Acute Renal Failure in Neonatal Intensive Care Unit (NICU)

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Case Study

- 28 week Premature infant 950g
  - Stormy antenatal course – premature rupture of membranes & chorioamnionitis
  - Poor Apgars – needed ventilation
- Week 1 develops PDA
  - Treated successfully with Indomethacin
- Also develops Sepsis
  - Rx Ampicillin / Gentamicin
- Necrotizing enterocolitis - oliguria
  - Bowel perforation - theatre
- Shocked, anuria & oedematous – fluid boluses
- Unable to adequately establish feeding

Incidence of Acute Renal Failure(ARF) in NICU

- ARF in the newborn is a very common problem:
  - 3 – 8% NICU admission - Agras PI Renal Failure 2004
  - 6 – 24% of newborns - Andreoli S. Sem in Perinatal 2004
  - Frequently multifactorial in origin
- Acute Renal Failure in PICU
  - 4.5% - Bailey D Ped Critic Care 2007
- Mortality in babies with ARF
  - 25 – 50% - Moghal N Sem in Fet & Neon Meds 2006

NICU

467 consecutive admissions/ 1 year

Lunn AJF et al. Arch Dis Child Fetal Neonated 2006;91:F388-390

- ARF plasma creat >100umol/l @ 48hrs age
- Total 8.8% admissions
  - 37% <28wks
  - 8% 28-32wks
  - 4% 33-36wks
  - 2% Term infants
- Causes - multifactorial:
  - Sepsis 39%
  - Perinatal asphyxia 17%
  - Hypotension 10%
- Prophylactic Indomethacin - Vent <1000g
- Death in 24%

Embryology

- Nephrogenesis continues to 34 weeks gestation
- Ischaemic/ Hypoxic and toxic insults
  - Potentially interrupts nephrogenesis
  - ARF
  - Also long term complications

ARF
Traditional Classification

Haycock GB. Semin Neonatol 2003 Aug;8(4):325-34

- Failure of Renal Perfusion
  - Pre-renal
- Damage to Renal Parenchyma
  - Intrinsic renal
- Obstruction of Urinary tract
  - Post-renal "obstructive"

ARF according to urine output

- Oligo/ anuria
  - Newborns with pre-renal failure
  - Due to hypoxia/ ischaemic insults – ATN
  - Cortical necrosis

- Normal urine output
  - Nephrotoxic insults – aminoglycoside and contrast nephropathy

Pre-renal Failure

Decreased renal perfusion in intrinsically normal kidney

- Restoration of normal renal perfusion results in return to normal renal function
- Acute tubular necrosis(ATN) implies kidney has suffered intrinsic damage
- Evolution of pre-renal to renal failure is not sudden
  - number of compensatory mechanisms work together

Renal Hypoperfusion

- Afferent arteriole
  - relaxes its vascular tone & decrease vascular resistance
  - maintaining renal blood flow
- Increased catecholamine secretion
- Activation of renin angiotensin system
- Generates Prostaglandins(PG's)
  - Vasodilatory PG's including prostacyclin
  - Mediates vasodilation of renal microvasculature
  - Maintains renal perfusion

Aspirin or NSAID's

- Inhibit PG's and thus affects compensatory mechanism
  - →precipitated renal insufficiency during hypoperfusion
- Indomethacin for PDA's – risk of renal insufficiency
  - 56% reduction in urinary flow rate
  - 27% reduction in GFR
  - 66% reduction in free water

Aspirin or NSAID's

- Indomethacin vs Ibuprofen

  Thomas RL. Europ J of Ped 2005;164(3):135-140

- Selective Cox-2 inhibitors no better

- Increased risk if:
  - Premature - 40% alteration in renal function
  - Infant abn renal function prior
  - Mothers received indomethacin
  - Chorioamnionitis

Case Study

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- Also develops **Sepsis**
  - Rx Ampicillin / **Gentamicin**
- Necrotizing enterocolitis - oliguria
  - **Bowel perforation** - theatre
- **Shocked, anuria & oedematous**
  - fluid boluses
- Unable to adequately establish **feeding**

Acute Tubular Necrosis(ATN)

- Pre-renal failure evolves if severe enough
  - to cause vasoconstriction & ATN
- **Urine analysis:**
  - Unremarkable or
  - Low grade proteinuria & granular casts
  - Abn tubular function – not conserving Na and H2O
- **Serum Creatinine** rises 0.5-1.0mg/dL/day
- **Radiology**
  - Normal size kidneys with loss of corticomedullary differentiation
- **Radionuleotide renal scan**
  - Poor function & delayed accumulation in renal parenchyma with no excretion of isotope

Prognosis of ATN

- Good
- Unless insult severe enough
  - Vasculature injury + microthrombi formation
  - Subsequent cortical necrosis
- Length of recovery variable
  - Days to weeks
- Diuretic phase – prevent additional injury
- Long term follow-up – late complications
- Mortality & morbidity worse in ARF in neonates with multiorgan failure

Andreoli S Curr Opin Peds 2002

Nephrotoxic Acute Renal Failure

- Endogenous agents
  - haemoglobinuria, myoglobinuria
- Drugs
  - Aminoglycosides
  - NSAID's
  - Intravascular contrast
  - 'Ampho-terrible'

Aminoglycosides

- Non-oliguric acute renal failure
- Urinanalysis – minimal urinary abnormalities
- Toxicity related to
  - Dose & duration
  - Level of renal function prior to drug
- Aetiology – lysosomal dysfunction of prox tubule and is **reversible**
- After discontinuation of drug – creatinine may continue to increase for few days
  - Ongoing tubular injury due to high levels
  - Once daily dosing

Vascular Insults

- Renal Artery Thrombosis
- Renal Vein Thrombosis

Vascular Insults
Cortical necrosis

- Assoc with hypoxic/ischaemic insults
- Gross/microscopic haematuria, oliguria, hpt
- Raised Urea and Creatinine
- Thrombocytopaenia
- U/S
  - normal(early)
  - then atrophy & decrease in size
- Nuclear Renal Scan
  - decreased/no perfusion with delayed/no function
- Partial or no recovery - risk of CRF later

Medical management

- Fluid management
- Electrolyte status
- Acid-base balance
- Nutrition
- Renal Replacement Therapy

