How I manage the sick transplant patient

Dr. Richard Baker

Renal Transplant Unit

St. James's Hospital, Leeds

RCP Advanced Medicine Course 6th February 2018

GJ

- 34 year old man
- End Stage Renal Failure – IgA Nephropathy
- Haemodialysis 2006
- Live donor transplant 2007 (mother)
- Tacrolimus and Mycophenolate mofetil (MMF)
- Creatinine 180 – 200 baseline
- June 2015 – creatinine 300 and 1-2 g protein
- Biopsy – no rejection, no recurrent disease – scarring
- Tacrolimus withdrawn – on MMF 750mg bd and Prednisolone 5mg od

GJ

- 20/10/17   Outpatient clinic
- Recurrent chest infections
- SOB
- Hb 116, WBC 8.41, Plts 277
- CRP 37
- Creatinine 596, Na^+ 132, K^+ 5.2
- Calcium 4.0

Question 1

This acute deterioration in function is classified as?

1. Stage 1 Acute Kidney Injury (AKI)
2. Stage 2 AKI
3. Stage 3 AKI
4. Chronic kidney disease stage 5

- Creatinine 159μmol/L
- Age 41, wt 95kg
- eGFR 44.5ml/min/1.73m^2
- CG 74.9ml/min
- DTPA GFR 144.9ml/min
- (116.2 ml/min/1.73m^2)

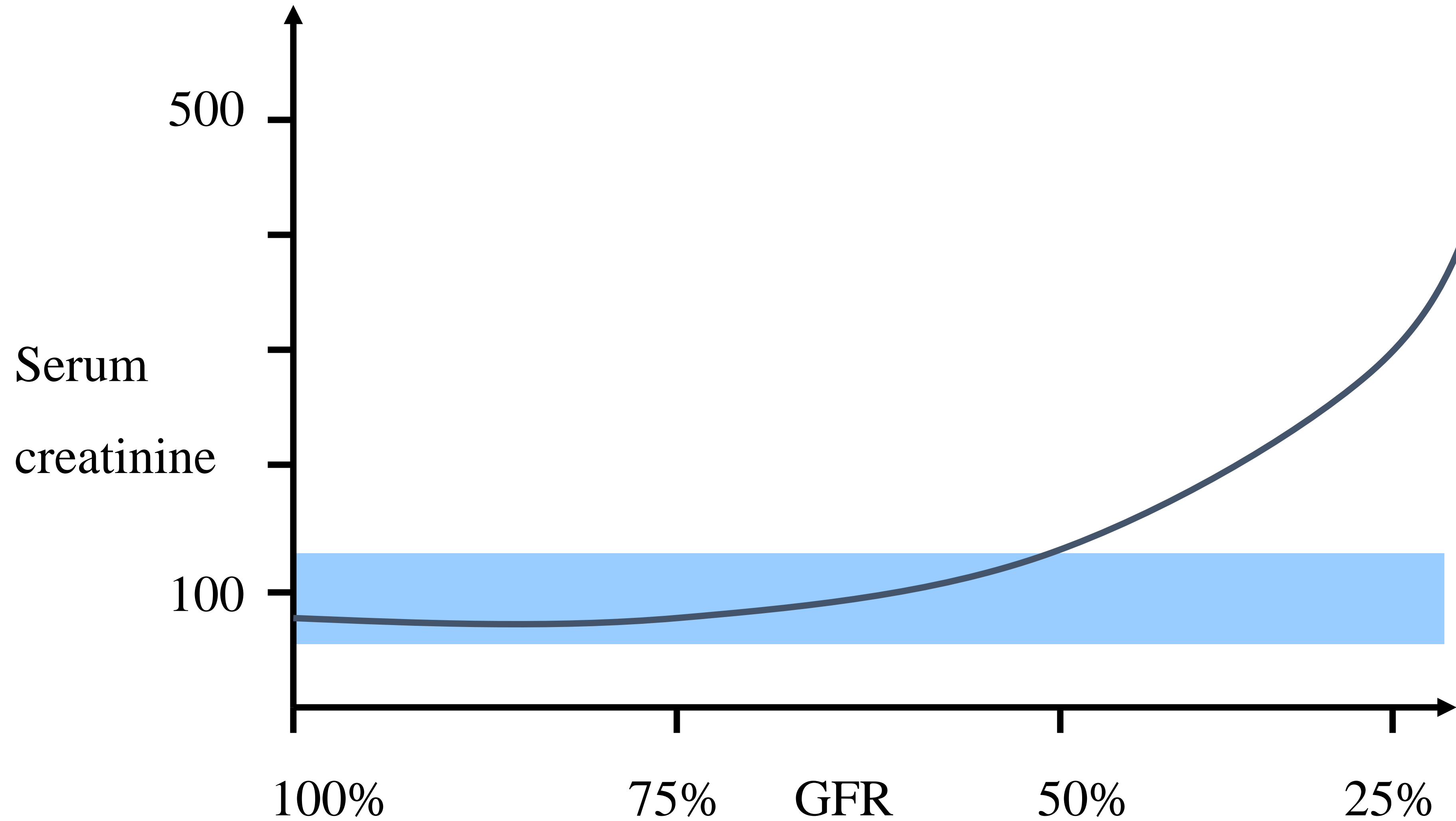
Question 2

How many nephrons does the average kidney have?

