Infectious Diseases with Public Health Impact for Dialysis Services

Dr Richard Fluck Consultant Renal Physician & Clinical Director, Royal Derby Hospital



#### Infection

 The leading preventable cause of mortality in the dialysis population

 Reducing the burden of infection should be the number one objective in the care of patients on dialysis

Discuss

## Outline

- Epidemiology
- Consequences
- Prevention (primary)
- Prevention (secondary)
- Treatment
- Summary

#### Catheter events & complications USRDS Figure 5.48



Prevalent hemodialysis patients age 20 and older, ESRD CPM data; only includes patients who are also in the USRDS database. Year represents the prevalent year & the year the CPM data were collected. Access is that listed as "current" on the CPM data collection form.

#### Change in hospital admissions since 1993 Figure 6.3



Period prevalent dialysis patients. Rates adjusted for age, gender, race, and primary diagnosis. ESRD patients 2005 used as reference cohort.

#### Adjusted admissions for principal diagnoses, by modality Figure 6.5



Period prevalent ESRD patients; adjusted for age, gender, race, & primary diagnosis. ESRD patients, 2005, used as reference cohort.

## UK RENAL REGISTRY VASCULAR ACCESS SURVEY

# UK RA Vascular Access Survey 2005

- Census of all dialysis patients
  - 62 centres returned
  - 4 unable to assist
  - 6 no return
- Census of chronic HD patients in hospital
- Proportion of above due to vascular access
- 2004 Staph. aureus septicaemias in chronic HD patients
- Proportion of those due to MRSA



Overall 13,343 (77%) of prevalent patients were having dialysis therapy delivered by definitive access.
Centres varied from 52% to 95%.
For HD patients only, definitive access was used in 69%, range from 44% to 94%.

UK RA Vascular Access Survey 2005

#### Renal Registry Vascular access survey – incident cohort



#### Infections

- 54 centres returned data
- 1547 episodes of Staph. aureus bacteraemias reported
- 462 episodes of MRSA (29%)
- Equivalent to 5-10% of all MRSA (relative risk 200-400 fold general population)

#### No of venous access vs Staph aureus episodes



# CONSEQUENCES

# Consequences: mortality in HD

- Role of access and outcome
- Single centre 143 SAB -111 hospitalised
  - Catheter 59.5%
  - Graft 36%
  - AVF 4.5%

Inrig et al Clin J Am Soc Nephrol 1: 518–524, 2006

#### **Morbidity and mortality**

Se:3 Im:13



# Consequences: mortality and morbidity in HD

#### **Mortality**

- 12 week mortality rate
  - 22.7% Catheter
  - 10.0% AVG
    - P=0.098

#### Morbidity

- Metastatic infection
  - N=34 (TC and AVG)
  - TC n=22 33.3%
  - AVG n=12 30.0%
- Endocarditis n=17
- Septic emboli n=8
- Abscess n=6
- Osteomyelitis n=6
- Mean IP days 10

*Inrig et al Clin J Am Soc Nephrol 1: 518–524, 2006* 



### **Consequences: Cost**

- MSSA and MRSA cost
  - Garau et al ESCMD April 2008
  - MSSA 11,079 Euro
  - MRSA 14859 Euro
- HPA 2002 Surveillance of Hospital Acquired bacteraemia
  - Nephrology only exceeded by ICU and haematology

• 80% associated with central lines

• £6029 per episode

Reducing reliance on catheters

## **'PRIMARY' PREVENTION**

#### Renal National Service Framework



Standard 3

"All children, young people and adults with established renal failure are to have timely and appropriate surgery for permanent vascular or peritoneal dialysis access, which is monitored and maintained to achieve its maximum longevity."

#### Three objectives

- An AVF is the optimal type of access to utilise
- Preserving access and extending its lifetime is essential
- Reduce complications

# Monitoring vascular access: the pyramid of care and delivery at the point of care

Advanced monitoring

Fistula complications or poor adequacy

Physical examination

Good needling technique

Nurse led examination

#### Principle of Vascular Access Maintenance Programme





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UK RA Vascular Access Survey 2005

### Vaccination - prevention

Pneumococcus

Hepatitis B

Influenza

If you have to use a line how do you reduce infection

## **'SECONDARY' PREVENTION**

## 'Secondary' Prevention

Colonisation

- Reduce carriage
- Risk
  - Improve modifiable risk factors
- Inoculation
  - Eliminate the chances of inoculation

# Suppression therapy for SA carriage



Figure 3. Kaplan-Meier Curves Showing Cumulative Hazard of Hospital-Acquired Staphylococcus aureus Infection in the Study Groups.

