14.–15. September 2017
Gemeinsame Jahrestagung SGI | GSASA
Réunion annuelle commune SSMI | GSASA
OLMA Messen, St. Gallen

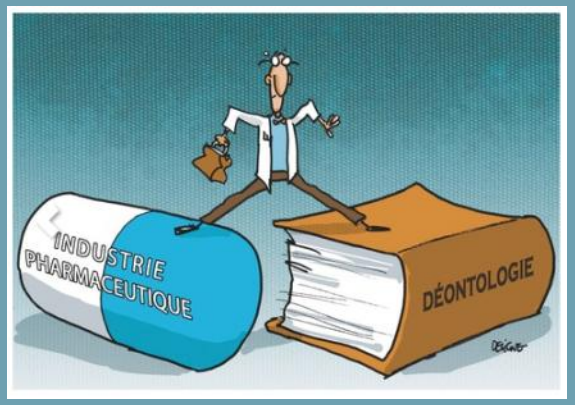
PHARMACOKINETIC IN THE NICU/PICU: WHAT DO YOU NEED TO KNOW?

Dre Caroline Fonzo-Christe
Dr Sébastien Fau
Service de néonatologie et soins intensifs pédiatriques
Pharmacie

Hôpitaux Universitaires Genève

Déclaration conflits d'intérêts ayant un lien avec la présentation

Les orateurs n'ont aucun conflit d'intérêts à déclarer avec la présentation qui suit



Our daily life

From the smallest to the biggest one…


ANNE GEDDES®

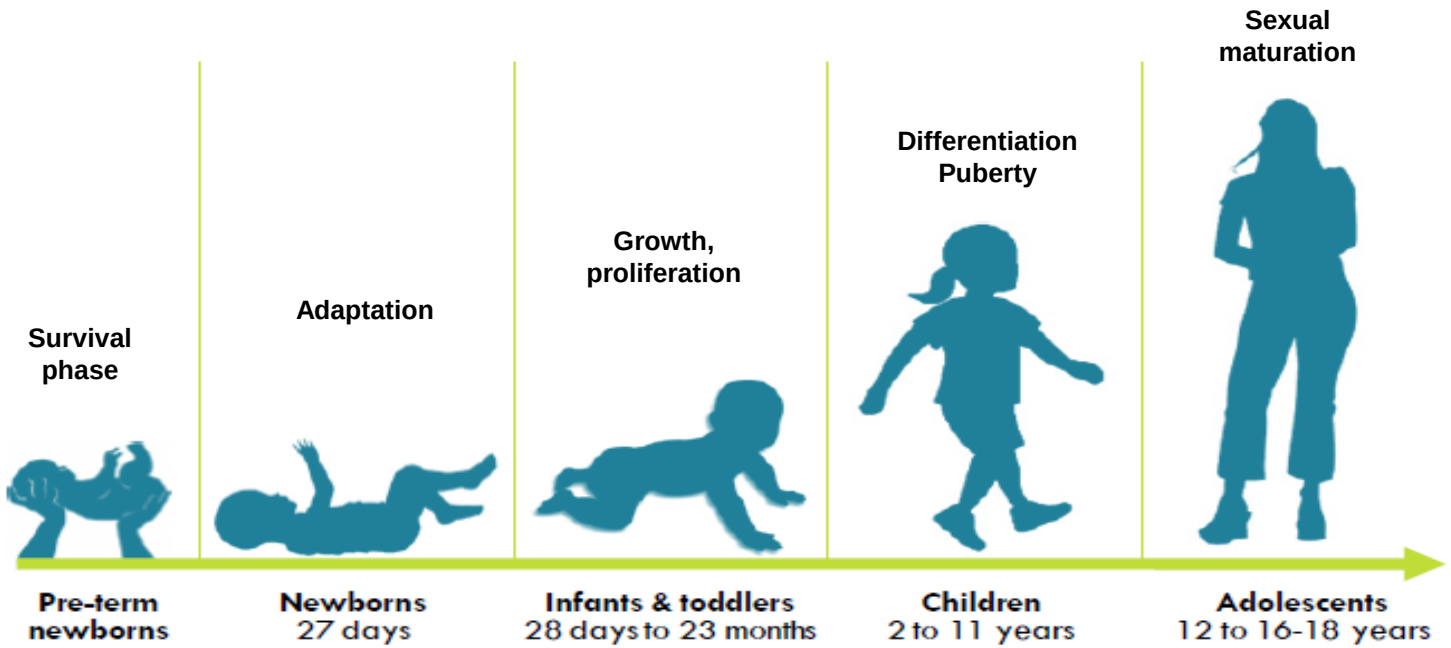
Children are not Little Adults


TWIX


TWIX
BOUNTY
Twix
SNICKERS
TWIX
Mars
SNICKERS
BOUNTY
SNICKERS
BOUNTY

Age categories: Variability

Evolving physiology

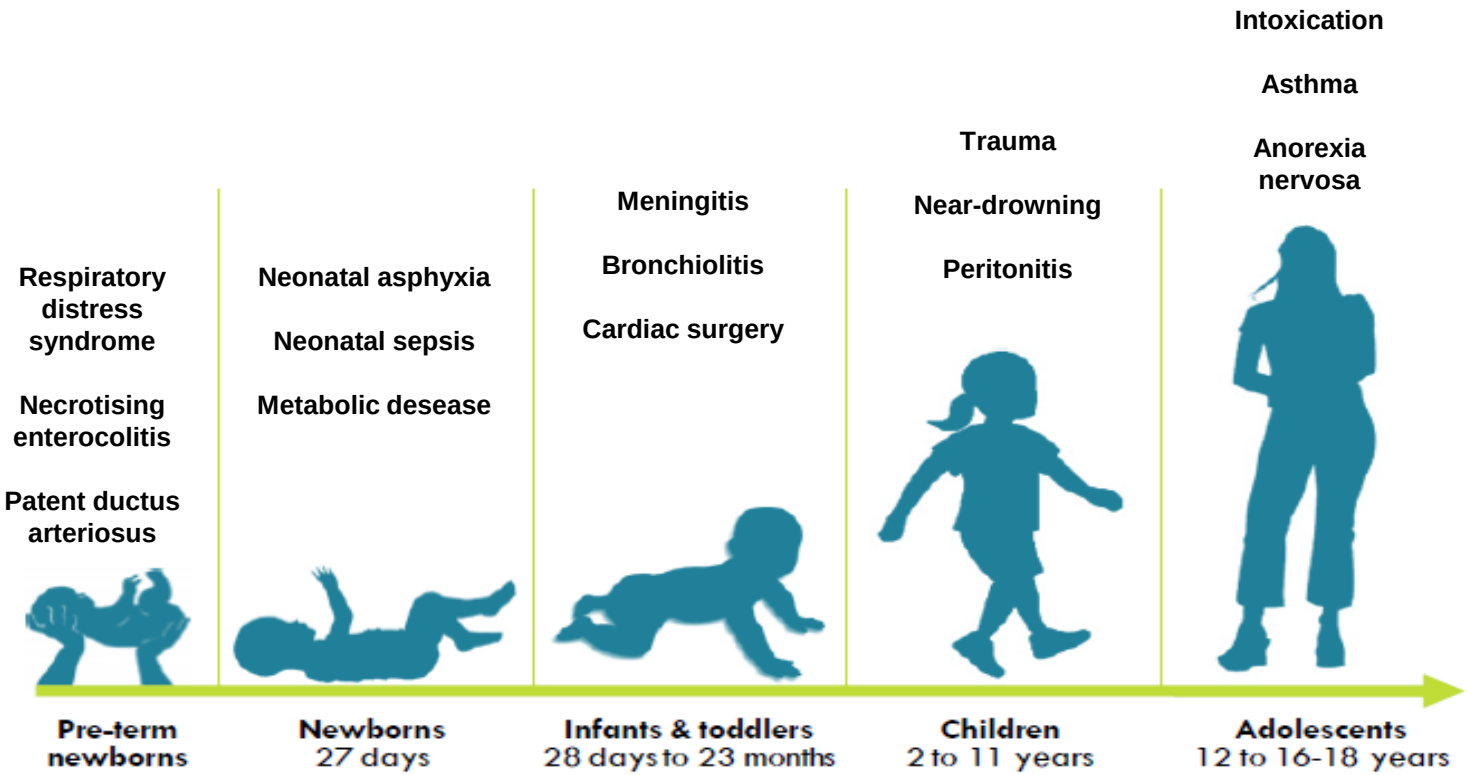


<500 g

>100kg

Adapted from : Tomlin S, EAHP 2014

VARIOUS DISEASES : EXEMPLES



<500 g

>100kg

Adapted from : Tomlin S, EAHP 2014

PATIENTS

27 beds

~ 1000 patients/year

12 PICU beds
(7 IC + 5 intermediate)

23 NICU beds
(13 IC + 10 intermediate)

20% Cardiac surgery (>200 patients/year)
50% Premature and neonates (>500 patients/year)

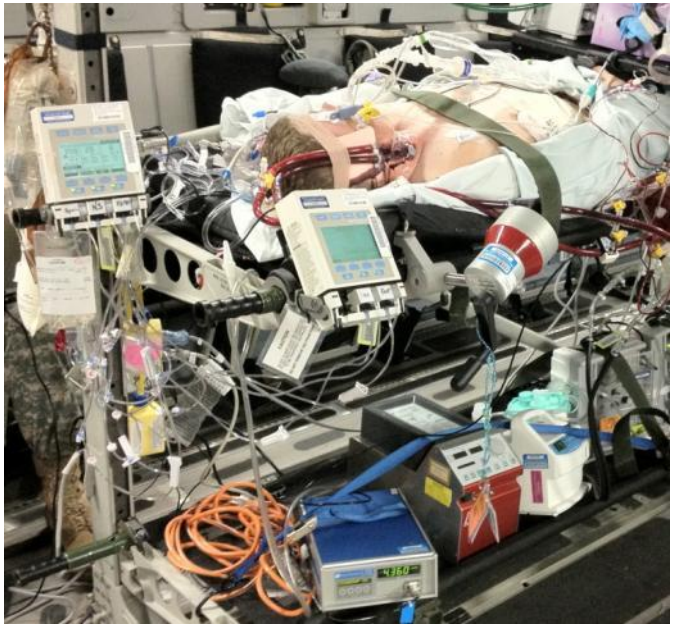
Liver transplantation (~10 patients/year)

