



spitäler schaffhausen

Clinical pharmacy service in an Intensive Care Unit for adults

Focus on antibiotics

Jahrestagung SGI / GSASA Donnerstag, 14.09.2017



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Conflict of Interest

financial interest or as an owner: **no**

activities for the pharmaceutical industry:
**I have no potential conflict of interest
to report**

other fundings/donations: **no**

personal entanglement: **nein**

Introduction ICU Spitäler SH

- Interdisciplinary
- 8 beds
- Category C
- Key data 2015
 - Staff: 27.4 nurses, 3.3 physicians
 - Entries: 667
 - Length of stay (d): 3.3 +/-6
 - Ventilation (hours per bed): 2389
 - Total of shift work: 7277
- PDMS (Software COPRA), since 2004



Clinical pharmacy Service

Clinical pharmacists take care of the appropriate, secure and cost-effective use of medication in collaboration with physicians and nurses.

The activities are:

- **patient**-oriented (e.g. education / counselling)
- **process**-oriented (assuring the adequate supply with medication)
- **therapy**-oriented (optimizing the medication therapy)

Clinical pharmacy Service SH: Activity

10 o'clock - office clinical pharmacy:
preparing the ICU ward round



11 o'clock - microbiology laboratory:
recording the results, discussing them with
laboratory assistants



11.45 o'clock - ICU:
discussing the new results from microbiology /
potentially a need to modify the
antibiotic therapy



typical examples from
hospital in Schaffhausen

Mrs K.S., 62 y

- 23.6.2017: Total laparoscopic Hysterectomy (TLH) and bilateral adnexectomy because of cervix carcinoma
- 30.06.2017: revision laparoscopy because of trokar hernia and ureter leakage because of necrotic ureter and 4-quadrants-peritonitis
- subsequently: septic shock with multiple organ dysfunction syndrome



antibiotic therapy?

Therapy (as of Friday, 30.06.17)

EMPFEHLUNGEN ZUR ANTIBIOTIKA-THERAPIE

6. Auflage
November 2012

Antibiotikagruppe:

Anästhesie: Dr. U. Denzler (8-540)
Chirurgie: Dr. B. Boldog (8-719)
Gynäkologie: PD Dr. Th. Roos (8-312)
Innere Medizin: Prof. Dr. S. Rüttimann (8-114)
Dr. H. Besrou (8-124)
Klin. Pharmazie: Fr. Dr. C. Grafein (8-417)
Fr. I. Vogel (8-439)
Spitalhygiene: Hr. C. Conrad (8-509)
Mikrobiologie: Fr. M. Wehrli (8-419)



Noradrenalin, Perf. 10mg/50 [µg/ml]	32	32	40	40	38	38	38	38	35	33	32
Tetraspan 6% [ml/h]	316										
Ringerfundin 500ml [ml/h]		500		500		500		500		500	
Ringerfundin 1000ml [ml/h]	41		41								
Glucose, 5% 1000ml [ml/h]	63		63								
Liquemin Perf. 25000IE/50 [IE/d]	9996		9996								
Midazolam, Perf. 100mg/50 [mg/h]	8		8								
Fentanyl Perf. 2.5mg/50 [mg/h]	0.1		0.1								
Humanaalbumin 20% i.v. [ml]: Dis					100						
Cefuroxim 1.5/100 i.v. [g]: Dis					500						
Metronidazole HCL 500mg/100 i.v.					1						
Novaiglim 100 NaCl 1/l/100 i.v. [g]: Dis					40						
Midazolam 5mg/1 i.v. [mg]: Dis		5	10		100						
Konakion MM 10mg/1 i.v. [mg]: Dis		2	2		2						
Solu Cortef 100mg/2 i.v. [mg]: Dis		2	2		2						
Midazolam 2mg/2 i.v. [mg]: Dis		2	2		2						
Bisolvon inhal. [mg]: Dis		2	2		2						
Lasix 5mg/0.50 i.v. [mg]: Dis		2	2		2						
					5						

Microbiological results (I)



Auftragsnummer: 803911

Datum: 30.06.2017 21:21

Befundtyp: Mikrobiologie

Dr.Breitling

Endbefund

Untersuchungsauftrag

Fragestellung

: Allg. Bakteriologie

Klinische Diagnose

: Keine Schwangerschaft, keine
Harnwegsinfektsymptome

Antibiotikabehandlung

: Cefuroxim

Antibiotikabehandlung

: Metronidazol

Sonstige Angaben

: Probe 1

Untersuchungsauftrag

Material

: Punktat

Untersuchungsauftrag

Lokalisation

: Flüssigkeit aus em Bauchraum

Position

: intraoperativ

Kommentar zum Auftrag:

Dr.Breitling

Mikroskopische Untersuchungen

Grampräparat

Gramnegative Stäbchen

viel

Kulturelle Untersuchungen

Leukozyten

mässig

Kultur aerob

Wachstum

Kultur anaerob

Kein Wachstum

1. E. coli

viel

AntibiogrammS = sensibel I = intermediär R = resistent f = folgt

	1.
Amoxicillin	S
Amoxicillin/Clavulansäure	S
Ceftazidim	S
Cefuroxim	S
Ciprofloxacin	S
Cotrimoxazol	S
Imipenem	S
Piperacillin/Tazobactam	S
Tobramycin	S

Microbiological results (II)

	Auftragsnummer: 804074	Datum: 02.07.2017 00:37	Befundtyp: Mikrobiologie	Status: Endbefund	Befundempfäng... ipschir
Untersuchungsauftrag					
Fragestellung	:	Allg. Bakteriologie			
Antibiotikabehandlung	:	Cefuroxim			
Antibiotikabehandlung	:	Metronidazol			
Untersuchungsauftrag					
Material	:	Trachealsekret			
Mikroskopische Untersuchungen					
Grampräparat		Gramnegative Stäbchen		wenig	
		Leukozyten		wenig	
Kulturelle Untersuchungen					
Kultur aerob		Wachstum			

Discussion with the laboratory assistant:

Have tests already been carried out to identify the «gram negative germ»?

- Catalase positive
- Oxidase positive



ICU: clinical pharmacy ward round

Monday 3.07.2017

- patient intubated and mechanical ventilation
- Unstable circulation, strong need of volume and norepinephrine



- reason?
- need for modification of the antibiotic therapy? If yes, which antibiotic?

Discussion in the ICU

- Cefuroxime + Metronidazole for the «bowel infection»: okay
- pulmonary situation? Antibiotic therapy of the identified gram negative bacteria?



Yes!

- Antibiotics against Pseudomonas which were in stock in Schaffhausen:
 - Imipenem / Cilastatin
 - Tobramycin
 - Ciprofloxacin
 - *currently unavailable: Pip/Taz, Ceftazidime*

