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

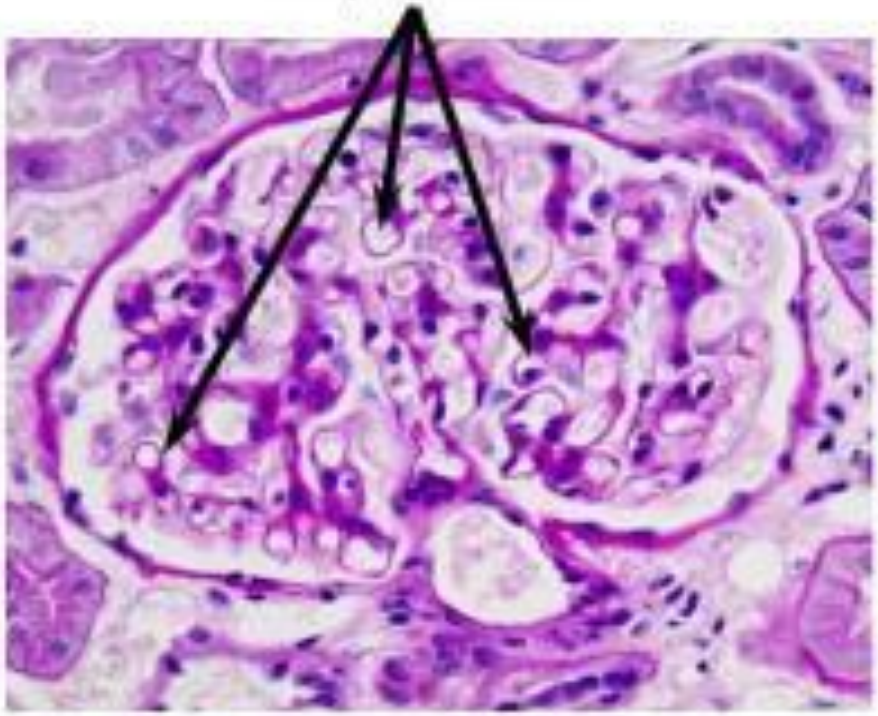
- Initially **Microalbuminuria** - urinary albumin which is undetected by dipstick testing

- Progress to intermittent albuminuria → persistent proteinuria

- LM – diffuse glomerulosclerosis

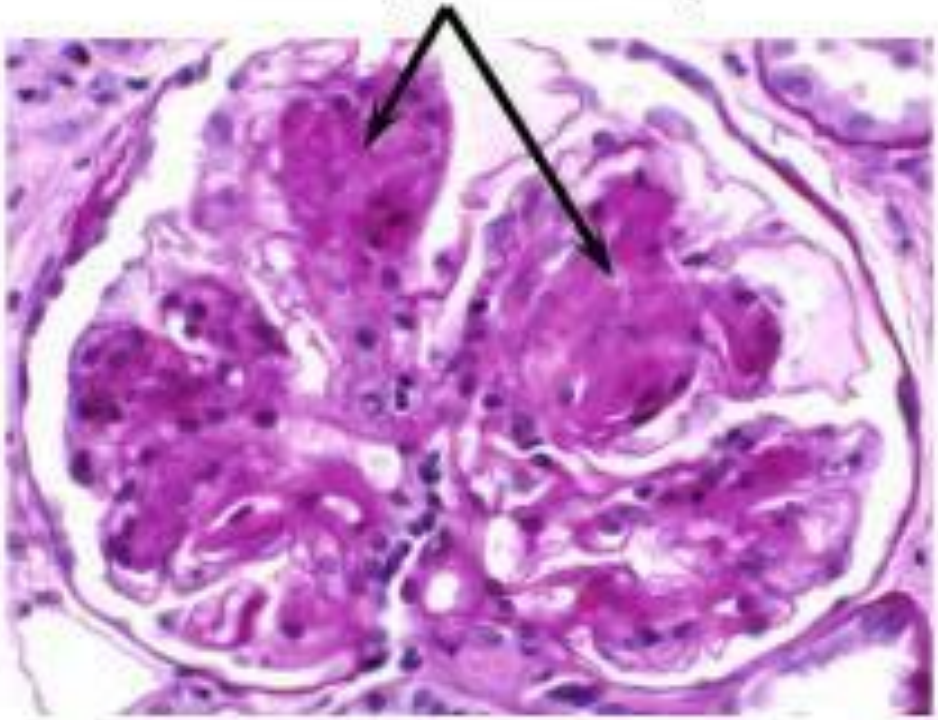
  nodular glomerulosclerosis (Kimmelstiel-Wilson lesion)

