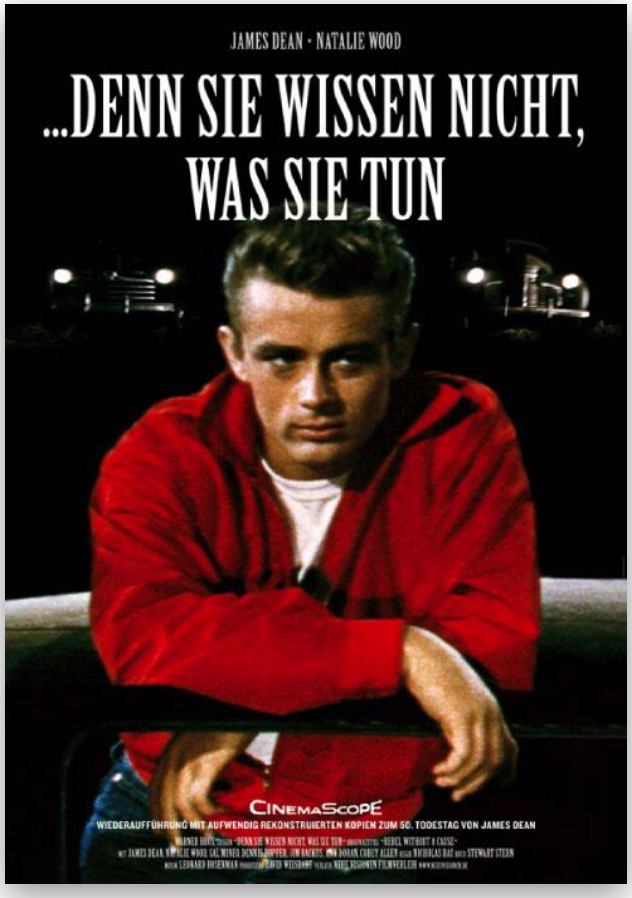
Antiinfektiva und Nierenersatzverfahren: Wie dosieren?



Jan T. Kielstein

Abteilung f. Nieren-und Hochdruckerkrankungen

Medizinische Hochschule Hannover

Medizinische Hochschule Hannover

Conflict of interest

Forschungsprojekte:	**Fresenius Medical Care**
	Novartis, Terumo BCT
Travel support:	**Novartis, Astellas, Sanofi,**
	FMC
Advisory Board:	**Sanofi, Terumo BCT**
	Fresenius Medical Care

Antiinfektiva und Nierenersatzverfahren: Wie dosieren?

1) Die klinische Notwendigkeit / Das Problem

2) CKD stage 5 / ESRD / Dialysepflichtigkeit

3) Acute kidney injury (Akutes Nierenversagen)

4) Empfehlungen / Dosierungsrichtlinien

Antiinfektive und Nierenersatzverfahren: Wie dosieren?

1) **Die klinische Notwendigkeit / Das Problem**

2) **CKD stage 5 / ESRD / Dialysepflichtigkeit**

3) **Acute kidney injury (Akutes Nierenversagen)**

4) **Empfehlungen / Dosierungsrichtlinien**

Atorvastatin in Patients with Type 2 Diabetes Mellitus Undergoing Hemodialysis

WANNER et al. *N Engl J Med* 353:238-48, 2005

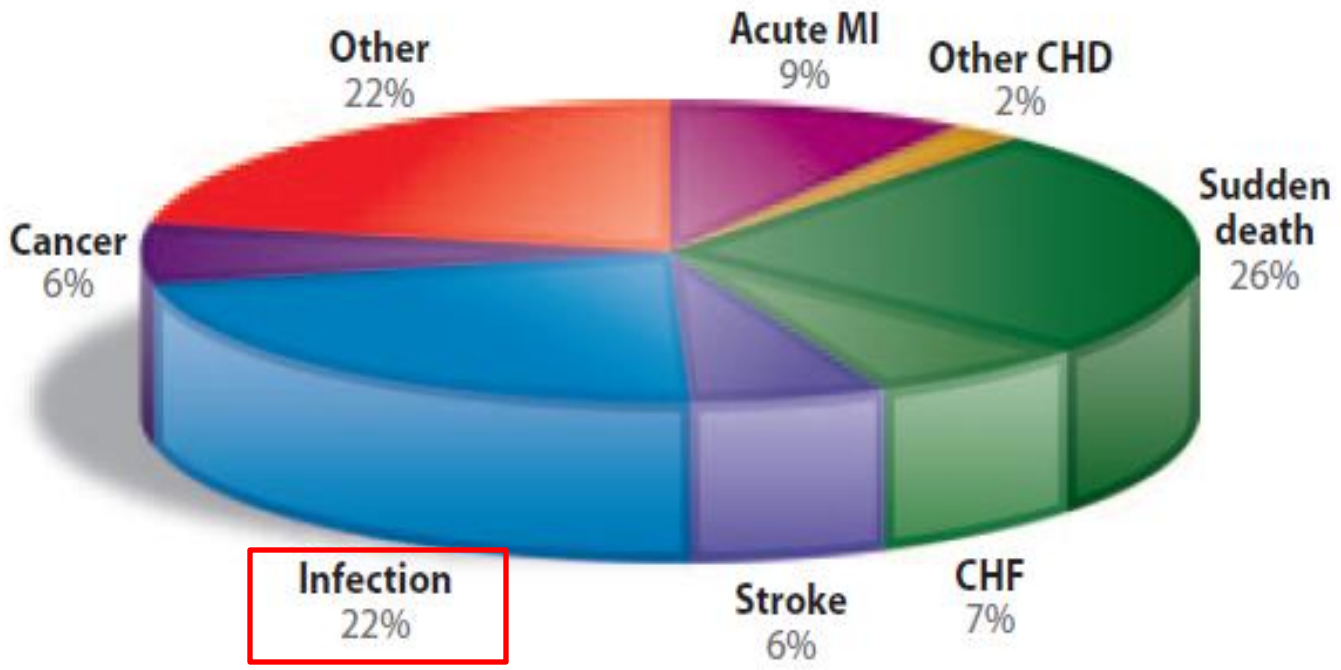


Figure 1. Causes of death in the 4D (Die Deutsche Diabetes Dialyse) study. MI, myocardial infarction; CHF, congestive heart failure; CHD, coronary heart disease.

Acute Renal Failure in critically ill patients (n=29,260)
A multinational, multicenter study

UCHINO et al. *JAMA* 294:813-818, 2005

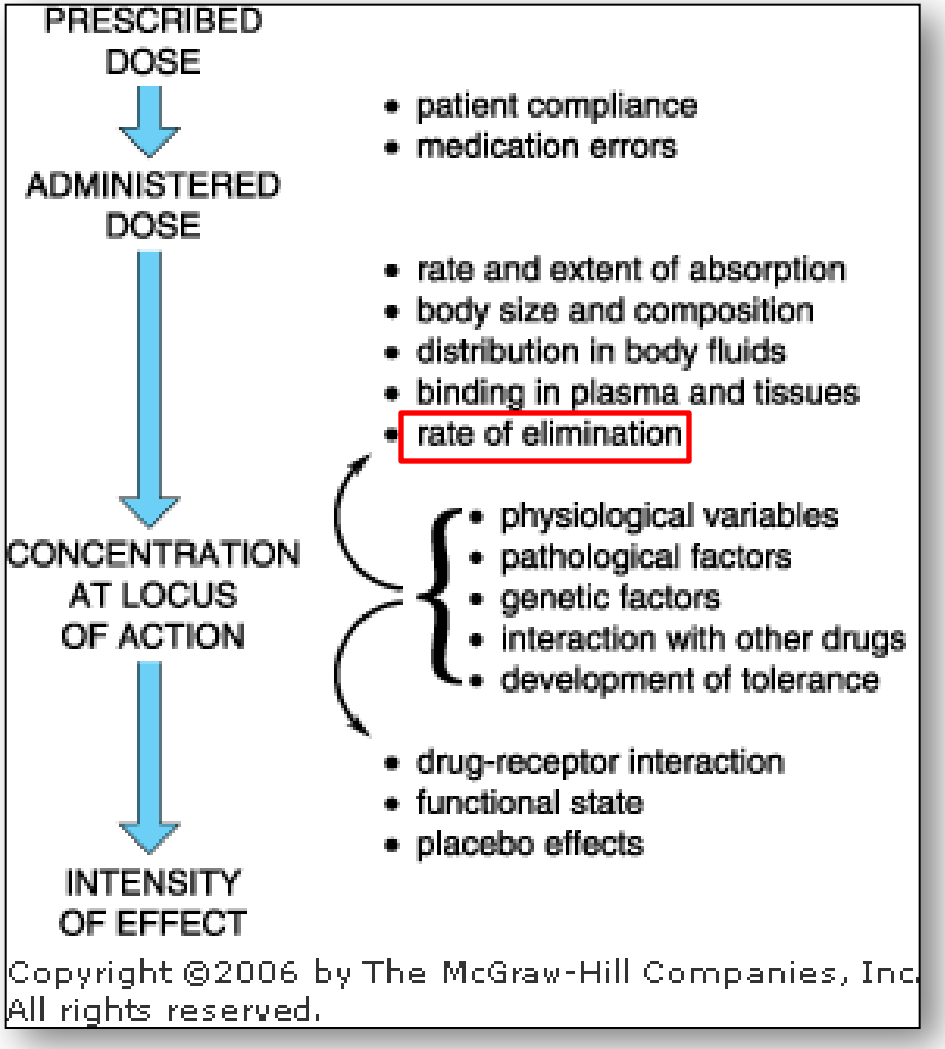
Contributing factors (n = 1726)	
Septic shock	820 (47.5)
Major surgery	592 (34.3)
Cardiogenic shock	465 (26.9)
Hypovolemia	442 (25.6)
Drug-induced	328 (19.0)
Hepatorenal syndrome	99 (5.7)
Obstructive uropathy	45 (2.6)
Other	211 (12.2)

Factors that determine the relationship between prescribed drug dosage and drug effect

Goodman & Gilman's The Pharmacological Basis of Therapeutics, 11th Edition

Specifics of RRT:

- treatment mode
- blood flow
- dialysate flow
- treatment time
- filter type
- ultrafiltration rate



Ambulante Dialyse

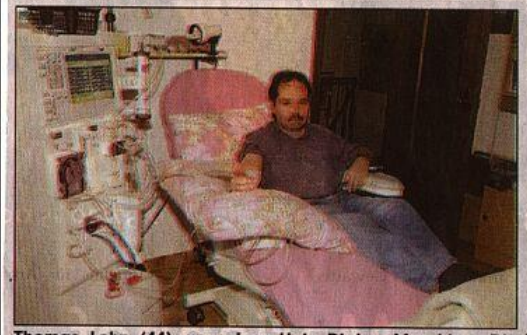
Alle zwei Tage zur Blutwäsche – Transplantation muss nicht sein

Ingelheimer lebt seit 30 Jahren ohne Niere

Von PILAR MAY

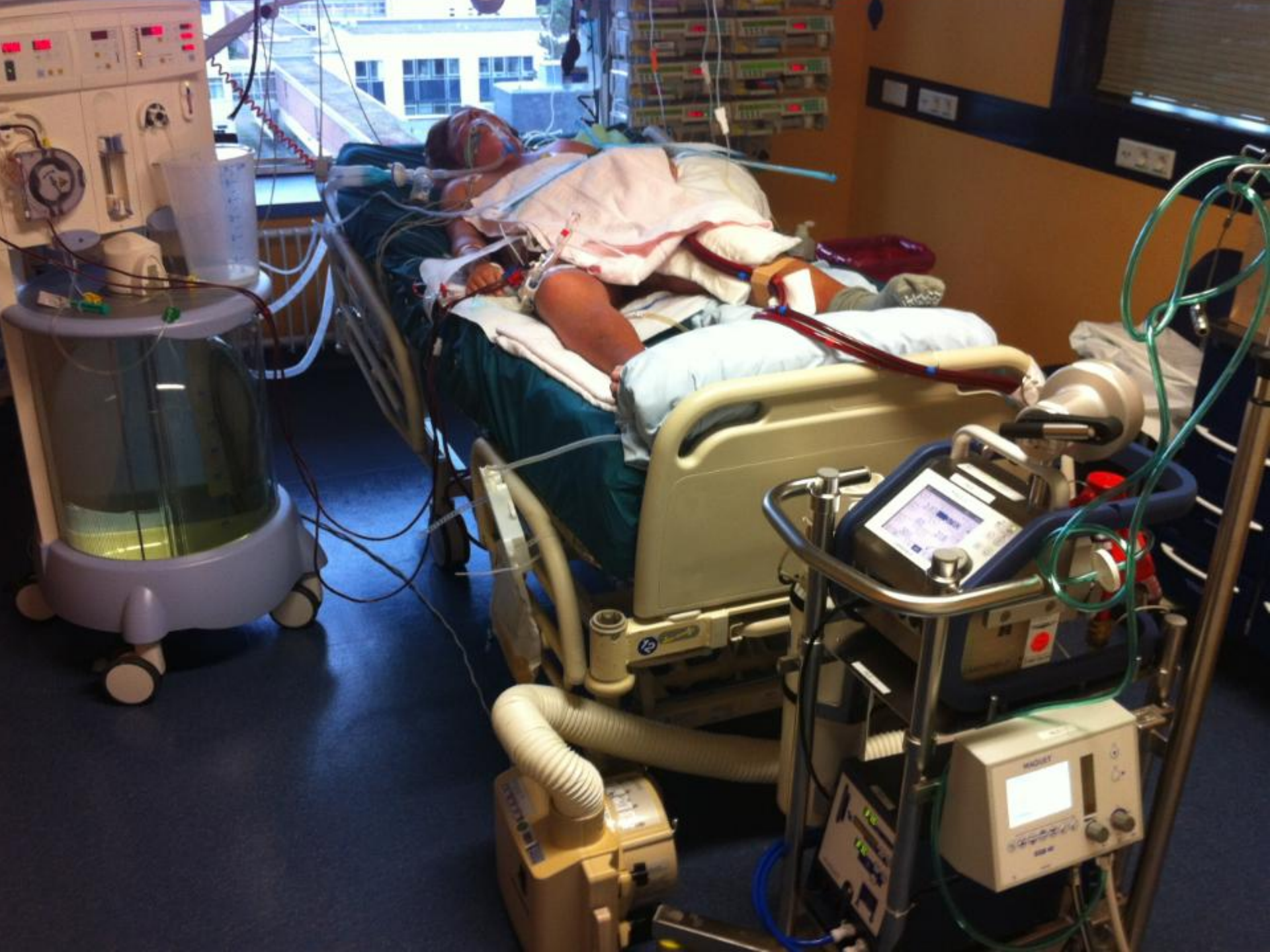
Ingelheim – **Thomas Lehn (44) arbeitet täglich acht Stunden als Systemtechniker im Datenzentrum in Mainz. Er unternimmt kleine Reisen, packt sogar im Garten mit an, führt scheinbar ein ganz normales Leben. Doch Lehn ist zu 100 Prozent schwerbehindert, ein leuchtendes Beispiel für Tausende Kranke. Er weiß: „Kein Deutscher geht länger zur Dialyse als ich. Am 19. August sind es 30 Jahre! Jetzt will ich anderen Mut machen."**

Schon im Alter von fünf Jahren musste Lehn die rechte Niere entfernt werden – eine angeborene Krankheit (Schrumpfniere) hatte sie zerstört. Doch auch die linke Niere war angegriffen, hörte in seinem 14. Lebensjahr auf zu arbeiten. Seitdem hängt Lehn alle zwei Tage für fünf Stunden an der Dialyse-Maschine. Sie übernimmt die Arbeit seiner Nieren, filtert überschüssiges Wasser und Giftstoffe aus seinem Blut. Ins Krankenhaus muss Lehn dafür nicht mehr: Er hat sich 1983 ein Dialyse-Zimmer in seinem Haus in Ingelheim eingerichtet. Eine Nieren-Transplantation lehnt er wegen der hohen Risiken ab. „Ich will mit meinem Fall zeigen, dass es möglich ist, auch ohne Transplantation so lange und gut zu leben. Viele Kranke gehen aus dem Beruf raus, in die Isolation. Das ist falsch." Hilfe und Informationen für Betroffene bietet er im Internet unter: http://www.main-rheiner.de/homepage/tlehn.



