Kidney disease and the requirements for renal replacement therapy (dialysis or transplant) continue to increase at an alarming rate. Manitoba has the highest prevalence and incidence in the country. The number of dialysis patients in Manitoba has tripled over the last decade.

**BY EARLY IDENTIFICATION OF PATIENTS WHO MAY BE AT RISK FOR DEVELOPING KIDNEY DISEASE, YOU CAN HELP PREVENT KIDNEY DISEASE AND PROGRESSION TO END STAGE RENAL DISEASE (ESRD).**

**Kidney Disease:** Patients with intrinsic renal disease with normal or supernormal renal function that may be at risk for progression to renal failure. This includes various chronic glomerulonephropathies (e.g., such as diabetic nephropathy, IgA nephropathy, glomerulonecrosis) and non-glomerular disease (e.g., FSGD, obstructive uropathy).

**Renal Failure:** Kidney disease associated with declining renal function (as determined by decreasing creatinine clearance).

**ESRD (End Stage Renal Disease):** The point at which renal replacement therapy; dialysis or transplant is required.

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**Patients with the following problems may be at high risk for developing kidney disease or failure:**

- Diabetes Mellitus
- Hypertension
- Urinary tract abnormalities
- Known systemic auto immune disorders such as SLE
- Excessive use of known toxins such as analgesics (NSAIDs), lithium and others
- Symptoms suggestive of a systemic illness

**Chronic Kidney Disease Stages**

Without intervention, once kidney function begins to decline it does so in a progressive downhill fashion. It is useful to divide the decline into stages, as shown.

**MRP Renal Management Guidelines**

The MRP Manitoba Renal Program has developed guidelines to help manage high-risk patients. These guidelines are recommended for patients that may require nephrologic care or assessment, and are evidence-based where possible. Where evidence was lacking, these recommendations are opinion-based and derived by consensus from a panel of Manitoba nephrologists and family physicians.

Non-diabetes nephropathy care is provided through the Renal Health Outreach (RHO). The RHO is a component of the Manitoba Renal Program (MRP) responsible for renal health promotion, disease prevention and management through education and clinical care for all of Manitoba.

Patients may require nephrologic care or assessment to:

- Determine etiology of presumed renal abnormality
- Determine their risk for progressive renal failure and/or
- Prevent them for end stage renal care management
- While it is best to identify high-risk patients early, they may present with acute abnormality or at various stages of chronic kidney disease where both focuses of investigations and therapies may be different.

Patients may present with:

- Asymptomatic hematuria or proteinuria noted on U/A, or
- Consistently positive results, confirm with 24-hour urine for microalbumin
- Normal creatinine clearance: 80-120 ml/min/1.73m²

**EARLY SYMPTOMS:**

- Asymptomatic
- Foaming, bloody (resembling cola or tea) or cloudy urine
- Gross hematuria, systemic symptoms such as anorexia, nausea and vomiting, pericarditis or purpura
- Either acute or chronic renal disease

**EARLY WARNING SIGNS:**

- Microscopic hematuria
- Proteinuria
- Albuminuria in patients with Diabetes Mellitus

**LATE SYMPTOMS:**

- Dyspnea and fluid retention
- Persistent generalized itching
- Bone or joint pain

**GLOMERULAR HEMATOLOGY (WBC, RBC, PLT):**

**OBTAIN:**

- CBC, blood urea, creatinine, electrolytes (Na, K, Cl, HCO₃), calcium, phosphorus, glucose and albumin

**IF URINALYSIS POSITIVE FOR PROTEIN**

**OBTAIN:**

- Consistently positive results, confirm with 24-hour urine for microalbumin
- Normal creatinine clearance: 80-120 ml/min/1.73m²

**EARLY DIAGNOSIS**

- Early detection usually occurs before the serum creatinine increases, i.e. Stage A, (Normal 100 – 120 umol/L) but at the latest when it is <250 umol/L, i.e. Stage B
- Normal creatinine clearance: 80-120 ml/min/1.73m²

**INDICATIONS:**

- Determine etiology of presumed renal abnormality
- Determine their risk for progressive renal failure and/or
- Prevent them for end stage renal care management
- While it is best to identify high-risk patients early, they may present with acute abnormality or at various stages of chronic kidney disease where both focuses of investigations and therapies may be different.