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

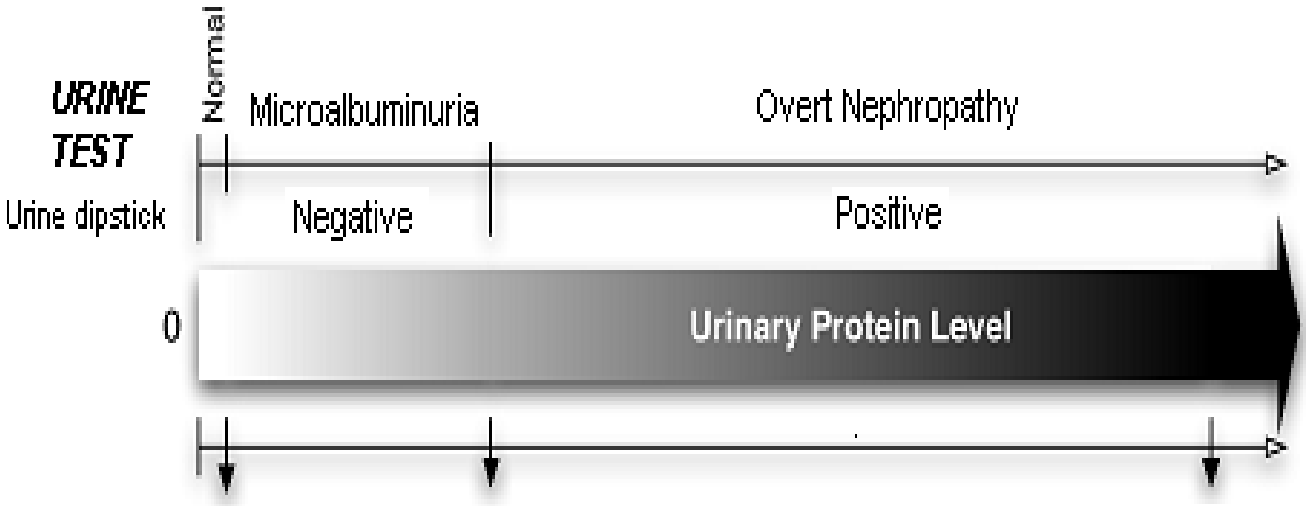
- Progress to overt nephropahy

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



24-hour	30mg/day	300 mg/day	1000 mg/day
ACR (Male)	2.0 mg/mmol	20.0 mg/mmol	66.7 mg/mmol
ACR (Female)	2.8 mg/mmol	28.0 mg/mmol	93.3 mg/mmol

