Update – Kidney Function

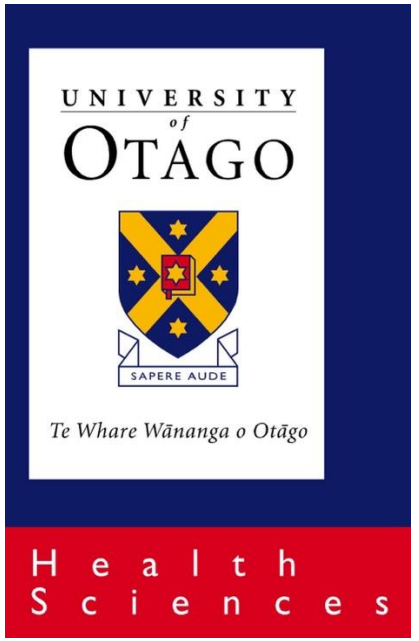
Professor Rob Walker

The organs of the human body were created to perform ten functions among which is the function of the kidney to furnish the human being with thought.

Leviticus Rabba 3 Talmud Berochoth 6_1b

Conflicts of Interest.

- This workshop is kindly sponsored by Boehringer-Ingleheim.
- The honorarium is paid into my research trust funds.



Objectives

Kidneys working!
- How?

- Measurement of kidney function? Assumptions and errors
- Serum biochemistry – creatinine, Estimates of kidney function – eGFR
- Urinalysis – dipstick ± microscopy, albuminuria and proteinuria, haematuria & sterile pyuria
- Urinary electrolytes – stone formation
- Hyponatraemia and hyperkalaemia
- Link changes in kidney function to common clinical scenarios
- Chronic kidney disease

Join at:
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ID:
116-882-760

Question 1

- Where is this?
- A: Rome
- B: Athens
- C: Rhodes
- D: Ephesus
- E: Cairo

Serum creatinine and estimated GFR

- Creatinine – derived from muscle mass
- Serum concentration: production versus elimination.
- Assumption for eGFR
  filtered only, no tubular secretion or uptake
- Remember inherent lab variation in determining serum creatinine
  Not an absolute number!

Table 2 eGFR calculations and subsequent CKD classification based on minimum and maximum serum creatinine results obtained for each pool

From: Routine serum creatinine measurements: how well do we perform?

Pool, µmol/L		1		2		3		4		5	
		35		70		112		296		934	
Min and max Scr, µmol/L		27	53	59	80	104	124	274	313	868	990
eGFR, ml/min/1.73 m ^{2}	**child 6y**	158	80[a,b]								
	CKD stage	G1	G2								
	man 18y			140	124	90[a,b]	73	28	24	7	6
	CKD stage			G1	G1	G1	G2	G4	G4	G5	G5
	woman 18y			128	93	68	55[a,b]	21	18	5	4
	CKD stage			G1	G1	G2	G3a	G4	G4	G5	G5
	man 65 y			101	89[a,b]	65[a,b]	52	20	17	5	4
	CKD stage			G1	G2	G2	G3a	G4	G4	G5	G5
	woman 65y			92[a,b]	67	49[a,b]	39	15	13[a,b]	4	3
	CKD stage			G1	G2	G3a	G3b	G4	G5	G5	G5

Hoste L et al. BMC Nephrol. 2015; 16: 21

Question 2

- Assuming you have normal kidney function (serum creatinine 70umol/l), If I were to remove one of your kidney as a kidney donor, what would your serum creatinine be tomorrow morning?
- A: Doubled (>150 umol/l)
- B: an increase by 25umol/l
- C: an increase by 50umol/l
- D: unchanged

Question 3

- Assuming you have normal kidney function (serum creatinine 70umol/l), If I were to remove both of your kidneys, what would your serum creatinine be tomorrow morning?
- A: Doubled (>150 umol/l)
- B: an increase of less than 25umol/l - essentially unchanged
- C: an increase by 50umol/l
- D: greater than 500umol/l

Estimated Glomerular Filtration Rate

- Provide a more valid way of ‘tracking kidney function’ and awareness of the development of chronic kidney disease.
- Derived from MDRD study.
  Accuracy around stage 3a CKD
  eGFR40 -59 ml/min/1.73m^2
- Less accurate above 60 ml/min/1.73m^2
- Underestimates GFR compared to Cockcroft & Gault (tends to over-estimate GFR).
- Currently use CKD-EPI – estimates of CKD more appropriate, but similar limitations at higher eGFR values.
- Must be at steady state

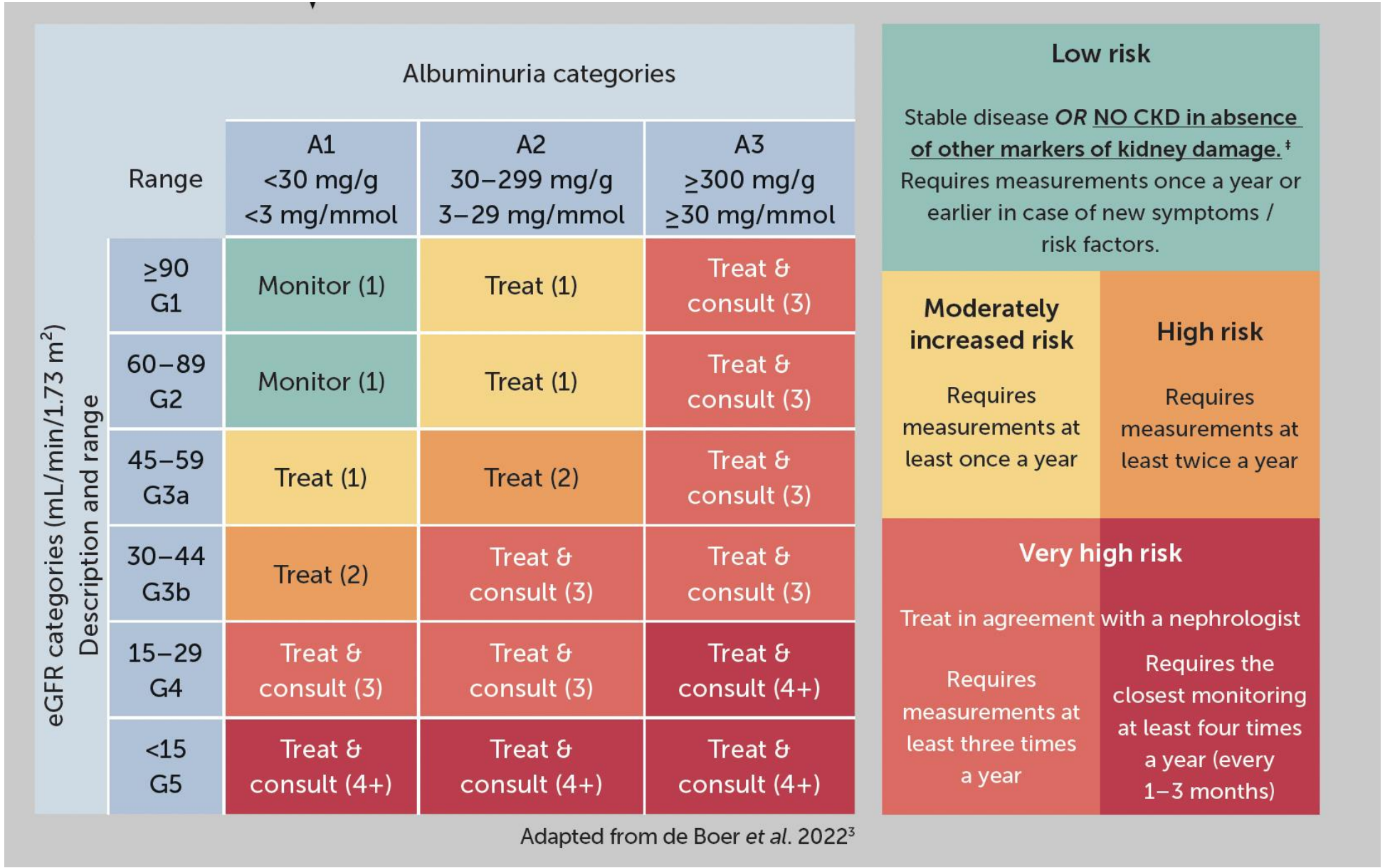
Variations in eGFR

- An All Black prop weighing 125kg with a serum creatinine of 125umol/l has an eGFR of 69ml/min/1.73m^2 (CKD grade 2) but has a normal calculated creatinine clearance of 141 ml/min.
- An anorexic 35 year female who is drastically underweight (42 kg) with a serum creatinine of 70umol/l has a falsely normal eGFR of 97ml/min/1.73m^2, but a calculated creatinine clearance of 66ml/min suggesting established CKD (grade 2).
- 20year old gym fanatic (Weight 95kg) has a serum creatinine of 115umol/l, eGFR of 78ml/min/1.73m^2 but calculated creatinine clearance 122ml/min. Taking large quantities of creatine supplements

Estimated Glomerular Filtration Rate: eGFR

- Major determinant is AGE in the denominator
- Lab variation in creatinine
  +/- 15 umol/l
- No estimation related to weight
  (muscle bulk) – source of creatinine
- Impact of diet, protein supplements etc

- Why use eGFR?



Adapted from de Boer *et al*. 2022[3]

Similar risk for Cardiovascular disease.

Kidney International 2022 102974-989DOI: (10.1016/j.kint.2022.08.012)

Question 4

- A 65yr old with COPD comes in with an infectious exacerbation and you start him on cotrimoxazole twice daily. A week later you check his kidney function as he is only slowly improving. Blood pressure remains at 136/80. His serum creatinine has gone from his baseline of 160umol/l to 220umol/l and K+ is 5.6 mmol/l
- A: Is this acute kidney injury?
- B: Is this a drug induced injury?
- C: Is this an expected response to the cotrimoxazole?
- D: Are you concerned about the K+?

Creatinine and CKD

- Once there is established CKD, tubular secretion of creatinine becomes important
  Creatinine is now delivered to proximal tubule with uptake by organic transporters
- Competition for these transporters can displace creatinine
  trimethoprim will falsely elevate serum creatinine.
- However, need to consider other reasons for elevated serum creatinine – fall in eGFR

	26.Jul.2011	06.Oct.2011	06.Mar.2012	11.Jun.2012
	08:50	08:45	08:30	09:14
Sodium	**147**	143	142	142
Potassium	4.5	4.6	4.4	4.4
Creatinine	**223**	**237**	**255**	**260**
Uric Acid				
eGFR	**27**	**25**	**23**	**22**
Urea	**12.6**	**12.7**	**11.7**	**12.6**

The GFR range for a young adult male is 87-167. From ag

65 year old male:
Please review deteriorating kidney function

	28.Nov.2009	27.Feb.2010	12.May.2010	21.Jun.2010	26.Jul.2010	01.Nov.2010	08.Feb.2011	08.Apr.2011	12.Jul.2011	26.Jul.2011	06.Oct.2011	06.Mar.2012	11.Jun.2012	09.Jul.2012
	09:30	10:04	08:15	09:45	08:39	08:25	08:40	08:30	08:35	08:50	08:45	08:30	09:14	08:38
Sodium	143	139	140	135	145	143	143	144	142	**147**	143	142	142	**146**
Potassium	4.5	**3.4**	**3.3**	4.5	4.5	4.7	4.7	4.5	4.6	4.5	4.6	4.4	4.4	4.6
Creatinine	**219**	**229**	**279**	**271**	**217**	**230**	**219**	**217**	**243**	**223**	**237**	**255**	**260**	**233**
Uric Acid			**0.67**											**0.51**
eGFR	**29**	**28**	**22**	**21**	**28**	**26**	**27**	**28**	**24**	**27**	**25**	**23**	**22**	**25**
Urea	**11.6**	**15.7**	**16.1**	**17.6**	**10.6**	**11.8**	**11.4**	**10.7**	**13.1**	**12.6**	**12.7**	**11.7**	**12.6**	

No change in eGFR over 3 years.

Variation around a mean.

Calculated creatinine clearances 42 – 36 ml/min.

Interpreting eGFR

- Does the result match the clinical picture?
- Extra serum creatinine values last 2- 4 years very useful.
- Important to add other variables
  proteinuria and blood pressure control.
  Medications
  Proportion muscle mass
  Intercurrent illness or excess physical activity.
  Creatine supplements and dietary intake

Progressive Nephropathy

- Overall in CKD
  - Lose the protective vasodilation or vasoconstriction
  - Kidney senses these highs and lows in perfusion pressure
  - Creatinine does rise and fall as you correct this
  - (a linear relationship almost)
  - Pre-glomerular pressure response lost and post-glomerular compensation lost

  - Loss of autoregulation.
  - In CKD fluctuations in serum creatinine and eGFR are normal

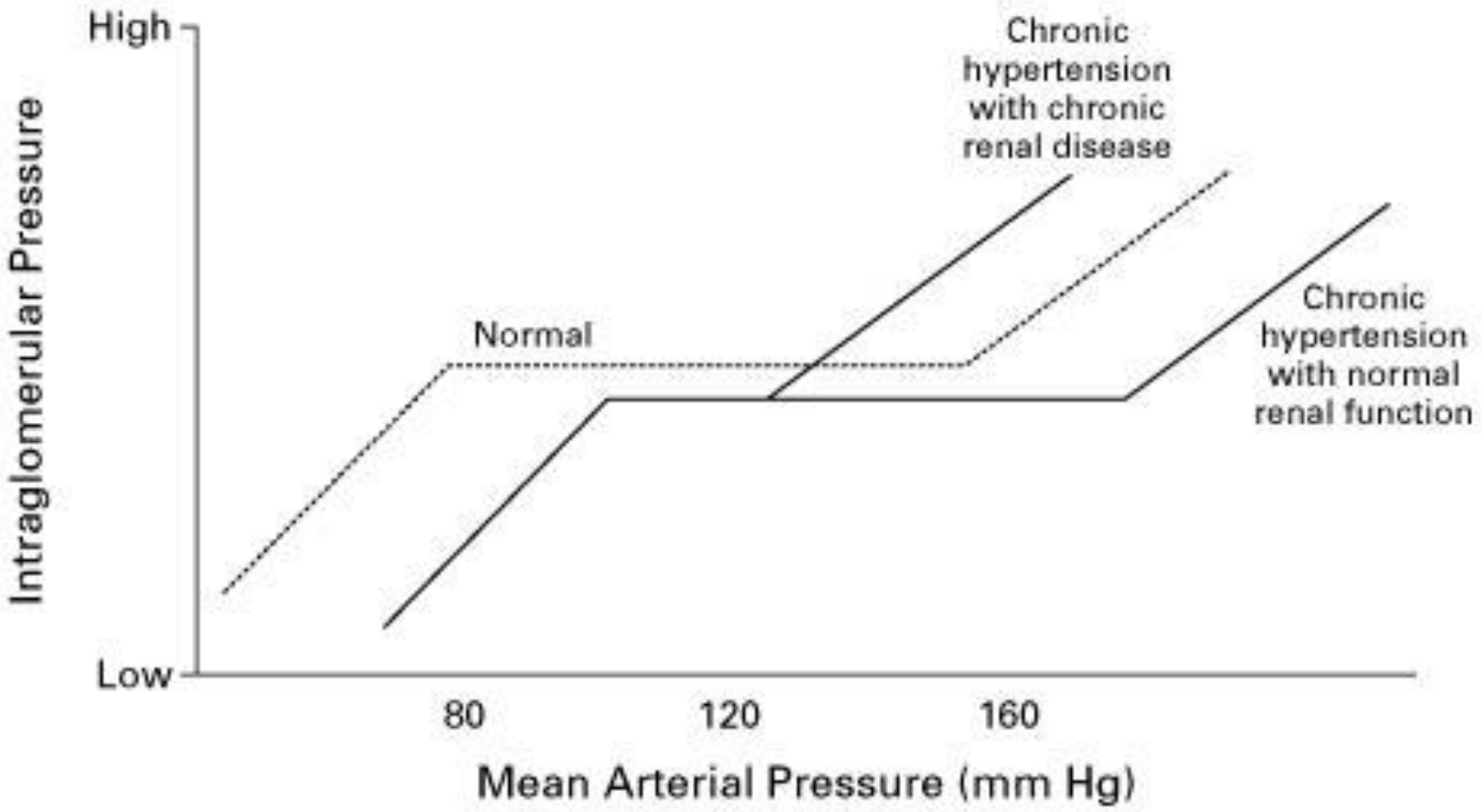
Case & question 5

- 65year old female, with hypertension and heart failure on an ACEI (BP was 136/80) frusemide increased due to some lower limb oedema, BP now 110/80, you check kidney function: serum creatinine was 130umol/l & eGFR 37ml/min/1.73m^2, now serum creatinine 148umol/l & eGFR 30ml/min/1.73m^2
- A: this is AKI - refer
- B: Stop ACEI as this has caused AKI
- C: withhold frusemide and recheck in a few days
- D: Do nothing just observe

