EARLY RENAL DISEASE: WHEN TO CALL THE NEPHROLOGIST?

McGill Refresher Course

Dr. Tiina Podymow

Associate Professor Nephrology

McGill University Health Centre

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DISCLOSURES

- None

OBJECTIVES

1. How to identify patients who are at the greatest risk of end-stage renal failure and dialysis
2. Interpret urine protein
3. Know the diagnostic features of nephrosclerosis vs. diabetic nephropathy
4. Management principles – what to expect

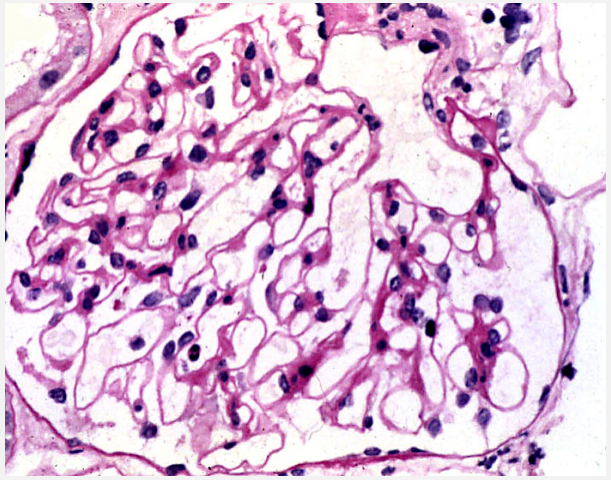
CASE

- 69 year old Afro Caribbean woman, Cr 146 µmol/L eGFR 35 ml/min
- Hypertension, DM2, longstanding pancytopenia
- Meds: ASA, candesartan, HCTZ, metformin
- O/E weight 76 kg, 135/84 mm Hg, HR 70's, no edema

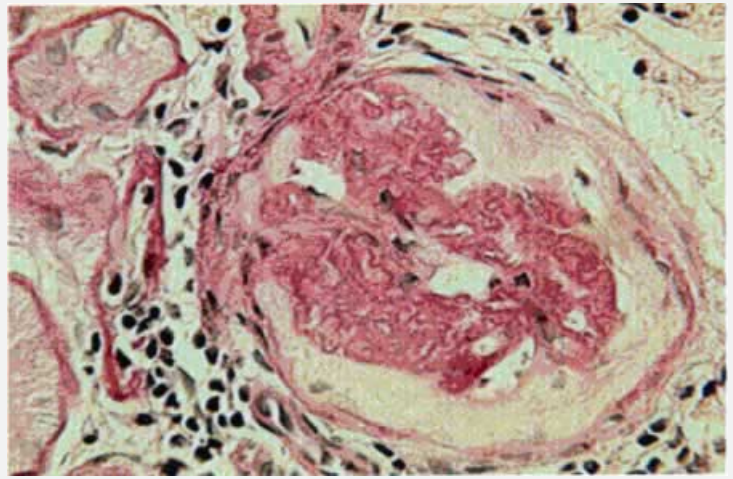
	Nov 3, 2008 14:12	Sep 21, 2012 11:41	Dec 20, 2013 11:15	Apr 1, 2014 12:24	Oct 10, 2014 11:55	Oct 20, 2014 13:33	Nov 27, 2014 10:59	Dec 15, 2014 09:50	Jun 8, 2015 12:42	Jul 24, 2016 11:51	Aug 24, 2016 15:38	Nov 28, 2016 13:30	Mar 20, 2017 15:05
CREATININE [umol/L]	132	115	125	133	152		151		152	147	154	164	146
UREA [mmol/L]		9.7		13			13.5				15.6		16.3
ESTIMATED GFR [mL/min/1]		50	45	42	36		36		35		35	32	36