Medical management Diuretics - Mannitol

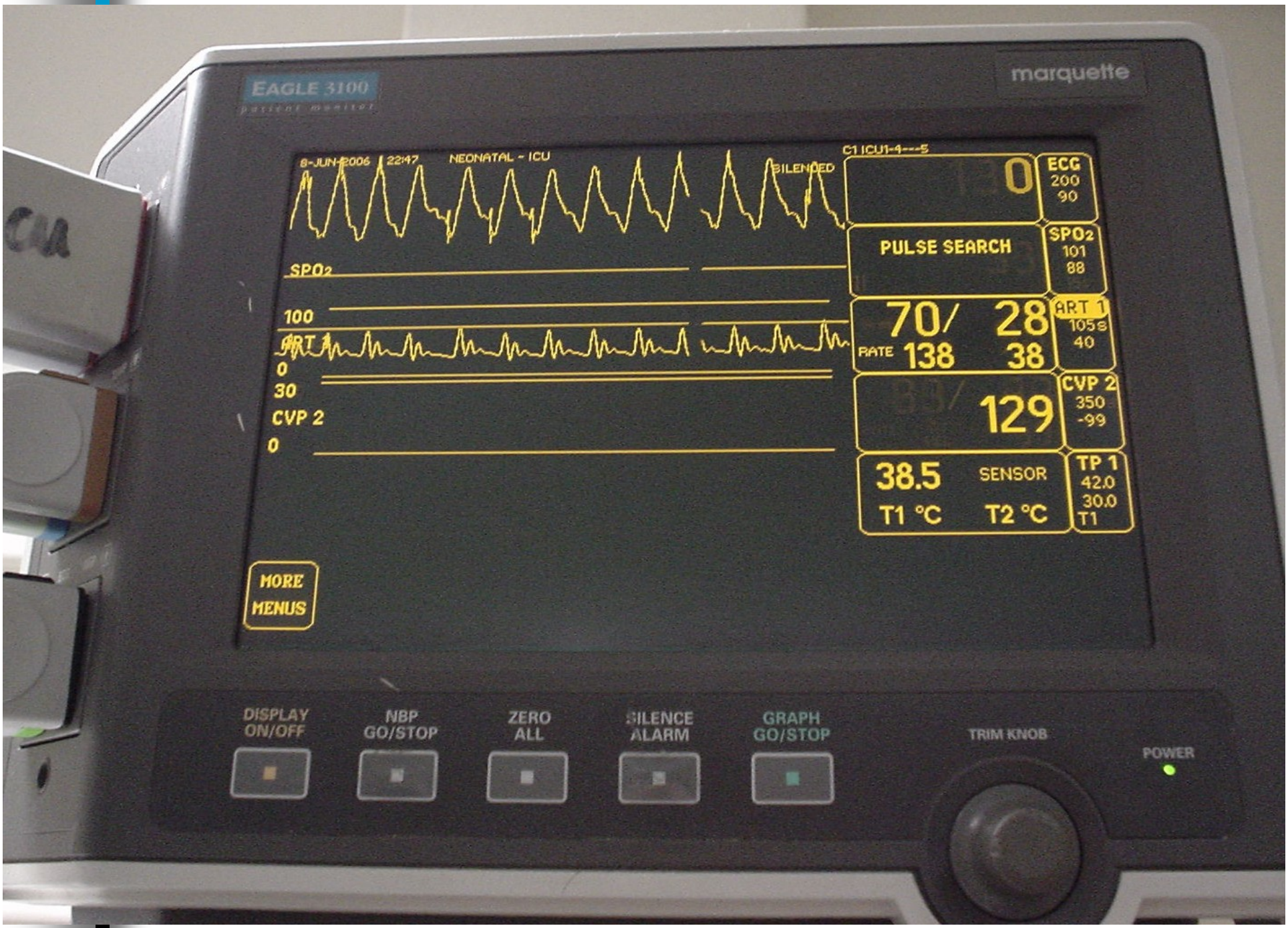
- Stimulates urine output
- Conversion of oliguric to non-oliguric ARF
  - does not alter course of ARF
- Mannitol 0.5 - 1g/kg may
  - Increase intra-tubular urine flow to limit tubular obstruction
  - Limit cell damage by prevention of swelling
  - Act as scavenger of free radicals
- Lack of response
  - Hyperosmolality and precipitates CCF

Medical management Diuretics - Frusemide

- Also increases urine flow rate to decrease intra-tubular obstruction
- Inhibits Na/K/ATPase
  - Impact on oxygen consumption in already damaged tubules with low O2 supply
- Problems: high doses in ARF assoc with ototoxicity
- Trial of therapy: 1-5 mg/kg/dose
  - Unresponsive to Rx - continued high doses unlikely to be beneficial
  - Do Respond - continuous infusion effective with less toxicity

Medical management Dopamine

- 'Renal Dose'
- Promote renal perfusion and improves urine output by promoting natriuresis
- But ...studies in adults does not
  - Decrease need for dialysis
  - Improve survival Denton MD Kidney Int 1996
- Not effective in paeds either ...but neonates ?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SILENCE ALARM
GRAPH GO/STOP
TRIM KNOB
POWER

Medical management
Hypokalaemia

Cochrane Database Syst Rev 2007 Jan 24;(1):CD005257

- Newborns with K>6.5mmol/l in absence of ARF
- **Cardiac toxicity** – tall peaked T's → v/tach & v/fib
- Combination of **insulin & glucose** preferred over cation resin
  - Borderline improvement of mortality
  - Reduction in incidence of IVH >grade 2
- **Albuterol** inhalation decreased K+ at 4 & 8hrs
- **Other Rx for ↑K+** - diuretics, xchange transfusion, PD and Calcium still needs RCT testing

Medical management

- Mild Hyponatraemia – very common in ARF
  - Fluid overload with dilutional hyponatraemia
  - Less commonly – hyponatraemic dehydration

  Management
  - >120meq/l – fluid restrict or dialysis
  - <120meq/l – correction to level of 125meq/l
- Hypocalcaemia – ionised Ca
- Hyperphosphataemia
- Acid base disorders

Medical management

- Marked catabolism
- Early Enteral feeding if possible
- Feeds compromised due to fluid balance issues
  - Earlier initiation of dialysis

"It's still hungry . . . and I've been stuffing worms into it all day."

Renal Replacement Therapy (CRRT)

- Peritoneal Dialysis(PD)
- Haemodialysis intermittently
- Haemofiltration/ Continuous Veno-veno haemofiltration(CVVH)
  - with or without dialysis circuit

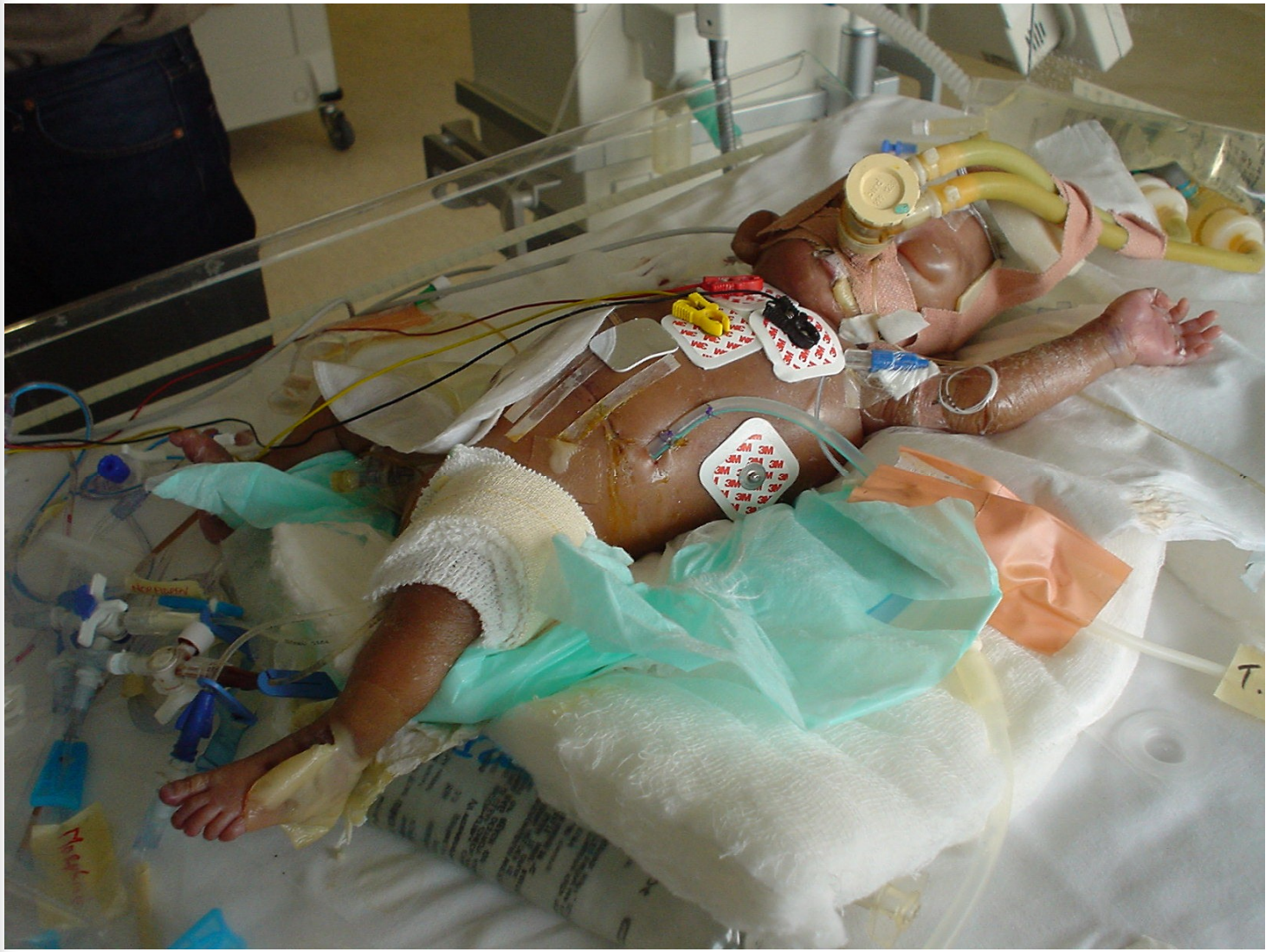
RRT
Peritoneal Dialysis

YES

- Easy to perform - practical & training
- Does not require heparinisation
- Difficult venous access
- Haemodynamically unstable babies