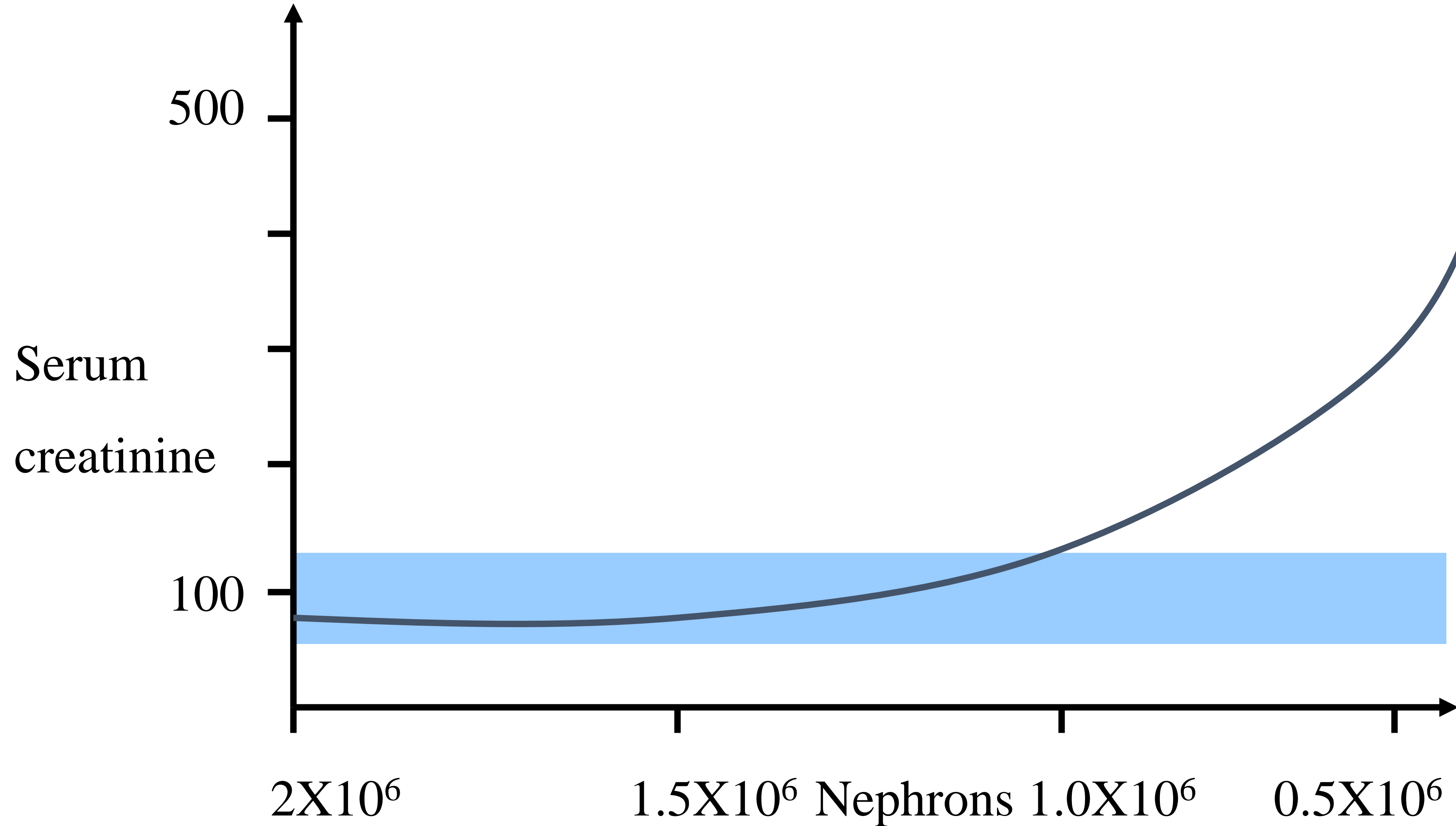
1. 10,000
2. 100,000
3. 1,000,000
4. 10,000,000
5. 100,000,000