Thomas Lehn (44) an seiner Heim-Dialyse-Maschine: Die Blutwäsche schwächt die Knochen, Lehn darf nur wenig trinken, muss Diät halten. Trotzdem sagt er: „Man kann damit gut leben." Fotos: Adalbert von Bremen

Vorbildlich: Trotz seiner Krankheit lässt Lehn sich nicht gehen, packt sogar im heimischen Garten mit an.



Dialyse auf der Intensivstation
Wohin geht der Weg?

KIELSTEIN *Intensivmed.* 46:228–234, 2009

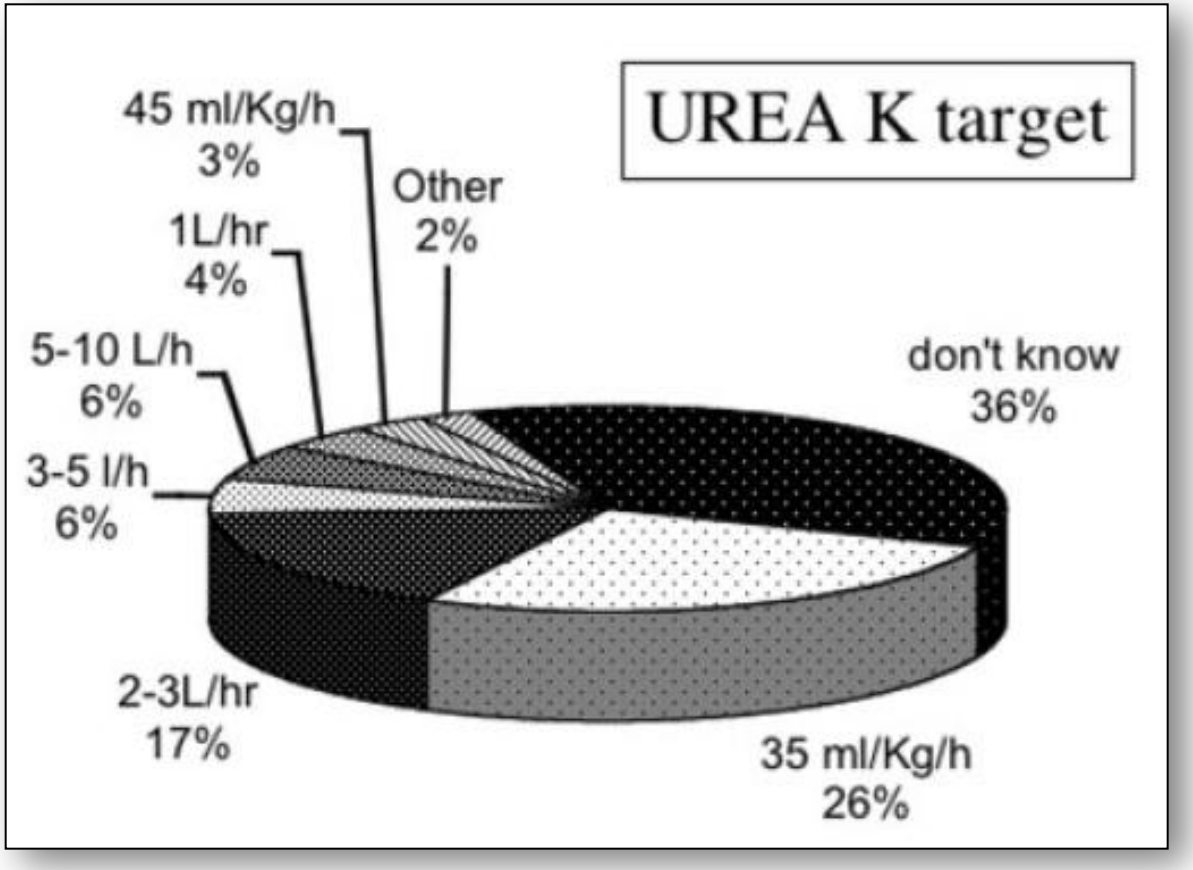
	Kontinuierliche Nierenersatztherapie	Intermittierende Nierenersatztherapie	„Extended dialysis", „GENIUS-Dialyse"
Elimination	Vorwiegend konvektiv	Vorwiegend diffusiv	Diffusiv
Membranen	High-flux	Low-flux	Low-flux/high-flux
Dialysatfluss	Niedrig (bei CVVHD)	Hoch	Niedrig
Flüssigkeitsentzug und Toxinelimination	Kontinuierlich (theoretisch)	Intermittierend (3–5 h)	Intermittierend 8–12 h
Antikoagulation	Kontinuierlich (theoretisch)	Intermittierend (3–5 h)	Intermittierend 8–12 h

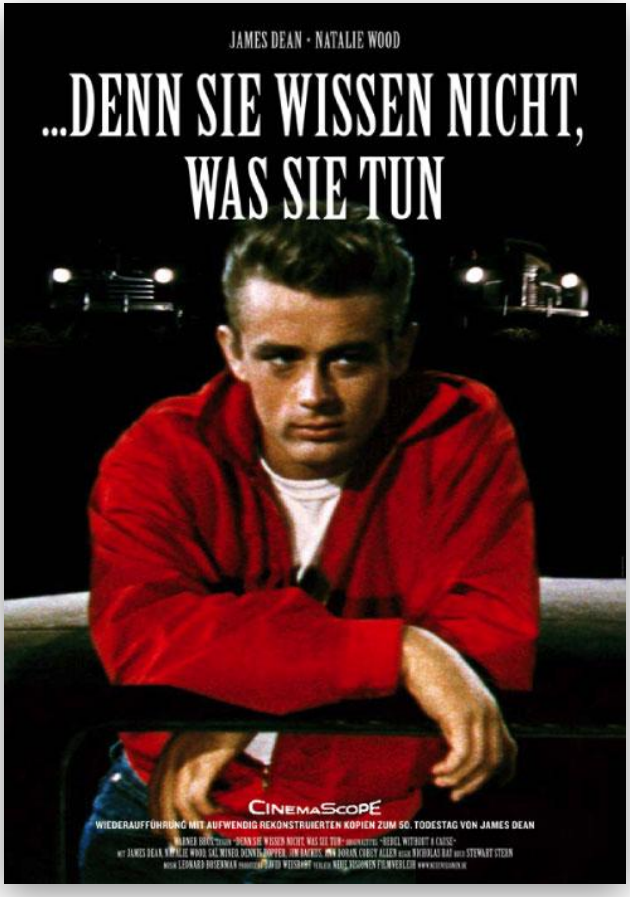
„Dialyse“ = „Auto“

„Dialyse“ = „Auto“

Practice patterns in the management of acute renal failure in the critically ill patient: an international survey

RICCI et al. *Nephrol Dial Transpl*, 21: 690–696, 2006





Antiinfektiva und Nierenersatzverfahren: Wie dosieren?

1) Die klinische Notwendigkeit

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4) Empfehlungen / Dosierungsrichtlinien

Vancomycin

Indication: invasive gram-positive infections

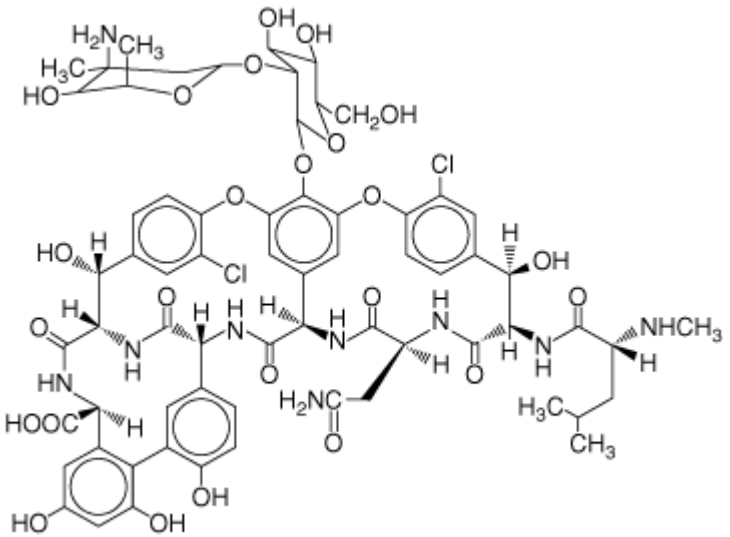
MW: 1449 Da

Protein bndg: 10-50%

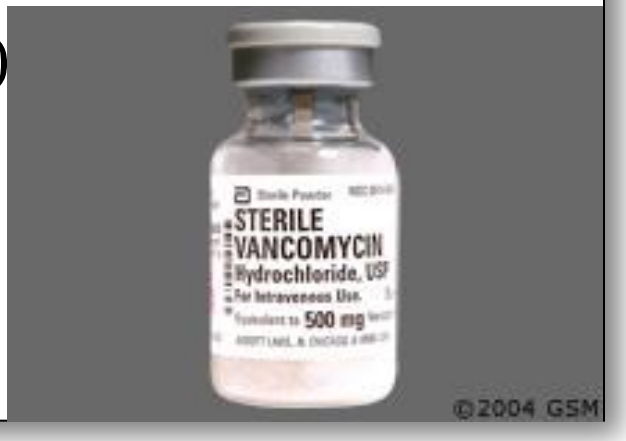
VOD: 0.6 L/kg

Elimination: urine
(80% to 90% as unchanged drug)

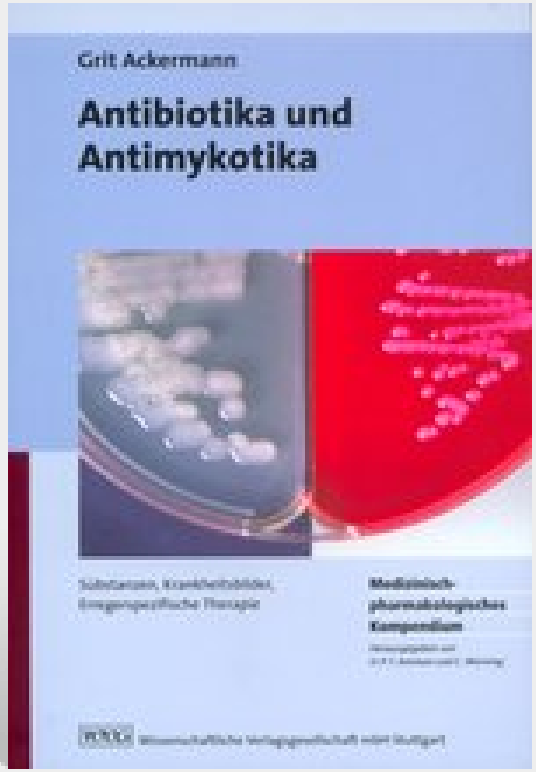
Half life: -4-6 h in healthy subjects
-200-250 h in ESRD



VANCOMYCIN



„Vancomycin bei Dialysepatienten alle 1-2 Wochen 1g“



Neuerscheinung

Ackermann, Grit (Hrsg.)

Antibiotika und Animykotika

Substanzen - Krankheitsbilder - erreger

Medizinisch-pharmakologisches Kompen

Band 8

ISBN 978-3-8047-2494-5

Breitband oder gezielter Einsatz?