NO

- Slower correction of metabolic parameters
- Potential for peritonitis
- Frequent exchanges required in babies
- Recent abdominal surgery



RRT
Peritoneal Dialysis

- Italian study: Neonates requiring RRT
  - Due to oligoanuria / fluid overload
  - 11/12 patients PD as only form of RRT
  - UF = 5 – 20ml/hr with up to 200ml/24 hr
  - Creat clearance 2-10ml/min/1.73m2
    - Morelli S et al. Contrib Nephrol **2007;**156:428-33
- USA: New Catheters – Multipurpose drainage catheter (Cook)
  - Bedside placement
  - Effective dialysis with satisfactory complication free survival

Auron A, Warady B et al Am J Kid Dis **2007** May;49(5)650-5

RRT
PD and Ultrafiltration

- Turkey: Complex Congenital Cardiac patients
  - Neonates & Infants <1yr - 756 patients
  - All cases received peri-operative ultrafiltration
  - 186 patients(24.6% of total) required PD
  - Combination of modalities
    - Post-op negative fluid balance with improvement of outcome
      - » Alkan T et al. ASAIO J 2006 Nov;52(6):693-7


CAUTION

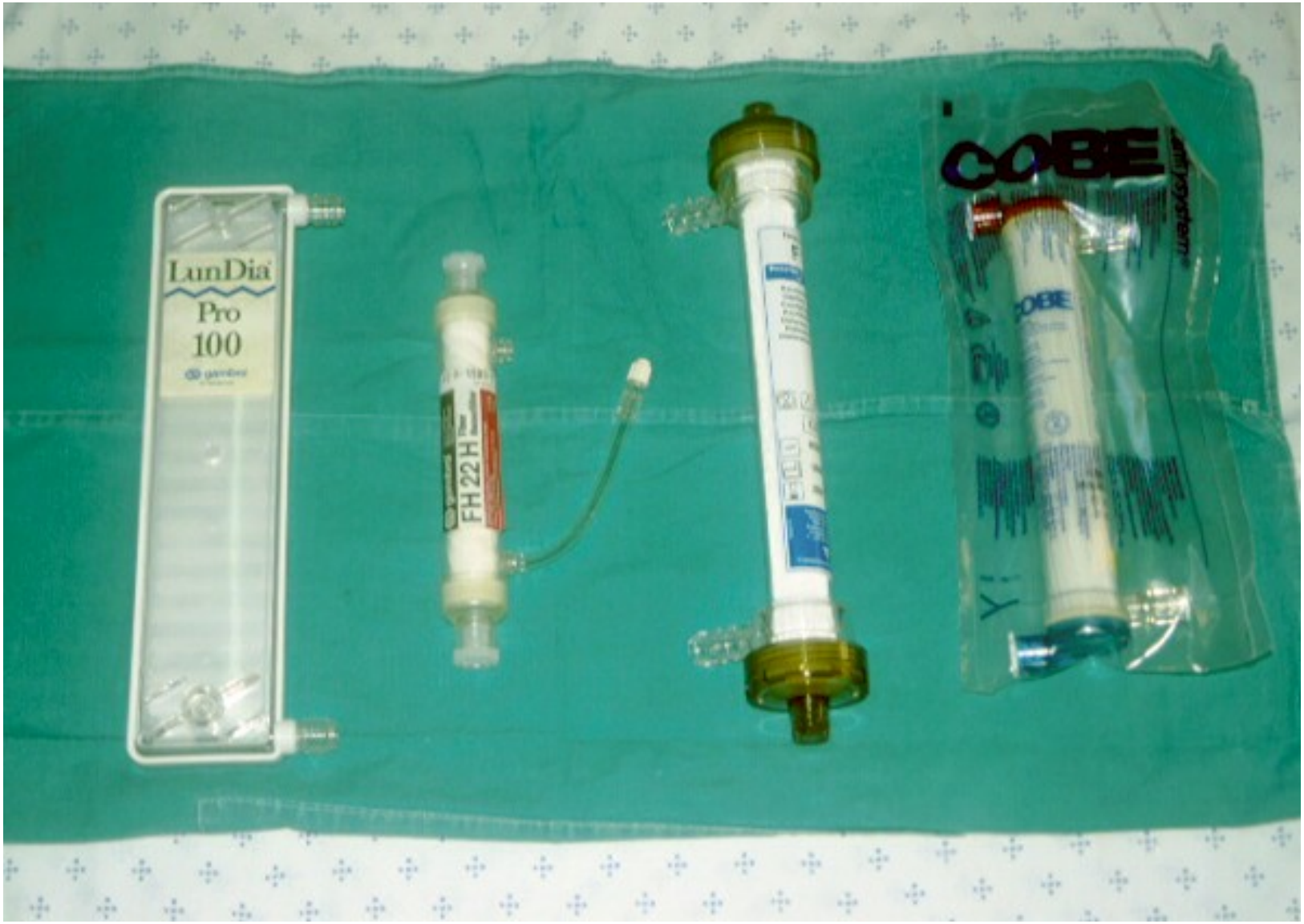
Haemodialysis for babies

- Technologically **'challenging'**
- Trained staff
- Equipment

  A machine for haemodialysing very small infants

  - Everdell NL et al. Ped Neph (2005)20:636-646
  - Everdell NL. Med Eng Phys 2007 May;29(4):516-24