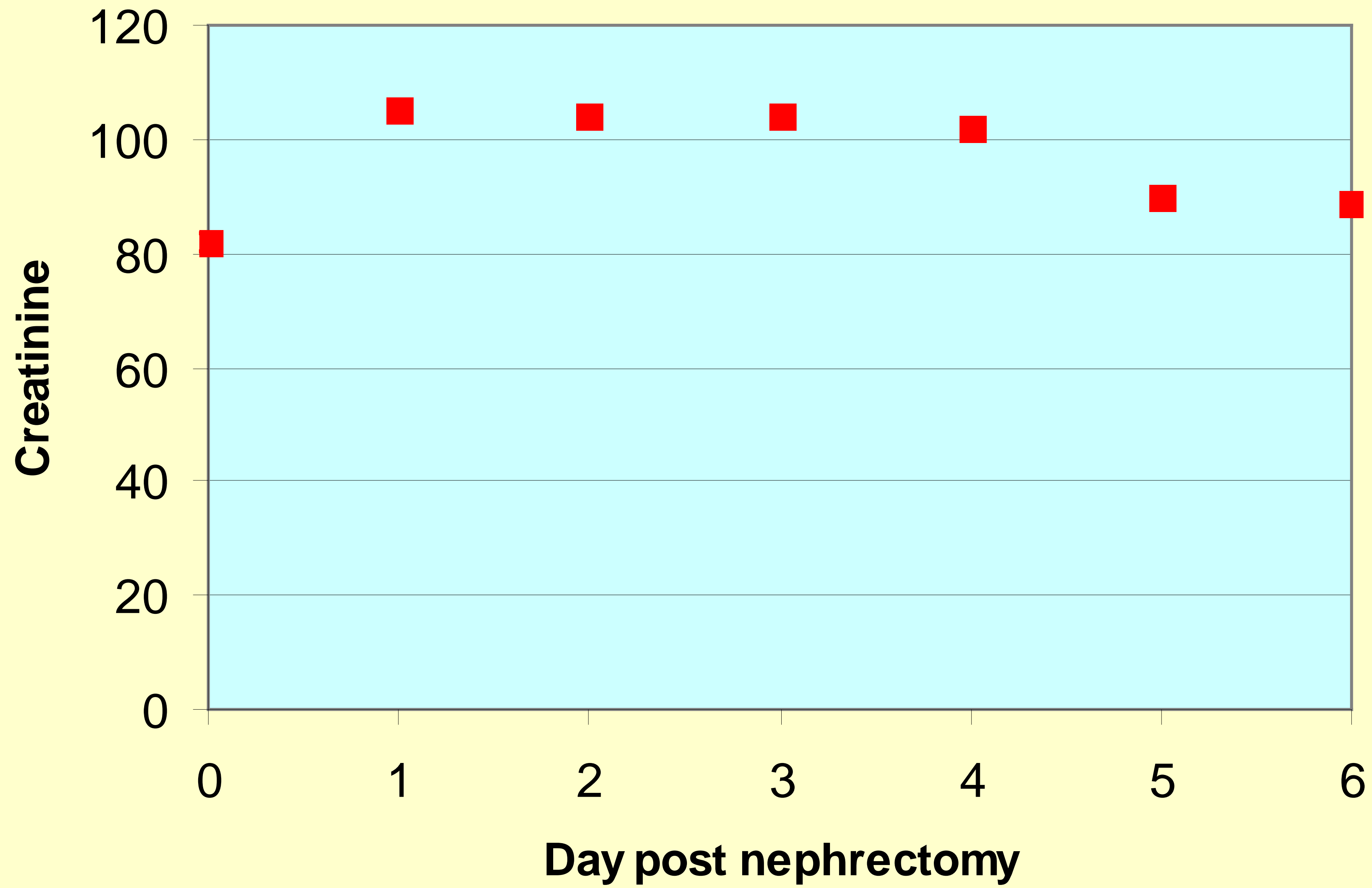
2,000,000

Estimating renal function

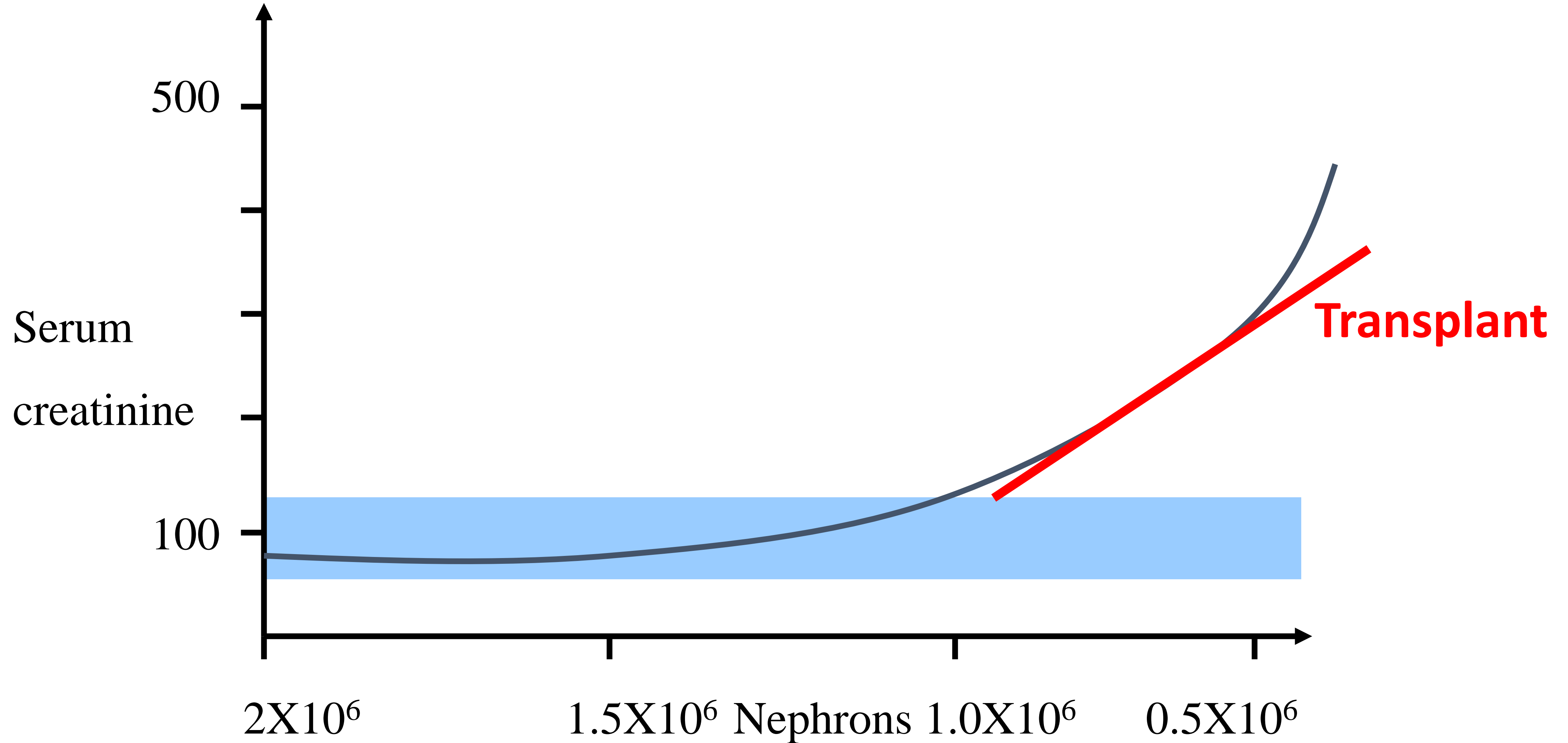


Estimating renal function




120
100
80
60
40
20
0
Creatinine
0
1
2
3
4
5
6
Day post nephrectomy

Estimating renal function



Question 3

What are the most likely cause of these findings?

1. Bacterial pneumonia
2. Left ventricular failure with pulmonary oedema
3. Non-bacterial pneumonia
4. Disseminated malignancy
5. Other

Microbiology

- 22.10.17 Sputum Respiratory flora and ***P. aeruginosa***
- 23.10.17 Sputum PCR Rhinovirus

AAFB, other viruses, Legionella, aspergillus IgG, aspergillus fumigatus all negative

Commenced i/v ciprofloxacin

Question 4

What would you do next?

1. Change empirically to broader spectrum antibiotics
2. Request a bronchoscopy with BAL
3. Stop all immunosuppression
4. Stop antibiotics and re-culture
5. Other

GJ Bronchoalveolar Lavage 3.11.17

- CMV +ve
- EBV +ve
- HHV6 +ve
- **Pneumocystis carinii +ve (consistent with a high organism load)**
- Co-trimoxazole 1920mg bd for 21 days
- Tapering prednisolone

Question 5

What is the most likely cause of the hypercalcaemia?

1. Underlying malignancy
2. Excessive Vitamin D supplementation
3. Tertiary hyperparathyroidism
4. Underlying sarcoidosis
5. Other

GJ

- Calcium **4.00**
- PTH 3.0
- ACE < 20
- ALP 49
- 25-OH Vitamin D 85
- Normal U/S neck
- Negative parathyroid antibodies
- PTH related protein <1

Clinical Kidney Journal

Clinical Kidney Journal, 2017, vol. 10, no. 6, 845–851

doi: 10.1093/ckj/sfx044
Advance Access Publication Date: 23 June 2017
Original Article

ORIGINAL ARTICLE

Hypercalcaemia preceding diagnosis of *Pneumocystis jirovecii* pneumonia in renal transplant recipients

Jonathan Ling[1], Tara Anderson[2], Sanchia Warren[2], Geoffrey Kirkland[1], Matthew Jose[1,3], Richard Yu[1], Steven Yew[1], Samantha Mcfadyen[1], Alison Graver[1], William Johnson[1] and Lisa Jeffs[1]

[1]Department of Nephrology, Royal Hobart Hospital, Hobart, Tasmania, Australia, [2]Department of Infectious Diseases, Royal Hobart Hospital, Hobart, Tasmania, Australia and [3]School of Medicine, University of Tasmania, Hobart, Tasmania, Australia

