Guidance for parallel clinic

The patients in this 'run-alongside' clinic will all have come from the main JRDC or their notes been reviewed by a Nephrologist and should have had non-diabetic/hypertensive-ischaemic causes for CRF excluded. Post-renal causes, e.g. obstruction from prostatic enlargement, are much more common than glomerulonephritis.

Patients with diabetic nephropathy will have a classic picture of microalbuminuria increasing over time to overt proteinuria accompanied by decreasing GFR. However, many people with diabetes (particularly type 2 diabetes) have CKD without proteinuria, with CKD attributed primarily to hypertension & vascular disease. They still need the same basic management.

As a minimum

- All patients should have had a renal ultrasound to document renal size, and to exclude obstruction and other unexpected lesions.

- All patients should have had a serum protein electrophoresis & urinary Bence Jones protein as this is usually an older age group with frequent abnormalities. Attached is the suggested algorithm from haematology for dealing with positive samples (note it needs to be unexplained renal failure and anaemia – there is a subjective element here as all these patients have renal failure by definition and many are anaemic due to their renal disease).

- Haematuria is not typical of diabetic or vascular renal damage. Remember infection is the commonest cause of haematuria (or menstruation in women). An MSU will also confirm the presence or absence of urinary RBCs. If no infection, in this age group genitourinary malignancy needs to be excluded. An up to date renal USS, urine cytology and cystoscopy should be arranged. Non-diabetic renal disease as a cause of the haematuria should have been excluded before referral into the clinic, but be observant for new conditions developing. A rapid change in creatinine and sudden increase in degree of proteinuria (vs. the usual gradual increase from microalbuminuria to overt proteinuria) may indicate intrinsic renal problems. All patients should have had renal immunology if appropriate before transfer into this clinic, but repeat if new features develop.

Bloods:
As a routine, request: **U&E, CAP (Calcium, albumin, phosphate), LFT, Lipids, PTH, FBC, TFT if not done recently**

Treatment
Set targets out in a letter very clearly to the patient & GP, including what you expect the GP to be doing to achieve these targets between clinic visits.

The best impact on slowing the rate of progression of renal disease ***and*** reducing cardiovascular complications is usually achieved by ***very*** aggressively addressing the following:

1. **Blood pressure control**
    - **<130/80 if proteinuria <1g/day, (PCR ~<100mg/mmol)**
    - **<120/75 if proteinuria >1g/day (PCR ~>100mg/mmol)**

Higher targets such as 140/80 are acceptable in older patients, especially those with low grade proteinuria and stable renal function.

The lower the BP, the slower the rate of CKD progression – this is probably the most effective renoprotection you can institute. While RAAS blockade is preferred for its specific anti-proteinuric effects, any drug reducing BP will reduce proteinuria. It is very common for CKD patients to need multiple agents (not infrequently up to 4). Try to maximise one drug first before adding in a second.

- A sensible order would be ACEi or ARB (with diuretic* as salt depletion enhances ACEi/ARB effect), CCB, alfa-blocker, beta-blocker.
- MRHA guidance is now NOT to combine ACEi and ARB

- *Fluid retention is common in advanced CKD and intravascular volume expansion will also increase BP. Most patients will need loop diuretics in addition to their BP meds (thiazides are less effective as antihypertensive agents in CKD but may increase K loss & so be useful).

2. Reduction in proteinuria

- **As low as you can go**

There is very good evidence that proteinuria is a risk factor for progressive renal failure and CV complications. In addition, lowering of proteinuria with ACE/ARB predicts better outcomes. Hence proteinuria should be quantified on a spot urine sample at every clinic visit. ACR is more sensitive at low levels of albuminuria and is used to screen for microalbuminuria (now called moderately elevated albuminuria). This is defined as >2.5mg/mmol in males and 3.5 mg/mmol in females (the difference is due to the fact that males excrete higher levels of creatinine in the urine and hence the ACR will be lower for a given level of albumin). The lab will not report values if urinary albumin >2000mg/L, therefore PCR is better for determining response to treatment in higher grade proteinuria).

Approximate conversion between ACR, PCR and 24hr proteinuria are given in the table below.