Cr relatively stable over years

GLOMERULOSCLEROSIS VS. GLOMERULONEPHRITIS

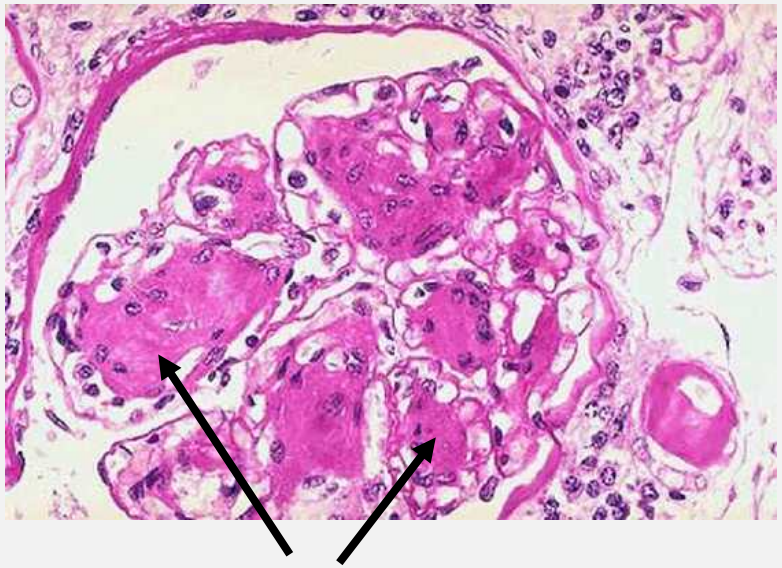


Normal glomerulus



Glomerulosclerosis

<1 g/day protein



3g/day u protein
GN e.g. Kimmelstiel Wilson lesions
Diabetic nephropathy (only 10-20% of diabetics)

URINE PROTEIN

- To diagnose renal disease, you need to know if there is protein in the urine or not
- Hint: Order both, can interpret them separately
- Urine albumin/Cr ratio (ACR) mg/mmol
- Urine protein/Cr ratio g/g

URINE PROTEIN INTERPRETATION

- Urine albumin/Cr ratio: answers the question: is the endothelium healthy?

  < 3 mg/mmol: yes

  >3 mg/mmol: no it might not be

- Urine protein/Cr in g/g is a surrogate for 24 hour urine collection and answers the question: is this a GN?

Prognosis of CKD by GFR and albuminuria category

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

Higher microalbumin level
Magnifies risk of renal function decline

All-cause mortality

	ACR <10	ACR 10–29	ACR 30–299	ACR ⩾300
eGFR > 105	1.1	1.5	2.2	5.0
eGFR 90–105	Ref	1.4	1.5	3.1
eGFR 75–90	1.0	1.3	1.7	2.3
eGFR 60–75	1.0	1.4	1.8	2.7
eGFR 45–60	1.3	1.7	2.2	3.6
eGFR 30–45	1.9	2.3	3.3	4.9
eGFR 15–30	5.3	3.6	4.7	6.6

Higher microalbumin level
Indicates greater cardiovascular mortality
A marker of endothelial health