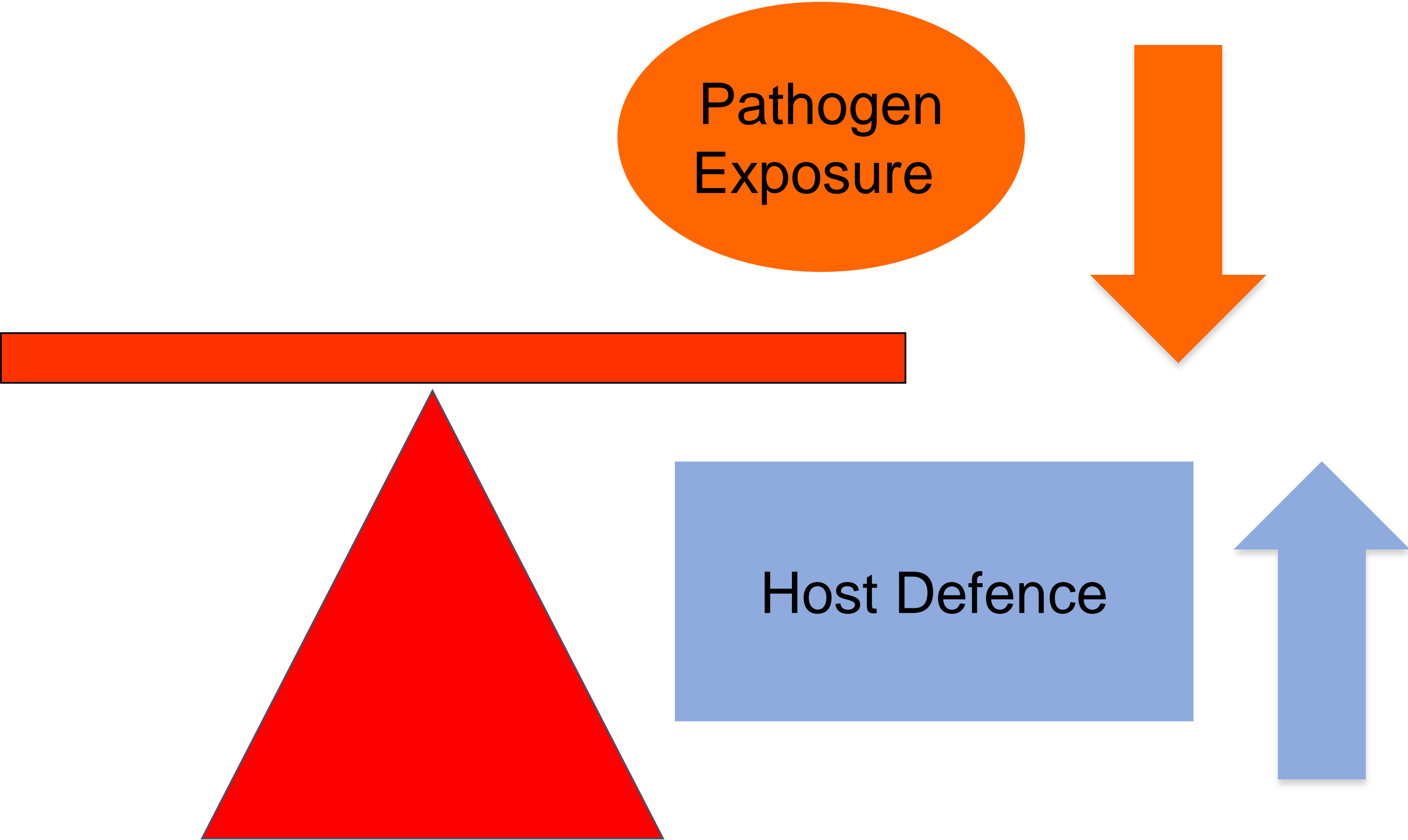
GJ – Serum Calcium

Question 6

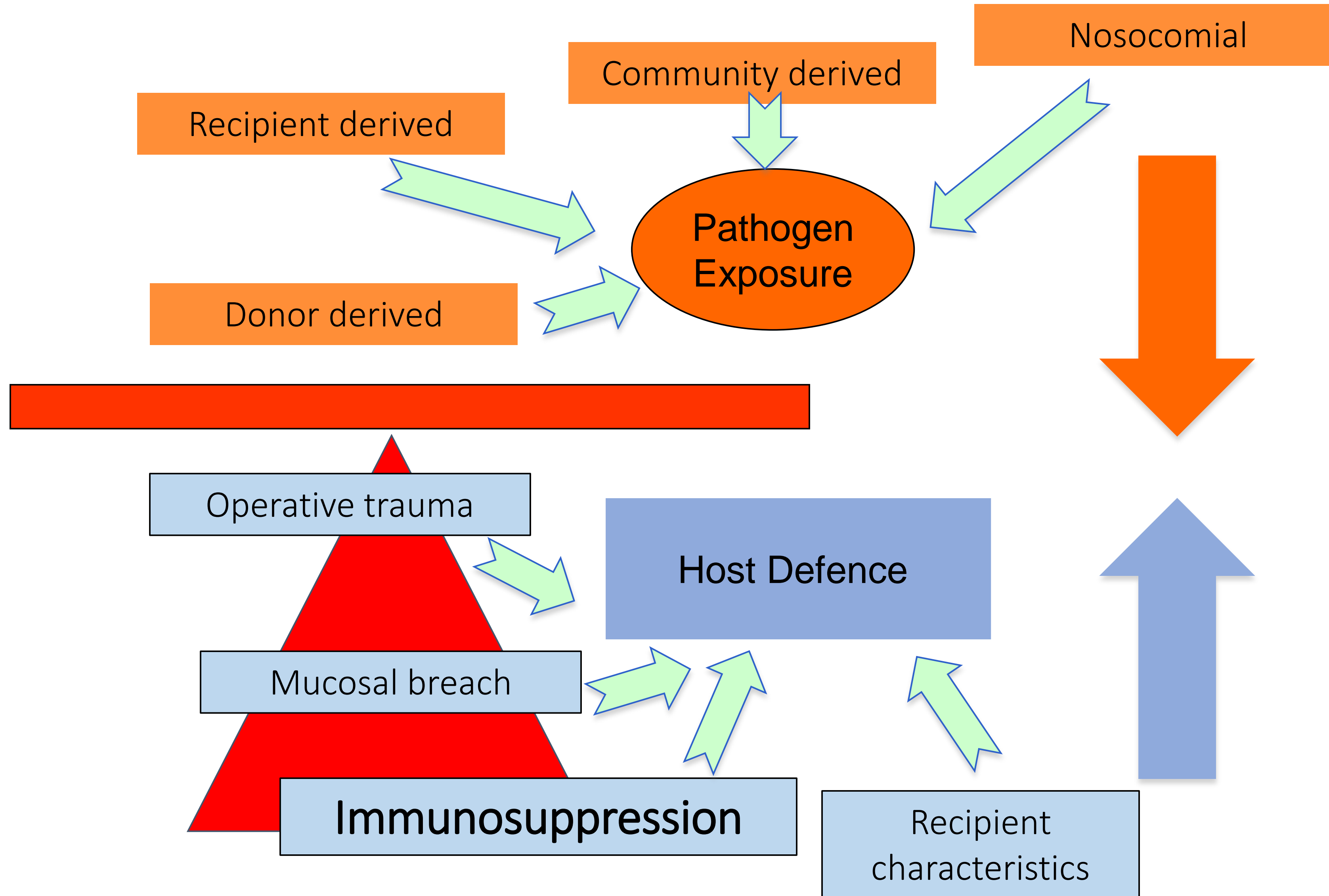
Which factor is most likely to have caused the PCP infection?