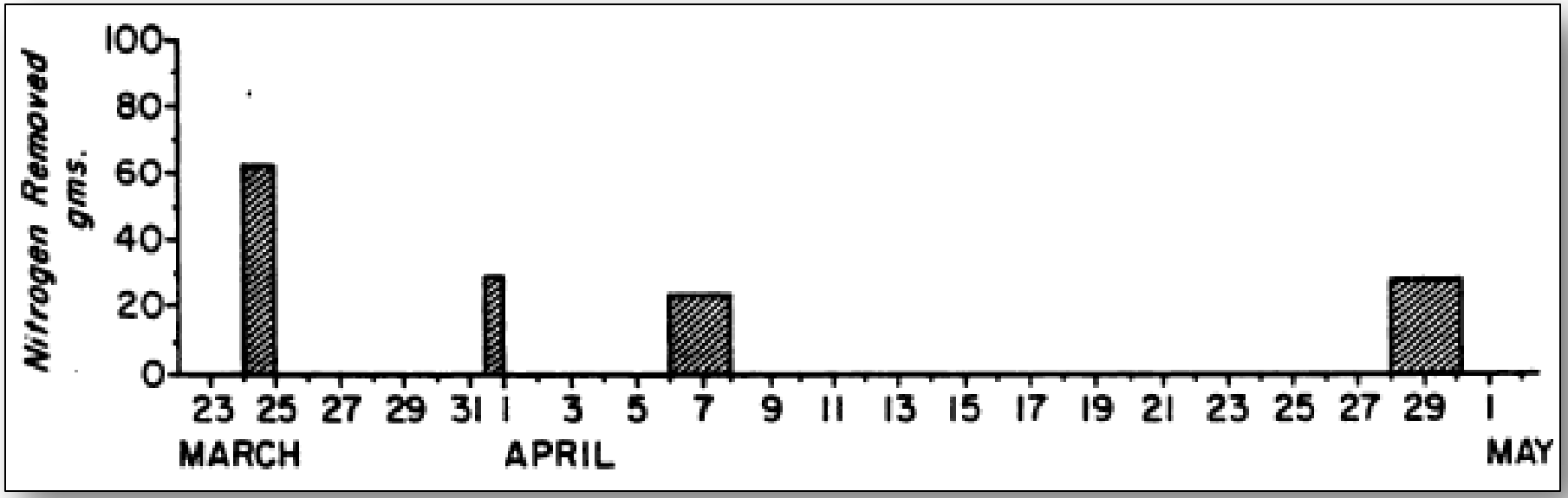
Der richtige Einsatz eines Antibiotikums
Fingerspitzengefühl, denn die Therapie s
kostengünstig und für den Patienten gut verträglich sein.
Ein Spezialistenteam hat in dieser komplett neu verfassten 3. Auflage alle Fakten zu Antibiotika und Antimykotika sowie Antituberkulotika für Sie zusammengestellt:

- Daten zur Pharmakokinetik und Dosierungen sämtlicher Wirkstoffe, auch für Patienten mit Nierenfunktionsstörungen,

The treatment of chronic uremia by means of intermittent hemodialysis: a preliminary report

SCRIBNER et al. ***Trans. Am. Soc. Antif. Intern. Organs 6: 114-122, 1960***

……on the fifth day of the infection, he was admitted to the hospital and started on a program of Vancomycin 1 .0 grams every 48 hours. The signs of infection cleared…….



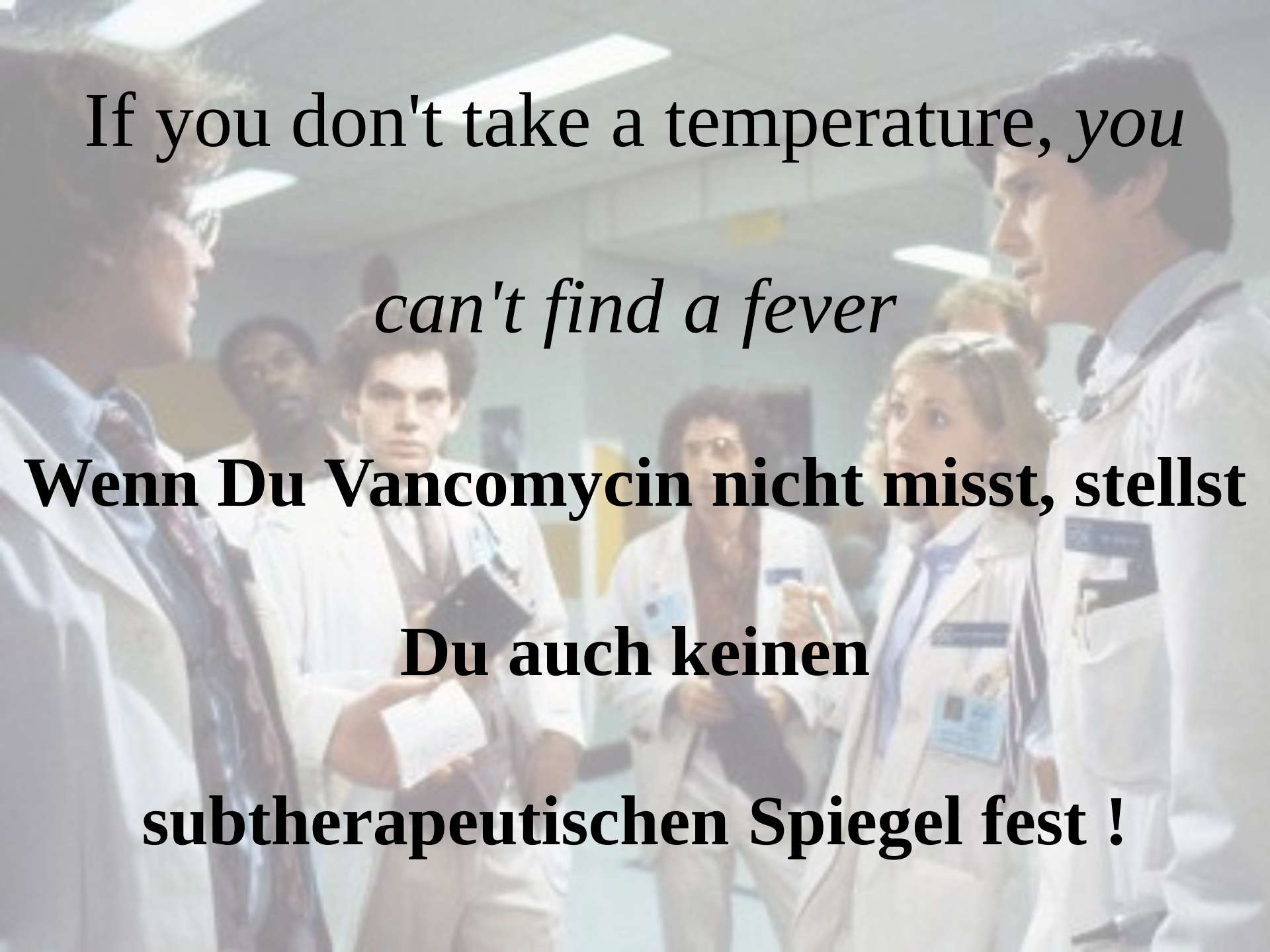
Markedly increased clearance of vancomycin during hemodialysis using polysulfone dialyzers

LANESE et al. *Kidney Int* 35(6):1409-12, 1989

Vancomycin Dosing in Patients on Intermittent Hemodialysis

VANDECASTEELE et al. *Seminars in Dialysis* 24:50-55, 2011

A weight-based loading dose of 20–25 mg⁄kg seems the most appropriate, with a preference for the higher dose range in patients with severe sepsis or higher BMI.



If you don't take a temperature, *you*

can't find a fever

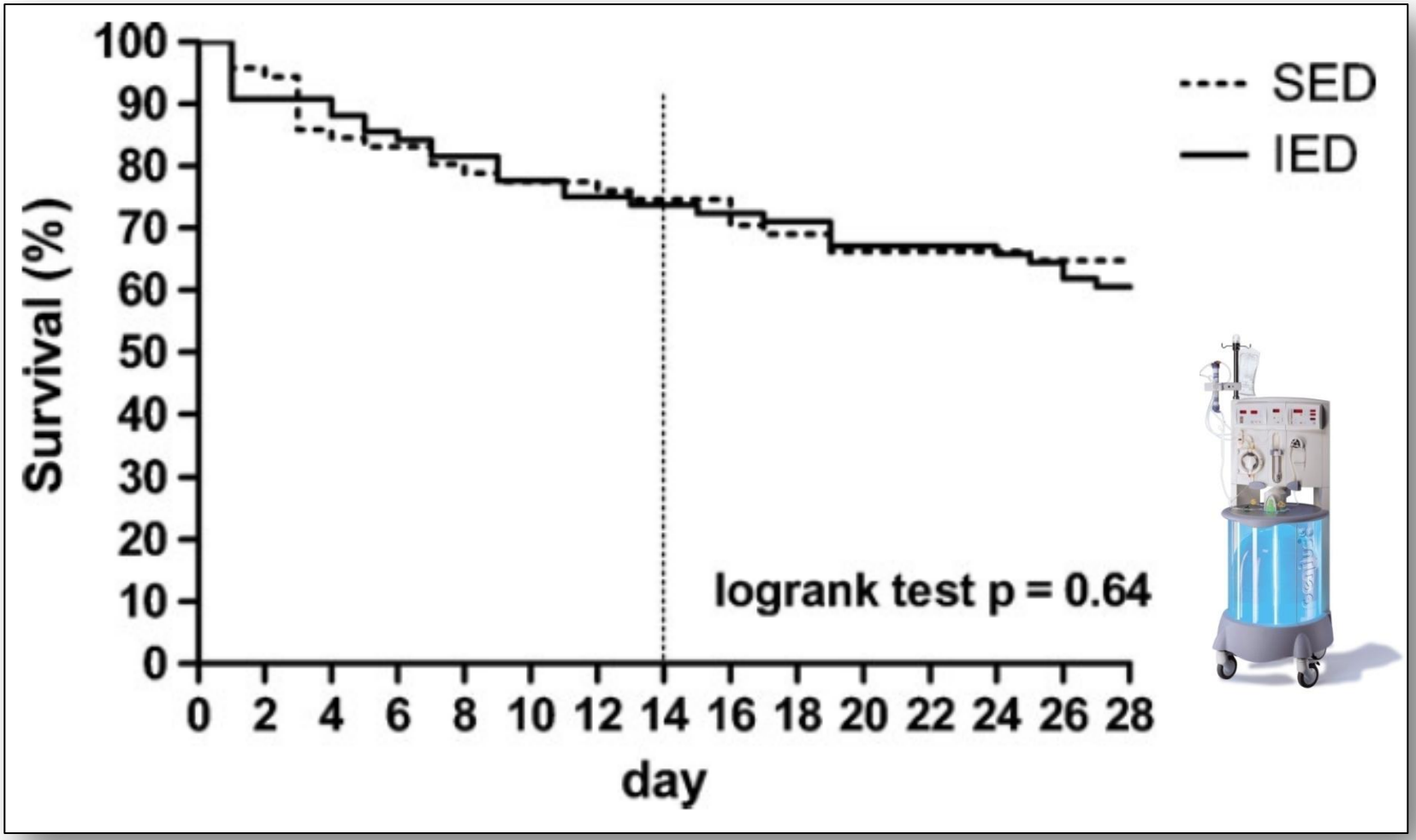
Wenn Du Vancomycin nicht misst, stellst

Du auch keinen

subtherapeutischen Spiegel fest !

The Hannover-Dialysis-Outcome (HAN-D-OUT)-study: Comparison of standard versus intensified extended dialysis in treatment of patients with AKI in the ICU

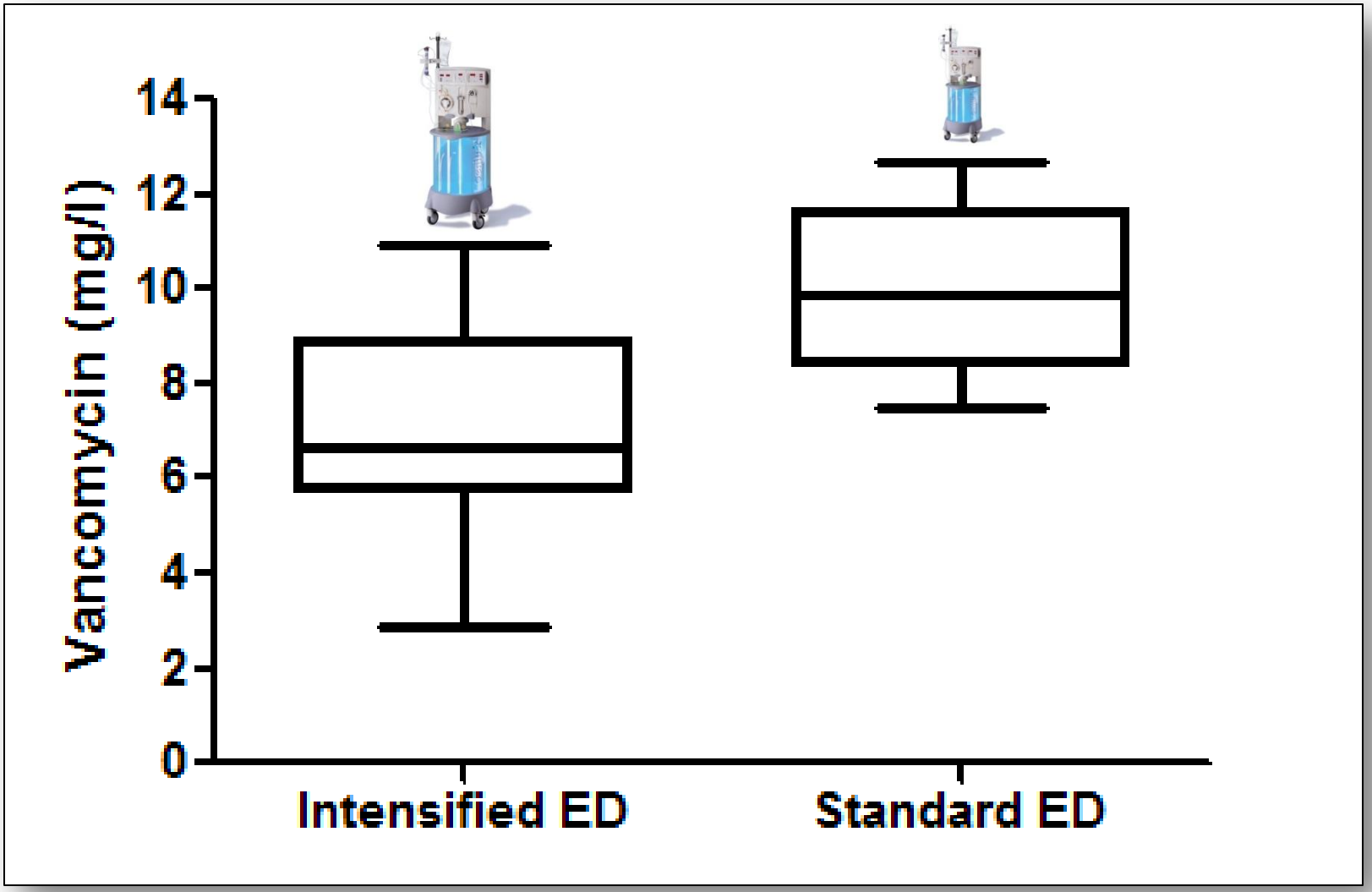
HAFER et al. *Nephrol Dial Transplant.* 24(7):2179-86, 2009