ACR = albumin to creatinine ratio

Diabetic Nephropathy – Natural History

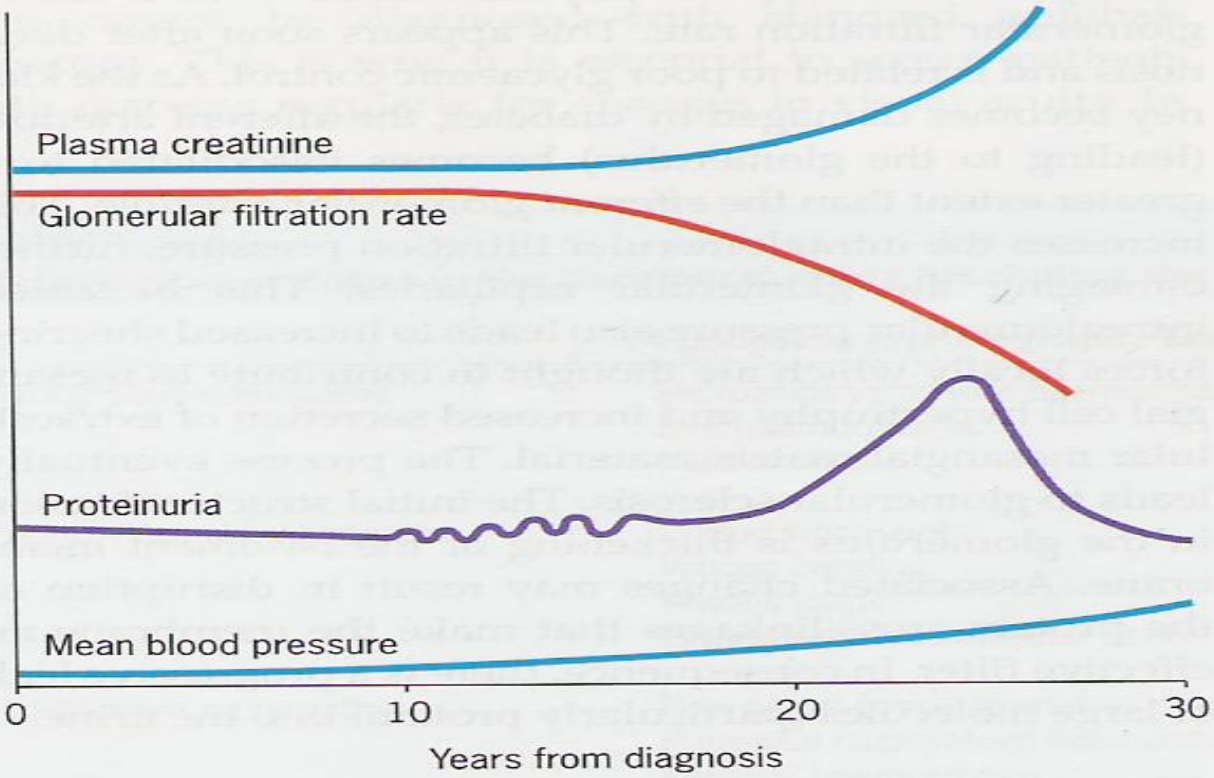


Fig. 19.15 Schematic representation of the natural history of nephropathy. The typical onset is 15 years after diagnosis. Intermittent proteinuria leads to persistent proteinuria. In time, the plasma creatinine rises as the glomerular filtration rate falls.

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

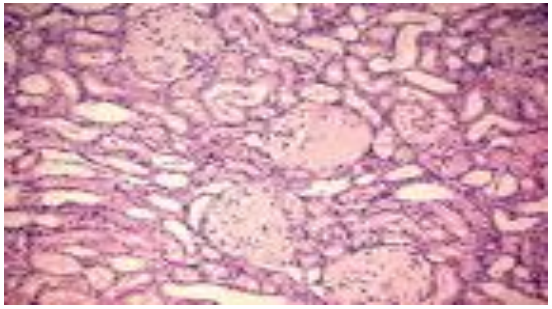
- As renal function deteriorates insulin sensitivity increases → need insulin dose reduction
- Retinopathy also progresses rapidly → blindness
- Develop other complications of DM –

  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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  Diabetic nephropathy

  Amyloidosis

- With active urinary sediment

  SLE

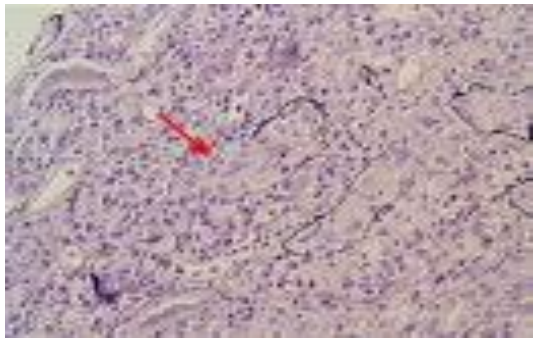
  Henoch-Schonlein syndrome (HSP)