24hr urine protein (g)	**PCR**	**ACR**	**Significance**
<0.3	<15	<2.5 (<3.5 females)	Normal
<0.3	<45	~3.5-30	Microalbuminuria
0.3-1.0	45-100	30-70	Dipstix positive
1.0-3.5	100-350	70-300	Heavy proteinuria
>3.5	>350	>300	Nephrotic range proteinuria

Proteinuria is reduced by BP control and use of ACE inhibitors & ARBs, *alone NOT in combination* (diltiazem & indapamide also have modest anti-proteinuric effects)

There is a very large amount of evidence supporting the renoprotective effect of ACEi & ARB (and cardioprotective effect of ACEi) in CKD, particularly diabetic nephropathy, including patients with advanced CKD. Where tolerated, these drugs should therefore be prescribed.
Main issues are **hyperkalaemia** (see below) and **rising creatinine**.
Because of the mechanism of action (preferential efferent arteriolar dilatation), GFR will fall when they are started as they reduce glomerular capillary pressure (part of how they protect the kidneys). **A fall in GFR of 15-20%, provided it then stabilises at this lower level, is acceptable**. Continuing decline suggests renovascular disease(RVD). As atherosclerosis is a systemic disease, RVD should be considered in any patient with major vascular issues. Femoral bruits are often associated. True renal bruits are rarer. If suspected, RAAS active drugs should be stopped and it should be discussed with one of the consultant nephrologist whether it is appropriate to arrange an MRA of the renal arteries to look for RVD, as it is potentially treatable by angioplasty & stenting, if appropriate (NB medical management may be as effective). Always write the eGFR on the request as the X-ray dept will be unenthusiastic about doing this in patients with an eGFR of <30ml/min/1.73m^2 due to the risk of developing nephrogenic fibrosing dermopathy with gadolinium. However, the reports for this are with the linear form of gadolinium and we use the cyclic form (Dotarem) for which there are currently no case reports of NFD (Drug Safety Update Vol 1, Issue 1,Aug 2007).

As with metformin (see below) ACEi/ARB should be stopped if there is an intercurrent episode that could provoke acute on chronic renal dysfunction, e.g. diarrhoea & vomiting with associated volume depletion, as they will exacerbate acute renal failure. However, this is **NOT** a reason to remain off them once the patient is well again. **Please ensure all patients have a medicine sick day card and understand it if they are on these medications.**

The main thing to remember is that any suggested changes in ACEi/ARB dose should be accompanied by an instruction to the patient & GP to check U&E in 1-2 weeks

3. Lipid control

- **Target Cholesterol in clinic <=4mmol/l**

There is now good evidence for reducing CV risk ***and*** slowing CKD progression with statins.
Remember to treat hypertriglyderidaemia also.

4. Diabetic control

- **Target HbA1c <=58 mmol/mol (7.5%)**

Metformin is a good oral hypoglycaemic agent that is accompanied by weight loss. However, it builds up in renal impairment and there is a risk of lactic acidosis (with a reported mortality of up to 50%) if it accumulates. Typically, we see this in patients with acute renal failure. Therefore it is important that metformin is temporarily stopped if there is an intercurrent episode that could provoke acute on chronic renal dysfunction, e.g. diarrhoea & vomiting with associated volume depletion. Patients should be told this (see medicine sick day cards).
Guidance in chronic kidney disease is harder. Current BNF guidance is that it is stopped in patients with 'mild' CKD – no further definition given. We have employed the following: If eGFR is <45ml/min/1.73m^2 *and falling steadily*, you need to start considering a switch away from metformin. Once eGFR has fallen below 30 ml/min/1.73m^2 this should have happened. However, *stability* is relevant here. If someone has a chronically stable eGFR of eg. >30 over years, they are probably safe to continue metformin provided arrangements are in place to regularly monitor creatinine. If there is clear evidence that CKD is progressing and eGFR steadily falling, an earlier switch would be better.

For patients on Insulin remember that some metabolism of Insulin takes place in the kidneys and it is not uncommon for patients to need less as GFR declines.

5. Lifestyle changes

These are very important and it is important to make the patient understand they have to take responsibility for these:

- **Weight loss** – almost universally required – monitor weight and reinforce with patient any losses (or gains!)
- **Salt restriction** – 6g/day – tell them to look on packets. Salt advice attached.
- **Smoking (not)** – good evidence now that smoking accelerates GFR decline as well as increasing CV risk.
- **Exercise** – any increase will be beneficial – walking is good exercise.

Sequalae of CKD

Likely to be encountered are anaemia, acidosis, hyperkalaemia and secondary hyperparathyroidism and hyperphosphataemia.

1. Anaemia (<105g/l)

The anaemia of CKD is due to lack of erythropoietin production by the failing kidneys and is normochromic, normocytic and characterised by a low reticulocyte count. It is uncommon above a GFR of 30ml/min/1.73m^2 and even below this **you should always exclude other causes of anaemia.**
All patients with Hb <=105g/l should therefore have reticulocytes, iron studies, B12 & folate as a minimum and any deficiencies of haematinics investigated (e.g. GP to do FOBs & refer for GI Ix if positive) and treated before any discussion about ESAs (erythropoiesis stimulating agents).
Please discuss with one of the consultant nephrologists if you then think a patient would benefit from ESA treatment.