Acute Kidney Injury - Altered Perfusion

- Certain pathophysiologic and pharmacologic factors may limit the effectiveness of autoregulatory responses to Kidney insults.
- Older age, chronic kidney disease, cardiovascular and peripheral vascular disease (including hypertensive or diabetic vasculopathy), infection, inflammation, sepsis, impair the reactivity of afferent & efferent arteriolar vessels to homeostatic stimuli.
- In these patients, even transient, mild hypotension may exhaust the ability of these arterioles to compensate for decreased renal perfusion, resulting in hypoperfusion and reduction in eGFR
  if prolonged then hypoperfusion-associated AKI.

Renal Autoregulation



Normal regulation

Myogenic tone

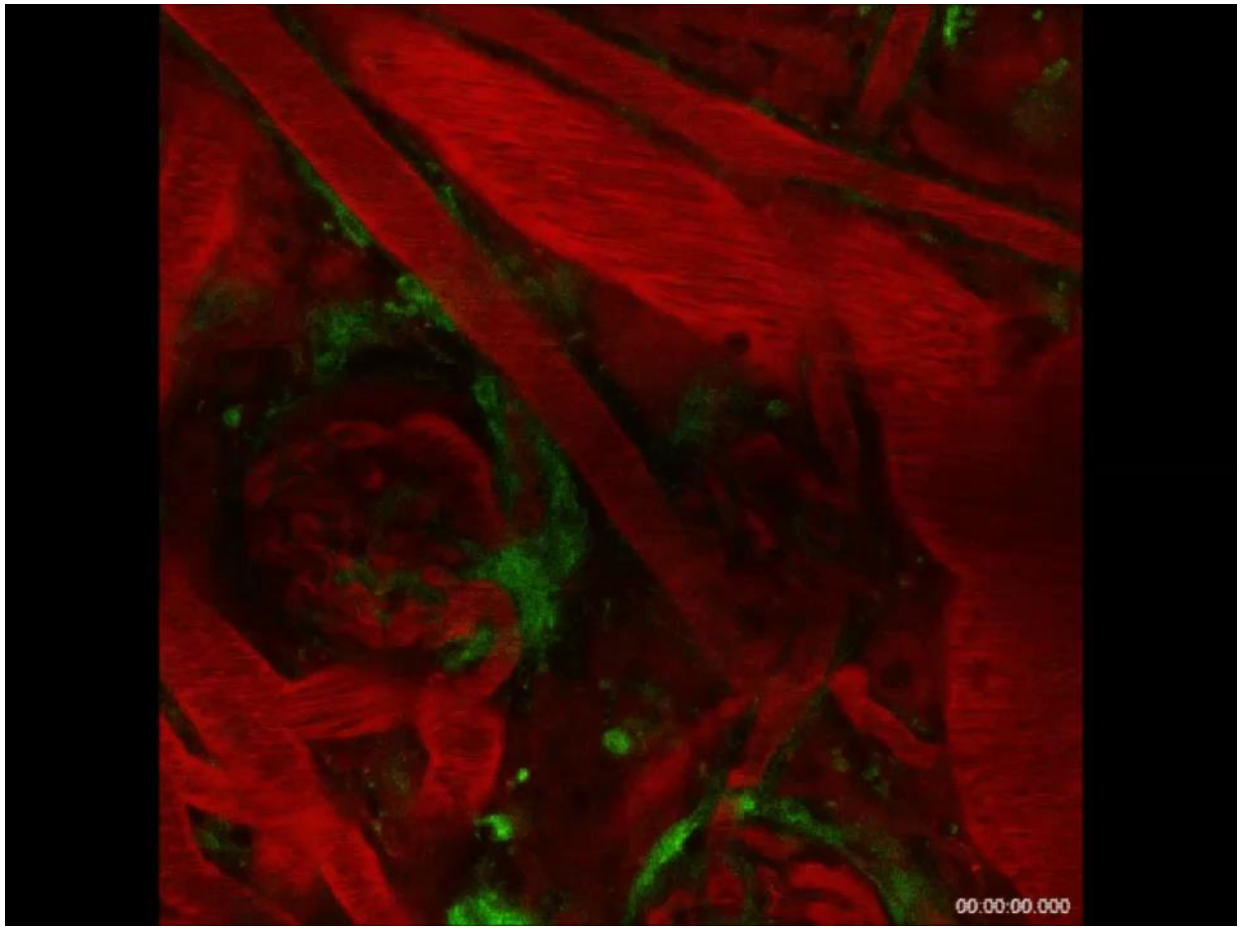
Tubulo-glomerular feedback

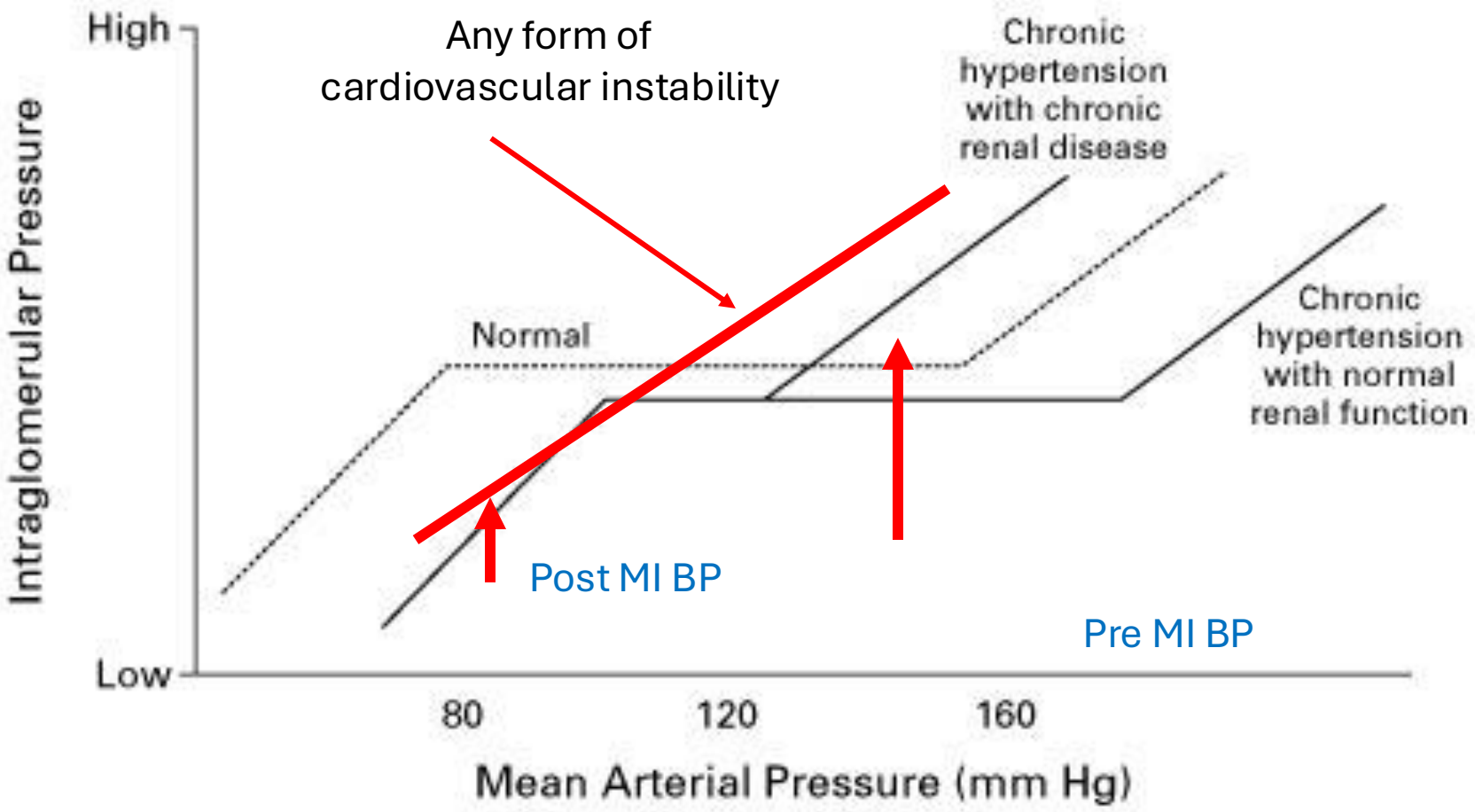
-Sodium balance

Neural input

vasoactive locally released hormones

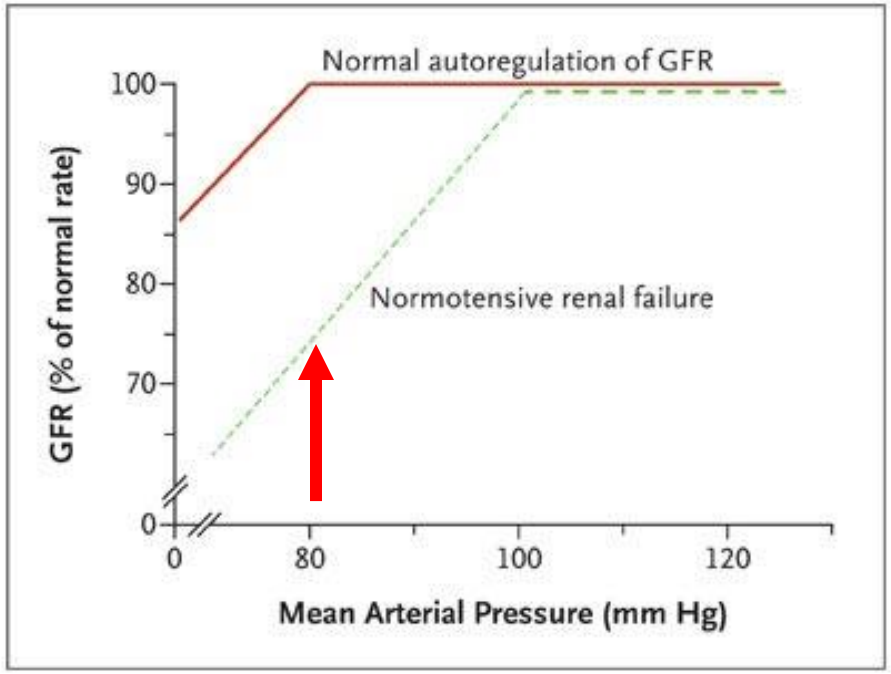
Myogenic oscillations afferent arterioles and glomerulus.
J Peti-Peterdi. Physiology 2009.




High
Low
Intraglomerular Pressure
Any form of
cardiovascular instability
Chronic
hypertension
with chronic
renal disease
Normal
Chronic
hypertension
with normal
renal function
Post MI BP
Pre MI BP
80
120
160
Mean Arterial Pressure (mm Hg)

Blood pressure (kidney perfusion) needs to be assessed in the clinical context

- MAP = 1/3 SBP + 2/3 DBP
- 60 yr old male BP 156/90: MAP = 112mmHg
- Post diuretics BP 110/70 MAP = 83mmHg



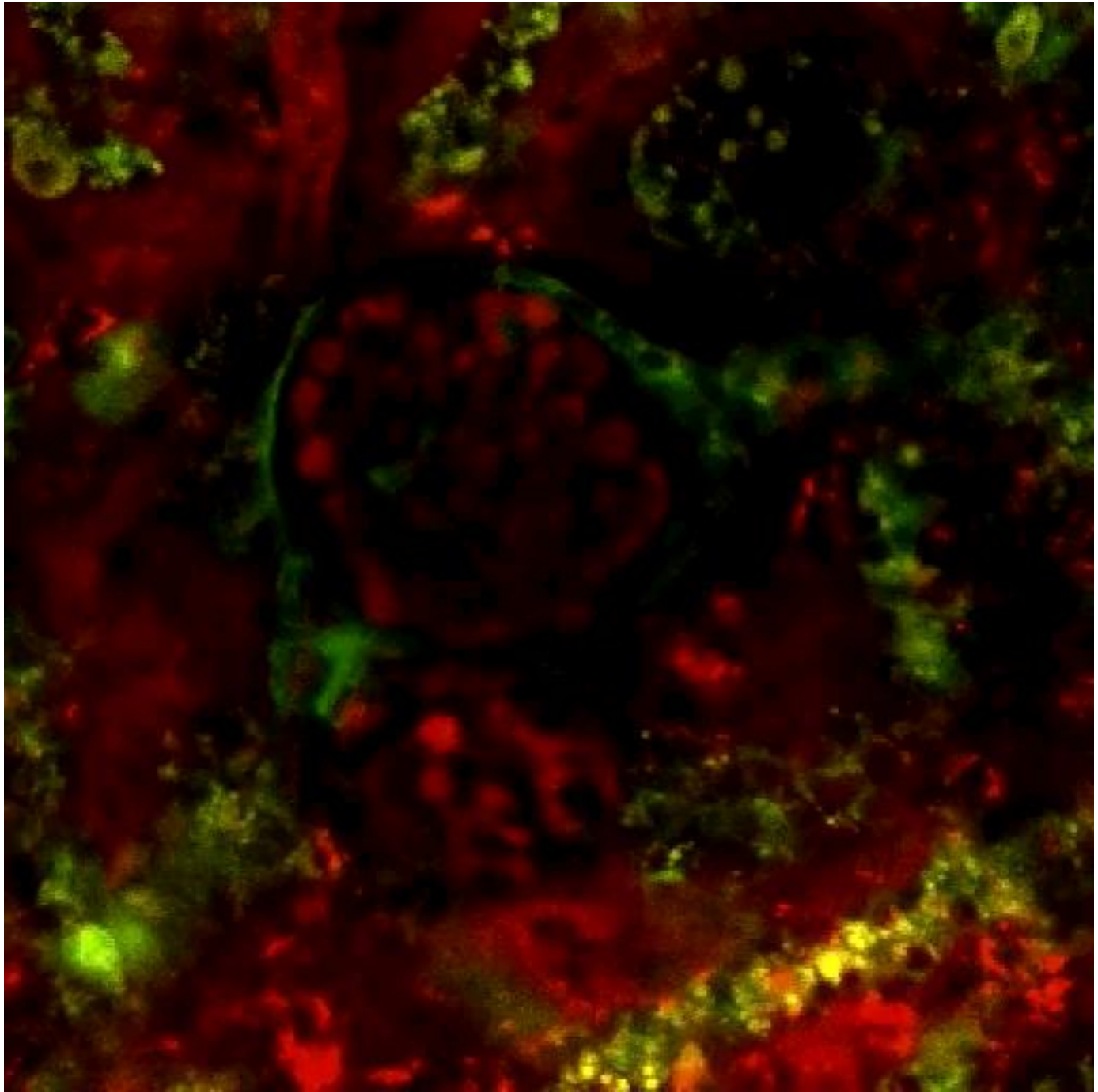
Stress Response – Pathophysiological Changes

