Kanton Zürich
Gesundheitsdirektion
Kantonsapotheke

# Pharmakokinetische Besonderheiten bei kritisch Kranken

# Particularités pharmacocinétiques en soins intensifs

**Marcel Rainer**
Apotheker Klinikbetreuung
Pharm. Dienste

# Agenda

1. Clinical pharmacy services in critical care units
2. Pharmacokinetics in critical ill patients
3. Case presentation
4. Pharmacist-led medication review
5. Take home messages

# Pharmacists involved in critical care?

PZ PHARMAZEUTISCHE ZEITUNG
DIE ZEITSCHRIFT DER DEUTSCHEN APOTHEKER

**August 2021**

Intensivstation

## Spezielle Aufgaben für Apotheker

Apotheker haben auf Intensivstationen viele spezielle Aufgaben. Im interdisziplinären Team tragen sie dazu bei, Patienten in oft lebensbedrohlichen Situationen rasch mit

**August 2022**

Untersuchung

## Mehr Apotheker auf Intensivstationen gebraucht

Eine neue Umfrage zeigt: Intensivmediziner wünschen sich apothekerliche Unterstützung bei ihrer Arbeit. Denn sie hilft, die Arzneimitteltherapiesicherheit zu steigern. Eine regelmäßige pharmazeutische Betreuung ist jedoch bislang erst bei etwa jeder dritten Intensivstation die Regel.

# Critical care pharmacists today?

## March 2022

Springer Link

Originalien | Open Access | Published: 08 March 2022

Arzneimitteltherapiesicherheit gefördert durch die interprofessionelle Zusammenarbeit von Arzt und Apotheker auf Intensivstationen in Deutschland

Erkenntnisse einer Umfrage

Drug therapy safety supported by interprofessional collaboration between ICU physicians and clinical pharmacists in critical care units in Germany

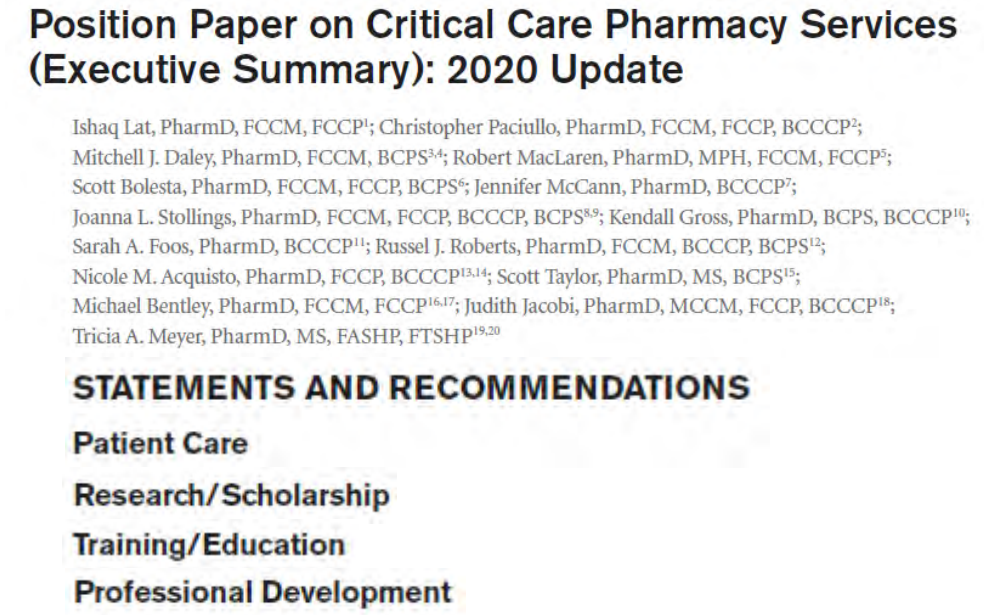
Results of a survey

Heike Hilgarth, Christian Waydhas, Frank Dörje MBA, Julia Sommer, Stefan Kluge & Karl Peter Ittner DEAA, EDIC

*Medizinische Klinik - Intensivmedizin und Notfallmedizin* (2022) | Cite this article

**1750** Accesses | **1** Citations | **15** Altmetric | Metrics

## September 2020: Society of Critical Care Medicine



Position Paper on Critical Care Pharmacy Services (Executive Summary): 2020 Update

Ishaq Lat, PharmD, FCCM, FCCP[1]; Christopher Paciullo, PharmD, FCCM, FCCP, BCCCP[2]; Mitchell J. Daley, PharmD, FCCM, BCPS[3,4]; Robert MacLaren, PharmD, MPH, FCCM, FCCP[5]; Scott Bolesta, PharmD, FCCM, FCCP, BCPS[6]; Jennifer McCann, PharmD, BCCCP[7]; Joanna L. Stollings, PharmD, FCCM, FCCP, BCCCP, BCPS[8,9]; Kendall Gross, PharmD, BCPS, BCCCP[10]; Sarah A. Foos, PharmD, BCCCP[11]; Russel J. Roberts, PharmD, FCCM, BCCCP, BCPS[12]; Nicole M. Acquisto, PharmD, FCCP, BCCCP[13,14]; Scott Taylor, PharmD, MS, BCPS[15]; Michael Bentley, PharmD, FCCM, FCCP[16,17]; Judith Jacobi, PharmD, MCCM, FCCP, BCCCP[18]; Tricia A. Meyer, PharmD, MS, FASHP, FTSHP[19,20]

**STATEMENTS AND RECOMMENDATIONS**

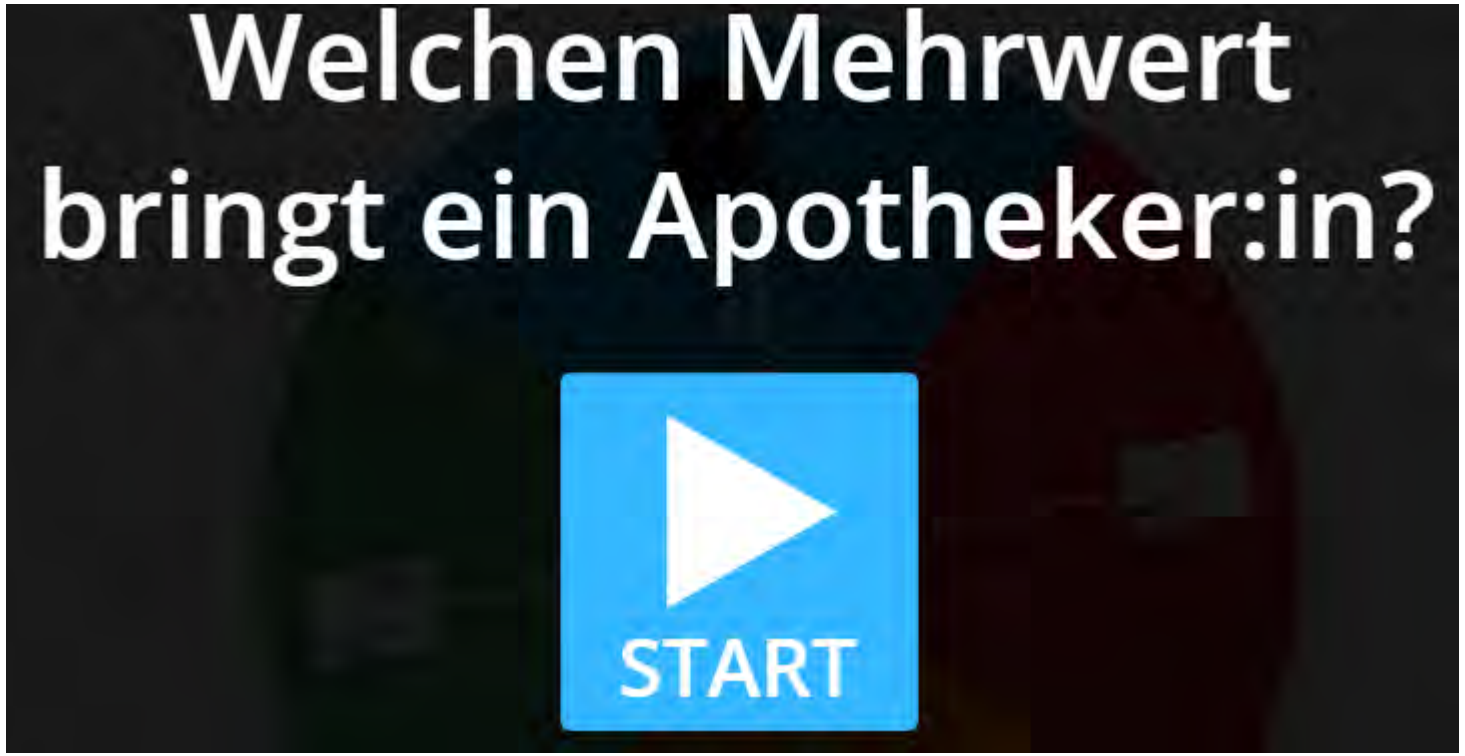
**Patient Care**

**Research/Scholarship**

**Training/Education**

**Professional Development**

# Pharmacy services in critical care units




Welchen Mehrwert bringt ein Apotheker:in? - Random wheel (wordwall.net)

# Clinical pharmacy services in critical care

Independent medication education for ther HCP

antimicrobial stewardship

antithrombotic stewardship

opioid stewardship

clinical nutrition counselling

TDM (safety, efficacy)

