I. Elevated Serum Creatinine

ISSUES:
- Determine if acute and rapidly rising versus chronic and stable
- Identify etiology, potential reversibility or attenuation of progression

1. OBTAIN AT LEAST TWO SERUM CREATININE MEASUREMENTS (2 to 6 weeks apart) in order to determine if stable or progressive

2. OBTAIN:
- History and physical examination with blood pressure assessment
- CBC, urea, electrolytes — Na, K, Cl, HCO₃,*, calcium, phosphorus, glucose, total protein and albumin
  *where readily available
- Urinalysis
- 24-hour urine for creatinine (and protein if dipstick has protein) along with a simultaneous blood sample for measurement of creatinine clearance

3. MAYBE INDICATED:
- Renal ultrasound: to assess kidney size, symmetry, consistency (echogenic kidneys) and to rule out obstruction

4. IF CREATININE CLEARANCE IS SUBNORMAL, DETERMINE IF COLLECTION IS ADEQUATE BY:
- Assessing 24-hour creatinine content (should be 0.15 mmol/kg +/- 0.03/kg)
- Calculate the estimated creatinine clearance without a 24-hour urine (based upon Gault-Cockroft formula):
  \[ \text{CrCl} = \frac{(140 - \text{age}) \times \text{Wt(kg)}}{\text{PCR (umol/L)}} \times 1.2 \text{ for males} \]

5. REFERRAL TO NEPHROLOGIST:
   a. Non-Urgent:
      - Persistently elevated but stable serum creatinine under 300 umol/L without an identifiable reversible cause
   b. Urgent:
      - If serum creatinine is rapidly rising (increases by 20% over 1 to 30 days; obtain a third to confirm)
II. Hematuria

*Defined as >3 RBC/Hpf 10% of adult patients may have up to 10 RBC/Hpf without identifiable cause, but still should be evaluated if persistent (i.e. two consecutive urine samples). Trace "blood" on dipstick without abnormal number of RBC does not require investigation unless suspicious for hemolysis (free Hgb) or muscle breakdown (free myoglobin).

**ISSUES:**
- Determine if Glomerular disease versus non-Glomerular, in particular urinary tract cancer
- Urgency dependent upon associated features such as symptoms or renal function
- Patient may present with gross or macroscopic hematuria (either red or tea coloured urine) or microscopic hematuria with or without associated symptoms

1. OBTAIN:
- History and physical examination with blood pressure assessment
- CBC, serum creatinine, urea, electrolytes — Na, K, Cl, HCO₃⁻, calcium, phosphorus, glucose, total protein and albumin
  *where readily available
- (Repeat) Urinalysis and urine culture
- 24 hour for creatinine clearance (and protein if dipstick has protein)
- Renal ultrasound (to assess kidney size, symmetry and rule out tumour, stones or cystic disease)

2. DETERMINE IF GLOMERULAR ORIGIN:
- If proteinuria >2.0 gm/day or RBC cast present on U/A, assume Glomerular
- If not, exclude anatomical abnormality with ultrasound
  - Urine cytology and referral to urologist for cystoscopy to exclude bladder tumour especially in patients over 40, who are at greatest risk for bladder cancer
  - If ultrasound and cytology/cystoscopy (if indicated and done) are negative, assume Glomerular

3. IF GLOMERULAR ORIGIN HEMATURIA:
- Do limited immune work-up: ANA, C3, C4
- If immune work-up negative:
  - With normal serum creatinine and BP with proteinuria <1.0 gm/day follow-up q3 to 6 months assessing renal function, protein excretion and BP (as likely good prognostic GN such as IgA nephropathy or Thin Membrane Nephropathy)
- If protein excretion >1.0 gm/day but <2.0 gm/day, consider ACE Inhibitor without referral to Nephrologist (see proteinuria section below)

4. REFER TO NEPHROLOGIST IF HEMATURIA and:
- Serum creatinine elevated
- Hypertensive
- Protein excretion >2.0 gm/day
- Immune work-up abnormal
- Family history of renal disease or neurosensory deafness (Alport's disease)
- Signs or symptoms such as malaise, weight loss, fever or hemoptysis

5. REFER TO UROLOGIST FOR CYSTOSCOPY and FURTHER EVALUATION IF HEMATURIA and
- No RBC cast on U/A and urine protein <2.0 gm/day and over 40 years old, or
- Associated with abdominal pain

III. Proteinuria

**ISSUES:**
- Determine if Glomerular disease versus non-Glomerular proteinuria
- Proteinuria is defined by protein excretion rate per day. Urinalysis is only a screening test for proteinuria. It is neither quantitative nor does it detect microalbuminuria required for diabetic nephropathy screening
• Glomerular range proteinuria may be any amount depending upon severity, but >2.0 gm/24 hrs/1.73m2 (referred as gm/day for simplicity) in the absence of an overflow cause or severe hypertension is usually a Glomerular disease
• Non-Glomerular causes include tubulo-interstitial (always <2.0 gm/day) and overflow (i.e. myeloma)
• Urgency of investigations dependent upon associated such as symptoms of renal function
• Patient may present with edema and associated symptoms, or asymptomatic proteinuria (+/- hematuria)