CENTRE SUISSE DES MALADIES DU FOIE DE L'ENFANT

Other: post chirurgical, traumatic injuries, infections (bronchiolitis, sepsis)

Using Drugs in ICUs

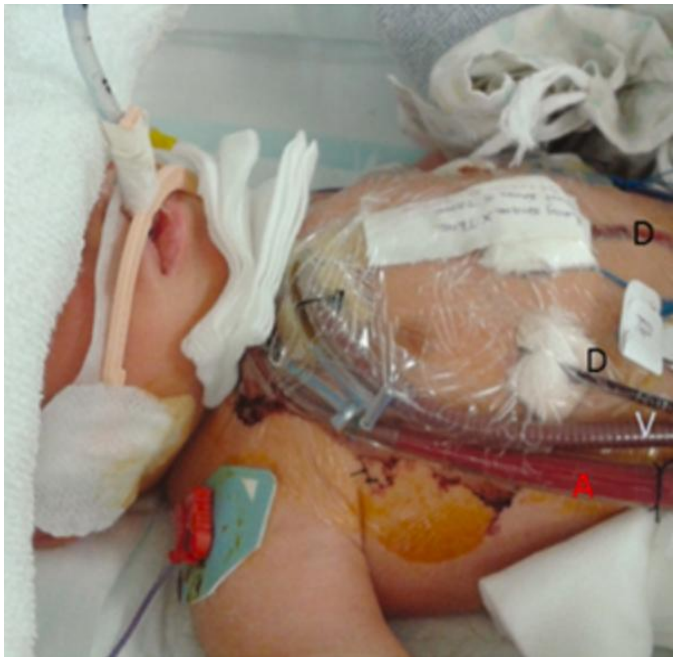
ADULT ICU



> 18 years

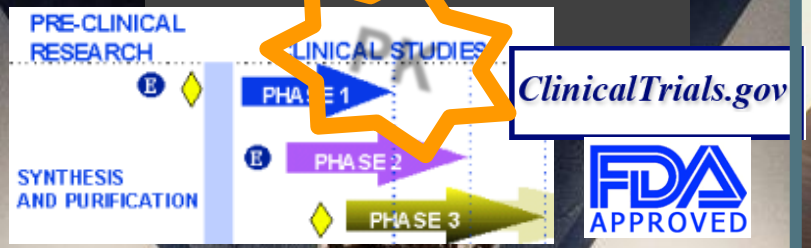
VS

PICU / NICU

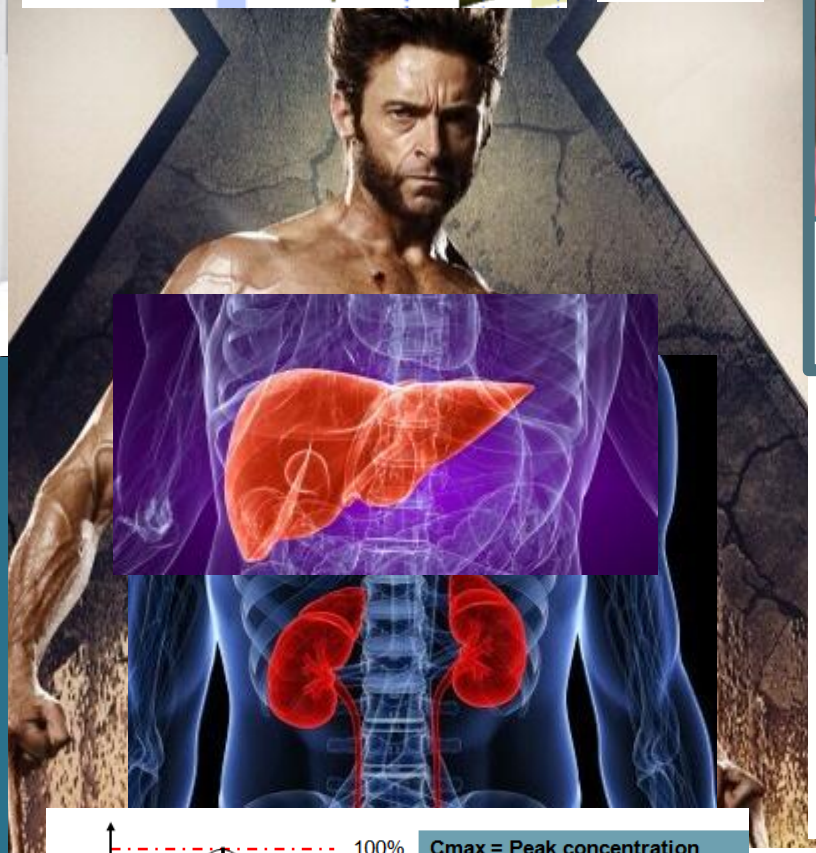


newborn

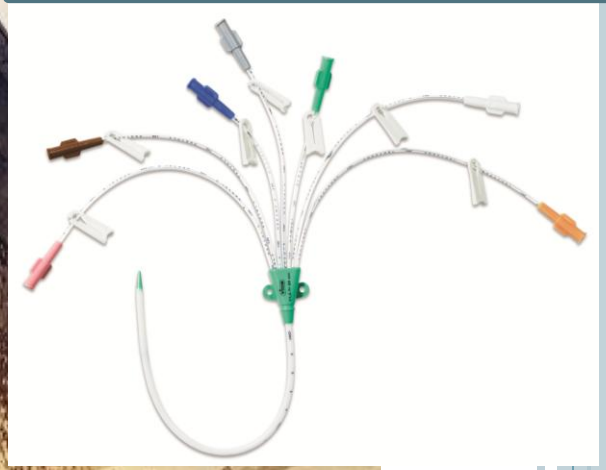

K
2011
Arzneimittel-Kompendium der Schweiz®

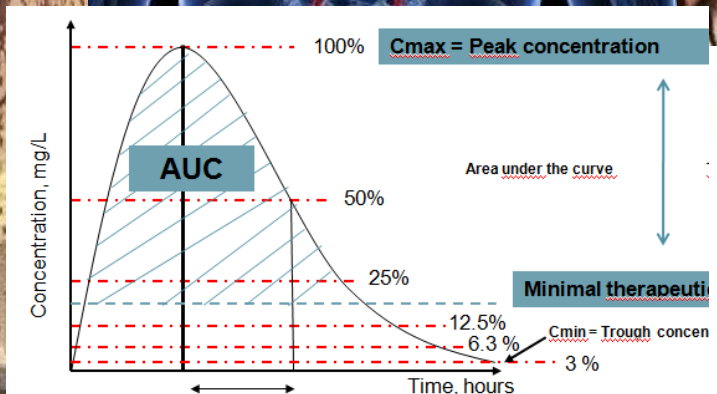

PRE-CLINICAL RESEARCH
CLINICAL STUDIES
SYNTHESIS AND PURIFICATION
PHASE 1
PHASE 2
PHASE 3
ClinicalTrials.gov
FDA APPROVED


0.9%
Sodium Chloride
Injection USP
50 mL
1 amp q 8h




SERIOUS ADVERSE SIDE EFFECTS
HEARING LOSS OR IMPAIRED HEARING
KIDNEY PROBLEMS
SEIZURES
SURPRESSED IMMUNE SYSTEM
ACUTE LIVER FAILURE
RESPIRATORY FAILURE

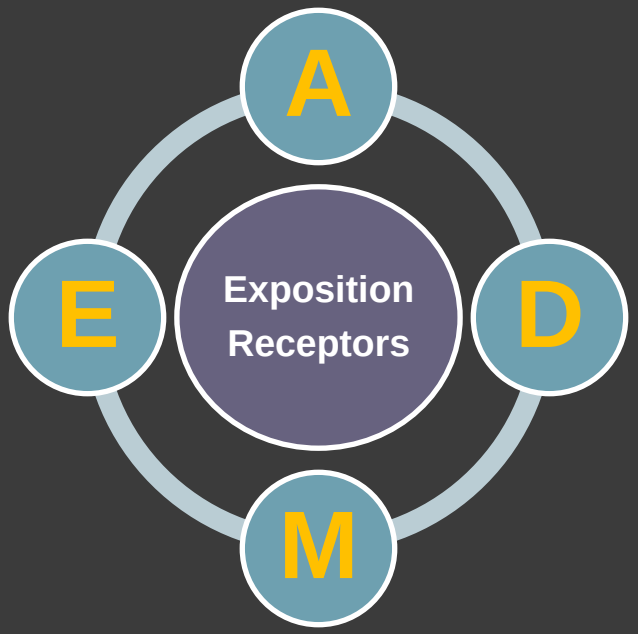



100%
Cmax = Peak concentration
AUC
Area under the curve
50%
25%
Minimal therapeuti
12.5%
6.3 %
Cmin = Trough concen
3 %
Concentration, mg/L
Time, hours


75% OFF LABEL
PRE-CLINICAL RESEARCH
STUDIES
PHASE 2
Forbidden
ClinicalTrials.gov
FDA APPROVED
« RCT so difficult... nearly impossible »
0.9% Sodium Chloride Injection USP 50 mL
80ml/kg/j = 80ml/j (total !)
1 amp q 8h
30mg/kg q8h
in 2ml
SERIOUS ADVERSE SIDE EFFECTS
HEARING IMPAIR
ACUTE LIVER FAILURE
SEVERE ALLERGIC REACTIONS
PSYCHOLOGICAL ISSUES
Long term adverse effects
(neurodevelopment, endocrine...)
No reliable Clearance measurement
7 Fr 2.3mm
1.2 Fr 0.4mm
Blood depletion (less transfusion)
Pain management (less puncture)
Single lumen 1.2F microcatheter (max flow 10 ml/h)

"I know that I know almost nothing"…

Concerning Drugs use and PK…
…Be pragmatic



Pharmacokinetic parameters

Pharmacokinetic

“what the body does to a drug”

-> profile of drug concentration over time

1. **A**bsorption
2. **D**istribution
3. **M**etabolism
4. **E**xcretion

Pharmacodynamic

“what a drug does to the body”

-> effect of the drug on the body (receptors)

What influence drug effect?