Interdisciplinary ward rounds

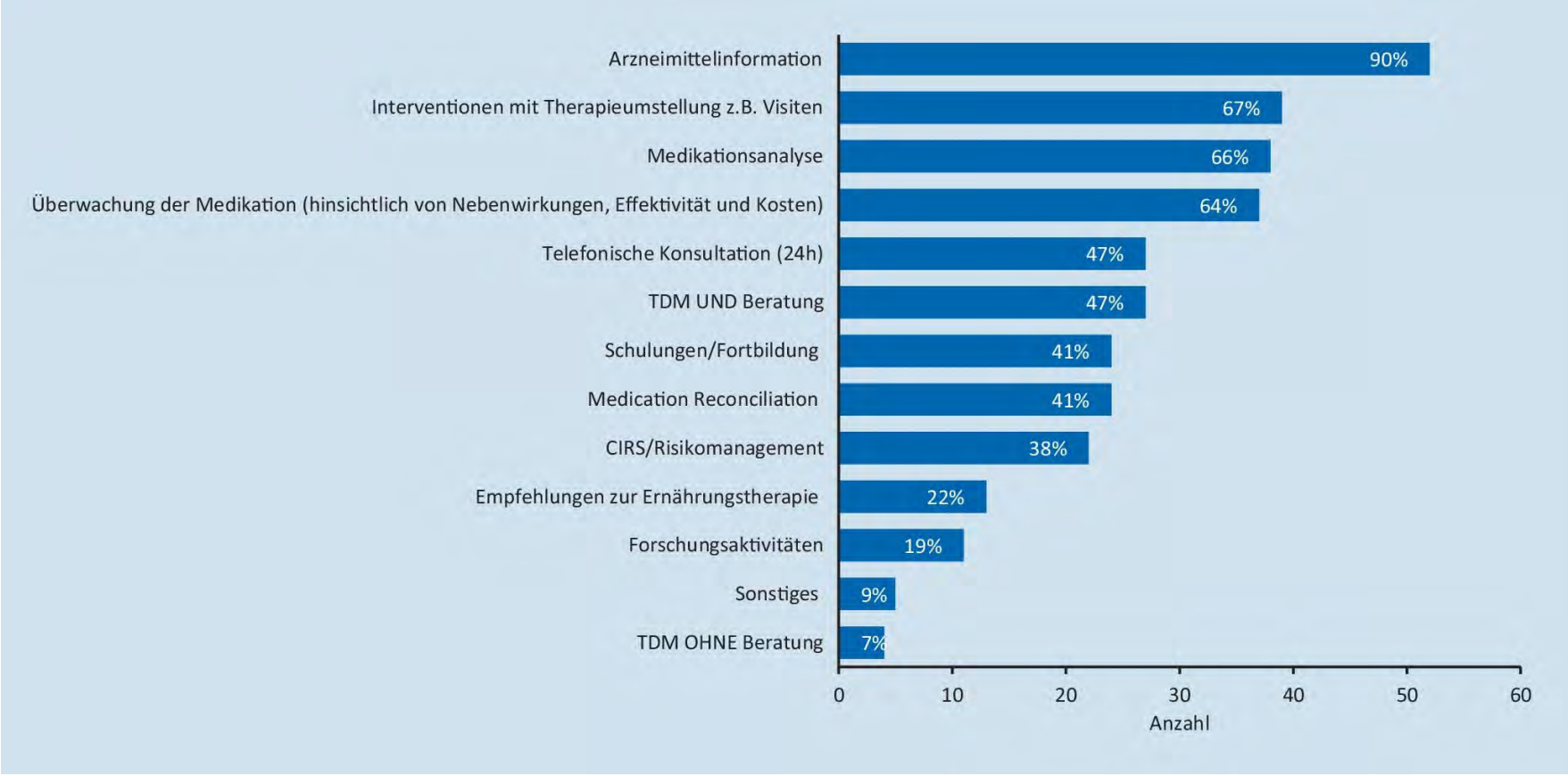
Dose individualization/
ADE management

Work up of drug standards

medication reconciliation

Preparing/maintaining prescription templates

# Clinical pharmacy services in critical care

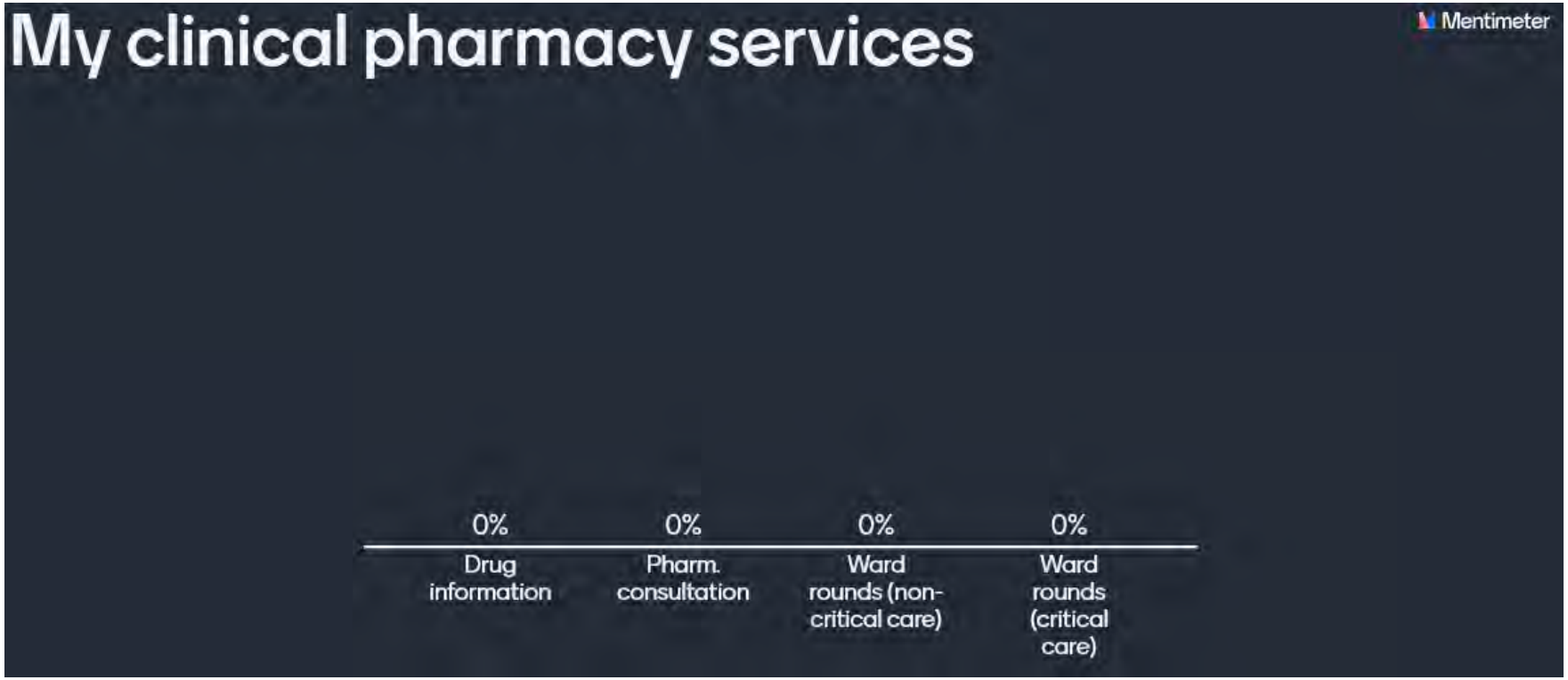



Pharm. support in 58 critical care units in Germany

# Clinical pharmacy services in critical care

| Pharmazeutische Tätigkeiten | Alle Teilnehmer /Teilnehmer ohne pharmazeutsiche Betreuung | Teilnehmer mit pharmazeutischer Betreuung |
|---|---|---|
| Bereitstellung von Arzneimittelinformation | Essenziell/unverzichtbar | Essenziell/unverzichtbar |
| Telefonische Erreichbarkeit (24 h) | Essenziell/unverzichtbar | Essenziell/unverzichtbar |
| Teilnahme an Visiten | Wünschenswert | Essenziell/unverzichtbar |
| Regelmäßige Evaluation der Verordnung (Medikationsanalyse) | Wünschenswert | Essenziell/unverzichtbar |
| Überwachung der Medikation (hinsichtlich Nebenwirkung, Effektivität, Kosten) | Wünschenswert | Essenziell/unverzichtbar |
| TDM und Beratung | Wünschenswert | Essenziell/unverzichtbar |
| Einbindung in das CIRS/Risikomanagement | Wünschenswert | Essenziell/unverzichtbar bzw. wünschenswert |
| Interventionen, die zur Therapieumstellung führen | Wünschenswert | Wünschenswert |
| Überprüfung der Medikation auf Vollständigkeit („medication reconciliation") | Wünschenswert | Wünschenswert |
| Empfehlungen zur Ernährungstherapie | Wünschenswert | Wünschenswert |
| Die Teilnahme und Durchführung von Schulungen/Fortbildungen | Wünschenswert | Wünschenswert |
| Forschungsaktivitäten | Optional | Optional |
| TDM ohne Beratung | Optional | Optional |

