



Integrating TDM into Pediatric Care: Practical Strategies

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Accreditation Statement

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A record of attendance will be provided to all registrants for requesting credits in accordance with state nursing boards, specialty societies or other professional associations.

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Available Credit

- 1.00 ACPE,
- 1.00 *AMA PRA Category 1 Credit™*
- 1.00 ANCC
- 1.00 Attendance
- 1.00 IPCE

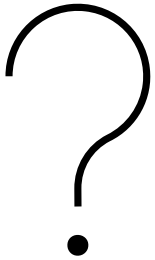
Disclosure:

No relevant financial disclosures to report and no mention of off-label use of any medications or products

Learning Objectives

- Define Therapeutic Drug Monitoring (TDM)
- Identify candidates for TDM
- Explain TDM integration steps

Polling Question



I have been involved with a TB case where TDM was utilized....

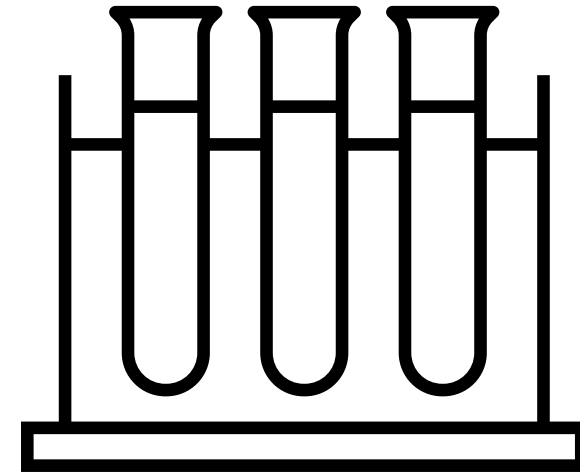
- A. Yes
- B. No
- C. Heard it was used but had no idea what for
- D. Unsure about TDM, looking forward to learning more during this presentation