Choice of antibiotic: characteristics of the patient

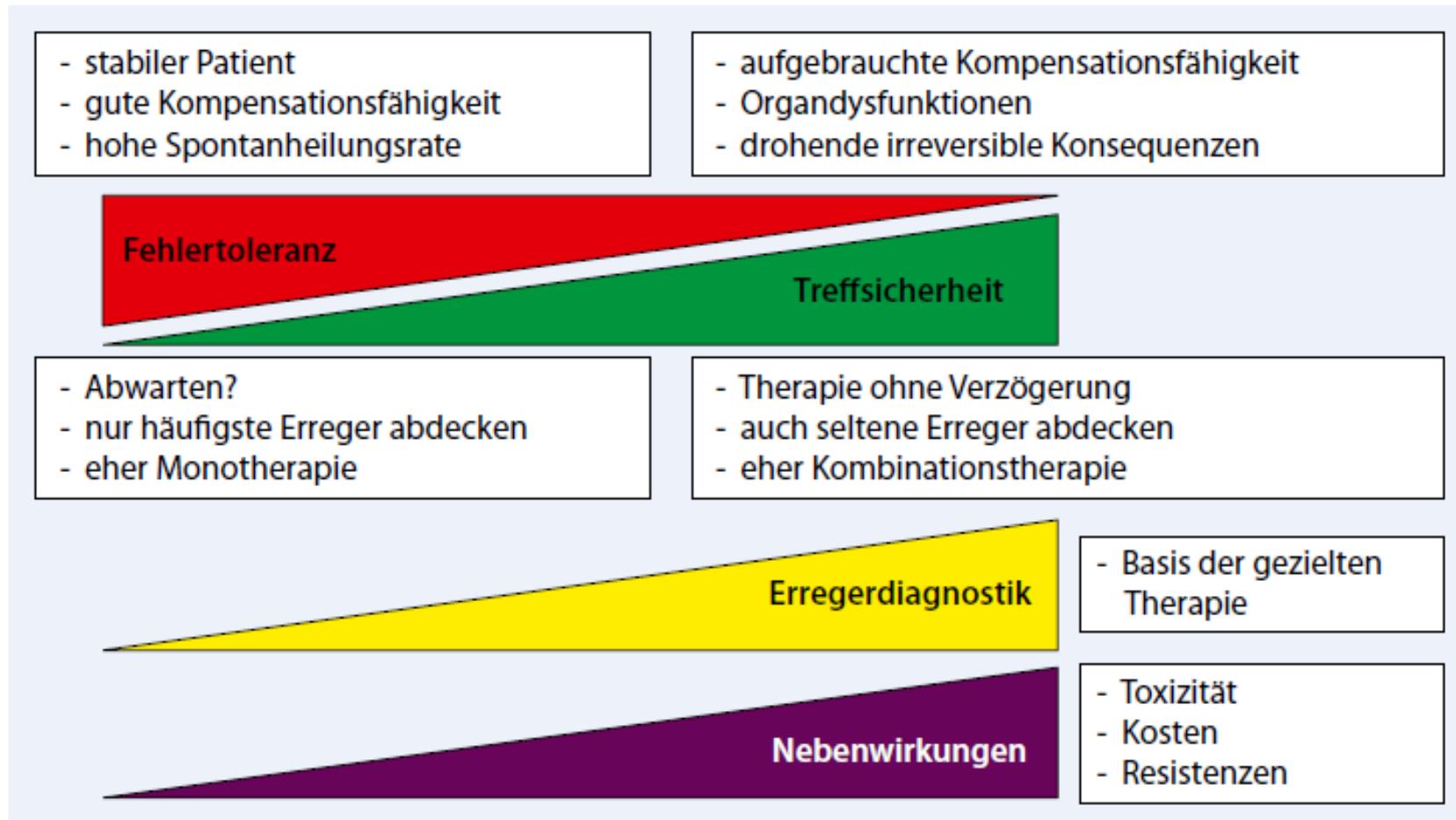
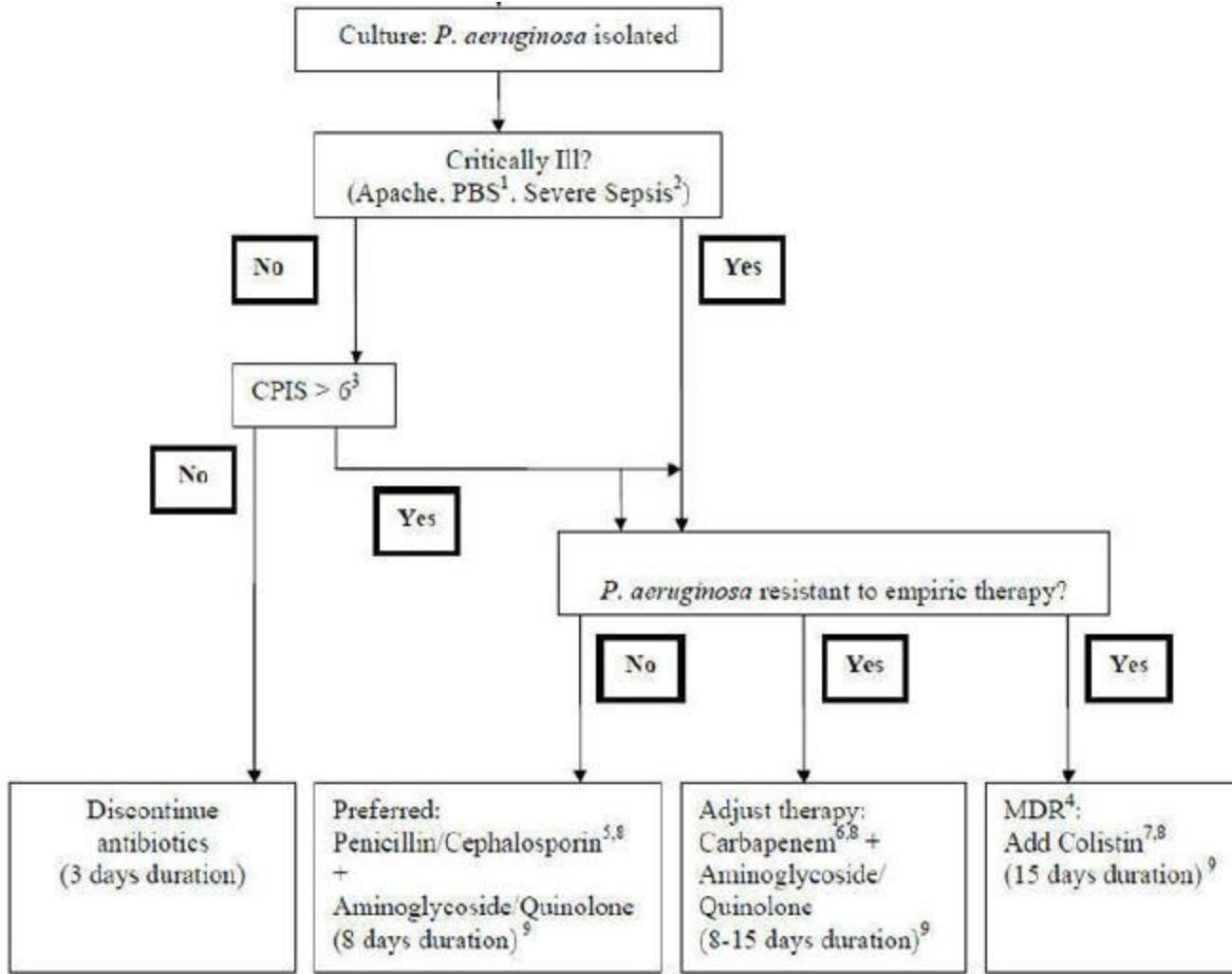