- Decrease in pressure in afferent arteriole - renin release in < 1 sec.
- Directly constricts pre-glomerular & post-glomerular vessels
- Pressure dependent changes in RAS - major cause behind hypotensive resetting of RBF autoregulation.
- Now a pathophysiological response which results in marked reduction of renal perfusion.
  decreased GFR
  decreased blood flow in the vasa recta

Peti-Peterdi. 2009

Seeliger 2009. Physiology

Infusion 10ng Ang II into afferent arteriole.
J Peti-Peterdi. Physiology 2009

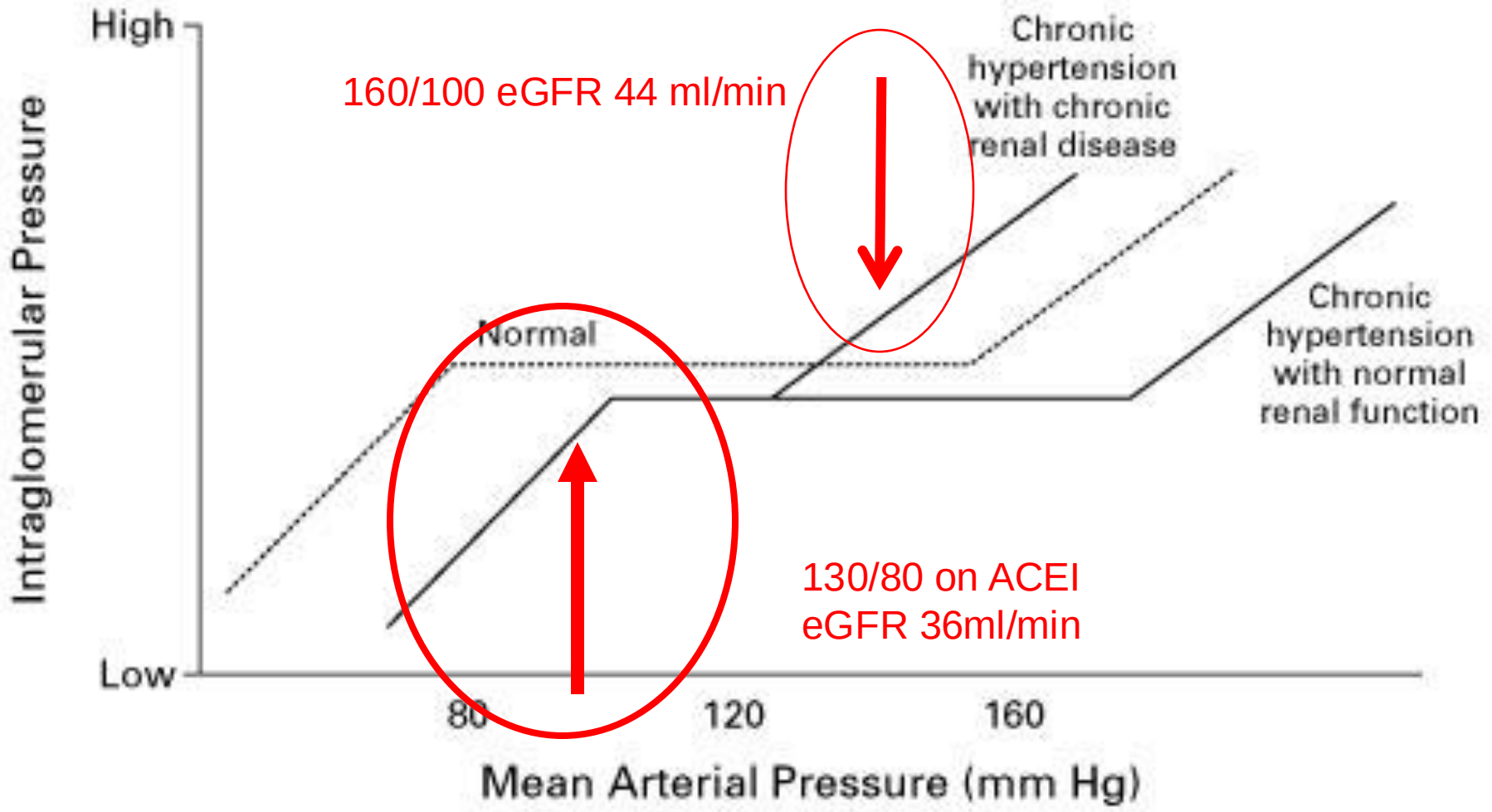


Impact of Vasoactive Drugs on Renal Function

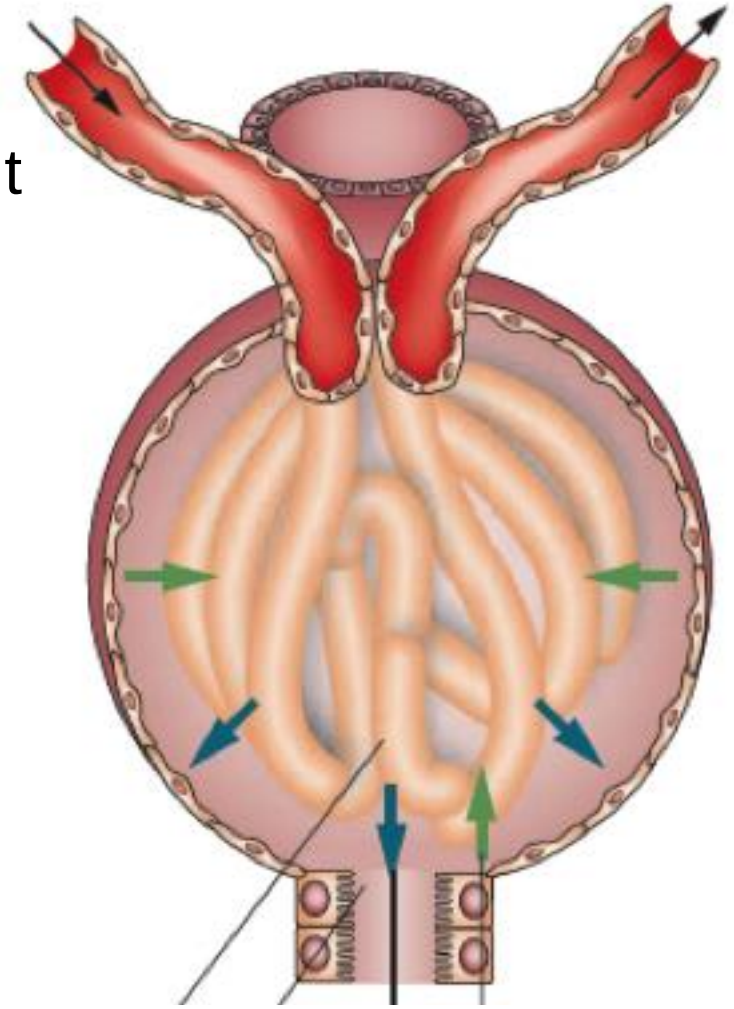
- Systemic effects vs local renal haemodynamic effects
- Need to remember changes over time
- GFR a continuous variable

Question 6

- Introduction of Candesartan in an individual with hypertension and CKD. eGFR falls from 44ml/min/1.73m^2 to 36ml/min/1.73m^2
- A: ARB needs to be stopped as causing AKI
- B: This confirms renal artery stenosis
- C: These drugs should not be used in CKD
- D: Expected physiological response to ARB


160/100 eGFR 44 ml/min
Chronic hypertension with chronic renal disease
Normal
Chronic hypertension with normal renal function
130/80 on ACEI
eGFR 36ml/min
High
Low
Intraglomerular Pressure
80
120
160
Mean Arterial Pressure (mm Hg)

Δ GFR



Slightly increased afferent vasodilation

SNGFR = Kf.NFP

Increased efferent arteriolar vasodilation

↑ Kf in glomerulus

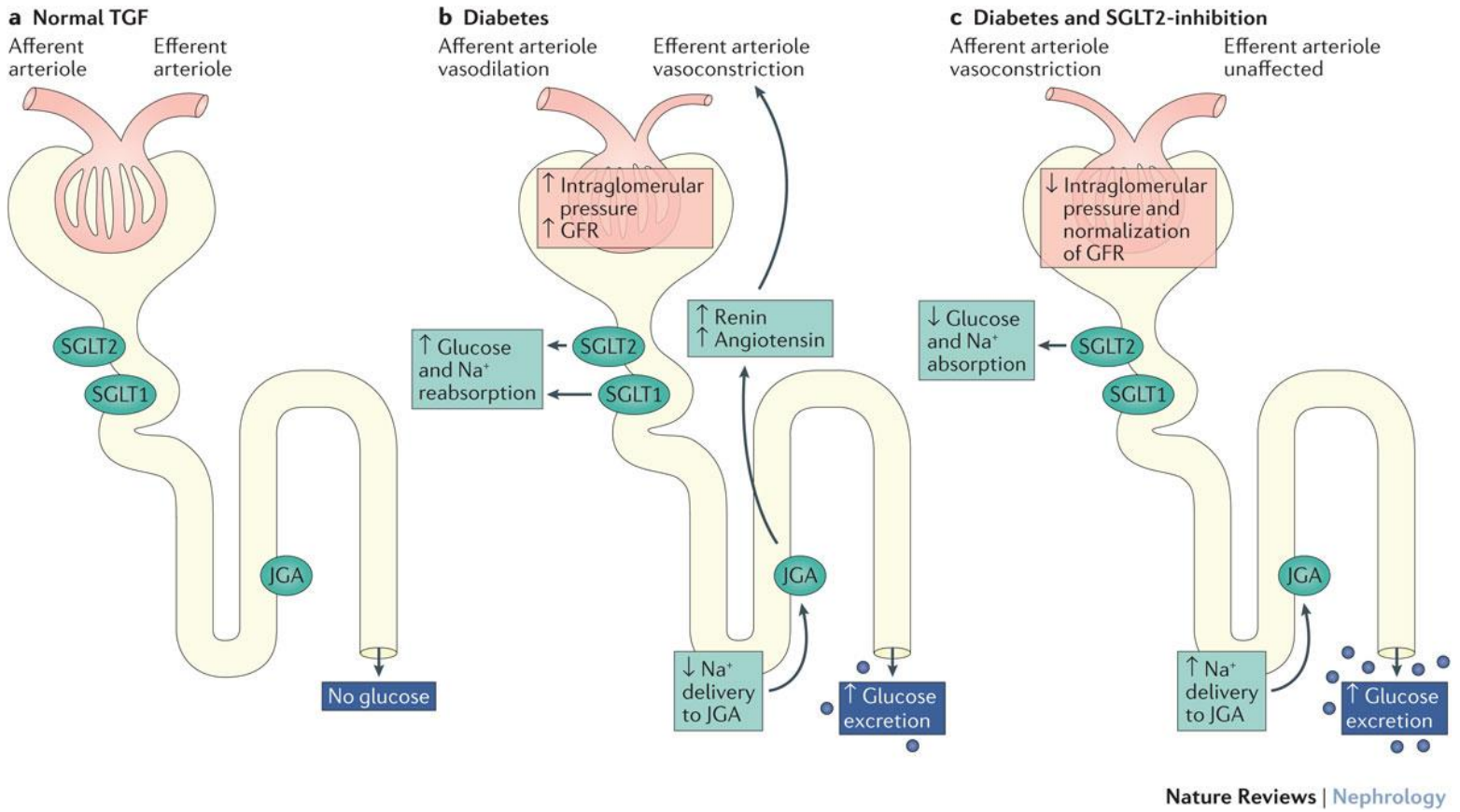
$P \propto 1/r^4$

Action of ACEI or ARB in CKD

Question 7

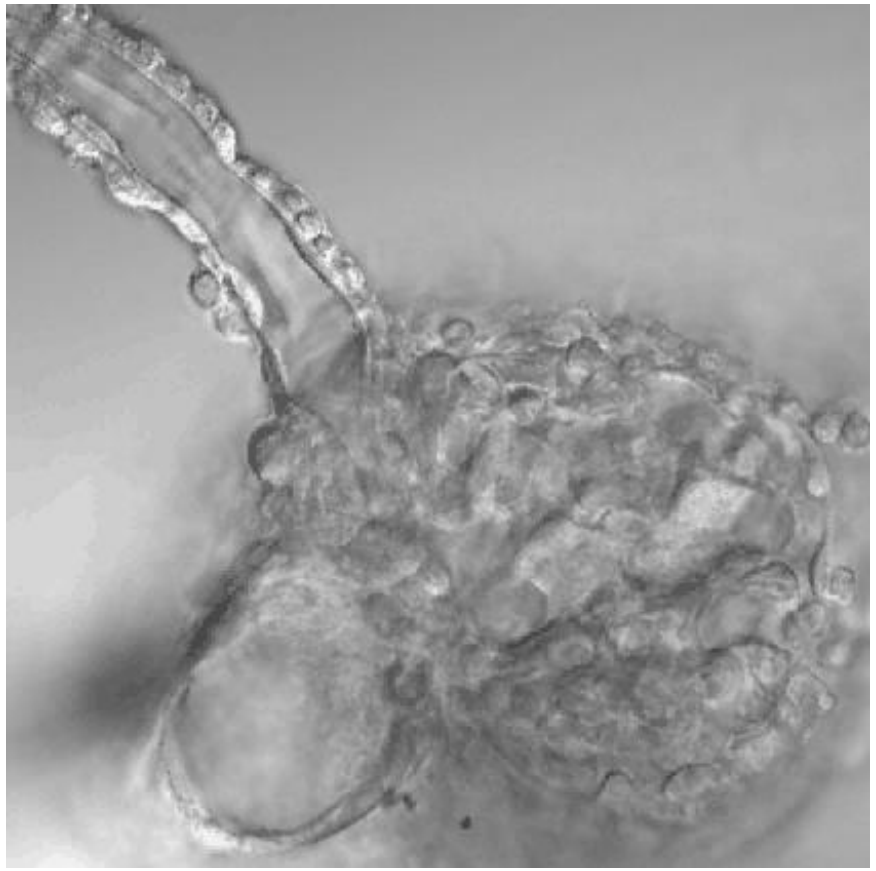
- Type 2 Diabetic with CKD and eGFR 32 ml/min/1.73m^2 is commenced on metformin and empagliflozin (500mg/5mg) BD.
  4 weeks later eGFR is now 26 ml/min/1.73m^2
- A: Empagliflozin is nephrotoxic and must be stopped
- B: eGFR now less than 30ml/min/1.73m^2 so empagliflozin needs to be stopped
- C: This is an expected change but need to review volume status
- D: Needs metformin stopped

