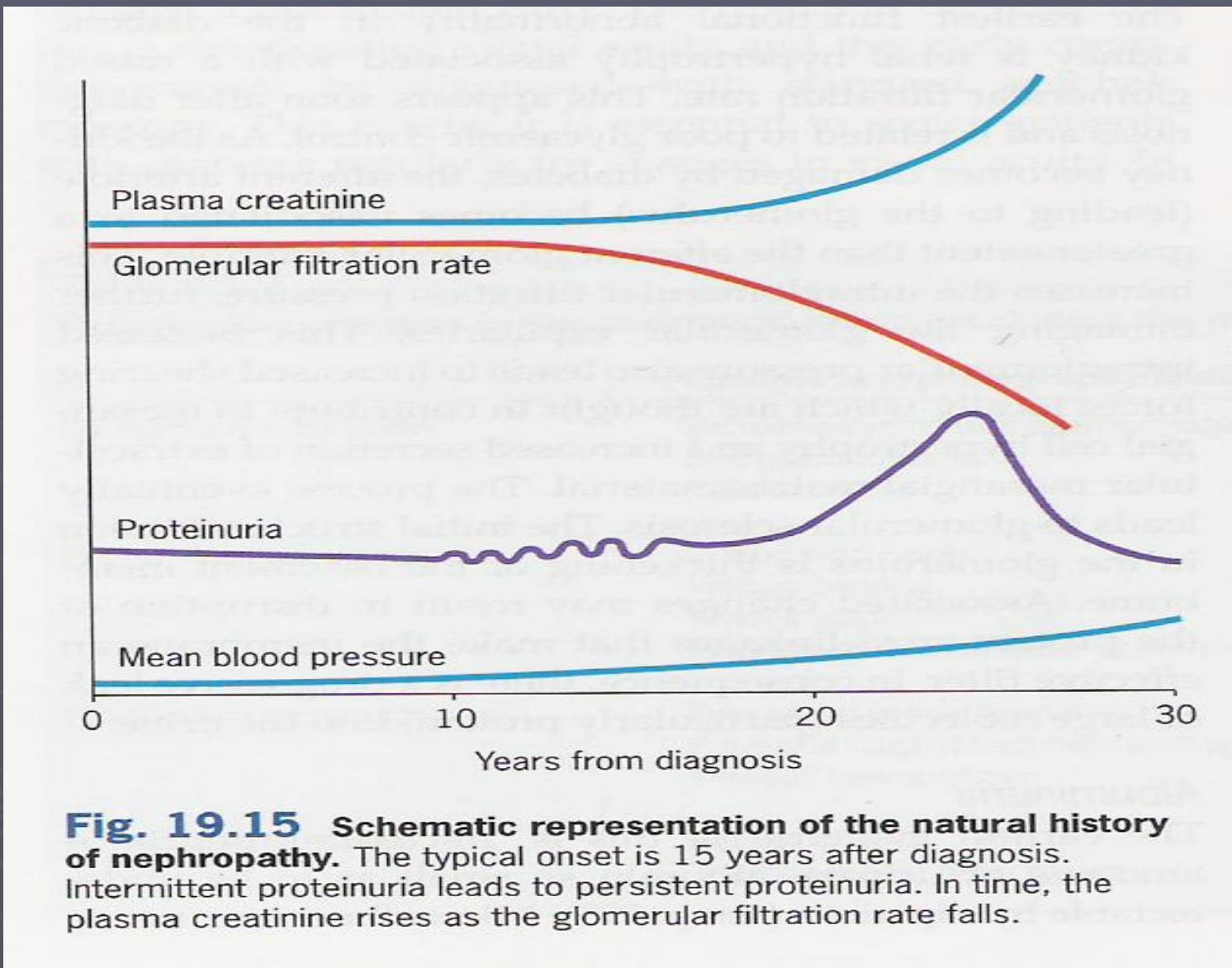
- ▶ Urinary albumin excretion **>300 mg/day**
- ▶ Overt nephropathy
- ▶ Once macroalbuminuria is present - creatinine clearance declines at a rate that varies widely from patient to patient  
(average reduction 10-12 ml/min/year if untreated)
- ▶ Hypertension and proteinuria accelerate decline in GFR and progression to ESKD

## STAGE OF NEPHROPATHY



ACR = albumin to creatinine ratio

# Diabetic Nephropathy – Natural History



**Fig. 19.15 Schematic representation of the natural history of nephropathy.** The typical onset is 15 years after diagnosis. Intermittent proteinuria leads to persistent proteinuria. In time, the plasma creatinine rises as the glomerular filtration rate falls.