# Status quo




Code: 6870 5479

# How confident do you feel?

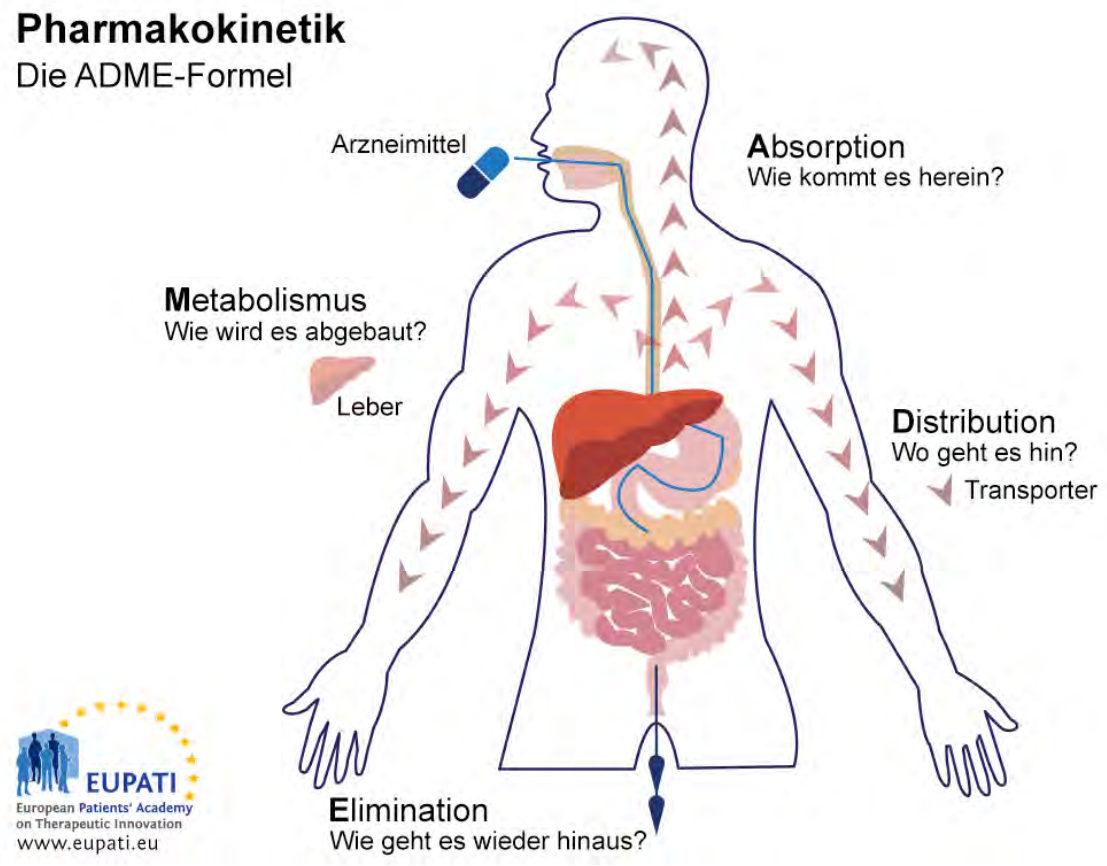
VERY CONFIDENT

KIND OF CONFIDENT

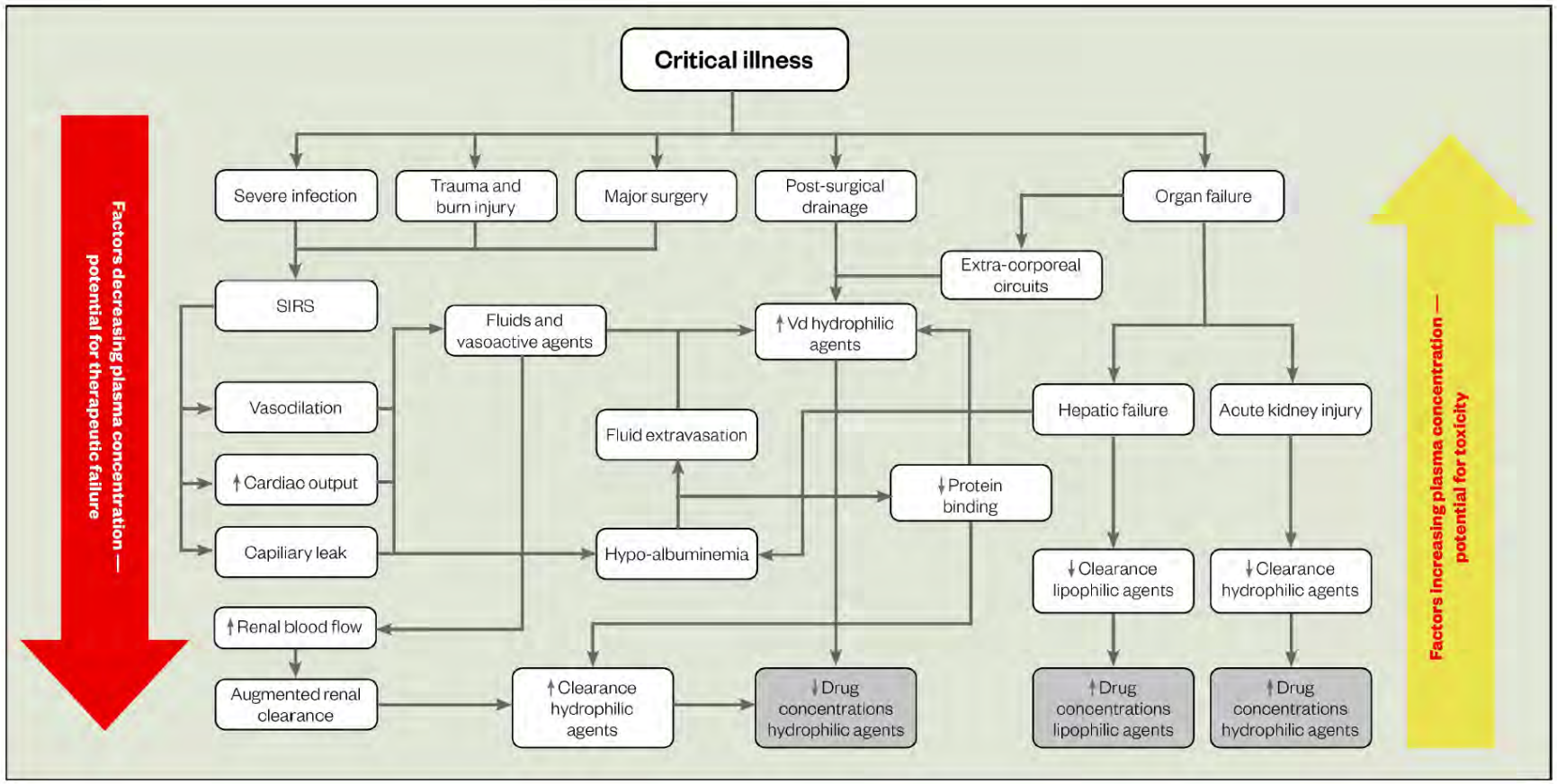
NOT CONFIDENT

Code: 1330 2048

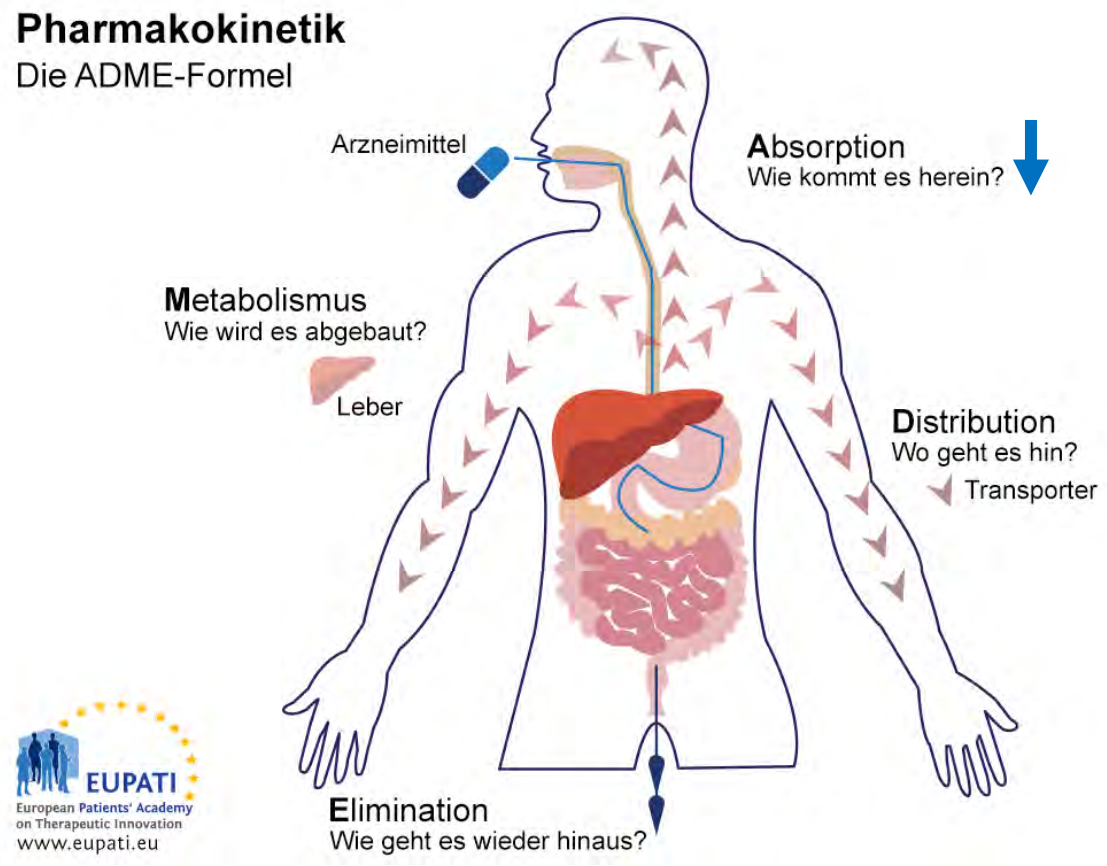
# Overview of pharmacokinetics



# Overview of pharmacokinetics

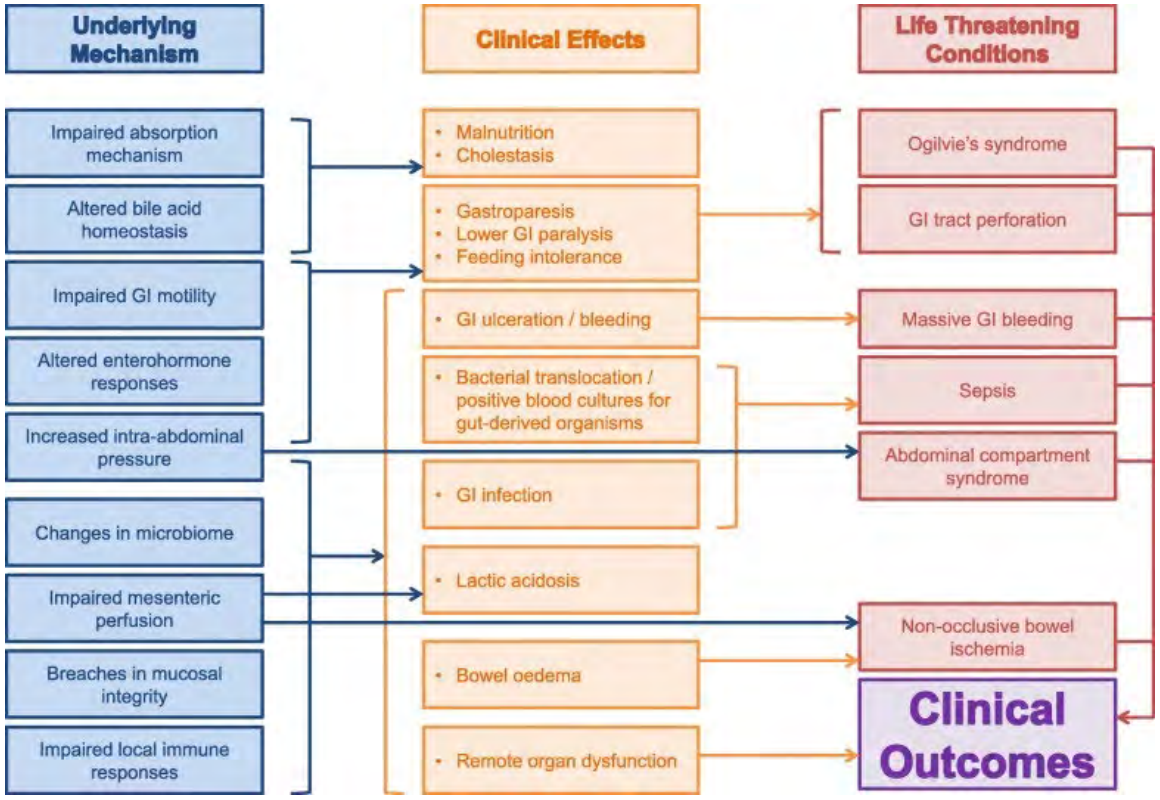


# Overview of pharmacokinetics



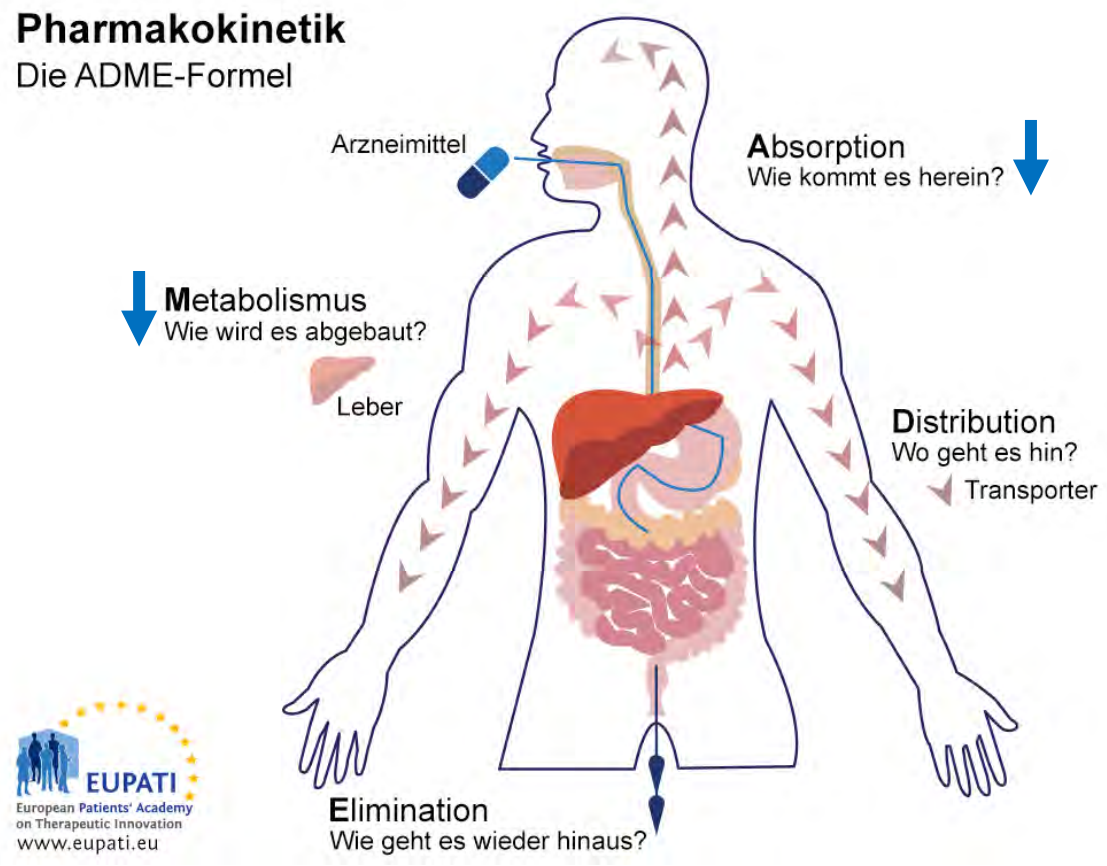
# Absorption

- gastroparesis
- increased gastric pH
- exocrine pancreatic dysfunction
- slow GI motility
- impaired mesenteric perfusion
- concomitant use of opioids



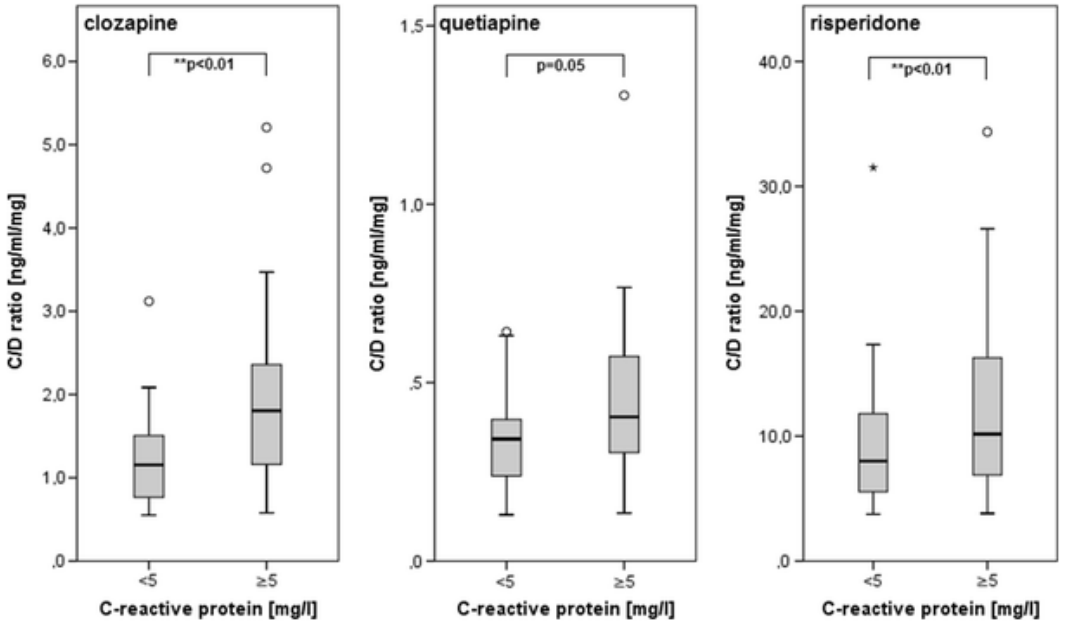

Blaser, A., et al. Crit Care (2020). Gastrointestinal dysfunction in the critically ill: a systematic scoping review and research agenda proposed by the Section of Metabolism, Endocrinology and Nutrition of the European Society of Intensive Care Medicine