  - Priming volumes as low as 6.8ml vs 15-40ml
  - Manual – now computer operated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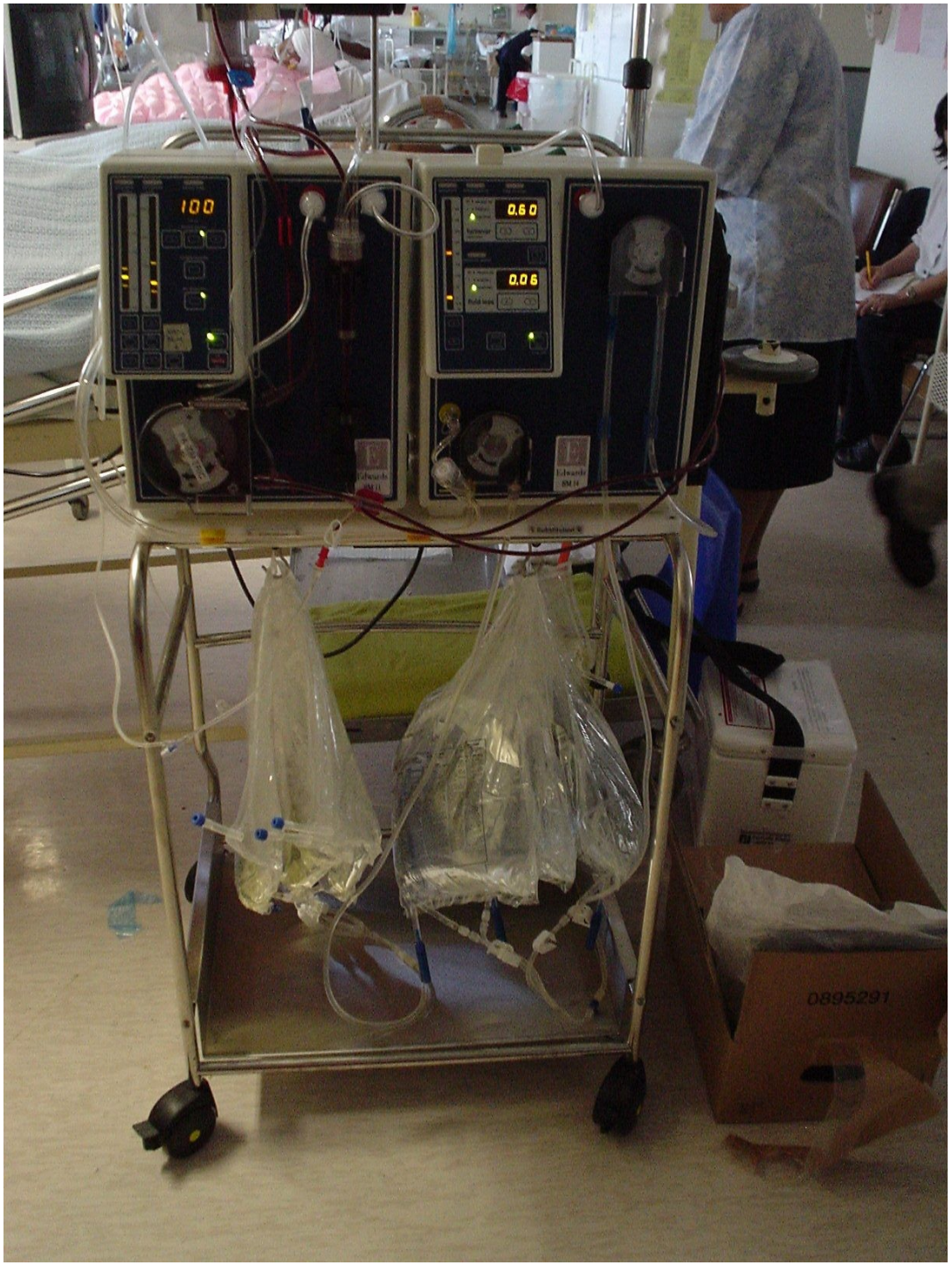
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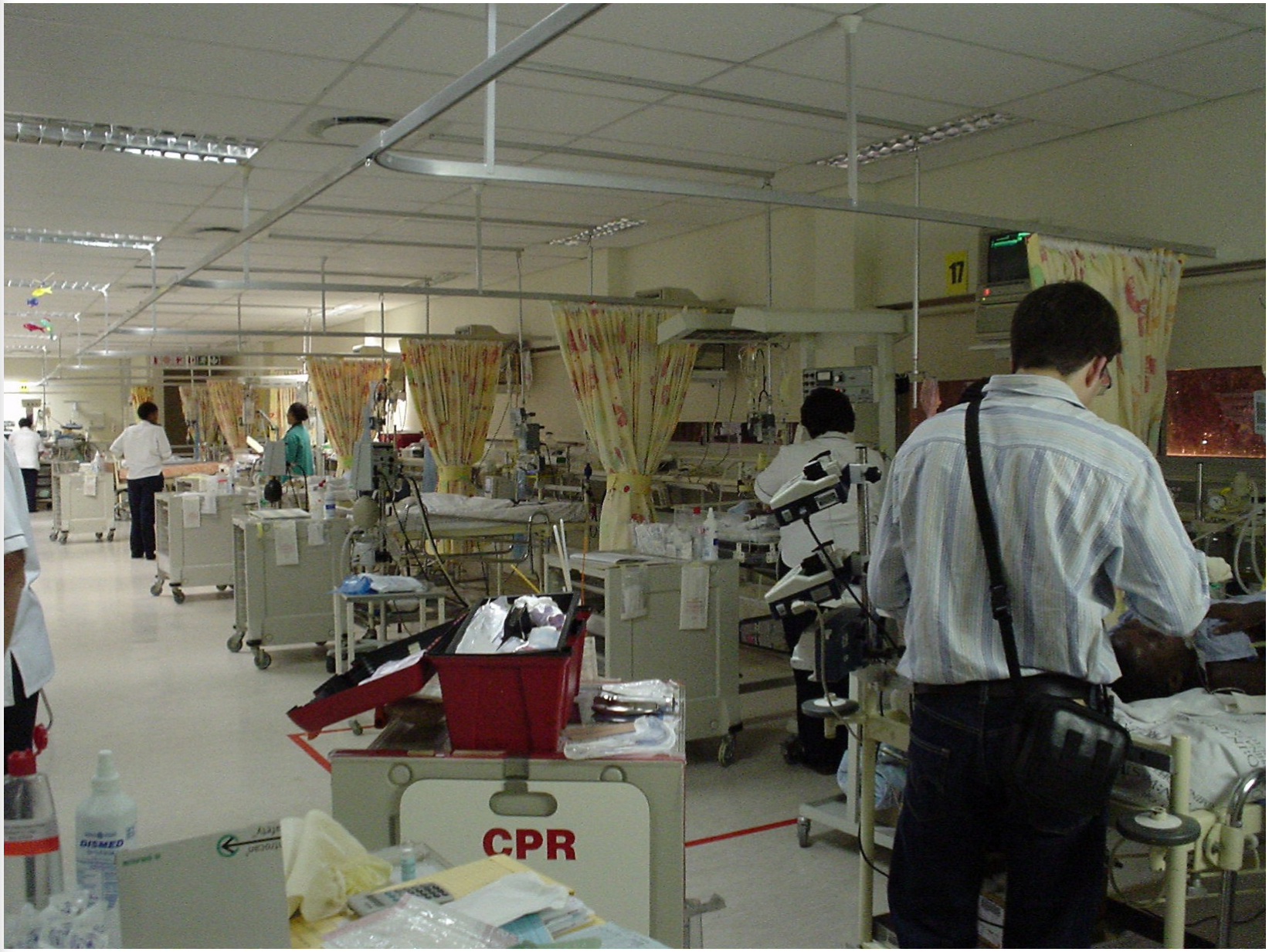
Long term follow-up after ARF

- ARF may result in long term renal dysfunction
- Low birth weight babies at risk

  Abitbol CL et al. Ped Nephrol 2003;18:887-893
- Signs of kidney injury
  - Microalbuminuria
  - Hyperfiltration (Schwartz GFR >150ml/min/1.73m2) or Decreased GFR
  - Haematuria
  - Hypertension
- Survival rate 56.8% (initial hospitalisation + those died subsequently)
  - High proportion of ARF deceased 3-5yrs after event

  Askenazi DJ, Goldstein SL et al Kidney Int (2006)69,184-189


CPR

Acute Renal Replacement Therapy

in Developing Countries

MI McCulloch, PJ Sinclair, P Gajjar, P Nourse, S Salie, S Singh, S Fisher, A Argent.