69F CR 146 µMOL/L

U Microalb/Cr Ratio [mg/mmol]	10.8
U Prot/ U Créat (g/g) (RPCU, UPCR) [g/g]	0.23

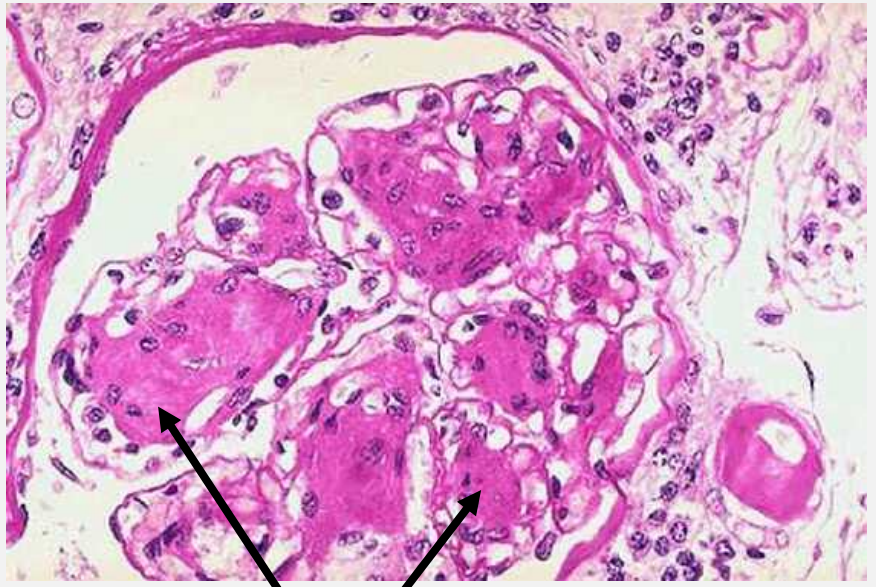
Dipstick: trace protein, no hematuria

Urine microalbumin is positive- but not at the higher risk level of >30 mg/mmol.
Urine total protein/Cr: This patient has CKD not due to diabetes

DOES THIS PATIENT WITH CR 146 AND URINE P/CR 0.23 G/G HAVE DIABETIC NEPHROPATHY? NO

Clinically DM nephropathy:

1. Microalbuminuria
2. Albuminuria
3. nephrotic proteinuria = 3/g/
4. THEN ↑ Cr
5. Progression to ESRD



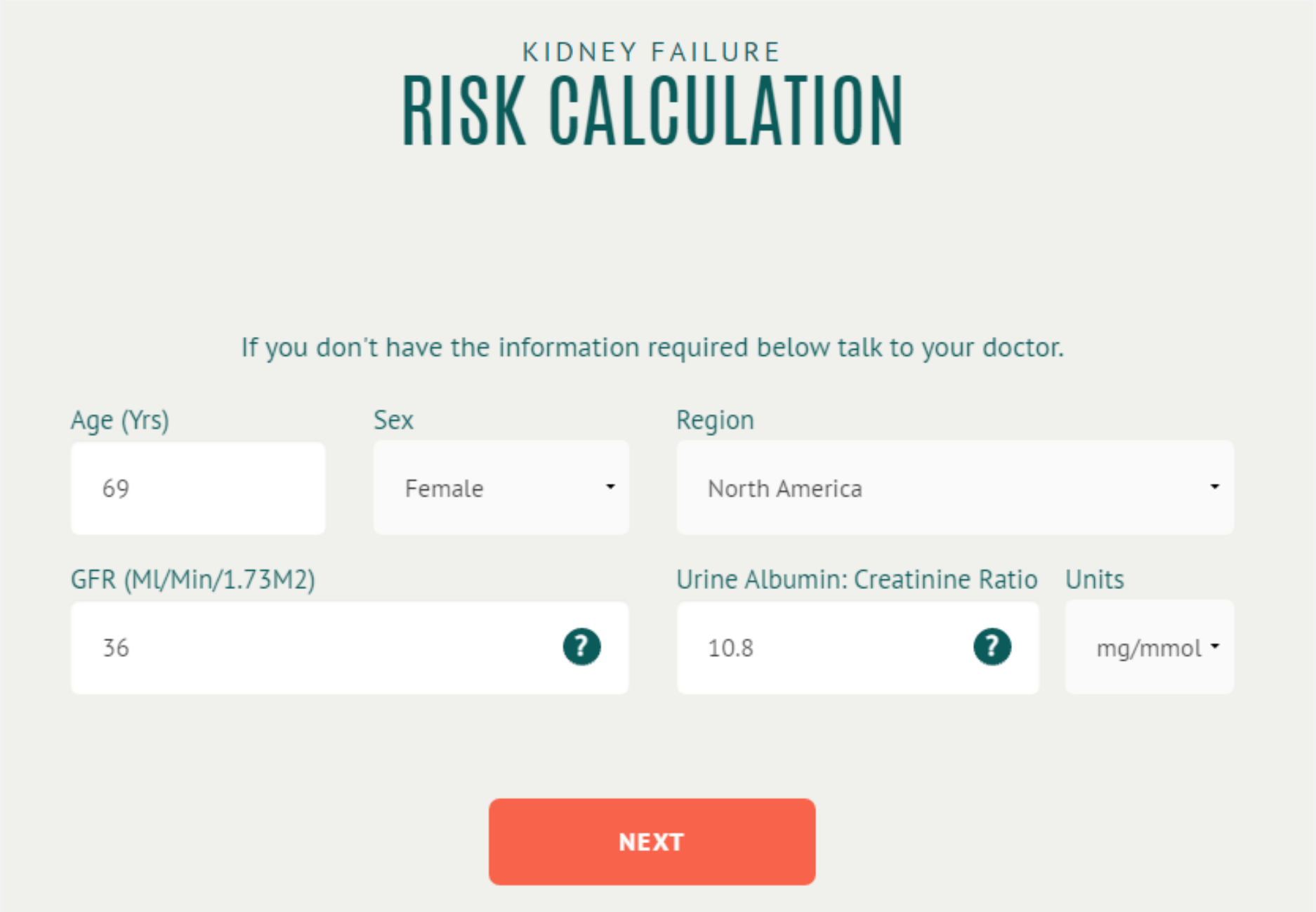
Kimmelstiel Wilson lesions

PATIENT DIAGNOSIS

- 69 year old woman
- Cr 146 eGFR 36 ml/min
- Urine microalbumin 10.8 mg/mmol
- U protein/Cr ratio 0.23 g/g

- = Glomerulosclerosis
- U protein ≤ 1 g/day
- Relatively stable Cr

- http://mdrd.com/ to calculate eGFR, KFRE http://kidneyfailurerisk.com/



KIDNEY FAILURE

RISK CALCULATION

A more accurate result can be calculated if you have the following information:
Albumin, Phosphorous, Bicarbonate and Corrected Calcium.
Do you have these details?

YES

NO, SKIP THIS STEP

STAGE 3

MODERATE DECREASE IN FUNCTION

Patient risk of progression to kidney failure requiring dialysis or transplant:

AT 2 YEARS	AT 5 YEARS
1.75 %	5.37 %

Risk thresholds used in health systems include:

- 3-5 % over 5 years for referral to a kidney doctor
- 10 % over 2 years for team based care (Kidney Doctor, Nurse, Dietician, Pharmacist)
- 20-40 % over 2 years for planning a transplant or fistula

WHAT TO EXPECT WITH GLOMERULOSCLEROSIS

- CKD associated with ≤ 1 g/d proteinuria and a slow decline in renal function
- Prognosis is actually quite good- e.g. at 5 years this patient only has a 5 % chance of needing dialysis
- Target BP ≤ 140/90 mm Hg
- Patients tend to be very "volume sensitive" - Cr fluctuates if they are volume contracted (hold sick day medications e.g diuretics)
- No NSAIDS – can cause AKI. Favor e.g. gout to be treated with short course prednisone rather than NSAID
- Dose meds to GFR 36 ml/min (use mdrd.com and Uptodate to easily calculate)

USES OF KFRE IN CANADA

- <3 % at 5 years (in the absence of uACR >100, hematuria or pregnancy)
- "Low risk letter"

- Management "secrets" of low-risk glomerulosclerosis patients:
- yearly urine albumin/Cr to recalculate KFRE
- BP targets <140/90 mm Hg
- no NSAIDs,
- dose medications to eGFR

- Clinic funding in Ontario and Alberta: need KFRE of 20% at 2 years or eGFR <15 to enter multidiscplinary pre-dialysis clinic

- >40% at 2 years need to plan for dialysis: PD education or vascular access creation

BLOOD PRESSURE

- Uncontrolled hypertension tends to accelerate all forms of renal disease
- Target: ≤ 130/80 mm Hg in CKD with ≥ 1 g/day proteinuria = uP/Cr of >1 g/g
- Glomerulosclerosis: ≤ 1 g/day proteinuria target ≤ 140/90 mm Hg.
- Note that for glomerulosclerosis ACEI or ARBS are <u>not</u> mandatory as they are in diabetic/proteinuric renal disease. If they are tolerated (e.g K is normal, no jump in Cr <15%), use them. If they are not tolerated CaCh blocker, beta blockers, alpha blockers, thiazide etc. to get the BP to target