# Overview of pharmacokinetics

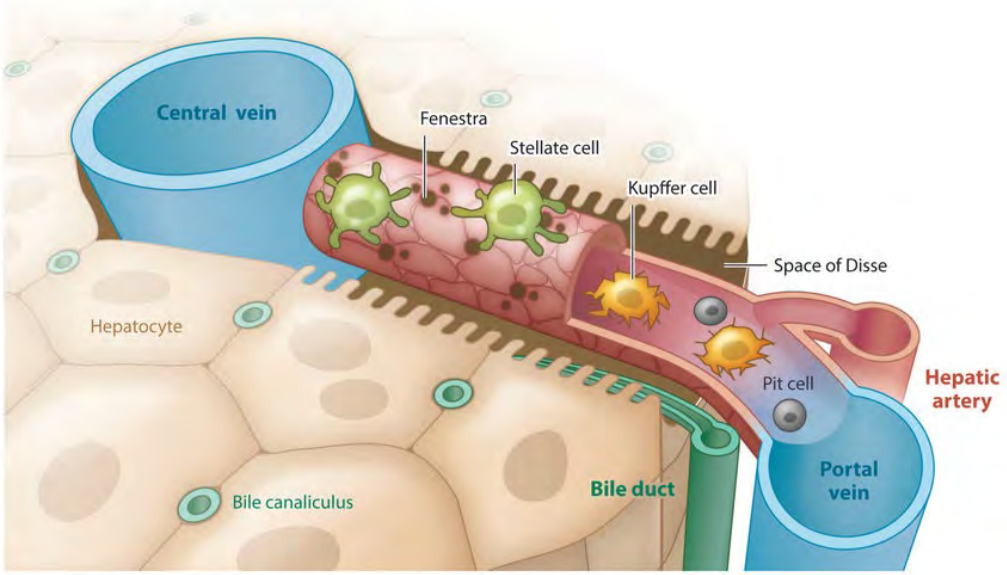


# Metabolism (I)

- hepatic hypoperfusion
- low activity of CYP-family (CYP3A, CYP2C19) due to systemic inflammation




Hefner, G., *et al.* Inflammation and psychotropic drugs: the relationship between C-reactive protein and antipsychotic drug levels. *Psychopharmacology*



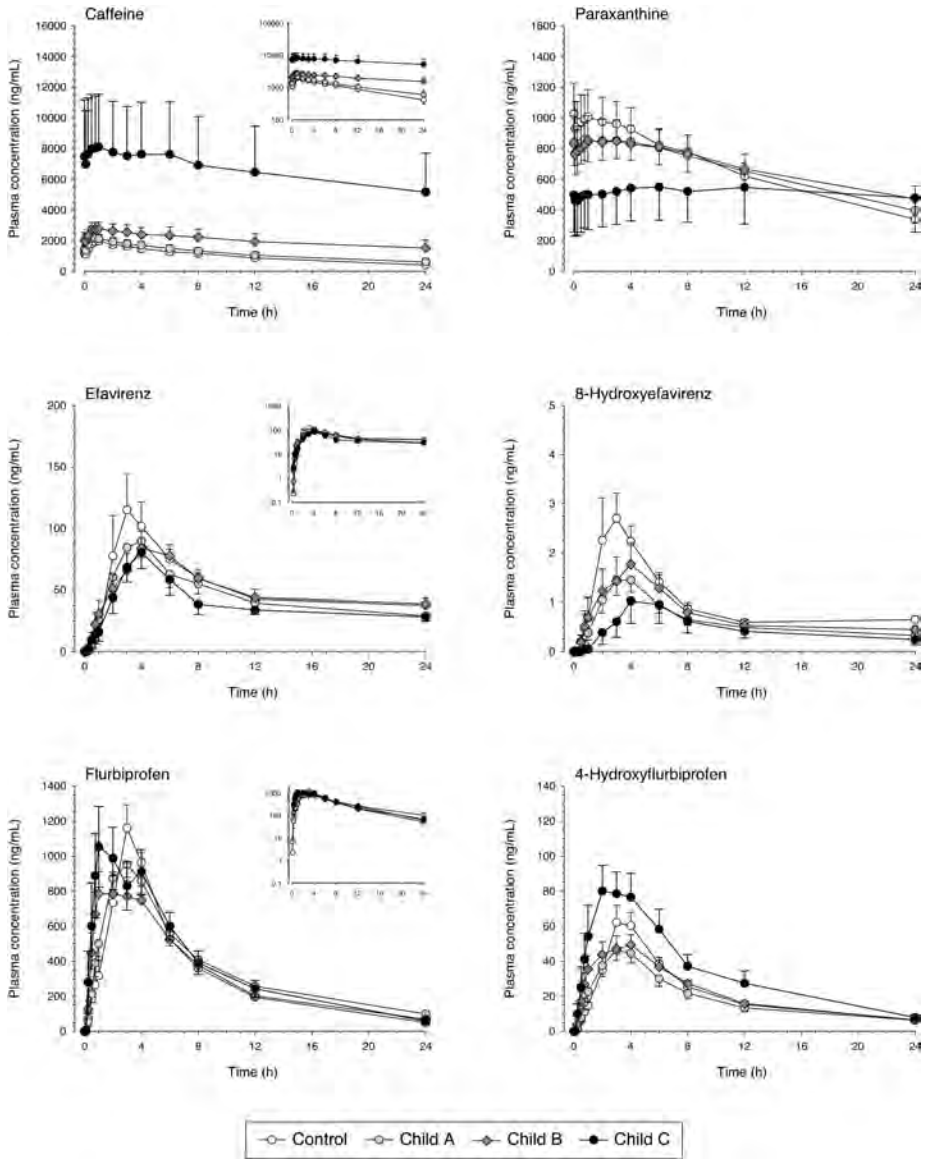

Schematic of the hepatic sinusoid. Ehrlich, A., et al. Annual Review of Biomedical Engineering (2019). Challenges and Opportunities in the Design of Liver-on-Chip Microdevices.

# Metabolism (II)

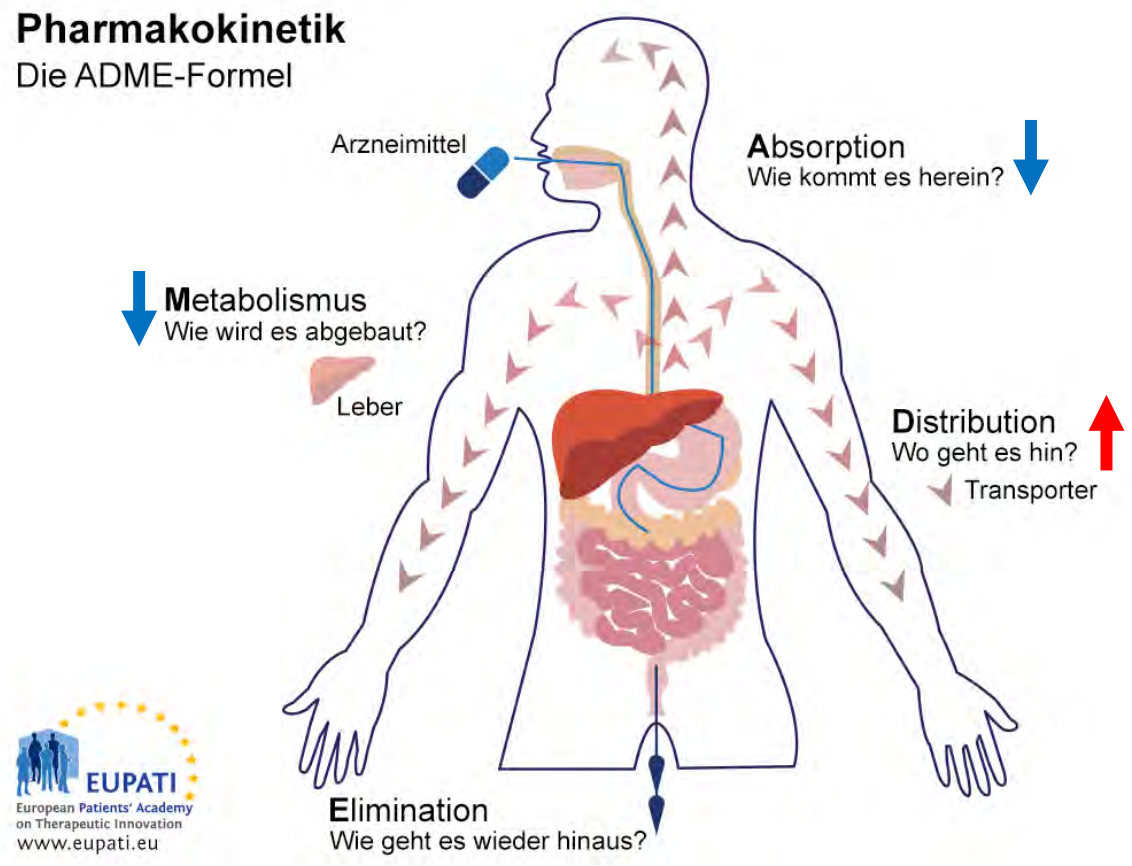
**Basler cocktail in liver cirrhosis**

Metabolic ratio altered of
drugs of high extraction rate

- CYP1A2
  Caffeine to Paraxanthine
- CYP2B6
  Efavirenz to 8-OH-Efavirenz
- CYP2C9
  Flurbiprofen to 4-OH-Flurbiprofen

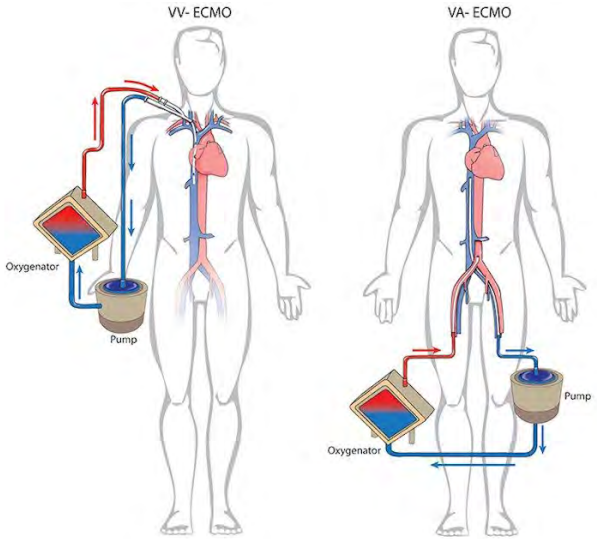


# Overview of pharmacokinetics



# Volume of distribution

- vasodilatation
- supportive fluid therapy (resuscitation)
- shift of plasma proteins to interstitial compartment (acidic to basic)
- metabolic pH changes (respiratory, renal, etc.)
- dermal perfusion alterations (ischemia or pyrexia)
- extracorporeal therapy




