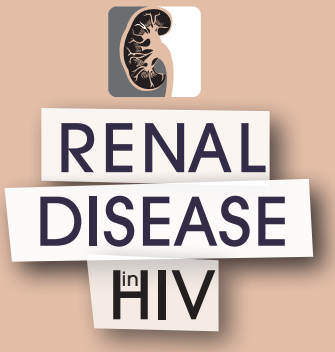
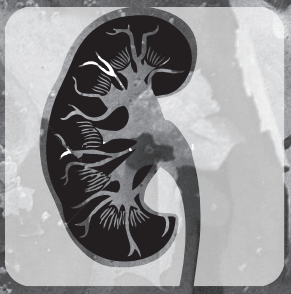


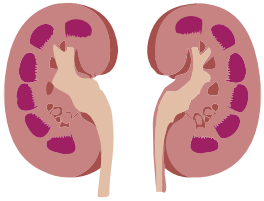
Education for capability must focus on supporting learners to construct their learning goals, receive feedback, reflect and consolidate their learning experience.
BMJ: Education for Capability

A practical manual for **primary care clinicians**



RENAL DISEASE in HIV

MEDECINS SANS FRONTIERES



introduction

There are several limitations to diagnosing and treating renal disease in the setting of a primary care HIV/TB clinic.

- It presents in non-specific ways so is not easily identified
- Urine dipsticks are not routinely performed as part of pre-ART work-up so some renal disease is missed
- When an elevated serum creatinine is encountered, the focus tends to be on avoiding tenofovir and reducing the ARV doses but the investigation and management of the renal disease is overlooked
- When identified, renal disease is generally not well understood so tends to be overlooked or referred early to higher level facilities.

The purpose of this booklet is to address these limitations by:

- Improving understanding of renal disease
- Increasing detection of renal disease in primary care
- Providing practical steps, in algorithm format, for diagnosing and managing renal disease

Acknowledgements

Appleseed Design for the layout, typesetting and design of the manual
www.appleseedesign.com

Colleen and Keith Begg for the cover photograph
www.niassareserve.com

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RENAL DISEASE in HIV

how to use this booklet

It is well recognised in clinical education that a good series of lectures on a disease does not necessarily translate into increased clinical competence in the consulting room.

A good theoretical foundation is of course essential but this needs to be followed by practical steps to apply it in the clinical setting, ideally with more experienced clinical oversight.

This booklet has been designed to attend to both.
It is essentially a manual to guide all the clinicians, doctors and nurses, in a primary care clinic into more informed management of renal disease.
Optimal use of it will be to follow the steps mentioned overleaf.

The optimal target group for this booklet is primary care clinicians in clinics or level 1 district hospitals.

This manual will assist clinicians in resource-limited settings. Where more advanced diagnostic and therapeutic options are available, they should be pursued.

STEP ONE
Gather together the interested clinicians, hopefully all in the clinic, and establish agreement for three separate meetings over approximately two months for training and implementation

STEP TWO
Set up routine urine dipstick screening as part the pre-ART work-up. A pre-ART room for doing routine observations is recommended as experience suggests that dipsticks are infrequently performed if left to the clinician during consultations. Routine observations usually done in this prep room are pulse, blood pressure, temperature, respiratory rate, urine dipstick and blood glucose. Ideally a register is kept of all patients with proteinuria ≥ 2+

STEP THREE
Establish links with a local clinician with some experience in renal disease with whom you can discuss problems or to whom you can refer patients for further management. Familiarise him/her with the algorithms you will be using

STEP FOUR
The first training session of approximately 90 minutes. Study section 1, the overview of renal disease in HIV and follow this with 20 minutes of review of the algorithms.

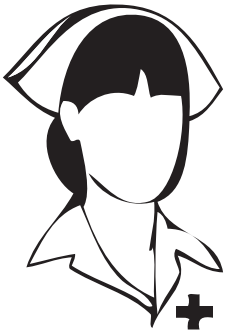
STEP FIVE
Establish agreement amongst clinicians to take a bit of extra time when renal abnormalities are encountered to apply the algorithms. The nurses need to understand clearly the dipstick alorithm and know when to refer patients with abnormal creatinines. Efficiency will increase with time as familiarity develops. Make a note of files of all patients with renal disease for discussion at the next training meeting. Use the identified local clinician as needed for difficult problems

STEP SIX
The second training session at the end of the first month. Meet to discuss patients with renal disease encountered during the previous month, ideally with a more experienced clinician lending expertise.

STEP SEVEN
Third training session at the end of the second month following a similar format to the second one.

The nurses need to understand the dipstick algorithm clearly and know when to refer patients with abnormal creatinines.

contents



AN OVERVIEW OF RENAL DISEASE IN HIV POSITIVE PATIENTS

1

Symptoms of renal disease are non-specific; mostly general malaise and nausea but, as these are so frequent in HIV/TB, renal disease is often overlooked. It therefore needs to be screened for more actively by looking for proteinuria and/or haematuria on dipstick or in the blood for an elevated creatinine.

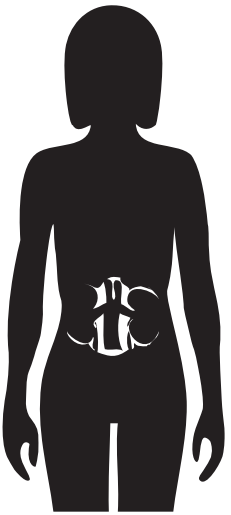
In the primary care HIV clinic renal disease will be identified by a small range of signs and symptoms

- Proteinuria and/or haematuria
- Elevated serum creatinine
- Ankle oedema
- Occasionally hypertension, nausea and vomiting, or a rash

These signs and symptoms can represent a variety of different types of renal disease, both HIV-related and incidentally discovered non-HIV related disease.

