

CKD and Transplant patients presenting to the DGH

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Objectives

Overview of the CKD population – definitions and aetiology

CKD stages and calculating eGFR

Long term principles of CKD management

Acute issues in managing CKD in the DGH

Acute issues in managing the Transplant patient in the DGH

Take home messages

Defining CKD

“ Irrecoverable bilateral abnormalities of the renal parenchyma”

KDIGO definition:

- eGFR < 60mls/min/1.73m²
or
- eGFR > 60mls/min/1.73m²
with evidence of renal structural damage

CKD stage 1

>90mls/min/1.73m²

CKD stage 2	61-89mls/min/1.73m²
CKD stage 3a/b	31-60 mls/min/1.73m²
CKD stage 4	16-30mls/min/1.73m²
CKD stage 5	<15mls/min/1.73m²

Thinking about eGFR

- Thinking in terms of eGFR rather than plasma Cr allows closer and safer drug-dosing
- More accurate reflection of actual functional changes over time
- Commonest bedside calculation is the Schwartz-Haycock formula

$$eGFR = \frac{height (cm) \times k (40)}{creatinine (umol/l)}$$



CKD Epidemiology

- True incidence is unknown (under-reporting and often presenting in early adulthood)
- Estimates between 8 and 16 cases per million child population (pcmp)
- Stable developed-world RRT incidence of 9-10 pmcp per year
- CKD incidence is higher in males (more CAKUT) and ethnic minorities/black Afro-Caribbean (APOL-1 risk association genes for FSGS)

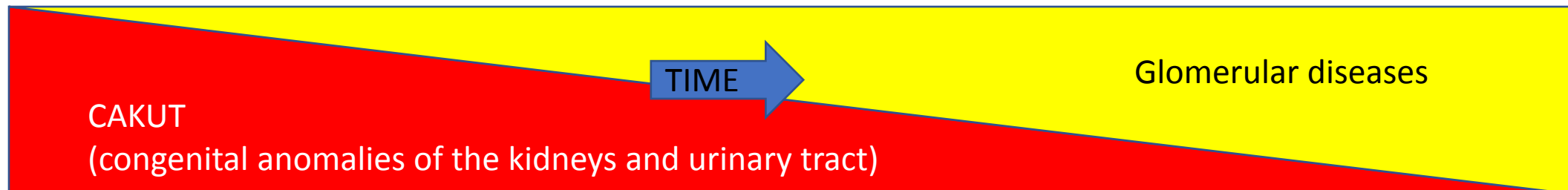
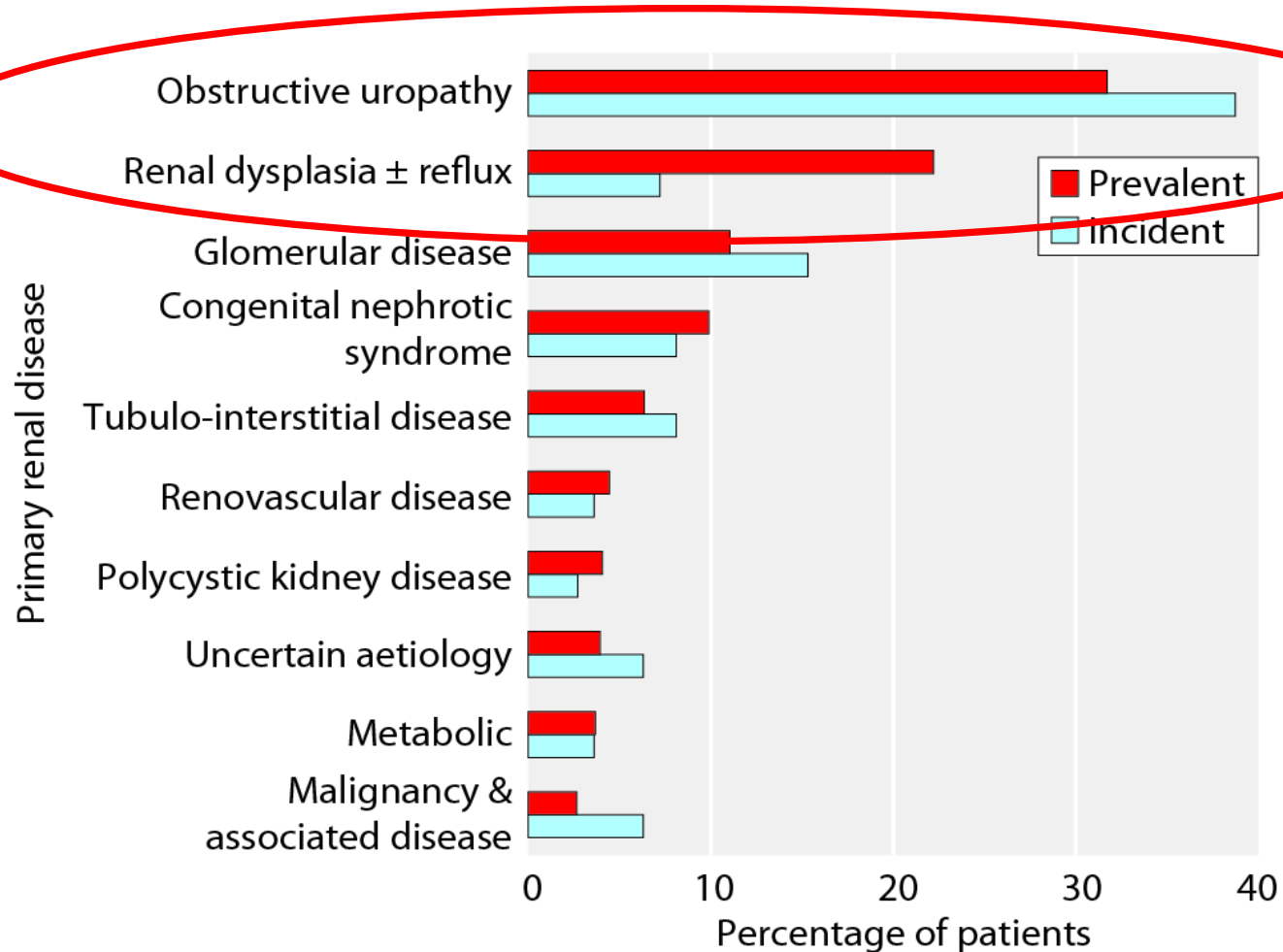