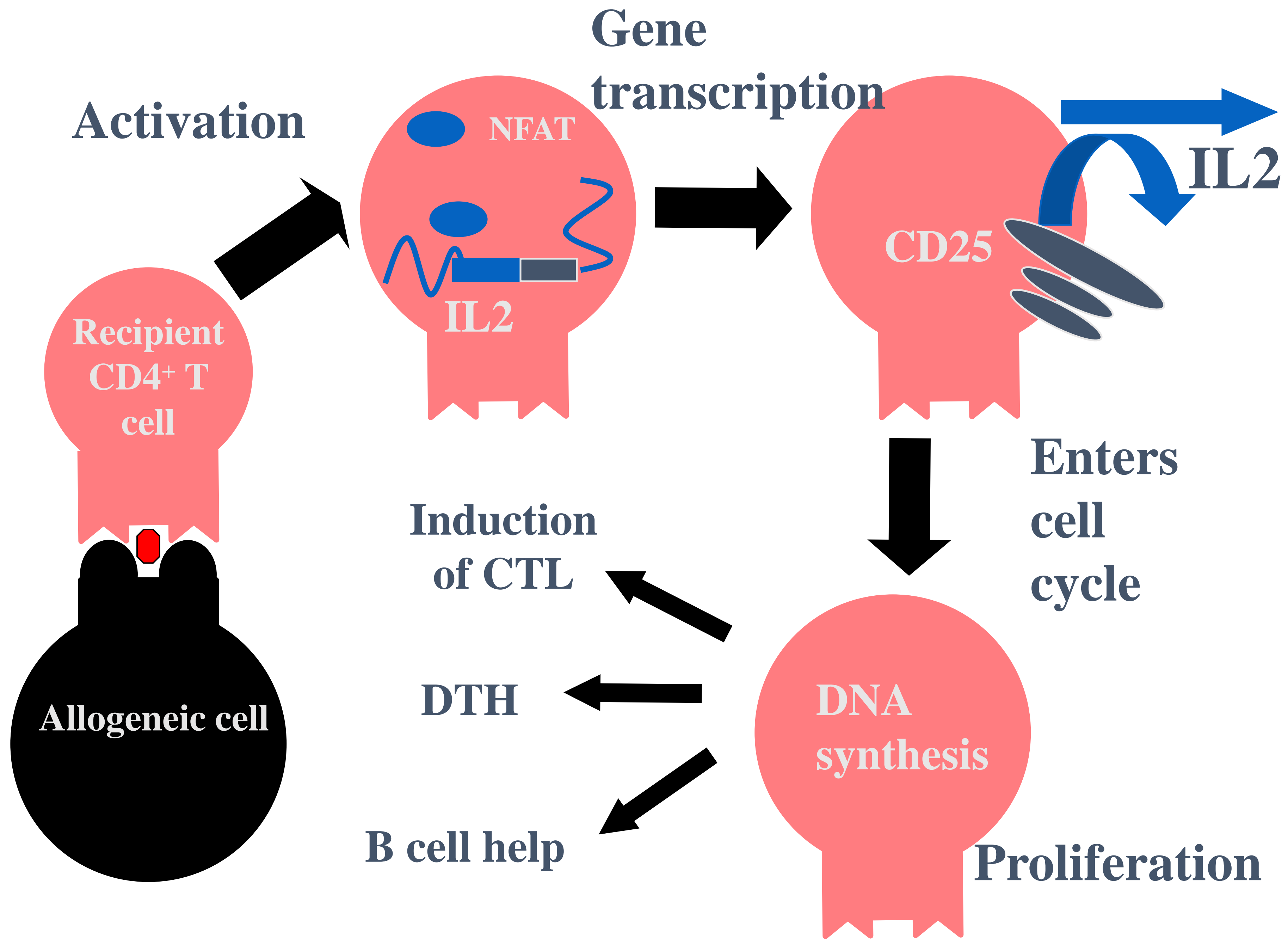
1. Damaged mucosal defences
2. Impaired cell mediated immunity
3. Reduced antibody titres
4. Overwhelming exposure to the organism
5. Other