Figure 6 Effect of diabetes and SGLT2 inhibition on afferent and efferent arteriolar tone, glomerular filtration rate (GFR), and sodium (Na^+) excretion

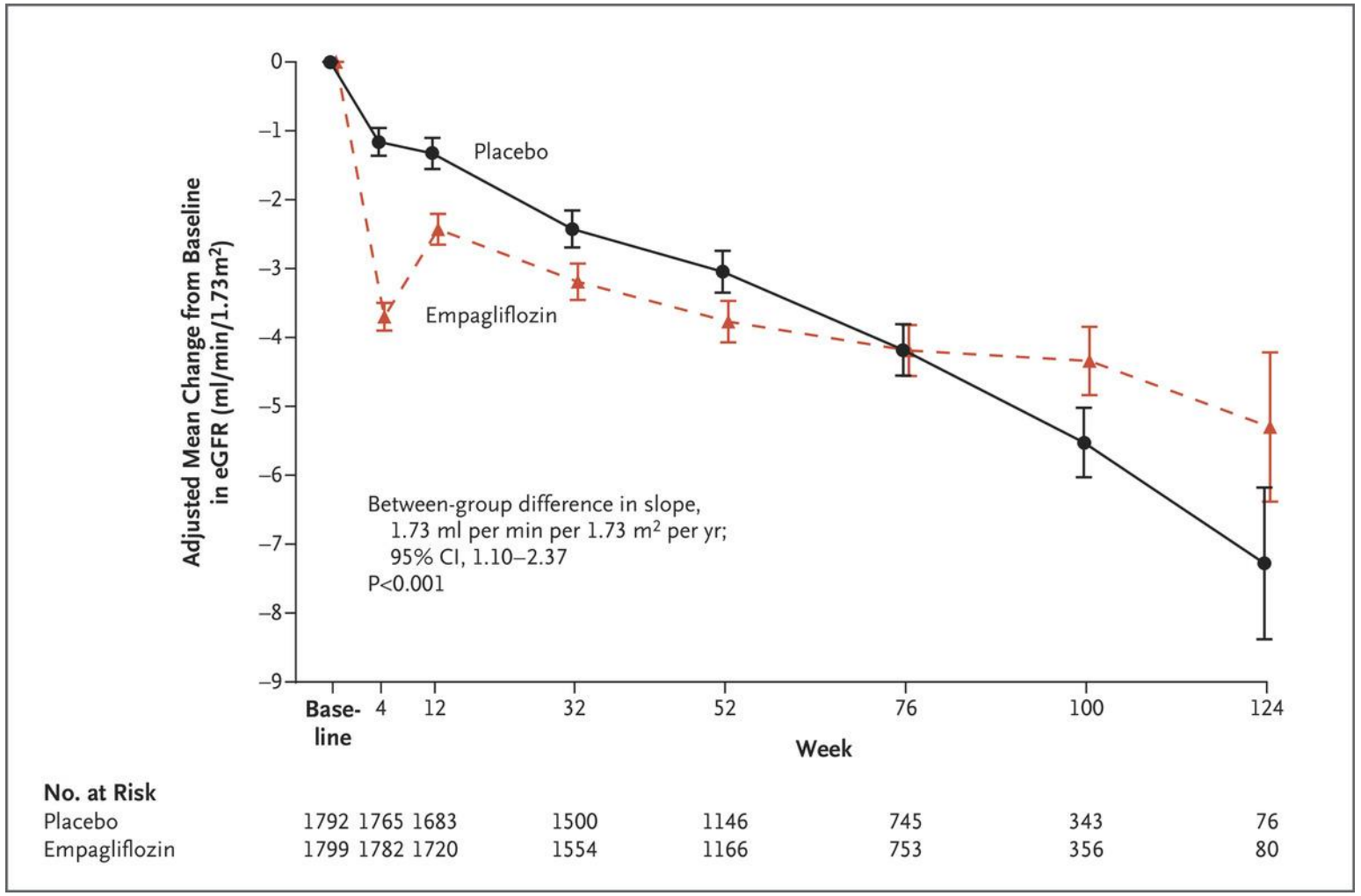


DeFronzo, R. A. *et al.* (2016) Renal, metabolic and cardiovascular considerations of SGLT2 inhibition
Nat. Rev. Nephrol. doi:10.1038/nrneph.2016.170

Isolated glomerulus – Tubuloglomerular feedback.
J Peti-Peterdi. Physiology 2009.



Changes in the Estimated Glomerular Filtration Rate.



Reduction in eGFR up to 30% acceptable

M Packer et al. N Engl J Med 2020;383:1413-1424.

The NEW ENGLAND JOURNAL of MEDICINE

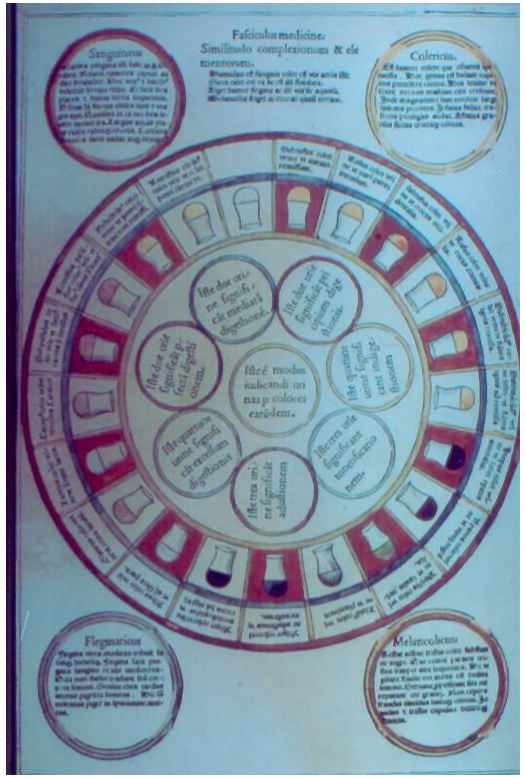
Key messages

- Variation in eGFR is expected once evidence of CKD
- Review contributing factors
  -changes in blood pressure and intravascular volume
  -factors affecting creatinine (muscle mass, high protein diet, supplements etc)
  -drugs
- Repeat test and compare longitudinal trend for serum creatinine /eGFR

Question 8

Where is this?
A: Milan
B: London
C: Paris
D: Rome
E: Athens

Urinalysis


Fasciculus medicine:
Sanguineus
Colericus.
Flegmaticus
Melancolicus


cobas
Roche

Question 9

- In reviews of General Practice assessment of kidney function, how often is urinalysis included in the assessment?
- A: 80%
- B: 60%
- C: 50%
- D: 40%
- E: less than 30%

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

KDIGO KIDNEY DISEASE IMPROVING GLOBAL OUTCOMES

Wonca World family doctors Caring for people. EUROPE

PCDE primary care diabetes europe

CKD is underdiagnosed and undertreated in the community[1]

Early identification, risk stratification, and treatment can reduce the morbidity and mortality rates from CKD and its related complications, such as CVD[2]

Step 2

Test high-risk adults to detect CKD
(not population-wide)

Evaluate kidney function – eGFR
- eGFR calculated based on serum creatinine and/or cystatin C

AND

Evaluate kidney damage – albuminuria
- UACR or dipstick* (if UACR is unavailable)

If UACR ≥30 mg/g (>3 mg/mmol) OR eGFR <60 mL/min/1.73 m²

If UACR <30 mg/g (<3 mg/mmol) AND eGFR >60 mL/min/1.73 m²

Re-test in 3 months

Step 3

Diagnose CKD

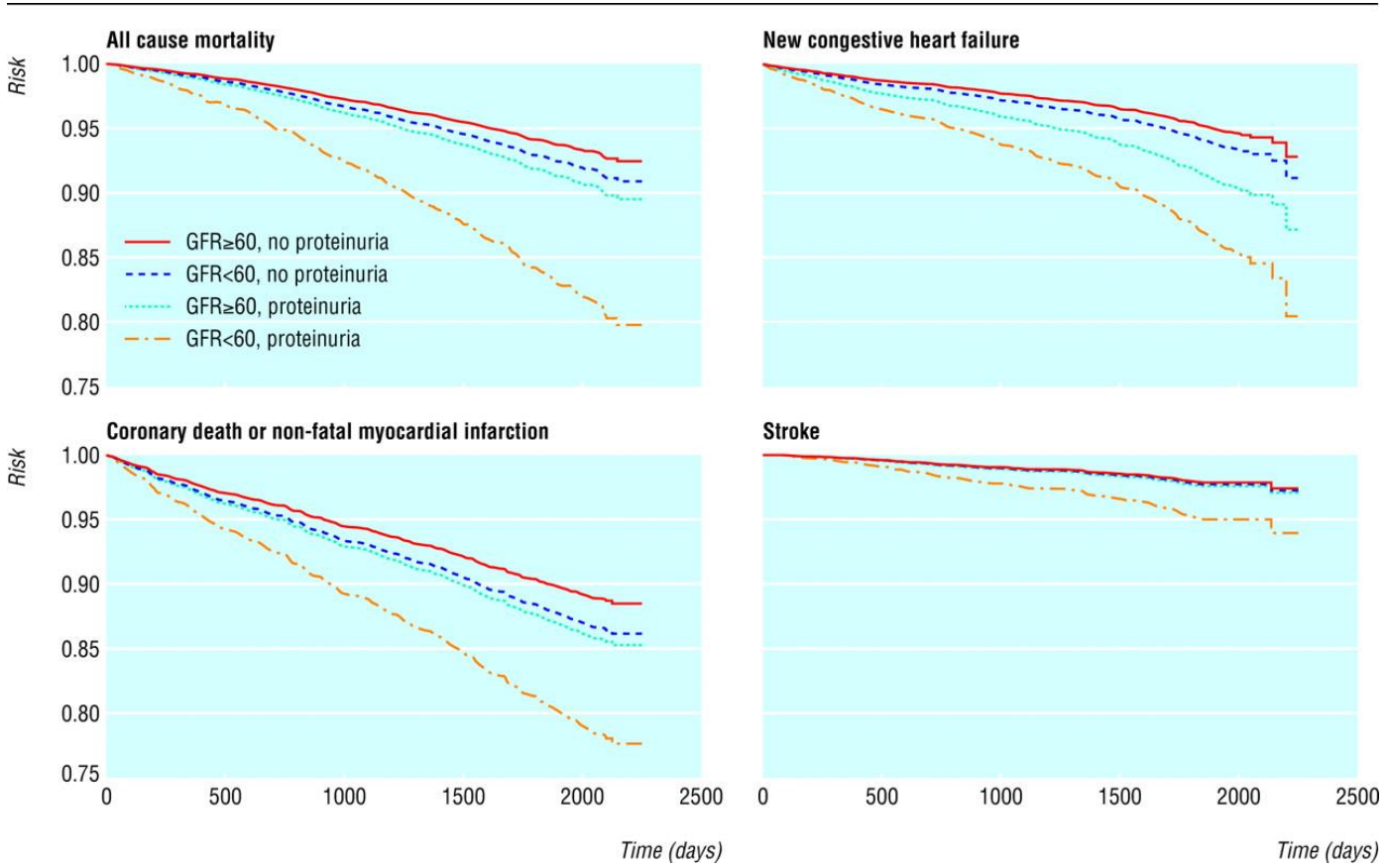
If low eGFR or high UACR are present for ≥3 months, diagnose CKD

Re-test at least once a year†

Do not forget the importance of urinalysis for CKD and CVD
Less than 25% had urinalysis!!

”bubbles appearing on the surface of the urine indicate renal disease with a prolonged course”

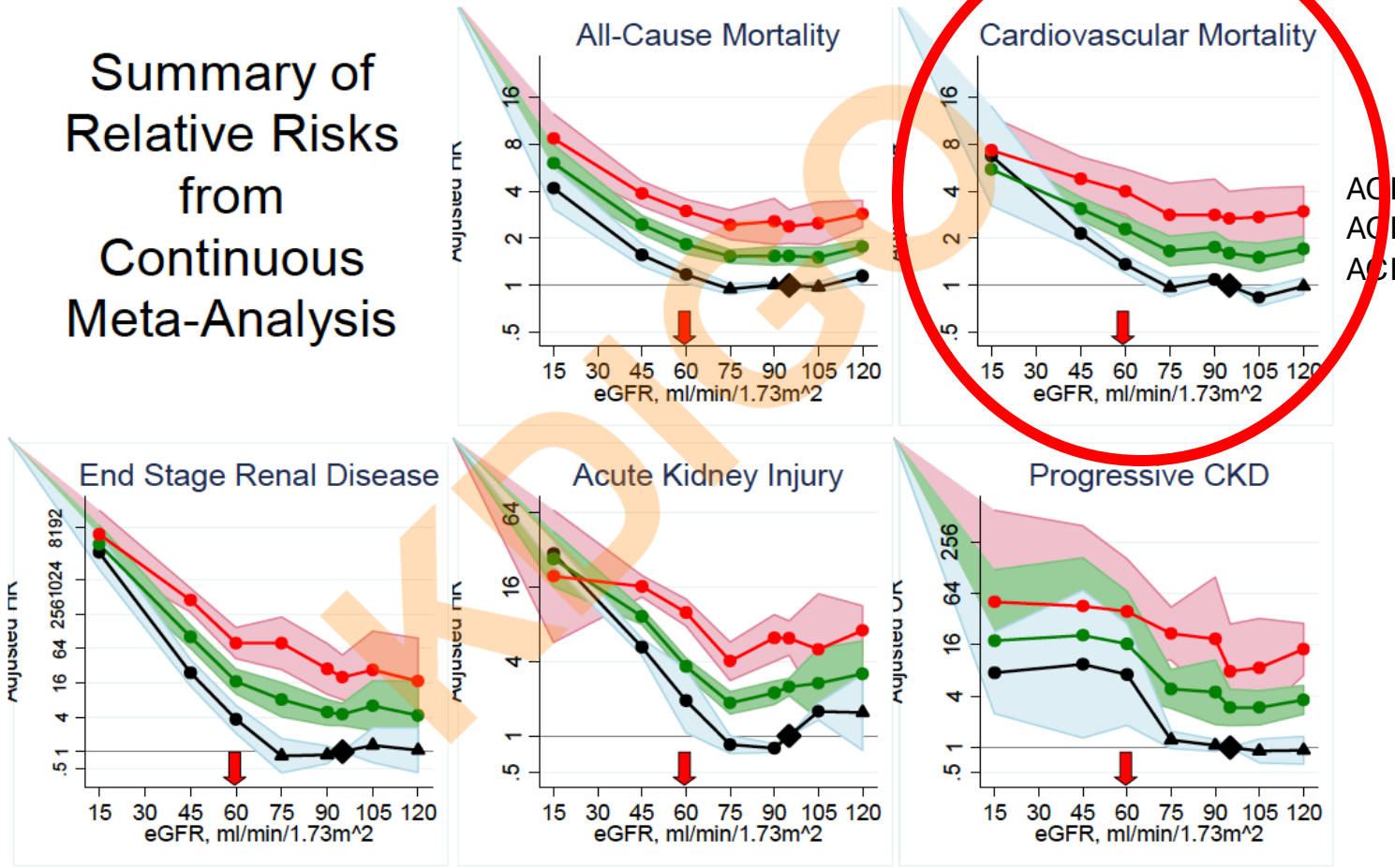
Fig 1 Time to clinical outcomes by proteinuria and kidney dysfunction