Medizinische Hochschule Hannover

Vancomycin concentration in the Hannover-Dialysis-Outcome (HAN-D-OUT)-study

unpublished



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Meropenem / Meronem ®

Indication: invasive gram-positive and gram negative infections ß—lactamase producers and pseudomonas aeruginosa

MW: 437 Da

Protein bndg: 2 %

VOD: 0.21 L/kg

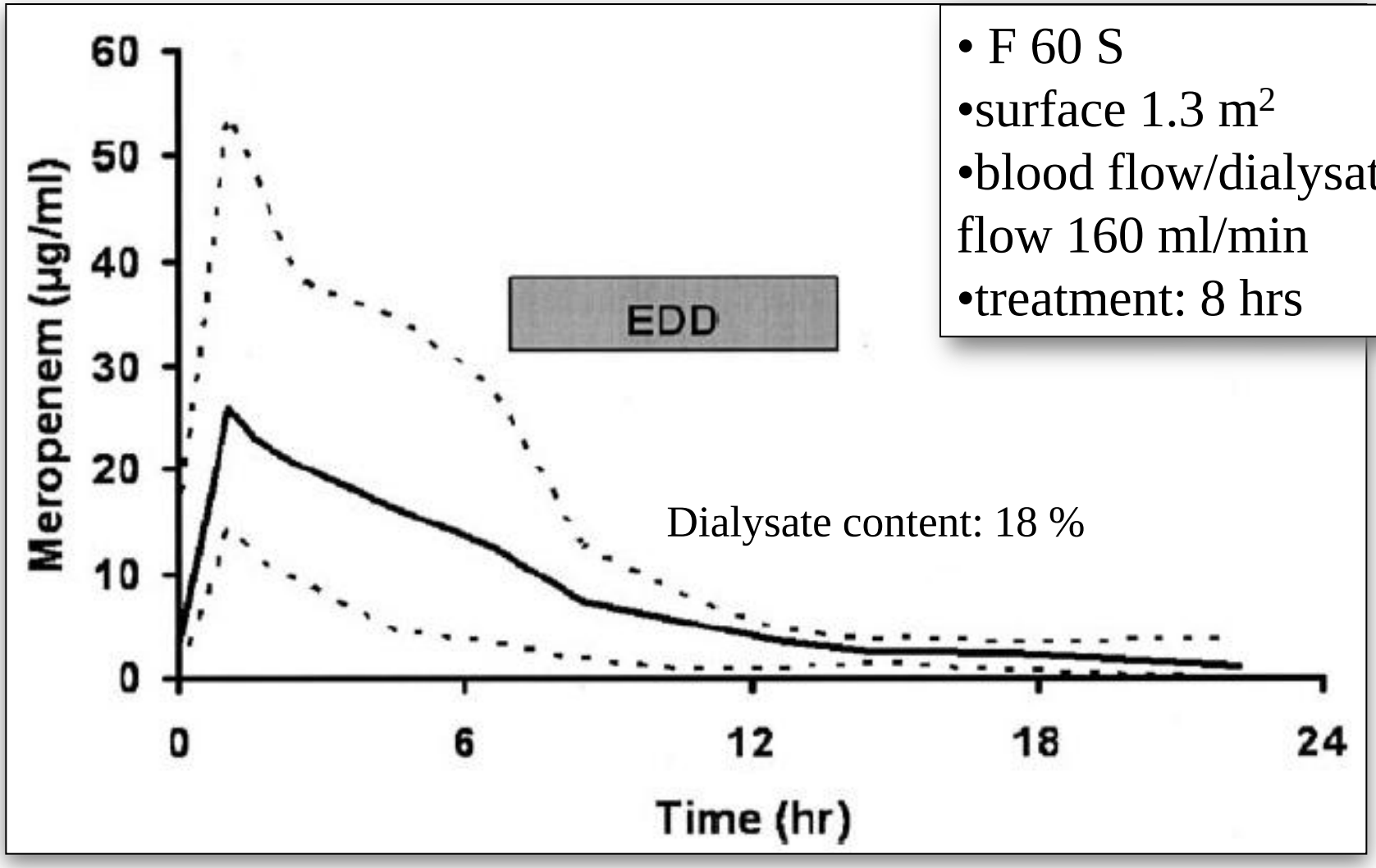
Elimination: 65% - 80% in urine as unchanged drug (glomerular filtration and tubular secretion)

Half life: 0.9 h in healthy volunteers

6.8 h in ESRD

Pharmacokinetics and total elimination of meropenem and vancomycin in ICU patients undergoing EDD

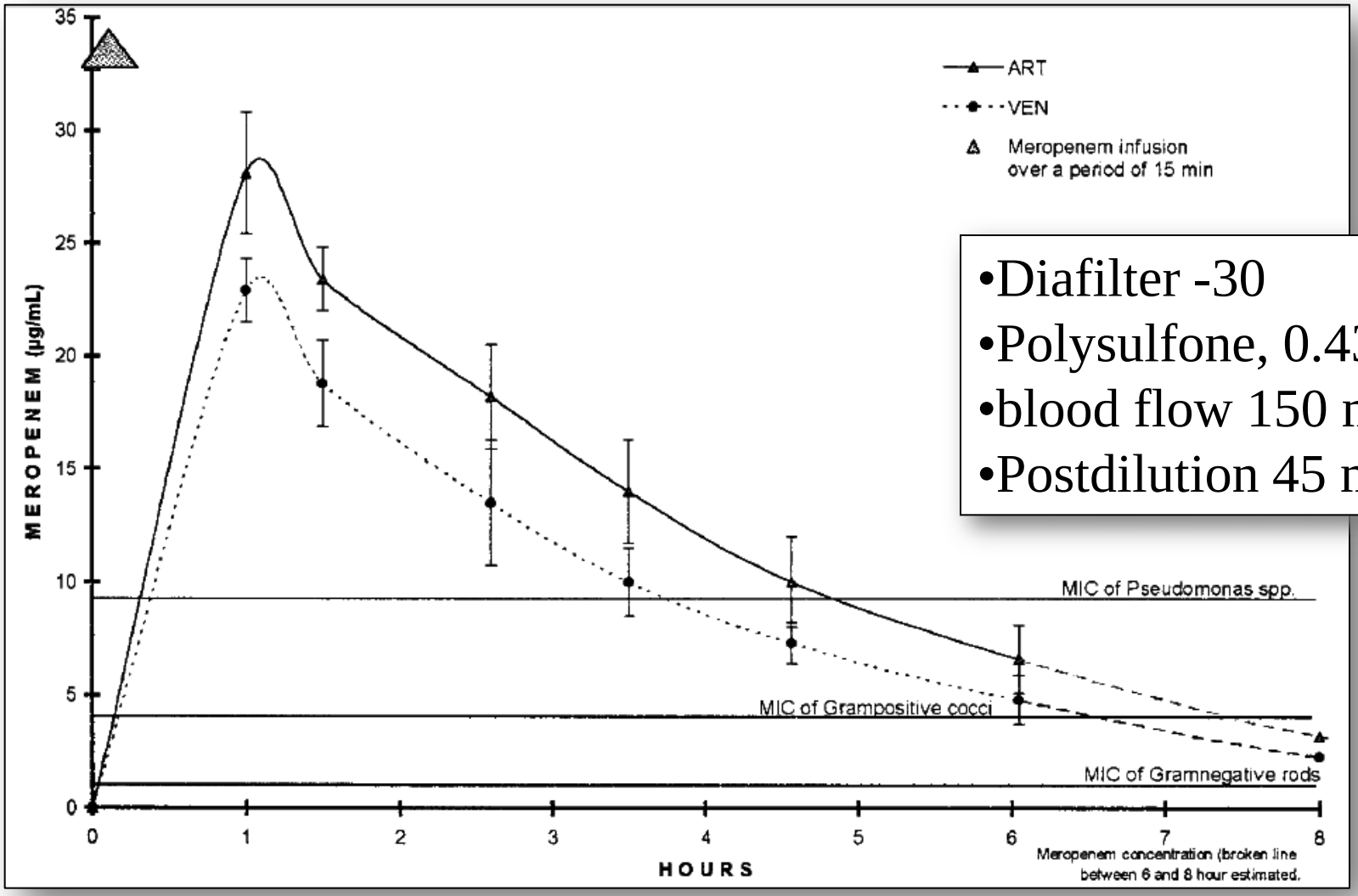
KIELSTEIN et al. *Critical Care Medicine* 34(1):51-56, 2006



- F 60 S
- surface 1.3 m^2
- blood flow/dialysate flow 160 ml/min
- treatment: 8 hrs

Single-Dose Pharmacokinetics of Meropenem during Continuous Venovenous Hemofiltration

THALHAMMER et al. *Antimicrob Agents Chemother* 42:2417–2420, 1998



- Diafilter -30
- Polysulfone, 0.43 m^2
- blood flow 150 ml/min
- Postdilution 45 ml/min

Meropenem / Meronem ®

	PubMed www.pub
No renal impairment	1g / 8 h
IHD + after HD	0.5 g / 24 h 0.5 g
CVVH	1g / 8 h
SLED	1g / 8 h

Ampicillin & Sulbactam / Unasyn ®

Indication: -skin and skin-structure infections
- respiratory infections

MW: ampicillin (365.4 D)
sulbactam (250.0 D)

Protein bndg: ampicillin 28 % / sulbactam 38 %

Elimination: urine (60% as unchanged drug)

Half life: -1.4 / 1.7 hrs in healthy subjects
-17 / 15 hrs in ESRD

Ampicillin & Sulbactam / Unasyn ®

UNASYN Dosage Guide For Patients With Renal Impairment

Creatinine Clearance ($mL/min/1.73m^2$)	Ampicillin/Sulbactam Half-Life (Hours)	Recommended UNASYN Dosage
≥30	1	1.5–3.0 g q 6h-q 8h
15–29	5	1.5–3.0 g q 12h
5–14	9	1.5–3.0 g q 24h

Pharmacokinetics of ampicillin (2.0 grams) and sulbactam (1.0 gram) coadministered to subjects with normal and abnormal renal function and with ESRD on hemodialysis.

BLUM et al. *Antimicrob Agents Chemother* 33(9):1470-6, 1989

- patients weighed 100 to 225 lb (45.4 to 102.3 kg)

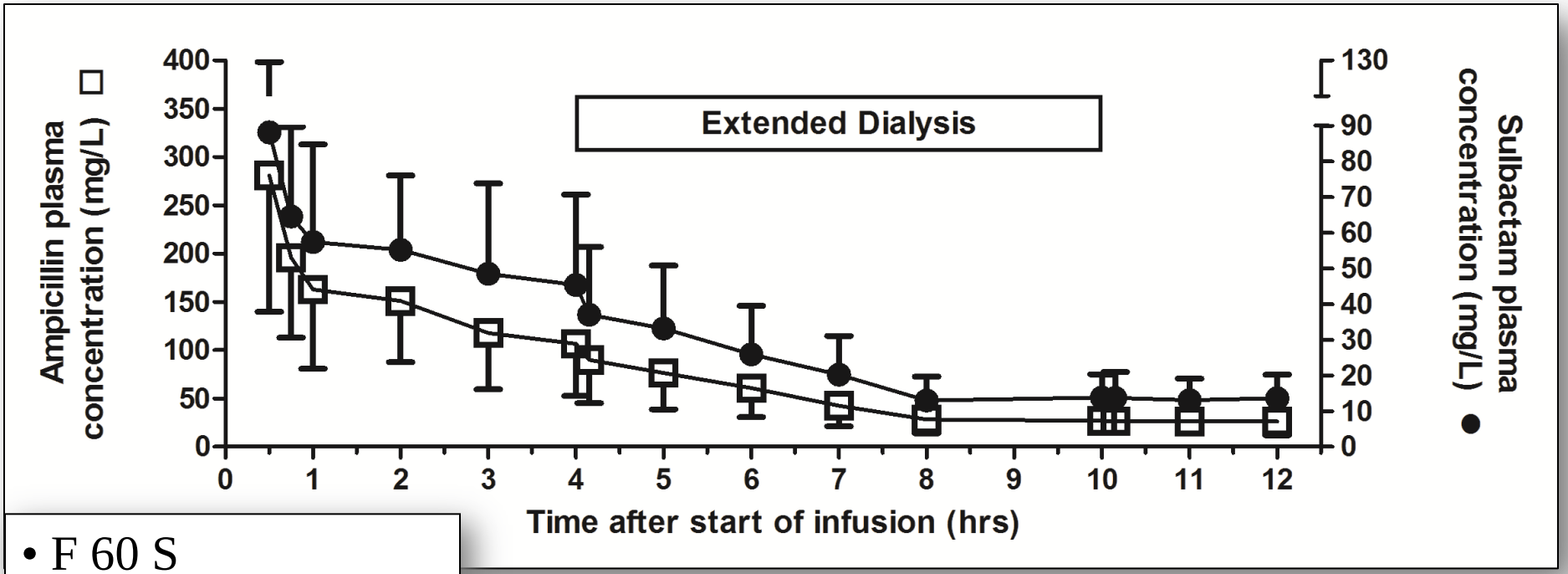
- the dialyzer used was the C-DAK model 3500, 1.0 m^2…"

- blood flow was 200 ml/min and dialysate flow was 500 ml/min for all four subjects.

- hemodialysis patients had normal laboratory tests except that hematocrit values as low as 22% were accepted.

Pharmacokinetics of Ampicillin/Sulbactam in critically ill patients with AKI undergoing extended dialysis

LORENZEN et al., ***Clin J Am Soc Nephrol. 2012 Jan 5. [Epub ahead of print]***



- F 60 S
- surface 1.3 m^2
- blood flow/dialysate flow 160 ml/min

Ampicillin / Sulbactam (Unacid ®)

	PubMed www.pub
No renal impairment	3-4 x 3 g
IHD	1 x 3 g
CVVH	-
SLED	2 x 3 g

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Urämietoxine
Antibiotika
Antibiotika
Urämietoxine

Dosierungsrichtlinien aus der Zeit der Schallplatte für Nierenersatzverfahren der i-Phone Ära?