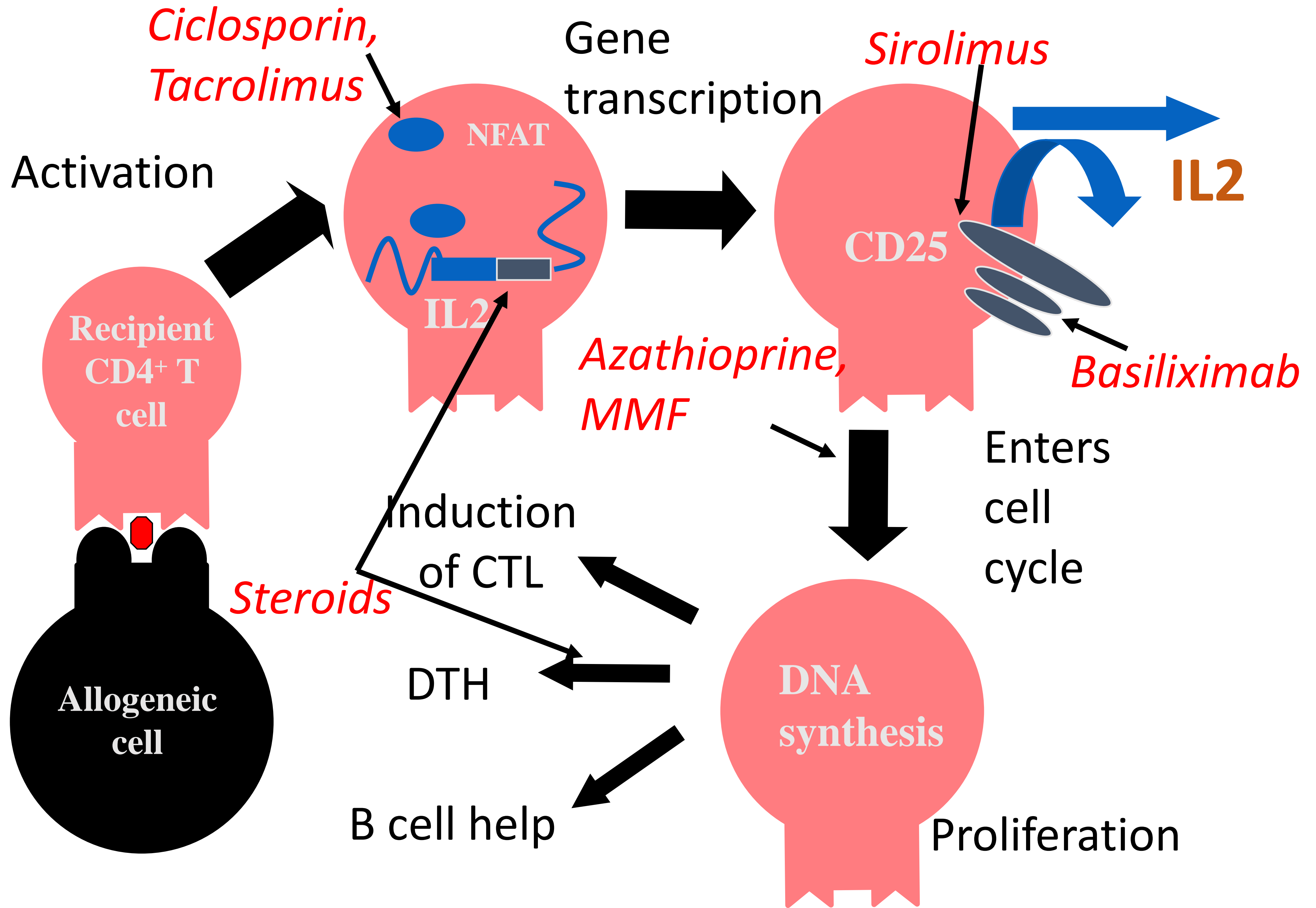
Outcome of host-pathogen encounter



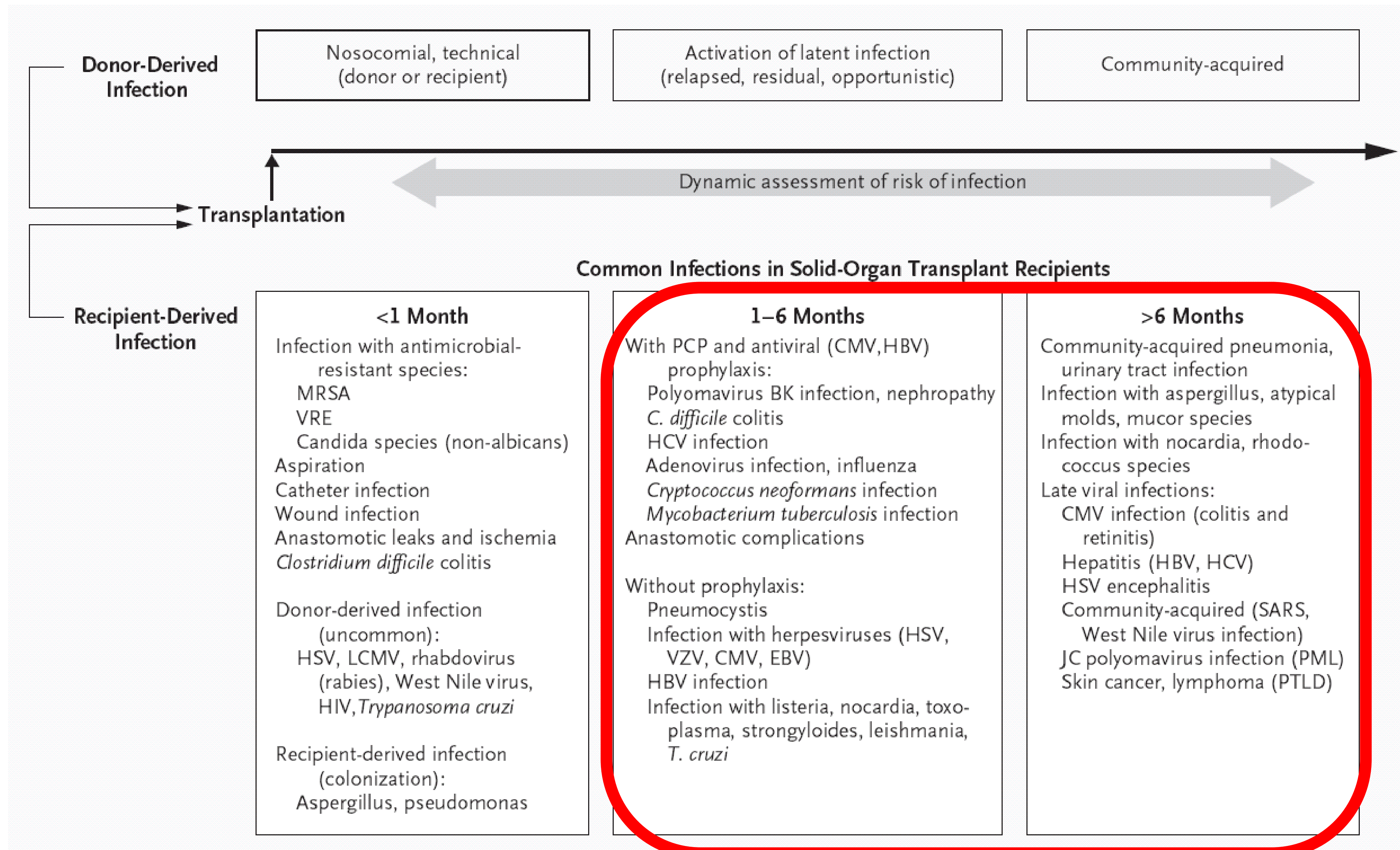
Outcome of host-pathogen encounter




Gene
transcription
Activation
NFAT
IL2
IL2
CD25
Recipient
CD4+ T
cell
Enters
cell
cycle
Induction
of CTL
DTH
Allogeneic cell
DNA
synthesis
B cell help
Proliferation