Abb. 1 ▲ Aspekte der kalkulierten Therapie



1 PBS = Pitt Bacteremia Score (139)

2 Severe Sepsis = sepsis with organ dysfunction (hypotension, hypoperfusion)

3 CPIS = Clinical Pulmonary Infection Score (106)

4 MDR = Multidrug resistant=resistant to antipseudomonal penicillins, cephalosporins, carbapenems, quinolones

5 Extended spectrum penicillin or antipseudomonal cephalosporin (Table 1)

6 Antipseudomonal carbapenem = imipenem, meropenem, doripenem

7 Add colistin as inhalation or parenteral therapy to the most active combination therapy.

8 Local antibiotic susceptibility patterns within that institution should be considered.

9 Duration of beta-lactam therapy should be 8-15 days. The aminoglycoside/quinolone can be discontinued at 3-5 days based on results from in vitro susceptibility testing and clinical responses

Choice of antibiotic: Literature



GENERAL PRINCIPLES OF TREATMENT — The following principles apply to the management of serious *P. aeruginosa* infections:

- The risk of antibiotic resistance, both intrinsic and acquired, is an important consideration when selecting empiric or directed therapy.
- Combination therapy is indicated in certain high-risk patients and in severe infections.
- Prompt initiation of antimicrobial therapy is important, as delayed therapy correlates with increased mortality.
- Source control is important. All infected catheters and removable devices should be removed, abscesses should be drained, and obstructions should be relieved whenever possible.

Choice of antibiotic: resistance data Switzerland



Antibiotic resistance data

The number of laboratories sending data to anresis.ch varies over time. Therefore data may not be comparable between years.

[Definition of selection](#)

[Modify query](#)

[New query](#)

[Footnotes](#)

Results:

Selected Criteria:

Microorganism: **Pseudomonas aeruginosa**; Antibiotic: **all**; Time interval: **2016**; Region: **Switzerland Nord-East**; Age: **>=15**; In-/outpatient: **hospitalized**; Anatomic localization: **all**;

Drug	2016			
	Susceptible %	Intermediate %	Resistant %	n
Aminoglycoside	77.9	2.2	19.9	1603
Carbapenem	58.3	4.5	37.2	1590
Cefepime	86.8	0.3	12.9	1469
Ceftazidime	83.3	0.0	16.7	1583
Ciprofloxacin	76.1	5.6	18.3	1584
Piperacillin-tazobactam	83.9	0.1	16.1	1412

Note: Due to rounding, the sum of susceptible, intermediate and resistant samples may differ from 100%.

Choice of antibiotic: resistance data SH

Imipenem / Cilastatin:

Jahr	<i>Pseudomonas aeruginosa</i>												<i>S. aureus</i> Resistenz gegen Imipenem = Resistenz gegen Flucloxacillin.	
	CH all		CH Mid		West CH		Ost CH all		SH all		SH Blut			
	R+I	n	R+I	n	R+I	n	R+I	n	R+I	n	R+I	n		
2004									7	54	0	2		
2005									7	86	0	2		
2006									5	92	0	1		
2007									8	93	0	2		
2008	22	7989	9	2794	21	2731	37	2464	11	95	11	9		
2009	22	8211	20	2829	16	2329	37	3053	6	111	12	8		
2010	19	9003	10	2946	18	3260	30	2797	8	149	0	3		
2011	20	9929	11	3306	25	3386	21	3237	11	109	50	2		
2012	20	9662	14	3036	24	3124	21	3502	7	161	0	1		
2013	28	10682	25	3736	25	3458	34	3468	9	116	0	1		
2014	30	11436	25	3921	29	3919	36	3596	17	153	0	2		
2015	30	12177	nd		nd		43	1988	8	141	0	3		
2016	29	10720	nd		nd		39	1874	12	146	0	2		

Choice of antibiotic: resistance data SH

Tobramycin

Jahr	<i>Pseudomonas aeruginosa</i>							
	CH all		Ost CH all		SH all		SH Blut	
	R+I	n	R+I	n	R+I	n	R+I	n
2004					0	54	0	2
2005					5	86	0	2
2006					0	92	0	1
2007					1	93	0	2
2008	14	8320	12	2497	1	95	0	9
2009	12	8603	13	3090	3	111	0	8
2010	13	9402	14	2809	2	117	0	3
2011	14	10147	13	3248	6	70	0	2
2012	13	9826	12	3518	3	161	0	1
2013	14	10691	17	3452	2	116	0	1
2014	14	11425	21	3618	1	153	0	2
2015	11	12193	23	2005	0	141	0	3
2016	11	10749	20	1888	1	146	0	2