NEW PATIENT 67F NO HISTORY OF DIABETES

Description [Unit]	Jan 25, 2016 08:44	Jan 25, 2016 09:50	Mar 9, 2016 07:46	Apr 27, 2016 08:40	Aug 5, 2016 00:42	Aug 5, 2016 01:06	Aug 5, 2016 06:15	Aug 5, 2016 21:30
CREATININE [umol/L]	64		80	105	155		162	
UREA [mmol/L]	3.3		3.9	6.5	6.4		8.1	
ESTIMATED GFR [mL/min/1]	>60		>60	48			28	
SODIUM [mmol/L]	135		138	133	128		131	
POTASSIUM [mmol/L]	4.4		4.7	4.9	4.9		3.8	
Bicarbonate Level [mmol/L]	29		27	27	23		22	
GLUCOSE RANDOM [mmol/L]					19.9		6.8	
ALBUMIN [g/L]								
U Prot/Creat Ratio [g/mmol]	2.87		1.1	1.31				1.23
U Microalb/Cr Ratio [mg/mmol]	1784.1		680					
U Créat (g/g) (RPCU, UPCR) [g/g]	27		10	12.3				11.3

Spot urine protein/Cr ratio is a surrogate for 24 hour collection. Units: g/g

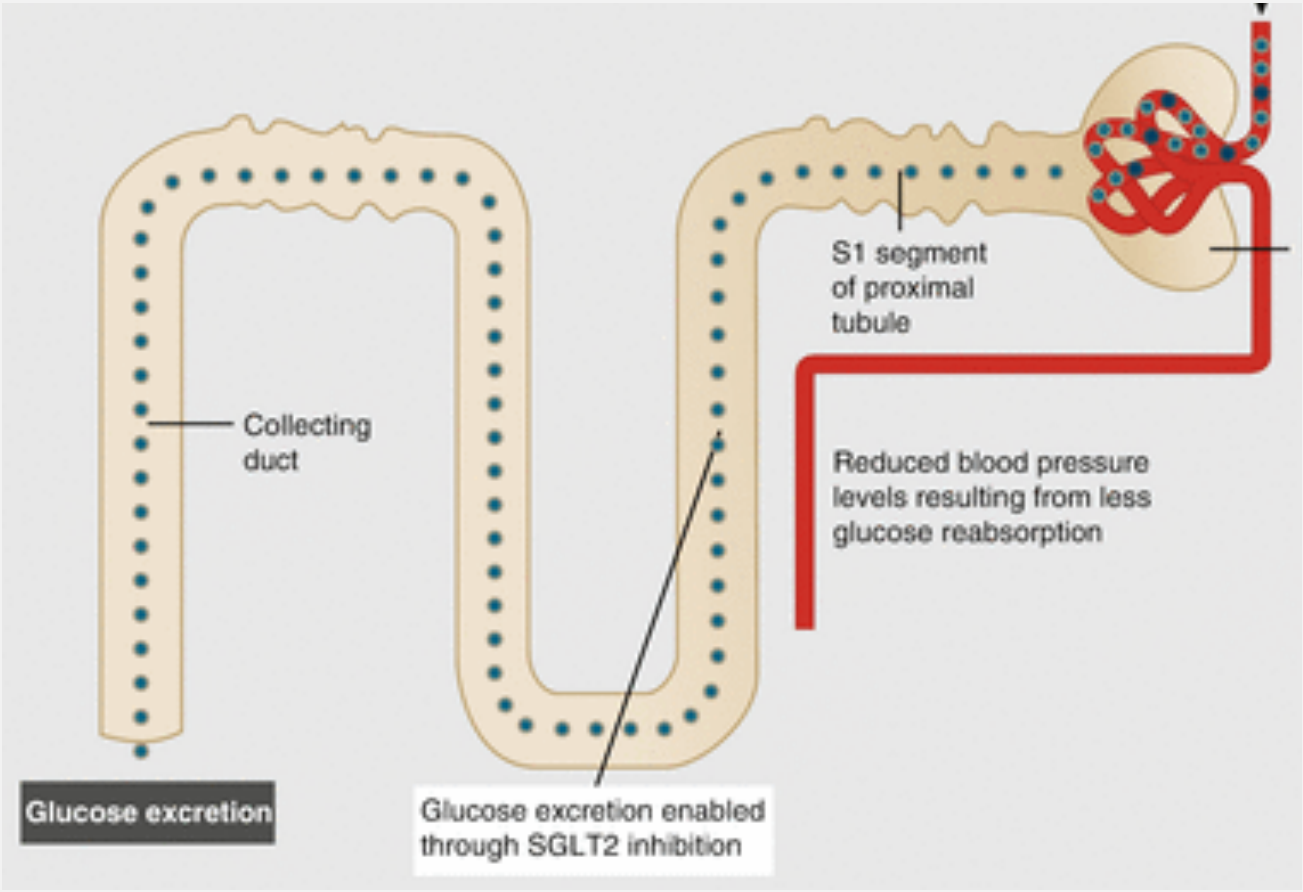
67F GN- PLEASE CALL NEPHRO