2. Acidosis (<=22mmol/l)

As GFR falls, so does bicarbonate. There is limited evidence for the benefits of correcting this but acidosis does enhance movement of potassium from cells into the plasma so bicarbonate supplementation may limit hyperkalaemia.
Use sodium bicarbonate 500mg tabs – start at bd or tds and titrate to achieve a serum bicarbonate of 23-25mmol
However, remember that this increases sodium intake and may predispose to fluid retention.

3. Hyperkalaemia (>=5.5mmol/l)

This is increasingly common as GFR declines and has multiple causes including drugs (ACEi/ARB/spironolactone), diet, acidosis and poor glycaemic control. Relative (exogenous or endogenous) Insulin lack (indicated by high glucose) will enhance movement of potassium from cells into the plasma. If a high potassium corresponds with a glucose of 20mmol/L or more, the chances are that it will be normal on repeat, if the glucose has fallen to normal. While it may be necessary to reduce or stop ACEi/ARB, given that the evidence for their renoprotective benefit is so strong, please try the following first.

- Correct acidosis.

- Ensure glycaemic control optimal.
- Dietary advice – basic sheet attached – dieticians can assist further.
- Stop other K sparing drugs e.g. spironolactone, amiloride.
- Consider K leaching drug e.g. thiazides, loop diuretic.
- If all this fails, try reducing RAAS active drugs before stopping unless K >6.5mmol/l (in which case, stop, do all the above, then try re-introducing at a lower level).

Most importantly, arrange a follow up blood test with the GP to ensure the interventions have been successful.
Any change in ACEi/ARB dose should be accompanied by an instruction to check K (& Creatinine) in 1-2 weeks.

4. Secondary hyperparathyroidism (>60pmol/l)

As GFR declines there is less hydroxylation of vitamin D by the kidneys, so less calcium absorption from the gut, leading to hypocalcaemia and activation of the parathyroid glands in response to this to restore plasma Calcium by taking it from bones (sometimes you will see an increase in alk phos also). This leads eventually to parathyroid bone disease. Again this is uncommon above an GFR of 30ml/min/1.73m^2.

Hyperparathyroidism can be treated by providing hydroxylated vitamin D. However, over-treatment leads to adynamic bone disease. We therefore aim to keep PTH levels between 2-9 times the lab upper limit. For RIE this means 13.8-62.1pmol/L, so start when PTH is reaching the top of this range & rising.

The starting dose of alfacalcidol is 250ng/day with an instruction to the GP to check Calcium at 2 & 4 weeks to ensure no hypercalcaemia, and is titrated to achieve a PTH within this range.

5. Hyperphosphataemia (>=1.7mmol/l)

This occurs **late** in CKD. It is treated by dietary restriction (see attached sheet but refer to a dietician as phosphate restriction usually results in protein restriction also – we no longer advocate this as a means of reducing the progression of CKD) and phosphate binders. Only calcium-containing phosphate binders are licensed for pre-dialysis patients currently. However, we are increasingly concerned about total calcium load in CKD patients as valvular & vascular calcification is a major problem.
If a person has hyperphosphataemia please discuss with a consultant nephrologist – they should probably be seen in a low clearance renal clinic.

Troubleshooting

1. Drug dosing

– alters as GFR falls for many drugs – consult appendix 3 of the BNF if in doubt or ask a consultant nephrologist.
e.g. Hyperuricaemia & gout (common if diuretics used) – allopurinol dose is 100mg in CKD

Finally

If a reciprocal creatinine plot (or eGFR plot) suggests that a person has progressively declining function, please discuss with a consultant nephrologist regarding referral to a low clearance clinic to prepare for renal replacement therapy.

