ACUTE RENAL FAILURE

John Feehally
ACUTE RENAL FAILURE

ACUTE KIDNEY INJURY
ACUTE KIDNEY INJURY

Outcomes

Causes

Diagnosis

Prevention & Management
MORTALITY IN ACUTE KIDNEY INJURY

[Graph showing mortality trends over the years from 1951 to 1990, with bars representing annual deaths and a cumulative trend line.]
AGE & OUTCOME IN ACUTE KIDNEY INJURY

[Diagram showing the relationship between age and survival percentage.]

The chart illustrates the survival percentage across different age groups in acute kidney injury.
Overall mortality remains 75%

Scoring systems [e.g. APACHE-II, POSSUM]

Age

Pre-existing vascular disease

Disease – specific data are needed
Effect of changes in serum creatinine on mortality after cardiac surgery

FALLING MORTALITY IN ACUTE RENAL FAILURE

Nationwide In-Patient Sample – USA – 1988-2002
- Increasing incidence of reported ARF
- Increasing co-morbidity

Waikar SS et al. JASN 2006; 17: 1143
ACUTE KIDNEY INJURY

HOW COMMON IS IT?

Problem of definitions

ESTIMATES

ADULTS ~200 – 500 pmp per year

CHILDREN ~7.5 pmp per year
The RIFLE criteria for ARF

GFR criteria

- Risk: Increased SCr × 1.5 or GFR decrease ≥25%
- Injury: Increased SCr × 2 or GFR decrease ≥50%
- Failure: Increased SCr × 3 or GFR decrease ≥75% or SCr ≥4 mg/dl or Acute rise ≥0.5 mg/dl

Urine output criteria

- Risk: UO < 0.5 ml/kg/h × 6 hr
- Injury: UO < 0.5 ml/kg/h × 12 hr
- Failure: UO < 0.3 ml/kg/h × 24 hr or Anuria × 12 hrs

Oliguria

High sensitivity

Loss

- Persistent ARF = complete loss of kidney function > 4 weeks

End-stage renal disease

- End-stage renal disease ( >3 months)

High specificity

ATN typically recovers in 3 days to 6 weeks
Progression to end-stage renal disease following acute renal failure

(Courtesy of P. Eggers, presented at the 2004 American Society of Nephrology Congress.)
RISK FACTORS FOR ACUTE KIDNEY INJURY

Emergency & planned admissions

- Older
- Comorbidity
  - Vascular disease
  - Pre-existing CKD
- Medication
- Younger
RISK FACTORS FOR ACUTE KIDNEY INJURY

Emergency & planned admissions

Older

Comorbidity
- Vascular disease
- Pre-existing CKD

Medication
- ACE inhibitors/ ARB
- NSAIDs
- Aminoglycosides

Younger
PREVENTION OF ACUTE KIDNEY INJURY

Role of the nephrologist

Risk awareness

Outside hospital
Medical wards
Surgical wards
Critical care

Education
ACUTE KIDNEY INJURY

Outcomes

Causes

Diagnosis

Management
Most important causes of community-acquired ARF

- ATN: 45%
- Prerenal: 21%
- ACRF: 10%
- Obstructive: 1.6%
- AIN: 1.5%
- Vascular: 1.5%
- Vasculitis: 1.5%
- Primary GN: 1.6%
- Secondary GN: 2.8%
- Cortex necrosis: 0.5%
- Other: 2%
- Unknown: 1%

Causes of ARF in hospital setting

- Acute tubular necrosis
- Acute interstitial nephritis
- Obstruction
- Acute-onset chronic renal failure
- Prerenal
- Vascular
- RPGN
ACUTE KIDNEY INJURY

INADEQUATE RENAL PERFUSION

ACUTE TUBULAR NECROSIS
ACUTE KIDNEY INJURY

INADEQUATE RENAL PERFUSION

TRUE HYPOVOLAEMIA

REDUCED ‘EFFECTIVE’ ECF VOLUME

ACUTE TUBULAR NECROSIS
ACUTE KIDNEY INJURY

INADEQUATE RENAL PERFUSION

TRUE HYPOVOLAEMIA

REDUCED ‘EFFECTIVE’ ECF VOLUME
- Cardiac failure
- Systemic vasodilatation
  - Sepsis
  - Cirrhosis
  - Anaphylaxis
- Impaired glomerular autoregulation