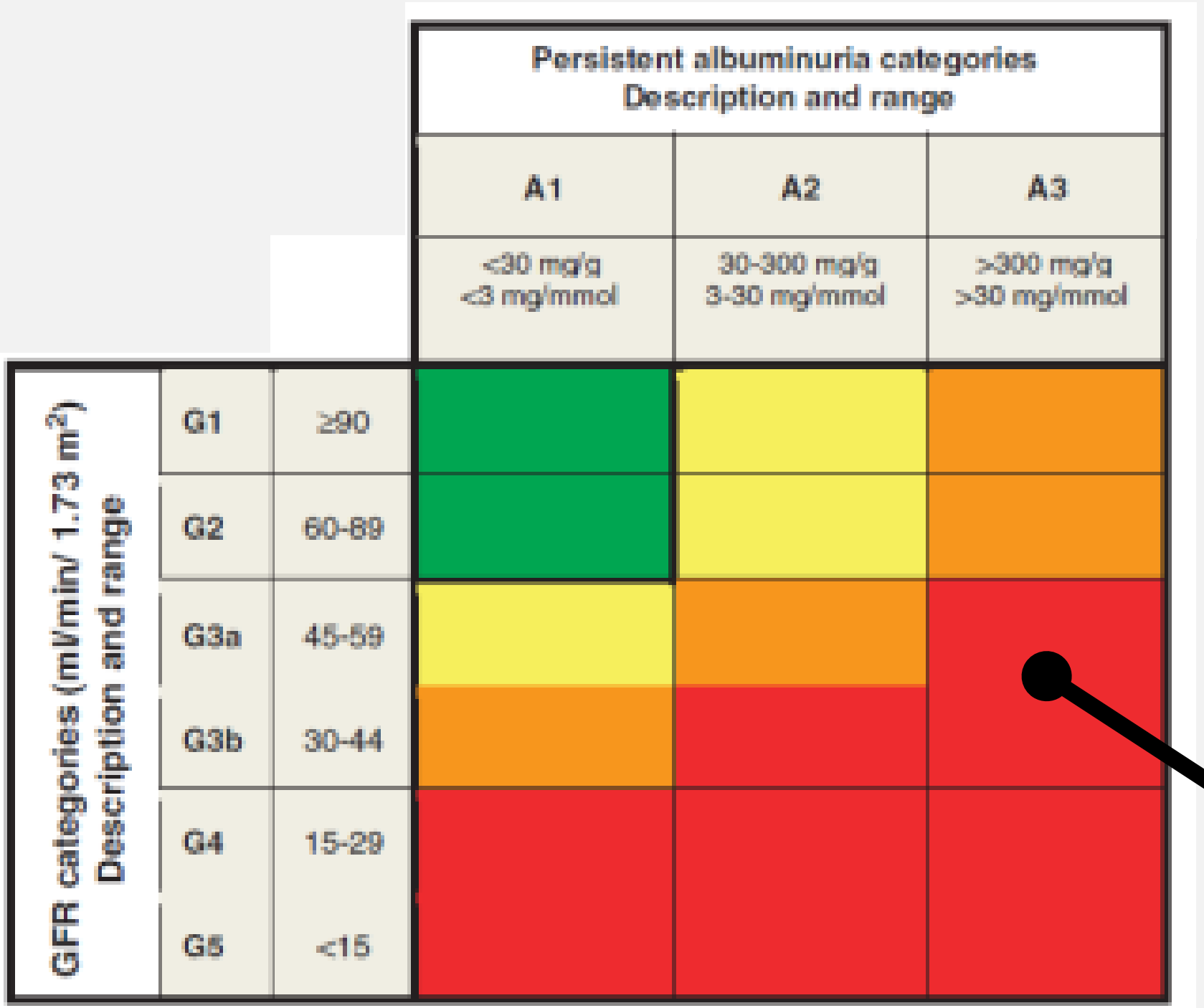
Description [Unit]	Nov 8, 2017 09:30	Nov 27, 2017 08:40	Jan 16, 2018 10:00	Jan 18, 2018 09:45	Mar 27, 2018 08:50	May 30, 2018 09:20	May 31, 2018 11:06	Jun 26, 2018 08:15	Sep 18, 2018 09:15	Oct 1, 2018 08:30	Oct 11, 2018 11:13
CREATININE [umol/L]	175	162	169		208	246		254	270	305	
UREA [mmol/L]								20.4			
ESTIMATED GFR [mL/min/1]	26	28	27		21	17		16	15	13	
SODIUM [mmol/L]	137	140	142		137	137		140	137	135	
POTASSIUM [mmol/L]	3.9	4.1	4.1		3.9	4.4		4.1	4.2	4.7	
Bicarbonate Level [mmol/L]								32		29	
GLUCOSE RANDOM [mmol/L]								5.4			
ALBUMIN [g/L]	30	30	30		33	36			33	36	
U Prot/Creat Ratio [g/mmol]	1.16	0.63									0.565
U Microalb/Cr Ratio [mg/mmol]	805.9	522.1									478.7
J Créat (g/g) (RPCU, UPCR) [g/g]	10	5.9									4.97