Departments of Paediatric Nephrology & PICU

Red Cross Children's Hospital (RXH)

Acute Renal Failure

- Increasing incidence in association with multi-organ failure in paediatric ICU's
- 1200 – 1400 admissions per year
  - Acute medical cases 600/yr
  - Cardiac cases 250/yr
  - Burns 50/yr
  - Head injuries 50/yr
  - Other Rest
- Mortality 10%
- Dialysis 3.5%

Causes of Acute Renal Failure

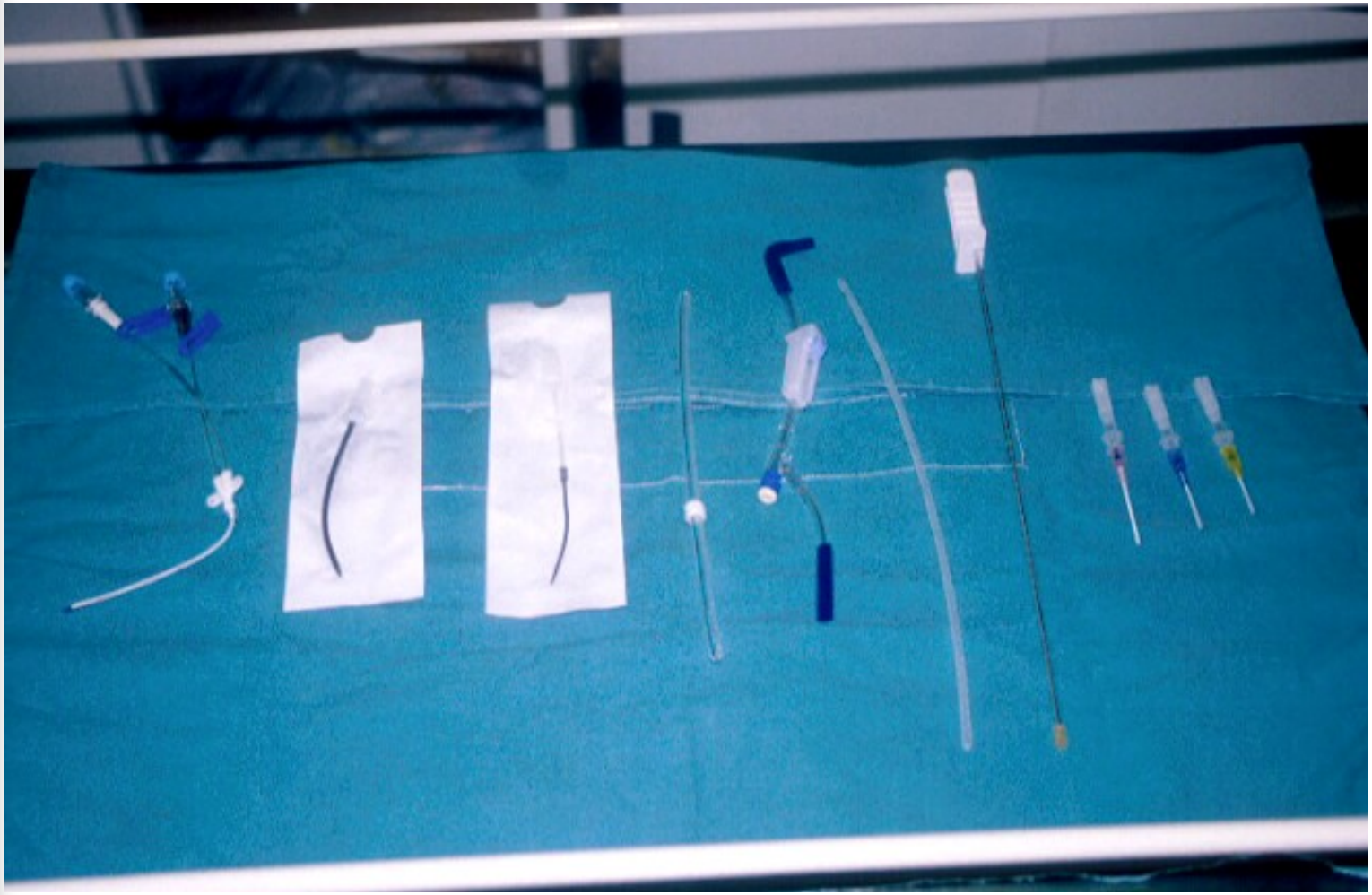
Sepsis	46(22%)
Post-cardiac surgery	36(17%)
Undiagnosed chronic renal disease	21(10%)
Gastroenteritis	19(9%)
Haemolytic uraemic syndrome	19(9%)
Necrotizing enterocolitis	15(7%)