Patient in NICU / PICU

Administration

Drug incompatibilities and in-line filters
Drug delivery and infusion material
…

A

E

Exposition Receptors

D

M

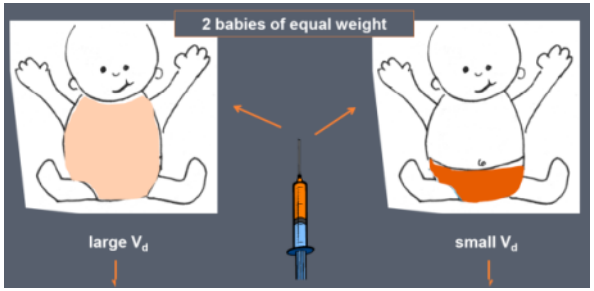
Drug effect

Ontogenesis
Pharmacogenetics
Environment
Nutritional state

Critically ill
- ECMO, renal dialysis
- Drug interactions
- Co-morbidity…

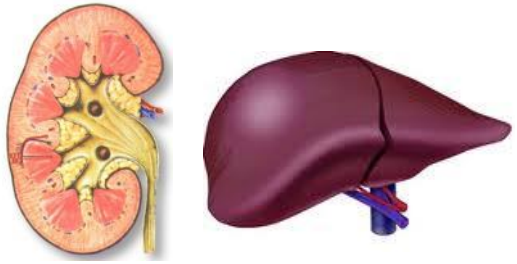
Two main PK parameters

- Volume of distribution (Vd)
  - ➔Loading dose

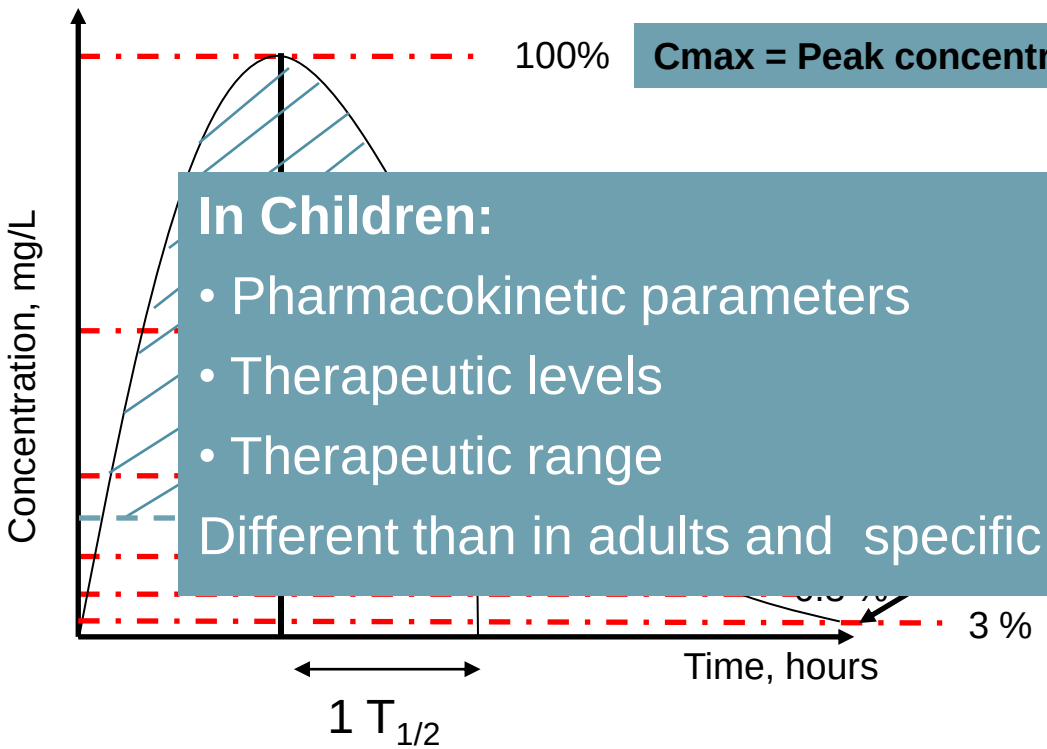


Adapted from Vaughan K, Dell Children's Medical Center of Central Texas

- Clearance
  - ➔Maintenance dose to reach a certain Css



PHARMACOKINETIC PARAMETERS



Cmax = Peak concentration

$$Cmax = \frac{dose}{Vd}$$

of distribution

In Children:

- Pharmacokinetic parameters
- Therapeutic levels
- Therapeutic range

Different than in adults and specific for age categories!

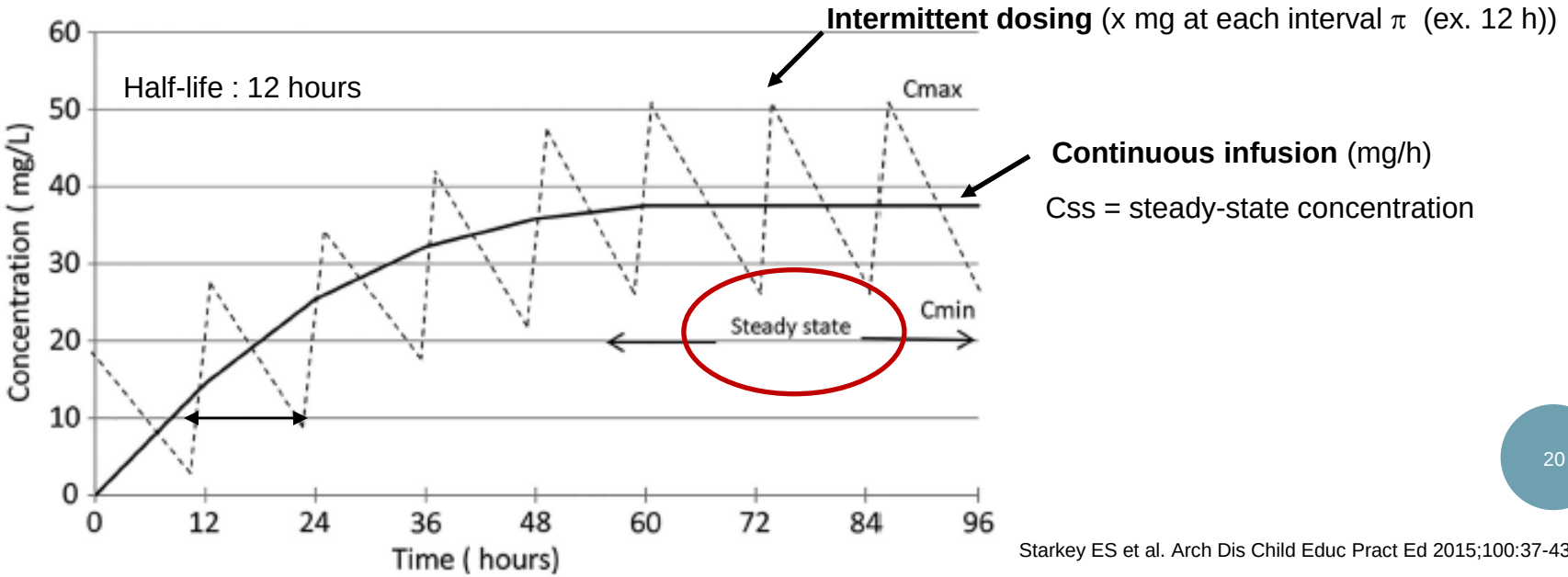
$$\text{Elimination half-life } T_{1/2} = \ln 2 \times \frac{Vd}{Cl}$$

T1/2: Time taken for plasma concentration to halve
Cl: Clearance
ln2 = 0.693

STEADY-STATE

- **Absorption or infusion rate balanced by elimination rate**
  - Plasma concentration does not increase anymore
  - Time to reach steady-state: **4-5** $T_{1/2}$

    Time to be completely eliminated: **4-5** $T_{1/2}$



Starkey ES et al. Arch Dis Child Educ Pract Ed 2015;100:37-43

Volume of distribution Vd

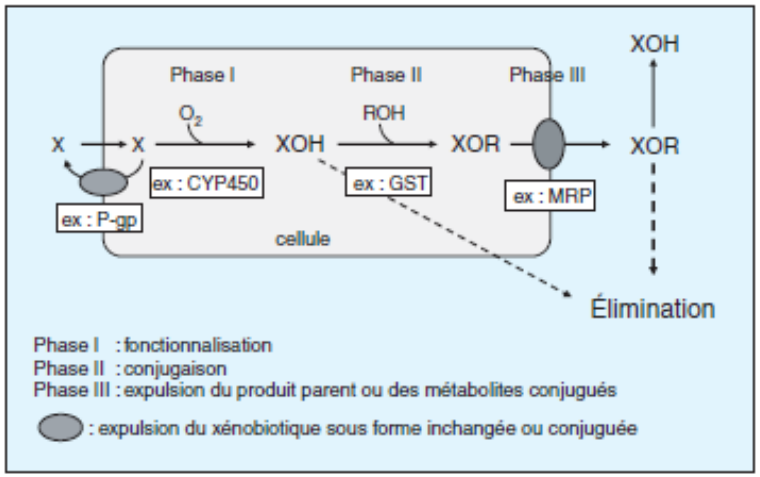
- Small Vd : drug mainly within systemic circulation
  - Plasma volume (Vd 0.05 L/kg): large MW or high protein binding (ex. heparin, aspirin)
  - Extracellular water (Vd 0.2 L/kg): ex. penicillins
  - Total body water (Vd 0.6 L/kg): ex. paracetamol, indometacine
- Large Vd (2-10 L/kg): drug distributed into peripheral compartments (ex. morphine)
- Useful to determine loading doses

$$C_{max} = \frac{dose}{Vd}$$

Starkey ES et al. Arch Dis Child Educ Pract Ed 2015;100:37-43

CLEARANCE CL

- Sum of drug clearance Cltot = hepatic + renal
- Hepatic clearance



Phase 1: oxidation, demethylation by enzymes (CYP450)
Phase II: conjugation
Phase III: excretion – elimination (renal or biliary)

Drug transport proteines:
P-gP (P-glycoproteine)
MRP (Multidrug resistance protein)

hydrophobic

hydrophilic

Cell protection

- Renal clearance: unchanged /metabolites
  - Glomerular filtration: aminoglycosides, digoxin
  - Proximal tubular secretion: penicillins, furosemide

Allorge D, Loriot A. Ann Biol Clin 2004;62:499-511
Starkey ES et al. Arch Dis Child Educ Pract Ed 2015;100:37-43

Basic Paediatric PK Principles and ontogenesis in the non - critically ill child

Challenge:

- Normal physiological and developmental changes

- Variability

3 PAPERS

Practical pharmacokinetics: what do you really need to know?