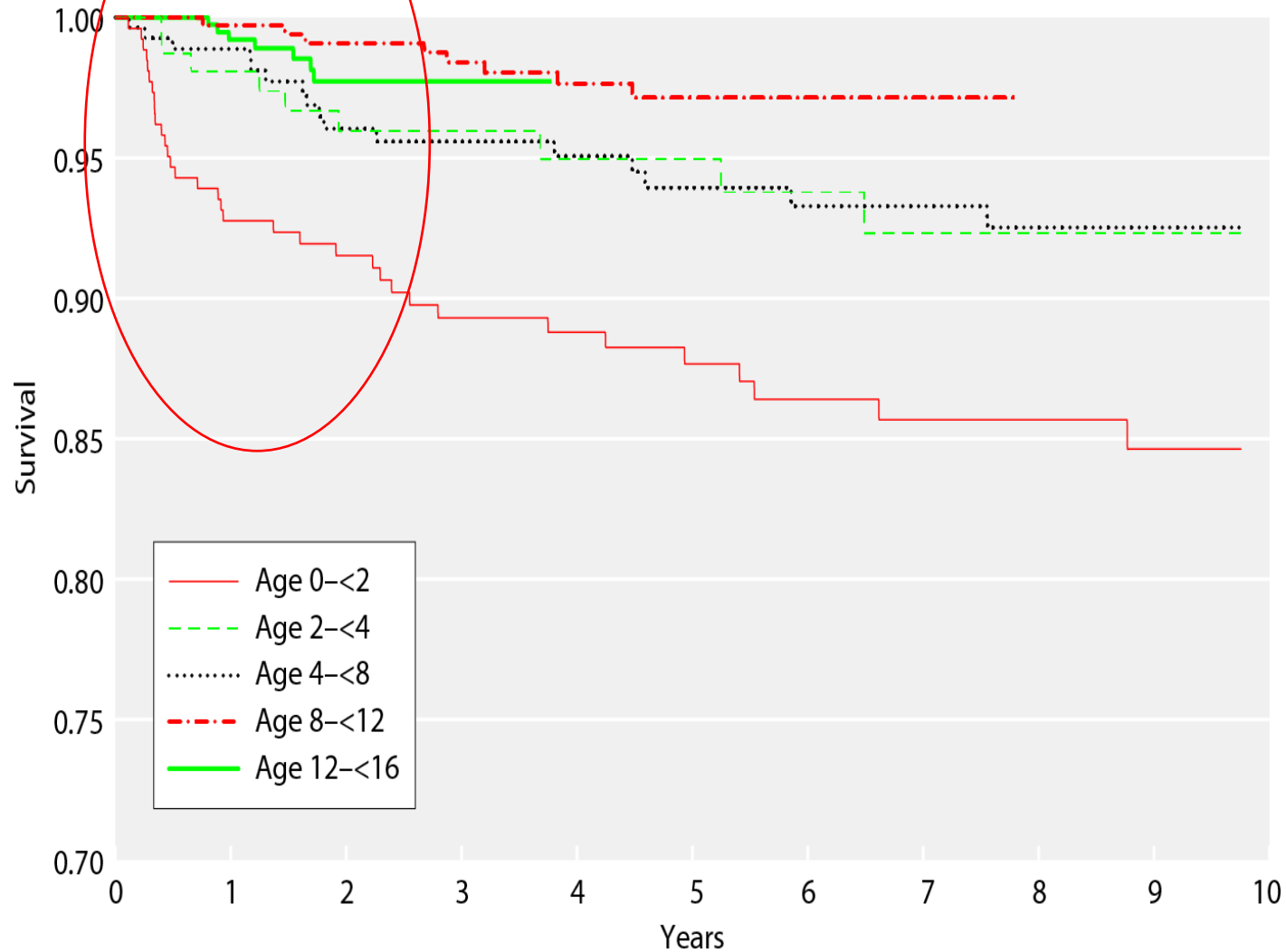


Figure 4.6. Proportion of primary renal disease by historic UKRR diagnostic groupings in incident and prevalent paediatric patients in 2016 for whom a causative diagnosis was reported



CKD aetiology in
the UK 2017
datapoints

Figure 4.5. Unadjusted Kaplan-Meier survival in the UK paediatric ERF population <16 years old starting RRT between 2002 and 2015, by age at start



Mortality is highest in infants and those who commenced RRT in infancy

Principles of long-term CKD management

Slowing the Progression

Volume and lyte control (most Na/biacarb/water losers in CAKUT)

Growth and Nutrition (PEG/high calories/protein control/growth hormone)

Management of BP and proteinuria (ACEi/ARB) + avoidance nephrotoxics (NSAIDS)

Management of CKD anaemia (Oral/IV Iron/ Erythropoetin)



Management of CKD MBD (25-OH Vit D, 1-alfacalcidol, calcimimetics)

Management of associated complex urological issues (CIC, surgeries)

Transplant at earliest opportunity (preferably LRDKT-pre-emptively)

VEIN PRESERVATION!! VEIN PRESERVATION!! VEIN PRESERVATION!!

Important general advice for DGH CKD treatment

- Parents are generally expert in their management – listen closely
- There is **no such thing as 'maintenance fluids'** ask the family about standard daily intake and urine output and match it plus losses
- They are generally SALT/WATER/BICARB losers (CAKUTs)
- DO NOT FEAR FLUIDS
- DO NOT AUTOMATICALLY FLUID RESTRICT on finding pCr  
- DO NOT BE REASSURED BY WET NAPPIES/UO
- Lookout for **ACEi (...prils)** and **ARBS (...sartans)** and **STOP when unwell**
- **Call your local friendly nephrologists** on admission but DO NOT BE AFRAID to act when unwell with fluids and antibiotics
- Aminoglycosides should give pause for thought but can be used appropriately even in CKD