Tonelli, M. et al. BMJ 2006;332:1426

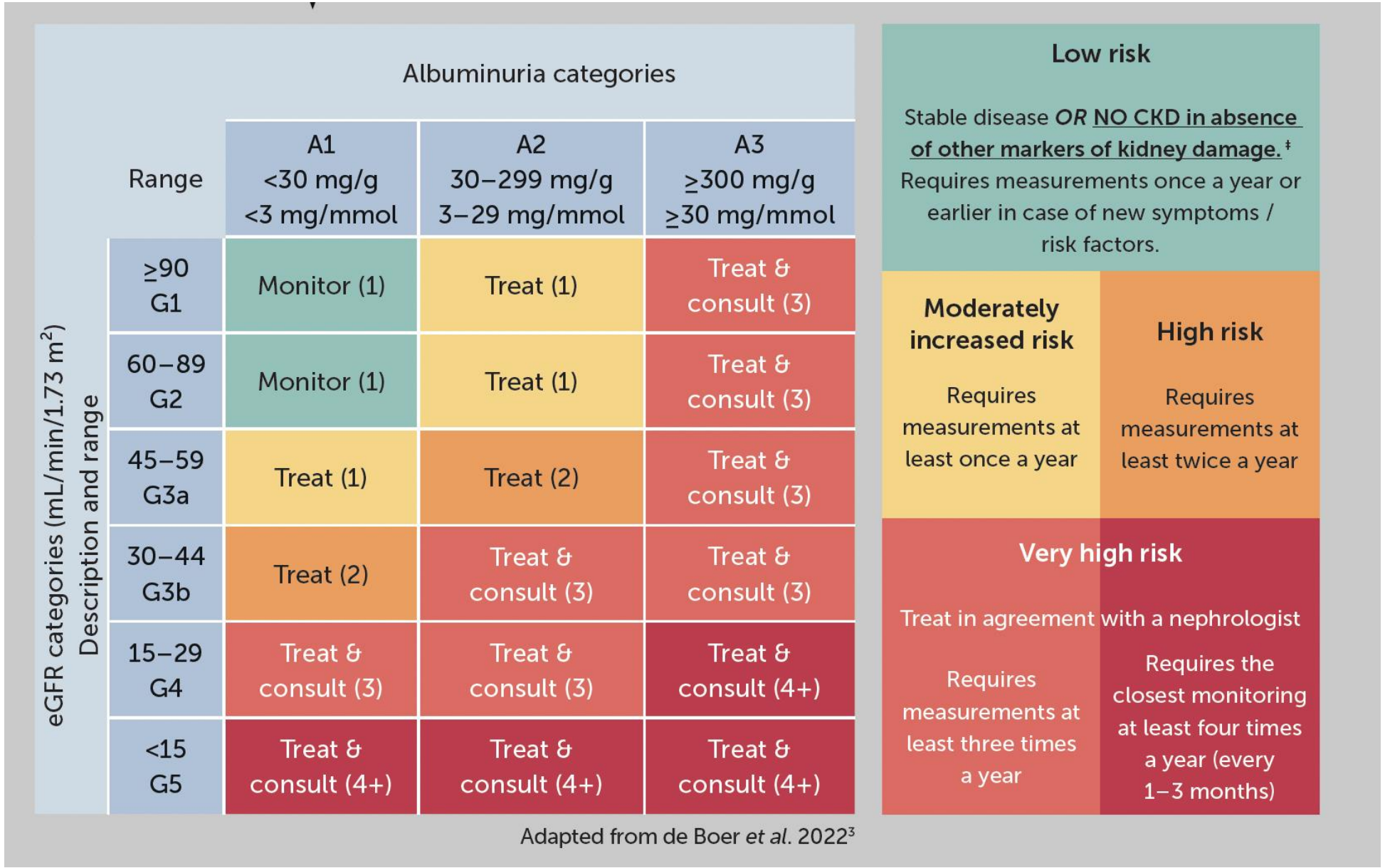
CV/renal prognosis related to GFR and ACR

Summary of Relative Risks from Continuous Meta-Analysis



ACR > 30mg/mmol
ACR 3– 30 mg/mmol
ACR < 3 mg/mmol

Matsushita K et al, Lancet 2010;375:2073-81 and Gansevoort RT et al Kidney Int 2011;80:93-104



Adapted from de Boer *et al*. 2022[3]

Similar risk for Cardiovascular disease.

Kidney International 2022 102974-989DOI: (10.1016/j.kint.2022.08.012)

Assessment of Albuminuria

- Albuminuria influenced by
  Exercise
  Obesity
  Hypertension
- Early morning urine – before physical activity
- Use urinary albuminuria/creatinine ratio
- Orthostatic benign proteinuria.

Risk management strategies

Table 1. Treat to slow CKD progression, reduce mortality risk, and manage comorbidities	
Lifestyle modification	
Smoking cessation; regular exercise; well-balanced diet (avoid excessive protein intake and processed food, limit sodium intake <2 g/day)	
Medical treatment	
Treat diabetes, hypertension, and CVD: Optimise blood pressure and glycemic control	Ensure guideline-directed medical treatment to slow down CKD progression and reduce CVD risk: maximally tolerated doses of **ACEIs/ARBs, SGLT2 inhibitors, nonsteroidal MRAs** with proven benefits in renal and cardiovascular outcome trials for T2D; also consider **lipid-lowering therapy (statins)** and/or **antiplatelet therapy** (for patients with CKD at risk of atherosclerotic events)
Considerations	
Adjust dosing of medications based on eGFR; exercise caution when prescribing analgesics, antimicrobials, hypoglycemics, chemotherapeutics, or anticoagulants; avoid nephrotoxins (e.g. NSAIDs) and some contrast media	

Standard of care for non-diabetic proteinuric CKD is identical

Question 10

- In a urinary albumin creatinine ratio result, you have the following information

Urine albumin concentration 795 mg/l

Urine creatinine concentration 26.4 mmol/l

UACR 30.11 mg / mmol

- A: total albumin concentration is more important than ratio
- B: amount of creatinine in urine reflects kidney function
- C: UACR results put this individual into a high-risk category
- D repeat to confirm

Proteinuria versus albuminuria Question 11

- 64 year old male routine health check has some minor lower limb oedema, has 4+ proteinuria on dipstick analysis, UACR only 35mg/mmol, serum albumin is 35g/l and total protein 72g/l, normal kidney function.
- A: UACR is wrong and you repeat it
- B: 4+ proteinuria reflects low grade proteinuria so with low UACR of no concern
- C: with 4+ proteinuria this is a nephrotic presentation?
- D: you request a urine protein/creatinine ratio in parallel with UACR

Proteinuria versus albuminuria Question12

- Urine protein/creatinine ratio comes back at 176 mg/mmol (UACR 35mg/mmol) what do you do next?
- A: this is exercise-induced proteinuria
- B: request serum free light chains urgently
- C: just repeat in 4 weeks time
- D: commence frusemide to treat the oedema

When is a 24 hr urine required?

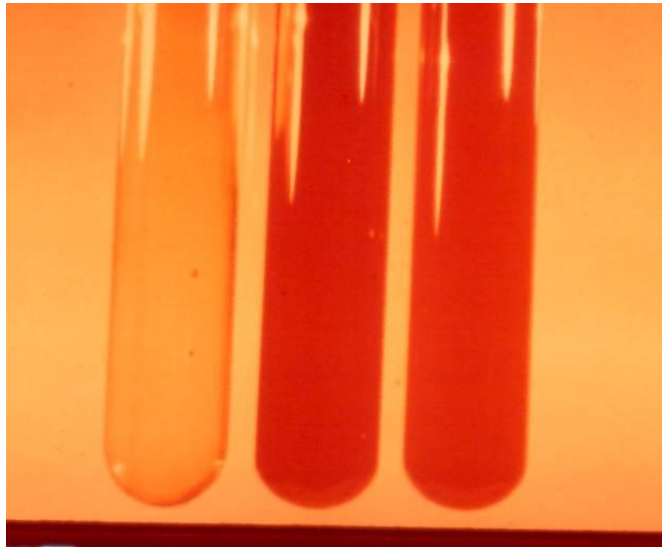
- Do we need a 24hr urine to assess proteinuria?
  - GN assessment?
  - Antenatal assessment?
- Do we need a 24hr urine for routine assessment of creatinine clearance?
- Do we need a 24hr urine for renal stone work up?

Question 13

In which European city is this Naval Training college located?

A: London
B: Hamburg
C: Copenhagen
D: Stockholm
E: Oslo

Haematuria



26 yr old male

Upper respiratory tract infection

Macroscopic haematuria 1 – 2 days later
“synpharyngitic haematuria”

Associated non-specific malaise and lethargy

3 days later haematuria persisting
Episode of R sided loin pain.

Case 2. Investigations Question 14

- Normal renal function, normal blood pressure, normal haematology, auto-antibody screen negative. Normal renal US

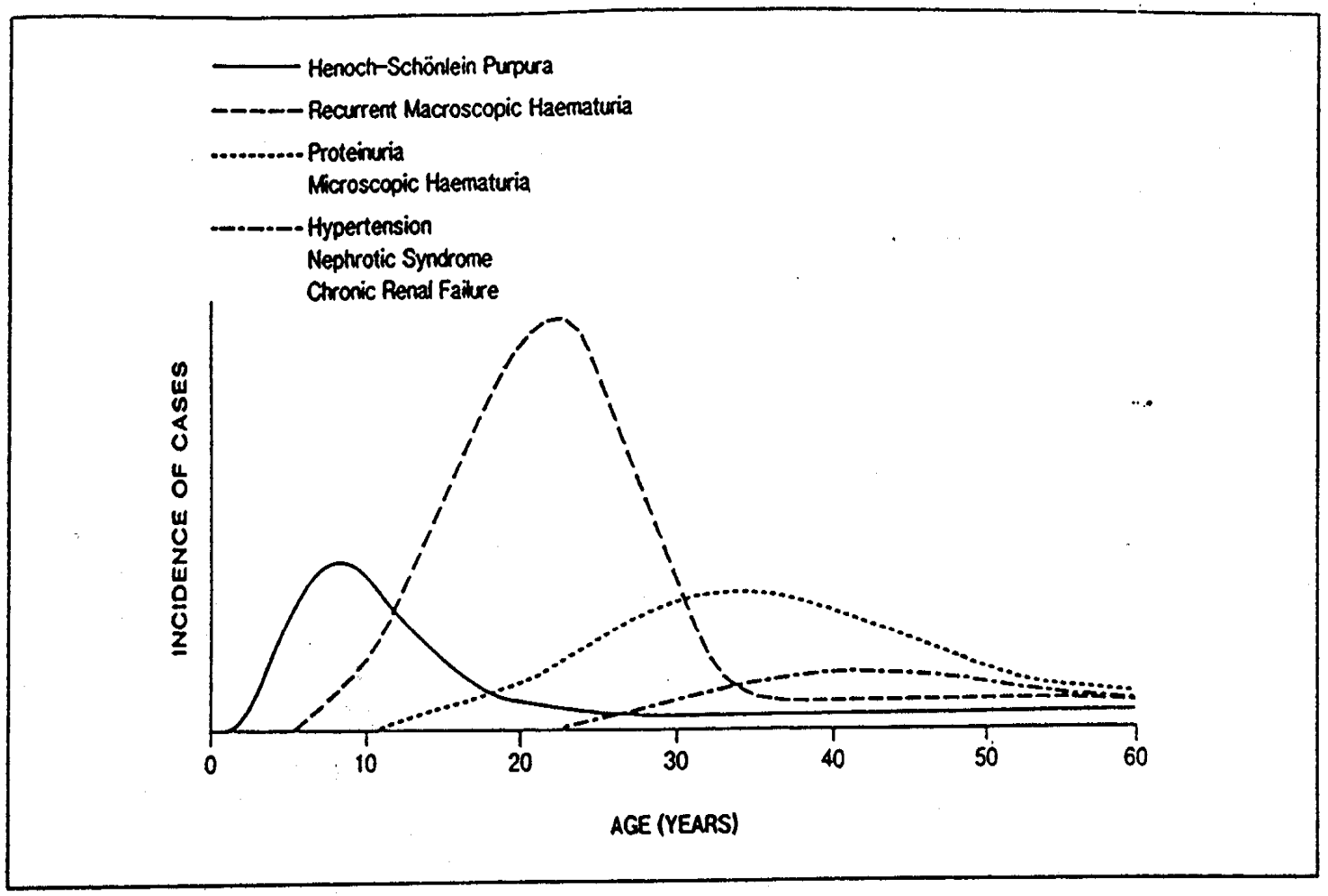
- A: is this post-streptococcal GN?
- B: Is this due to a renal calculus?
- C: Is he presenting with a nephritic syndrome?
- D: Does he need a cystoscopy?
- E: Is this consistent with a glomerulonephritis?