# Diabetic Nephropathy – History

- ▶ Diabetes
- ▶ Passing frothy urine
- ▶ Otherwise unexplained proteinuria
- ▶ Diabetic retinopathy, neuropathy, etc
- ▶ Fatigue and foot oedema - if nephrotic syndrome is present
- ▶ Other associated disorders
  - ie - PVD, HPT, IHD

# Diabetic Nephropathy – Examination

## □ Features of long standing DM –

- Diabetic retinopathy
- Diabetic neuropathy

(decreased fine sensations, diminished tendon reflexes)

- Non-healing skin ulcers/osteomyelitis
- PVD

(decreased peripheral pulses, carotid bruits)

## □ Hypertension

# Diabetic Nephropathy – Diagnosis

- ▶ **Check annually for proteinuria**

random/early morning sample

- ▶ **If positive → exclude UTI**

Repeat on 2 occasion over next 3 months

Confirmed if positive on 2/3 occasions

# Suspect Non-diabetic Cause of Proteinuria if -

- ▶ No retinopathy or neuropathy
- ▶ Family h/o non-diabetic renal disease (PCKD)
- ▶ Short duration of DM
- ▶ Features of systemic disease
  
- ▶ Persistent haematuria
- ▶ Rapidly rising creatinine

# Diabetic Nephropathy – Management

► Avoid risk factors - long-term NSAIDs

► Aggressive treatment of hypertension

Slows rate of deterioration of renal failure

Target BP **130/80**

ACE Inhibitors or ARB — maximum tolerated doses

Can also be used if normotensive + persistent microalbuminuria

# Diabetic Nephropathy – Management

- ▶ Tight glycaemic control

Targets → HbA1c <6.5%, FBS 70-110 mg/dl

- ▶ Improve lipid profile

Targets (mg/dl) →      LDL <100, TG <150,  
                                  HDL >40 (males) & >50 (females)

- ▶ Intensify IHD protection

Aspirin, stop smoking, regular exercise

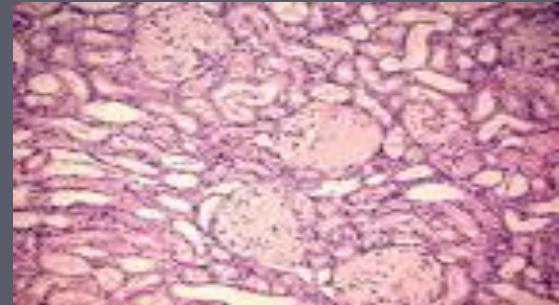
- ▶ Check proteinuria annually

- ▶ Check s.creatinine every 6 months

# Diabetic ESKD

- ▶ As renal function deteriorates insulin sensitivity increases → need insulin dose reduction
- ▶ Retinopathy also progresses rapidly → blindness
- ▶ Develop other complications of DM – autonomic neuropathy, PVD
- ▶ Dialysis (HD or PD) – infections, calcification
- ▶ Transplants – failure rates higher
- ▶ Future – pancreatic grafts

# Amyloidosis



- ▶ Disorder of protein metabolism  
Extra-cellular deposition of pathological insoluble fibrillar protein
- ▶ May be –
  - a) acquired - chronic infections, inflammation, myeloma
  - b) inherited
- ▶ Asymptomatic proteinuria  
Nephrotic syndrome  
Chronic kidney disease

# Amyloidosis

- ▶ Diagnosis made clinically when features of Amyloidosis are present elsewhere – heart failure, neuropathies, organomegaly, large tongue
- ▶ Imaging – large kidneys
- ▶ May need renal biopsy
- ▶ Treat underlying cause
- ▶ Progress to ESKD requiring dialysis



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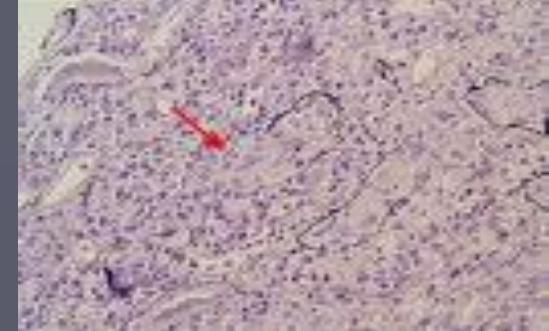
Cryoglobulinaemia

# SLE



- ▶ Auto-immune disorder with vasculitis
- ▶ Affects females more
- ▶ GN with Ag-Ab complexes – Ag is host DNA
- ▶ Can present as,
  - microscopic haematuria
  - proteinuria
  - nephrotic syndrome
  - acute nephritic syndrome
  - acute kidney injury
  - chronic kidney disease

# SLE



- ▶ Kidney most commonly involved organ
- ▶ Only 50% develop clinically evident renal disease  
But on renal biopsy - some degree of renal involvement in almost all
- ▶ Glomerular disease develops within first few years after onset  
Usually asymptomatic
- ▶ Acute nephritic disease – hypertension, haematuria
- ▶ Nephrotic syndrome - oedema, weight gain, hyperlipidemia
- ▶ Acute on chronic kidney disease – uremia & fluid overload symptoms

# Classification of Lupus Nephritis

- ▶ WHO Classification based on histology
- ▶ 25% change from one type to another during course of illness
- ▶ Better prognosis in Types I, II & V