Wehrmedizinische Relevanz der Extrakorporalen Membranoxygenierung (ECMO) –

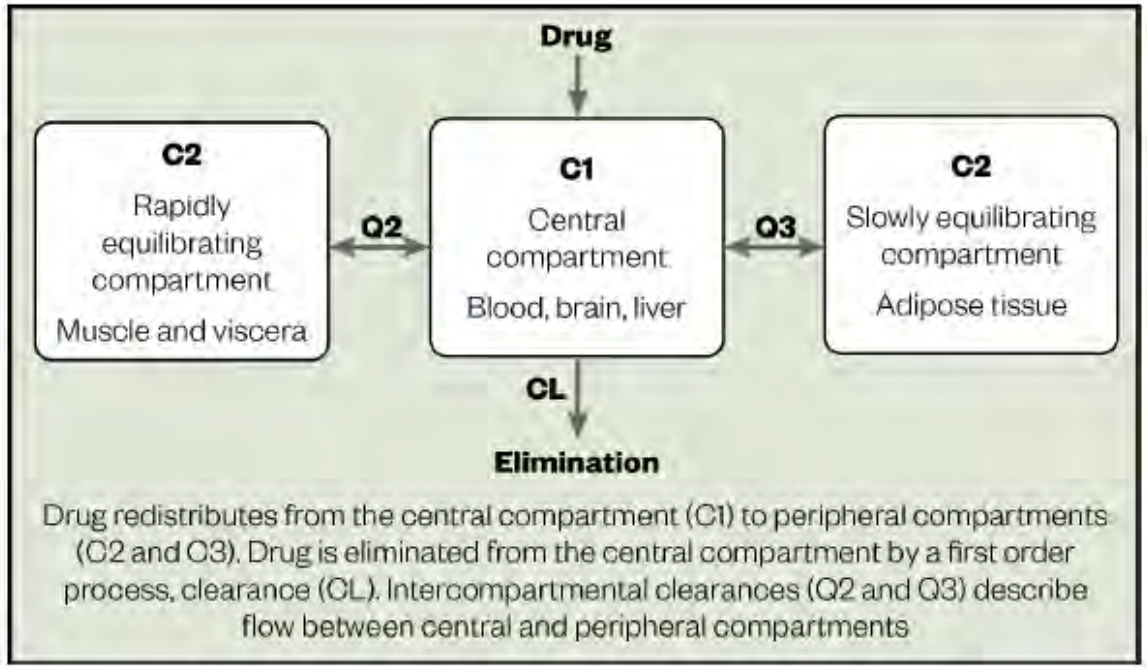
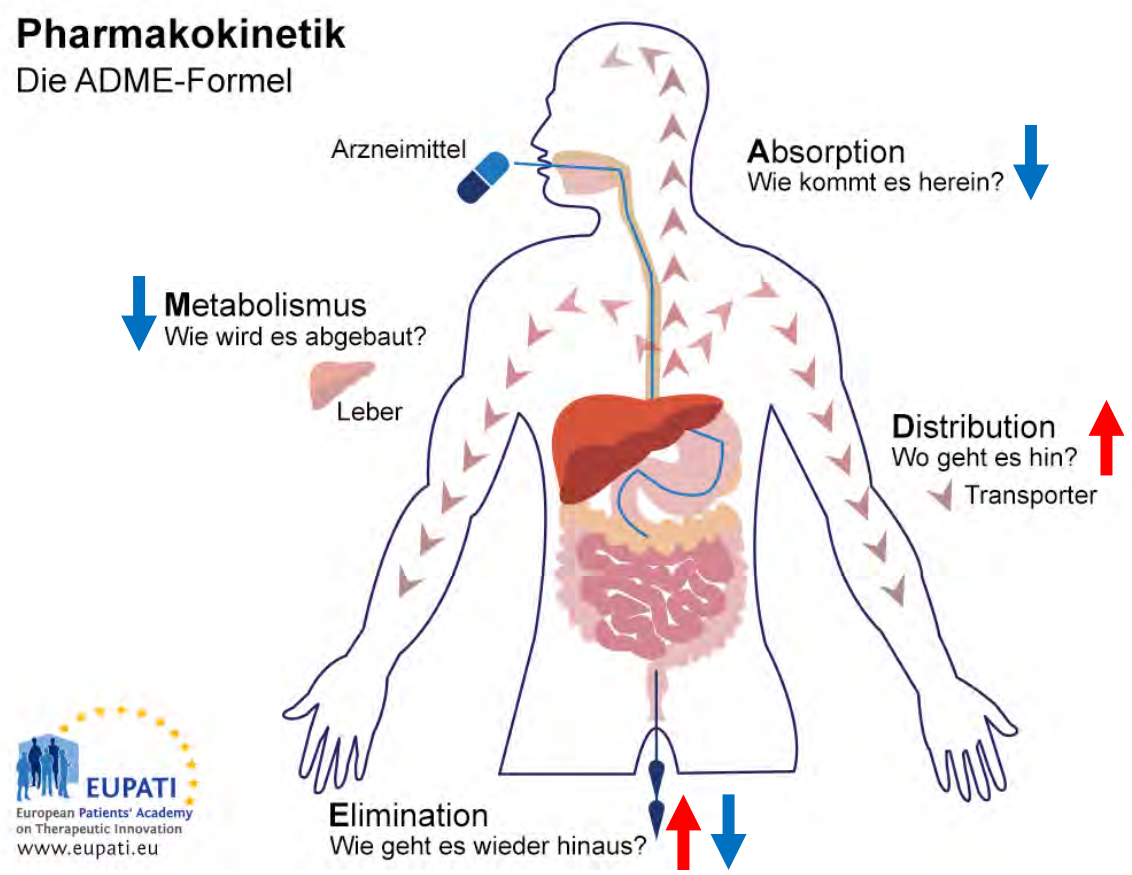


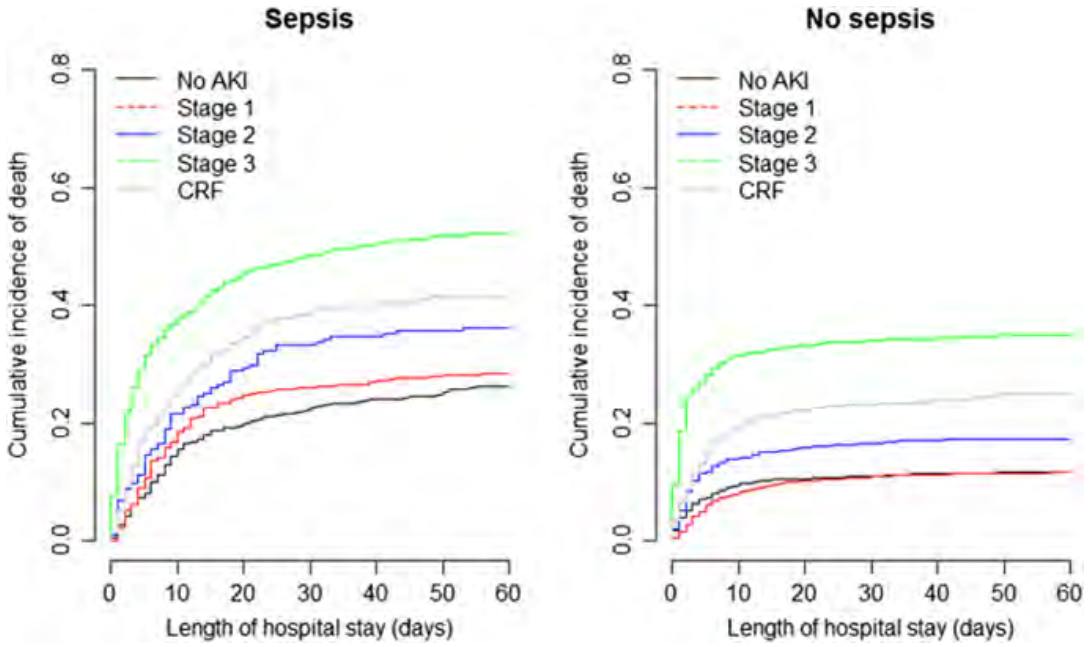

Figure 2: The 'Three compartment model' for highly lipophilic drugs[9]

# Overview of pharmacokinetics

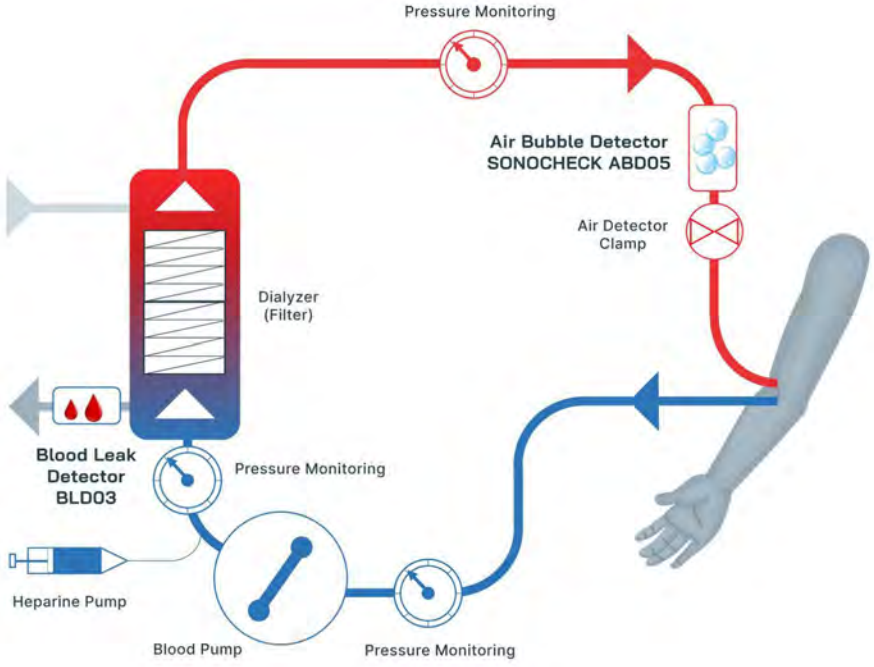


# Elimination

- augmented renal clearance
- hypoxemic damage
- hemodialysis (1000-1500 Da, hydrophilic)




Peters, E., *et al.* A worldwide multicentre evaluation of the influence of deterioration or improvement of acute kidney injury on clinical outcome in critically ill patients with and without sepsis at ICU admission: results (2018).




Hemodialysis SONOTEC ©

# Case presentation

Patient PB, m, 36 years old, 190 cm, 180 kg BW

Chief complaint/main problem:
Acute promyelocytic leukemia, first diagnosed (FD) 19.08.2022

Past medical history:
- Recurrent thrombophlebitis, FD 05.2022
- COVID-19 infection, FD 06.2022
- Metabolic syndrome: art. hypertension, dyslipidemia
- General anxiety syndrome, episodes of depression, first manifestation 2018

Medication upon entry:
- Xarelto® 20 mg coated tbl 1-0-0-0
- Venlafaxin ER Sandoz® 150 mg cps 1-0-0-0

Allergies/family history/social history: former smoker, 2010

# Course of hospitalisation

**01.09.** Start of curative chemotherapy: ATRA, Arsenic trioxide according to Lo-Coco scheme

**05.09.** Endocarditis of the mitral valve
Begin of Gentamycine, Cefepime, Metronidazol i.v.

**09.09.** Progredient number of promyelocytes
Start cytoreductive therapy: Hydroxycarbamide

**11.09.** Acute renal insufficiency DD Gentamycine DD tumor lysis syndrome

**13.09.** Oxygen saturation drop 85% despite oxygen mask 5-6L/min

**14.09.** Entry critical care unit

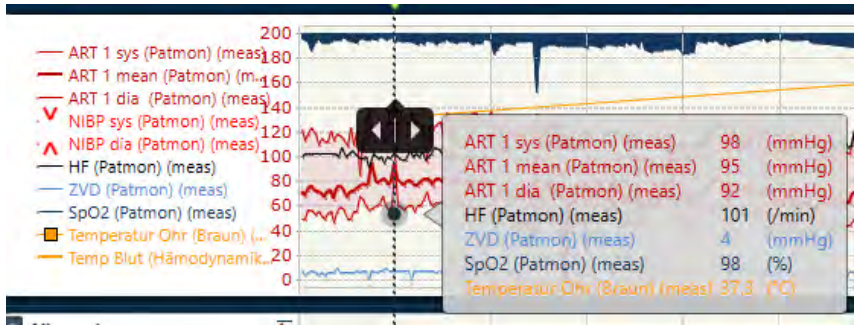
**15.09.** Start continuous renal replacement therapy, invasive ventilation