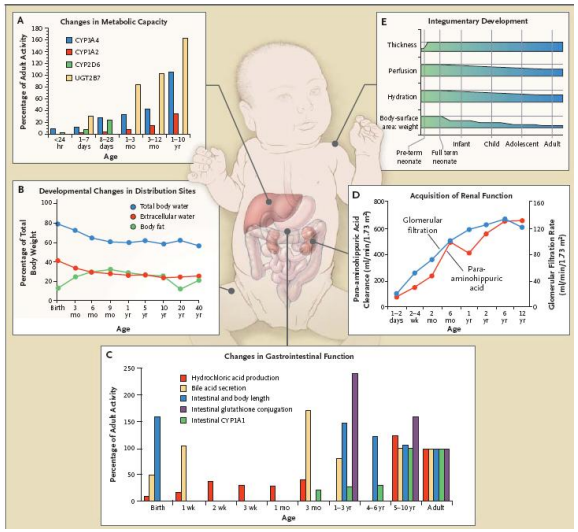
E S Starkey,[1] H M Sammons[2]

Starkey ES, *et al*. *Arch Dis Child Educ Pract Ed* 2015;**100**:37–43.

Drug metabolism for the paediatrician

Saskia N de Wildt,[1] D Tibboel,[1] J S Leeder[2]

de Wildt SN, *et al*. *Arch Dis Child* 2014;**0**:1–6.



Developmental Pharmacology — Drug Disposition, Action, and Therapy in Infants and Children

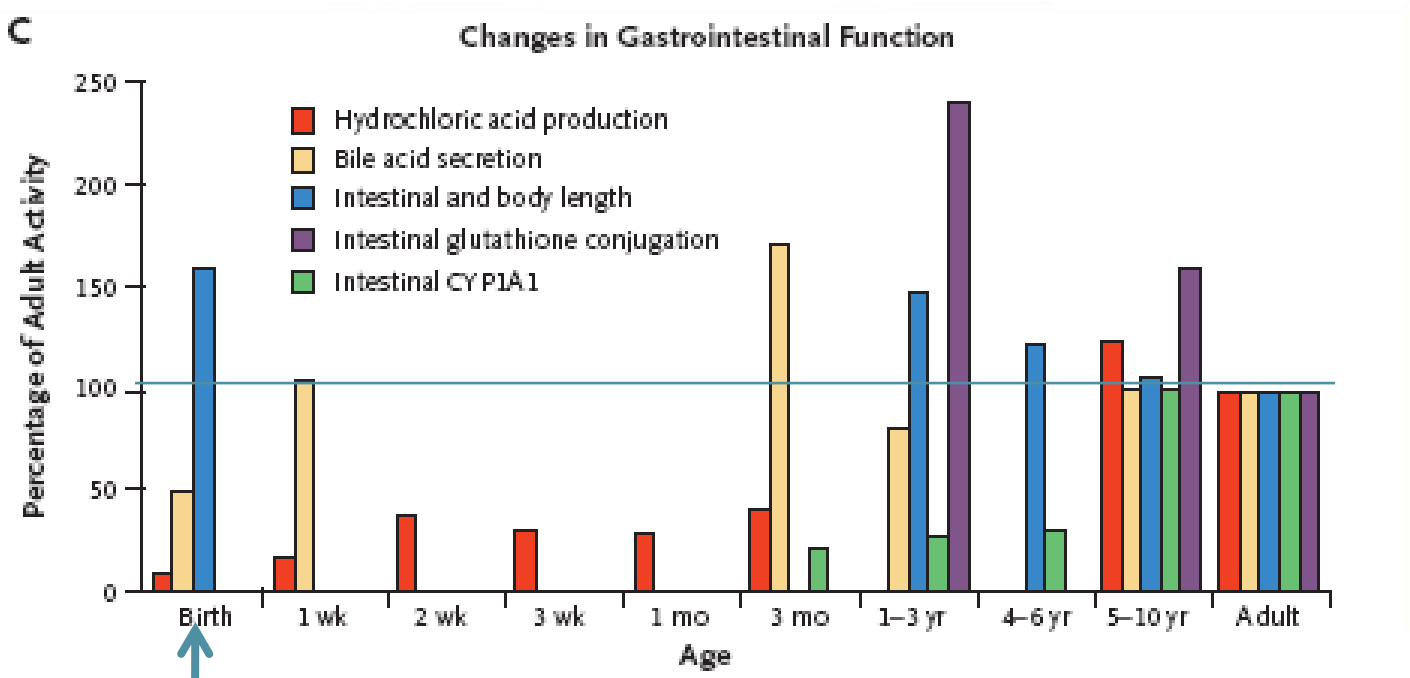
Gregory L. Kearns, Pharm.D., Ph.D., Susan M. Abdel-Rahman, Pharm.D., Sarah W. Alander, M.D., Douglas L. Blowey, M.D., J. Steven Leeder, Pharm.D., Ph.D., and Ralph E. Kauffman, M.D.

Kearns GL et al. N Engl J Med 2003;349:1157-67

1. **A**bsorption
2. **D**istribution
3. **M**etabolism
4. **E**xcretion

Gastro-intestinal absorption

ABSORPTION



> adult

adult

< adult

Day 1: pH 1 – 3
At 24h and for 1 to 2 weeks: pH neutral

Kearns GL et al. N Engl J Med 2003;349:1157-67

ABSORPTION

Bioavailability

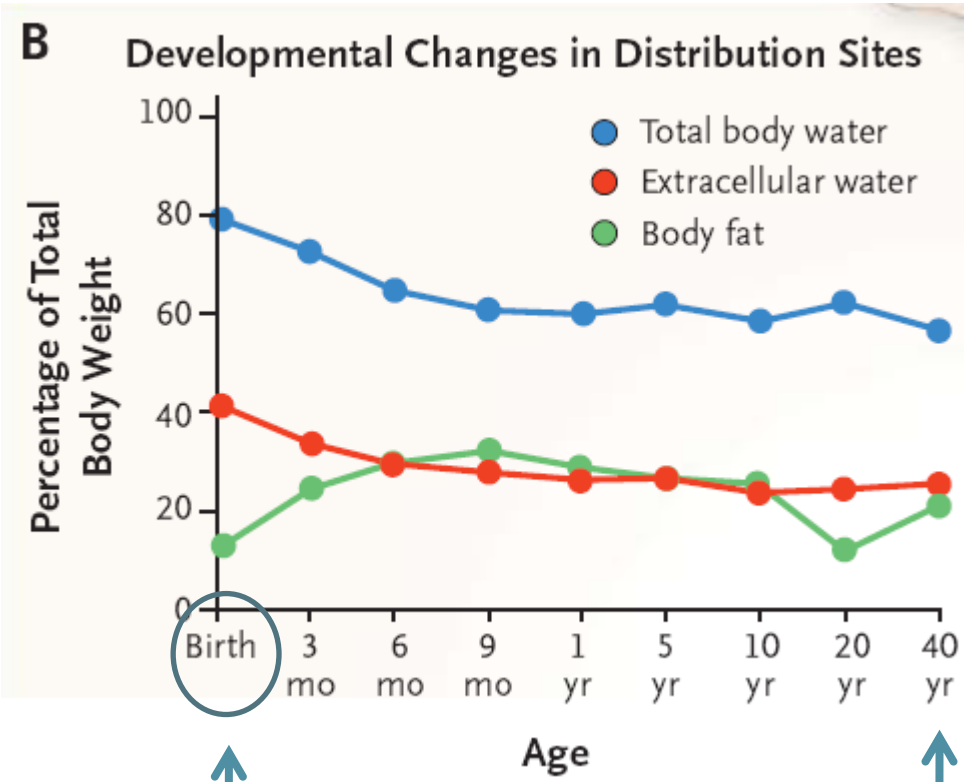
	Neonate	Infant	Child
Gastric emptying	Delayed ↓ Absorption time	Enhanced	Slighltly enhanced
Gastric pH	pH >5 1-2 weeks of life ↓ progressively	4-2	>2 years age: Adult value (pH 3)
Intestinal transit time	Decreased ↓ Delayed absorption time	Enhanced	Slighltly enhanced
Biliary system	Immature ↓ Fat absorption	Almost adult value	Adult value
Intestinal enzyme **CYP1A1, CYP3A** **PgP**	 Immature Unclear	 Immature Unclear	 Adult value Unclear

Kearns GL et al. N Engl J Med 2003;349:1157-67
Bartelink IH. Clin Pharmacokinet 2006; 45;1077-1097

1. **A**bsorption
2. **D**istribution
3. **M**etabolism
4. **E**xcretion

DISTRIBUTION

Body composition



80% water
20% fat

60% water
20% fat

Vd

Neonates

- larger Vd for hydrophilic drugs (aminoglycosides) -> risk of underdosing
- lower Vd for fat-soluble drugs (fentanyl, midazolam) -> risk of toxicity

Kearns GL et al. N Engl J Med 2003;349:1157-67

VD AND GENTAMICINE

- A larger Vd requires a higher loading dose of the drug (in mg/kg) to reach the same plasma concentration

Vd ↓

Dosing Chart

PMA *(weeks)*	Postnatal *(days)*	Dose *(mg/kg)*	Interval *(hours)*
≤29*	0 to 7 8 to 28 ≥29	5 4 4	48 36 24
30 to 34	0 to 7 ≥8	4.5 4	36 24
≥35	ALL	4	24

* or significant asphyxia, PDA, or treatment with indomethacin

$$C_{max} = \frac{dose}{Vd}$$

Message 1:
Increased volume of distribution means **increase the dose (loading dose)**, to " fill up all the spaces "