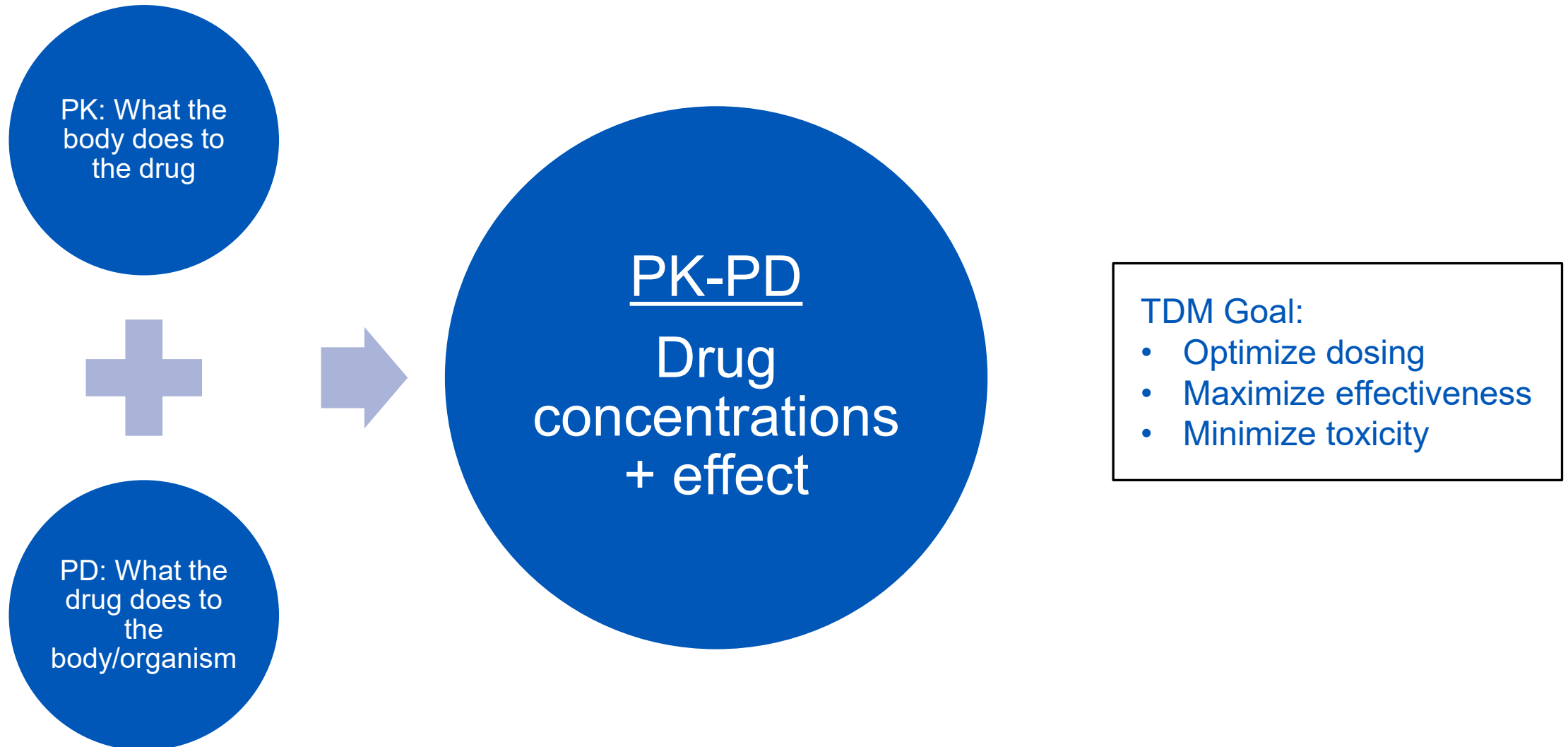
Define Therapeutic Drug Monitoring

Therapeutic Drug Monitoring

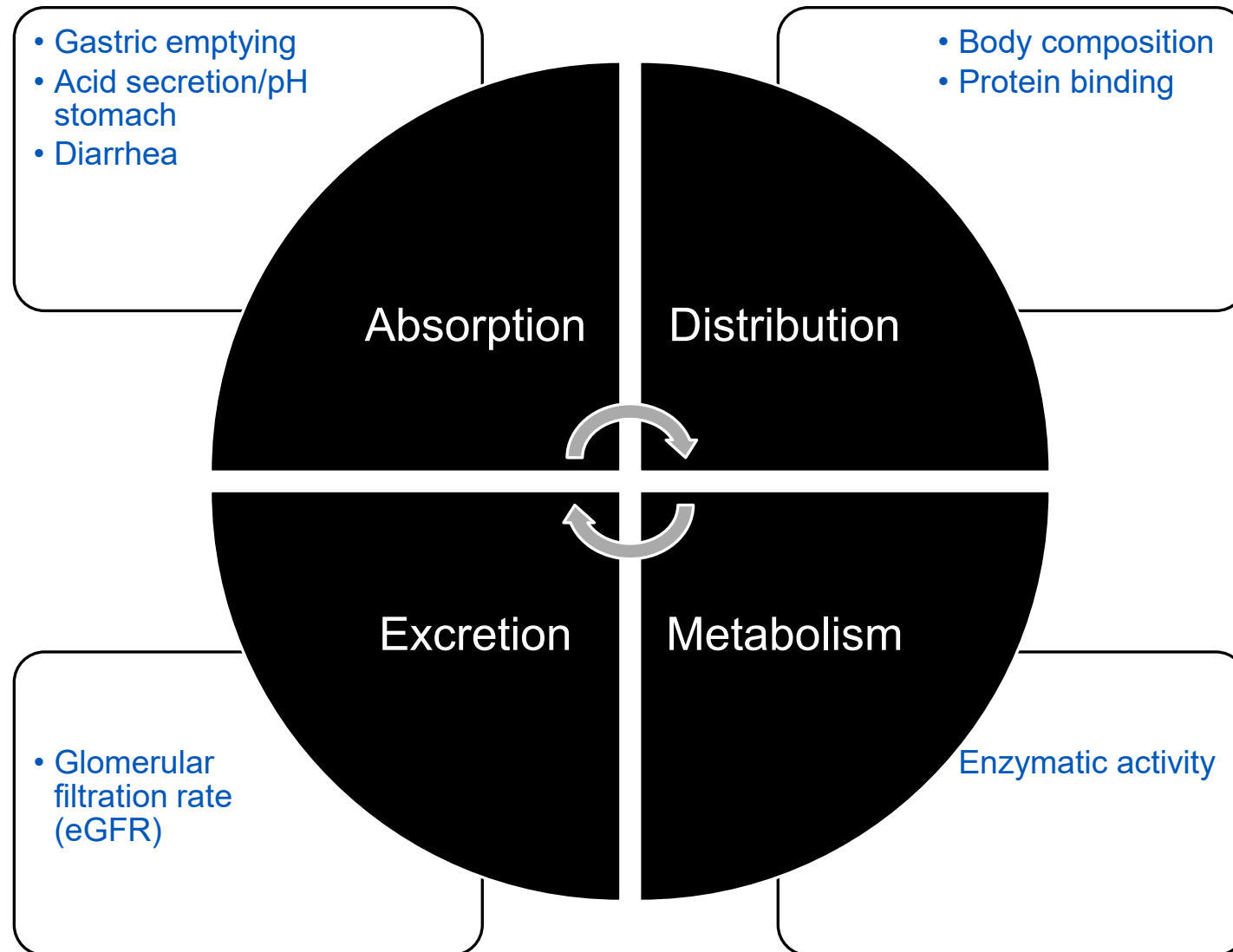
- Process of quantifying drug concentrations in patients
- Typically measured as total drug concentration; it is only the unbound (free) drug concentration that has activity against pathogens
- Using these measurements to design individualized therapeutic regimens
 - Dose
 - Formulation
 - Route
 - Frequency of administration