ACUTE TUBULAR NECROSIS
ACUTE KIDNEY INJURY

INADEQUATE RENAL PERFUSION

Preglomerular (afferent) constriction
- Sepsis
- Hypercalcaemia
- Hepatorenal syndrome
- Drugs
  - NSAIDs
  - CNIs
  - Amphotericin
  - Adrenaline

Postglomerular (efferent) dilatation
- ACE inhibitors
- ARBs

TRUE HYPOVOLAEMIA

REDUCED ‘EFFECTIVE’ ECF VOLUME

Cardiac failure
Systemic vasodilatation
- Sepsis
- Cirrhosis
- Anaphylaxis

Impaired glomerular autoregulation
ACUTE KIDNEY INJURY

INADEQUATE RENAL PERFUSION

TRUE HYPOVOLAEMIA

REDUCED ‘EFFECTIVE’ ECF VOLUME

ACUTE TUBULAR NECROSIS
ACUTE KIDNEY INJURY

INADEQUATE RENAL PERFUSION

SEPSIS

ACUTE TUBULAR NECROSIS
ACUTE KIDNEY INJURY

INADEQUATE RENAL PERFUSION

SEPSIS

NEPHROTOXINS

ACUTE TUBULAR NECROSIS
Intrarenal vasoconstriction

Flattened tubular epithelium

Luminal debris

ATN
ACUTE TUBULAR NECROSIS

ATN is reversible

ATN describes the histology [which is variable]

It is not an ideal term – but widely used
ACUTE RENAL FAILURE

‘ACUTE RENAL SUCCESS’?

Tubular dysfunction

Isosmolar urine

Thurau 1976
ACUTE RENAL FAILURE

‘ACUTE RENAL SUCCESS’?

Tubular dysfunction → Isosmolar urine

Vasoconstriction → Tubuloglomerular feedback

RPF ↓ GFR ↓

Thurau 1976
ACUTE KIDNEY INJURY

INADEQUATE RENAL PERFUSION + SEPSIS

NEPHROTOXINS
ACUTE KIDNEY INJURY

INADEQUATE RENAL PERFUSION

SEPSIS

NEPHROTOXINS

ENDOGENOUS

Myoglobin
Bilirubin
Urate
MYOGLOBINURIA

TRAUMATIC
- Crush Injury
- Extreme exertion
  - Exercise
  - Fits
  - Tetanus
- Ischaemia
- Burns

NON-TRAUMATIC
- Influenza
- Myopathies
  - McArdles
  - alcoholic
  - Polymyositis
- Prolonged coma
  - Alcohol
  - Narcotics
ACUTE KIDNEY INJURY

INADEQUATE RENAL PERFUSION + SEPSIS

NEPHROTOXINS

ENDOGENOUS
Myoglobin
Bilirubin
Urate
ACUTE KIDNEY INJURY

INADEQUATE RENAL PERFUSION

+ SEPSIS

NEPHROTOXINS

EXOGENOUS
- Medicines
- Contrast
- Poisons
- Endotoxin

ENDOGENOUS
- Myoglobin
- Bilirubin
- Urate
ACUTE KIDNEY INJURY

Inadequate Renal Perfusion

Sepsis

Nephrotoxins

Exogenous

Medicines

Contrast

Poisons

Endotoxin

Endogenous

Myoglobin

Bilirubin

Urate

Aminoglycosides

NSAIDs

ACEi & ARB
ACUTE KIDNEY INJURY

Not all AKI is ATN

- PRE-RENAL ?
- RENAL ?
- POST-RENAL ?
ACUTE KIDNEY INJURY

PRE-RENAL ?

RENAL ?