**17.09.** Switch from cvvHD to SLED, non-invasive ventilation

**22.09.** Clinical pharmacy ward round

# Ward round:
# Clinical presentation

Cardial:




Pulmonal:

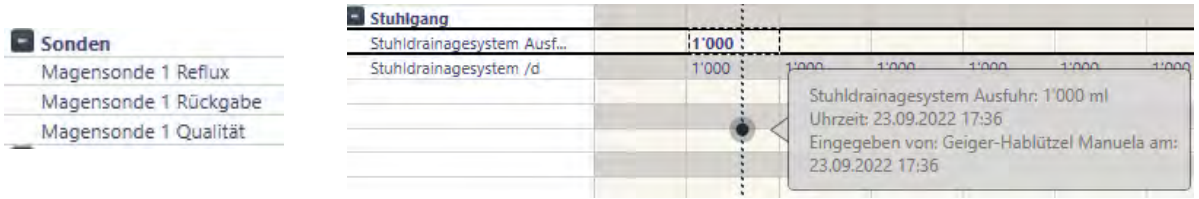
| | | | |
|---|---|---|---|
| FIO2 (BGA arteriell nicht spez.) | | 30.0 | % |
| sO2 (BGA arteriell nicht spez.) | | 0.963 | fraction |
| FHHb (BGA arteriell nicht spez.) | | 0.036 | fraction |
| FO2Hb (BGA arteriell nicht spez.) | | 0.929 | fraction |

Neurology:

| | |
|---|---|
| Punkte total (GCS) | 13 |
| RASS (RASS) | +1 Ruh... |
| Punkte total (ICDSC) | 7 |
| Ergebnis (ICDSC) | Delir |

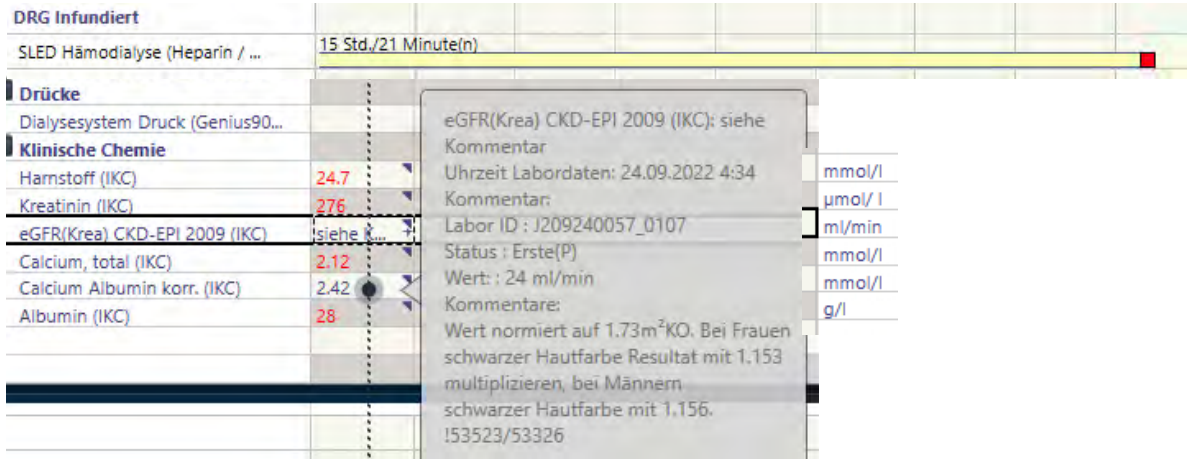
| | |
|---|---|
| Pupillenform li (status) | rund |
| Pupillengrösse li (status) [mm] | 3 |
| Pupillenreaktion li (status) | prompt |
| Pupillenform re (status) | rund |
| Pupillengrösse re (status) [mm] | 3 |
| Pupillenreaktion re (status) | prompt |

Abdominal:

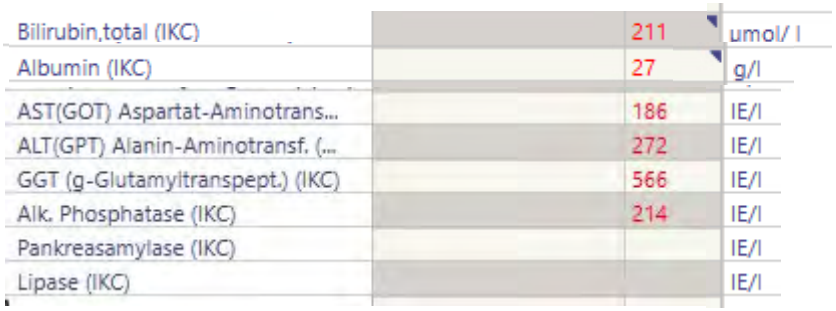


# Ward round:
# Clinical presentation

Renal:




Hepatic:



# Ward round:
# Clinical presentation

## Hematology:

| | | |
|---|---|---|
| Hämoglobin H (Hämatologie) | 68 | g/l |
| Hämatokrit H (Hämatologie) | 0.219 | l/l |
| Erythrozyten (Hämatologie) | 2.11 | T/l |
| Thrombozyten, automatisch (H... | 89 | 10^9/l |
| Neutrophile (Hämatologie) | 0.77 | 10^9/l |
| Monozyten H, automatisch (H... | 0.06 | 10^9/l |
| Eosinophile H, automatisch (H... | 0.01 | 10^9/l |
| Basophile H, automatisch (Hä... | 0.00 | 10^9/l |
| Lymphozyten (Hämatologie) | 0.37 | 10^9/l |
| IG abs., automatisch (Hämatol... | 0.02 | 10^9/l |
| Retikulozyten %, automatisch ... | 8 | % |
| Retikulozyten, automatisch (H... | 168 | 10^9/l |
| Retikulozyten-LFR (automat.) (... | 67 | % |
| Reti.-MFR (automatisch) (Häma... | 18 | % |
| Reti.-HFR (automatisch) (Häma... | 15 | % |
| RET-He (Hämatologie) | 31.3 | pg |

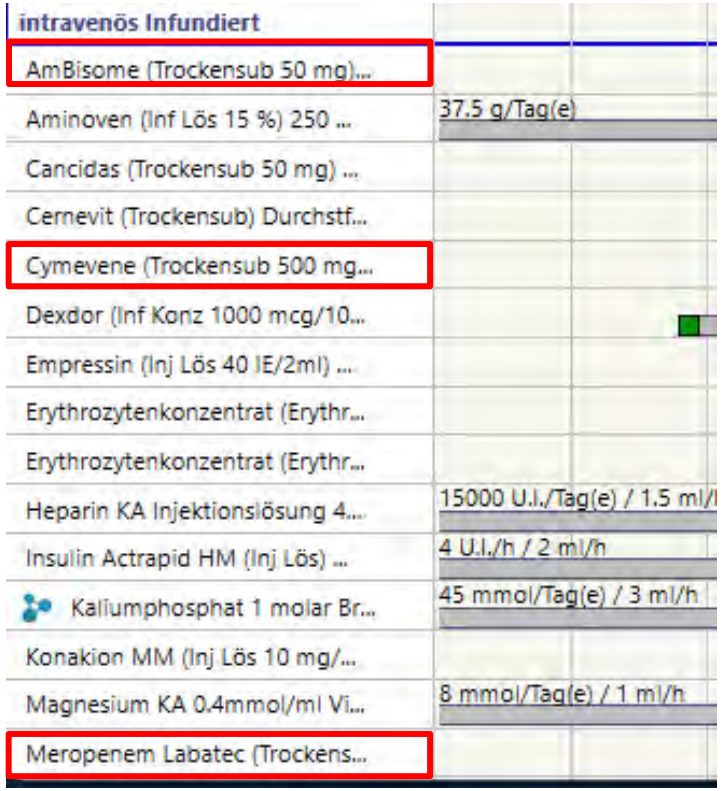
## Electrolytes:

| **Elektrolyt Ergebnis** | | |
|---|---|---|
| cK+ (BGA arteriell nicht spez.) | 4.6 | mmol/l |
| cNa+ (BGA arteriell nicht spez.) | 141 | mmol/l |
| cCl- (BGA arteriell nicht spez.) | 111 | mmol/l |
| cCa++ (BGA arteriell nicht spez.) | 1,11 | mmol/l |
| Anion gap (BGA arteriell nicht... | 11.6 | mmol/l |
| **Metabolit Ergebnis** | | |
| cLac (BGA arteriell nicht spez.) | 1.7 | mmol/l |
| cGlu (BGA arteriell nicht spez.) | 7.9 | mmol/l |
| mOsmc (BGA arteriell nicht spez.) | 289.5 | mmol/ kg |

# Ward round

| | 22.09. | 21.09. | 20.09. | 19.09. | 18.09. | 17.09. | |
|---|---|---|---|---|---|---|---|
| **Entzündung (all. klin. Chemie)** | | | | | | | |
| CRP (IKC) | 94.0 | 95.0 | 70.0 | | 58.0 | 52.0 | mg/l |
| PCT (Procalcitonin) (IKC) | 15.20 | 19.10 | 17.30 | | 16.90 | 15.00 | µg/l |
| Interleukin-6 (Roche) (IKC) | | | | | | | ng/l |

| | | |
|---|---|---|
| 17.09.2022 | 2x2BK | folgt |
| | **GalactomannanS** | **negativ** |
| 18.09.2022 | Katheter V. jug re | **C. albicans, C. dubliensis** |
| 19.09.2022 | Clostridien | negativ |
| | Bakterielle BS-PCR | negativ |
| | atypische Erreger PCR | negativ |
| | **panfungale PCR** | **Candida albicans, Candida dubliensis** |
| 20.09.2022 | 2x2 BK | ausstehend |
| 23.09.2022 | 2x2 BK | ausstehend |



# Ward round: MAI

*Group 1+2 - Meropenem:*
**D**isease? Right **D**rug? **D**ose and intervall? **D**elivery to infection site? **D**uration?

*Group 3+4 - Liposomal Amphotericin B:*
**D**isease? Right **D**rug? **D**ose and intervall? **D**elivery to infection site? **D**uration?

*Group 5+6 - Ganciclovir:*
**D**isease? Right **D**rug? **D**ose and intervall? **D**elivery to infection site? **D**uration?

# Ward round: MAI

*Meropenem:*
Empiric therapy febrile neutropenia

| Parameter | Standard pharmacokinetics |
|---|---|
| Volume of distribution (L/Kg) | 0.25 L/kg |
| Protein binding | 2% |
| Half-life (hours) | 1 hour (healthy subjects) |
| Clearance (L/h) | 12.4 L/h[5]<br>7.7 to 15.4 L/h[9] |
| Metabolism | Metabolised by hydrolysis of the beta-lactam ring generating an inactive metabolite |
| Renal elimination | Mainly excreted in urine by tubular secretion and glomerular filtration<br>70% excreted unchanged in urine within 12 hours |
| Other elimination | Faecal 2% |

# Ward round: MAI

*Meropenem:*
Empiric therapy febrile neutropenia

### Extremes of body-weight

> **Obesity**
> Body mass index (BMI) has minimal effect on the PK/PD target attainment in critical illness. Using a higher dose of 2 g every 8 hours as prolonged infusion enabled coverage of 90% of *P. aeruginosa* and susceptible *A. baumanii*.[25]

### Sustained low-efficiency dialysis (SLED)

Drug clearance is dependent on the effluent flow rate, filter type, and method of renal replacement.

Consider initial loading dose.

Dosing recommendations based on 8- to 10-hour daily PIRRT sessions with effluent rates of 4 to 5 L/hour[36] and 6 to 12 L/hour.[37] The PK is significantly influenced by the degree of residual diuresis.

# Ward round: MAI

*Meropenem:*
Empiric therapy febrile neutropenia

- MW = 383.5 g/mol
- Vd = 0.25 L/kg
- Q0 = 0.1
- PB = 2%
- Half life = 1 h, 70% after 12 h
- Duration of dialysis = 15 h

**Decision: 1 g every 8 h**
MIC: unknown
Trough level: 40 mg/L (> 44 mg/L nephrotoxic, > 64 mg/L neurotoxic)
Peak level: 105 mg/L (comparable to 2g Meropenem in non-impaired renal function)

# Ward round: MAI

*Group 1+2 - Meropenem:*
**D**isease? Right **D**rug? **D**ose and intervall? **D**elivery to infection site? **D**uration?