Pharmacokinetics (PK) + Pharmacodynamics (PD)

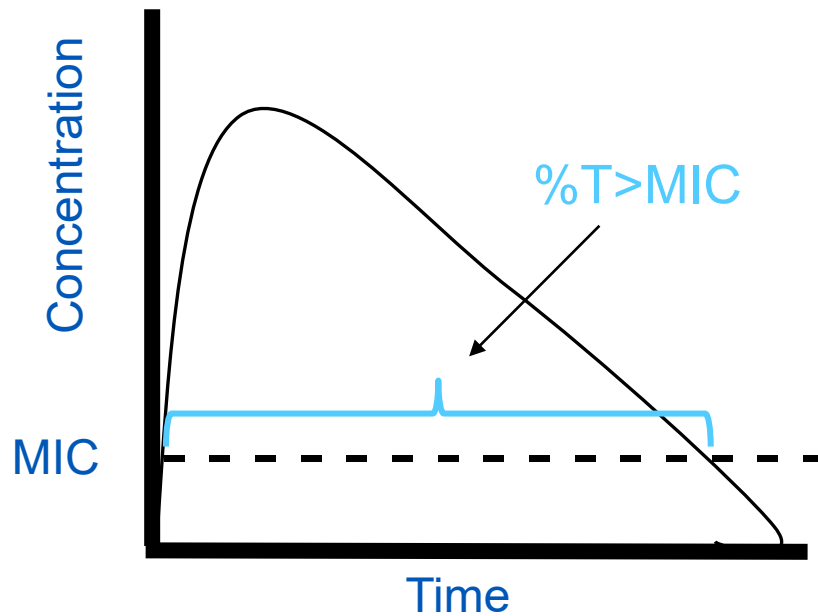


Pharmacokinetics

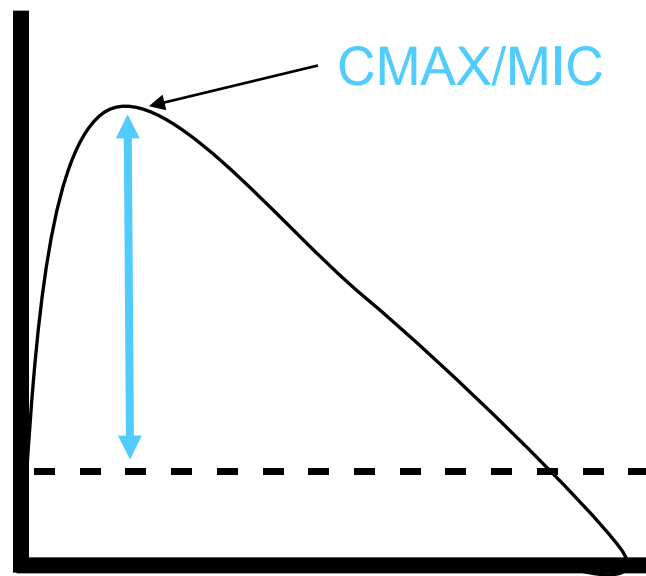


Pharmacodynamic Classification

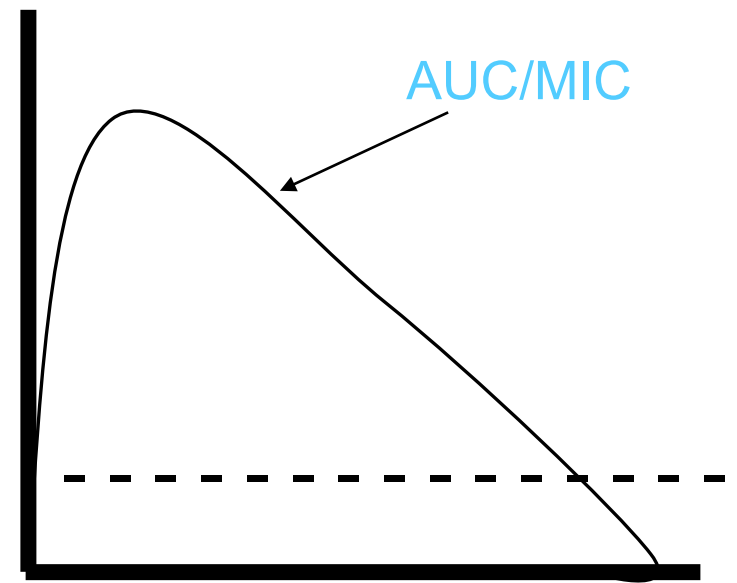
TIME
DEPENDENT



CONCENTRATION-
DEPENDENT



AREA UNDER THE
CURVE (AUC)