Typical CAKUT patient presenting to DGH

5 year old male
PUV/dysplasia/VUR
CKD IV last eGFR 20
mls/min/1.73m²



-1000mls overnight pump feed
(*Renastart*)
-500mls as daytime boluses -
Additional 500mls water
(2L total 24h)
(would be 1.3L if maintenance
wrongly prescribed)



Mitrofanoff channel for CIC
and PEG

Nacl 30% 60mmols/day, Na bicarbonate 30mmols/day,
enalapril 5mg OD , 1 alfacalcidol 0.5mcg OD ,
colecalciferol, cefalexin prophylaxis, growth hormone,
Aranesp 40mcg fortnightly



Presents to St Elsewhere with 4
day history of Fever, D+V, weight
loss, abdo pain and cloudy urine

What Investigations do you request?
What information do you want?

Baseline weight 16Kg current
weight **15.5Kg (down 0.5Kg)**
UO - ongoing 1.8L day at last
measure
Ht 98cm
BP 90/50mmHg
HR 110bpm RR normal
CRF <2secs
Dry mucous membranes
Multiple recent klebsiella UTIs ESBL
producing
Now eGFR = 13mls/min/1.73m2

Day	Last clinic	Day 1
Na mmol/l	135	129mmol/l
K mmol/l	3.9	5.8
Cl mmol/l	95	88
Bicarb mmol/l	25	15
Urea mmol/l	18	29
Creatinine umol/l	200	300
cCalcium mmol/l	2.7	2.8
Phosp mmol/l	1.9	2.2
pH/BE	7.38/-2	7.25/-10
Hb g/l	108	94
MC+S	-	WCC > 100 culture awaited
eGFR <small>ml/min/1.73m2</small>	19.6	13

1. Volume: (correct shock if present)

2. Volume: IVI 2L straight conversion plus 500mls (2.5L starting point)

Contents: 0.9% Nacl plus separate bicarb correction (half/whole)

0.45% Nacl plus 20mmol bicarbonate per bag and RV

OR

As soon as is possible switch over to enteral feeds/water and enteral supplements – much easier to manage

3. Withhold: **Enalapril**, calcium carbonate, colecalciferol, 1-alfacalcidol, saizen, cefalexin -non essentials

4. Monitor K+ should improve with Na+/water delivery to DCT and stopping ACEi.

Management 1.

5. Treat Infection –
high likelihood UTI
(history and Sx)

6. Decide on
empirical therapy
ESBL+ve past =
Meropenem

7. Review eGFR and dose
(half normal dose 12h BNFC
eGFR 10-25mls/min/1.73m²)

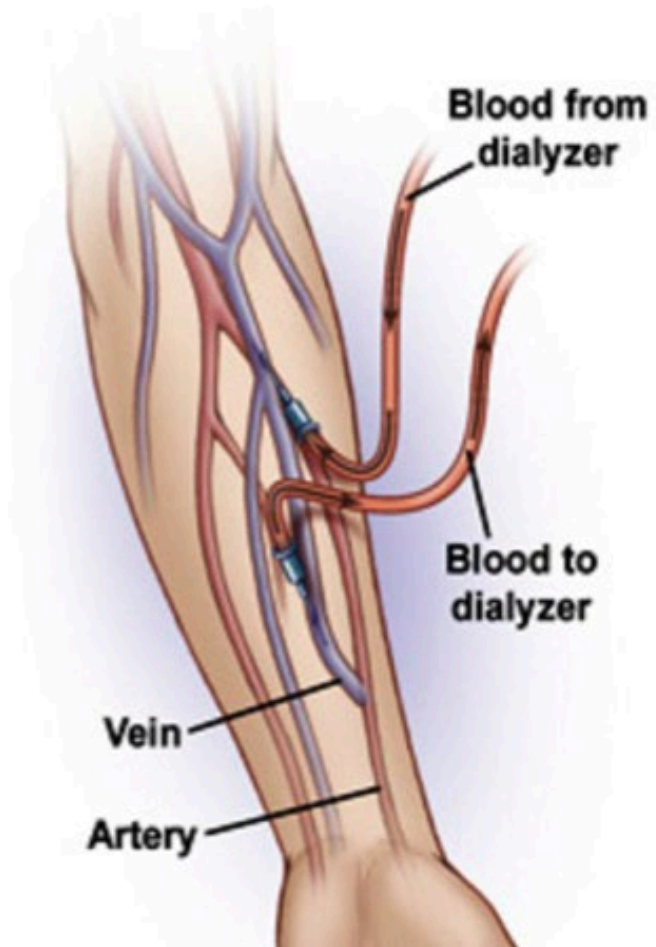
Catheterize bladder
and Free drainage
until better

Management 2.