A simple way of classifying them is as follows:

1. CHRONIC KIDNEY DISEASE (CKD)
2. HIV associated nephropathy (HIVAN)
3. ACUTE KIDNEY INSULT (AKI)



1. CHRONIC KIDNEY DISEASE (CKD)

CKD is at least 3 times more frequent in Africa than in developed countries. Common presentations seen in an ARV clinic are chronic hypertensive and diabetic nephropathy. Also seen are chronic HIVAN or other AGN, missed previously. By the time they present with elevated creatinine or proteinuria there is already significant renal disease. However, careful management from this point onwards can slow the progression to end stage renal disease (ESRD).

The stark reality in South Africa and many developing countries is that most people with ESRD and HIV face a very high risk of mortality and many of them have limited access to dialysis.

Diagnosis

- Usually elevated creatinine with proteinuria and/or haematuria. The patient is often a known diabetic or hypertensive with poor control.
- An FBC often shows a normochromic, normocytic anaemia
- An ultrasound, if obtainable, usually shows small kidneys (<9cm)

Management

a. The following have been shown to slow the progression to ESRD:
- Stop smoking
- Treat blood pressure effectively
- Tighten diabetic control
- Avoid NSAIDs

b. Adjust renally excreted drug doses as needed (see section 7)

c. Monitor creatinine and urine six- monthly and re-stage (renal staging - see page 17)

d. Consider referral for renal replacement – ie dialysis and transplantation. HIV patients may be considered if:
- Creatinine rising above 450
- CD4 > 200
- VL LDL
- ARVs for more than 3 months
- If so, contact local nephrology department

The progression to ESRD can be slowed by carful attention to specific risk factors.

The following will not be accepted for renal replacement
- patients > 60 years;
- diabetics > 50 yrs
- patient with BMI > 35
- history of substance abuse;
- patient with poor adherence to medication

Note:
HIVAN is the 2nd commonest cause of nephrotic syndrome at Groote Schuur Hospital

2. HIV ASSOCIATED NEPHROPATHY (HIVAN)

Summary points

- The histological appearance is of collapsing glomeruli, hence the pathology term for it, focal collapsing glomerulosclerosis – FSGS
- Can have rapidly rising creatinine that can progress to end stage renal disease (ESRD) in a few months
- Variable CD4 count, but is a stage 4 disease requiring fast-tracking for ARVs
- Usually nephrotic range proteinuria (> 3.5 g protein per day or urine protein/creatinine ratio > 0.35) but can be as low as 0.1)
- There is rarely hypertension or oedema
- There are frequently enlarged echogenic kidneys on ultrasound

HIVAN can present with proteinuria only and a normal serum creatinine

Diagnosis

- Prevention and early detection is of paramount importance. This needs to be implemented at the primary care level with routine dipstick screening and serum creatinine measurement
- Can be confirmed only by biopsy. However, a combination of all the above findings is highly suggestive.
- In a setting where biopsy is not available, proteinuria (≥ 2+ and or a protein/creatinine ratio > 0.1) coupled with absence of hypertension and oedema is enough for a presumptive diagnosis in primary care
- It can be helpful to do a Hep BsAg and VDRL to exclude two possible causes of AGN.

Treatment

- Start ARVs as soon as possible as clear evidence of the benefit. In a study ART reduced mortality of HIVAN by 57%
- Treat proteinuria with enalapril. (Protein damages the kidney). Start with 2.5 mg bd and watch the blood pressure (can drop) and potassium (can rise, so check at one month)
- Continue to monitor the proteinuria and serum creatinine.

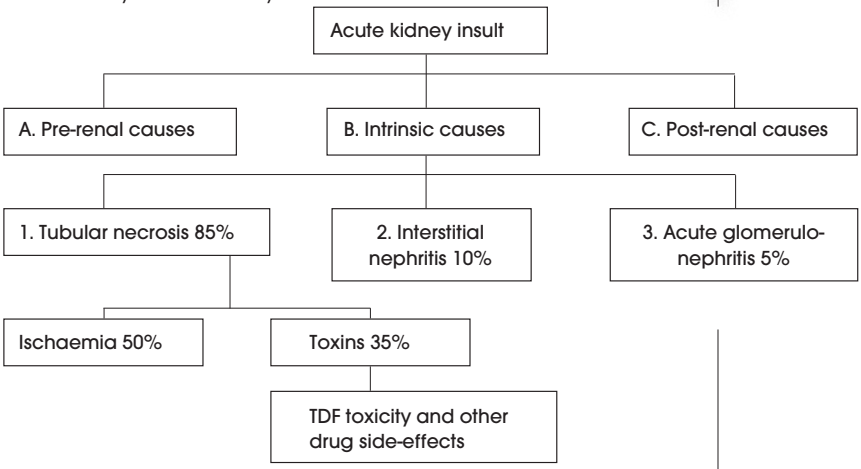
Missing the early diagnosis and treatment of HIVAN can result in long-term renal morbidity

3. ACUTE KIDNEY INSULT

The causes of an acute kidney insult can be categorized as:

a. Pre-renal
b. Intrinsic
c. Post-renal

Once pre-renal and post-renal causes have been excluded, one is left with intrinsic causes, which are associated with high rates of morbidity and mortality



a. Pre-renal causes

Main precipitants which act by decreasing blood pressure in glomerulus

- Sepsis
- Hypovolaemia – especially in setting of diarrhoea
- Hypotension

A mildly elevated serum creatinine (100 –150) in the setting of dehydration is a common presentation in sicker patients presenting for the first time to an HIV clinic. If the cause of the pre-renal failure is rapidly corrected, renal function can soon improve. But, beware a delayed or inadequate intervention. The kidney is highly sensitive to hypoperfusion so, if blood flow is sufficiently compromised, ischemia-induced ATN develops. Several days to weeks are then necessary to recover and the patient may need dialysis.