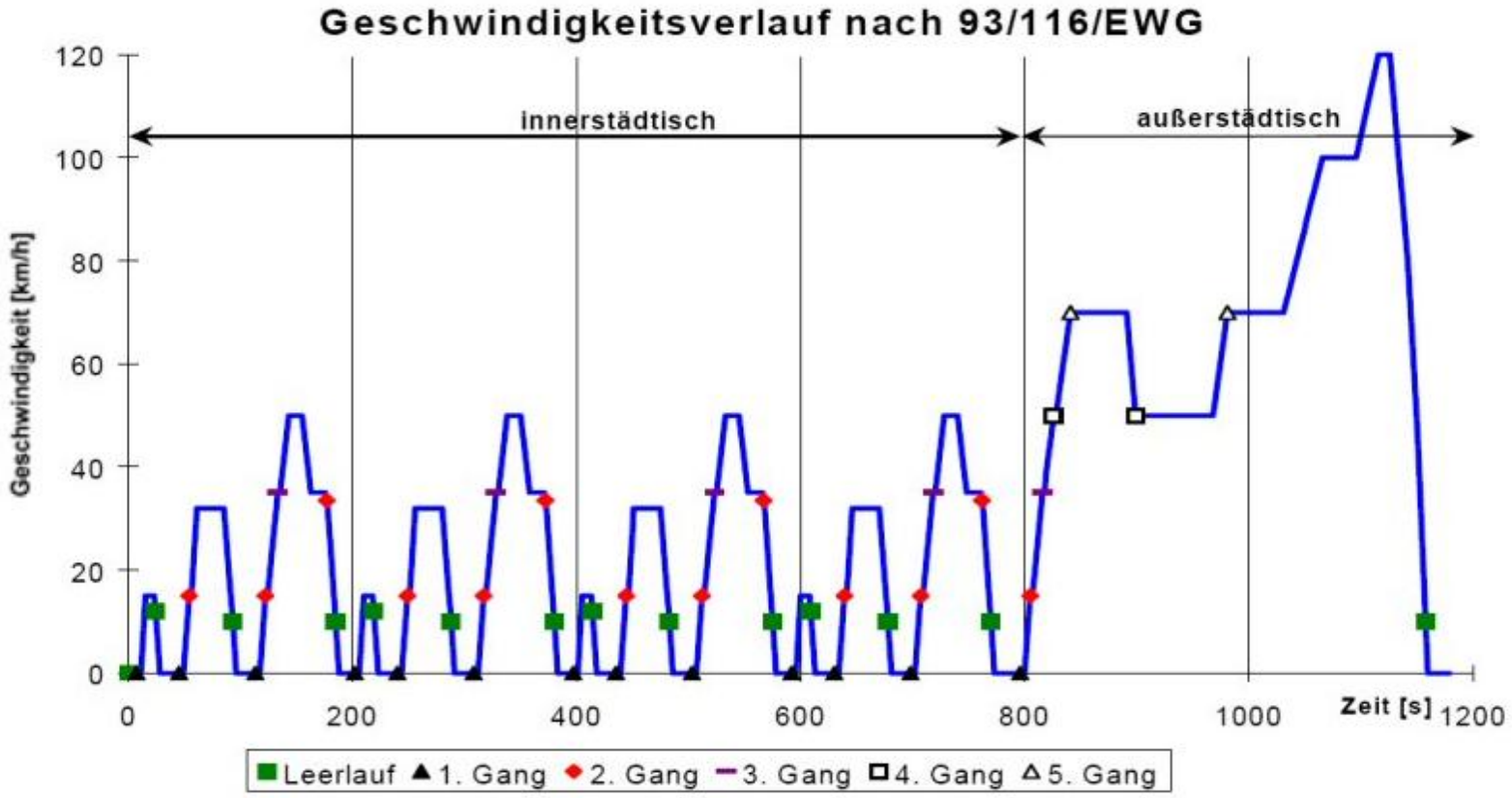
Antiobitikadosierung bei RRT
Allgemeine Grundsätze

1. **Immer (mindestens) volle Initialdosis des Antibiotikums geben**

   Effektivität = Medikament * Conzentration^2 E=m*c^2
2. **Individuell verordnen (pro kg KG dosieren, Nebenwirkungen)**
3. **Renale Rest-Funktion beachten (bei nephrotoxischen Meds.)**
4. **Bestimmung der Plasmaspiegel TDM UND Dosis-Adaptation**
5. **Umstellung auf orale Therapie 1 Tag nach deutlicher klinischer Besserung wenn möglich (Verfügbarkeit, Compliance, etc.)**
6. **Dosisadaptation bei Veränderung der GFR oder RRT**
7. **Beendigung der Therapie nach Klinik &Procalcitonin im Verlauf**

“Neuer europäischer Fahrzyklus“ (NEFZ)

ADAC

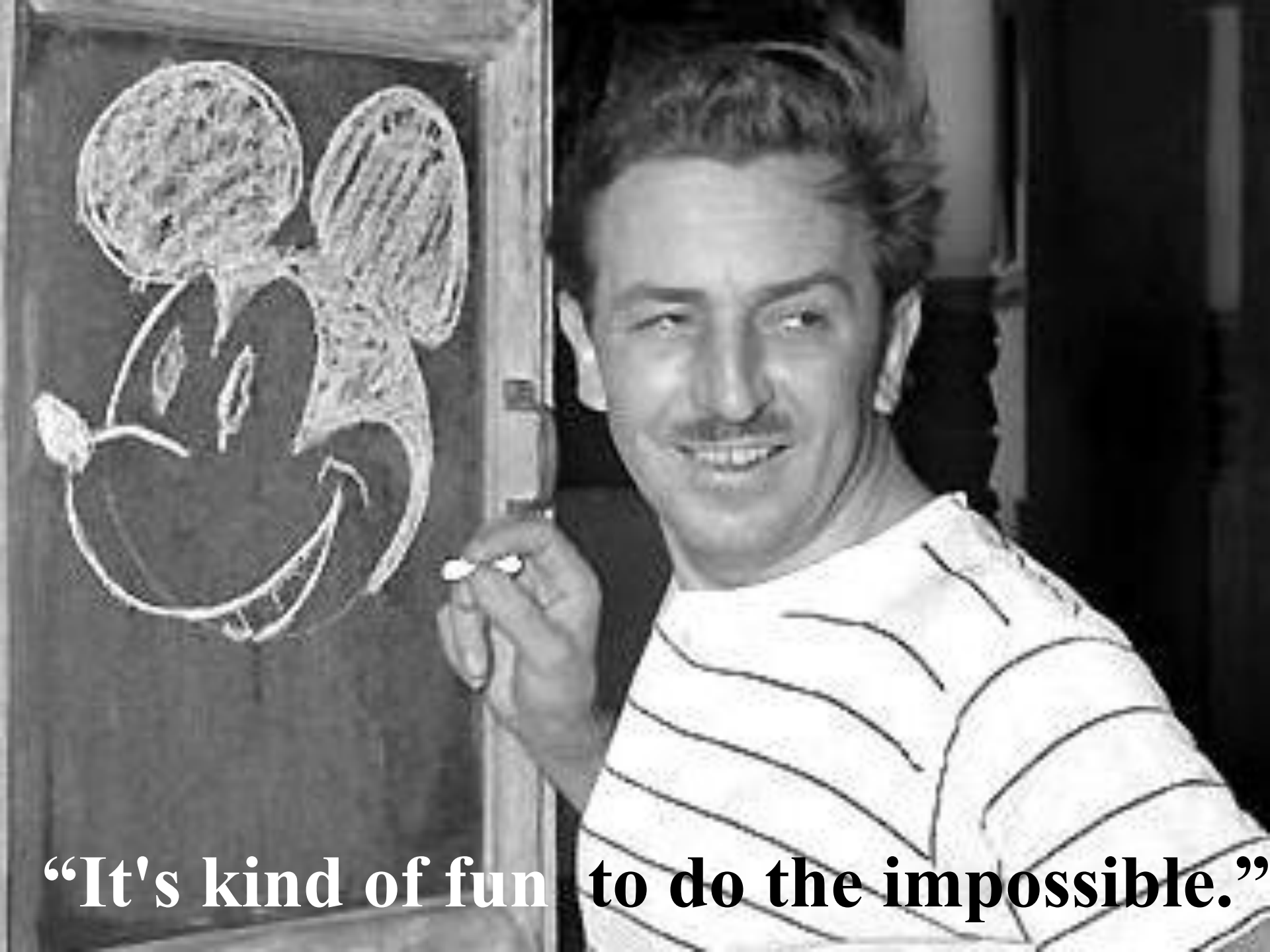


http://www.kidney-international.org

Drug dosing consideration in patients with acute and chronic kidney disease—a clinical update from Kidney Disease: Improving Global Outcomes (KDIGO)

Gary R. Matzke[1], George R. Aronoff[2], Arthur J. Atkinson Jr[3], William M. Bennett[4], Brian S. Decker[5], Kai-Uwe Eckardt[6], Thomas Golper[7], Darren W. Grabe[8], Bertram Kasiske[9], Frieder Keller[10], Jan T. Kielstein[11], Ravindra Mehta[12], Bruce A. Mueller[13], Deborah A. Pasko[14], Franz Schaefer[15], Domenic A. Sica[16], Lesley A. Inker[17], Jason G. Umans[18] and Patrick Murray[19]

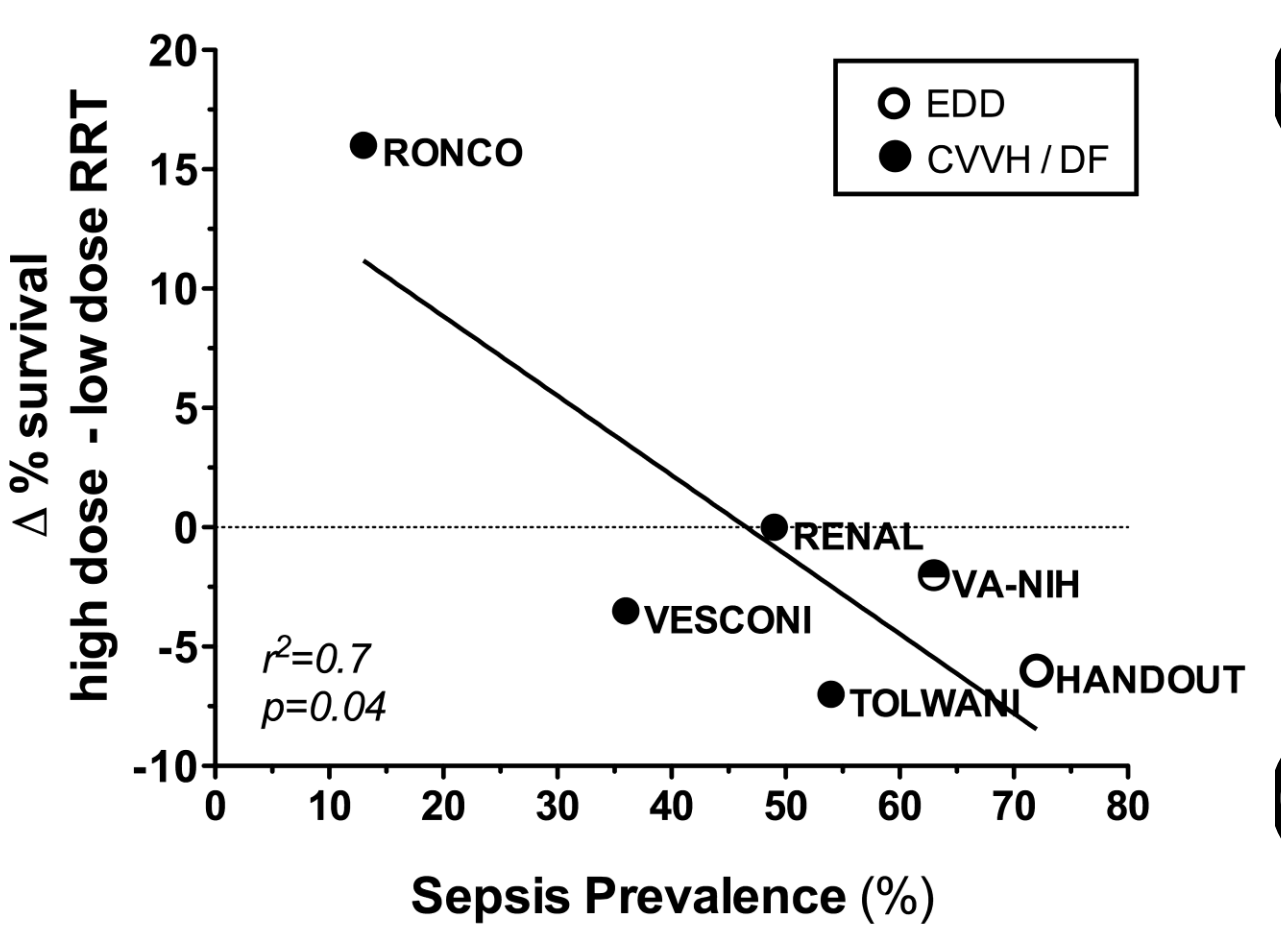
[1]Virginia Commonwealth University, School of Pharmacy, Richmond, Virginia, USA; [2]University of Louisville, Louisville, Kentucky, USA; [3]Northwestern University, Chicago, Illinois, USA; [4]Legacy Transplant Services, Portland, Oregon, USA; [5]Indiana University School of Medicine, Indianapolis, Indiana, USA; [6]University of Erlangen-Nuremberg, Erlangen, Germany; [7]Vanderbilt Medical Center, Nashville, Tennessee, USA; [8]Albany College of Pharmacy and Health Sciences, Albany, New York, USA; [9]Hennepin County Medical Center, Minneapolis, Minnesota, USA; [10]Nephrology, Ulm University, Ulm, Germany; [11]Medical College of Hannover, Hannover, Germany; [12]University of California San Diego, San Diego, California, USA; [13]University of Michigan-School of Pharmacy, Ann Arbor, Michigan, USA; [14]University of Michigan Health System, Ann Arbor, Michigan USA; [15]Heidelberg University Hospital, Heidelberg, Germany; [16]Virginia Commonwealth University, School of Medicine, Richmond, Virginia, USA; [17]Tufts Medical Center, Boston, Massachusetts, USA; [18]Georgetown University Medical Center, Washington, DC, USA; [19]University College, Dublin School of Medicine and Medical Science, Dublin, Ireland


“It's kind of fun to do the impossible.”