More plots can be obtained from

http://renux.dmed.ed.ac.uk/EdREN/Handbookbits/HDBKgfrest.html#reciprocalcreat

Parallel 'renal' Checklist **Clinic date:_____**

Name etc
(Label)

DM1/DM2 **Duration**____yrs (**Date of diagnosis** _____)

Rx:_____

Wt:_____kg **Ht:**_____m

ACEI/AII **Drug(s):**_____
If no give reason:_____

Aspirin? **Y/N**
If no give reason:_____

Smoker **Y/N/Ex** (details) _____

Sick Day card **Y/N Date:**_____

Results this visit: **BP** _____/_____

Cre:_____μmol/L **MDRD GFR**_____ml/min/1.73m^2 Hb_____g/L

ACR:_____mg/mmol **Protein (spot)**:___g/L **Urine Cre**: _____mmol/L

PCR:_____mg/mmol **Urine dipstix:** bld:___prot____

IFCC this visit _____mmol/mol **HbA1c** this visit:_____%

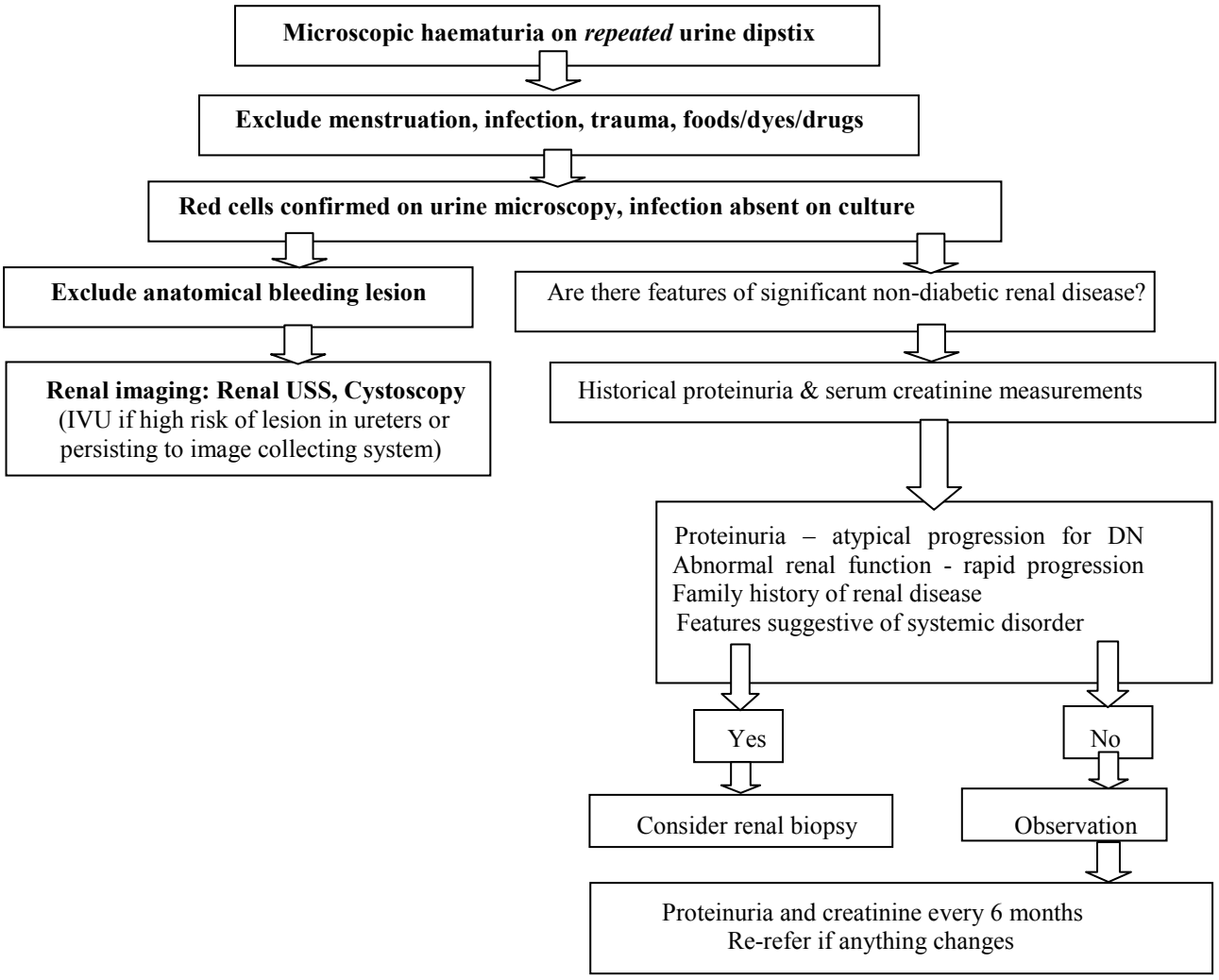
Chol this visit:_____mmol/l **On Rx:** Y/N **Drug(s)**_____

PTH this visit:_____pmol/l **On 1-alpha?**_____

TFT: Last check:_____ **OK?** Y/N **On Rx:** Y/N

Comments:

Algorithm for haematuria



Guideline for investigation of a paraprotein