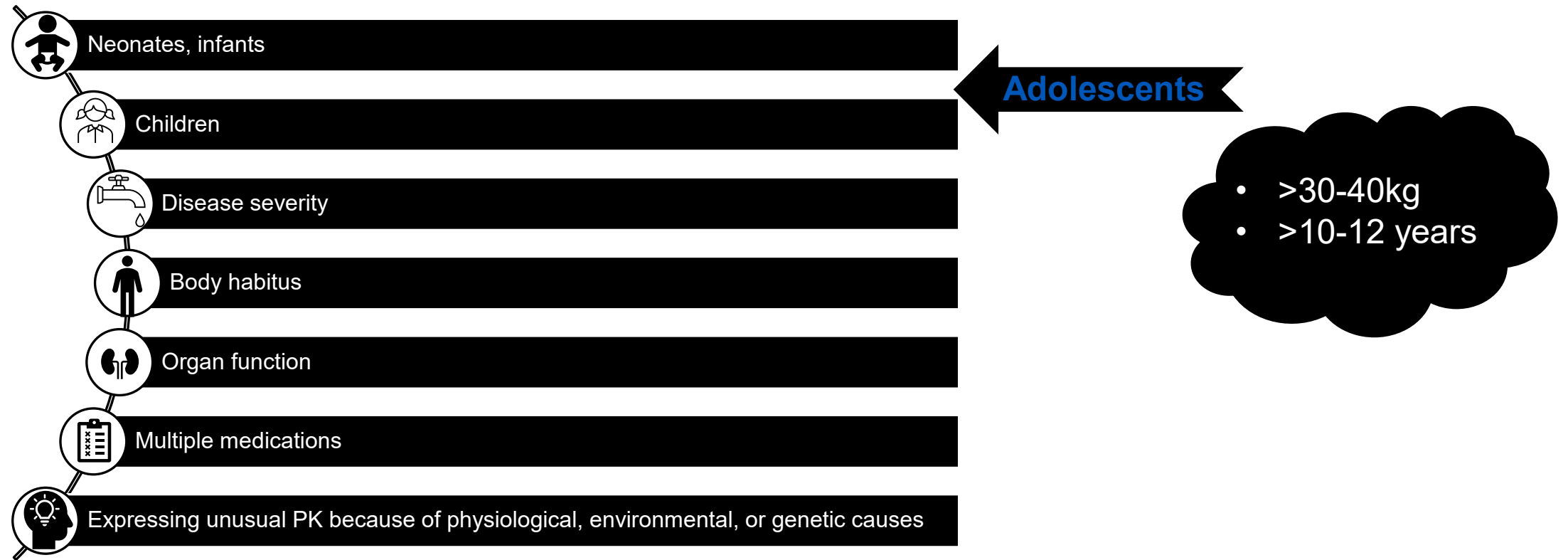
Identify Candidates for TDM

“TDM can be useful for some drugs in any patient, and for most drugs in some special populations”

Pediatrics = Special Population

- Prone to under or over respond to usual dosing regimens
- Less able to tolerate, recognize, or communicate drug effects
- Intentionally or accidentally mis-dosed
- Adherence/compliance
- Assessing crushing, absorption

Pediatrics = Special Population



RESEARCH

Open Access



Analysis of factors influencing plasma concentrations of anti-TB drugs in pediatric TB patients

Yunlian Huang^{1,2}, Qin Guo^{1,2}, Yang Wen^{1,2}, Qiong Liao^{1,2}, Chaomin Wan^{1,2} and Yu Zhu^{1,2*}

- Retrospective analysis, January 2022–November 2023
- 110 inpatients, West China Second University Hospital of Sichuan University
- Majority 6–18 years old
- Oral administration only, for at least 5 days
- Incidence of subtherapeutic plasma levels: 31.4% for isoniazid, 30.1% for rifampin, and 3.9% for pyrazinamide
- Mg/kg dosing was a key determinant of exposure
- Maturation principles + body weight should be used to individualize anti-TB therapy

Practical Challenges in Therapeutic Drug Monitoring



Availability of testing



Ability to obtain extra blood and at specific time points



Resources to perform testing and analyze results



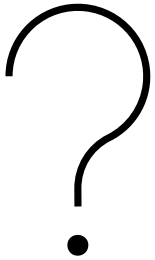
Cost



Unclear/lack of therapeutic level

“Appropriate” drug levels alone do not ensure efficacy or safety.

Polling Question



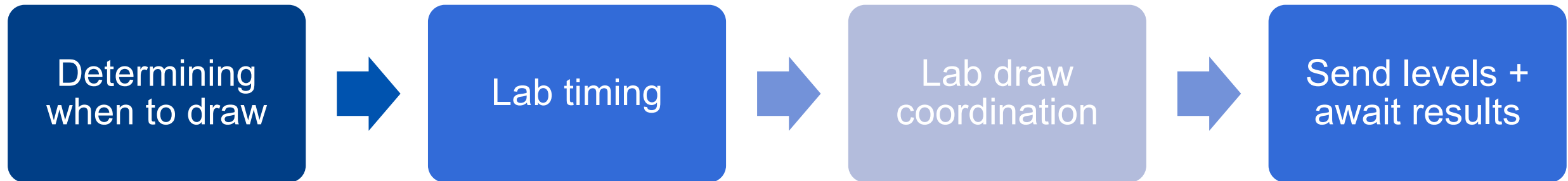
Which patient would be most likely to benefit from TDM?

- A. 6Y, MDR TB, family describes compliance with medications
- B. 11Y, MDR TB, 35kg, history of partial bowel resection as an infant
- C. 15Y, post bone marrow transplant, drug sensitive TB
- D. 17Y, normal body habitus, no underlying renal or hepatic dysfunction, no other medications, drug sensitive TB



Explain TDM Integration

TDM Process



Step 1: Determining when to draw

Steady State

- Amount of drug entering the body is approximately equal to what is eliminated – blood levels remain in a consistent, predictable range between doses
- Reached after 4-5 half-lives
- Sampling prior to steady state underestimates the true level which may lead to inappropriate dose increases

Half-life

- Time for the blood concentration to fall by half
- Controls time to steady state
- Can be prolonged in renal or hepatic impairment or with interacting drugs

Step 1: Determining when to draw

Rifampin can auto-induce metabolism at ~1 week into therapy so may take up to a few weeks to truly be at steady state