Neofax 2010

1. **A**bsorption
2. **D**istribution
3. **M**etabolism
4. **E**xcretion

Hepatic metabolism

Metabolic capacity and developpement

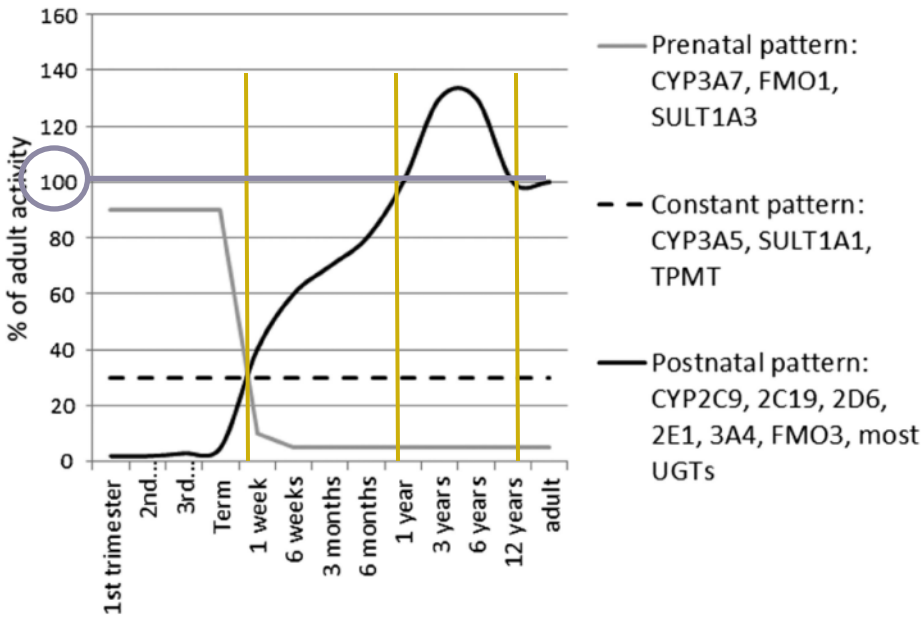


Table 2 Drug metabolism and age

Age	CYP3A4	CYP1A2	Glucuronidation	Sulphation
Preterm neonates	+	+	+	+++
Term neonates	+	+	+	+++
Infants	+++	++	++	++
Children	+++	+++	+++	+
Adolescents	++	+++	+++	+

Hepatic Clearance

Neonates

- Reduced hepatic clearance -> risk of toxicity

Child

- Increased hepatic clearance for some drugs -> risk of underdosing

de Wildt SN, et al. Arch Dis Child 2014
Choonara I, et al. Arch Dis Child 2014;99:1143–1146

IMPACT ON HALF-LIFE

	midazolam CYP3A4	ibuprofen CYP2C9, 2C19	indomethacin CYP2C9	caffeine CYP1A2	morphine UGT2B7	paracetamol UGT1A6,1A9
$T_{1/2}$ NN	6-12h	PNA 3j: 43h PNA 5j: 27h	PNA<2sem: 20h PNA>2sem: 11h	NN: 72-96h	Premature: 10-20h NN: 8h	NN: 2-5h Sulphation
$T_{1/2}$ child	1-1.5h	1-2h	-	5h (at 9 months)	1-2h	Sulphation
$T_{1/2}$ adult	1.5-3.5h	2-4h	-	3-5h	2-4h	1-3h Glucuro-conjugation

PNA: post natal age
NN: neonate

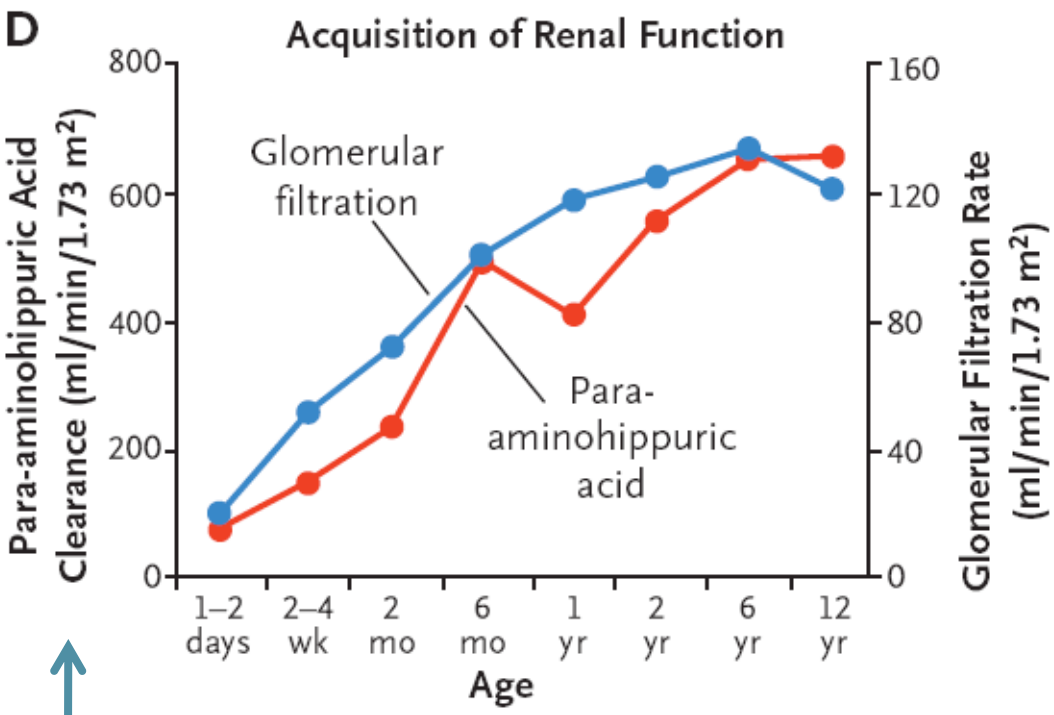
Reduced hepatic clearance and longer half-life in NN
Increased hepatic clearance in childhood

Message 2:
Metabolic clearance of drugs matures at different rates, depending on the drug metabolism pathways involved

1. **A**bsorption
2. **D**istribution
3. **M**etabolism
4. **E**xcretion

Renal excretion

RENAL FUNCTION



Proximal tubular secretion

Adult values (100 – 120 ml/min) at about 1 year

Renal Clearance

Reduced renal clearance in the first year of age for:

- Drugs with high renal excretion (aminoglycosides, penicillines, furosemide)
- Active metabolites (morphine-6-glucuronide)

Kearns GL et al. N Engl J Med 2003;349:1157-67

CLEARANCE AND GENTAMICINE

- Renal Clearance is affected by immature glomerular filtration
- A decreased Clearance requires a longer dosing interval to maintain trough concentrations low (to limit toxicity)

Cl ↑

Dosing Chart

PMA *(weeks)*	Postnatal *(days)*	Dose *(mg/kg)*	Interval *(hours)*
≤29*	0 to 7 8 to 28 ≥29	5 4 4	48 36 24
30 to 34	0 to 7 ≥8	4.5 4	36 24
≥35	ALL	4	24

* or significant asphyxia, PDA, or treatment with indomethacin

Message 3:
Decreased clearance
means longer half-life and higher plasma concentrations
Need to **increase dosing interval**

Neofax 2010

Therapeutic Drug Monitoring

At HUG:

- No specialist for interpretation of drug levels
- N
  m
- P
  - n
  - which interval
  - How to adapt trough level if to high or to low

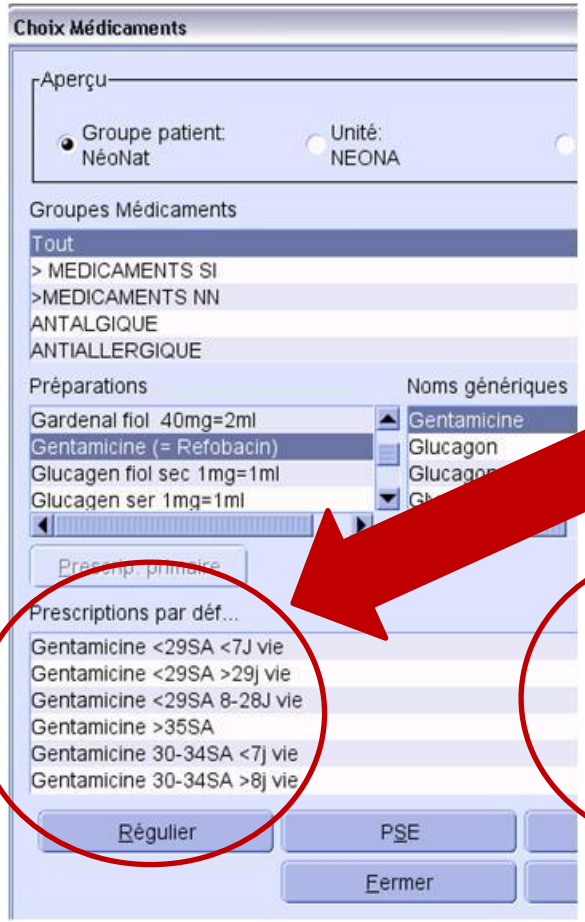
Message 4:

…changing dose and interval all the time !

To change trough level,
adapt dosing interval

Steady-State?

Electronic prescribing



GENTAMICINE chez le NOUVEAU-NE et PRÉMATURÉ

Carte de poche

HUG Hôpitaux Universitaires Genève

GENTAMICINE

Posologie et administration

GENTAMICINE	Age gestationnel [semaines]	Age postnatal [Jours de vie]	Dose [mg/kg/dose]	Intervalle [heures]
Taux résiduel ciblé : ≈ 1 mg/L	≤ 29	≤ 7	5	48
		8-28	4 – 5	36
		≥ 29	4 – 5	24
	30 – 34	≤ 7	4 – 5	36
		≥ 8	4 – 5	24
	≥ 35	tou	4 – 5	24

- Perfusion IV sur 30 min. Dilution avec G5% ou N… conc. finale 0.1-2 mg/mL, max 10 mg/mL.