POST-RENAL ?
CAUSES OF ACUTE KIDNEY INJURY

PRE-RENAL 30%

RENAL
- ATN 55%
- Other parenchymal renal disease 5%
  - GN
  - Acute interstitial nephritis
  - Thrombotic microangiopathy
  - Myeloma kidney

POST-RENAL 10%
CAUSES OF ACUTE KIDNEY INJURY

PRE-RENAL  30%

RENAL

ATN 55%

Other parenchymal renal disease  5%
GN
Acute interstitial nephritis
Thrombotic microangiopathy
Myeloma kidney

POST-RENAL  10%
ACUTE KIDNEY INJURY

Outcomes

Causes

Diagnosis

Management
Clinical Assessment of Acute Kidney Injury

<table>
<thead>
<tr>
<th>History</th>
<th>drug history</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>evidence of CKD</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Physical examination</th>
<th>fluid and volume status</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Chart Review</th>
<th>drug charts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BP + fluid charts</td>
</tr>
<tr>
<td></td>
<td>anaesthetic records</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Urine examination</th>
<th>stick test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>microscopy</td>
</tr>
<tr>
<td></td>
<td>biochemistry</td>
</tr>
</tbody>
</table>
Look at the ‘numbers’

BUT

Look at the patient first
ACUTE KIDNEY INJURY

Pre-renal
- Are the kidneys underperfused?
- Are nephrotoxins implicated?

Renal
- Is ATN established?
- Is there a parenchymal renal disease other than ATN?

Post-renal
- Is there renal tract obstruction?
ATN does not cause ABSOLUTE ANURIA

Consider ……

- OBSTRUCTION
- VASCULAR OCCLUSION
ATN does not cause ABSOLUTE ANURIA

Check bladder catheter

Most obstructed patients are polyuric

Ultrasound shows PC dilatation in 95% misses ureteric stones so combine with KUB or CT

Clinical pelvic examination is mandatory

Relieve obstruction rapidly
<table>
<thead>
<tr>
<th>Observation</th>
<th>Clue to Diagnosis Of</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shrunken kidneys</td>
<td>Chronic intrinsic renal disease</td>
</tr>
<tr>
<td>Normal-sized kidneys</td>
<td></td>
</tr>
<tr>
<td>Echogenic</td>
<td>Acute glomerulonephritis, acute tubular necrosis</td>
</tr>
<tr>
<td>Normal echo pattern</td>
<td>Prerenal acute renal failure, acute renal artery occlusion</td>
</tr>
<tr>
<td>Enlarged kidneys</td>
<td>Malignant infiltration, renal vein thrombosis, amyloid, human immunodeficiency virus (HIV)—associated nephropathy</td>
</tr>
<tr>
<td>Pelvicalyceal dilatation*</td>
<td>Obstructive nephropathy</td>
</tr>
</tbody>
</table>
ATN does not cause ABSOLUTE ANURIA

Bilateral arterial occlusion → ANURIA

Incomplete occlusion + circulatory failure → ANURIA

Widespread atheromatous vascular disease

Anuria may not = infarcted kidney
# Urine Examination in AKI

<table>
<thead>
<tr>
<th>Condition</th>
<th>Proteinuria</th>
<th>Haematuria</th>
<th>Microscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-renal failure</td>
<td>-</td>
<td>-</td>
<td>Normal</td>
</tr>
<tr>
<td>Vascular occlusion</td>
<td>-</td>
<td>-</td>
<td>Normal</td>
</tr>
<tr>
<td>Acute GN</td>
<td>+++</td>
<td>+++</td>
<td>RBC casts, dysmorphic RBCs</td>
</tr>
<tr>
<td>Acute interstitial nephritis</td>
<td>++</td>
<td>+</td>
<td>Pyuria, WBC casts</td>
</tr>
<tr>
<td>HUS/TTP</td>
<td>-</td>
<td>+</td>
<td>Normal</td>
</tr>
<tr>
<td>ATN</td>
<td>-</td>
<td>-</td>
<td>Granular casts</td>
</tr>
</tbody>
</table>
Thrombocytopenia is not a feature of AKI *per se*