Data were censored at the end of the follow-up period or at the time of death.

#### n engl j med 362;1 january 7, 2010

#### Bode et al

#### Prevention

Screening and decolonisation
Out patient HD population (n=136)
42% nasal MSSA
12% nasal MRSA
Carriage treated with mupirocin

- No MRSA infections at 1 year
- Eur J Med Res. 2007 Jul 26;12(7):284-8 Lederer et al

### Secondary prevention

Exit site options

- Mupirocin to exit site
- Meta-analysis Clin Infect Dis. 2003 Dec 15;37(12):1629-38
- 80% reduction in SAB in HD
- Resistance?
- Connection technology
- Antibiotic locks

#### Chlorhexidine–Alcohol versus Povidone– Iodine for Surgical-Site Antisepsis



#### Figure 2. Kaplan–Meier Curves for Freedom from Surgical-Site Infection (Intention-to-Treat Population).

Patients who received chlorhexidine–alcohol were significantly more likely to remain free from surgical-site infection than were those who received povidone–iodine (P=0.004 by the log-rank test). In the chlorhexidine–alcohol group, 39 patients had events (9.5%) and data from 370 patients (90.5%) were censored; in the povidone–iodine group, 71 patients had events (16.1%) and data from 369 patients (83.9%) were censored.

#### Darouiche et al

#### N Engl J Med 2010;362:18-26.

#### Antibiotic lock solutions



McIntyre et al Kidney International 2004

Study or sub-category	rate ratio (SE)	rate ratio (random) 95% Cl	Weight %	rate ratio (random) 95% Cl
01 Gent vs heparin Dogra, GK Nori, MD (gent) McIntrye CW Subtotal (95% Cl) Test for heterogeneity: Chi <sup>z</sup> = 10 Test for overall effect: Z = 6.68	14.0000 (1.4640) 8.0000 (1.4640) 13.3000 (1.0480) 184, df = 2 (P = 0.004), I <sup>2</sup> = 81.5% (P < 0.00001)	_	<ul> <li>11.73</li> <li>11.73</li> <li>12.60</li> <li>36.07</li> </ul>	14.00 (11.13, 16.87) 8.00 (5.13, 10.87) 13.30 (11.25, 15.35) 11.83 (8.36, 15.29)
02 Citrate vs heparin Weijmer, MC Subtotal (95% CI) Test for heterogeneity: not appli Test for overall effect: Z = 9.92	3.7300 (0.3760) cable (P < 0.00001)	•	13.52 13.52	3.73 [2.99, 4.47] 3.73 [2.99, 4.47]
03 Taurolidine vs heparin Betjes, MGH Subtotal (95% CI) Test for heterogeneity: not appli Test for overall effect: Z = 2.80	4.2000 (1.5000) cable (P = 0.005)	-	- 11.65 ► 11.65	4.20 [1.26, 7.14] 4.20 [1.26, 7.14]
04 Minocycline vs heparin Nori MD (minocl) Subtotal (95% Cl) Test for heterogeneity: not appli Test for overall effect: Z = 9.35	10.0000 (1.0690) cable (P < 0.00001)		→ 12.57 ◀ 12.57	10.00 [7.90, 12.10] 10.00 [7.90, 12.10]
05 Cefazolin/gent vs heparin Kim SH Subtotal (95% Cl) Test for heterogeneity: not appli Test for overall effect: Z = 6.64	7.1000 (1.0690) cable (P < 0.00001)		12.57 12.57	7.10 [5.00, 9.20] 7.10 [5.00, 9.20]
06 Cefotaxime vs heparin, (diab Saxena AK Subtotal (95% Cl) Test for heterogeneity: not appli Test for overall effect: Z = 10.88	etics) 2.3600 (0.2170) cable )(P < 0.00001)	:	13.62 13.62	2.36 [1.93, 2.79] 2.36 [1.93, 2.79]
Total (95% Cl) Test for heterogeneity: Chi² = 22 Test for overall effect: Z = 5.80	4.64, df = 7 (P < 0.00001), I² = 96.9% (P < 0.00001)	_	100.00	7.72 [5.11, 10.33]
	-10 Favo	-5 0 5	10 ervention	

Jaffer Y, Taal MW, Fluck RJ, McIntyre CW. AJKD 2007

Rates of CRI in tunneled lines only, when comparing ALS and heparin. Includes the five studies that assessed tunneled lines

