Indicators for Combined Peritoneal Dialysis plus Hemodialysis Therapy

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What are the physiological indications?

- Why is HD so bad?
- Why might PD be better?
- What is it that lets PD down?
- What should we do about it?

Systemic circulatory stress in HD -Effects of HD on $ScVO_2$

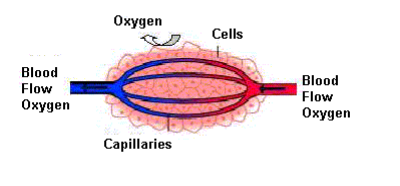
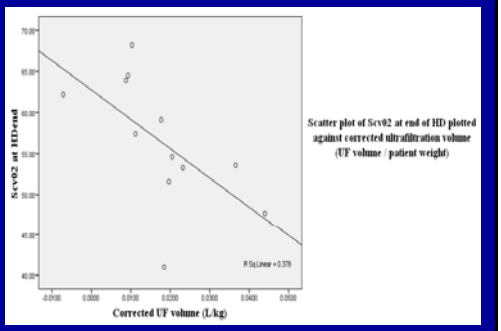


Table 1 Limits of mixed venous oxygen saturation

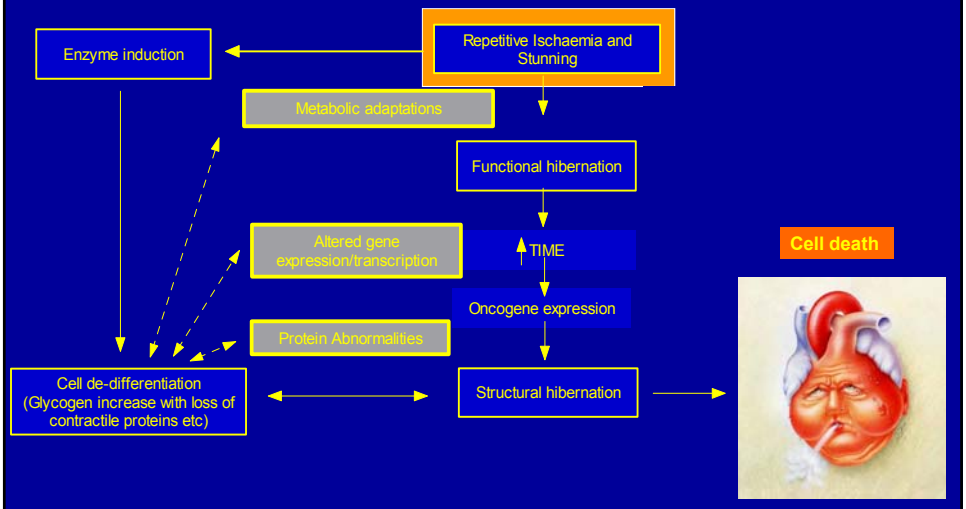
SvO_2 >75%	Normal extraction O_2 supply >O_2 demand
75% >SvO_2 >50%	Compensatory extraction Increasing O_2 demand or decreasing O_2 supply
50% >SvO_2 >30%	Exhaustion of extraction Beginning of lactic acidosis O_2 supply <O_2 demand
30% >SvO_2 >25% SvO_2 <25%	Severe lactic acidosis Cellular death

$ScVO_2$ Pre HD 63.5 ±1 3%, post HD 56.4 ± 8% (p=0.04)*

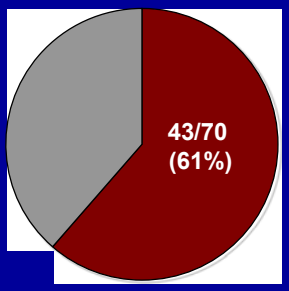


*Harrison L, Selby NM, McIntyre CW. ASN 2010

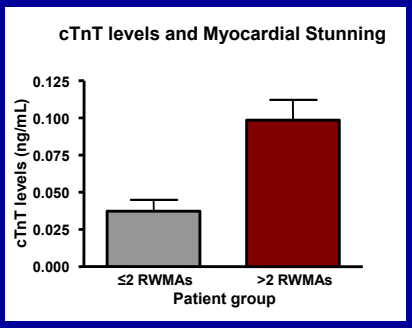
Repetitive cardiac injury- Hibernation and heart failure