- Sepsis → ATN
- Lupus
- Myeloma
- Thrombotic microangiopathy
<table>
<thead>
<tr>
<th>Causes of acute renal failure and liver disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prerenal uremia</strong></td>
</tr>
<tr>
<td><strong>Hepatorenal syndrome</strong></td>
</tr>
<tr>
<td><strong>Acute tubular necrosis</strong></td>
</tr>
<tr>
<td><strong>Drugs</strong></td>
</tr>
<tr>
<td><strong>Infections</strong></td>
</tr>
<tr>
<td><strong>Other</strong></td>
</tr>
<tr>
<td>Causes of acute renal failure in patients with cancer</td>
</tr>
<tr>
<td>-----------------------------------------------------</td>
</tr>
<tr>
<td><strong>Prerenal</strong></td>
</tr>
<tr>
<td>Nausea and vomiting, hypercalcemia, cardiomyopathy secondary to chemotherapy</td>
</tr>
<tr>
<td><strong>Vascular</strong></td>
</tr>
<tr>
<td>Thrombotic microangiopathy (adenocarcinoma of stomach, pancreas, prostate; radiation nephropathy), renal vein thrombosis secondary to hypercoagulability, disseminated intravascular coagulation (acute promyelocytic leukemia)</td>
</tr>
<tr>
<td><strong>Glomerular</strong></td>
</tr>
<tr>
<td>Rapidly progressive glomerulonephritis</td>
</tr>
<tr>
<td><strong>Acute tubular necrosis</strong></td>
</tr>
<tr>
<td>Sepsis and antibiotic nephrotoxicity, hypercalcemia</td>
</tr>
<tr>
<td><strong>Malignant infiltration</strong></td>
</tr>
<tr>
<td>Lymphoma, acute lymphoblastic leukemia</td>
</tr>
<tr>
<td><strong>Intraluminal obstruction</strong></td>
</tr>
<tr>
<td>Tumor lysis syndrome, cast nephropathy</td>
</tr>
<tr>
<td><strong>Postrenal obstruction</strong></td>
</tr>
<tr>
<td>Transitional cell carcinoma of the ureters/bladder, extrinsic ureteral compression (tumor, nodes, retroperitoneal fibrosis)</td>
</tr>
<tr>
<td><strong>Chemotherapeutic agents</strong></td>
</tr>
<tr>
<td><strong>Tubular toxicity</strong></td>
</tr>
<tr>
<td>Cisplatin, ifosfamide, plicamycin (mithramycin); 5-fluorouracil, thio guanine (6-thioguanine), cytarabine</td>
</tr>
<tr>
<td><strong>Thrombotic microangiopathy</strong></td>
</tr>
<tr>
<td>Mitomycin C, bleomycin, cisplatin, calcineurin inhibitors</td>
</tr>
<tr>
<td><strong>Other mechanisms</strong></td>
</tr>
<tr>
<td>Capillary leak syndrome (IL-2 therapy), acute interstitial nephritis (interferon-α), intraluminal obstruction (methotrexate)</td>
</tr>
<tr>
<td>Causes of acute renal failure in patients with HIV infection</td>
</tr>
<tr>
<td>-------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Prerenal</strong></td>
</tr>
<tr>
<td>Diarrhea, nausea and vomiting, cirrhosis and hepatorenal syndrome, sepsis</td>
</tr>
<tr>
<td><strong>Vascular</strong></td>
</tr>
<tr>
<td>Thrombotic microangiopathy</td>
</tr>
<tr>
<td><strong>Glomerular</strong></td>
</tr>
<tr>
<td>Immune complex glomerulonephritis (MPGN secondary to hepatitis C virus, postinfectious glomerulonephritis), HIVAN</td>
</tr>
<tr>
<td><strong>Acute tubular necrosis</strong></td>
</tr>
<tr>
<td>Sepsis, hypotension, nephrotoxins (aminoglycosides, amphotericin, acyclovir, cidofovir, tenofovir, pentamidine), rhabdomyolysis</td>
</tr>
<tr>
<td><strong>Acute interstitial nephritis</strong></td>
</tr>
<tr>
<td>Drug induced (cotrimoxazole, rifampicin, foscarnet, nevirapine), CMV infection, DILS</td>
</tr>
<tr>
<td><strong>Drug-induced intratubular obstruction</strong></td>
</tr>
<tr>
<td>Sulfadiazine, indinavir, foscarnet, acyclovir</td>
</tr>
<tr>
<td><strong>Postrenal obstruction</strong></td>
</tr>
<tr>
<td>Stones, tuberculosis, fungal ball, tumor</td>
</tr>
<tr>
<td><strong>Associated with IV drug use</strong></td>
</tr>
<tr>
<td>Sepsis, endocarditis, heroin-associated nephropathy (FSGS), rhabdomyolysis</td>
</tr>
</tbody>
</table>
ACUTE KIDNEY INJURY