  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

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

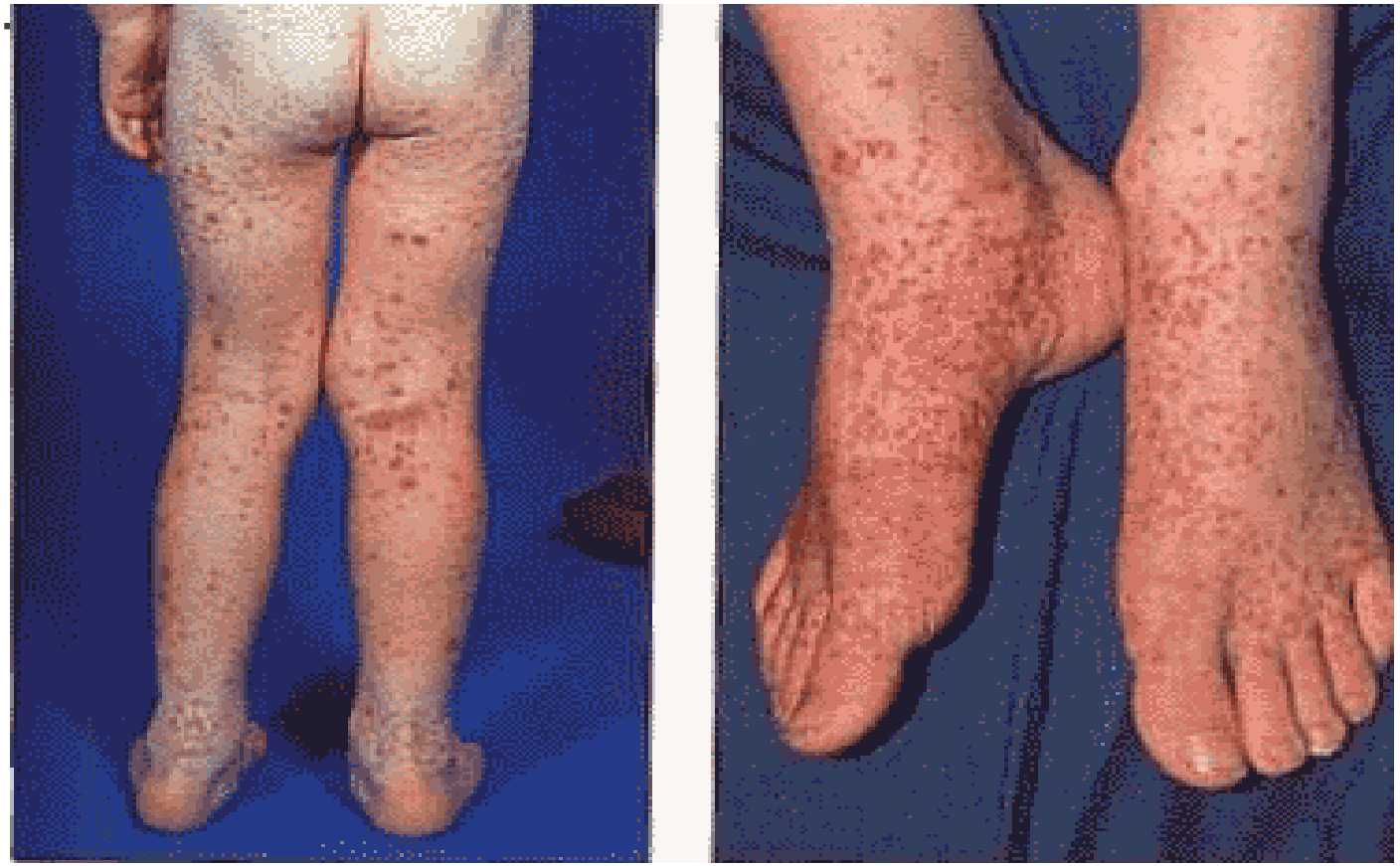
Henoch-Schonlein Syndrome (HSP)

- 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



Other Systemic Diseases Affecting the Kidney

- Systemic Sclerosis
- Myeloma
- HUS
- Infections

Systemic Sclerosis

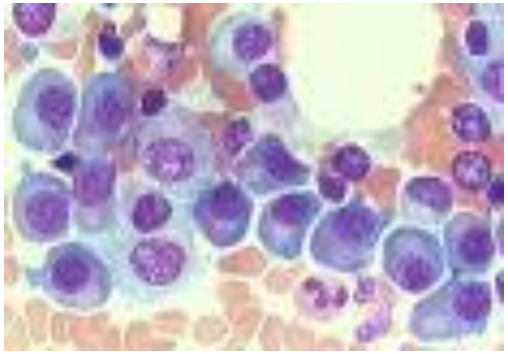
- Multi-system disease of unknown cause

- 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, Prostocycline, 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?