HD induced RWMA – prevalence and cTnT levels



>2 RWMAs ≤2 RWMAs



- The higher the cTnT, the greater the reduction in SF

Burton JO, Korsheed S, McIntyre CW. Clin J Am Soc Nephrol. 2009 May;4(5):914-20

Factors associated with the presence of RWMAs

- Factors associated with development of >2 RWMAs (r^2=0.602)

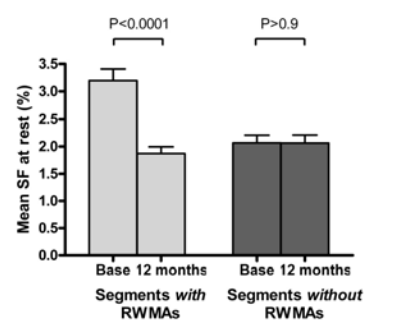
Factor associated with development of myocardial stunning	*OR*	*P value*
UF volume during HD of 1L	5.1	0.007
UF volume during HD of 1.5L	11.6	
UF volume during HD of 2L	26.2	
Max SBP reduction during HD of 10 mmHg	1.8	0.002
Max SBP reduction during HD of 20 mmHg	3.3	
Max SBP reduction during HD of 30 mmHg	6.0	

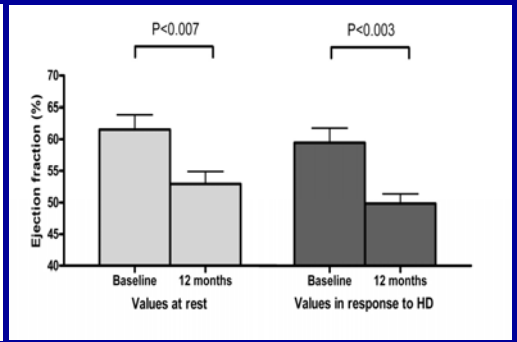
cTnT	1.26	1.04 – 1.54	0.004
Age	1.07	1.01 – 1.128	0.018

Burton JO, Korsheed S, McIntyre CW. Clin J Am Soc Nephrol. 2009 May;4(5):914-20

HD Induced Myocardial Stunning Lead to Myocardial Hibernation and Reduction in Overall Systolic Function

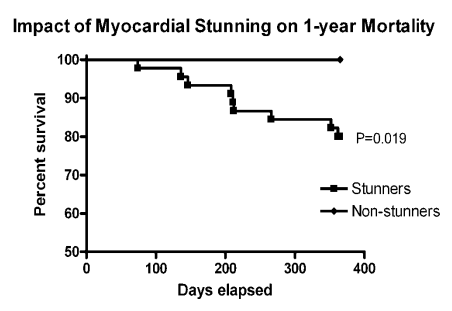
- Hibernation of segments co-localised with stress induced RWMAs
- Reduction in LVEF ~ 10% (absolute)
  - At rest
  - At peak stress on HD

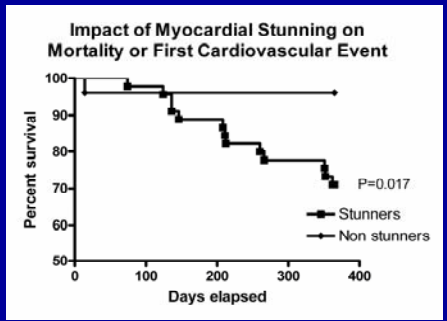




Burton JO, Korsheed S, McIntyre CW. Clin J Am Soc Nephrol. 2009 May;4(5):914-20
Burton JO, Jefferies HJ, *McIntyre CW* . Clin J Am Soc Nephrol. 2009 Dec;4(12):1925-31

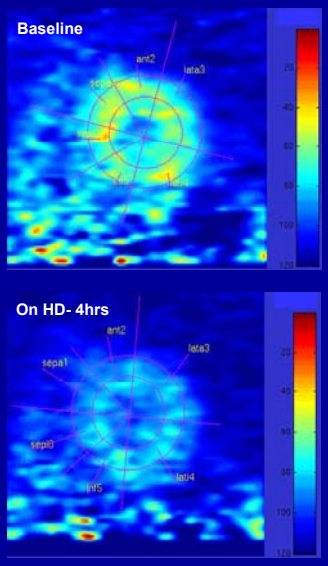
Mortality and time to CV event





Burton JO, Korsheed S, McIntyre CW. Clin J Am Soc Nephrol. 2009 May;4(5):914-20

Effect of HD on global and segmental Myocardial Blood Flow



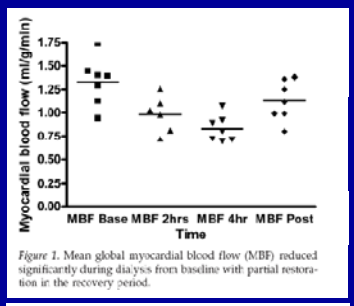


Figure 1. Mean global myocardial blood flow (MBF) reduced significantly during dialysis from baseline with partial restoration in the recovery period.