Pre-renal

Are the kidneys underperfused?

Renal

Is ATN established?
ACUTE KIDNEY INJURY

Pre-renal

Are the kidneys underperfused?

Renal

Fluid challenge?

or

Fluid restrict?

Is ATN established?
SERUM UREA:CREATININE RATIO IN ACUTE KIDNEY INJURY

**HIGH**
- Pre-renal failure
- High urea production
  - Catabolic
  - G-i bleed
  - Corticosteroids

**LOW**
- Low urea production
- Malnutrition
- Severe liver disease
- High creatinine release
- Rhabdomyolysis
### Urine Chemistry in Acute Kidney Injury

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre-renal</th>
<th>ATN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine: plasma osmolality</td>
<td>&gt; 1.5</td>
<td>&lt; 1.1</td>
</tr>
<tr>
<td>Urine: plasma urea</td>
<td>&gt; 8</td>
<td>&lt; 3</td>
</tr>
<tr>
<td>Urine sodium - mmol/L</td>
<td>&lt; 10</td>
<td>&gt; 40</td>
</tr>
<tr>
<td>Fractional excretion sodium FENa+</td>
<td>&lt; 1%</td>
<td>&gt; 2%</td>
</tr>
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### URINE CHEMISTRY IN ACUTE KIDNEY INJURY

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<th>ATN</th>
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Helpful if parameters are ‘pre-renal’

Parameters of ‘ATN’ cannot be interpreted if –
- a) already had diuretic
- b) elderly
- c) pre-existing renal disease
The most promising candidates to be in a ‘panel’ for AKI prediction are:

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Name</th>
<th>Indicates</th>
</tr>
</thead>
<tbody>
<tr>
<td>KIM-1</td>
<td>Kidney Injury Molecule -1</td>
<td>Proximal ischaemic injury</td>
</tr>
<tr>
<td>NGAL</td>
<td>Neutrophil gelatinase-associated lipocalin</td>
<td>Ischaemic/nephrotoxic injury</td>
</tr>
<tr>
<td>IL-18</td>
<td>Interleukin-18</td>
<td>Ischaemic injury</td>
</tr>
<tr>
<td>CYC</td>
<td>Cystatin C</td>
<td>Reduced GFR</td>
</tr>
</tbody>
</table>
BIOMARKERS PREDICTING AKI

CARDIAC SURGERY

In first 6 hours after surgery ….

Rise of urine NGAL & urine Cystatin C predicts AKI

Kayner J et al. 2008 Kidney Int epub 23 July
BIOMARKERS PREDICTING AKI

EMERGENCY ROOM

Single measurement of urine NGAL predicted AKI

95% sensitivity - 99% specificity

Also predicted need for
Nephrology referral
Dialysis
Transfer to ICU

BIOMARKERS PREDICTING AKI

Promising, but need ....

Rapid point of care testing

Prospective testing of multiple parameters

Interventions which make a difference
MANAGEMENT OF OLIGURIA

Correct volume
Clinical assessment, CVP

Correct BP - inotropes

What is the correct BP for this patient?
MANAGEMENT OF OLIGURIA

Correct volume
Clinical assessment, CVP

Correct BP - inotropes
‘RENAL DOSE’ DOPAMINE

2 µg/kg/min

NORMAL KIDNEYS

Vasodilatation & diuresis

... but what does it do in sick oliguric patients?
DOPAMINE DOES NOT PREVENT AKI

RCT - dopamine 2µg/kg/min throughout ITU stay

Survival

- - - - Dopamine
- - - - Placebo

Log-rank p = 0.88

Time (h)