Treatment

Essentially raise the perfusion pressure in the glomerulus
Rehydrate, treat the sepsis, treat the diarrhoea. Because of the sensitivity of the kidney to hypo-perfusion the patient will need IV fluids and preferably in-patient management till renal function has normalised.

b. Intrinsic causes

1. Acute tubular necrosis
2. Acute Interstitial nephritis (AIN)
3. Acute glomerulonephritis (AGN)

1. Acute tubular necrosis

ischaemia

Nephrotoxins
- Rhabdomyolysis
- Contrast media
- Tenofovir

Ischaemia

Prolonged pre-renal failure leading to ischaemia as mentioned above

Treatment

Refer to hospital for in-patient management

Tenofovir toxicity

Pharmacology and pathology

Tenofovir may be directly cytotoxic to the tubular cell or cause damage via mitochondrial injury. A study in Johannesburg in 2011 showed a prevalence of tenofovir toxicity of 2.4%

Clinical manifestations: Tenofovir can cause AKI and CKD

AKI

1. Most common manifestation is Fanconi syndrome. Often presents with normal eGFR and variable levels of bicarb, glucose, amino acids, uric acid and phosphate in the urine

2. Acute Tubular Necrosis - usually non-oliguric.

CKD

ATN-associated ARF **may not** *resolve with tenofovir withdrawal. The reversibility of ATN is usually a function of baseline renal function as well as the length of exposure to the tenofovir insult*

Those at risk of TDF toxicity: pre-existing renal impairment; older age; advanced HIV disease; use of other nephrotoxic drugs or PIs; low BMI

TDF usage and monitoring

Routine government guidelines

a. Baseline creatinine and calculation of creatinine clearance with Cockroft- Gault or MDRD

b. Creatinine is to be repeated at 1, 4, 12 months then annually in patients with normal baseline creatinine clearance. (If baseline clearance is 50 – 60, monitor more closely)

c. Tenofovir should be avoided with Cr Cl < 50ml/min (not introduced <30ml/min)

Consider dipstick for glycosuria & serum phosphate as a marker of TDF toxicity.

NB: If glycosuria is noted incidentally, it may be due to TDF toxicity

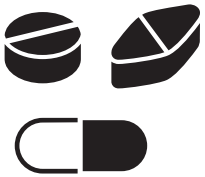
Treatment

Stop drug if TDF toxicity is suspected and monitor the return to normal renal function by following the abnormalities used to diagnose the problem

2. Acute Interstitial nephritis (AIN)

An immunologically mediated hypersensitivity reaction to an antigen

- Classically drug or infectious antigen
- Not dose dependent
- **May** occur with extra-renal manifestations of hypersensitivity - rash, fever, joint pain, eosinophilia, eosinophiliuria
- Recurs on re-exposure
- May also involve delayed type hypersensitivity (granulomas)



Causes

2.1 Drugs – any drug can potentially do it

- Antibiotics (penicillins, cephalosporins, quinolones, sulfa drugs **(Bactrim)**
- **Rifampicin**
- Herbal remedies / traditional medications
- NSAIDs
- Diuretics (thiazides and furosemide)
- Allopurinol
- Phenytoin

2.2 Infections:

- TB
- Leptospirosis

2.3. Systemic disease

- Sarcoid
- DILS- diffuse inflammatory lymphocytic syndrome
- Lymphoma

Renal TB
At the time of writing this booklet (2012) there is a significant lack of literature on renal TB. Several studies are currently in the planning stages

Bactrim

A frequently encountered cause of severe acute interstitial nephritis
Also causes crystal nephropathy
Bactrim can also inhibit tubular secretion of creatinine and lead to increased levels

Rifampicin

AIN due to rifampicin generally occurs when the antibiotic is **re-introduced** after an interval.
Flu-like symptoms, flank pain, oliguria, fever and ARF are common
Not normally associated with eosinophilia
Can also cause acute tubular necrosis
Rifampicin may be associated with low platelets and haemolytic anaemia

Treatment of drug-induced AIN

Cessation of the drug normally results in recovery of renal function (may take time)

If no improvement within a few days:

- High dose prednisone; Eg – stat dose of 500mg of methylprednisone IV or prednisone 200 mg orally stat followed by 1mg/kg of prednisone and taper over 1 month. Promptly starting steroids after diagnosis of AIN lessens subsequent interstitial fibrosis and incomplete recovery of renal function
- Consider referral for renal biopsy.

3. Acute glomerulonephritis (AGN)

Usually presents with a combination of several of the following: haematuria, proteinuria, hypertension, oedema and sometimes a rash.

There are several causes. The full diagnostic work-up and management are outside the range of the primary care clinic but awareness of the possibility of an AGN is important so that the diagnosis is not missed. In reports from secondary or tertiary institutions the following may be seen as the work-up for a diagnosis:

- ASOT for post-streptococcal GN
- Anti-dsDNA and ANA for lupus
- ANCA for Wegener's granulomatosis
- Complement – levels vary depending on the disease Complement levels helps stratify
- RPR as syphilis can cause an AGN
- HepBsAg & Hep C – both can cause an AGN.

c. Post-renal causes

In the HIV clinic the commonest cause is bilateral ureteric obstruction due to large TB nodes. Occasionally the nodes can be from a malignancy such as CA cervix or lymphoma. The clinical setting will alert the clinician and the diagnosis will have to be confirmed with an ultrasound showing hydronephrosis.