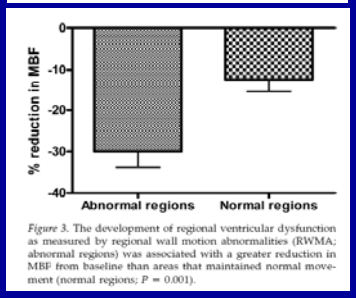


Figure 3. The development of regional ventricular dysfunction as measured by regional wall motion abnormalities (RWMA; abnormal regions) was associated with a greater reduction in MBF from baseline than areas that maintained normal movement (normal regions; $P = 0.001$).

McIntyre CW et al. Clin J Am Soc Nephrol. 2008 Jan;3(1):19-26

HD Induced Myocardial Stunning Lead to Myocardial Hibernation and Reduction in Overall Systolic Function

- Hibernation of segments co-localised with stress induced RWMAs
- Reduction in LVEF ~ 10% (absolute)
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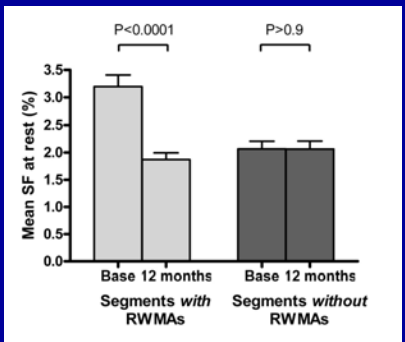

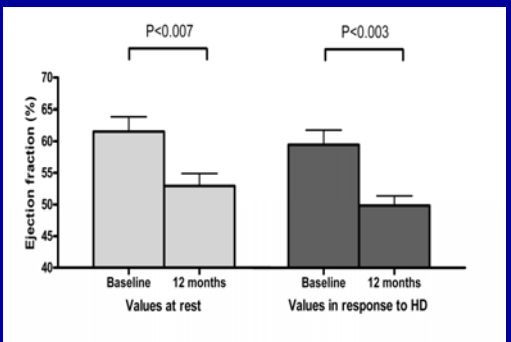

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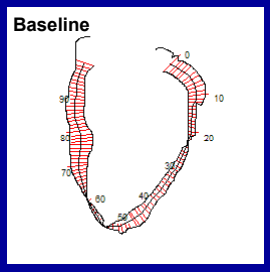
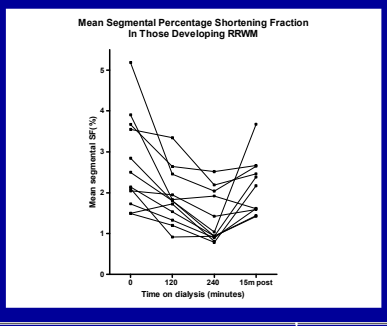
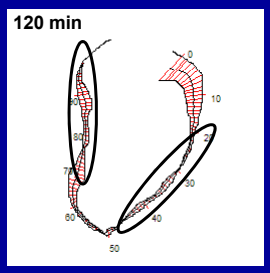
Burton JO, Jefferies HJ, *McIntyre CW* . Clin J Am Soc Nephrol. 2009 Dec;4(12):1925-31