TDM (th… toring)

- Le schéma de posologie p… maturité de la fonction rénale. Mesurer le taux résiduel avant la 3ème … est poursuivi pendant > 48 heures.
- En cas de sus… rénaux particuliers (diurèse <1 mL/kg/h dès 2j de vie) au début du … protocole 1ère dose » tenant compte de l'accumulation à venir. En cas … très bas, s'assurer qu'il n'y a pas de surdosage, un intervalle raccourci / … eur de prélèvement.

… prolongé pendant >10 jours, répéter TDM et consulter les infectiologues au 33763.

… aux pic ne doit pas être contrôlé en routine. Indication : Prescription d'une posologie différente de ces recommandations, présence d'un 3ème secteur ou non réponse au traitement. Moment du dosage : après la 3ème dose, 30 min après la fin de la perfusion.

PROTOCOLE STANDARD, DOSAGE A L'EQUILIBRE

PROTOCOLE STANDARD, DOSAGE A L'EQUILIBRE

Taux résiduel ciblé ≈ 1 mg/L

Résiduel	Intervalle actuel	Action proposée
< 0.5 mg/L	24 heures	Si la dose est correcte, continuer le traitement sans changement
	36 heures	Diminuer l'intervalle à 24 heures. Refaire un dosage après deux doses.
	48 heures	Diminuer l'intervalle à 36 heures. Refaire un dosage après deux doses.
> 2 mg/L	24 heures	Augmenter l'intervalle actuel à 36 heures, continuer avec cet intervalle. Refaire un dosage après deux doses.
	36 heures	Augmenter l'intervalle actuel à 48 heures, continuer avec cet intervalle. Refaire un dosage après deux doses.
	48 heures	Ne pas donner la prochaine dose. Contrôler la conc. dans 24 heures.
> 3 mg/L	(correcte pour l'âge)	Ne pas donner la prochaine dose. Contrôler la conc. dans 24 heures.

< 1.1 mg/L	Donner la prochaine dose, continuer avec un intervalle de 24 heures
1.2 - 2.3 mg/L	Donner la prochaine dose dans 12 heures, continuer avec un intervalle de 36 heures
2.4 - 3.2 mg/L	Donner la prochaine dose dans 24 heures, continuer avec un intervalle de 48 heures
> 3.3 mg/L	Ne pas donner la dose, contrôler la concentration dans 24 heures

Pharmacie des HUG / Document créé le : 25.09.09 / auteur ; CZ / dernière révision le 19.06.2017 par cefl/tlp/fl/pb
Validation initiale : Profs A. Gervaix, P. Rimensberger, J. Desmeules, Drs R. Pfister, K. Posfay Barbe, R. Corbelli, O. Karam 1/2
La pharmacie des HUG décline toute responsabilité en cas d'utilisation des informations disponibles sur son site Internet hors des HUG. Seule la version la plus récente visible sur le site Internet de la pharmacie des HUG fait foi. (http://pharmacie.hug-ge.ch)

http://pharmacie.hug-ge.ch/informedic/utilsmedic/tdm_vanco_amino_neo_poche.pdf

Impact of Clinical Decision Support Guidelines on Therapeutic Drug Monitoring of Gentamicin in Newborns

Caroline Fonzo-Christe, MSc, PhD, Bertrand Guignard, MSc, PhD,* Claudia Zaugg, MSc,* Ana Coehlo, MSc,* Klara M. Posfay-Barbe, MD,† Alain Gervaix, MD,‡ Jules Desmeules, MD, PhD,§¶ Victoria Rollason, MSc, PhD,§¶ Christophe Combescure, PhD,|| Regula Corbelli, MD,** Peter Rimensberger, MD,** Riccardo Pfister, MD, PhD,** and Pascal Bonnabry, MSc, PhD*¶*

	BEFORE (Control-group)	AFTER (Case-group)	Statistical analysis
ODD scheme	61.6%	97.7%	p<0.001
% peak level measurement	17.2%	0.9%	p<0.001
mean number of levels sampled	1.7 ± 1.4	0.8 ± 1.0	p<0.001
% of trough levels ≤ 1 mg/L	33.0%	68.5%	p<0.001

Fonzo-Christe C et al. Ther Drug Monit 2014 ;36:656-62

Critically ill and pharmacokinetic

IMPACT ON DRUG PK

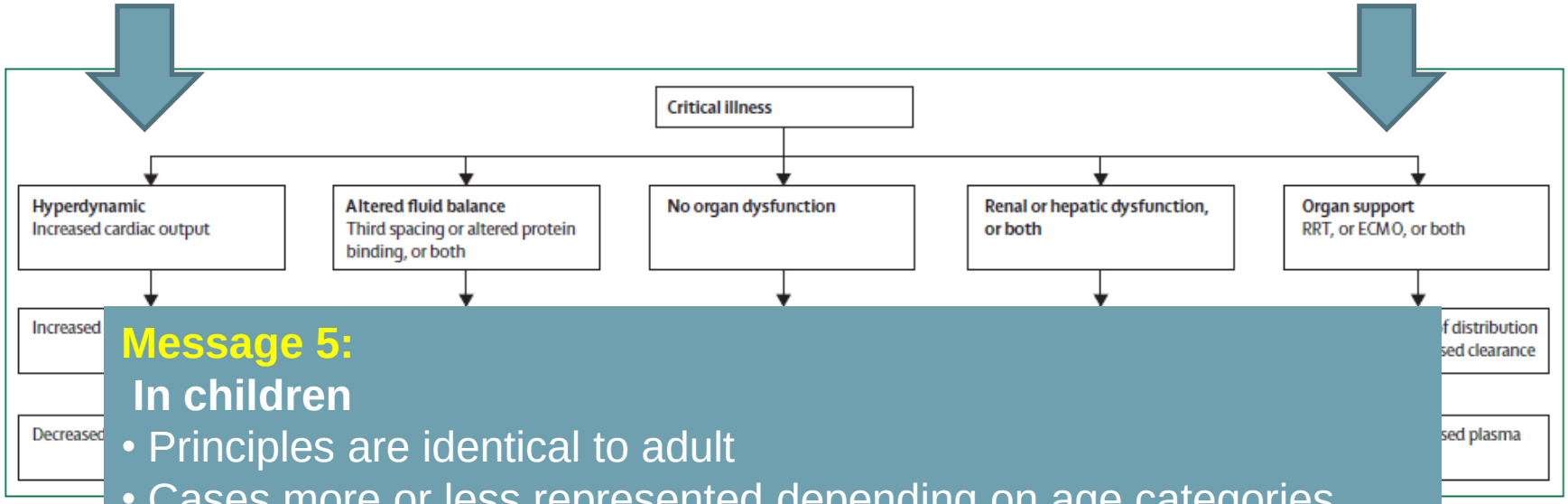


Figure: The
RRT–renal r

Message 5:

In children

- Principles are identical to adult
- Cases more or less represented depending on age categories
- Renal function difficult to evaluate < 1 year
- Congenital malformations (heart, kidney…)

Therapeutic failure

Toxicity

Therapeutic failure or Toxicity

$$C_{max} = \frac{dose}{Vd}$$

Vd: Volume of distribution

$$\text{Elimination half-life } T_{1/2} = \ln 2 \times \frac{Vd}{Cl}$$

Roberts JA et al. Lancet Infect Dis 2014;14:498-509

Enhanced renal Clearance

Antibiotics

RENAL CLEARANCE

- **Enhanced** in some critically patients (adult)

  ARC: augmented renal clearance

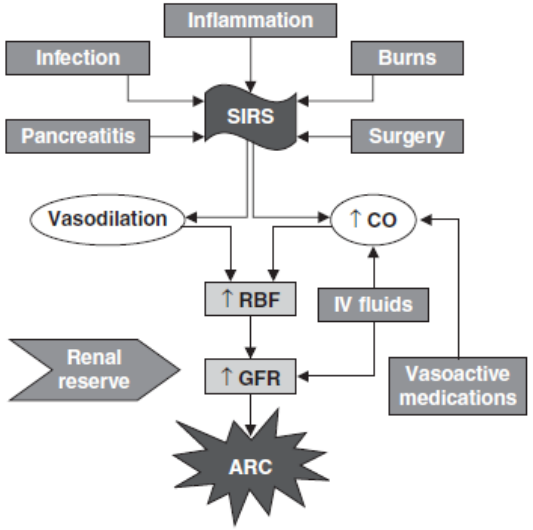
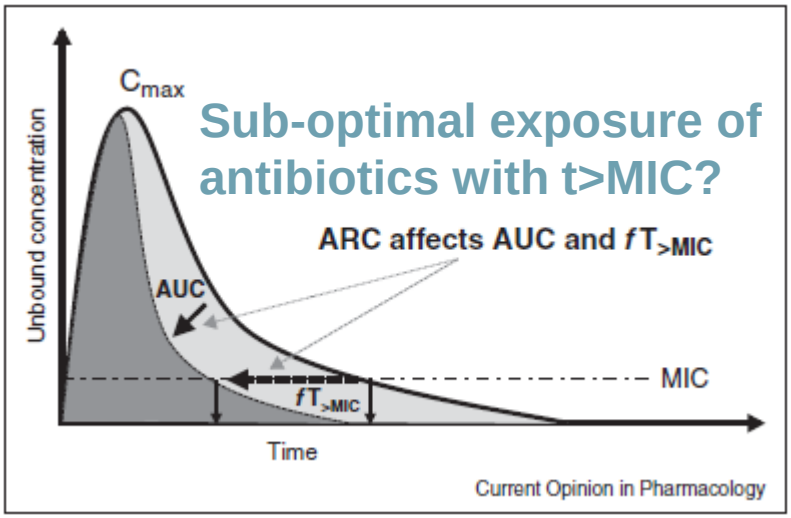


Fig. 2. Mechanisms underlying augmented renal clearance (ARC) in the critically ill. **CO** = cardiac output; **GFR** = glomerular filtration rate; **IV** = intravenous; **RBF** = renal blood flow; **SIRS** = systemic inflammatory response syndrome; ↑ indicates increase.



Udy AA et al. Clin Pharmacokinet 2010; 49:1-16
Sime FB et al. Curr Opin Pharmacol 2015;24:1-6

ARC IN CRITICALLY ILL CHILDREN

- Has not been reported in children
- In two PK modelling studies in critically ill children :
  - high mean clearance for amoxicillin estimated -> ARC?