Treatment

Treat the underlying condition, whilst monitoring the renal function to ensure it returns to normal. May need specialist advice.

IMPLEMENTING ROUTINE URINE DIPSTICK TESTING IN A PRIMARY CARE HIV CLINIC

2

- Some renal diseases can have **abnormal dipsticks but normal renal function**, and other renal diseases can have **normal dipsticks with abnormal renal function**
- In order not to miss potentially damaging renal disease it is important to be doing both screening dipsticks and serum creatinine in all our patients as soon as possible after HIV diagnosis, ideally in the wellness clinics.

A. Dipstick tests in the clinic:
An enrolment room for doing routine vital signs, including urine dipsticks, on all new HIV positive patients would be ideal as this has benefits for many other aspects in the enrolment of a new patient to an HIV clinic. Routine observations usually done in this prep room are pulse, blood pressure, temperature, respiratory rate, urine dipstick and blood glucose. Ideally a register is kept of all patients with proteinuria ≥2+. The result is documented in the clinical records and the responsibility passed on to the managing clinician. (A urine register can be kept to document total dipsticks performed as well as proteinuria ≥2+)

B. Serum creatinine is now routinely performed prior to starting tenofovir. This provides a useful compulsory renal pathology screen

A FEW PRACTICAL POINTS IN THE USE OF THE ALGORITHMS

3

- Because renal disease may present with an abnormal dipstick and not necessarily an elevated creatinine (or vice versa) an algorithm has been created for both presentations.
- Algorithm 1 tracks the management of an abnormal dipstick. Oriented more towards nurse clinicians
- Algorithm 2 guides the evaluation of a serum creatinine result in combination with the urine dipstick
- Algorithm 3a and 3b are one continuous document and guide the clinician through the approach to an elevated creatinine. It is not entirely algorithmic as there is a degree of clinical judgment needed. Rather, it helps the clinicians gather the relevant evidence and directs them towards a likely disease scenario. Alternatively it provides the clinician with the information the specialist will need if contacted.

Please note

- Proteinuria and haematuria, especially associated with oedema and/or hypertension and/or a vasculitic rash could be an acute glomerulonephritis and requires urgent referral.
- Low level proteinuria is common in any acute illness Therefore do a follow up urine check after the acute illness has settled before assuming renal disease
- The US National Kidney Foundation describes five stages in the progression of kidney disease according to creatinine clearance:

1. > 90 2. 60-90 3. 30-60 4. 15-30 5. <15

A creatinine clearance of 55 is considered acceptable for the use of tenofovir but does not mean that there is no renal impairment. It is stage 3 renal disease so continued monitoring of renal function is important especially if using tenofovir

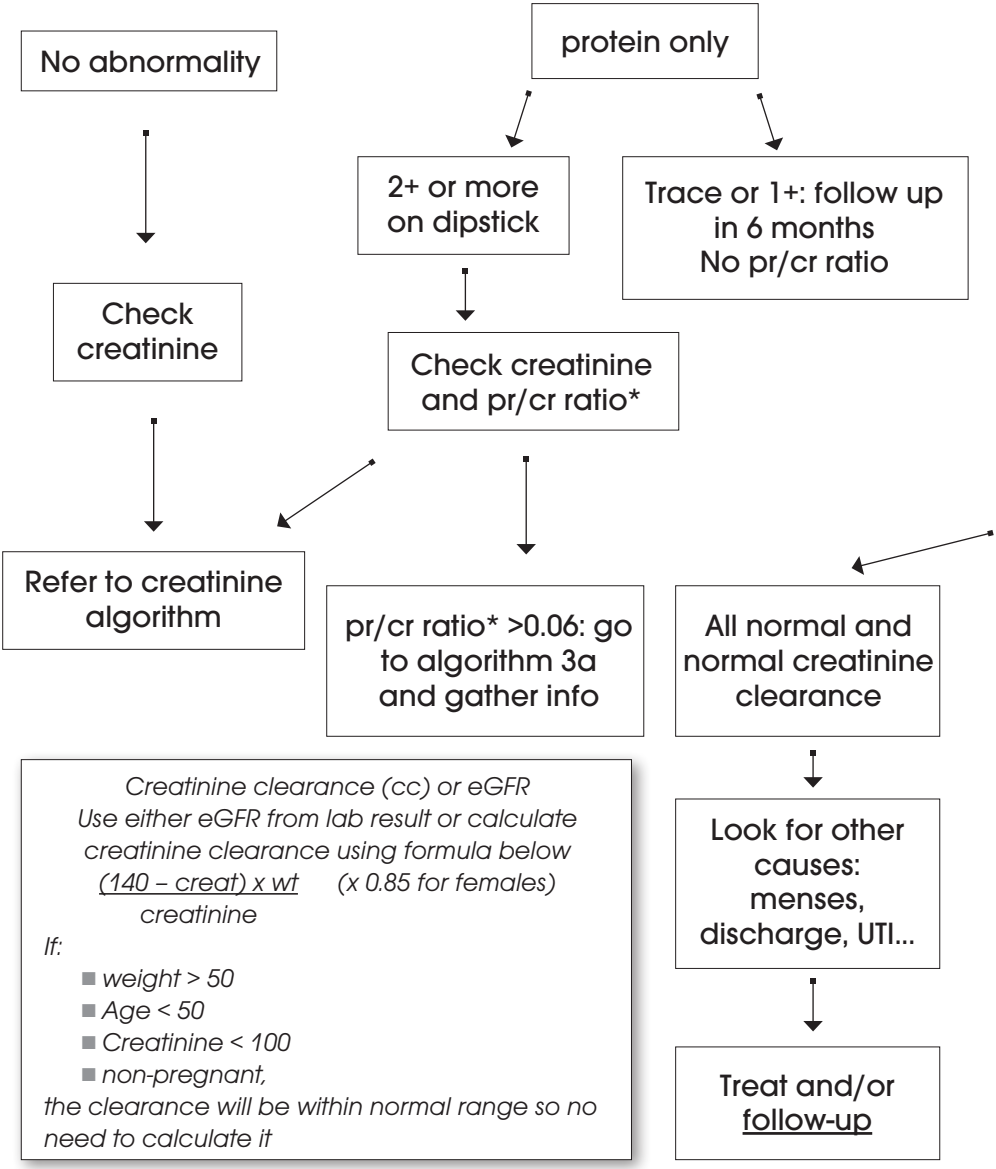
There are three important actions that need to be taken when encountering renal disease in the setting of HIV:

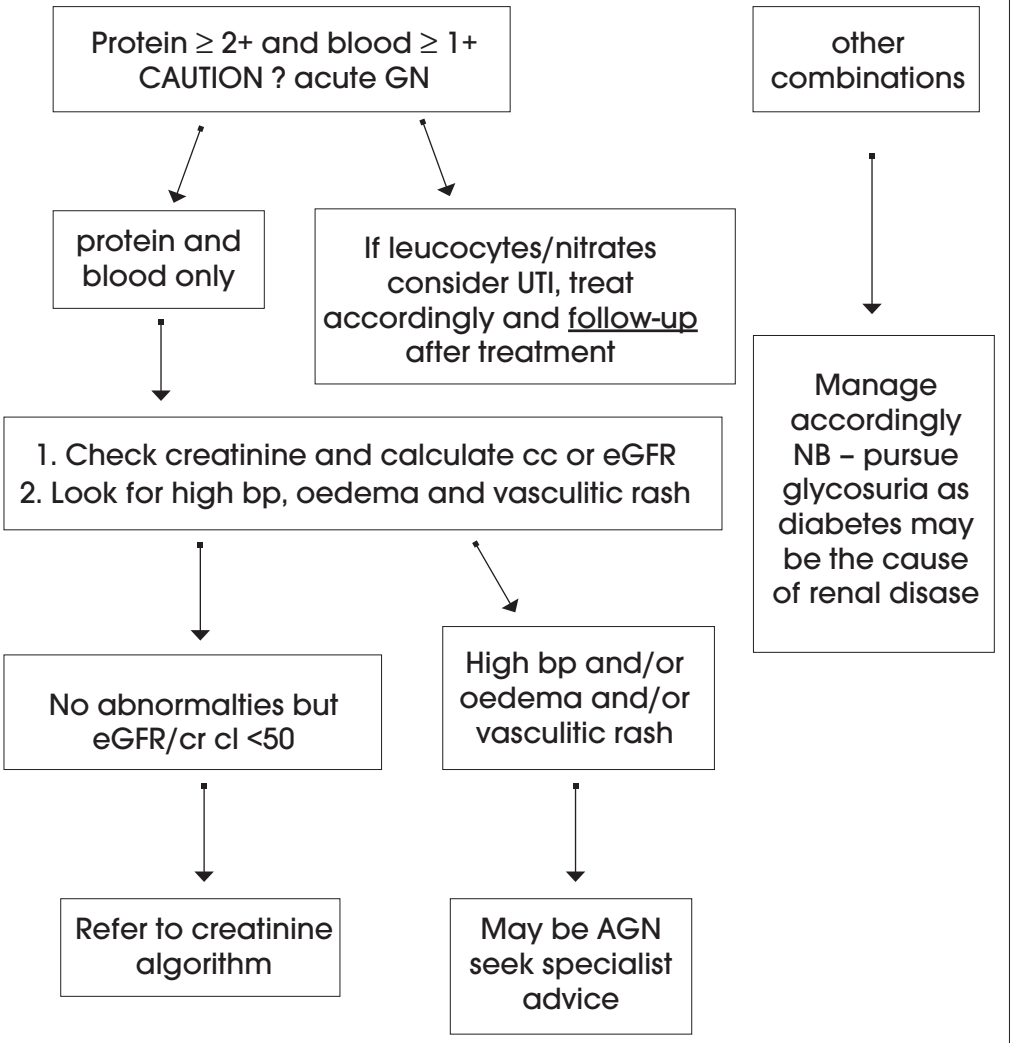
1.
Avoid or take great caution with tenofovir

2.
Remember to adjust doses of renally excreted drugs
(see dosage charts)

3.
Pursue a cause of the renal impairment

URINE DIPSTIX ALGORITHM 1.