Recurrent HD induced myocardial stunning in children



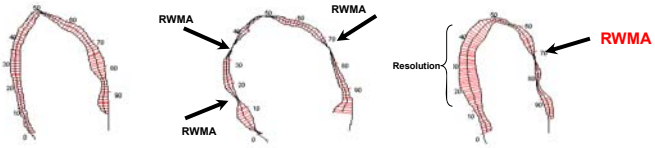




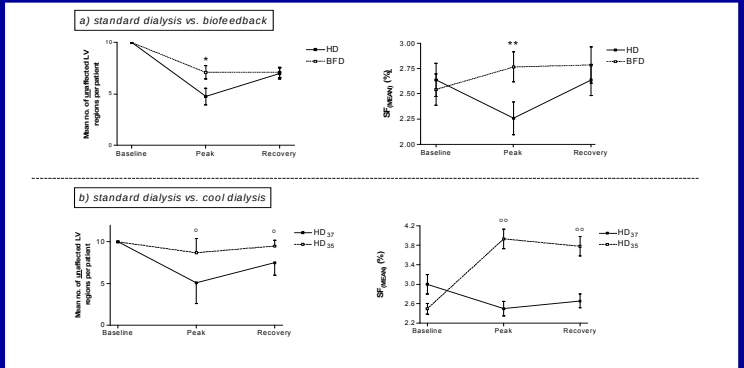
Proportion stunning	11/12
Age (years)	12.4(2-17)
UF volume(L)	1.2± 079
Delta BP (mmHg)	25.5± 9
Pre HD LVEF (%)	55± 8.3
Post HD LVEF (%)	54.6± 7.5

Hothi D, Rees L, McIntyre CW. Clin J Am Soc Nephrol. 2009 Apr;4(4):790-7

Reduction in HD induced circulatory stress ameliorates myocardial stunning

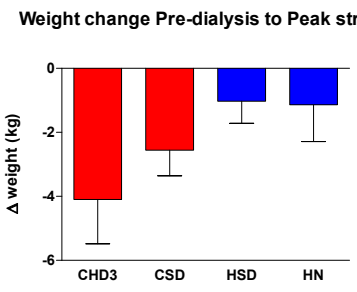


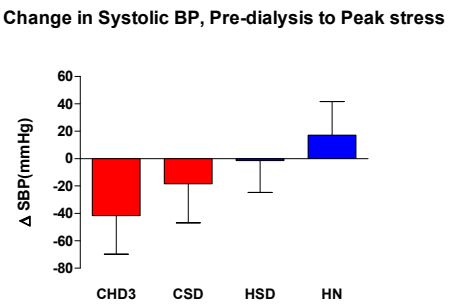
HD baseline | HD 240min | HD post



N Selby, S Lambie, C Baker, P Camici, C McIntyre. AJKD 2006
Selby NJ, Burton JO, McIntyre CW. Clin J Am Soc Nephrol 2006

Daily dialysis impact on UF and BP

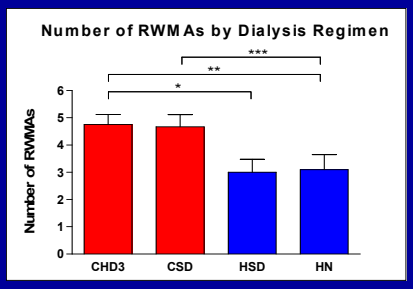


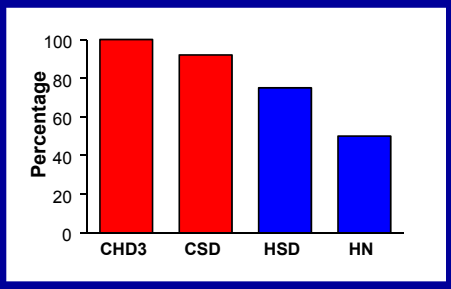


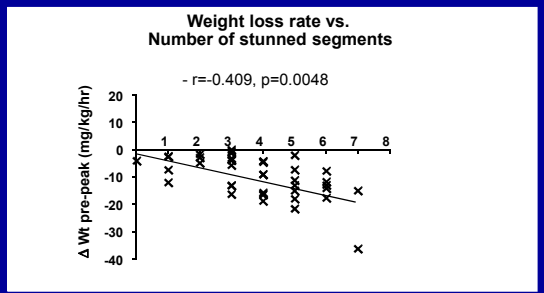
Patients fully matched for age, sex, history of IHD and dialysis vintage

Jefferies HJ, Schiller B, Moran J, McIntyre CW. Accepted for publication CJASN 2010

Impact of dialysis schedule- Intradialytic cardiac stunning



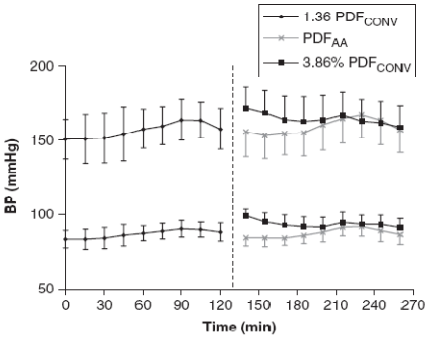




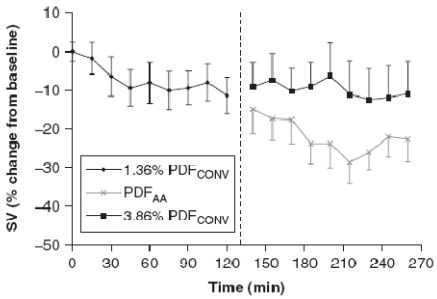
Jefferies HJ, Schiller B, Moran J, McIntyre CW. Accepted for publication CJASN 2010