Ciprofloxacin

Jahr	<i>Pseudomonas aeruginosa</i>							
	CH all		Ost CH all		SH all		SH Urin	
	R+I	n	R+I	n	R+I	n	R+I	n
2004							7	54
2005							11	85
2006							7	92
2007							4	94
2008	16	8366	18	2477	4	93	3	36
2009	15	8675	17	3078	4	111	8	51
2010	14	9432	17	2765	6	149	6	71
2011	15	10352	16	3249	13	109	18	62
2012	17	10102	19	3224	9	161	13	101
2013	18	11006	21	3489	3	116	6	69
2014	17	11557	21	3619	11	153	7	68
2015	16	12342	22	2161	6	141	8	76
2016	15	10905	22	1868	1	146	0	75

Choice of antibiotic and dose

patient 65kg

creatinine (3.7.17): 160 μ mol/l (eGFR 29ml/min)

Imipenem/Cilastatin 1000mg loading dose,
after that 3x 500mg i.v. +

Tobramycin 1x 180mg i.v. (ca. 3mg/kgKG),
if necessary adapt corresponding the plasma level

Microbiological results (III) one day later

Auftragsnummer:	804074	Datum:	02.07.2017 00:37	Befundtyp:	Mikrobiologie	Status:	Endbefund	Befundempfäng...	ipschir
Untersuchungsauftrag									
Fragestellung	:	Allg. Bakteriologie							
Antibiotikabehandlung	:	Cefuroxim							
Antibiotikabehandlung	:	Metronidazol							
Untersuchungsauftrag	:	Trachealsekret							
Material	:								
Mikroskopische Untersuchungen									
Grampräparat		Gramnegative Stäbchen			wenig				
		Leukozyten			wenig				
Kulturelle Untersuchungen									
Kultur aerob		Wachstum							
1. Pseudomonas aeruginosa		mässig							
2. Candida albicans		wenig							
<hr/> AntibiogrammS = sensibel I = intermediär R = resistent f = folgt									
		1.							
Ceftazidim		S							
Ciprofloxacin		S							
Imipenem		S							
Piperacillin/Tazobactam		S							
Tobramycin		S							



Microbiological results (III) one day later

Auftragsnummer: 804186 Datum: 03.07.2017 00:35 Befundtyp: Mikrobiologie Status: Endbefund Befundempfäng... ipschir

Endbefund
Untersuchungsauftrag
Fragestellung : Allg. Bakteriologie
Antibiotikabehandlung : Cefuroxim
Antibiotikabehandlung : Metronidazol
Untersuchungsauftrag
Material : Blutkultur peripher punktiert

Mikroskopische Untersuchungen
Grampräparat aerobe Blutkultur Gramnegative Stäbchen nachweisbar
Kulturelle Untersuchungen
Blutkultur aerob Wachstum
Blutkultur anaerob kein Wachstum nach 7 Tagen

1. Pseudomonas aeruginosa nachweisbar

Antibiogramm S = sensibel I = intermediär R = resistent f = folgt

Ceftazidim	1.
Ciprofloxacin	S
Imipenem	S
Piperacillin/Tazobactam	S
Tobramycin	S

from 4.7.2017: patientin on hemofiltration

Dosage of the antibiotics?

- Tobramycin: according to literature, env. half of the dose
our recommendation: 1x 180mg i.v./d (the same as to date, if necessary adapt corresponding TDM)

		Datum	05.07.2017 14:05	10.07.2017 15:48	13.07.2017 15:56	
	Befundtyp	Zentrallabor	Zentrallabor	Zentrallabor	Zentrallabor	
	Status	Endbefund	Endbefund	Endbefund	Endbefund	
	Befundempfänger	ipschir	ipschir	ipschir	ipschir	
Name	Einheit	Referenz	Wert			
Medikamente						
<input checked="" type="checkbox"/> Tobramycin Tal	mg/l	Therapeutische	i 0.7	i 0.8	i 0.7	

- Imipenem/Cilastatin: according to literature, normal dose
our recommendation: increase to 4x 500mg i.v./d