Patients may present with:

- Asymptomatic hematuria or proteinuria noted on U/A, or
- Elevated serum creatinine
- Protein electrophoresis abnormal
- Family history of renal disease
- Immune work-up abnormal
- Protein electrophoresis abnormal

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**THERAPEUTIC FOCUS/ GOAL AT EACH STAGE**

**A • PREVENT KIDNEY FAILURE**

**B • ANTI-PROGRESSION THERAPY**

**C • MANAGEMENT OF CHRONIC DISEASE/FAILURE COMPLICATIONS**

**D • PREPARATION FOR RENAL REPLACEMENT THERAPY**

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**IV. Diabetic Nephropathy**

**ISSUES:**

- Screen diabetics for risk progression:
  - Type 1: Screen @ 5 years diabetes duration over the age of 15 years old.
  - Type 2: Screen @ diagnosis
- Determine if alternative diagnosis for renal abnormality

**METHODS:**

- Blood pressure (BP) assessment
- Diabetic retinopathy
- If negative or trace for protein, then screen for microalbuminuria with albumin/creatinine ratio
- If negative for microalbuminuria, screen annually

**2. IF POSITIVE FOR MICROALBUMINURIA:**

- Confirm results; repeat 2 to 3 times over 3 months
- Consistently positive results, confirm with 24-hour urine for microalbumin
- Monitor 24-hour urinary protein and creatinine clearance every 6 to 12 months
- Check fasting lipid profile

**3. IF URINALYSIS POSITIVE FOR PROTEIN (greater than a trace):**

- Proceed to quantitative 24-hour urine 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 tumors) or serology for CR, C3, C4, ASMA, ANA, dsDNA, RF, lupus anticoagulant
- Obtain renal ultrasound (to assess kidney size, symmetry and rule out stones or tumors) or serology for CR, C3, C4, ASMA, ANA, dsDNA, RF, lupus anticoagulant
- Onset 10 years before other features of SLE
- Prompt treatment of active SLE
- Monitor renal function and proteinuria
- Monitor proteinuria
- Monitor renal function

**II. HEMATURA**

- Determine if alternative diagnosis for renal abnormality
- Renal replacement therapy
- Anti-progression therapy
- Management of chronic kidney disease and the requirements for renal replacement therapy (dialysis or transplant) is required.

**GOAL AT EACH STAGE**

**PREPARATION FOR RENAL REPLACEMENT THERAPY**

**PREVENT KIDNEY FAILURE**

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**II. HEMATURA**

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- Renal replacement therapy
- Anti-progression therapy
- Management of chronic kidney disease and the requirements for renal replacement therapy (dialysis or transplant) is required.
4. INTERVENTION FOR INCipient NEPHROPATHY
(microalbuminuria – albumin 30-300 mg/day):
• Treat hypertension: target blood pressure <125/80 mmHg
  - Type 1: Treat with ACE inhibitors or ARB for kidney protective effect even in the absence of hypertension
  - Type 2: Treat with ACE inhibitors or ARB for kidney protective effect even in the absence of hypertension
• Monitor serum potassium and creatinine at routine follow-up visits or within two weeks of dose change for those taking ACE inhibitors or ARB
• Monitor 24-hour urinary protein and creatinine clearance every 6 to 12 months
• Maintain optimal glycemic control

5. INTERVENTION FOR OVERT NEPHROPATHY
(macroalbuminuria >300 mg/day):
• Treat hypertension: target blood pressure <125/75 mmHg
• Treat with ACE inhibitors or ARB for kidney protective effect even in the absence of hypertension
• Monitor serum potassium and creatinine at routine follow-up visits or within two weeks of dose change for those taking ACE inhibitors or ARB
• Monitor 24-hour urinary protein and creatinine clearance every 6 to 12 months
• Maintain optimal glycemic control

6. ASSESS FOR OTHER RISK FACTORS SUCH AS LIPIDS, SMOKING AND NUTRITION

7. REFER TO NEPHROLOGIST IF:
• Clinical presentation atypical:
  - Associated with hematuria
  - Early onset overt nephropathy
• Serum creatinine is discongruent
• Refractory hypertension

Kidney disease in its early stages is often asymptomatic. It is important for high-risk individuals to be tested regularly to reduce the progression of kidney disease and ultimately reduce the need for dialysis.