<b>Class I</b>	<b>Minimal mesangial</b>	Normal LM Abnormal EM Asymptomatic
<b>Class II</b>	<b>Mesangial proliferative</b>	Hypercellular on LM Mild renal disease
<b>Class III</b>	<b>Focal proliferative</b>	<50% of glomeruli Haematuria & proteinuria
<b>Class IV</b>	<b>Diffuse proliferative</b>	>50% of glomeruli segmental or global NS, HPT, CKD
<b>Class V</b>	<b>Membranous</b>	Predominantly nephrotic disease Haematuria, HPT
<b>Class VI</b>	<b>Advanced sclerosing</b>	Chronic sclerosis Progressive CKD

# Lupus Nephritis - Investigations

- ▶ FBC, ESR, CRP
- ▶ ANA positive in almost all
- ▶ dsDNA positive in most
- ▶ Urine microscopy
- ▶ SE, BU & s.creatinine
- ▶ 24 hr urine protein
- ▶ Creatinine clearance
- ▶ Renal imaging
- ▶ Renal biopsy

# Lupus Nephritis - Management

- ▶ Induce remission with steroids & cyclophosphamide
- ▶ Maintain remission with azathioprine & mycophenolate mofetil
- ▶ Treat if – urine RBC or RBC casts  
impaired renal function  
deteriorating renal function
- ▶ Biopsy MUST pre-treatment
- ▶ Pregnancy –
  - HPT
  - premature delivery
  - rapid progression of renal lesion following delivery

# Henoch-Schonlein Syndrome (HSP)

- ▶ Syndrome of –
  - skin rash
  - abdominal colic
  - joint pains
  - GN
- ▶ Mainly in early childhood
- ▶ Men : Women = 2:1
- ▶ Recent infection (URTI)
- ▶ Mainly supportive treatment

# Henoch-Schonlein Purpura

- ▶ Typical skin rash



# Other Systemic Diseases Affecting the Kidney

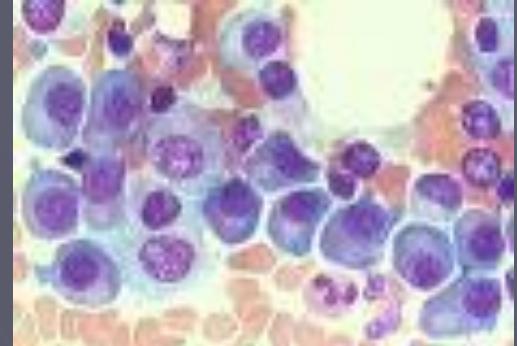
- ▶ Systemic Sclerosis
- ▶ Myeloma
- ▶ HUS
- ▶ Infections

# Systemic Sclerosis



- ▶ Multi-system disease of unknown cause
- ▶ Male:female = 3:1
- ▶ Peak incidence 30-50 yrs
- ▶ Limited to skin or diffuse (renal, gut, heart, lungs)
- ▶ Acute or chronic renal symptoms
- ▶ Acute hypertensive renal crisis may be fatal
- ▶ Drug of choice → ACE Inhibitors
- ▶ IV prostacycline

# Myeloma



- ▶ Acute kidney injury in 20-30%
- ▶ Cause renal impairment by many different mechanisms -
  1. Light chain cast nephropathy
  2. AL Amyloidosis
  3. Light chain deposition disease
  4. Radio-contrast Nephropathy
  5. Hypercalcaemic Nephropathy
  6. Hyperuricaemic Nephropathy

# Myeloma



- ▶ ‘Myeloma kidney’ –
  - proteinuria
  - nephrotic syndrome
  - acute & chronic renal impairment
  
- ▶ Treat myeloma –
  - steroids, melphalan, BM transplantation

# Haemolytic Uraemic Syndrome (HUS)

- ▶ Syndrome of –
  1. Micro-angiopathic haemolysis → intra-vascular haemolysis with RBC fragmentation
  2. Thrombocytopenia
  3. Acute renal failure
- ▶ Follows febrile URT/GI infection
- ▶ *Escherichia coli* sp O157 strain



# Haemolytic Uraemic Syndrome (HUS)

- ▶ May be – Recurrent, Familial
- ▶ Most children recover spontaneously
- ▶ Elderly – high mortality
- ▶ Heparin, FFP, Prostacycline, plasma exchange

# Infections

- ▶ Severe sepsis from any cause can cause renal impairment by hypotension & dehydration
- ▶ Leptospirosis
  - hepato-renal syndrome with acute tubular necrosis
- ▶ HIV associated nephropathy (HIVAN)
  - commonly focal glomerulosclerosis

# PBL

- A 56 year old man has Type 2 Diabetes Mellitus. His urine analysis on 3 separate occasions shows -
  - protein ++
  - pus cells 1-2/hpf
  - red cells 1-2/hpf
- ❖ What is the likely underlying diagnosis?
- ❖ How would you manage this patient?