CO FOLLOW WITH NEPHROLOGY

- CKD with kidney failure risk score calculated ≥3% at 5 years
- More than the equivalent of 1 g/day proteinuria or 100 mg/mmol albuminuria and any Cr
- Proteinuria with hematuria- need to rule out glomerulonephritis
- Pregnancy or contemplating pregnancy with any degree of renal impairment or proteinuria (because of the high risk of renal deterioration and preeclampsia)

A WORD ABOUT SGLT-2 INHIBITORS





SLGT-2 Inhibitors: PRESERVED RENAL FUNCTION in trials

CREDENCE
DAPA-CKD
EMPA-KIDNEY

DECISION ALGORITHM FOR SGLT2-I

eGFR	< 3 mg/mmol	< 3-30 mg/mmol	> 30 mg/mmol
>60 ml/min per 1.73 m^2	SGLT2i or GLP-1 RA[a]	SGLT2i is preferred. GLP-1 RA as an alternative if SGLT2i is contraindicated or not tolerated, and as an add-on for uncontrolled metabolic risk[b]	SGLT2i should be initiated. GLP-1 RA as an add-on for uncontrolled metabolic risk[c]
30–60 ml/min per 1.73 m^2	SGLT2i is preferred. GLP-1 RA as an alternative if SGLT2i is contraindicated or not tolerated, and as an add-on for uncontrolled metabolic risk[b]		SGLT2i should be initiated. GLP-1 RA as an add-on for uncontrolled metabolic risk[c]
15–29 ml/min per 1.73 m^2	GLP-1 RA (dulaglutide) is preferred. Initiation of SGLT2i is currently contraindicated[d]		

Li et al. CJASN. 2020; 15: 1678–1688

SUMMARY

- When to call the nephrologist?
- In CKD, use urine albumin/Cr ratio (ACR) and KFRE to risk stratify, >5-10% consider referral
- If nephrotic proteinuria (total protein/Cr ratio > 3 g/g) always refer
- If low risk, annual or semi-annual serum Cr, eGFR, urine ACR and monitor targeted blood pressure, avoid NSAIDs. The lower the GFR, the more they could cause AKI.
- Presence of albuminuria and proteinuria: powerful markers for the tempo of renal disease and >30 mg/mmol always accelerate it
- Hypertension accelerates the loss of kidney function. Urine protein quantification helps establish BP treatment targets (<130 vs. 140/90 mm Hg per Canadian Hypertension Guidelines)