Drug	Half-life	Time to steady state
Rifampin	1-4 hours	~6-10 hours
Isoniazid	2-3 hours	~1 day
Pyrazinamide	7-10 hours	~2 days
Ethambutol	8 hours	~2 days
Bedaquiline	5.5 months	Weeks-months
Pretomanid	16 hours	~4-5 days
Linezolid	4-7 hours	~2 days
Moxifloxacin	12 hours	~3 days

Step 2: Lab timing



Draw once the drug has reached steady state



Trough: draw within 30 minutes before the next dose – this is the most reproducible point and the standard for TDM with most drugs



Peak: drawn at a specific time after the dose (drug-specific), used to determine the highest level within the interval



The peak can shift when a patient has “delayed absorption” and this can be evaluated by drawing 2 levels after a dose (e.g. 2h and 6h levels)

Polling Question – Patient Case 1



AJ is a 6yo male (20kg), newly diagnosed with pulmonary TB. Poor weight gain and possible malabsorption were noted by the team who is following him. He is on rifampin 300mg daily, isoniazid 200mg daily, pyrazinamide 600mg daily, and ethambutol 400mg daily. His medications were started on 06/01/26

- When would be the best time to draw 2h and 6h post-dose levels to evaluate for malabsorption?

A. Draw for all medications on 09/17/26

B. Draw for isoniazid, pyrazinamide, and ethambutol on 09/17/26 and then for rifampin on 09/24/26

C. Draw for all medications on 09/24/26

D. AJ does not have an indication to have TDM drawn

Step 3: Lab draw coordination

Patient
understanding

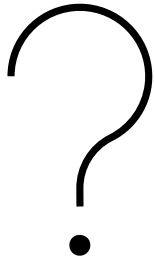
Minimize lab
draws

Dose timing

Lab
scheduling

Ability to draw
and send
TDM

Polling Question – Patient Case 1 (continued)



What education would you like to provide to AJ's mother before setting up the lab visit(s) for them?

- A. Give the morning dose at the usual scheduled time and be prepared to tell the nurse the exact clock time the dose was taken.
- B. Make sure AJ has taken his medications without missed or doubled doses, and report any missed doses.
- C. Plan for AJ to be available for 2 blood draws on the appointment day at 2 hours and 6 hours after the dose(s), rather than leaving after a single draw.
- D. All of the above

Step 4: Send levels

Two main labs that perform tests on these medications

- Infectious Disease Pharmacokinetic Laboratory (IDPL) at University of Florida
- Advanced Diagnostic Laboratories (ADL) at National Jewish Health

Requirements for lab draws

- Considerations for how much sample is needed, whether it needs to be sent on ice, etc
- Who will handle the shipping and necessary paperwork for your facility

Step 4: Send levels – IDPL @ UF Health

Sample Handling Instructions

Serum and Plasma Collection & Sample Shipping and Handling Instructions

- Extensive website with all details of how and what to send and where to address everything for the shipping.

Step 4: INFECTIOUS DISEASE PHARMACOKINETICS LABORATORY

1600 SW Archer Rd., P4-30
Gainesville, FL 32610
Phone: 352-273-6710 Fax: 352-273-6804
E-mail: idpl@cop.ufl.edu
Website: <http://idpl.pharmacy.ufl.edu>



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levels

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Patient Last, First Name, M.I. (Required)		☐ Male ☐ Female	Facility Name & Address (Required)
Date of Birth:	Patient ID:		
Referring Physician (Required):		Physician Phone #	
Fax #	Facility Phone #		
Please note: We do not bill 3 rd party payers. The laboratory or office shipping the samples accepts responsibility for payment.			
Bill to / Contact Name:			