	Day 2
Na	134
K	4.2
Cl	92
Bicarb	21
Urea	20
Creat	225
ccA	2.7
Phosp	1.8
pH/BE	7.38/-2
Hb	89
MCS	Klebsiella a ESBL
eGFR	17



Arterio**V**enous **F**istula

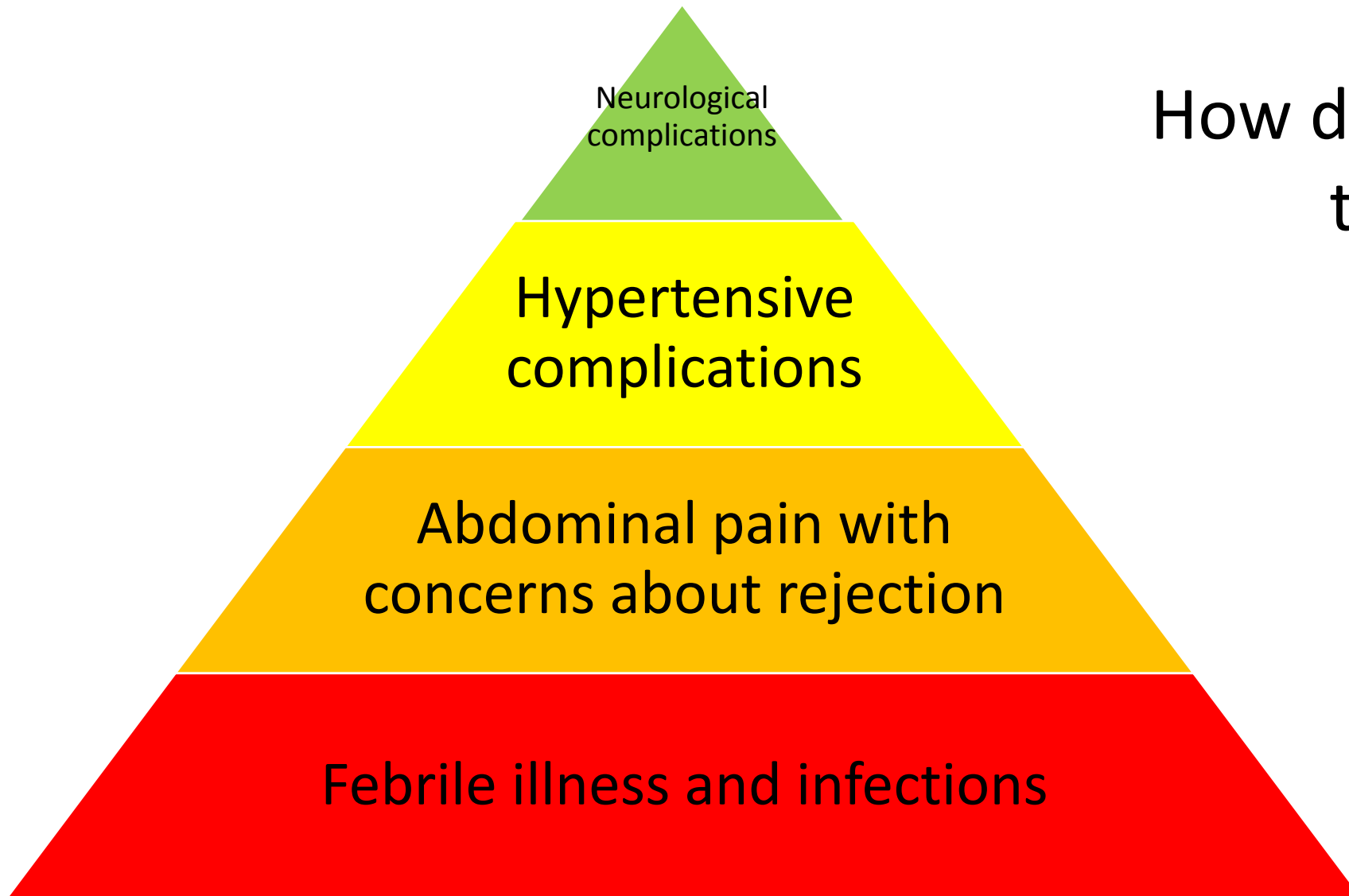


VEIN preservation

- One of the most important issues DGHs can help with
- Avoid antecubital venous sampling/cannulation where possible
- Avoid subclavian veins where possible in PICU settings
- Advanced CKD predicts a future of transplant and re-transplant plus punctuated periods of RRT – blood vessels must be seen as lifeline to preserve for the long-term.

The transplant patient in the DGH setting

- Should be considered as *CKD+ special case* patients
- Added issues of solid organ transplant
- Added issue of immunosuppression
- Special case of drug-level monitoring (tacrolimus)
- Vulnerable to infection, sepsis and AKI
- Vulnerable to chronic viraemia
- Special cases – JC/BK/EBV/CMV virus, PMLE (progressive multifocal leucoencephalopathy) , PTLD (post-transplant lymphoproliferative disease)
- Acute cellular and vascular rejection



How do they present
to DGHs?

Basic Investigations at DGH

- FBC
- Children's profile + LFT/Bone profile
- CRP
- Urine dip/MC+S, +/- uACR/PCR
- EBV/CMV/JC/BK PCR (if none recently and suggestive signs symptoms)
- USS graft if pCr elevated– allows R/O pyelonephritis/obstruction (that's *all* USS gives)
- 12h trough tacrolimus level (limited timely availability in DGH)
- **Calculate eGFR!!** These are CKD patients (50% nephron mass whatever blood results say)

Specific history features to elicit

What was the underlying renal disease (disease recurrence?)

Was it a living-related or deceased-donor transplant