Summary case 1

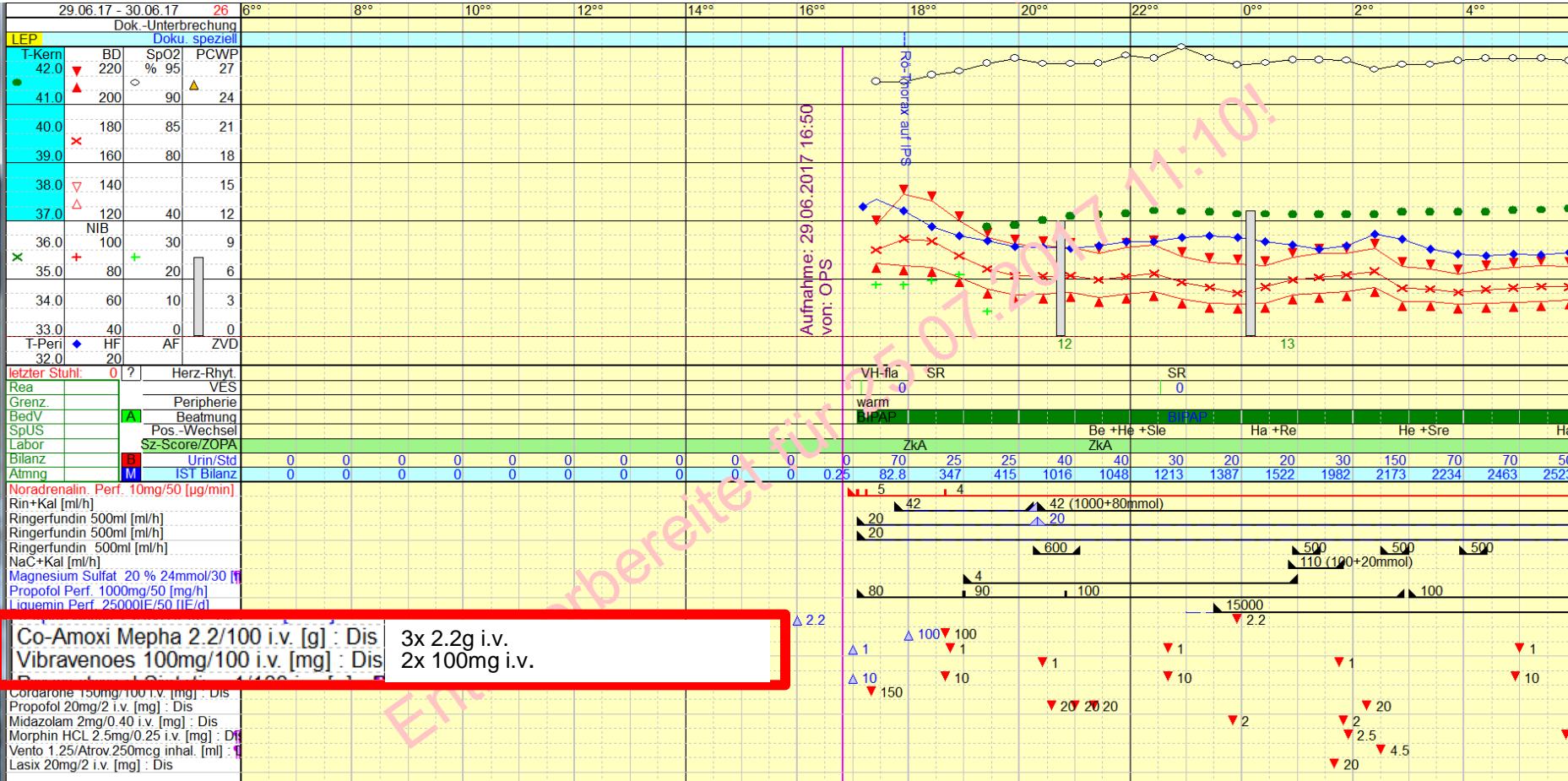
- Due to interdisciplinary teamwork, the therapy can be discussed and optimised related to choice of drug, dose, monitoring
- Because of closely working together with the microbiology laboratory, the antibiotic therapy can be adapted rapidly
- Resistance data can help in the selection of initial therapy

Mrs H.M., 63 y

- 28.6.2017: sepsis with complicated myometritis and infection in lesser pelvis with fibrinous all-quadrants-peritonitis unknown etiology
 - Status after copper-IUD for 20 years
- Diagnostic hysteroscopy and curettage, drainage insertion transvaginal to douglas (29.6.17)

- arterial hypertension
- chronic venous insufficiency both sides (Widmer III)
- adipositas per magna (128kg, 165cm)
- alcoholism until 2016

29.6.2017



Microbiological results (I)

Erfassung: 28.06.2017 15:16
Abnahme: 28.06.2017 14:10

Auftragsstellung

Material Urethra (Abstrich)
Fragestellung Chlamydia trachomatis / Gonokokken PCR

Spezielle Untersuchungen

Chlamydia trachomatis PCR	negativ
Gonokokken PCR	negativ

Erfassung: 28.06.2017 15:16
Abnahme: 28.06.2017 14:10

Auftragsstellung

Material Vagina (Abstrich)
Fragestellung Allg. Bakteriologie

Mikroskopische Untersuchungen

Grampräparat	Mikroorganismen	nicht nachweisbar
	Leukozyten	wenig
	Plattenepithelien	wenig
	Clue Cells	nicht nachweisbar