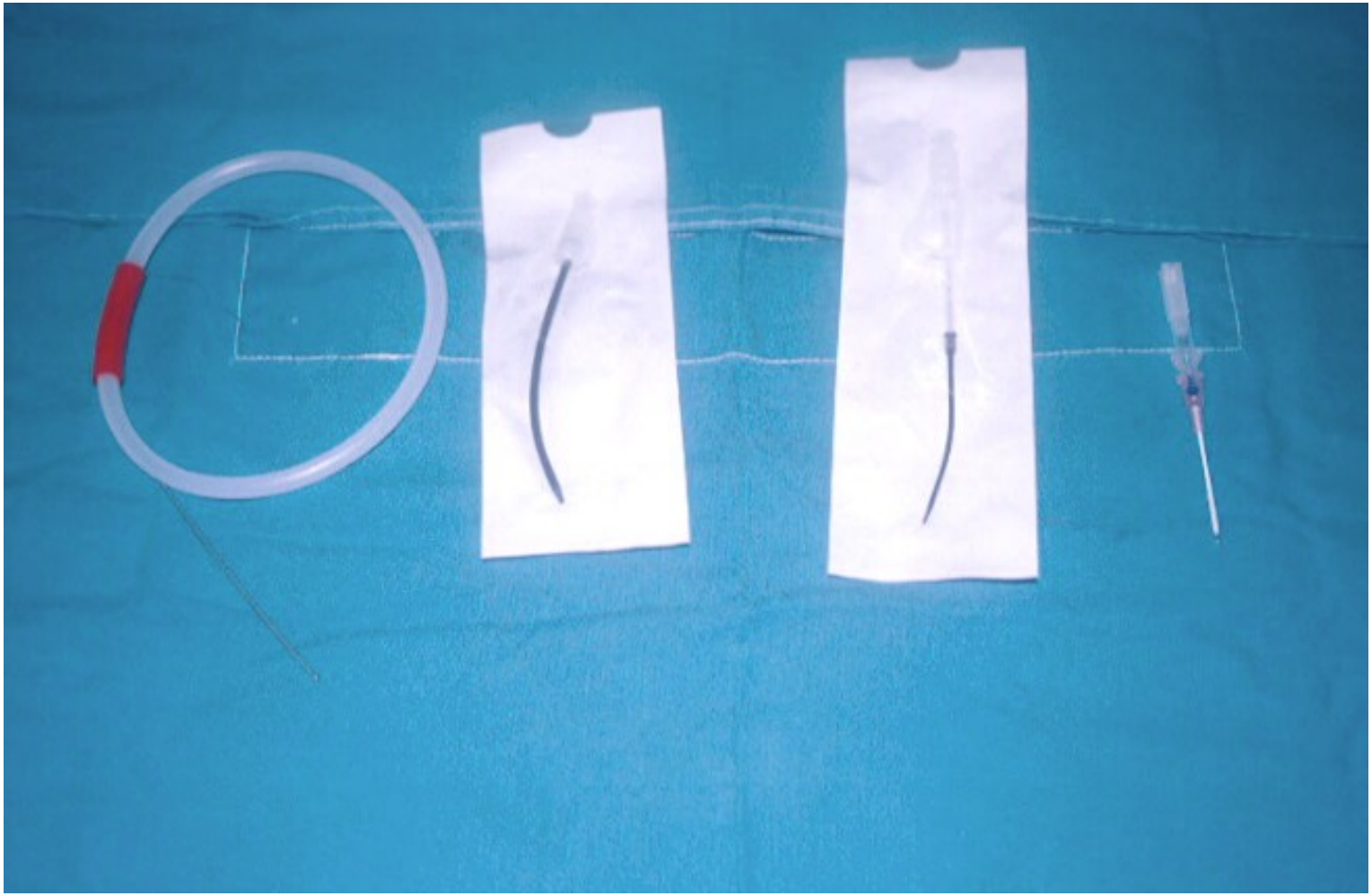
Causes of Acute Renal Failure

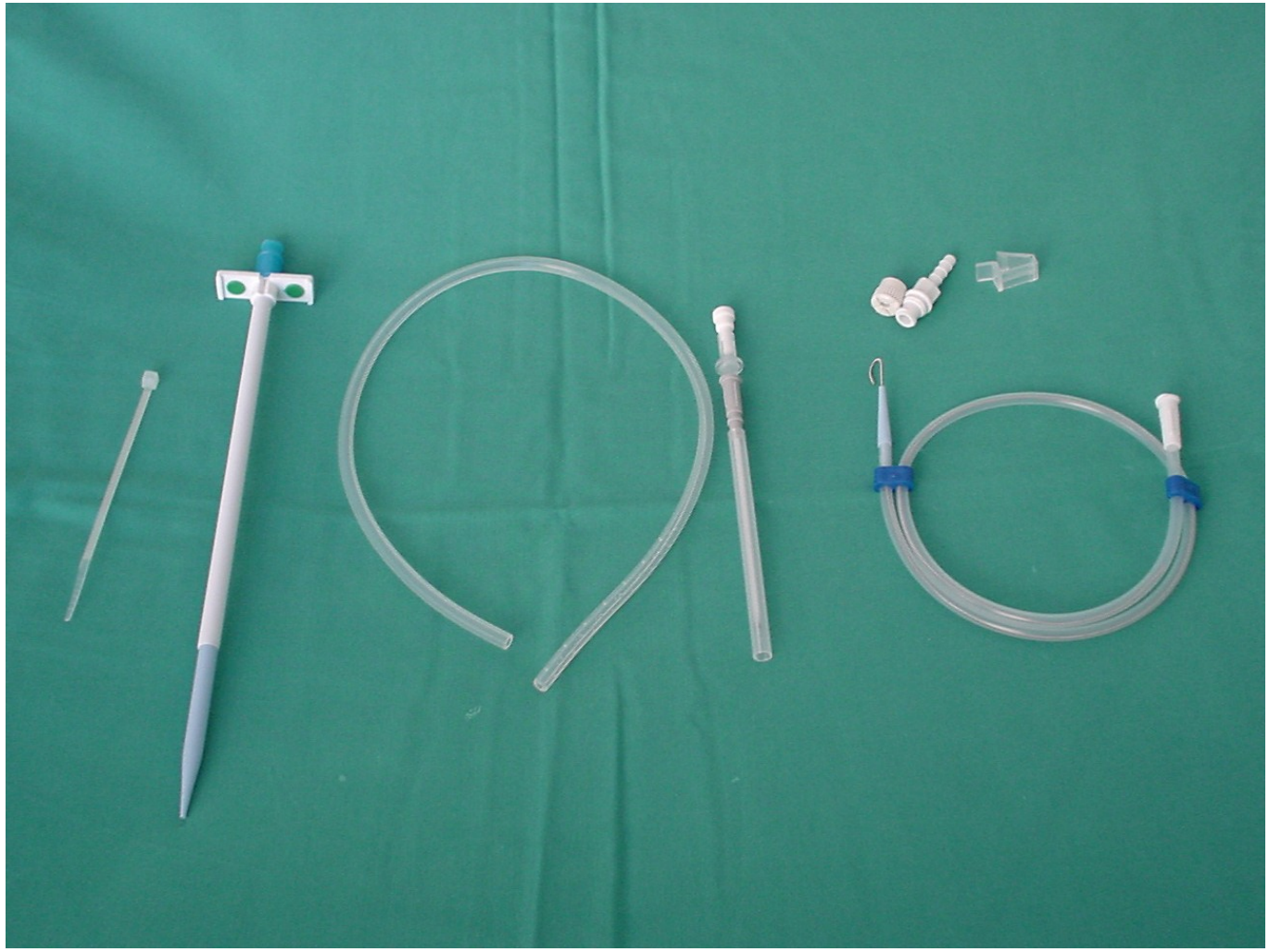
Leukaemia/ Lymphoma	14(6%)
Myocarditis	11(5%)
Rapidly progressive nephritis	10(5%)
Trauma/ Burns	8(4%)
Toxin ingestion	7(3%)
Kwashiorkor**	6(3%)

Equipment

Total catheters used	260
Cook - 5 Fr Neonatal - 8 Fr Paediatric - 11 Fr Adult	(62%) 53 106 4
Kimal "peel away" Percutaneous Tenckhoff	46 (18%)
Surgical inserted Tenckhoff	51 (20%)







Complications related to PD Jan 2000 – Dec 2001

- 68 patients received acute peritoneal dialysis
- 17 Catheter related problems(25%)
  - Blockage in 16 – all Cooke catheters
  - Bowel perforation in 1 case
- Infection seen especially if catheter left in longer than 5 days

Perit Dial Int 2001

Flynn et al (Brophy & Bunchman)

	RXH	Flynn (USA)
Time period	2 yrs	10 yrs
Nos of patients	68	63
Complication Rate	25%	25%
Commonest problem	Catheter blockage	Catheter malfunction
Survival	61%	51%

Acute Peritoneal Dialysis

January 1999 to January 2004

TOTAL NUMBER OF PATIENTS	**212**
Male: Female	102:110
Age at dialysis:	
< 3 months	**79(38%)**
3 months - 1yr	**45(21%)**
1 – 6 years	38(18%)
6 – 12 years	30(14%)
>12 years	20(9%)

Acute PD
Long term outcome

Survival following Acute PD	**130(61%)**
Chronic PD required following Acute PD	26(12%)
Total nos of patients requiring CVVHD (PD not possible)	20(9%)
Survival following CVVHD	11(55%)

Peritoneal Dialysis as a Form of CRRT for Infants in a Developing Country

McCulloch M, Argent A.
Red Cross Children's Hospital
University of Cape Town


CT-ICU
PATIENTS
NO BP
NO SATS
NO DRIPS
!! LEFT ARM !!!
APRONS

Red Cross Children's Hospital Experience

Aug 1998 - Feb 1999

- 70 Children <13 years old dialysed
- 25 of these patients were <5kg
- 15/25 Infants (60%) survived
- Age range from 2 - 138 days
- Male:Female 2:1