Study or sub-category	Rate ratio (SE)		Rate ratio (random) 95% Cl	2	Weight %	Rate ratio (random) 95% Cl	
Betjes, MGH	3.4000 (	1.7320)	-		16.07	3.40	[0.01, 6.79]
Dogra, GK	14.0000 (	1.4640)			16.42	14.00	[11.13, 16.87]
Nori, MD (gent)	8.0000 (	1.4640)		-	16.42	8.00	[5.13, 10.87]
Nori MD (minocl)	10.0000 (	1.0690)		$\rightarrow$	16.85	10.00	(7.90, 12.10)
MoIntrye CVV	13.3000 (	1.0480)			16.87	13.30	[11.25, 15.35]
Saxena AK	2.3600 (	0.2170)			17.36	2.36	[1.93, 2.79]
Total (95% CI)					00.00	8.50	3.54, 13.46]
Test for heterogeneity: Chi	<sup>2</sup> = 212.62, df = 5 (P <	0.00001), I <sup>2</sup> = 97.6%		10.144			and the second second
Tool for overall offect: 7 -	3.36 (P = 0.0008)	and the second					

Jaffer Y, Taal MW, Fluck RJ, McIntyre CW. AJKD 2007

#### Local data from Derby

Focus on bacteraemia
 NOTE NOT CRB but all episodes

- High usage of venous catheters
- High admission rate
- High complication rate
- High mortality rate

# Blood Cultures (HD) 1999-2004

Data	99/00	00/01	01/02	02/03	03/04
Patients having a + blood	54	74	77	58	46
culture					
No. of positive blood	102	183	179	103	101
cultures					
Gram positive isolates	70%	82%	67%	55%	69%
Staph epid as % of all	43%	61%	35%	22%	28%
isolates					
MRSA as % of Staph	24%	13%	12%	11%	30%
aureus isolates					
Gentamicin resistance in	16%	11%	18%	4%	10%
GNBs					
Ciprofloxacin resistance	30%	19%	14%	6%	10%
in GNBs					
HD Patients (December)	127	143	173	189	199

# Blood Cultures (HD) 2005-9

Data	2005	2006	2007	2008	2009
Patients having a + blood	17	17	12	14	16
culture					
No. of positive blood	18	20	12	15	17
cultures					
Gram positive isolates	61%	45%	42%	53 %(8)	41% (8)
	(10)	(9)			
Staph epid as % of all	28% (5)	10% (2)	0%	7%	6% (1)
isolates				(1)	* Gent
					Res
MRSA as % of Staph aureus	17%	43%	0	28.5%	14.3%
isolates	(1/6)	(4/7)		2/7	1/7
Gentamicin resistance in	0%	0%	0%	0%	0%
GNBs					
Ciprofloxacin resistance in	0%	0%	0%	0%	0%
GNBs					
HD Patients (December)	205	210	221	245	255

TC 0.36/1000 Pt days AVF 0.11/1000 Pt days 2005 6 of 17 had tunnelled access 2006 6 of 17 had tunnelled access 2007 4 of 12 had tunnelled access and 1 had NTC 2008 7 of 15 had tunnelled access

2009 7 of 16 had tunnelled access

## Cost for gentamicin locks

- Gentamicin
  - Additional cost £1.80 per session
- Total cost per annum
  - •£260
- Total cost for Derby programme
  - £11000 per annum
  - Saving in bacteraemia costs (100 episodes per annum) ~£600000 per annum

#### For every person treated .....

- At least 0.5 Staph. Aureus bacteraemias are prevented
- At least 2.5 bacteraemias are prevented
- The NHS saves at least £15000
- In patient beds are not filled with catheter associated sepsis
- Risk is reduced for patients receiving haemodialysis



#### Treatment

• Systemic Antibiotic strategy

- High recurrence/failure rate
- E.g Clin Infect Dis. 2007 Jan 15;44(2):190-6
- Antibiotic Line locks
  - High failure rate
  - E.g 59% Am J Kidney Dis. 2007 Aug;50(2):289-95.
- Guide wire exchange
  - Less successful in MSSA/MRSA
- Line removal

#### Summary

- Staphylococcus aureus bacteraemia is a major cause of concern within the HD population
- Improvement in incidence of infections can be made
  - Systems approach
  - Medical management
- Targeting a single organism may improve overall infection rates

## Conclusion

- Bacteraemia in the dialysis population is
  - Common
  - Harmful
  - Preventable

Questions? THANK YOU