1. OBTAIN:
• History and physical with blood pressure assessment
• CBC, serum creatinine, urea, electrolytes — Na, K, Cl, HCO3; calcium, phosphorus, glucose, total protein and albumin
  *where readily available
• (Repeat) Urinalysis
• 24 hour for creatinine clearance and protein
• Renal ultrasound (assess kidney size, symmetry and rule out cystic disease)
• If over 40 years old, serum and urine protein electrophoresis

2. DETERMINE IF GLOMERULAR ORIGIN:
• If proteinuria >2.0 gm/day or RBC cast, Glomerular origin
• If proteinuria <2.0 gm/day and no RBC cast, exclude:
  - Anatomical abnormality with renal ultrasound
  - Obvious tubulo-interstitial (i.e. analgesic or recurrent pyelonephritis) or overflow cause where applicable
  - If no urologic, tubulointerstitial or overflow cause identified, assume Glomerular

3. IF ASSUMED GLOMERULAR ORIGIN:
• Do limited immune work-up: ANA, C3, C4
• If immune work-up negative:
  - With normal serum creatinine and BP with proteinuria <1.0 gm/day, follow-up q3 to 6 months assessing renal function, protein excretion and BP (as likely good prognostic GN) (see intervention)
• Assess for other progression risk factors such as hyperlipidemia and smoking

4. INTERVENTION FOR GLOMERULAR PROTEINURIA
• Target blood pressure <130/80 using ACE Inhibitor (if intolerant because of cough use ARB) There is some evidence to support a target <125/75 in patients with >1.0 gm protein excretion/day.
• If proteinuria >2.0 gm/day, while awaiting assessment by nephrologist and BP below target, use an ACE Inhibitor to reduce proteinuria and progression
• If proteinuria >1.0 gm/day but <2.0 gm/day, consider ACE Inhibitor without referral to nephrologist
• If ACE Inhibitor or ARB used, always check serum potassium and creatinine after 7 to 10 days. A static 15 % increase in serum creatinine is acceptable
• Check lipid profile and manage according to CV guidelines

5. REFER TO NEPHROLOGIST IF PROTEINURIA and:
• If serum creatinine elevated
• Protein excretion >2.0 gm/day — start ACE Inhibitor (or ARB if ACE intolerant due to cough) even if at target BP
• Immune work-up abnormal
• Family history of renal disease
• Protein electrophoresis abnormal

IV. Diabetic Nephropathy

ISSUES:
• Screen people with Diabetes Mellitus for risk progression
  - Type 1: Screen at five years diabetes duration over the age of 15
  - Type 2: Screen at diagnosis
• Determine if alternative diagnosis for renal abnormality

1. OBTAIN:
• History and physical with blood pressure assessment
• Dipstick urinalysis
• CBC, serum creatinine, urea, electrolytes — Na, K, Cl, HCO3; calcium, phosphorus, glucose, total protein and albumin
  *where readily available
• If negative or trace for protein, then screen for microalbuminuria with albumin/creatinine ratio (ACR)
• If negative for microalbuminuria: screen annually

2. IF POSITIVE FOR MICROALBUMINURIA (MIA):
• Confirm results: repeat twice between 1 and 8 weeks apart;
  - If both negative, repeat in one year
• If one of them is positive diabetic nephropathy is confirmed; see intervention
3. IF URINALYSIS POSITIVE FOR PROTEIN (GREATER THEN A TRACE):
- Proceed to quantitative 24-hour urinary protein plus baseline creatinine clearance to determine the presence of Overt Nephropathy
- Obtain:
  - renal ultrasound (to assess kidney size, symmetry and rule out stones or cystic disease)
  - CBC, urea, serum creatinine, electrolytes — Na, K, Cl, HCO₃⁻, calcium, phosphorus, glucose, total protein and albumin
  * Where readily available

4. INTERVENTION FOR DIABETIC NEPHROPATHY (INCIPIENT AND OVERT):
- If serum creatinine elevated exclude non-diabetic cause
- Treat hypertension: target blood pressure <130/80 mmHg
- ACE Inhibitor or ARB for renoprotective effect even in the absence of hypertension. Monitor serum potassium and creatinine at routine follow-up visits and as indicated for those taking ACE inhibitor or ARB (i.e. 7 to 10 days after initiating or changing dose.)
- Target: MiA = normal albumin excretion:
  - Overt Nephropathy = <500-1000 mg/day
  (depending upon pre-treatment proteinuria)
- Once at target, monitor ACR or 24-hour urinary protein and creatinine clearance every six months.
- If Overt Nephropathy and not at target, consider combination ACEI and ARB or addition of non-dihydropyridine Calcium Channel Blocker
- Targeting LDL <2.5 mmol/L**, maintaining optimal glycemic control* plus, smoking cessation and ECASA (81 mg or 325 mg OD if no contraindications) in addition to general vascular effects may also infer renoprotection

5. REFER TO NEPHROLOGIST IF DIABETIC NEPHROPATHY and:
- Clinical presentation atypical:
  - associated with hematuria
  - early onset Overt Nephropathy
- If serum creatinine >150 umol/L
- Refractory hypertension

**Current CDA guidelines (http://www.diabetes.ca/cpg2003/chapters.aspx)
Lipid guidelines (http://www.heartandstroke.ca/Page.asp/PageID=27&CategoryId=1&Src=heart)