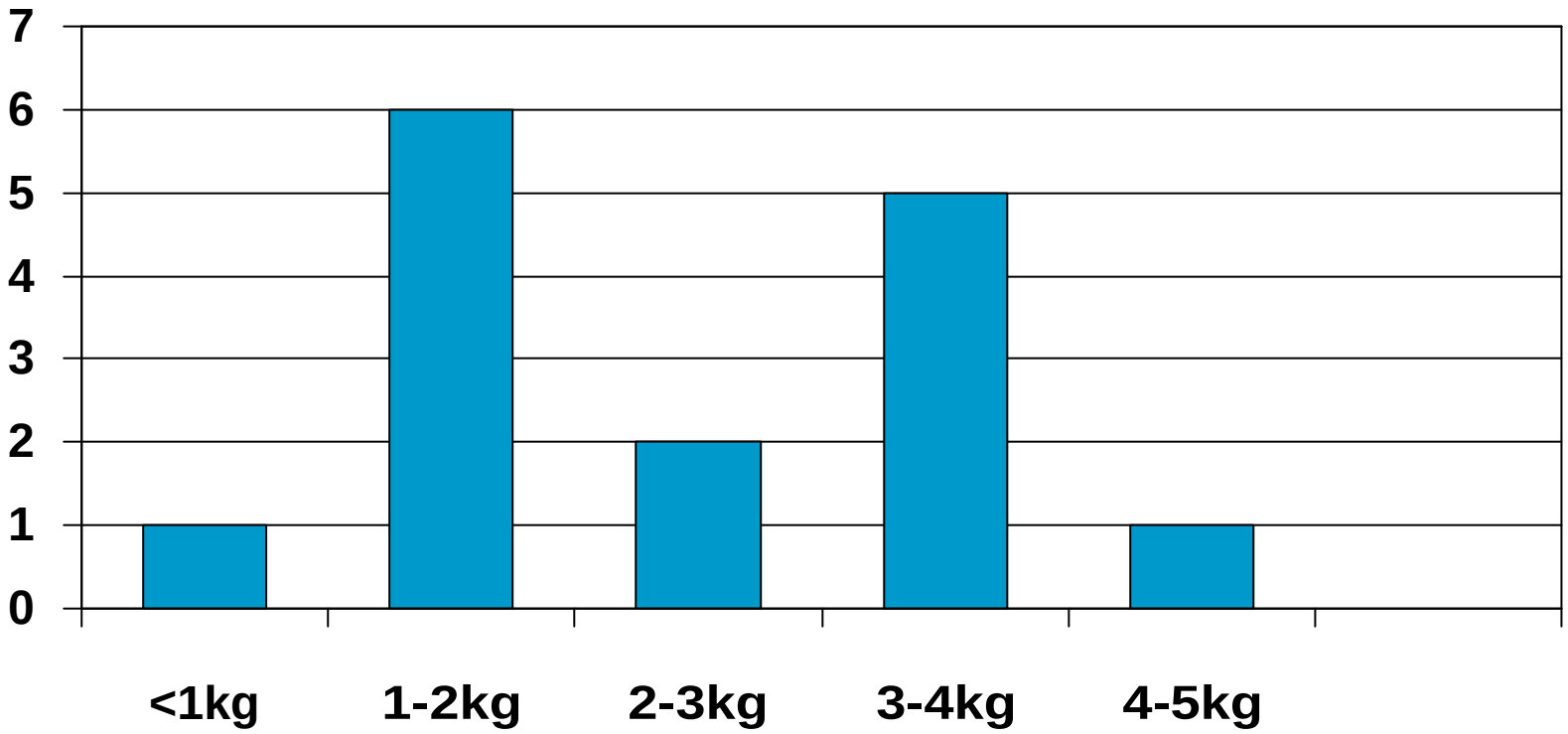
Diagnosis of Infants Surviving Dialysis

- INFECTIVE CAUSES
  - Septicaemia
  - Diarrhoea
  - Fungal sepsis
- SURGICAL CAUSES
  - Necrotising Enterocolitis
  - Cardiac Surgery - TGA's
  - Abdominal Surgery

DRUGS

- 13/15 patients received large doses of Furosemide e.g. 5mg/kg/dose pre-dialysis
- 10/13 patients were on Dopamine infusions at time of dialysis
- 2 patients received Adrenaline infusions in addition
- 7/14 patients were on an Aminoglycoside antibiotic (amikacin/gentamicin) pre-dialysis

Weight of Infants surviving Dialysis



Advantages of Acute PD Catheters

- No bleeding complications
- 2/15 catheters blocked - day 3 and 4 on dialysis
- Replaced 1 catheter by "re-wiring"

Practicalities of Dialysis

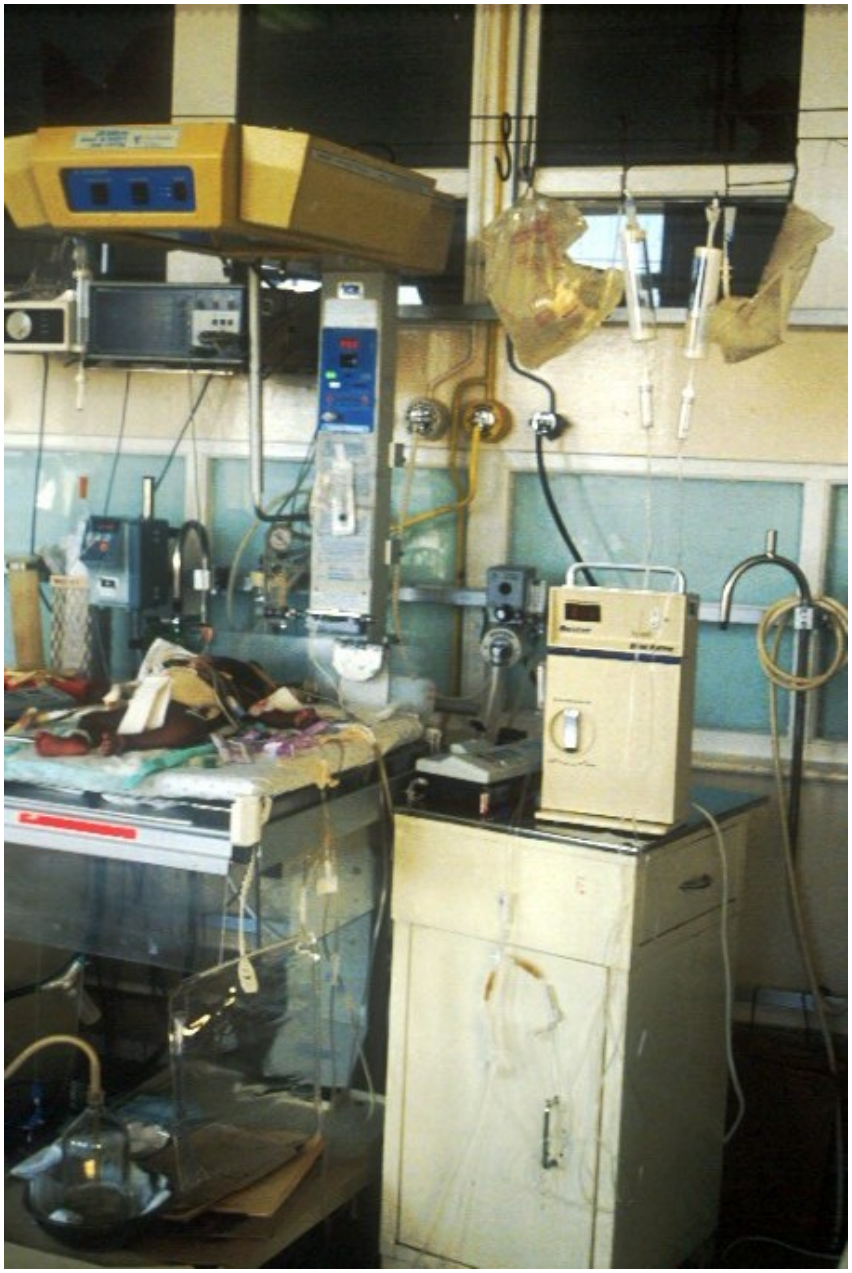
Fluid Volumes:

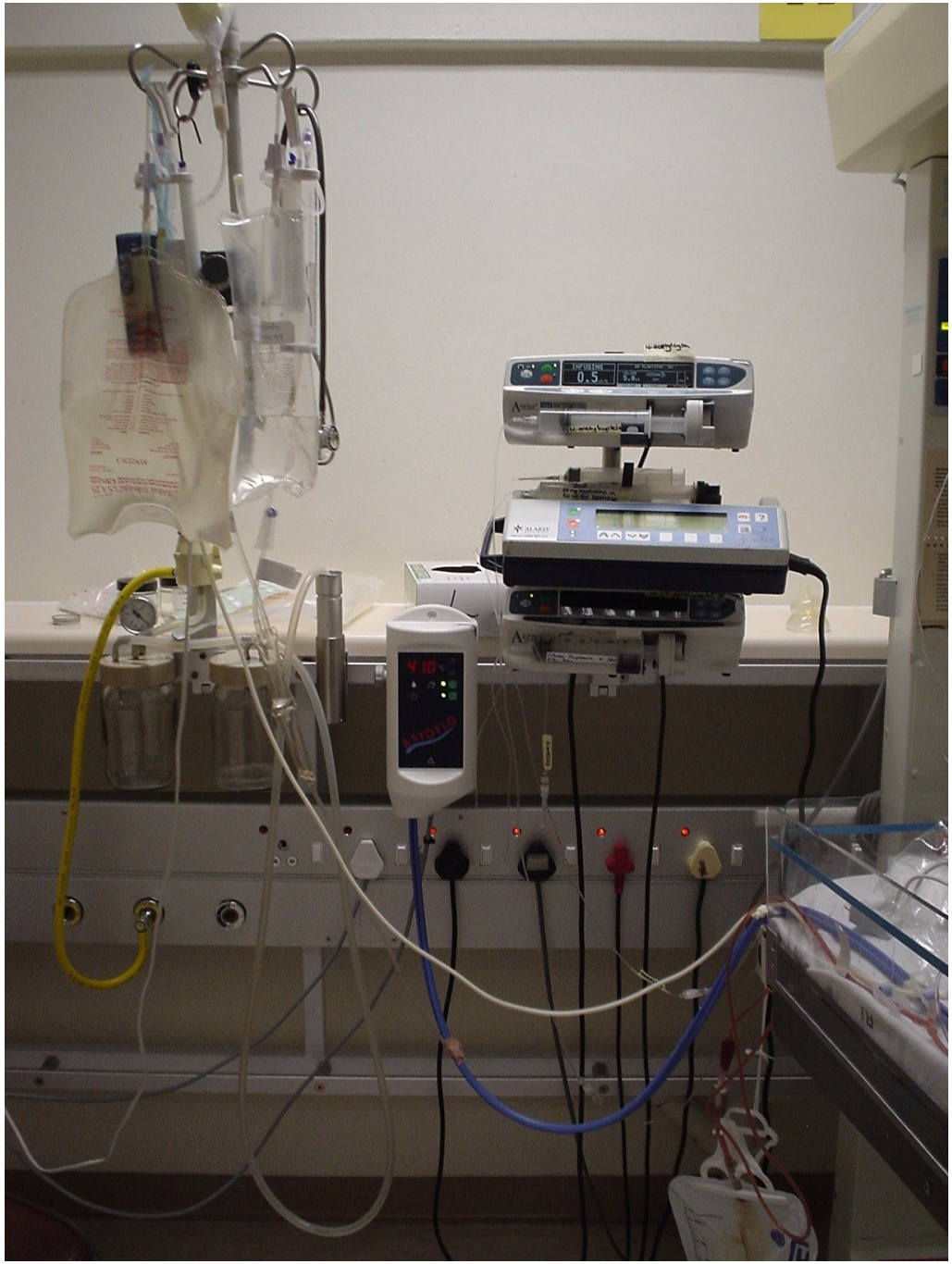
- Small volumes to avoid raised intra-abdominal pressure
  Fischbach M. Perit Dial Int 1996
- 20 ml/kg/cycle
- Adapted to ventilatory requirements