Haematuria

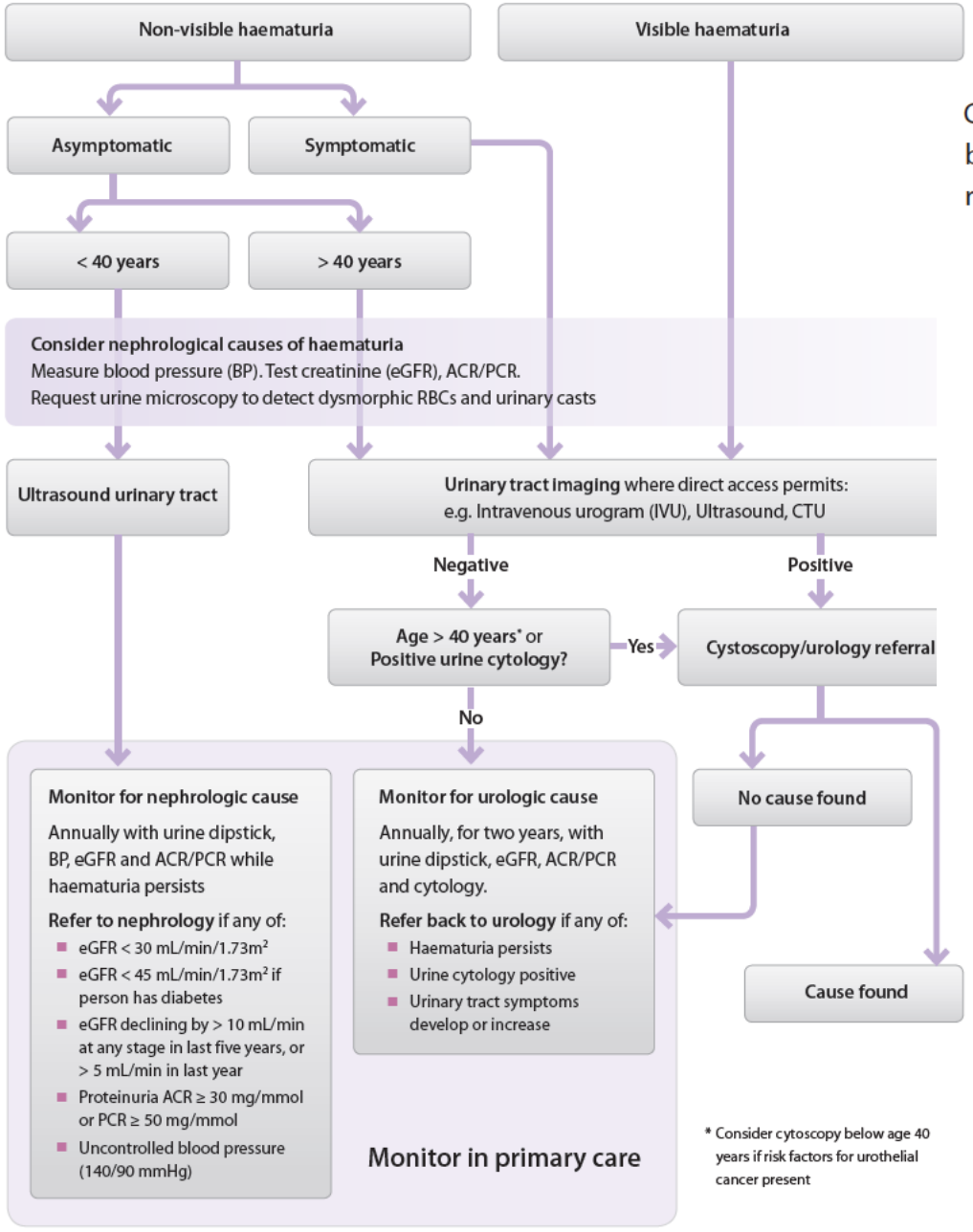
- With proteinuria & absence UTI symptoms (culture negative)
  GN until proven otherwise.
- Haematuria in absence of urological findings
  Also consider GN.
- Warrants nephrological review – discussion.

- In this case – renal biopsy warranted.

Presenting Patterns of IgA Nephropathy



World-wide it is the most common form of primary glomerulonephritis.



Clinical suspicion of significant urological disease should be raised in people with haematuria with the following risk factors:[4]

- History of recurrent visible haematuria
- Age over 40 years
- Current smoker or recent history of smoking
- History of recurrent urinary tract infection (UTI) or other urological disorders
- Occupational exposure to chemicals or dyes
- Previous pelvic irradiation
- History of excessive analgesic use
- Treatment with cyclophosphamide

Haematuria in the absence of dysuria is not a UTI

Case and Question 15

- 68year female presents with non-specific symptoms of anorexia, and tiredness. Denies any urinary symptoms, still passing good volumes of urine, nocturia x1. BP 136/80
  Meds Quinapril for hypertension, omeprazole for indigestion, cholecalciferol and a vitamin supplement.
- Kidney function has deteriorated over past 2 months eGFR falling from 46ml/min/1.73m^2 to 24ml/min/1.73m$^{2.}$ Urinalysis demonstrates WBC >100 x 10^6/l but no growth on culture. UACR 26mg/mmol.

- A: do you treat as a presumptive UTI
- B: withhold her ACEI as this has caused her change in function
- C: Stop her omeprazole and refer to nephrology
- D: Organise a CT scan

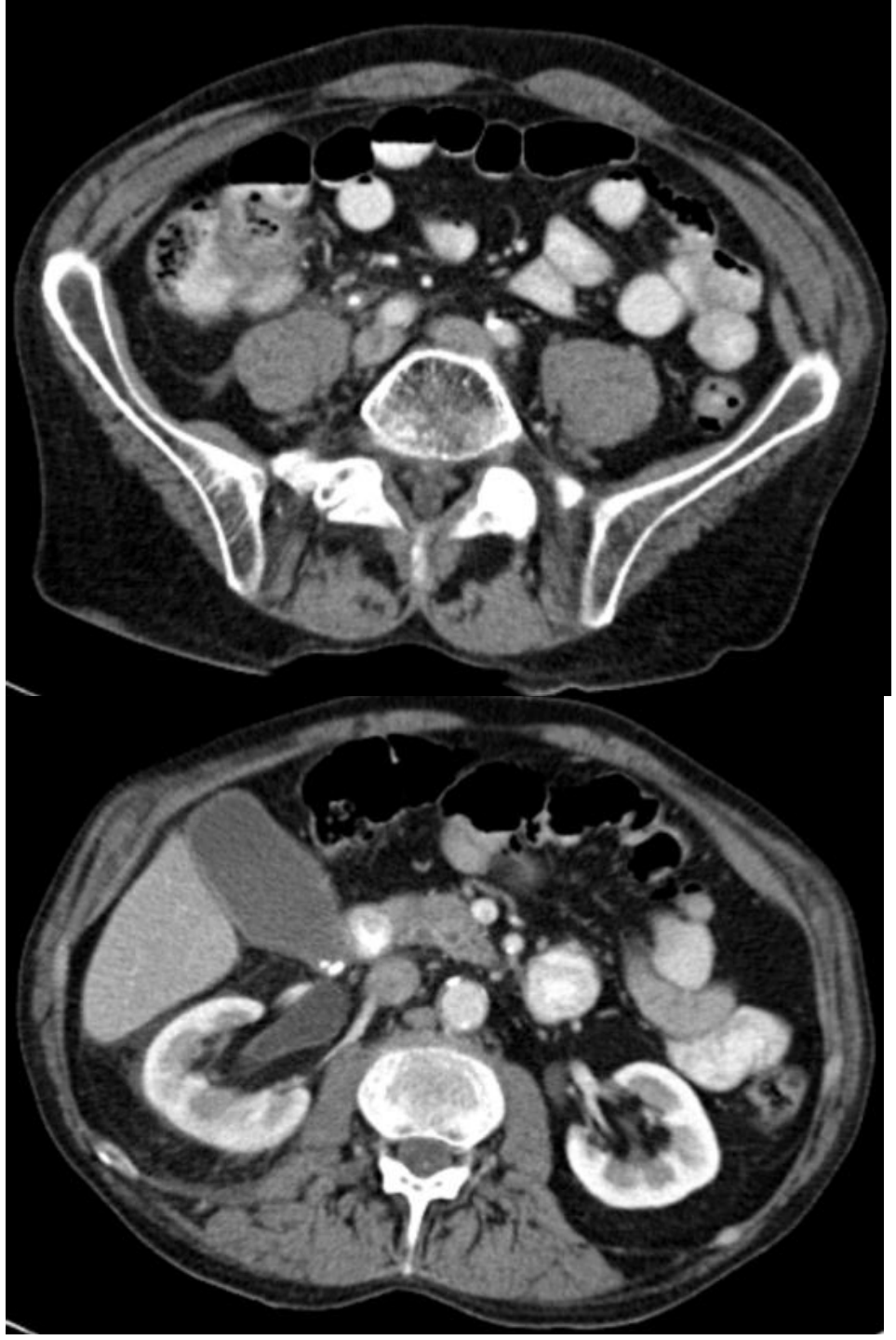
Sterile pyuria

- Marker of kidney inflammation
- Causes of inflammation
  - chronic infection – TB
  - GN primary or secondary such as SLE vasculitis
  - acute interstitial nephritis
- AIN most common aetiology
  Drug induced – PPIs
  less common antibiotics and NSAIDs

- Take home message – in the absence of symptoms sterile pyuria is NOT an UTI

Case 3

- 45 year old male sudden onset severe R sided flank pain.
- Pain radiating from flank to groin, severe 9/10 intense with waves of colic.
- Episode of macroscopic haematuria associated with pain.



What is the most usual composition of the renal calculus? Question 16

- A: Uric acid?
- B: Struvite (magnesium ammonium phosphate)?
- C: Calcium oxalate?
- D: Calcium hydroxyapatite?

Renal Stone Types

- Calcium oxalate 36 -70%
- Calcium phosphate (hydroxyapatite) 6 -20%
- Mixed calcium oxalate and phosphate 11 – 30%
- Struvite stones 6 – 20 % (associated with infection)
- Uric acid stones 6 -17% (radiolucent).
- Cysteine stones 0.5 – 3%

What is the major contributor to kidney stone formation? Question 17

- A: Too much calcium in the diet?
- B: Excess uric acid excretion?
- C: Excess urinary oxalate excretion?
- D: Excess urinary calcium excretion?
- E: Concentrated urine?

Stone Investigations

- History – bowel disease and pancreatic disease
  oxalate handling by gut – absorption small bowel excretion large bowel.
- Investigations
  Stone analysis
  Serum calcium, phosphate, uric acid,
  consider electrolytes and pH
- 24 hour urinary excretion calcium, oxalate, phosphate, citrate, uric acid. (total volume helpful)
- Dietary review
  Dietary calcium (needs to be high normal) and salt intake (needs to be low)
  Foods rich in oxalate, vitamin C excess, Vitamin D supplementation.

Stone Prevention

- Fluids fluids and more fluids – dilute urine > 2.5 liters
- Non opaque stones (Uric acid) : Fluids, alkalinisers, allopurinol and surveillance.
- Calcium oxalate stones
  High normal dietary calcium, reductions sources oxalate, low dietary salt intake
  consider allopurinol (uric acid levels & possible seeding)
- Can consider potassium citrate for recurrent stone formers
- Hypercalcuria – thiazides but of limited value

Question 18

In which city is this famous building?

1. London
2. Paris
3. Venice
4. Florence
5. Madrid

Hyponatraemia

Question 18

- A: Is hyponatraemia determined by total body sodium?
- B: Is hyponatraemia determined by total body water?

Hyponatraemia

- 3 main categories
- Hypovolaemic hyponatraemia
  - severe GI losses
  - osmotic diuresis
  - mineralocorticoid deficiency
- Hypervolaemic hyponatraemia
  - heart failure, liver failure
  - iatrogenic
- Euvolaemic hyponatraemia
  - Drugs
  - SIADH
  - potomania
  - Addisons & hypothyroidism

Hyponatraemia

- 75year old female, moderately confused, not coping at home. History of depression. Meds Citalopram and metoprolol.
- BP 132/88, JVP 2cm, normal neuro exam, weight 62kg
  Na+ 119mmol/l, K+ 3.7mmol/l, urea 4.2mmol/l, creatinine 67umol/l
- What type of hyponatraemia?
- What tests to help with diagnosis?
- Mechanisms of hyponatraemia

Hyponatraemia

- Investigations:
- Serum osmolality 265 mosm/kg
  Urine osmolality 620 mosm/kg

- How do you interpret this?

Hyponatraemia

- 75year old female, moderately confused, not coping at home. History of depression. Meds Bendrofluazide and metoprolol.
- BP 112/88, JVP not visible, normal neuro exam. Weight 58kg Na+ 119mmol/l, K+ 3.7mmol/l, urea 4.2mmol/l, creatinine 67umol/l
- What type of hyponatraemia?
- What tests to help with diagnosis?
- Mechanisms of hyponatraemia

Hyponatraemia

- Investigations:
- Serum osmolality 295 mosm/kg
  Urine osmolality 620 mosm/kg

- How do you interpret this?

Drugs and Hyponatraemia

- Drugs that stimulate vasopressin release
  -SSRIs, anti-depressant, opioids
- Others that cause hyponatraemia
  - anticonvulsants, anti-psychotics, vincristine, NSAIDs
- Party drugs
  – MDMA and ecstasy
- Activation of AVP and excess water intake/retention

Question 20

- Where is this Banksie' art work?
- A: London
- B: Manchester
- C: Bristol
- D: Cardiff
- E: Glasgow

Question - hyperkalaemia

- Which is more arrythmogenic?
  Hypokalaemia or Hyperkalaemia?

Hyperkalaemia Case Question 21

- 69year old with CKD due to hypertensive nephrosclerosis (eGFR 36ml/min/1.73m^2) on candesartan and amlodipine.
- Echo shows diastolic dysfunction and started on bisoprolol.
- Repeat blood tests 4 weeks later demonstrate serum K+ has risen from 5.1mmol/l to 5.8mmol/l

- A: do you stop the candesartan?
- B: do you stop the bisoprolol?
- C: do you just observe?
- D: do you request an ultrasound exclude renal artery stenosis?

Question 22

- In proteinuric kidney disease, standard of care is now ARB or ACEI, SGLT2inhibitor, and now suggest adding a mineralocorticoid receptor antagonist as well
- Many patients are also on a β blocker as well.
- Baseline serum K+ in your diabetic individual is 5.6mmol/l and you wish to start spironolactone as still hypertensive (156/90).
- A: do not start spironolactone because of hyperkalaemia?
- B: Stop ARB/ACEI because of hyperkalaemia
- C: stop β blocker
- D: ignore K+ and start

Question 23

- You have started spironolactone. BP now fallen to 128/80 but follow up K+ is now 6.1. Your ECG is normal
- A: stop spironolactone
- B: stop β blocker
- C: continue to watch and provide dietary advice
- D: add frusemide

Assessing impact of kidney function in CKD

- Extra kidney manifestations
- Anaemia – assessment?
  Hb and blood film, iron studies
- CKD metabolic bone disease – assessment?
  Calcium, phosphate, PTH, vitamin D
- Uric acid and gout
- Metabolic acidosis

64year old female. History of hypertension, complaining of some lethargy.