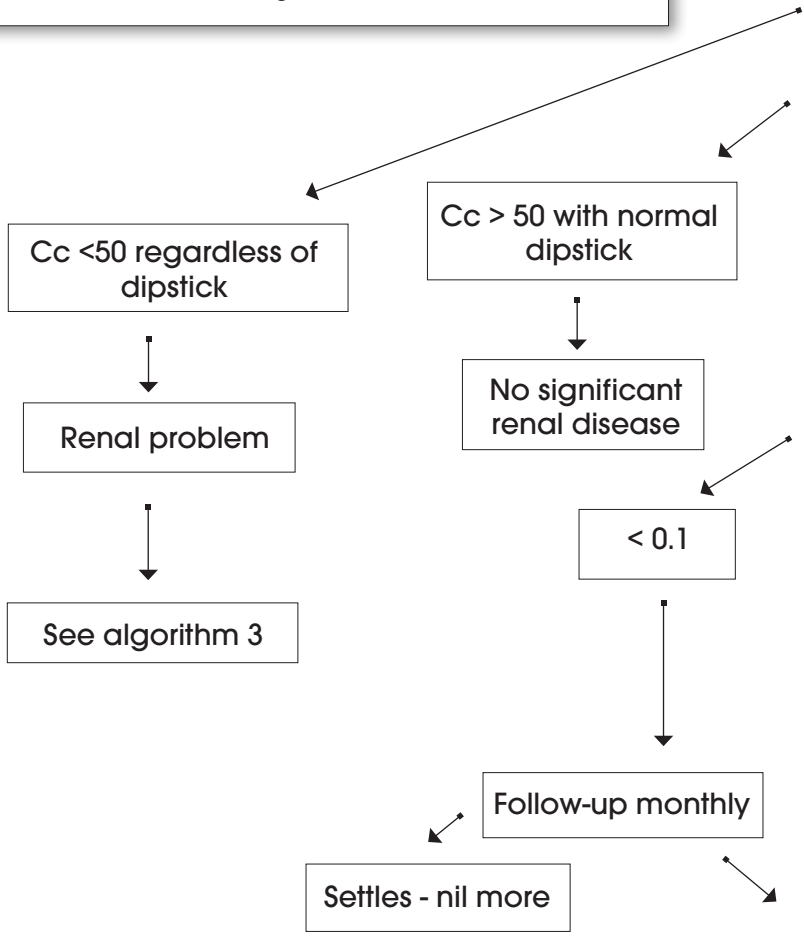
*pr/cr ratio – see details on page 16

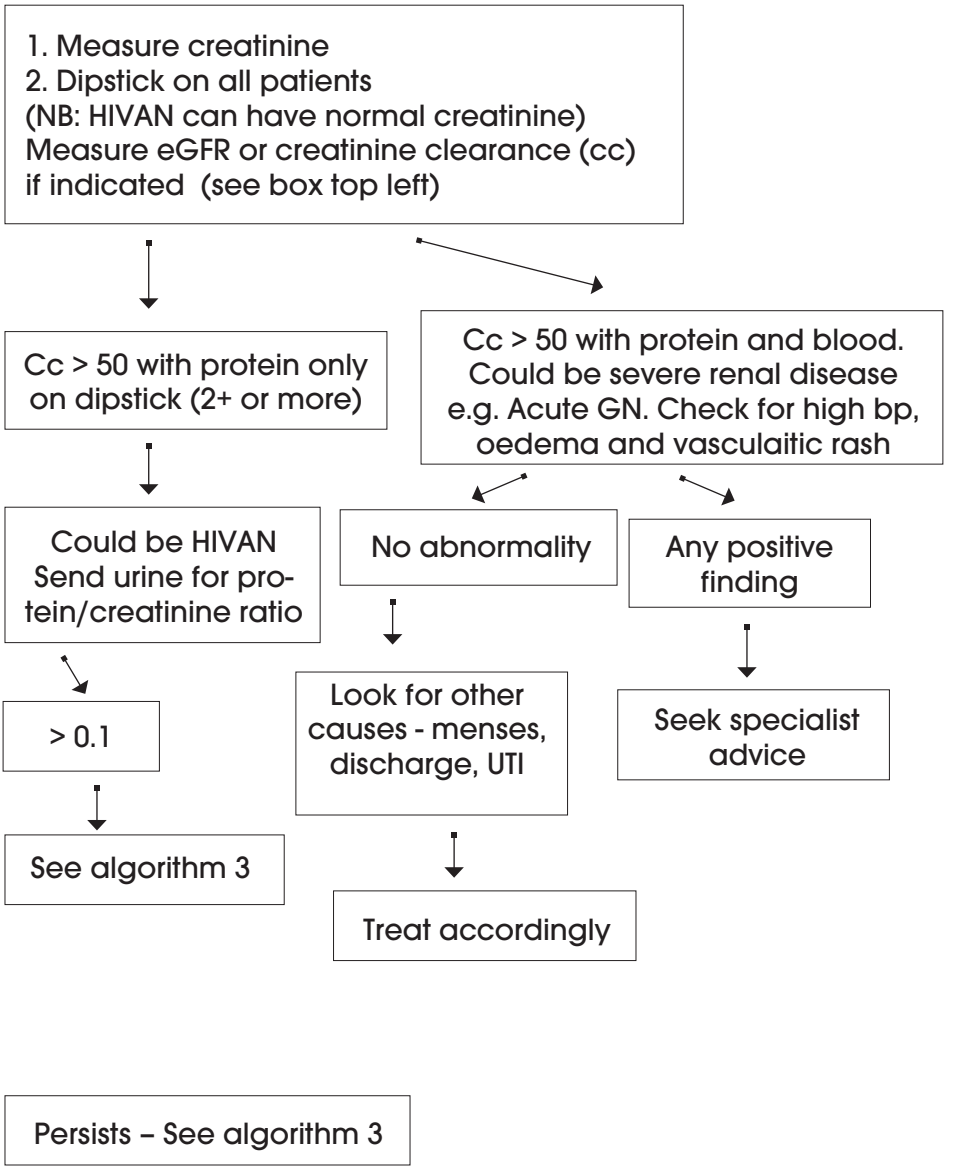
CREATININE EVALUATION ALGORITHM 2.