Haemodynamic consequences of Nutrineal vs Dianeal- effect of hypertonic glucose

Continuous BP



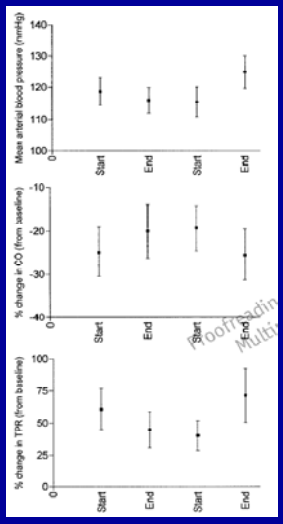
Continuous stroke volume

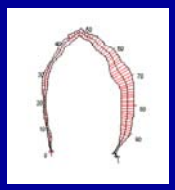


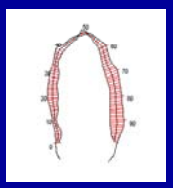
Selby NJ, McIntyre CW. Nephrol Dial Transplant. 2007 Mar;22(3):870-9
Selby NJ, McIntyre CW. Nephrol Dialysis Transplant 2006;9:1848-1853.

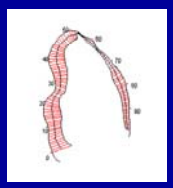
NO DIFFERENCES IN LV SYSTOLIC OR DIASTOLIC DIMENSIONS

Peritoneal dialysis is not associated with myocardial stunning









baseline **Drain/fill** **Post UF**

Limited evidence (<5% of segments during drain/fill cycle)

Studied during drain/fill and at peak ultrafiltration
Patients studied had little structural cardiac disease

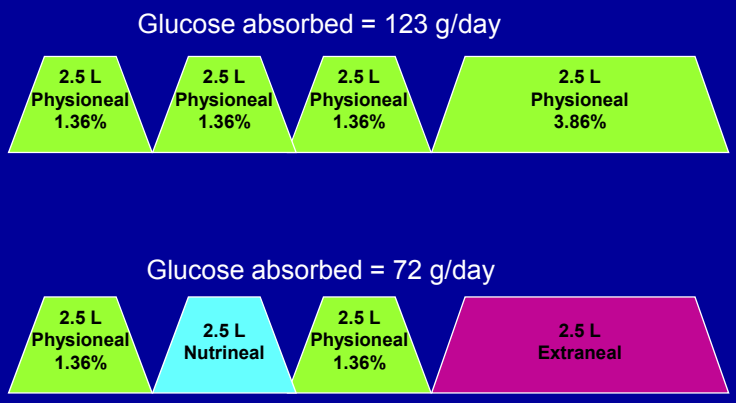
Selby NM, McIntyre CW. PDI 2010

So why does PD not have a clear survival advantage?

METABOLIC STRESS

FLUID OVERLOAD

Impact of non-glucose solutions on glucose load



Holmes et al, PDI 2000

New Buffers and Osmotic Agents

Multi-bag, glucose based
(Physioneal[1]/Trio/Balance)

- ↓ GDPs and AGEs
- ↓ Lactate
- Physiologic pH and pCO_2
- ↑ Membrane and immune cell function

Amino acid based[2]

- No glucose exposure
- No GDPs or AGEs
- ↑ pH
- ↑ Membrane and immune cell function

'Vanilla' Glucose fluids

Glucose

Low pH

Glucose degradation products (GDPs)

Advanced glycation end products (AGESs)

Icodextrin based[2]

- Isosmolar to plasma
- No glucose exposure
- ↓ GDPs and AGEs
- ↑ Membrane and immune cell function