	10-Jan-2024 11:43	02-May-2024 12:20	06-Dec-2024 10:52	04-Feb-2025 13:11	05-Mar-2025 12:03
Haemoglobin	**109**	**104**	**105**	**101**	**100**
Hct	**0.34**	**0.34**	**0.34**	**0.33**	**0.33**
MCV	92	94	93	93	90
MCH	30	28	29	28	28
Platelets	241	272	236	346	277
WBC	8.3	9.1	9.1	**11.5**	8.2
Neutrophils	5.1	6.1	5.8	**10.1**	5.0
Lymphocytes	1.3	1.8	1.8	1.1	2.0
Monocytes	**1.7**	0.8	1.0	0.2	0.8
Eosinophils	0.1	0.3	0.4	0.1	0.4
Basophils	0.0	0.0	0.1	0.1	0.0
COMPLETE BLOOD COUNT					

Sodium	137
Potassium	**5.4**
Urea	**14.9**
Creatinine	**118**
eGFR	**37**
Comment	

Question 24

- What further investigations do you want?
- A: bowel screening
- B: serum EPO levels
- C: CRP
- D: full iron studies

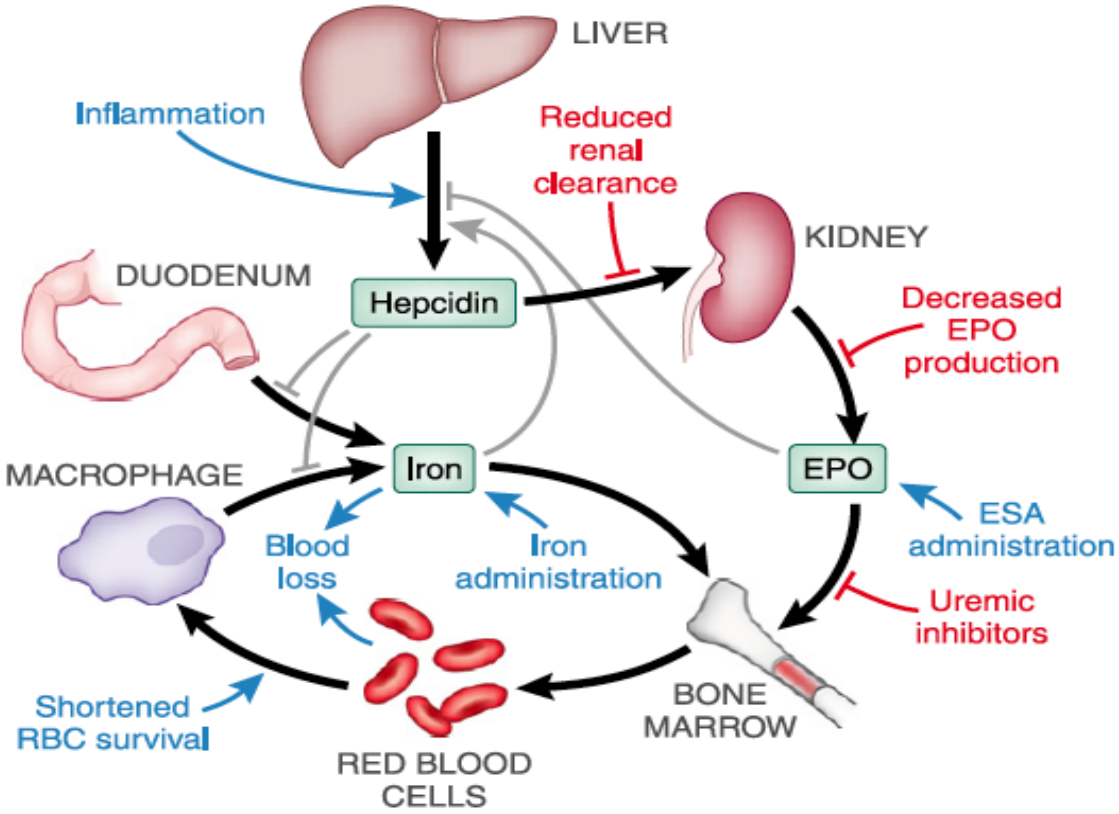
Question 25. How do you interpret these results

	16-Nov-2023 14:01	16-Nov-2023 14:01	10-Jan-2024 11:43	04-Feb-2025 13:11	04-Feb-2025 13:11
Serum Iron					10
Ferritin					87
Transferrin					2.5
Transferrin saturation					16

- A: they are normal
- B: no evidence of iron deficiency
- C: reflects chronic inflammation
- D: requires iron infusion

Extrarenal Manifestation: Haemopoetic system

- Normochromic normocytic anaemia
- Decreased EPO production
- Decreased iron availability. Inflammation – increased hepcidin with decreased iron absorption & recycling



Babbitt JASN 2012.

CKD alterations in calcium, phosphate and PTH

Calcium		2.11
Phosphate		1.8
Adjusted Calcium		2.17
Sodium	140	
Potassium	5.8	
Urea	24.3	
Creatinine	298	
eGFR	13	
Comment		

	09-Jan-2024 12:18	09-Apr-2024 11:38	04-Jul-2024 11:52	02-Oct-2024 10:38	23-Jan-2025 13:51
Parathyroid Hormone (intact)	59.4	31.2	70.9	87.1	93.5
Comment					
PARATHYROID HORMONE					

Question 26:
How do you interpret these results

- A: Primary hyperparathyroidism
- B: secondary hyperparathyroidism
- C: tertiary hyperparathyroidism
- D: hyperphosphataemic rickets

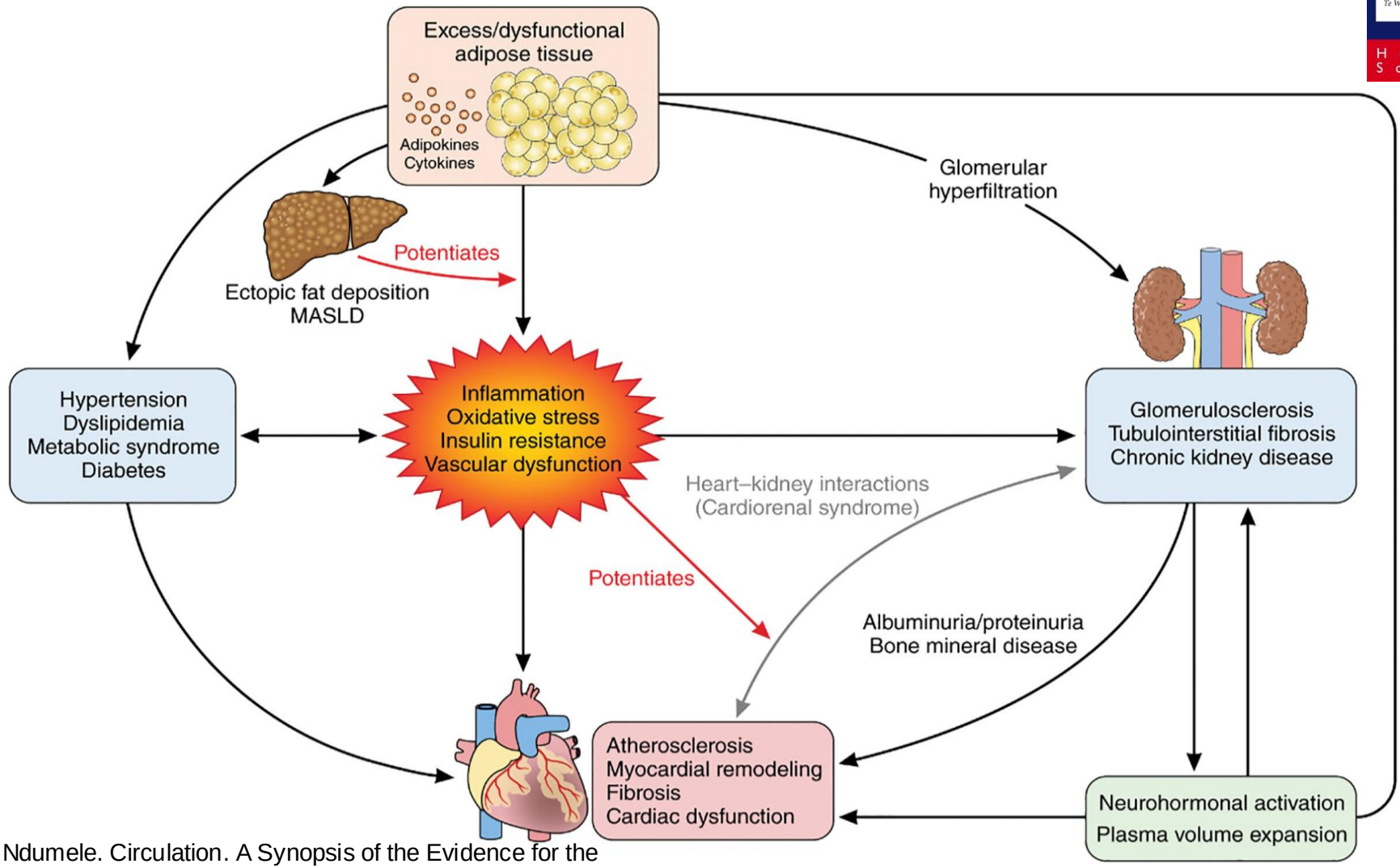
Cases from General Practice for Discussion

Newer Concepts removing Silos

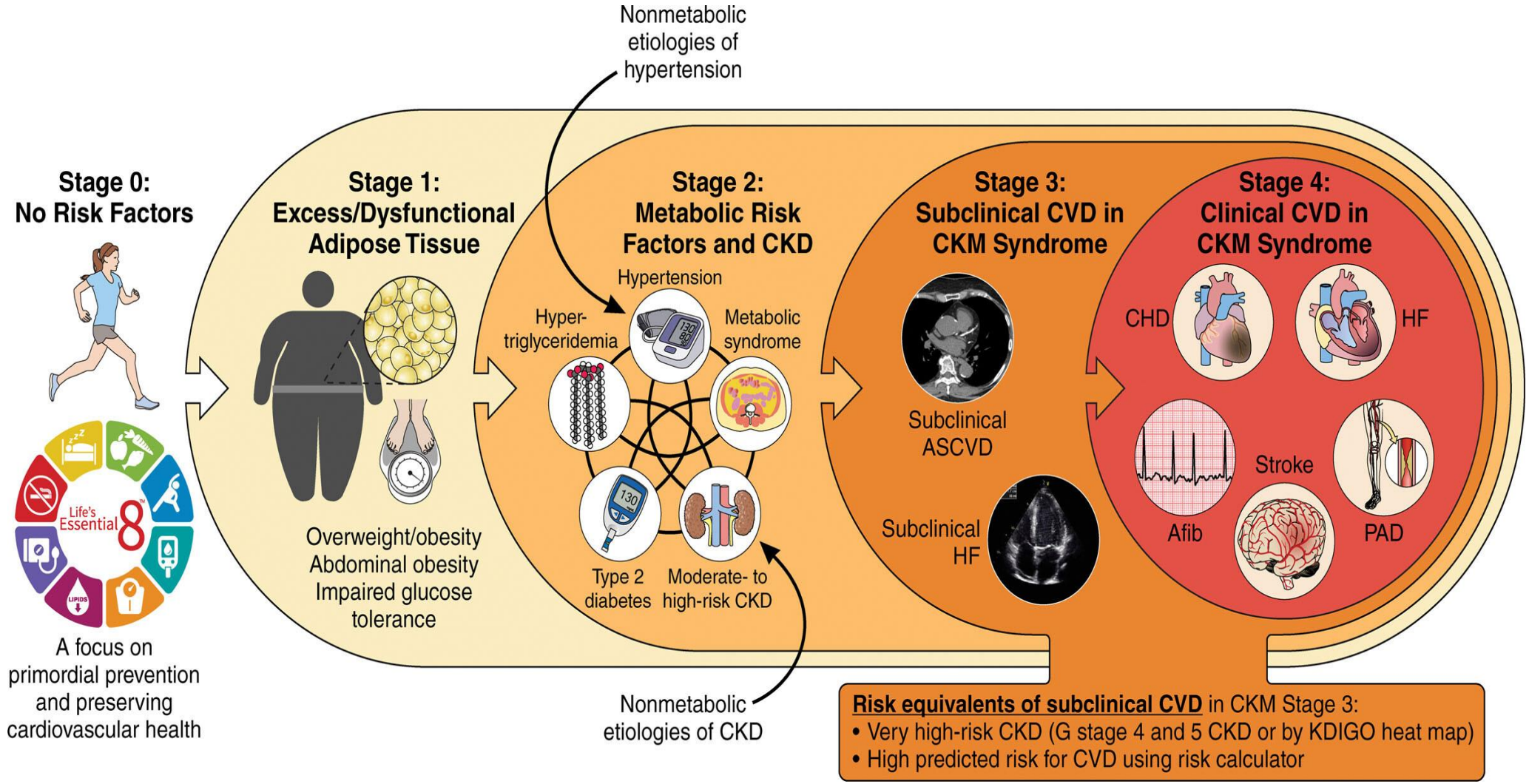
- Cardiovascular-Kidney-Metabolic Syndrome Pathophysiological interactions between metabolic risk factors, chronic kidney disease and the cardiovascular system leading to multiorgan dysfunction.

- Recognise the importance of close interaction between cardiac, metabolic and renal pathophysiology.