**DID YOU KNOW:**
• Up to 50% of new dialysis patients present abruptly requiring urgent dialysis.
• Late referral increases the patient’s mortality (with increased pulmonary edema, acidosis, temporary access, and prolonged hospitalization).
• Late referral also negates any opportunity for life-prevented kidney failure if at least attempted the rate of decline.
• Late referral prevents appropriate renal replacement therapy planning that includes preemptive transplantation (i.e. before ever being dialyzed), offtake creation or vascular access and initiation of immunosuppression and prophylaxis of postrenal dialysis. Patients with end-stage renal disease should be started on replacement therapy before they become symptomatic.
• 30% of patients starting dialysis have diabetes as the underlying etiology, but diabetes is also associated with an increased incidence of non-diabetic kidney disease.
• Many of the remaining 70% of new dialysis patients may have had asymptomatic kidney disease that if identified earlier may have been prevented.

Although there are clinical symptoms associated with renal failure, people who have kidney disease are frequently asymptomatic.
• Urgency of investigations dependent upon associated features such as symptoms or renal function
• Patient may present with edema and associated symptoms, or asymptomatic proteinuria

1. OBTAIN:
• Blood pressure (BP) assessment
• CBC
• Blood urea, creatinine, electrolytes (Na, K, Cl, HCO3), calcium, phosphorus, glucose, total protein and albumin
• Repeat urinalysis
• 24-hour for creatinine clearance and protein
• Renal ultrasound (assess kidney size, symmetry and R/O cystic disease)
• If over 40 years old, serum and urine protein electrophoresis

2. DETERMINE IF GLOMERULAR ORIGIN:
• If proteinuria >2.0 gm/24hrs /1.73m2 or RBC cast, assume glomerular
• If not, exclude:
  - Anatomical abnormality with renal ultrasound
  - Obvious tubulo-interstitial or overflow cause where applicable
  - If negative, assume glomerular

3. IF 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 3-6 months assessing renal function, protein excretion and BP (as likely good prognostic GN)
  - If protein excretion >1.0 gm/day but <2.0 gm/day, consider ACE Inhibitor without referral to Nephrologist

4. REFER TO NEPHROLOGIST IF:
• Serum creatinine elevated
• Protein excretion >2.0gm/24hrs/1.73m2

1. Elevated Creatinine

ISSUES:
• Determine if acute and rapidly rising vs. 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:
• Blood pressure (BP) assessment
• CBC
• Blood urea, electrolytes (Na, K, Cl, HCO3) (if readily available), calcium, phosphorus, glucose, total protein, albumin
• Urinalysis
• 24-hour urine for creatinine (and protein if dipstick has protein) along with a simultaneous blood sample for measurement of creatinine clearance

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

4. IF SERUM CREATININE NORMAL BUT CREATININE CLEARANCE SUBNORMAL, DETERMINE IF COLLECTION IS ADEQUATE BY:
• Assessing 24-hour creatinine content (should be 0.15 mmol/kg +/- 0.03)
• Calculate the estimated creatinine clearance without a 24-hour urine (based upon Gault-Cockroft formula): CrCl = 140 x Wt (kg) / Serum creatinine x 1.2 (multiply by 1.2 for male) (PCr umol/L)

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

ISSUES:
- Determine if glomerular vs. non-glomerular disease, 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:
   - Blood pressure (BP) assessment
   - CBC
   - Blood urea, creatinine, electrolytes (K, Cl, Na), Hct, Hgb (if readily available), calcium, phosphorus, glucose and albumin
   - (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 tumor, stones or cystic disease)

2. DETERMINE IF GLOMERULAR ORIGIN:
   - If proteinuria > 2.0 gm/24hrs/1.73m² or RBC cast present on U/A, assume glomerular
   - If not, exclude anatomical abnormality with ultrasound:
     - Urine cytology
     - Consider referral to Urologist for cystoscopy to exclude bladder tumor or if persistent urinary tract symptoms especially in patients over 40, who are at greatest risk for bladder cancer
   - If ultrasound and cytology/cystoscopy negative, assume glomerular

3. IF 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 assuming complete 24-hour urine collection, follow-up q3-6 months assessing renal function, protein excretion and BP (as likely good prognostic CN such as Lp 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:
   - Serum creatinine elevated
   - Hypertensive
   - Protein excretion >2.0gm/24hr/1.73m²
   - Immune work-up abnormal
   - Family history of renal disease or neurosensory deafness
   - Ominous signs or symptoms such as malaise, weight loss, fever, or hemolytic
   - You are unsure

III. Proteinuria

ISSUES:
- Determine if glomerular vs. 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 screening diabetics
- Glomerular range proteinuria may be any amount depending upon severity, but >2.0 gm/24hr/1.73m² 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 (as in myositis, may be any amount)