Kulturelle Untersuchungen

Kultur aerob Wachstum

1. Normale Vaginalflora wenig

Microbiological results (II)

Erfassung: 29.06.2017 16:31
Abnahme: 29.06.2017 16:06

Auftragsstellung

Material	Fremdmaterial, Spirale, intraoperativ
Fragestellung	Allg. Bakteriologie
Antibiotikabehandlung	Keine
Sonstige Angaben	Probe 2

Kommentar zum Auftrag:

Dr.Breitling

Kulturelle Untersuchungen

Kultur aerob	Kein Wachstum nach 14 Tagen
Kultur anaerob	Kein Wachstum nach 14 Tagen

Erfassung: 29.06.2017 16:31
Abnahme: 29.06.2017 16:16

Auftragsstellung

Material	Douglas-Punktat, Punktat Douglas, intraoperativ
Fragestellung	Allg. Bakteriologie
Antibiotikabehandlung	Keine

Mikroskopische Untersuchungen

Grampräparat	Grampositive Kokken Leukozyten	wenig mässig
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Kulturelle Untersuchungen

Kultur aerob	Kein Wachstum
Kultur anaerob	Wachstum

1. Anaerobe Mischflora

wenig

Informationen zur Resistenzsituation von anaeroben Bakterien sind in der Analysenliste vom Labor (Intra-/Internet) unter dem Begriff Anaerobier zu finden.

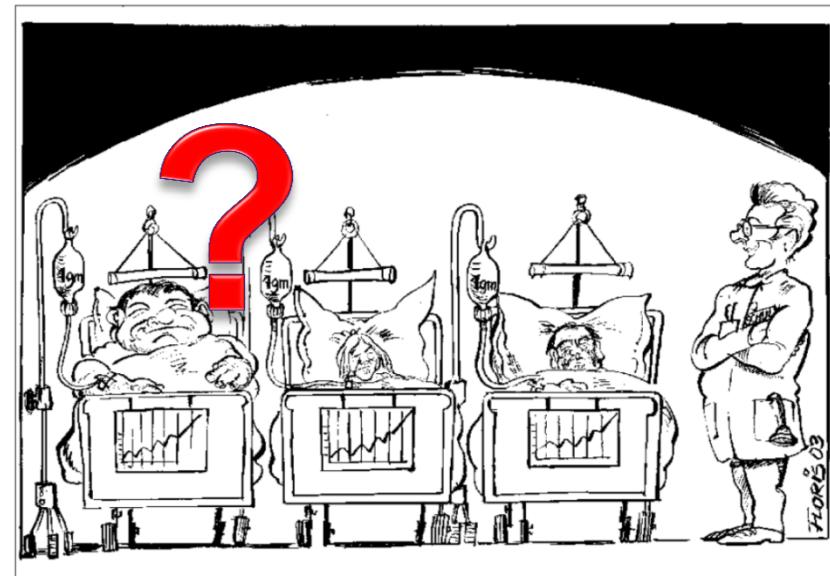
ICU: clinical pharmacy ward round

Thursday, 29.6.17

discussion

- Stop tetracycline, because there is no evidence of atypical bacteria (Chlamydia)
- Dose of Co-Amoxi in this patient?

NRS 2002	3	Gewicht	Gewicht	Datum	Vis	BMI	Gr. cm	BMI	Cal	kCal
			128.1	29.06.2017	agas		165	47		2530



Recommendation (Literature)

Beta-lactams

Despite widespread use, there is very little information regarding appropriate dosing of beta-lactams in obese patients. Lower concentrations have been observed in obese patients receiving conventional doses of beta-lactam antibiotics. Beta-lactams can experience alterations in both V_d and overall clearance in obese patients, which may suggest standard doses are no longer sufficient to achieve target attainment (40–60% $T > MIC$) for bacteria with higher MICs (1,15).

Clinicians should consider higher dosing of beta-lactam antibiotics to effectively treat infections in obese patients.

Our recommendation:
Co-Amoxi 3 to 4x
2.2g i.v./d

Dosing should at the very least be on the upper end of recommended doses or the highest effective dose safely administered with minimal side effects (Table 3). To ensure target attainment for resistant infections, extended or continuous infusions can be utilized.