Antibiotikadosierung unter CVVH und GENIUS-Dialyse

KielBurk-Liste zur angepassten Medikamentendosierung bei CRRT- und GENIUS® SLEDD-Behandlungen										
Substanz/ Handelsname	**PB (%)**	**MW**	**TDM**	**Dosis GFR >90**	**Dosis IHD**	**Dosis CRRT**	**Dosis SLEDD**	**Q_{Blut} / $Q_{Dialysat}$**	**Filter**	**T (h)**
Anidulafungin/ Ecalta™	84	1140	-	100 mg/ 24 h	100 mg/ 24 h[1]	Keine Daten	100 mg/ 24 h[2]	180/180	Fresenius Polysulfon 1,3 m²	7 h
Ampicillin/Sulbactam Unacid™	28/45	371/255	-	3 g / 6 h[3]	3 g / 24 h	Keine Daten	3 g / 8 h[4]	160/160	Fresenius Polysulfon 1,3 m²	8 h
Daptomycin/ Cubicin™	92	1620	-	6 mg/kg/d	6 mg/kg nach HD[5]	Keine Daten	6 mg/kg/d[6]	160/160	Fresenius Polysulfon 1,3 m²	8 h
Ertapenem/ Invanz™	90-95	497	-	1.0 g/d	500 mg/d[7]	Keine Daten	1.0 g/d[8]	160/160	Fresenius Polysulfon 1,3 m²	8 h
Levofloxacin/ Tavanic™	24-38	370	-	250-500 mg / 12 h	250-500 mg / 48 h[9]	500 mg / 24 h[10]	500 mg/ 24 h[11]	160/160	Fresenius Polysulfon 1,3 m²	8 h
Linezolid/ Zyvoxid™	31	337	(+)	600 mg / 12 h	600 mg / 12 h	600 mg / 12 h[12]	600 mg / 12 h[13]	110-150 110-150	Fresenius Polysulfon 1,3 m²	12-24 h
Meropenem/ Meronem™	2	437	-	1 g / 8 h	0.5 g/d 0.5 g nach HD	1g / 8 h[14]	1 g / 12 h[15]	160/160	Fresenius Polysulfon 1,3 m²	8 h
Moxifloxacin/ Avalox™	54	437	-	400 mg/d	400 mg/d	400 mg/d[16;17]	400 mg/d[11]	160/160	Fresenius Polysulfon 1,3 m²	8 h
Vancomycin/ Vancomycin™	10-50	1449	++	1000 mg/12h	1000 mg nach jeder HD	1000 mg/ 12h[18]	1000 mg/ 12h[15]	160/160	Fresenius Polysulfon 1,3 m²	8 h
nach **Kiel**stein und **Burk**hardt										

Renal Replacement Trauma
Reverse Paracelsus
Kielstein & David, submitted



Medizinische Hochschule Hannover

Daptomycin / Cubicin ®

Indication: -skin and skin-structure infections
-right heart endocarditis
-MRSA, sepsis

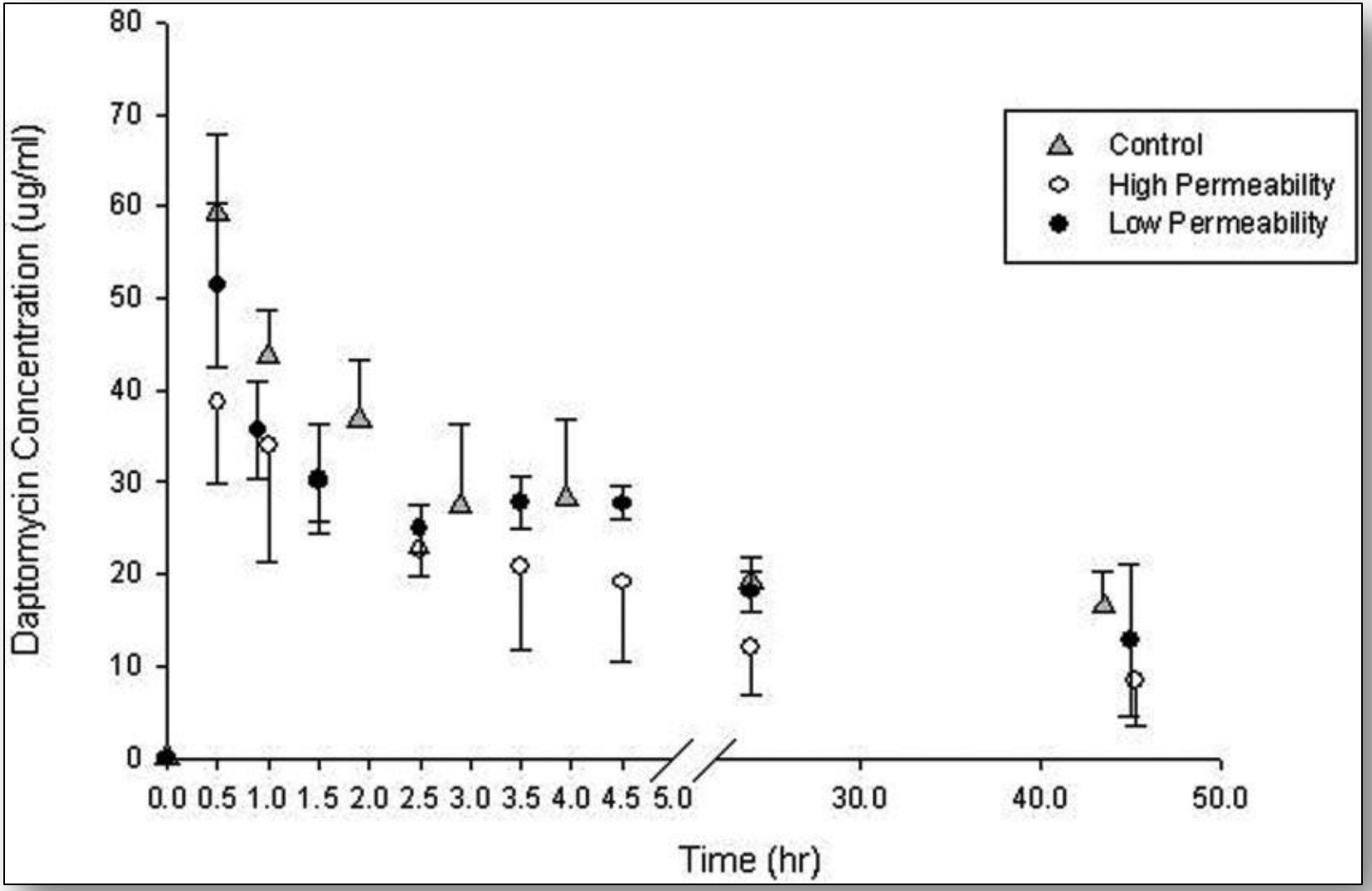
MW: 1620 Da
Protein bndg: 92 %
VOD: 0.01 L/kg

Elimination: urine
(80% to 90% as unchanged drug)

Half life: -7.8 hrs in healthy subjects
-29.3 hrs in ESRD

Intradialytic Administration of Daptomycin in End Stage Renal Disease Patients on Hemodialysis

SALAMA *CJASN* 4: 1190–1194, 2009



A simplified thrice weekly daptomycin dosing regimen for chronic hemodialysis patients

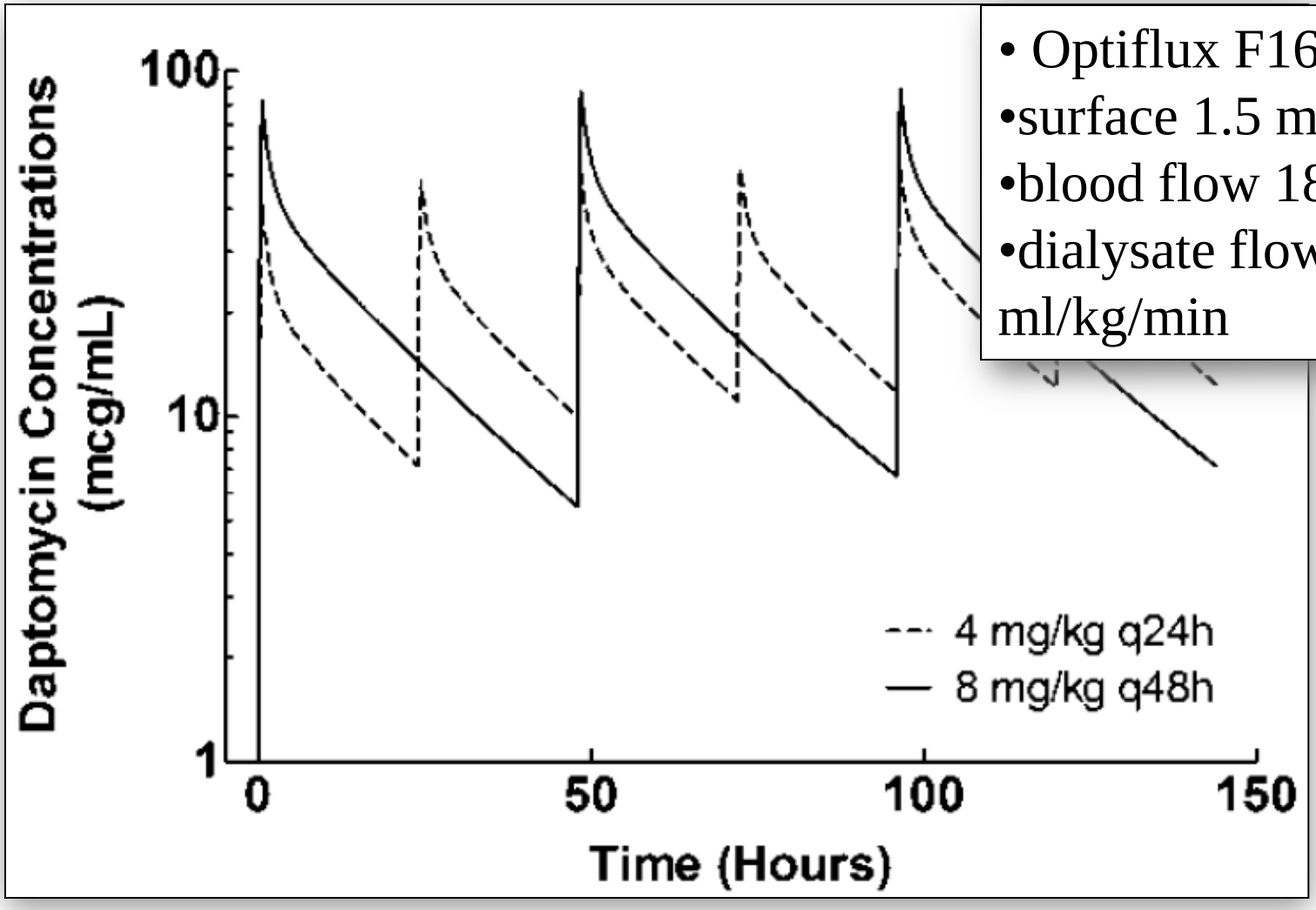
BURKHARDT & KIELSTEIN Expert Rev Anti Infect Ther, 8 (1), 2010

Table 1. Three-times weekly daptomycin dosing: differences depending on the dialyser used.

Flux	Recommended dose three-times weekly*	Dialyzer	Blood flow/ dialysate flow	Treatment time
Low flux	7 mg/kg body weight	F-8 1.8 m^2 Kuf 11 ml/h per mmHg polysulfone	400 ml/700 ml	?
High flux	9 mg/kg body weight	F-200NR 2.0 m^2 Kuf 62 ml/h per mmHg polysulfone	400 ml/700 ml	?

Daptomycin pharmacokinetics in critically ill patients receiving CVVHD

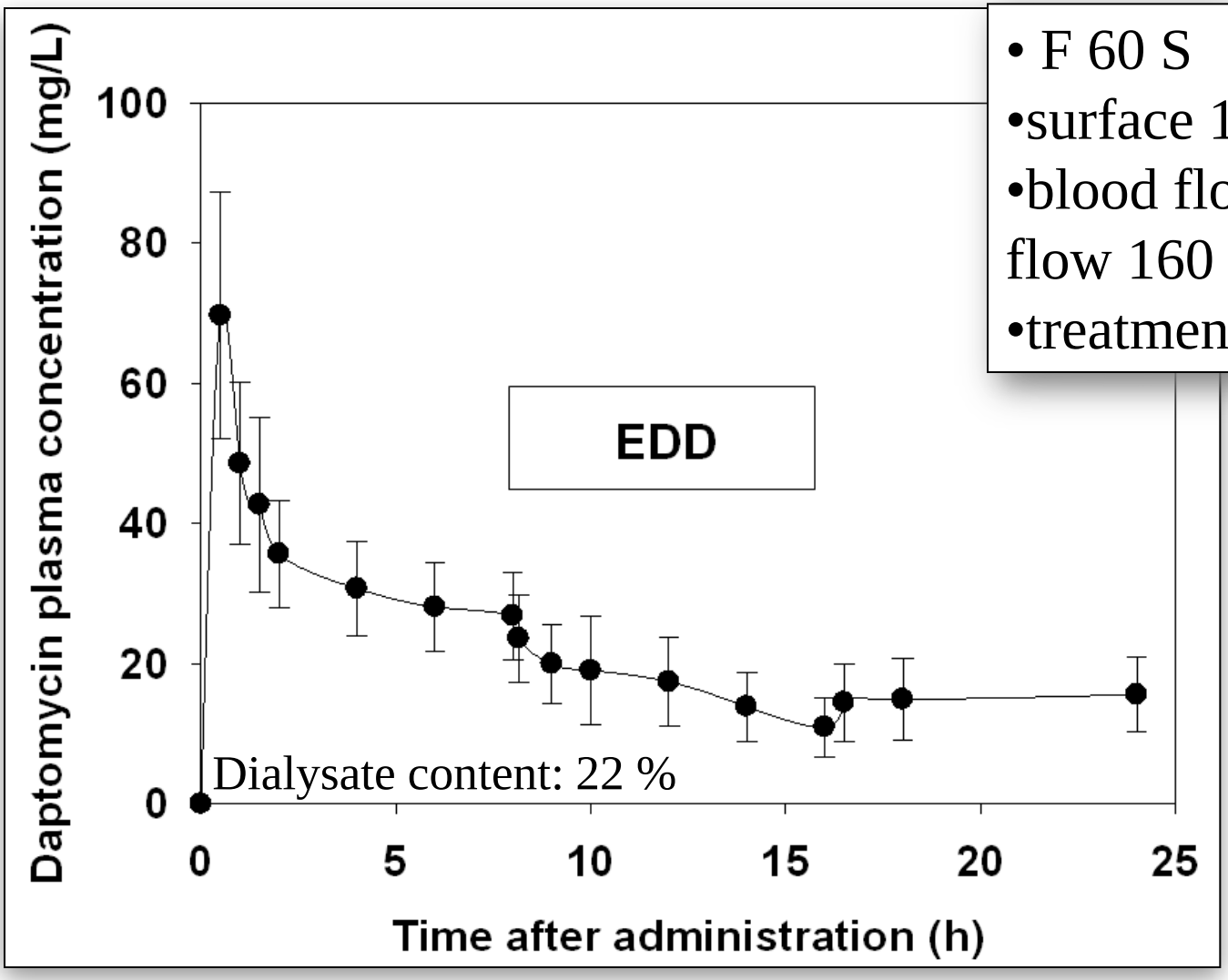
VILAY et al. *Crit Care Med*, 39:19 -25, 2011