*Group 3+4 - Liposomal Amphotericin B:*
**D**isease? Right **D**rug? **D**ose and intervall? **D**elivery to infection site? **D**uration?

*Group 5+6 - Ganciclovir:*
**D**isease? Right **D**rug? **D**ose and intervall? **D**elivery to infection site? **D**uration?

# Ward round: MAI

*Liposomal Amphotericin B:*
Febrile neutropenia *C. albicans, C. dubliensis* in blood samples

| Parameter | Standard pharmacokinetics |
|---|---|
| Volume of distribution (L/kg) | 0.10 to 0.44 L/kg[3]<br>0.2 to 1.6 L/kg[4]<br>0.77 L/kg at steady state[17]<br>20 L[11] |
| Protein binding | 90%[18] |
| Half-life (h) | 6.3 to 10.7 h[3]<br>Terminal half-life 152 h[17] |
| Clearance (L/h) | 11 to 51 mL/hour/kg[3] (0.011 to 0.051 L/h/kg)<br>1.6 L/h in 15 patients with haematological malignancy[11] |
| Metabolism | A pharmacokinetic study in 10 healthy subjects given a single 2 mg/kg dose of liposomal amphotericin or 0.6 mg/kg amphotericin B deoxycholate found no metabolites, suggesting that amphotericin B is not extensively metabolised[17] |
| Renal Elimination | With conventional amphotericin, 2 to 5% is excreted unchanged in urine, but due to the size of the liposomes there is no glomerular filtration and renal elimination of liposomal amphotericin, thereby reducing the potential for nephrotoxicity (in distal tubuli) that is seen with conventional amphotericin formulations[3,18] |

# Ward round: MAI

*Liposomales Amphotericin B:*
Febrile Neutropenie *C. albicans, C. dubliensis*

ClinCalc.com

**Drug Dosing in Obesity Reference Table**

| Drug | Comments |
|---|---|
| A | |
| Acyclovir [1] | ▸ Dose using a 40% adjusted body weight |
| Amikacin [2] | ▸ Dose using a 40% adjusted body weight |
| Amphotericin B (liposomal) [3] | ▸ Consider capping body weight to 100 kg |
| Atracurium [4] | ▸ Dose using ideal body weight<br>▸ The use of ideal body weight has been shown to be associated with a more predictable muscle strength recovery within 60 minutes and a lack of need for antagonism compared to total body weight |

**Decision: 0.5 g every 24 h**

- No renal elimination
- Dose capping due to morbid weight

# Ward round: MAI

*Group 1+2 - Meropenem:*
**D**isease? Right **D**rug? **D**ose and intervall? **D**elivery to infection site? **D**uration?

*Group 3+4 - Liposomal Amphotericin B:*
**D**isease? Right **D**rug? **D**ose and intervall? **D**elivery to infection site? **D**uration?

*Group 5+6 - Ganciclovir:*
**D**isease? Right **D**rug? **D**ose and intervall? **D**elivery to infection site? **D**uration?

# Ward round: MAI

*Ganciclovir:*
CMV-infection in immune suppressed patients *or*
CMV prophylaxis after heart/lung transplantation

Universität Zürich
Institut für Medizinische Virologie
STS 263

Winterthurerstrasse 190, CH-8057 Zürich Tel.: 044 634 26 57 Fax: 044 634 26 83 Tel. NZR 044 634 38 08
e-mail: Virusdiagnostik@virology.uzh.ch

| | | | | | |
|---|---|---|---|---|---|
| **Bericht vom:** | 22.09.2022 13:39:49 / IMV | **Version:** | 4 | **Letzte Änderung:** | 22.09.2022 19:36:46 / IMV |
| | | **Labornr:** | VDCI220004 | | |
| **Auftragsnr:** | 186822094 | | | **Status:** | abgeschlossen |
| **Material vom:** | 21.09.2022 18:15 | | | | |
| **Eingang am:** | 22.09.2022 07:58 | | | | |

Klinische Angaben — Einsendergrund: Krankheit

| Untersuchungen | Resultat | Einheit | Referenzbereich |
|---|---|---|---|
| Material Diagnostik | EDTA-Blut | | |
| **Humanes Herpes Virus** | | | |
| HHV-6 DNA-Nachweis ql (PCR) | positiv (1) | | |

**Bemerkungen**

(1) Auf Anfrage quantifiziert: 129'000 Kopien/ml. Die Quantifizierung dieser Analyse ist ausserhalb des akkreditiertenBereiches.

Hinweis:
Das Vademecum des IMV (www.virology.uzh.ch) ist integrierender Bestandteil des vorliegenden Befundes. Dieses enthält Angaben über Probenmaterialien, Stichprobenrelevanz und über die analytische Messunsicherheit. Letztere kann im Labor nachgefragt werden. Dieser Befund darf nicht auszugsweise kopiert werden, dagegen ist die Weiterverwendung einzelner Resultate unter der Angabe der Quelle erlaubt. Die in Befund festgehaltenen Resultate beziehen sich ausschliesslich auf das untersuchte klinische Material.

# Opportunistic infections

| Family | HHV-X | Herpesviridae | Commentary |
|---|---|---|---|
| Alpha | HHV-1 | Herpes-simplex-Virus 1 (HSV-1) | Sensitive to acyclovir |
| | HHV-2 | Herpes-simplex-Virus 2 (HSV-2) | Sensitive to acyclovir |
| | HHV-3 | Varizella-Zoster-Virus (VZV) | Sensitive to acyclovir, famcyclovir, brivudine |
| Beta | HHV-5 | Cytomegalovirus (CMV) | Sensitive to gancyclovir, foscarnet, fomivirsene |
| | HHV-6 | Human Herpes Virus 6 | High level of endemic infection |
| | HHV-7 | Human Herpes Virus 7 | High level of endemic infection |
| Gamma | HHV-4 | Epstein-Barr-Virus (EBV) | Oncogenic properties |
| | HHV-8 | Kaposi-Sarkom-Virus (KSHV) | Oncogenic properties |

# Opportunistic infections

## Hepatic encephalopathy

Despite high frquency, pathogenesis still not fully understood

| Grade | Signs of clinical manifestation |
|---|---|
| I | Changes in behaviour, mild confusion, slurred speeach, disordered sleep |
| II | Lethargy, moderate confusion |
| III | Marked confusion, incoherent speech, sleepign but arousable |
| IV | Come, unresponsive to pain |

Uptodate © 2022

**Pharmacological management:** Lactulose, Rifaximin

Antibiotic therapy to reduce ammonia producing bacteria and prophylactic protection from bacterial translocation from guts to peritoneum/blood stream as part of liver cirrhosis (spontaneous bacterial peritonitis)

# Opportunistic infections

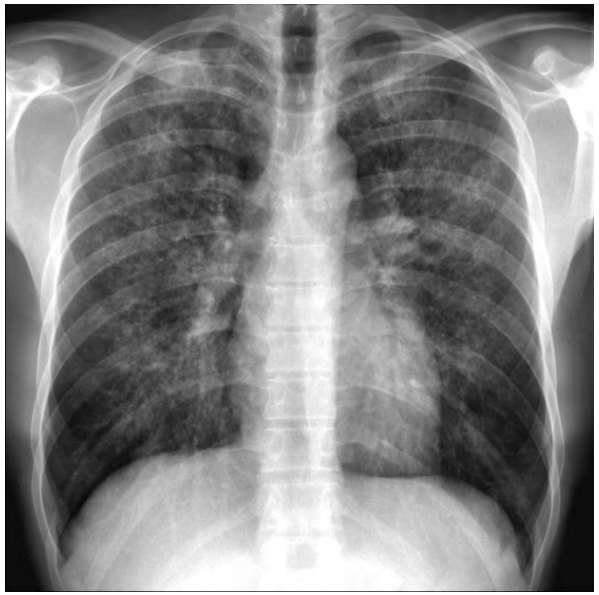
**Pneumocystis pneumonia (PCP)**

*P. jirovecii* ubiquitous fungus that specifically infects human lungs in immunsuppressed patients

**Drug of choice:** Trimethoprim-sulfamethoxazole (TMP-SMX)

**Example indications for chemoprophylaxis:**

- HIV+ and/or CD4 count below 200 cells/mm3
- Hematological neoplasia (prolonged leukopenia)
- Iatrogenic immunsuppression (calcineurin inhibitors)



Radiopaedia ©

# Ward round: MAI

*Ganciclovir:*
HHV-6 reactivation as part of acute promyelocytic leukemia

- MW = 255.2 g/mol
- Q0 = 0.05
- PB = 1-2%
- Adjusted BW = 120 kg
- Duration of dialysis = 15 h

**Decision: 150 mg every 48 h**
- 1.25 mg/kg BW
- Leukopenia monitoring

# Course of hospitalisation

**23.09.** Start ganciclovir, continuation meropenem, liposomal amphotericin B

**23.09.** CMV-PCR negative, HHV-6 positive, Aspergillus antigen positive

**25.09.** Stool samples C. difficile positive, toxin negative
Deescalation to ceftriaxon, start metronidazol

**27.09.** Bacterial broad spectrum blood PCR negative; regredient CRP, PCT

**28.09.** HHV-6 PCR positive but almost no copies per ml

**29.09.** Clinical pharmacy ward round

# Ward round

| | 29.09. | 28.09. | 27.09. | 26.09. | |
|---|---|---|---|---|---|
| **Entzündung (all. klin. Chemie)** | | | | | |
| CRP (IKC) | 11.0 | 53.0 | 53.0 | 86.0 | mg/l |
| PCT (Procalcitonin) (IKC) | | | 0.20 | 1.39 | µg/l |

*Group 1+2* *Group 3+4* *Group 5+6*

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**Universitätsspital Zürich**
**Rämistr. 100, WEST J 28**
**8091 Zürich**

Patient:
Beh. Arzt:
Auftrag:

Arbeitsplatz: v04 2022269383
Material: Urin - Mittelstrahl

**Mikrobiologischer Endbefund**

**Kulturergebnisse**

Candida glabrata: 10E4/ml

Ohne klinische Angaben oder Fragestellung beschränken wir die Untersuchung auf mikrobiologisch releva Erreger.

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Patient:
Beh. Arzt:
Auftrag:

Arbeitsplatz: v10 2022867244
Material: Tracheal-/Bronchialsekret

**Mikrobiologischer Endbefund**

**Kulturergebnisse**

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Patient:
Beh. Arzt:
Auftrag:

Arbeitsplatz: v04 2022269383
Material: Liquor

**Mikrobiologischer Endbefund**

**Kulturergebnisse**

Candida glabrata: 10E4/ml

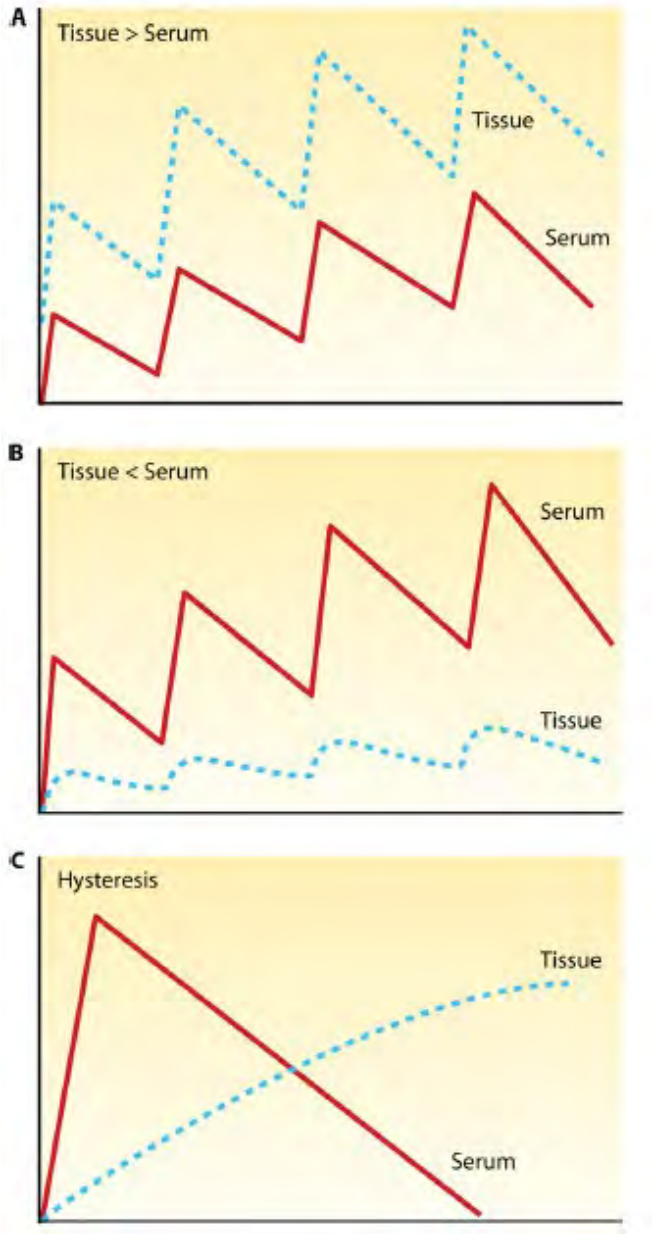
Ohne klinische Angaben oder Fragestellung beschränken wir die Untersuchung auf mikrobiologisch relevante Erreger.