Lancet 2000;356:2139
DOPAMINE DOES NOT PREVENT AKI

RCT - dopamine 2µg/kg/min throughout ITU stay

...and no effect on development of AKI

Lancet 2000;356:2139
MANAGEMENT OF OLIGURIA

Correct volume
Clinical assessment, CVP

Correct BP - inotropes

dopamine not indicated
MANAGEMENT OF OLIGURIA

Correct volume
Clinical assessment, CVP

Correct BP - inotropes

dopamine not indicated

DIURETIC

Mannitol 20% 100ml [if jaundiced]

Furosemide 250-500mg [not with aminoglycosides]
LOOP DIURETICS IN AKI

n = 92

Pre-renal corrected
Post-renal excluded

All received mannitol for 3 days and low dose dopamine

DOUBLE BLIND RCT OF LOOP DIURETIC

Furosemide or Torasemide

Shilliday I et al. NDT 1997; 12: 2592
LOOP DIURETICS IN AKI

n = 92 - double blind RCT

Significant increase in urine volume over first 24 hrs

*but*……..

**No effect on**

Mortality

Need for dialysis

Renal recovery

Shilliday 1997 NDT;12:2592
PREVENTION OF ACUTE KIDNEY INJURY

Volume loading

Mannitol [if jaundiced]

There is no evidence that ‘renal dose’ dopamine or furosemide prevent AKI in high risk patients
MANAGEMENT OF AKI

Fluid balance

Potassium

Acidosis

Uraemia
MANAGEMENT OF AKI

Fluid balance

Potassium

Acidosis

Uraemia
FUROSEMIDE IN ACUTE KIDNEY INJURY

OLIGURIA – incipient AKI

No evidence furosemide prevents AKI

ESTABLISHED AKI

No evidence furosemide improves outcome or speeds recovery

It may produce a small rise in urine volume
NUTRITION IN AKI

AKI is a catabolic illness

Starvation worsens catabolism

Low protein diet aggravates negative nitrogen balance

Feed early and maximally

If this → fluid overload : DIALYSE
MANAGEMENT OF AKI

Fluid balance

Potassium

Acidosis

Uraemia
HYPERKALAEMIA

ECG changes may not correlate with serum K level

Hyperkalaemia aggravated by

- acidosis
- sepsis
- catabolism
- dead tissue
TREATMENT OF HYPERKALAEMIA

- Protect heart
  - no change in serum K
  - Calcium

- Shift K into cells
  - Insulin/glucose
  - Bicarbonate
  - Salbutamol

- Remove K from body
  - Calcium resonium
  - Dialysis
MANAGEMENT OF AKI

Fluid balance

Potassium

Acidosis

Uraemia
METABOLIC ACIDOSIS IN AKI

ANION GAP > 20

Na – Cl – HCO₃

URAEMIA
50-100 mmol/day

LACTIC ACIDOSIS

Circulatory failure
Liver failure
Poisoning
Diabetic ketoacidosis
......
It may be severe and resistant

... especially if there is dead tissue

Think of: compartments? ischaemic bowel?
BICARBONATE DEFICIT

Deficit [mmol] =

0.4 x lean body weight

x [desired – measured] serum bicarbonate
TREATMENT OF METABOLIC ACIDOSIS IN AKI

- **iv NaHCO$_3$**
- Haemodialysis
- Haemofiltration
TREATMENT OF METABOLIC ACIDOSIS IN AKI

When to treat?

pH < 7.2  ITU pH < 7.3

Why treat?

Acidosis causes inotrope resistance?

How to treat?

Sodium bicarbonate

Risks unproven

Prefer isotonic 1.4%

Problem of volume overload
TREATMENT OF METABOLIC ACIDOSIS

Possible risks of sodium bicarbonate therapy

Volume overload & hypertonicity

Intracellular acidosis

Respiratory acidosis

CNS acidosis

In practice these are less than expected...