Cardiovascular-Kidney-Metabolic Syndrome Multi-directional relationships

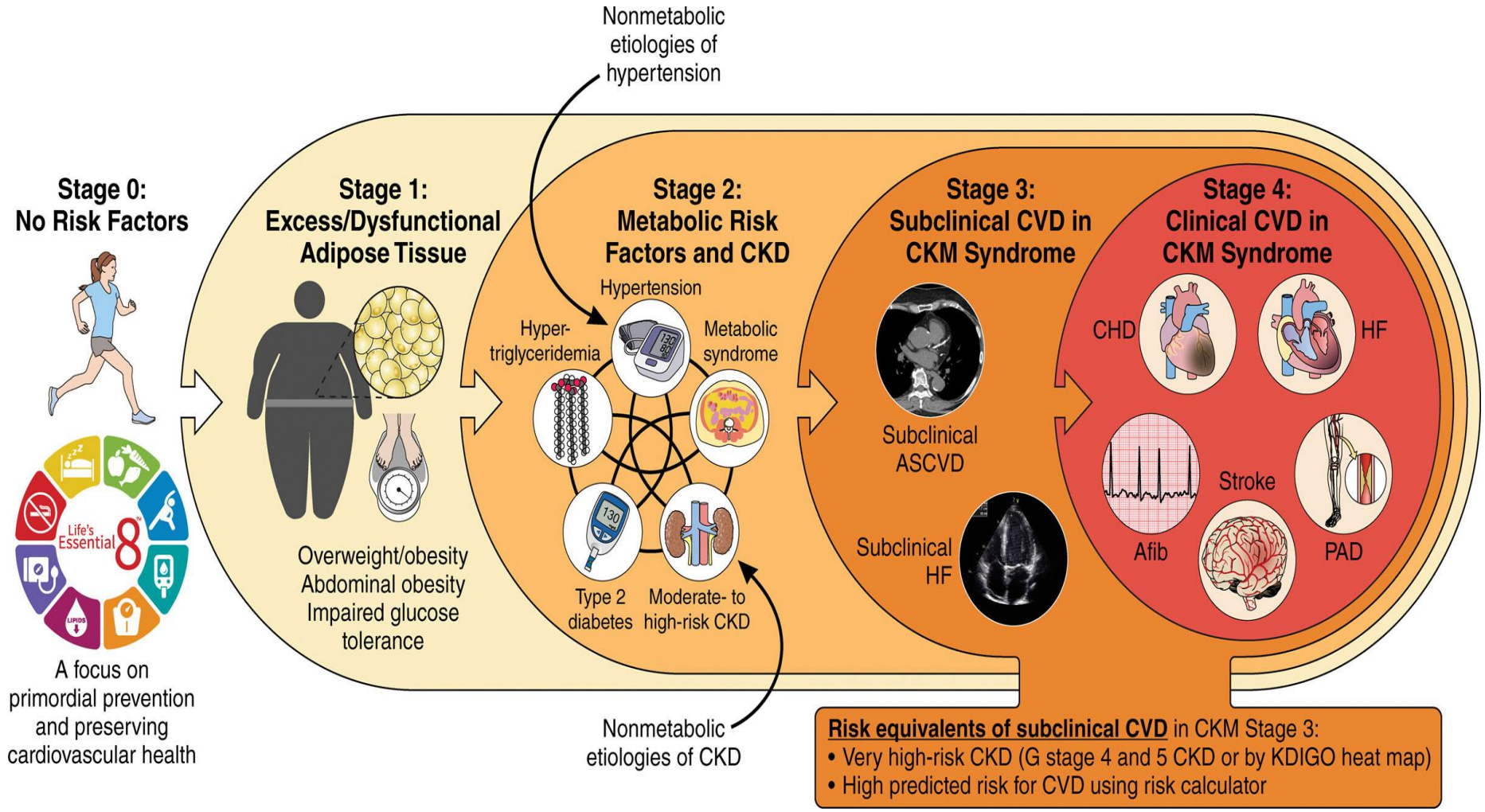


Chiadi E. Ndumele. Circulation. A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic (CKM) Syndrome: A Scientific Statement From the American Heart Association, Volume: 148, Issue: 20, Pages: 1636-1664, DOI: (10.1161/CIR.0000000000001186)



Chiadi E. Ndumele. Circulation. Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association, Volume: 148, Issue: 20, Pages: 1606-1635, DOI: (10.1161/CIR.0000000000001184)

Stage 2: strategies are similar for hypertension, diabetes
CKD regardless of cause.
May or may not have dysfunctional adiposity



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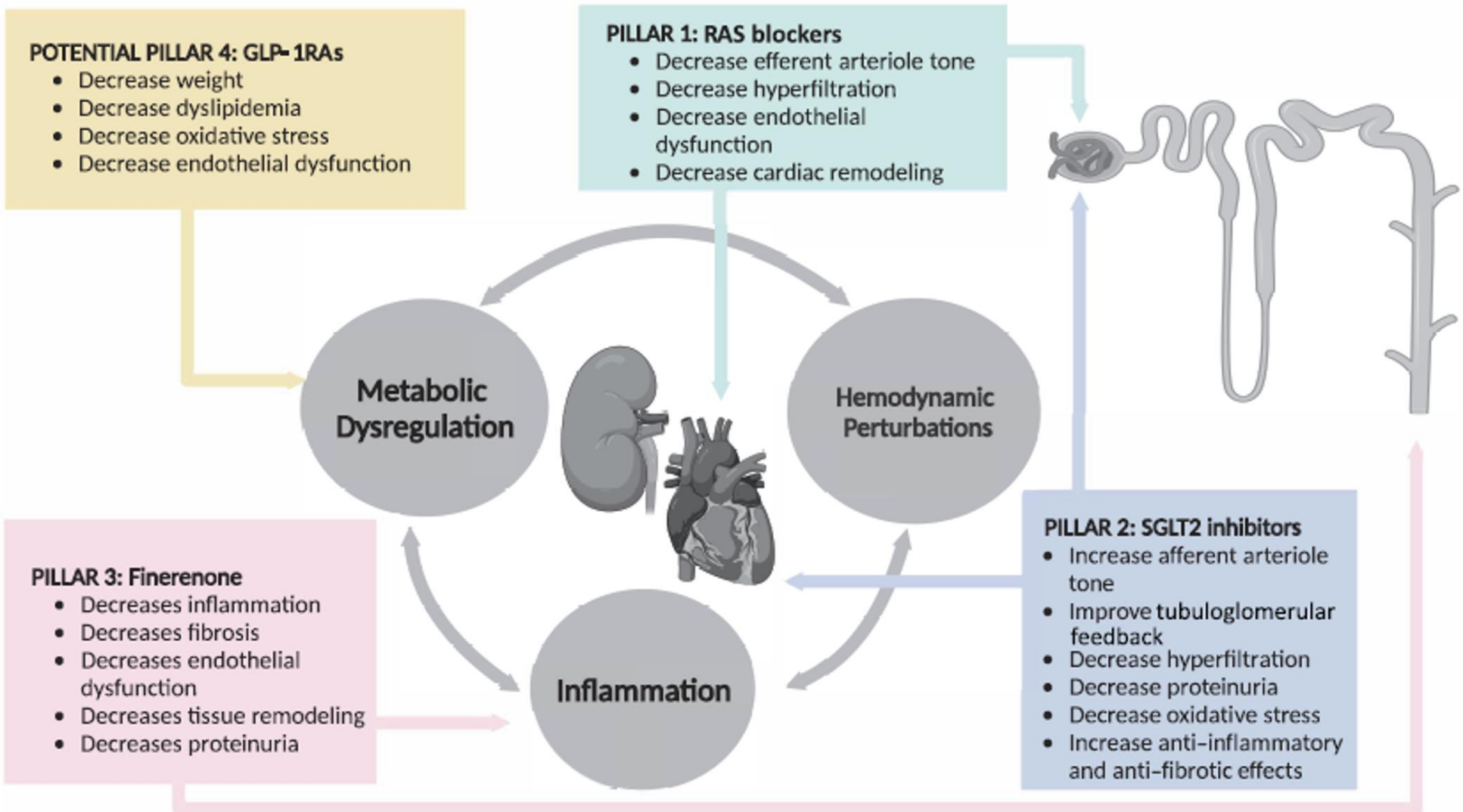
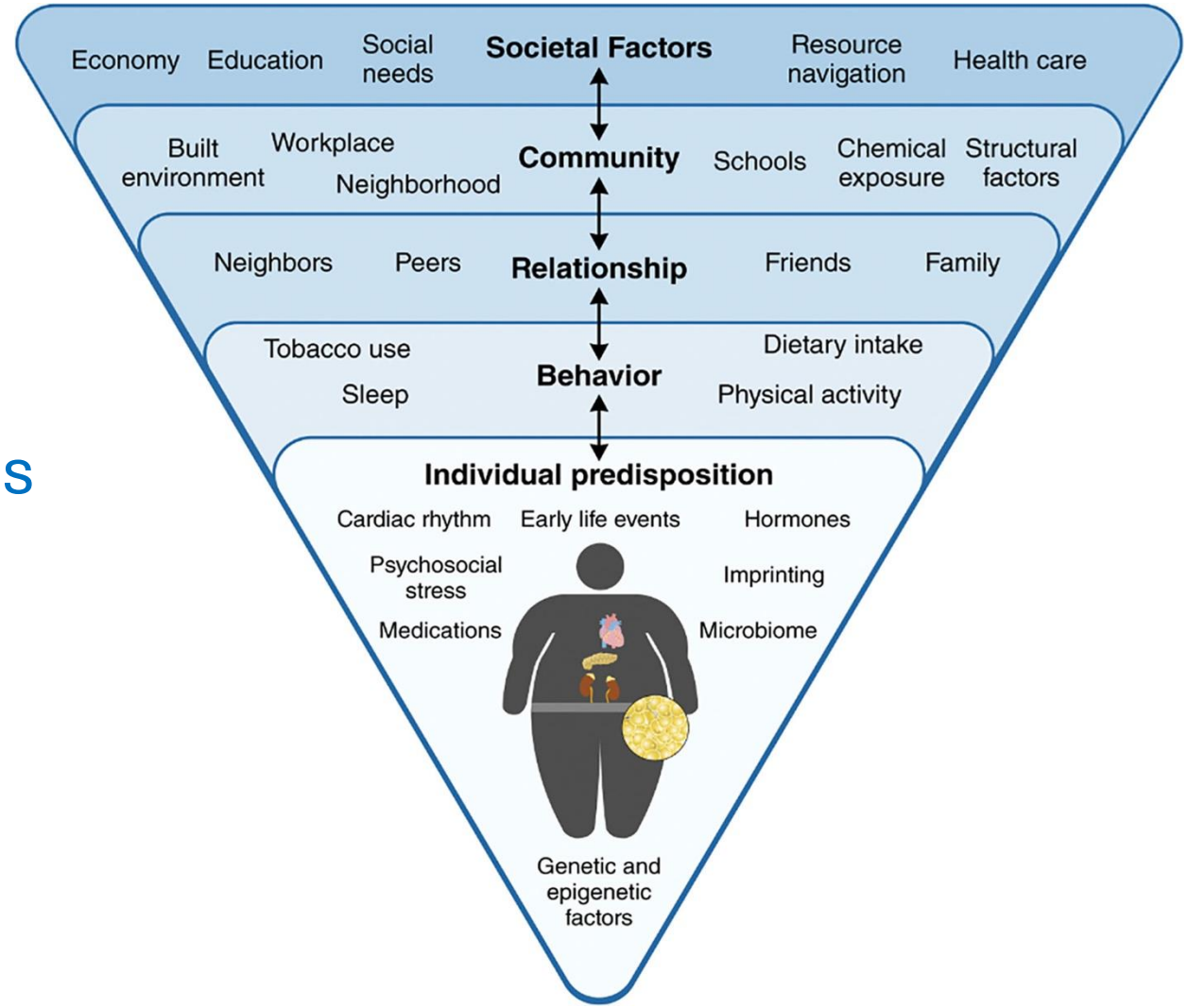
Management of Cardiovascular-Kidney-Metabolic Syndrome

- The availability of new therapies that protect heart, kidneys and improve metabolic health underscores the need for a combined multi-disciplinary approach to maximise prevention and treatment.

- Focus on the social determinants of health are also essential as part of the management of the cardiovascular disease, kidney and metabolic disease.


POTENTIAL PILLAR 4: GLP-1RAs
Decrease weight
Decrease dyslipidemia
Decrease oxidative stress
Decrease endothelial dysfunction
PILLAR 1: RAS blockers
Decrease efferent arteriole tone
Decrease hyperfiltration
Decrease endothelial dysfunction
Decrease cardiac remodeling
Metabolic Dysregulation
Hemodynamic Perturbations
Inflammation
PILLAR 3: Finerenone
Decreases inflammation
Decreases fibrosis
Decreases endothelial dysfunction
Decreases tissue remodeling
Decreases proteinuria
PILLAR 2: SGLT2 inhibitors
Increase afferent arteriole tone
Improve tubuloglomerular feedback
Decrease hyperfiltration
Decrease proteinuria
Decrease oxidative stress
Increase anti-inflammatory and anti-fibrotic effects

Social Determinants of Health Remain a critical part of our management



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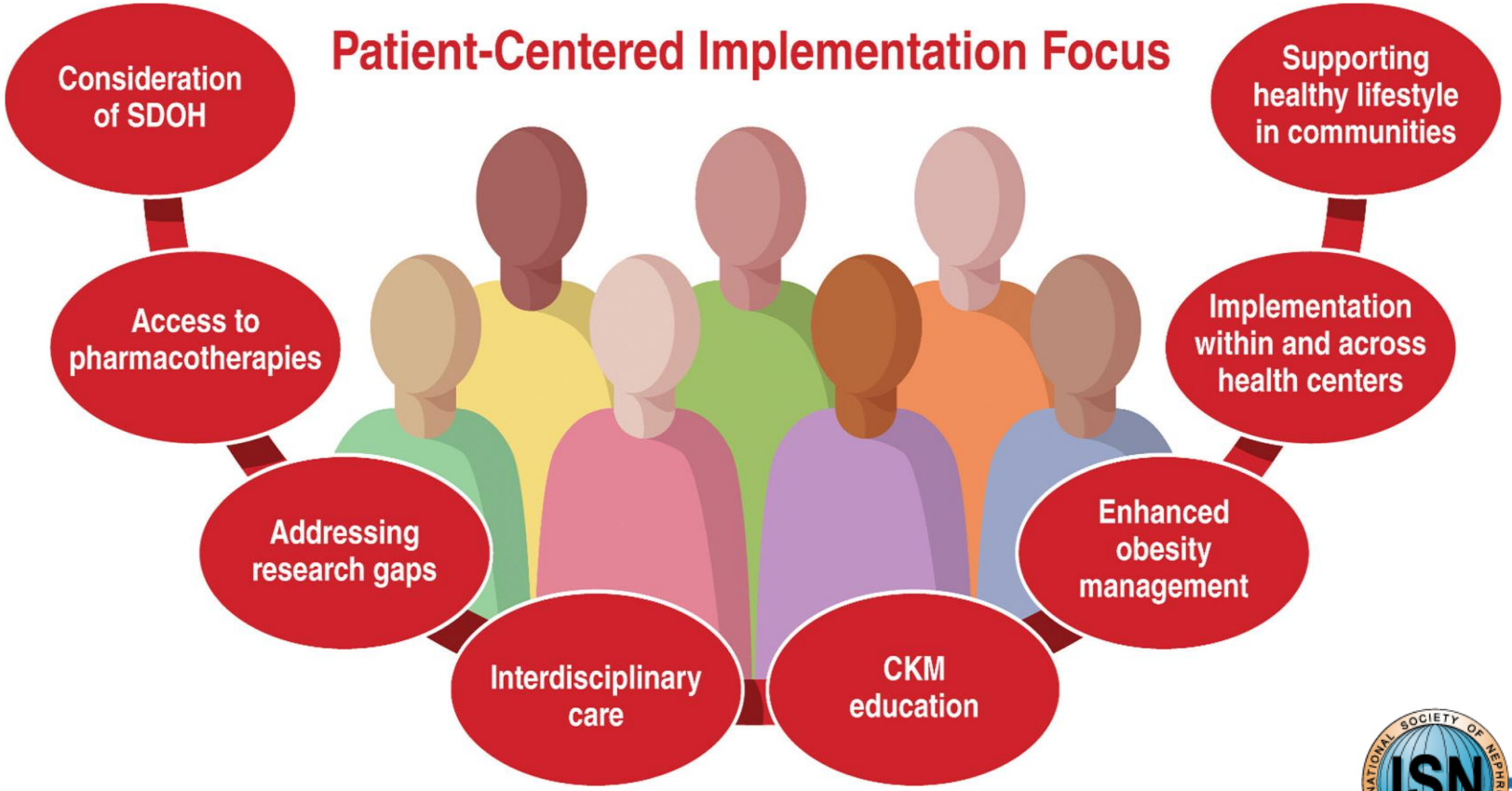

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“Once in a while
You may come across a place
where everything
is as close to perfection
as you will ever need”

“Place” Brian Turner