Continuation of case report

- Clinical deterioration with fever, increasing dyspnea/tachypnea, increasing signs of inflammation
- Analysis of

Material	Trachealsekret
Fragestellung	Allg. Bakteriologie
Antibiotikabehandlung	Amoxicillin/Clavulansäure
Mikroskopische Untersuchungen	
Grampräparat	Leukozyten Gramnegative Stäbchen
viel wenig	
Kulturelle Untersuchungen	
Kultur aerob	Wachstum
1. Enterobacter cloacae-Komplex mässig	
Der Stamm bildet hohe Mengen an AmpC-Betalactamase (dereprimiert). Der Keim ist dadurch resistent auf Penicilline, 1., 2. und 3. Gen. Cephalosporine, Piperacillin/Tazobactam und Aztreonam. Carbapeneme und 4. Gen. Cephalosporine bleiben in der Regel empfindlich.	
Multiresistenter Keim, Spitalhygiene kontaktieren!	

Antibiogramm	S = sensibel	I = intermediär	R = resistent
1.			
Amoxicillin	R		
Amoxicillin/Clavulansäure	R		
Cefepime	I		
Ceftazidim	R		
Cefuroxim	R		
Ciprofloxacin	S		

Cotrimoxazol	S
Doxycyclin	S
Ertapenem	R
Imipenem	I
Piperacillin/Tazobactam	R
Tigecyclin	S
Tobramycin	I

Change to Cotrimoxazole: dose?

- lipophilic molecule

Table 4 Lipophilicity (9.48)

Hydrophilic	Lipophilic
Penicillins	Fluoroquinolones
Cephalosporins	Macrolides
Monobactams	Clindamycin
Carbapenems	Linezolid
Aminoglycosides	Vancomycin
Polymyxins	Tetracyclines
Fosfomycin	Tigecycline (glycylcyclines)
Daptomycin	Trimethoprim-sulfamethoxazole
	Rifamycins
	Chloramphenicol

- Predominantly renal elimination
- Renal function of the patient is good
- Severe infection
- Strongly (!) resistant bacteria

Body weight	Equation	Weight-based drug recommendations
IBW	Men: 50 kg + 2.3 kg/each inch over 5 feet Women: 45.5 kg + 2.3 kg/each inch over 5 feet	Acyclovir Amphotericin (lipid-associated) Flucytosine Isoniazid Pyrazinamide Rifampin Acyclovir Amikacin Ganciclovir Gentamicin Streptomycin Tobramycin Trimethoprim-sulfamethoxazole
ABW or LBW	IBW + 0.4 (ABW – IBW) Men: $1.1 \times \text{Wt (kg)} - 128 (\text{Wt}^2 \text{ (kg)}/(100 \times \text{Ht (m)})^2)$ Women: $1.07 \times \text{Wt (kg)} - 148 (\text{Wt}^2 \text{ (kg)}/(100 \times \text{Ht (m)})^2)$	
TBW	Patient's actual weight	Amprioterin (conventional) Daptomycin Quinupristin-dalfopristin Telavancin Vancomycin Voriconazole

Table 2 Recommendations for body weight formulas and weight-based drugs (9,10)

Our patient:
IBW: 57 kg
ABW: 86 kg
TBW: 128 kg

Ideal body weight (IBW): a weight that is believed to be maximally healthful for a person, based chiefly on height and gender.

Adjusted body weight (ABW): based on the theory that as certain percentage (25–40%) of body weight greater than IBW is metabolically active tissue.

Lean body weight (LBW): a person's body weight minus fat, which can be roughly calculated by measuring height, weight, girth and gender.

Our recommendation

- Choose the higher standard dose (3x 2 Ampoules Bactrim forte i.v.)
- + Metronidazole (because of the detection of the anaerobic bacteria)
- contact isolation precautions

Summary case 2

- Support the physicians in the selection of the dose of the antibiotics by
 - Search of scientific literature
 - Pharmacokinetic calculations

Clinical pharmacists support

- Definition of the dose (renal function, dialysis, weight, TDM) and interval
- Change the medication in the case of side effects
- Search for alternatives in the case of shortages
- Check the interactions
- Search the literature
- Definition of the length of the therapy
- Selection of reasonable microbiological investigations
- Provide consumption statistics, resistance data
- ...the physicians by assisting to «think of...»

«think of»

- Change urinary catheter during the antibiotic therapy?
- Search for a thrombus in case of positive blood culture of central catheter?
- Endocarditis excluded in case of detection of staphylococcus aureus in urine samples?
- Vaccination after splenectomy
- Take more blood cultures after detection of yeasts
- Check the liver enzymes in case of Rifampicin
- TDM Vancomycin / Aminoglycosides
- etc

Clinical pharmacy service in an Intensive Care Unit for adults

Additional benefit for all!

- Relief the physicians (search the literature, contact the microbiology laboratory, test for interaction...)
- Optimal care for the patient (focus infectiology)
- Teaching for the resident physicians
- Contribution against the resistance development
- A fascinating job for clinical pharmacists