Ciclosporin,
Tacrolimus
Gene
transcription
Sirolimus
NFAT
Activation
IL2
CD25
IL2
Recipient
CD4+ T
cell
Azathioprine,
MMF
Basiliximab
Enters
cell
cycle
Induction
of CTL
Steroids
DTH
Allogeneic
cell
DNA
synthesis
B cell help
Proliferation

Infection Timeline



Fishman J NEJM 2007

Diagnostic Difficulties

- Diverse pathogens – Geography important
- Decreased and delayed signs and symptoms
- Indolent course
- Delayed seroconversion
- Emphasis on Tissue diagnosis

Question 7

What would you do with the immunosuppression (MMF 750mg bd and Prednisolone 5mg od)?

1. Stop it all
2. Continue as before
3. Stop the MMF
4. Stope the MMF and increase the prednisolone (e.g. 20mg od)

Calcineurin Inhibitor

Tacrolimus – Adoport, Prograf, Gengraf, Advagraf

Ciclosporin – Neoral, Sandimmune

TDM

Tac 5-9ng/ml

Cic <100ng/ml

Antiproliferative

Mycophenolate Mofetil - Myfortic

Azathioprine - Imuran

WITHOLD

Corticosteroids

Prednisolone

INCREASE

Can be given nasogastrically or intravenously

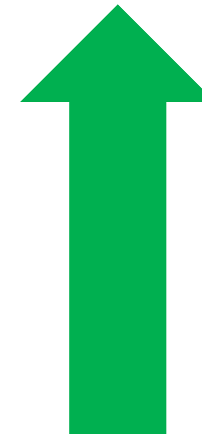
Question 8

Which of the following will not affect Tacrolimus levels?

1. Rifampicin
2. Trimethoprim
3. Ritonavir
4. Itraconazole
5. Clarithryomycin

CNI Interactions

- Tacrolimus
  - Impaired glucose tolerance
  - Tremor
  - Hypertension
  - Hyperkalaemia
- Ciclosporin
  - Hirsutism
  - Gingival hyperplasia
  - Tremor
  - Hypertension
  - Hyperkalaemia



Inducers	Inhibitors	
Aminoglutethimide	Amiodarone	Nifedipine
Amprenavir	Amprenavir[a]	Nilotinib
Aprepitant	Aprepitant[a]	Norfloxacin
Carbamazepine	Atazanavir[b]	Pomegranate
Dexamethasone	Chloramphenicol	Posaconazole[b]
Efavirenz	Cimetidine	Pazopanib
Ethosuximide	Ciprofloxacin	Prednisone
Etravirine	Clarithromycin[b]	Propoxyphene
Garlic supplements	Cyclosporine	Quinine
Glucocorticoids	Danazol	Ranolazine
Glutethimide	Delavirdine	Ritonavir[b]
Griseofulvin	Diltiazem[a]	Saquinavir[a]
Modafinil	Darunavir/ritonavir[b]	Synercid
Nafcillin	Dronedarone[a]	Telithromycin[b]
Nevirapine	Erythromycin[a]	Tipranavir/ritonavir[b]
Oxcarbazepine	Ethinyl estradiol	Verapamil[a]
Phenobarbital	Everolimus	Voriconazole[b]
Phenytoin	Fluconazole[a]	Zafirlukast
Primidone	Fluoxetine	
Rifabutin	Fluvoxamine	
Rifampin	Fosamprenavir[a]	
Rifapentine	Grapefruit[a]	
Ritonavir	Indinavir[b]	
St. John's wort	Imatinib	
	Isoniazid	
	Itraconazole[b]	
	Ketoconazole[b]	
	Lapatinib	
	Methylprednisolone	
	Mifepristone	
	Nefazodone[b]	
	Nelfinavir[b]	
	Nicardipine	