How far from transplant are you? (helps with relative rejection risk and tac level interpretation)

What is your daily fluid target? How much of it have you had?

What is your last known weight?

What medications are you taking (immunosuppression regimen)?

Any previous issues with infections/rejection episodes

Are you known to have any chronic viraemias (EBV/CMV/JC/BK)?

Any plastic stents still indwelling (JJ- stents)

Standard history of presenting complaint

Common findings in Medication History

- **TACROLIMUS** (*Prograf/Modigraf/Adoport/Advagraf*)

Calcineurin inhibitor: Staple Immunosuppressant BD (except advagraf)

Toxicity common esp GI disturbance (levels high) – directly nephrotoxic

Other s/e – tremor, hypertension, hyperkalaemia, hypomagnesaemia

Long list of interacting drugs in BNFc (macrolides/PPI/grapefruit/fluconazole commonest)

- **MYCOPHENOLATE MOFETIL** (*MMF, Cellcept, Myfortic, Myfenax*)

Anti-proliferative – BD oral agent

No levels monitoring – MPO active drug

s/e GI disturbance, weight loss, infections – ENT/Resp/bronchiectasis, viraemias, marrow suppression

- **AZATHIOPRINE**: Purine analogue (AZT) OD drug S/e marrow suppression/LFT derangement (TPMT assay before use)

- **SIROLIMUS**: mTOR inhibitor alternative to tacrolimus OD drug s/e dyslipidaemia, poor wound healing, pleural effusions

- **PREDNISOLONE**: used with tac/aza protocol – s/e well documented

Examination features



General thorough
paediatric examination



Volume status and
weight/nutritional
status

(GI s/e common with
MMF)



Blood Pressure and
urinalysis (Dip, MC+S
plus uPCR/uACR)



Lymphadenopathy?