.. and can mostly be avoided
MANAGEMENT OF ARF

Fluid balance

Potassium

Acidosis

Uraemia
URAEMIC BLEEDING DIATHESIS

Platelet aggregation and adhesion

von Willebrand factor is the main platelet ‘glue’
URAEMIC BLEEDING DIATHESIS

Defective platelet adhesion and aggregation

Inhibited by uraemic factors

von Willebrand factor is the main platelet ‘glue’
URAEMIC BLEEDING DIATHESIS

Treatment

Remove uraemic factors

DIALYSIS

Provide additional vWF

CRYOPRECIPITATE

DDAVP
RENAL REPLACEMENT THERAPY IN AKI

Peritoneal dialysis

Haemodialysis

Haemofiltration
CONTINUOUS RENAL REPLACEMENT THERAPY FOR AKI

Convenience ?

Technical simplicity ?

Cardiovascular tolerability ?

Biocompatibility ?

Clearance of toxins, mediators ?
RENAL REPLACEMENT THERAPY FOR AKI

Haemodialysis or Haemofiltration?

Intermittent or Continuous?

Dose?
RENAL REPLACEMENT THERAPY FOR AKI

Haemodialysis or Haemofiltration?

Intermittent or Continuous?

Dose?

OUTCOME MEASURES

Survival

Duration of oliguria

Recovery GFR
RENAL REPLACEMENT THERAPY IN ITU
Continuous or Intermittent?

RCT  n = 166

Intermittent Haemodialysis vs. Continuous Haemodiafiltration

There was no difference in –

Recovery of renal function

ITU stay

In-hospital mortality

Mehta R et al. KI 2001; 60: 1154
RENAL REPLACEMENT THERAPY IN ACUTE KIDNEY INJURY

What is the most effective dose?
HIGHER DOSE RRT BENEFICIAL IN ACUTE KIDNEY INJURY

RCT    n = 425

Post-dilutional CVVH

20 ml/hr/kg vs. 35 ml/hr/kg vs. 45ml/hr/kg

Survival significantly reduced [41% vs. 57%]
if only receive 20 ml/hr/kg

HIGHER DOSE RRT BENEFICIAL IN ACUTE KIDNEY INJURY

RCT - Intermittent HD

DAILY better than THREE TIMES WEEKLY

.... but three times weekly group probably underdialysed

Mean pre-dialysis urea 37 mmol/l

Schiffl H et al. NEJM 2002; 346: 305
HIGHER DOSE RRT NOT BENEFICIAL IN ACUTE KIDNEY INJURY

LESS INTENSIVE

3 / week Intermittent HD or SLED

OR

CVVH Mean 21.5 ml/kg/hr

MORE INTENSIVE

Mean 5.4 / week Intermittent HD or SLED

OR

CVVH Mean 36.2 ml/kg/hr

Palevsky P et al. NEJM 2008; 359: 7
HIGHER DOSE RRT NOT BENEFICIAL IN ACUTE KIDNEY INJURY

LESS INTENSIVE

3 / week
Intermittent HD
or
SLED

OR

CVVH
Mean 21.5 ml/kg/hr

MORE INTENSIVE

Mean 5.4 / week
Intermittent HD
or
SLED

OR

CVVH
Mean 36.2 ml/kg/hr

Patients changed modalities as clinically indicated

Palevsky P et al. NEJM 2008; 359: 7
HIGHER DOSE RRT NOT BENEFICIAL IN ACUTE KIDNEY INJURY

4340 screened 1124 randomised

LESS INTENSIVE

3 / week
Intermittent HD
or
SLED

OR

CVVHDF
Mean 21.5 ml/kg/hr

MORE INTENSIVE

Mean 5.4 / week
Intermittent HD
or
SLED

OR

CVVHDF
Mean 36.2 ml/kg/hr

Patients changed modalities as clinically indicated

Palevsky P et al. NEJM 2008; 359: 7
HIGHER DOSE RRT NOT BENEFICIAL IN ACUTE KIDNEY INJURY

Palevsky P et al. NEJM 2008; 359: 7
CHOICE OF RRT MODALITY IN AKI

On available evidence....

Use convenient technique

Providing cardiovascular stability

Use conventional clinical markers of adequacy