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Augmented Renal Clearance Implies a Need for Increased Amoxicillin-Clavulanic Acid Dosing in Critically Ill Children

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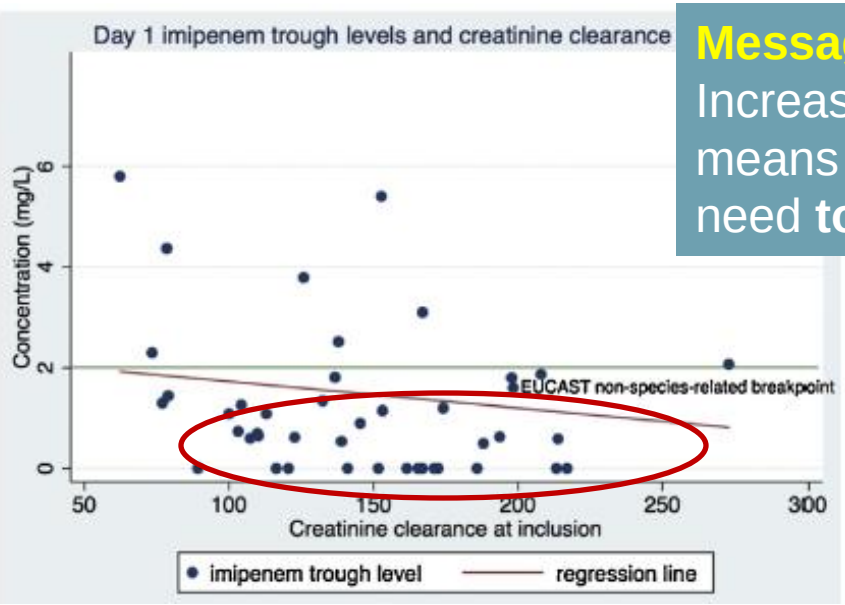
De Cock PAJG et al. Antimicrob Agents Chemother 2015; 59:7027–7035

ARC AND BETA-LACTAM AB

Augmented renal clearance, low β-lactam concentrations and clinical outcomes in the critically ill: An observational prospective cohort study

Angela Huttner[a,*], Elodie Von Dach[a], Adriana Renzoni[a], Benedikt D. Huttner[a],



Message 6:
Increased clearance
means low troughs for AB's that needs t>MIC
need **to increase frequency** (reduce interval)

Clinical implications for time-dependent (t>MIC) AB

- More frequent dosing (shorter dosing interval)
- Increased total daily dose
- Continuous/extended infusions?
- TDM

Huttner A et al. Int J Antimicrobiol Agents;2015:45:385-92
Udy AA et al. Intensive Care Med 2013;39:2070–82
Sime FB et al. Curr Opin Pharmacol 2015;24:1-6

QUESTIONS

- ARC and antibiotics resistance? No data
- Antibiotics as a continuous infusion: pharmaceutical considerations
  - Stability of drugs

Tableau 6 Stabilité de différentes bêta-lactamines en fonction de la température.

Durée de stabilité (heures) : dégradation < 10 %		
	37 °C	25 °C
Aztréonam	> 24	—
Pipéracilline	21	30
PIP + tazobactam	> 24	72
Ceftazidime	8	24
Céfépime	13	20
Cefpirome	7	23
Imipénème	3	3,5
Méropénème	1,5	5

➔ Need to change the drug solution (syringe) regularly

  - Drug compatibility (IV line « occupied » during 24h)
  - Potential for vasculitis and extravasation?

Jehl F et al. Réanimation 2009;18:343-52

ECMO

Antibiotics, sedation/analgesia

ECMO: Impact on PK

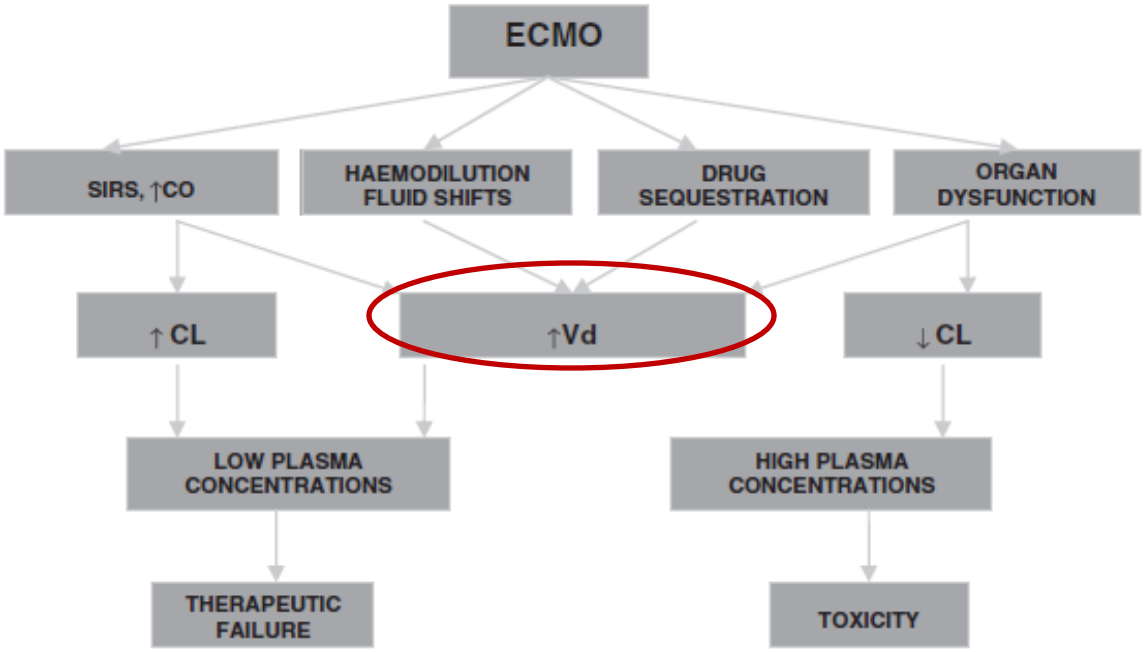


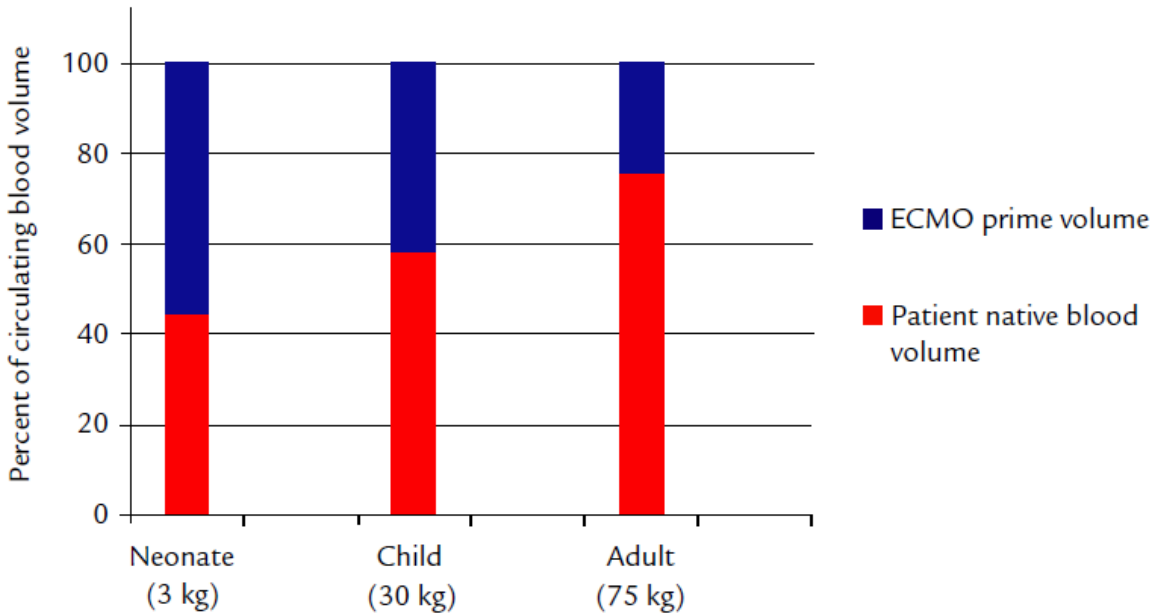
Fig. 2 Impact of critical illness, inflammation, and ECMO on drug PK. SIRS indicates systemic inflammatory syndrome; CO, cardiac output.

Often ECMO and CRRT combined !

Shekar K et al. J Crit Care 2012; 27: 741.e9–741.e18

HEMODILUTION

- Inversely proportional to age
- Impact mainly for hydrophilic drugs with small Vd (AB)



Graphic representation of the proportion of circulating blood volume attributable to patient's own native blood volume and the amount added with priming of the ECMO circuit. This assumes a blood volume of 80ml/kg for a neomate and 70 ml/kg for an older child and adult. ECMO prime volumes are per our institution's ECMO protocols: approximately 300 ml PRBCs for children <20 kg and 1.5 L crystalliod for children >20 kg and adults.