- Optiflux F160 NR
- surface 1.5 m^2
- blood flow 180 ml/min
- dialysate flow 26 ml/kg/min

Elimination of daptomycin in septic patients in the ICU with acute kidney injury undergoing ED

KIELSTEIN et al., *Nephrol Dial Transplant*, 25: 1537–1541, 2010



- F 60 S
- surface 1.3 m^2
- blood flow/dialysate flow 160 ml/min
- treatment: 8 hrs

Daptomycin / Cubicin ®

	PubMed www.pub
No renal impairment	6 mg/kg/24 h
IHD	7-9 mg/kg post HD
CVVH	8 mg/kg/48 h
SLED	6 mg/kg/24 h

Linezolid / Zyvoxid ®

Indication: -skin and skin-structure infections
-pneumonia
-vancomycin-resistant strains of *Enterococcus faecalis*
-MRSA, sepsis

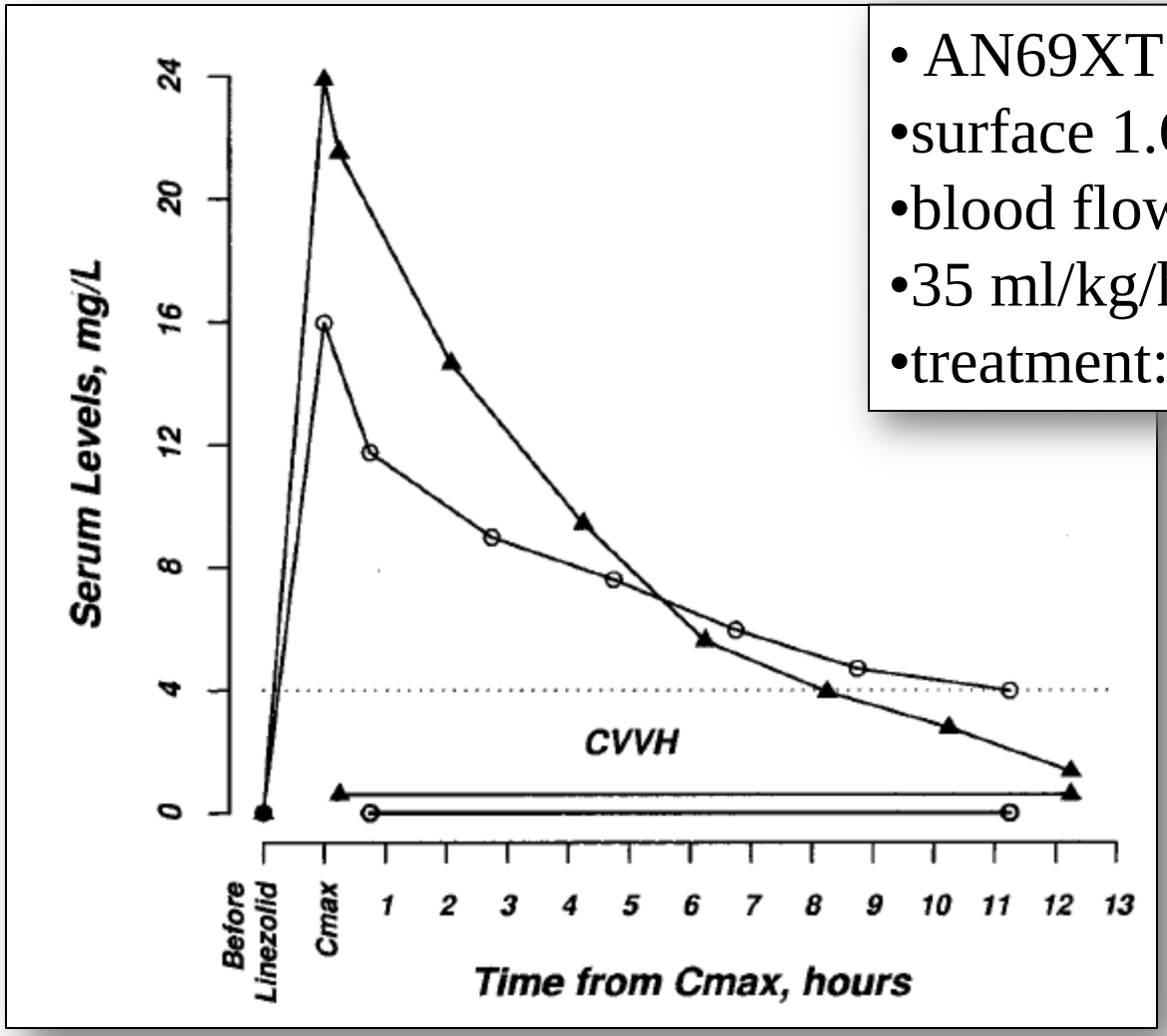
MW: 337 Da
Protein bndg: 31 %
VOD: 0.5-0.8 L/kg

Elimination: urine (30% as parent drug, 50% as metabolites)
liver 50 %

Half life: -4-5 hrs in healthy subjects

Removal of linezolid by conventional IHD, SLED, or CVVH in patients with acute renal failure

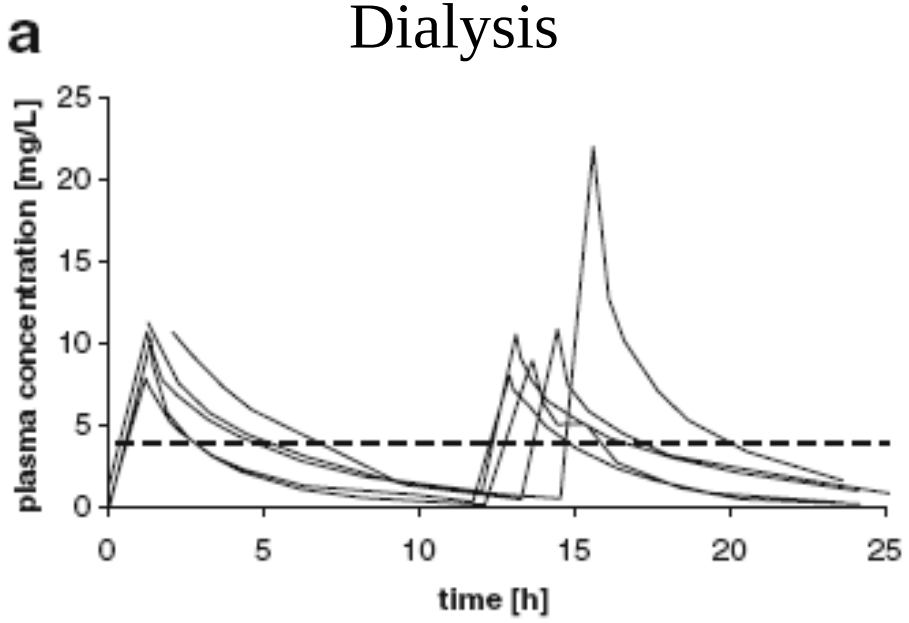
FIACCADORI et al. *Crit Care Med* 32:2437–2442, 2004

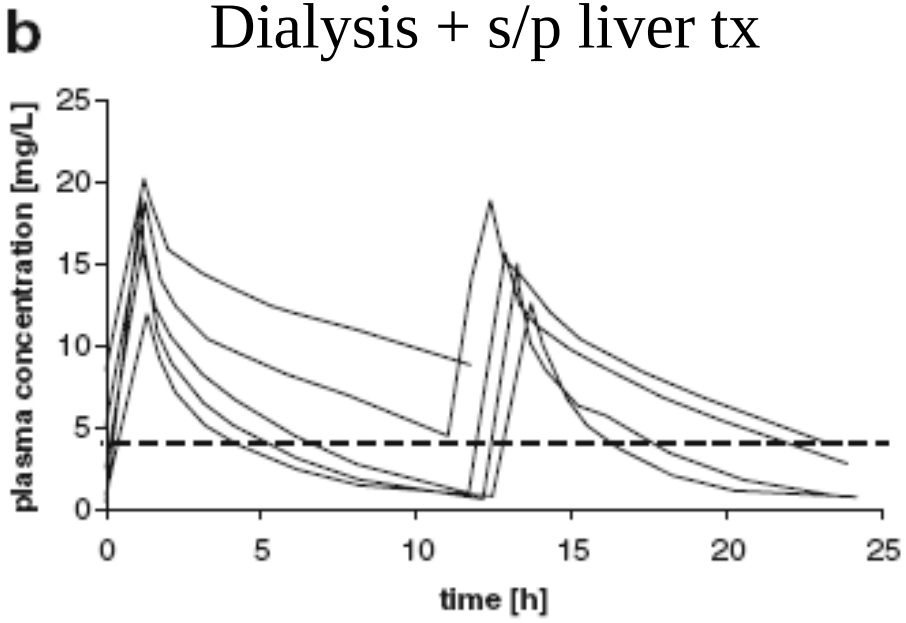


- AN69XT
- surface 1.65 m^2
- blood flow 150 ml/min
- 35 ml/kg/h pre-dilution
- treatment: 12 hrs

Pharmacokinetics of linezolid in septic patients with and without extended dialysis

SWOBODA et al. *Eur J Clin Parmacol* e-pub 16.12.2009





Pharmacokinetics of linezolid in septic patients with and without extended dialysis

SWOBODA et al. *Eur J Clin Parmacol* e-pub 16.12.2009

in the course of ED, linezolid plasma concentrations can be reduced to subtherapeutic values. Septic patients with and without ED—but not septic patients with liver transplantation/resection or patients with severe liver failure—may require higher doses. More data are necessary for the latter two groups of patients. The best method for achieving effective antimicrobial therapy in critically ill patients would be a TDM approach to dosing.

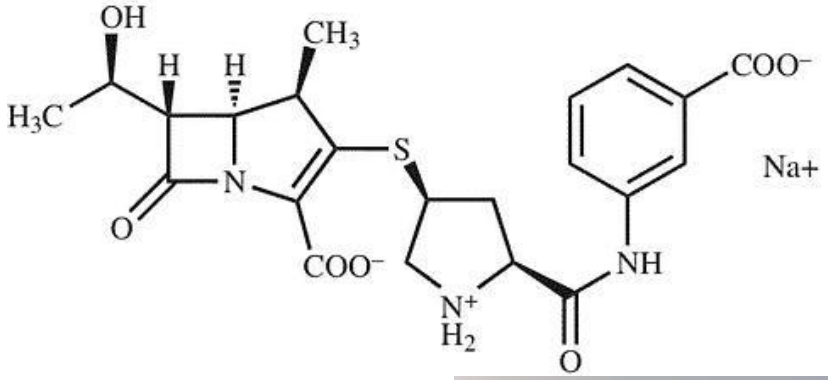
Ertapenem / Invanz ®

Indication: anaerobes, Gram-positives and Gram-negatives, incl. extended-spectrum β-lactamase (ESBL) and AmpC-producing Enterobacteriaceae