Think PTLD

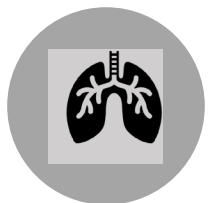


Warts hands/feet

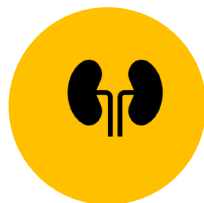
(Common MMF)



Opportunistic fungal
infestations
(mouth/perineum/nails)



Within 6 months at risk
of PCP (co-trimoxazole
prophylaxis)



Graft site tenderness and bruit (mostly now in
RIF, graft tenderness/redness rarely present
with modern immunosuppression)

Example transplant presentation to DGH



5yo female - Cloacal abnormality with bilateral renal dysplasia – unsafe bladder drainage– CIC 2-3 hrly via Mitrofanoff channel



12 months post LRDKT (Mother 0-1-1 mismatch)



No previous rejections but multiple post-Tx UTIs



2-day history of Intermittent fever 39 degrees and D+V (10 vomits and 8 episodes loose stools siblings also affected)



Admission Obs: T 38.9 HT 120bpm BP 99/70 CRF 2 secs skin turgor normal dry MMs



Meds: Tacrolimus 5mg BD, MMF 500mg BD, cefalexin 5mls nocte,



Previous knowns: Wt 25Kg, baseline creatinine 50umol/l 2L/day oral fluids

Management

- APLS get weight (24Kg) and recent height (112cm)
- Establish IV access (sparing antecubital veins *where possible*)
- FBC/Profile/CRP/BC/gas/BM/
- Urine sample MC+S/dip/stool
- Start IVF at 2L/day with 0.9% NaCl/5% dextrose with 20mmol KCL
- Cover with IV ceftriaxone pending 48hBC or positive samples?
- Catheterize and free drainage
- USS where possible
- Inform Tertiary nephrology team and discuss plan and results:

Day	1	2
Na	128	136
K	2.9	3.9
Bicarb	19	22
Urea	12	6
Creat	100	65
cCa	2.67	2.67
Ph	1.2	1.2
CRP	55	18
pH/BE	7.32/-5	7.38/0
Hb	132	124
WCC	15	12
eGFR	45 (CKD III equiv)	68
MC+S	50 WCC	No growth
	24Kg (down 1Kg)	24.6kg

Increase IVF rate to 2.5L/day in view of acute 1Kg weight loss (correct over 48hrs) plus ongoing losses = c100mls/hr 48 hrs

Deranged Creatinine where cause not obvious

The Big 6

1. Dehydration
2. Obstruction
3. Tacrolimus Toxicity
4. Ischaemia
5. Rejection
6. Infection

Challenge with Volume and pCr ↓

USS graft (hydronephrosis) +/-contrast

12h trough tacrolimus levels (?D+V)

Mag-3 and USS doppler

Renal Biopsy only reliable marker

MCS, BC, stool virology, Viral PCR

FAQ

- Q. Does every transplant patient require transfer to tertiary centre?
- A. **Not every one** – in example above if clearly defined cause of disturbance (viral GE) with rapid signs of improvement negating need for acute tacrolimus levels - can be managed locally
- A. **Other examples** would include uncomplicated UTI (+/- fever), LRTI, viral URTI, tonsillitis etc.

NB - Timely tacrolimus levels can only be done at RMCH – diarrhoeal illnesses cause abnormal elevation of levels and transfer often required for dose titration.

NB - Acute rejection can be triggered by intermittent infections if pCr still rising think again

Every transplant and CKD patient seen /admitted locally must be discussed with the RMCH nephrology team

Take Home messages

- CKD and Transplant patients are part of the same continuum
- Both are vulnerable to infection, dehydration and AKI
- The commonest reasons for presentation are infection and dehydration
- Calculation of eGFR is vital to safeguarding renal function and drug dosing
- Thorough history and examination are essential
- Do not fear giving volume in acute illness since most are obligate polyuric salt losers – resuscitate then call
- Discuss early at outset with RMCH nephrology for advice on investigations, therapy, monitoring and need for acute transfer

FAMOUS KIDNEYS



BILLY THE KIDNEY



NICOLE KIDNEY



HELLO KIDNEY



JOHN F. KIDNEY



THE KIDNEY AND I



KIDNEY ROCK