# Ratio of penetration

$$PR = AUC_{\tau\ tiss} / AUC_{\tau\ pl}$$

**Factors**

- Log P value (polarity)
- Molecular weight
- Ionisation
- Carriers/Protein binding
- Metabolic extraction rate
- Route of administration
- PGx, etc.




Felton et al. 2014 Clin Microbiol Rev 27:68–88

# Relevant compartiments

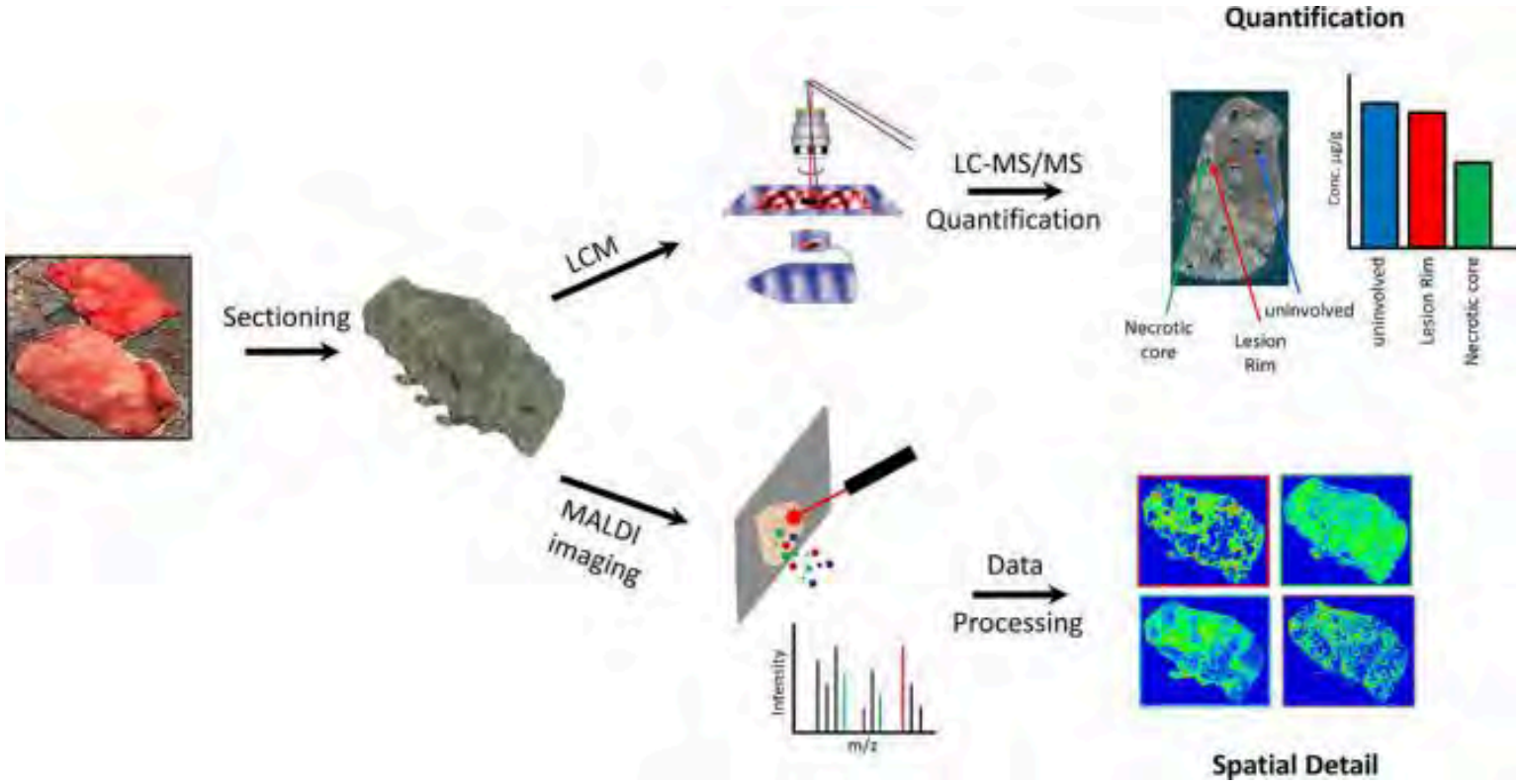
**Tissue**

- Brain
- Eye
- Lungs
- Liver, GI-Tract, Pancreas
- Spleen
- Myocard
- Skeletal muscle, skin
- Bone

**Body fluids**

- Blood/Plasma/Serum
- Liquor
- Alveolar „Epithelial Lining Fluid“
- Pleurisy effusion
- Pericardial effusion
- Ascites
- Biliary system/Bile
- Urine

# Drug exposure analysis




Workflow of analysis by integrating MALDI imaging with LC-MS/MS

# Ratio of penetration

| Compound | Eye | | | Skin | | | Vagina | | Heart | | Liver | Pancreas | Kidney | Bone | | Prostate | | Brain | | Lung | | | Spleen | Muscle | Reference |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Aqueous | Vitreous | Cornea | Tissue | Interstitial fluid | Nail | Tissue | Fluid | Tissue | Pericardial fluid | | | | Tissue | Synovial fluid | Tissue | Fluid | Tissue | CSF | Tissue | Alveolar cells | ELF | | | |
| Fluconazole | X | X | O | X | X | X | X | X | X | X | X | X | X | X O | X | X X | X | X | X | X | | O | X | X | (67, 70, 72, 120, 137, 200-203, 205, 219, 237, 238) |
| Itraconazole | O X | O | | X | X | X | X X | X X | O | | X | O | X | X | X | X | X | O | X | X | X | | X | X | (25, 56, 73, 74, 120, 121, 140, 220, 221, 239-242) |
| Voriconazole | X | X | | O | O | | | | X | X | X X | | X X | X | X | | | X | X | X X | X | X X | X X | O | (58, 80, 81, 83, 114, 142, 153, 154, 208, 224, 243, 252, 253) |
| Posaconazole | | X | | X | | X | | | | | | | | | | | | O | X | | X | X | | | (57, 59, 85-89, 223, 244) |
| AmBd | X X | X | | | | | | | O | | X | X X | X | O | X | | | X X | X | O | | O | X | | (37, 52, 53, 91, 115, 123, 148, 151, 156, 210, 245-247, 249) |
| ABLC | | | | | | | | | X | | X | | X | O | | | | O | X | | | X | X | | (90, 92, 117, 125, 147, 155, 210, 246, 249) |
| L-AMB | | | | | | | | | X | | X | | X | O | | | | X | X | | | X | X | | (34, 53, 60, 90, 125, 147, 155, 210, 248, 249) |
| 5-FC | O | X | | O | | | | | O | | O | | O | O | | | | | X | | | | O | O | (91, 96, 115, 116, 151, 156, 174, 250) |
| Anidulafungin | | | | O | | | | | O | | O | | O | O | | | | | O | O | X | | | | (58, 100, 102, 175, 251) |
| Caspofungin | O | | O | | | | | | O | | | | O | | | | | | | | X | | O | | (44, 103, 105, 113, 126, 130, 149) |
| Micafungin | | | | | | | | | | | O | | O | | | | | | X | O | X | | | | (61, 62, 106-108, 127, 150, 252) |

<0.5x plasma conc.
>0.5x plasma conc.
>5.0x plasma conc.

AmBd = Amphotericin B

ABLC = lipid complex Amphotericin B

L-AMB = liposomal Amphotericin B

5-FC = 5-Fluorouracil

X = human data, O = animal data; Felton et al. 2014 Clin Microbiol Rev 27:68–88

# Ward round

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|---|---|---|---|---|---|
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| PCT (Procalcitonin) (IKC) | | | 0.20 | 1.39 | µg/l |

*Group 1+2* *Group 3+4* *Group 5+6*

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Beh. Arzt:
Auftrag:

Arbeitsplatz: v04 2022269383
Material: Urin - Mittelstrahl

**Mikrobiologischer Endbefund**

**Kulturergebnisse**

Candida glabrata: 10E4/ml

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Fluconazol

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Auftrag:

Arbeitsplatz: v10 2022867244
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**Kulturergebnisse**

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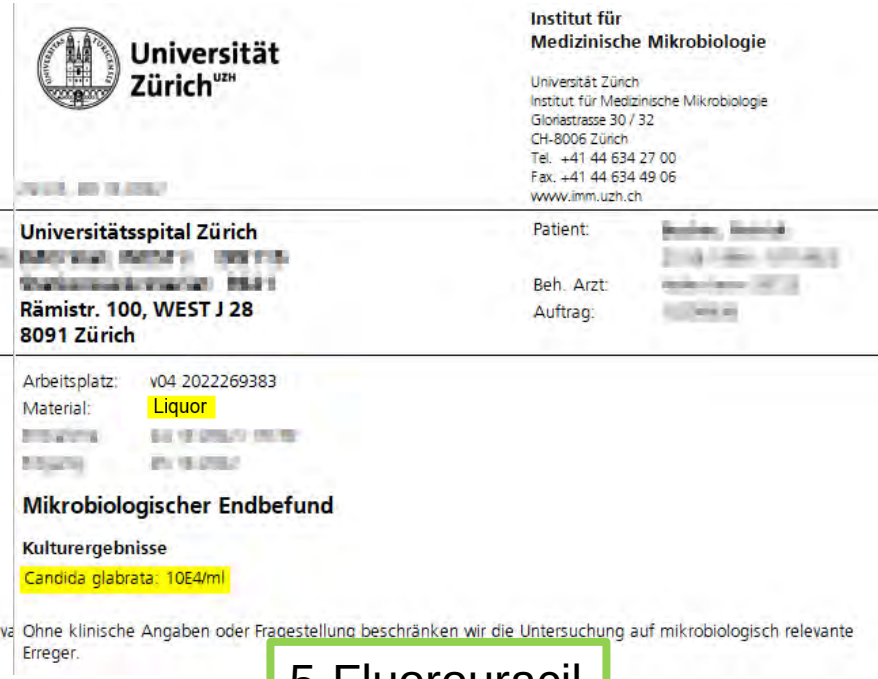
Posaconazol



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Patient:
Beh. Arzt:
Auftrag:

Arbeitsplatz: v04 2022269383
Material: Liquor

**Mikrobiologischer Endbefund**

**Kulturergebnisse**

Candida glabrata: 10E4/ml

Ohne klinische Angaben oder Fragestellung beschränken wir die Untersuchung auf mikrobiologisch relevante Erreger.

5-Fluorouracil

# Course of hospitalisation

**30.09.** Deterioration of respiratory function

**01.10.** Rapid weight loss, persistent normocytic anemia

**03.10.** hemodynamic stabilization, SPONT of breathing

**04.10.** Rotation to oncologic ward

# How confident do you feel?

VERY CONFIDENT

KIND OF CONFIDENT

NOT CONFIDENT

Code: ??????

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