P450 CYP3A

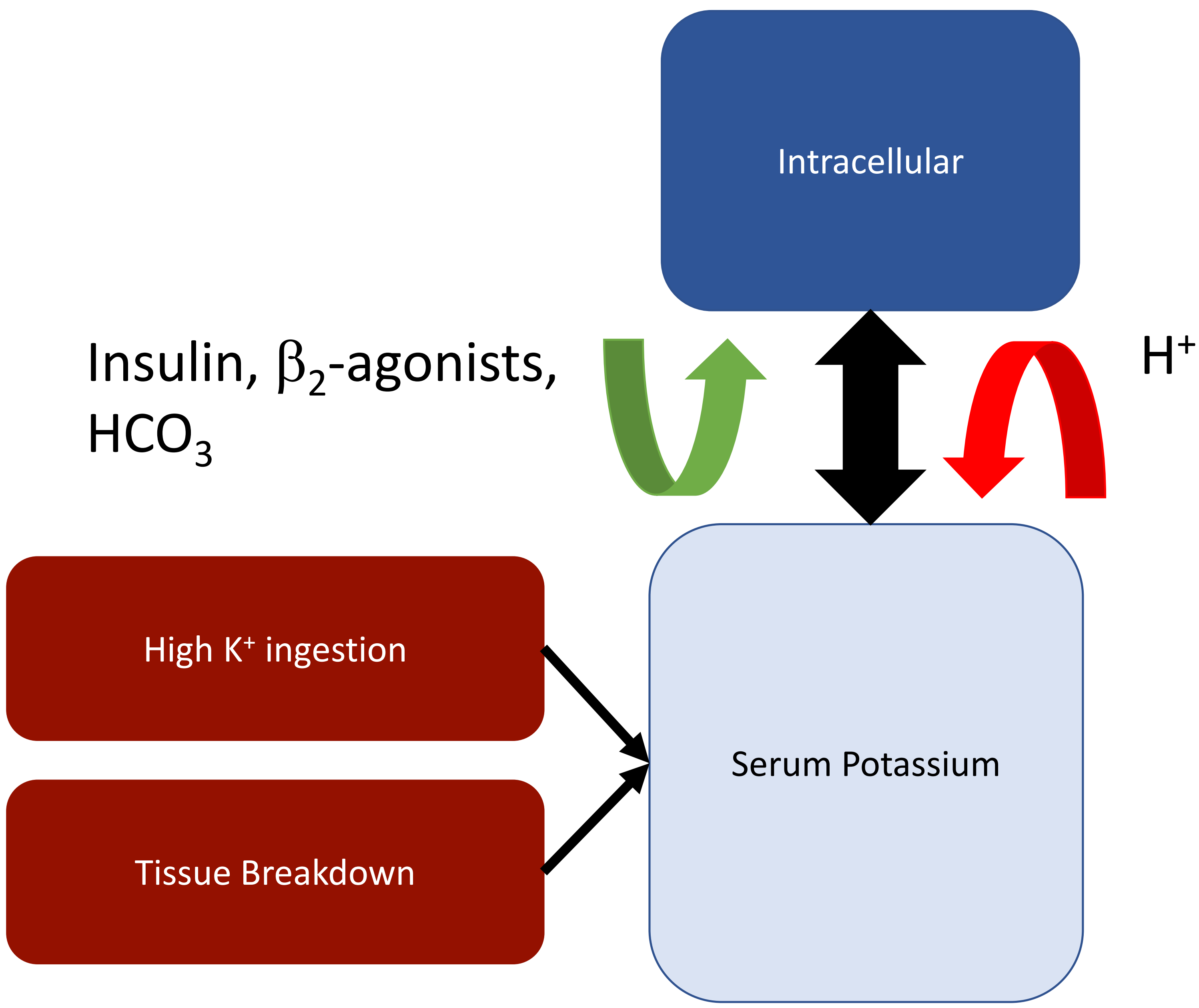
GJ

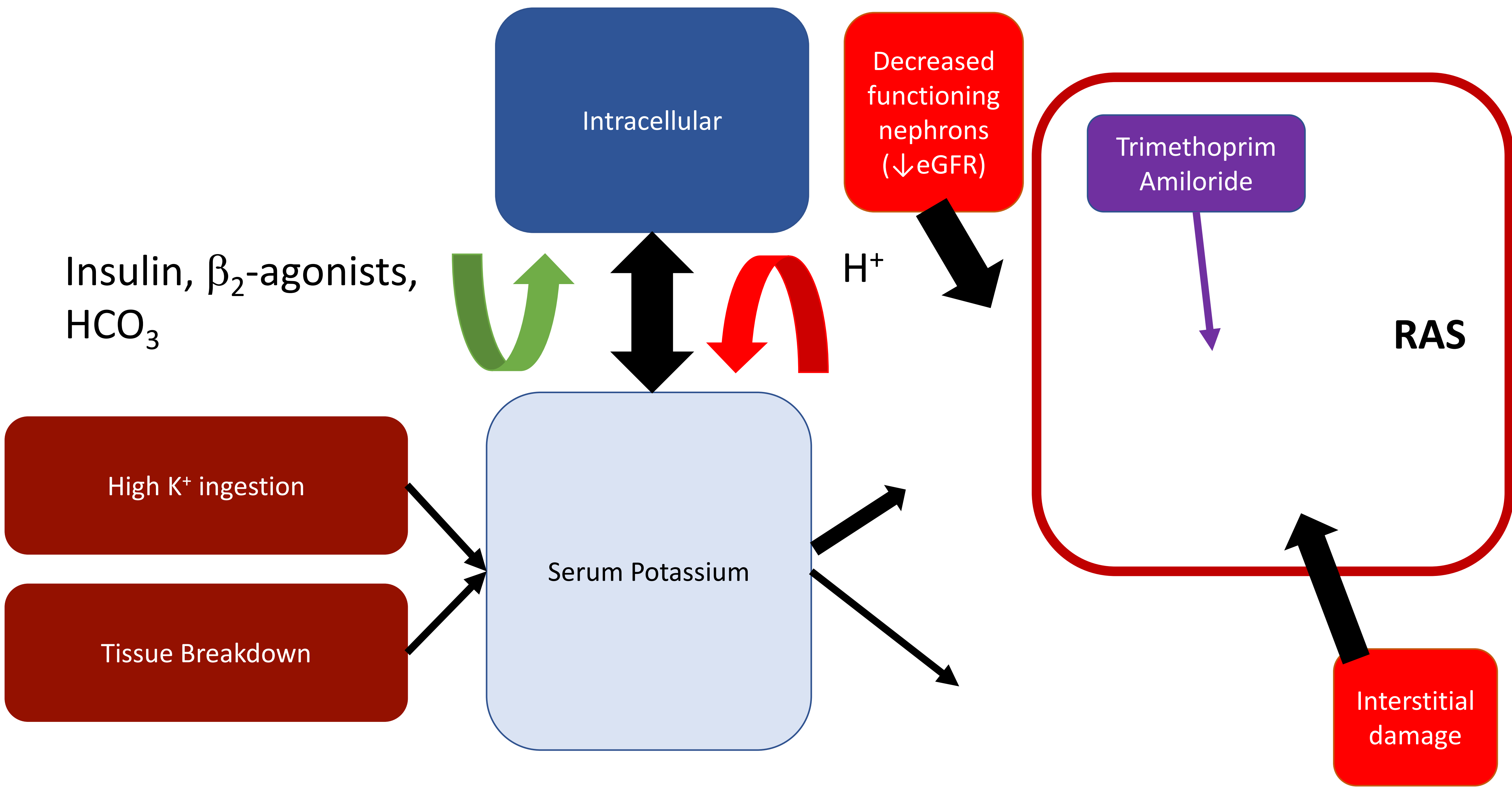
- 17.11.17 Creatinine 445, Na^+ 132, **K^+ 6.7**

Question 9

What is the most important contributor to his hyperkalaemia?

1. Medications
2. Uraemic metabolic acidosis
3. Dietary input
4. Low activity of the Renin Angiotensin System


Intracellular
Insulin, β_2-agonists, HCO_3
H^+
High K^+ ingestion
Tissue Breakdown
Serum Potassium


Intracellular
Decreased functioning nephrons (↓eGFR)
Trimethoprim
Amiloride
Insulin, β_2-agonists, HCO_3
H^+
RAS
High K^+ ingestion
Tissue Breakdown
Serum Potassium
Interstitial damage

Question 10

His creatinine was resolutely increased three weeks into therapy. What was the best course of action?

1. Ultrasound of kidney?
2. Transplant renal biopsy?
3. Wait another fortnight?
4. Administer treatment for rejection?

Question 11

How long would you administer PCP prophylaxis (Cotrimoxazole 480 mg od)?

1. Not necessary
2. 6 weeks
3. 6 Months
4. Indefinitely

THE END

Thank you