Cycle duration:

- Short dwell times to optimize ultrafiltration
- 45 - 60 minute dwell cycles
- Continuous dialysis over 24 hours

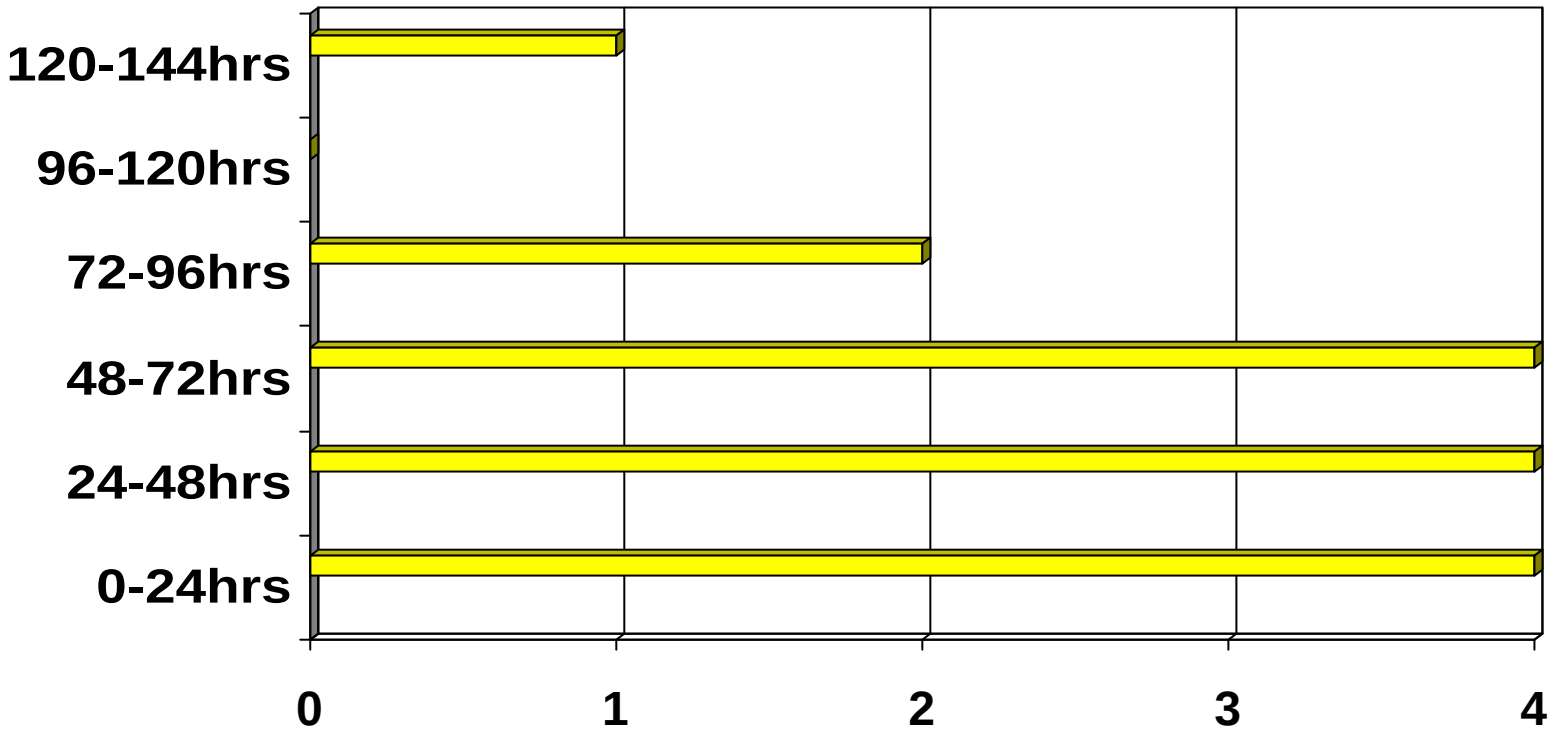
Manual dialysis





Automated Dialysis
Home choice machine

Duration Of Dialysis



Added Benefit of Dialysis

- Fluid overloaded infants - "Wet lungs" with difficult ventilation
- Reduce maintenance fluid volumes to minimum e.g. 40 ml/kg/day
- Use combination of 1.5% or 4.25% dianeal to maintain blood glucose
- Use glucose concentration in dianeal to allow severe fluid restriction (not usually tolerated in these small infants)

→ **Allows space for feeding/fluids**

OUTCOME

- 15/25(60%) Infants survived to come off dialysis
- Nil required long term dialysis
- 3 Subsequently demised - not related to dialysis:
  - 1 accidental extubation
  - 1 Cerebral Palsy and developed septicaemia 1 year later
  - 1 Shock & Dehydration due to excessive colostomy losses 3 months later

COMPLICATIONS RELATED TO DIALYSIS

- 2 blocked catheters - 1 case size 5Fr catheter changed for a 8Fr catheter
- No bleeding problems related to catheter
- No infections related to peritoneal dialysis
- Hyponatraemia related to dialysis not a problem
  - Na ranged from 129-138mmol/l

CONCLUSIONS

- Peritoneal Dialysis is a safe and effective method of continuous renal replacement therapy in infants
- Rapid insertion and safety profile makes it possible for use even in smallest infants
- Glucose content in dianeal allows severe fluid restriction without hypoglycaemia

Conclusion

- Peritoneal Dialysis is a relatively easy procedure for acute dialysis even in small babies.
- It can be life saving for children.
- It is appropriate in the African setting, as it does not depend on expensive technology.
  - Even in adequately resource countries
- Survival rate is comparable to our previous audits and also to continuous haemodialysis used in other paediatric units


Nigeria
Kenya
Training for Africa
Nigeria
Benin
Uganda

Take home message

- Prevention of ARF in Neonates NB
- Identify high risk infants
- Beware toxins – especially drugs
- Dialysis is possible even in smallest infant
  - Peritoneal dialysis still has a role
  - Especially in low resource countries
- Long term follow-up necessary
  - Call a friend – paeds nephrologist !