Creatinine clearance (cc) or eGFR. Use either eGFR from lab result or calculate creatinine clearance using formula below

(140 – creat) x wt (x 0.85 for females)
creatinine

If: weight > 50 / Age < 50 / Creatinine < 100 / non-pregnant, the clearance will be within normal range so no need to calculate it




1. Measure creatinine
2. Dipstick on all patients
(NB: HIVAN can have normal creatinine)
Measure eGFR or creatinine clearance (cc)
if indicated (see box top left)
Cc > 50 with protein only on dipstick (2+ or more)
Cc > 50 with protein and blood. Could be severe renal disease e.g. Acute GN. Check for high bp, oedema and vasculaitic rash
Could be HIVAN Send urine for protein/creatinine ratio
No abnormality
Any positive finding
> 0.1
Look for other causes - menses, discharge, UTI
Seek specialist advice
See algorithm 3
Treat accordingly
Persists – See algorithm 3

ABNORMAL CREATININE CLEARANCE (CC) OR eGFR

3A

Remember to adjust renally excreted drugs as per guidelines

Cc or eGFR 30-50
Stage 3 renal disease

Cc or eGFR 15-30
Stage 4 renal disease

Cc or eGFR < 15
Stage 5 renal disease

Gather information as follows:

History

- PH of renal disease
- Hypertension or diabetes
- Fever
- Rash
- Meds history
  - Co-trimoxazole
  - Tenofovir
  - NSAIDs
  - Penicillins
  - Aminoglycosides
  - Amphotericin B
  - Rifampicin
  - Cephalosporins
- Recent significant diarrhoea and vomiting.
- Is patient passing urine? Anuria? Oliguria?
- Recent significant strep infection

Examination

- Hydration
- Elevated temp
- Blood pressure
- Oedema
- Rash – allergic or vasculitic

Side room

- Urine dipstix for infection, protein or blood
- Finger prick glucose

Laboratory

Urine: protein/creatinine ratio* – only if protein ≥ 2+ on dipstix or unexplained oedema

Blood:
- RPR – can cause an acute GN
- Urea, elecs, creatinine
- HBV – can cause an acute GN
- FBC – low Hb can be chronic renal disease
- CD4 (VL if indicated)

Ultrasound – if available

- Small kidneys suggest chronic renal disease
- Normal or large, echogenic kidneys suggest acute renal disease including HIVAN

Using above information follow guidelines in **3B opposite**

Will need specialist advice.

Gather as much information as possible from the list opposite as it will help the consultant you are discussing the problem with.

***protein/creatinine (pr/cr) ratio**

- replaces the old 24 hour urine protein measurement
- units are grams protein per mmol creatinine
- multiply by 10 to get approx equivalent of grams protein excreted per 24 hours. Eg u pr/cr ratio of 0.21 = approx 2.1 g protein/24 hrs
- 1+ protein on dipstick is approx 0.3 g = pr/cr ratio of 0.03

ABNORMAL CREATININE CLEARANCE OR eGFR (contd)

3B

(See section 1, "renal disease overview" for details)

1. Does this look like chronic kidney disease (CKD)?

- Commonly poorly controlled diabetes and/or hypertension
- Other known CKD

If so, refer to the appropriate clinic for improved management of the chronic condition

Commence CKD management principles to prevent further damage
- Stop smoking
- Treat bp
- Treat diabetes
- Avoid NSAIDs
- Adjust drug doses as needed
- Highlight condition in the file

Consider referral for dialysis and/or transplantation.

Referral criteria:
- creatinine rising above 450
- CD4 > 200
- VL LDL
- ARVs for more than 3 months.

2. Could this be HIVAN?

– Proteinuria – usually ≥ 2+ on dipstick, urine pr/cr ratio > 0.1 and no haematuria
– Usually normal bp, no oedema and no rash
– CD4 not necessarily low. Can be > 500

No definitive diagnosis without biopsy but diagnosis highly suggestive of HIVAN if, in addition, other conditions are excluded by the acute kidney insult screening process below.

If so:

Start ARVs as soon as possible (stage 4 condition)
Start enalapril, initially 2.5 mg bd, and watch the bp and potassium
Monitor the creatinine and proteinuria
(see details in section 1, the renal disease overview)

3. Could this be an acute kidney insult? (see AKI diagram in section 1, renal review notes)

First, exclude pre-renal causes and obstructive nephropathy. If excluded, evaluate for intrinsic renal disease.

A. Could this be pre-renal?

Usually associated with hypovolaemia and low bp – associated with dehydration, diarrhoea or sepsis. Can be from a previous visit when patient was much sicker and is now better. If this is suspected, repeat creatinine and urine dipstick and see the patient again within the week. If still low bp, will need IV fluids and in-patient monitoring

C. Could this be an obstructive nephropathy?

Large lymph nodes due to TB or a malignancy
If so, will need an ultrasound to confirm diagnosis. Arrange within the week and manage with specialist advice.

ABNORMAL CREATININE CLEARANCE OR eGFR (continued overleaf)

ABNORMAL CREATININE CLEARANCE OR eGFR (contd)

3B

B. Could this be an intrinsic nephropathy?

1. Tubular necrosis – usually follows an episode of severe dehydration or sepsis (pre-renal)
   Will need hospitalisation, IV fluids and monitoring

   > **TDF toxicity** involves the tubules by direct damage or via mitochondrial damage
   > Can occur in weeks to months; hence screening creatinine at 1 and 4 months
   > Can present as rising creatinine, glycosuria or even oedema

2. Acute interstitial nephritis
   May occur with extra-renal manifestations of hypersensitivity
   - Rash, fever, joint pain, eosinophilia, eosinophiliuria

   Can look like pyelonephritis with fever and flank pain
   Recurs on re-exposure
   More common causes in setting of HIV/TB – **cotrimoxazole, rifampicin**
   Treatment is to stop offending drug and sometimes give steroids
   (See section 1, renal overview notes, for more detail)