Sherwin J et al. Clin Ther. 2016;38:1976–1994

Drug sequestration

Table 1 Drug recoveries in *ex vivo* circuits and controls relative to baseline and their relationship to lipophilicity and protein-binding characteristics[a]

Drug	Mean (SD) drug recovery (%) from controls at 24 hr	Mean (SD) drug recovery (%) from circuits at 24 hr	Lipophilicity (log *P*)	Protein binding (%)
Ciprofloxacin	119 (4)	96 (17)	2.3	20 to 40
Fluconazole	102 (1)	91 (4)	0.4	12
Linezolid	102 (4)	91 (4)	0.9	31
Ceftriaxone	102 (1)	80 (6)	−1.7	95
Caspofungin	99 (8)	56 (13)	0.1	97
Thiopentone	102 (8)	12 (5)	2.3	80
Fentanyl*	82 (6.3)	3 (3.8)	3.9	85
Midazolam*	100 (3.6)	13 (2)	3.9	92
Meropenem*	42 (1.5)	20 (7)	−0.6	2
Vancomycin*	98 (9)	91 (11)	−3.1	55
Morphine*	103 (11)	97 (2.6)	0.8	30

-90%

- 3 key factors: drug stability, lipophilicity and protein binding
- Dependent of
  - oxygenator and circuit type (silicone vs polypropylene hollow fiber membrane, coated vs uncoated circuit)

Shekar K et al. Critical Care 2015;19:164
Shekar K et al. J Crit Care 2012; 27: 741.e9–741.e18

THERAPEUTIC IMPLICATION

Factors
1. **Priming / fluid**
2. **Circuit / Filter**
3. **Patient**
4. **Drug caracteristics**

		Therapeutic implication	Drugs affected
		↑ Loading dose	Hydrophilic drugs, eg, β-lactams and aminoglycosides
ations		↑ Loading dose ↑ Frequency	Highly protein-bound drugs, eg, teicoplanin and ceftriaxone
Circuit-related factors			
Drug sequestration Sorption	↑ Vd ↓ Cmax	↑ Loading dose	Lipophilic drugs, eg, fluoroquinolones fentanyl, and midazolam
Drug inactivation Ex. photodegradation	↑ CL ↓ Bioavailability	↑ Frequency regarding dose	Furosemide, nitroprusside,
Patient factors			
Systemic inflammation/sepsis	↑ Vd ↓ Cmax ↑ CL		
Organ failures	↓ CL ↑ Vd		
Drug factors			
Hydrophilicity	↑ Vd ↓ Cmax ↑↓ CL (dependent on renal function)		
Lipophilicity	Vd largely unchanged ↑ Circuit sequestration ↓↑ CL (dependent on hepatic function)	↑ Loading dose ↑ Frequency	For example, fluoroquinolones, macrolides, and propofol

Cmax indicates peak concentrations.

Message 7:
Increased Vd means increase the loading dose
Decreased clearance means increase interval
Increased clearance means reduce interval
For Abs, do TDM
For sedation/analgesia, titration (morphine 1st choice)

Shekar K et al. J Crit Care 2012; 27: 741.e9–741.e18

Pharmacokinetic in the critically ill:

« If you do not understand it, Drugs don’t work! »

True and important, but even more important in NICU/PICU:

Where is the drug?

Drug preparation and administration

Drug preparation

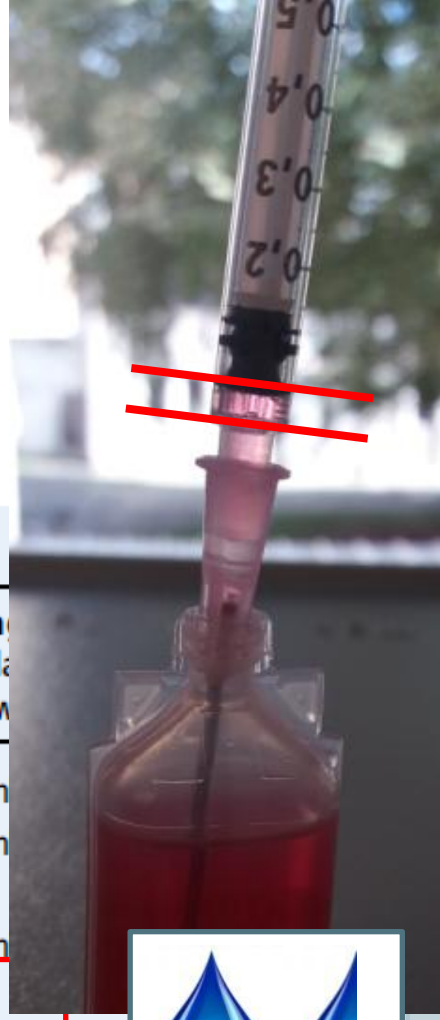


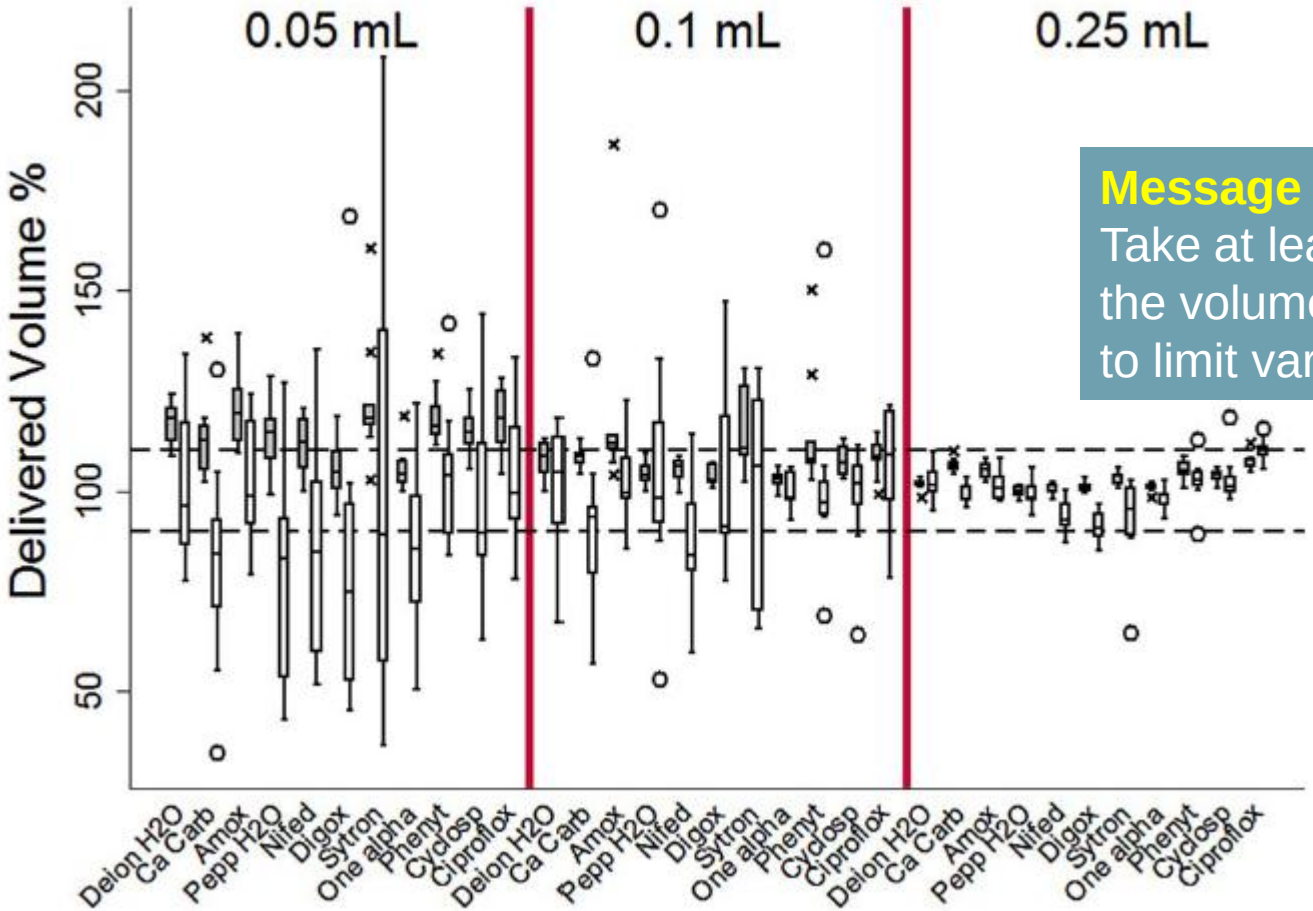
Table 1 Examples of 'not measurable' doses

Prescribed drug	Administration route	Concentration of drug available on ward	Prescribed dose	Calculated volume to be given/taken	Syrin avail the w
Chloral hydrate	Oral	500 mg/5 mL	50 mg	0.5 mL	2.5 m
Cefotaxime	Intravenous	250 mg/mL	580 mg	2.32 mL	2.5 m
Dexamethasone	Intravenous	3.3 mg/mL	1.4 mg	0.424 mL	1 mL
Gentamicin	Intravenous	80 mg/2 mL	66.5 mg	1.663 mL	2.5 m
Hydrocortisone	Intravenous	50 mg/mL	1.6 mg	0.032 mL	1 mL
Metronidazole	Oral	200 mg/5 mL	175 mg	4.375 mL	5 mL
Morphine	Oral	10 mg/5 mL	1.48 mg	0.74 mL	1 mL
Phenobarbitone	Intravenous	60 mg/mL	5 mg	0.0833 mL	1 mL
Phenytoin	Oral	30 mg/5 mL	5 mg	0.8333 mL	1 mL
Vancomycin	Intravenous	50 mg/mL	88 mg	1.76 mL	2.5 mL

Morecroft CW, et al. Arch Dis Child 2013;98:831–832

Accuracy of enteral syringes with commonly prescribed paediatric liquid medicines

Sara Arenas-López,[1] Karuna Gurung,[2] Shane M Tibby,[1]
Miguel Ángel Calleja Hernández,[3] Catherine Tuleu[2]



Message 8:
Take at least 25% of the volume of a syringe to limit variability

Arenas_Lopez S et al. Arch Dis Child 2017, doi: 10.1136/archdischild-2016-312492
De Giorgi I, 2007 http://pharmacie.hug-ge.ch/rd/posters/jfsph06_idg_precision_seringues.pdf

Conclusion and key messages

Whenever « Drug Culture » is lacking…

A « bedside » pharmacist as a « translational Drug Specialist »

Teaching

PK TDM

Good practice survey

Drug Safety

Prescription → Preparation → Administration

Literature research

IT tools

Clinical research

…

To Care for the patient …

Take also Care of the drug!

Sick Kids …
… Pragmatism Needed

- Prefer « no drugs » if possible
- Prefer « old drugs » if possible
- Prefer « safe drugs » in adults if possible
- Fight fuzziness (or even mistakes)

  in prescription, preparation, delivery
- Fill the Vd
- Think to the kidney
- In some cases, do TDM
- ECMO, give more and monitor
- No effect… **Where is the drug ?**
- Ask the pharmacist!

Thanks for your attention !