MW: 497 Da

Protein bndg: 85-95 %

VOD: 0.12 L/kg



Elimination: 80% urine

38 % unchanged

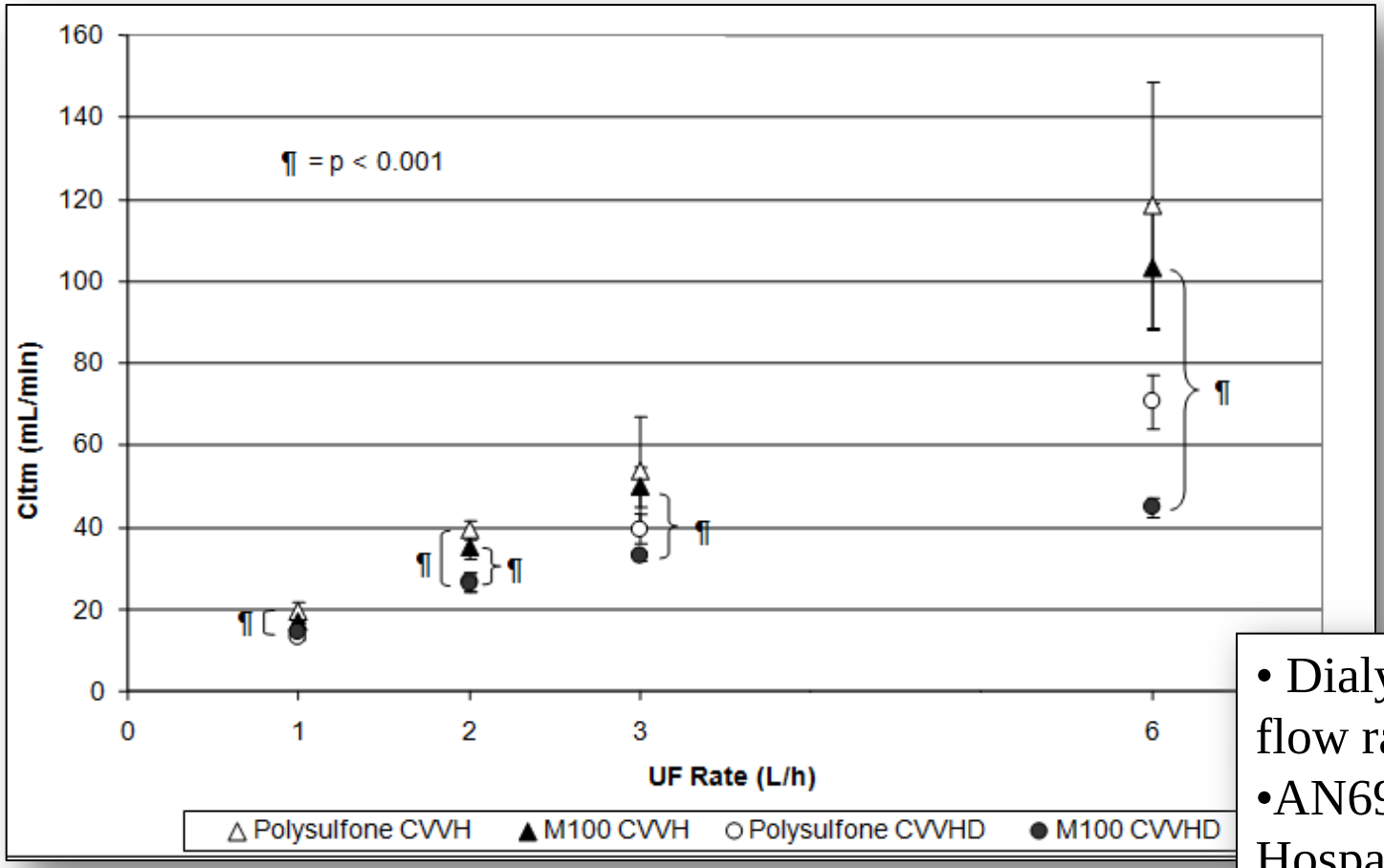
42 % hydrolytic metabolite

Half life: -3.8 hrs in healthy subjects

-14 hrs in ESRD

Ertapenem Clearance during Modeled Continuous Renal Replacement Therapy

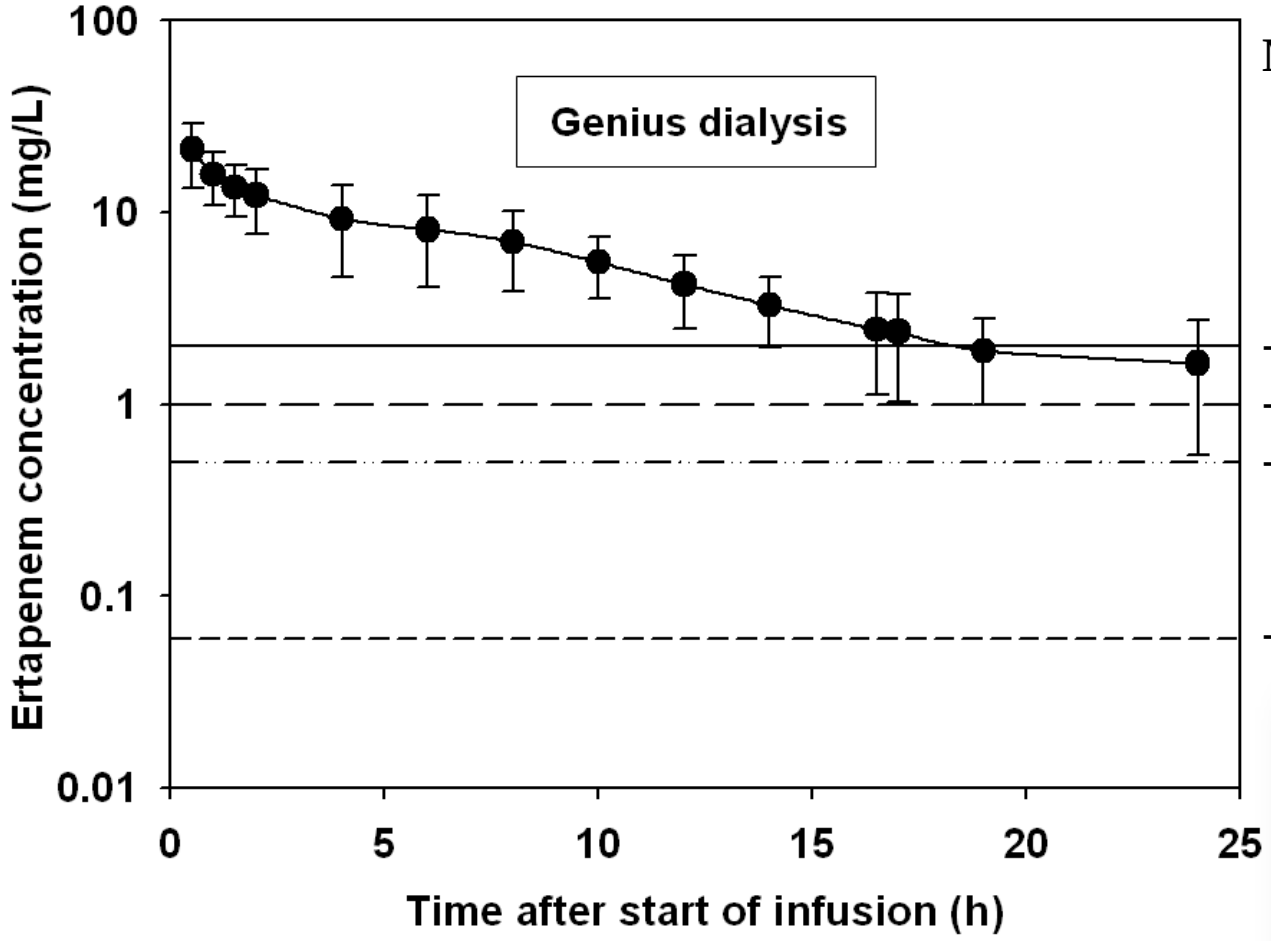
STEVENSON et al. *Int J Artif Organs* 31(12):1027-34, 2008



- Dialysate/ultrafiltrate flow rates (1, 2, 3, 6 L/hr)
- AN69 (Multiflow 100, Hospal) 1.0 m^2
- polysulfone (Optiflux F160, Fresenius)1.6 m^2

Ertapenem in patients with acute renal failure undergoing EDD

BURKHARDT et al. *NDT*, 24(1):267-71, 2009



MIC_{90} values for

-*Streptococcus pneumoniae*
-*Staphylococcus aureus*
-*Klebsiella pneumoniae*

-Enterobacteriaceae

- F 60 S
- surface 1.3 m^2
- blood flow/dialysate flow 160 ml/min
- treatment: 8 hrs

Ertapenem / Invanz ®

	PubMed www.pub
No renal impairment	1g / 24 h
IHD + after HD	0.5 g / 24 h 0.15 g
CVVH	1g / 24 h
SLED	1g / 24 h

Moxifloxacin / Avalox ®

Indication: -skin and skin-structure infections
-community acquired pneumonia / sinusitis
- complicated intra-abdominal infections

MW: 437.9 D
Protein bndg: 54%

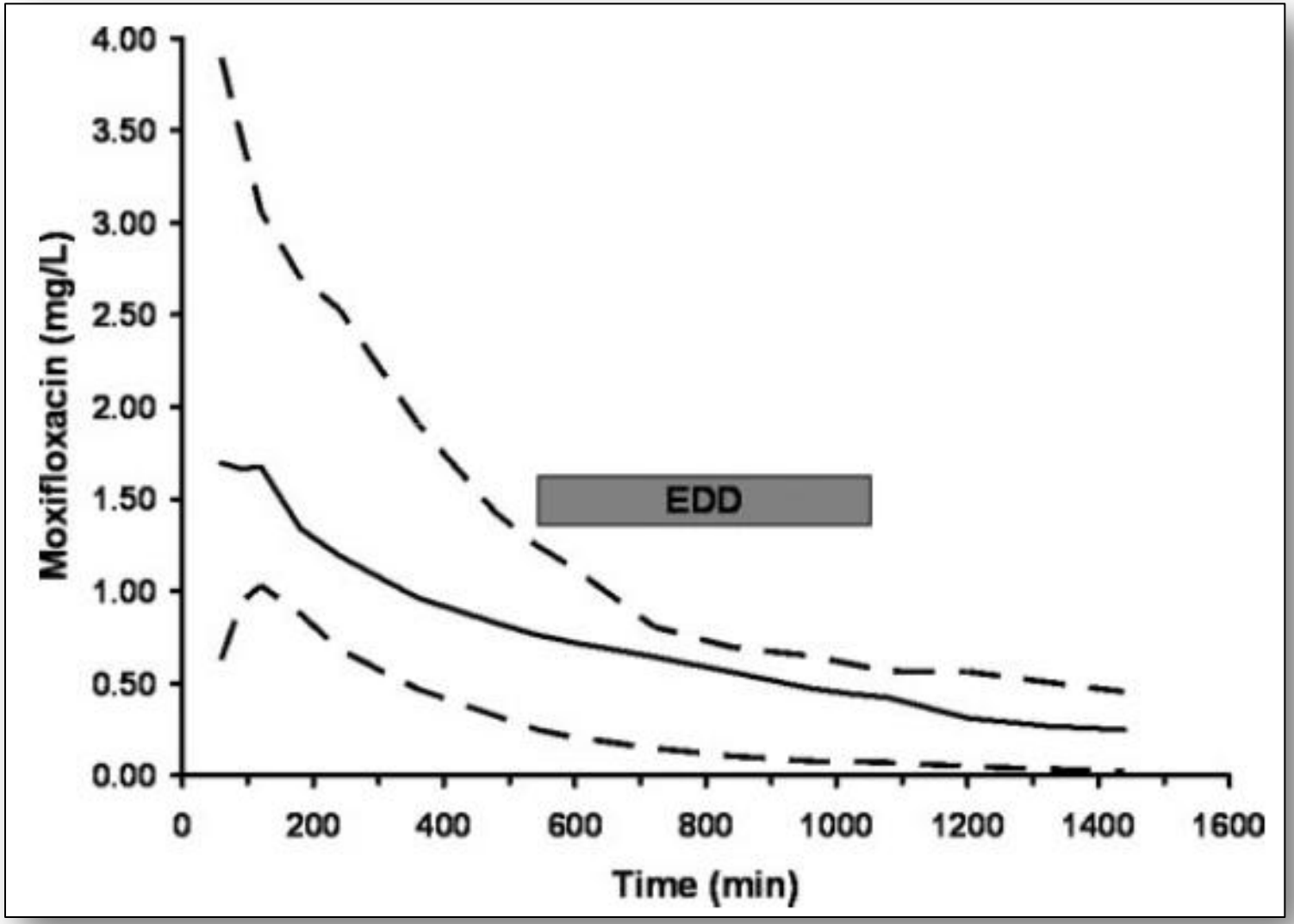
Elimination: 20 % urine as unchanged drug

Half life: -12 hrs in healthy subjects

Price: 400 mg i.v. = 36.61 € ORAL 3.37 € !!!!!!!!

Pharmacokinetics of Moxifloxacin and Levofloxacin in Intensive Care Unit Patients Who Have Acute Renal Failure and Undergo Extended Daily Dialysis

CZOCK et al. *Clin J Am Soc Nephrol* 1: 1263–1268, 2006



Pharmacokinetics of Moxifloxacin and Levofloxacin in Intensive Care Unit Patients Who Have Acute Renal Failure and Undergo Extended Daily Dialysis

CZOCK et al. *Clin J Am Soc Nephrol* 1: 1263–1268, 2006

Parameter	EDD	IHD	CRRT
Membrane	Polysulfone 1.3 m^2	—	Polyacrylonitrile 0.9 m^2 (R
Q_B, Q_D (ml)	160, 160	—	150, —
$T_{1/2off}$ (h)	12.3 (3.7 to 34.0)	14.1 ± 1.23 (Ref. 28)	
$T_{1/2on}$ (h)	6.0 (3.9 to 11.0)	11.6 ± 1.57 (Ref. 28)	9.87 ± 3.26 (Ref. 23)
Vd (L)	266 (154 to 514)		270 ± 133 (Ref. 23)
Vd (L/kg)	3.8 (1.9 to 7.1)		
CL_{off} (L/h)	15.7 (8.1 to 49.3)	10.8 ± 7.6 (Ref. 28)	
CL_{dial} (L/h)	2.0 (0.0 to 4.9)[b]	5.72 ± 7.6 (Ref. 28)	1.63 ± 0.33 (Ref. 23)
	3.1 (2.6 to 4.3)[c]		
$fract_D$ (%)	8 (0 to 23)[d]		
	34 (0 to 60)[e]		9.99 ± 4.25 (Ref. 23)
	35 (0 to 50)[f]		
A_{dial} (mg)	7 (0 to 34)		

Moxifloxacin / Avalox ®

	UpToDate ONLINE	University of Pennsylvania Health System	PubMed www.pub
No renal impairment	400 mg / d	400 mg / d	400 mg / d
IHD	400 mg / d	400 mg / d	400 mg / d
CVVH	400 mg / d	-	400 mg / d
SLED	-	-	400 mg / d

Gentamicin

Indication: -skin and skin-structure infections
- respiratory infections

MW: ampicillin (371.39 D)
sulbactam (255.22 D)

Protein bndg: ampicillin 28 % / sulbactam 38 %

Elimination: urine (60% as unchanged drug)

Half life: -1.1 hrs in healthy subjects
-24 hrs in ESRD

Drug Dosing Consideration in Patients with Acute and Chronic Kidney Disease -- A Clinical Update from Kidney Disease: Improving Global Outcomes (KDIGO)

Kidney Disease: Improving Global Outcomes

Epidemiology of Acute Infections among Patients with Chronic Kidney Disease

DALRYMPLE et al. *Clin J Am Soc Nephrol* 3: 1487–1493, 2008

- **Risiko für Pneumonie x 10**
- **Risiko für Sepsis x 100**
- **Risiko für invasive MRSA Infektion x 100**
- **MRSA Kolonialisierung von Dialysepatienten:**
  - **30 % Europa**
  - **60 % USA**
- **15 % aller MRSA Infektionen bei Dialysepatienten**

Using population pharmacokinetics to determine gentamicin dosing during extended daily diafiltration in critically ill patients with AKI

ROBERTS et al. *Antimicrob Agents Chemother* 54(9):3635-40, 2010