3. Acute glomerulonephritis (AGN)
   Usually presents with haematuria, proteinuria, hypertension, oedema and sometimes a rash.
   Needs fuller work-up in a hospital setting. Refer soon to establish diagnosis and prevent long-term damage
   (See section 1, renal overview notes, for more detail)

Intrinsic nephropathy can result in long term renal damage. If unsure, seek experienced advice soon to establish diagnosis and prevent long-term damage

DRUG DOSING CHARTS IN RENAL IMPAIRMENT

Drug	Creatinine clearance or eGFR				
ARVs					
3TC	Clearance > 50	Clearance 30 – 49	Clearance 15 – 29	Clearance 5 – 14	Clearance < 5
	150 mg bd or 300 daily	150 mg daily	150 mg stat then 100 mg daily	150 mg stat then 50 mg daily	50 mg stat then 25 mg daily
DDI	Clearance > 60	Clearance 30 – 59	Clearance 10 – 29	Clearance < 10	
	>60 kg 400 mg daily <60 kg 250 mg daily	>60 kg 200 mg daily <60 kg 125 mg daily	>60 kg 125 mg daily <60 kg 125 mg daily	>60 kg 100 mg daily <60 kg no formulation	
D4T	Clearance > 50	Clearance 25 – 50	Clearance 10 – 25		
	30 mg bd	15 mg bd	15 mg daily		
Cr clearance / eGFR	> 50 Usual dose	10 – 50 % of usual dose	<10 % of usual dose		
AZT	300 mg bd	No adjustment needed	300 mg daily		
TDF	300 mg nocte	AVOID	AVOID		
abacavir	No adjustment needed	No adjustment needed	No adjustment needed		
nevirapine	No adjustment needed	No adjustment needed	No adjustment needed		
efavirenz	No adjustment needed	No adjustment needed	No adjustment needed		
PIs	No adjustment needed	No adjustment needed	No adjustment needed		
Anti-hypertensives					
enalapril	2.5 – 10 mg bd	75 – 100%	50%		
atenolol	25 – 50 mg daily	50%	25%		
HCTZ	12.5 – 25mg daily	100%	avoid		
amlodipine	5 – 10 mg daily	No adjustment needed	No adjustment needed		
doxazosin	2 – 4 mg daily	No adjustment needed	No adjustment needed		
Diabetic meds					
gliclazide.	40 – 80 mg bd	AVOID	AVOID		
g;ilibenclamide	2.5 – 5 mg bd	AVOID	AVOID		
metformin	500 – 1000 mg bd	25 %	AVOID		
Anti-fungals					
fluconazole	200 – 400 daily	50%	50%		
itraconazole	100 – 200 bd	100%	50% IV form contra-indicated		
Anti-virals					
acyclovir	200 – 800mg 4 – 12 hourly	100%	200 mg bd		

DRUG DOSING CHARTS IN RENAL IMPAIRMENT contd

Drug	Creatinine clearance or eGFR		
	> 50	10 – 50	<10
	give usual dose	% of usual dose	% of usual dose
Antibiotics			
amoxycillin	250 – 1000 mg tds	Every 8 – 12 hours	Every 24 hours
azithromycin	500 mg daily	No adjustment needed	No adjustment needed
ceftriaxone	1 – 2 g daily	No adjustment needed	No adjustment needed
clarithromycin	250 – 500 mg bd	50% – 100%	50%
ciprofloxacin	250 – 750 mg bd	50% – 75%	50%
clindamycin		No adjustment needed	No adjustment needed
co-trimoxazole prophylaxis	2 tabs daily	No adjustment needed	No adjustment needed
co-trimoxazole treatment	2 bd – 4 qid	50%	Seek advice
erythromycin		No adjustment needed	No adjustment needed
penicillin g	0.5 – 4 MU 4 – 6 hourly	75%	25%
TB drugs (see separate document opposite)			
Miscellaneous			
NSAIDs	AVOID	AVOID	AVOID
metoclopramide	10 mg tds	75%	50%
omeprazole	20 – 40 mg daily	No adjustment needed	No adjustment needed
ranitidine	150 – 300 mg nocte	50%	25%

DR TB DRUGS IN RENAL IMPAIRMENT

Monitor creatinine clearance regularly for all DR TB patients, especially for those at high risk of renal impairment (diabetic >60 years of age)

If patient has renal impairment with **creatinine clearance < 30ml/min** they will need some of their DR TB meds to be adjusted as follows:

Table 9: Dosing of selected antituberculosis drugs in renal failure

Drug	Change in frequency	Recommended dose and frequency for patients with creatinine clearance < 30 ml/min or for patients receiving haemodialysis
Isoniazid	No change	300 mg once daily, or 900 mg 3 x per wk
Rifampicin	No change	600 mg once daily, or 600 mg 3 x per wk
Pyrazinamide	Yes	25 – 35 mg/kg/dose 3 x per wk
EthambutoL	Yes	15 – 25 mg/kg/dose 3 x per wk
Ofloxacin	Yes	600 – 800 mg/kg/dose 3 x per wk
Moxifloxacin	No change	400 mg once daily
Terizidone	Yes	250 mg once daily, or 500 mg 3 x per wk
Ethionamide	No change	250 – 500 mg/dose daily
PAS	No change	4 g/dose, twice daily
Streptomycin	Yes	12 – 15 mg/kg/dose 2 or 3 x per wk
Capreomycin	Yes	12 – 15 mg/kg/dose 2 or 3 x per wk
Kanamycin	Yes	12 – 15 mg/kg/dose 2 or 3 x per wk
Linezolid	No change	600mg daily

Adapted from American Thoracic Society / Centers forDisease Control and Prevention / Infectious Disease Society of America. Treatment of Tuberculosis. Am J Respir Crit Care Med 2003;167