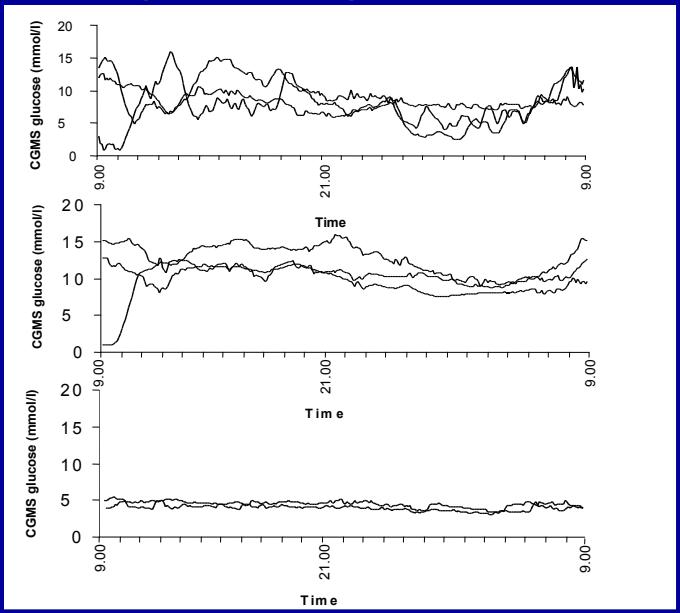
McIntyre CW. Kidney Int. 2007 Mar;71(6):486-90.

ISF glucose single patient

DDDD

PPPP

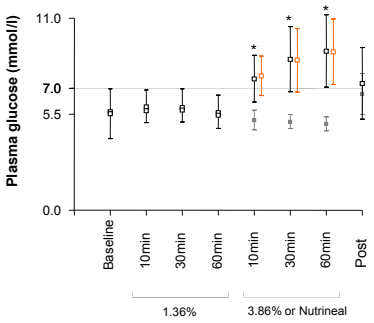
NEPP



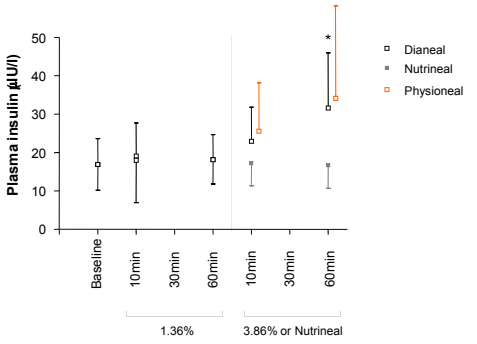
Marshall J, McIntyre CW. Kidney Int 2003 64:1480-1486

Hyperglycaemia and hyperinsulinaemia induced in fasting non-diabetic CAPD patients

Plasma glucose



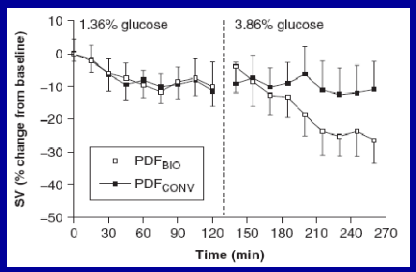
Plasma insulin

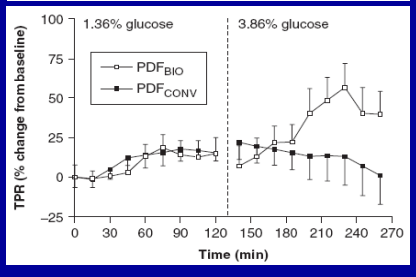


* p<0.001 Dianeal versus Nutrineal, p<0.05 Dianeal versus baseline by ANOVA

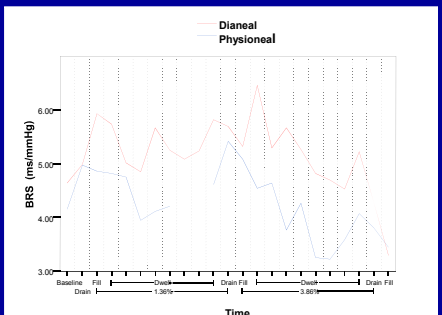
Selby NJ, McIntyre CW. Nephrol Dial Transplant. 2007 Mar;22(3):870-9.

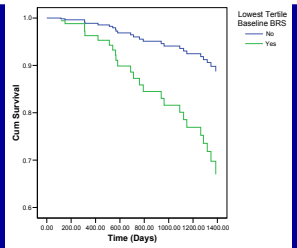
Cardiovascular function and baroreflex sensitivity (BRS) -effects of glucose containing fluid biocompatability





Selby NJ, McIntyre CW. Nephrol Dial Transplant. 2007 Mar;22(3):870-9





John S, Selby NJ, McIntyre CW. Kidney Int 2008

Tissue AGE deposition- Cutaneous autofluoresence

- Well correlated with biopsy AGE levels
- Relates to vascular complications and out comes in
  - HD
  - Diabetes
  - PET
  - Hypertension
  - Diastolic cardiac dysfunction

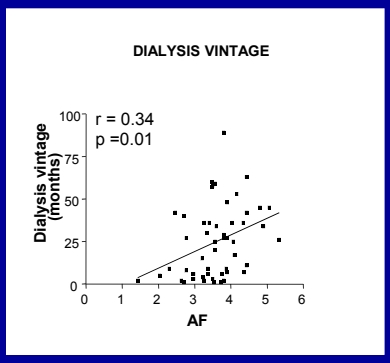
McIntyre CW et al. NDT+ 2008

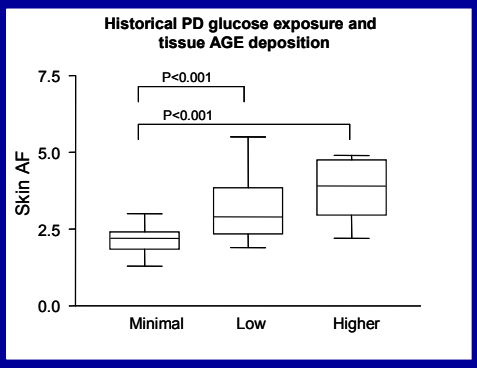
Tissue AGE in CKD 3 patients -Renal Risk in Derby Study

Table 1.Significant Correlations with skin AF		
	r	P-value
Age (years)	0.214	<0.0001
Calculated GFR (mL/min/1.73m^2)	-0.228	<0.0001
Total Cholesterol (mmol/L)	-.0.147	<0.0001
Hb (g/dL)	-0.218	<0.0001
Albumin (mmol/L)	-0.124	<0.0001
Glucose (mmol/L)	0.135	<0.0001
Diastolic BP (mmHg)	-0.149	<0.0001
PWV (m/sec)	0.112	<0.0001
Waist:Hip Ratio	0.110	<0.0001
IMD Score (Indices of Multiple Deprivation)	0.068	0.005
Bicarbonate	-0.067	0.006
Uric Acid (mmol/L)	0.070	0.004
HDL Cholesterol (mmol/L)	0.057	0.019

McIntyre NJ, McIntyre CW, Taal MW. ASN 2010

Effect of dialysis on tissue AGE

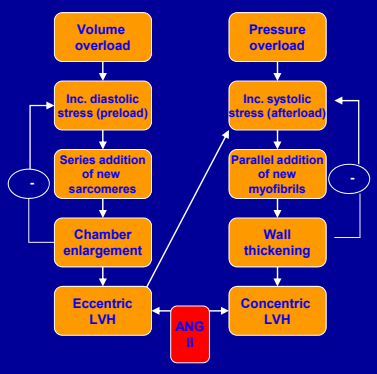


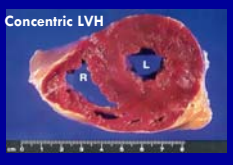


- AF grossly elevated
- 3.58 ± 0.75 vs 3.7 ± 0.88

McIntyre et al Clin J Am Soc Nephrol 2009

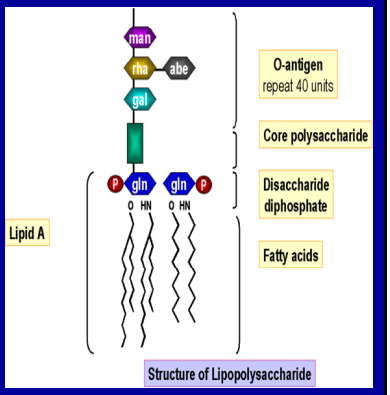
PD is associated with chronic volume overload





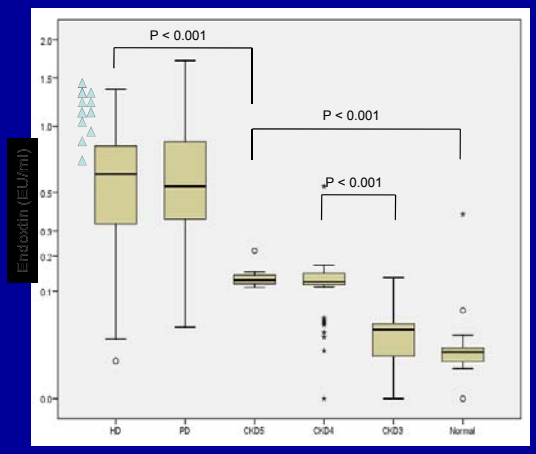
Endotoxin and heart failure

- Bacterial endotoxin is a lipopolysaccharide (LPS) comprising over 70% of the total bacteria in the **human gut**
- Stimulus for immune activation in the pro-**inflammatory** state of congestive heart failure (CHF)*
- ET enters the circulation via bacterial translocation from the gut
  - bowel **oedema**
  - **hypoperfusion**
- Endotoxinaemia reduces with
  - Reduction in **venous congestion**
  - Selective **gut detoxification**



*Anker, S.D., et al. Am J Cardiol, 1997

Endotoxaemia in CKD 3- 5D



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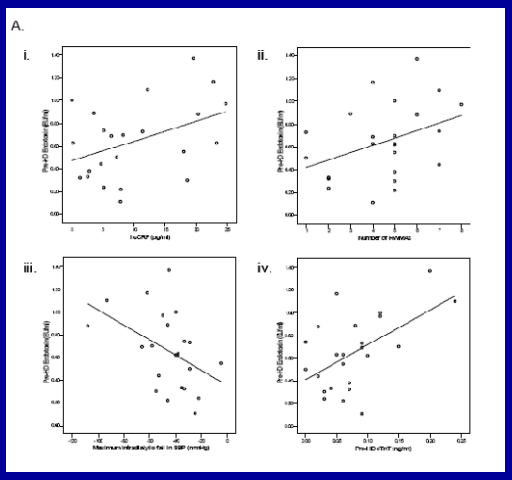
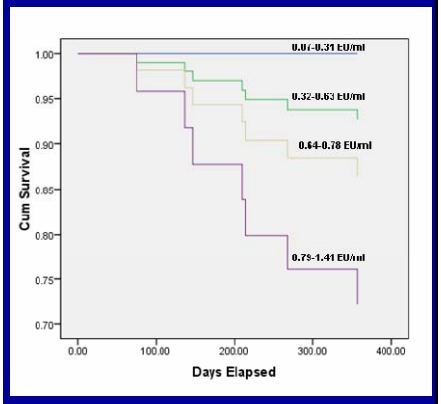
Effect of haemodialysis related factors on Endotoxaemia





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If you can't beat them, join 'em -Bimodal dialysis

	T_0	$T_{6\ MONTHS}$	$T_{12\ MONTHS}$
Kt/V HD	1.5±0.24 (1.2-1.8)	1.45±0.22 (1.1-1.8)	1.5±0.14 (1.3-1.7)
Weekly Kt/V PD	1.0±0.13 (0.8-1.1)	0.95±0.14 (0.8-1.1)	1.0±0.14 (0.8-1.2)
Cr EDTA Cl /1.73 m^2	13.6±3.4 (8-16)		12.4±2.0 (9-14)
PD ultrafiltration volume l/24 hours	1.55±0.58 (0.95-2.6)	1.65±0.76 (1.1-2.55)	1.58±0.32 (1.3-2.1)

	T_0	$T_{6\ MONTHS}$	$T_{12\ MONTHS}$
LVMI G/m^2	194±25.3 (161-265)*		156±21.2 (138-189)*
Ejection fraction %	50.4±11.1 (38-67)		48±8.0 (48-67)
Mean arterial blood pressure MmHg	80.2±9.4 (58-105)	74.8±17.0 (55-94)	72.6±16.3 (56-91)
Number of antihypertensive medications	3.8±0.8 (3-5)	1.6±0.5 (1-2)*	1.4±0.5 (1-2)**
Hb G/dl	11.3±1.5 (9.7-13.4)		11.4±0.9 (9.9-12.1)
Serum phosphate Mmol/l	1.67±0.3 (1.3-2.0)	1.8±0.18 (1.65-2.1)	1.66±0.14 (1.55-1.9)
Albumin G/l	27.4±4.9 (21-33)	28.0±3.0 (24-32)	28.0±2.8 (25-31)

* p=0.05, ** p= 0.04

McIntyre CW. Perit Dial Int. 2004 Nov-Dec;24(6):547-53
Kawanishi H, McIntyre CW. Kidney Int 2009

Additional potential benefits

- Initial start
  - 'Seamless' time line changes
  - Facilitated holiday options
  - Informed final modality choice
- Conversion from PD
  - Assisted UF
  - Assisted solute clearance
  - Domiciliary dialysis prolongation
- Conversion from HD
  - Reduction is circulatory stress