AZL	Azithromycin (2-3 H & 6-7 H)	INH	Isoniazid (1-2 H & 6 H)	RBN	Rifabutin (3 H & 7 H)	Intravenous Drugs (intravenous doses) (30-60 min. post infusion & trough)	
BDQ	Bedaquiline (trough 2 & 5-6 H)	ISA	Isavuconazole (trough & 2-3H)	RIFH	Rifampin (2 H & 6 H)		
BIC	Bictegravir (trough & 2 H)	ITRL	Itraconazole (trough & 3-4 H)	RPNT	Rifapentine (trough & 5-6H)	AMOX	Amoxicillin
CIPH	Ciprofloxacin (2 H & 6 H)	LDV	Ledipasvir (trough & 4 H)	RILP	Rilpivirine (trough & 4-5H)	AMPI	Ampicillin
CLART	Clarithromycin (2-3H & 6-7 H)	LFLHL	Levofloxacin (2 H & 6 H)	SOF	Sofosbuvir (trough & 1 H)	AZTRE	Aztreonam
CFH	Clofazimine (2-3 H & 6-7 H)	LNZL	Linezolid (trough, 2 & 5-6 H)	VORL	Voriconazole (trough & 2 H)	CEFAZ	Cefazolin
CSH	Cycloserine (2-3 H & 6-7 H)	LOPV	Lopinavir (trough & 4-6H)	VEL	Velpatasvir (trough & 3-4 H)	CEFE	Cefepime
DARU	Darunavir (trough & 2-4 H)	MINO	Minocycline (2 H & 6 H)			CTL	Ceftaroline
DTG	Dolutegravir (trough & 2 H)	MXFL	Moxifloxacin (2 H & 6 H)			CEFT	Ceftriaxone
DOXY	Doxycycline (2-3 H & 6-7 H)	OMADA	Omadacycline (2-3 H & 6-7 H)			DAPTO	Daptomycin
EFVL	Efavirenz (trough & 5 H)	PMD	Pretomanid (trough 2 & 5-6 H)			IMIP	Imipenem
EMBH	Ethambutol (2-3 H & 6-7 H)	POSA	Posaconazole (trough & 3H)	PIPE	Piperacillin	MERO	Meropenem
ETAH	Ethionamide (2 H & 6 H)	PZAH	Pyrazinamide (2 H & 6 H)	OXA	Oxacillin	NAFC	Nafcillin

# Doses per week				
Date of last dose				
Time of last dose (For IV: Start/End)				
Date blood drawn				
Time blood drawn				

Step 4: Send levels – ADL @ National Jewish Health



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Pharmacokinetics & Pharmacodynamics: Therapeutic Drug Monitoring

For more than two decades, National Jewish Health Advanced Diagnostic Laboratories has been helping physicians optimize pharmacological therapies for their patients by measuring, analyzing and interpreting drug levels.

PK/PD Diagnostic Tests

- Comprehensive anti-mycobacterial, anti-fungal, anti-HIV drug monitoring and steroid serum concentrations measured by high-performance liquid chromatography (HPLC), Gas Chromatography Mass Spectrometry (GC/MS) and Liquid Chromatography Mass Spectrometry (LC/MS)

[View Advanced Diagnostic Labs Test Catalog](#)



Rifampin Level

 [Download Requisition](#)

Test Code

PKRIF

Description

Rifampin (RIF) is a first-line anti-tuberculosis (TB) and antimicrobial agent used in combination therapy for Mycobacterium tuberculosis infections, nontuberculous mycobacterial (NTM) infections, and certain bacterial infections such as Staphylococcus aureus endocarditis. Due to its complex pharmacokinetics and significant interpatient variability, therapeutic drug monitoring (TDM) is recommended to optimize efficacy while minimizing toxicity and drug resistance.

Collection/Transport	+
Test Detail	+
Result Interpretation	+
Fees/Coding	+
Licensing & Certification	+

Step 4: Send levels ADL @ National Jewish Health

Advanced Diagnostic Laboratories National Jewish Health®
Pharmacokinetics Laboratory | 800.550.6227 phone | 303.270.2175 fax | njlabs.org

SHIP TO: National Jewish Health
Pharmacokinetics Laboratory
1400 Jackson Street, K425
Denver, CO 80206

Assays may require up to ten business days for completion. Please submit a separate requisition for each sample collection time.

- Requisition level
- PDF

Indication levels

1. PATIENT INFORMATION					
Patient Name (Last, First)				DOB ____ / ____ / ____	
☐ Male ☐ Female ☐ Neutral/Other ☐ Unknown					
Address		City		State	Zip
Phone		Ethnicity		Race	
2. BILLING INFORMATION			3. REPORT DELIVERY INFORMATION		
National Jewish Health Advanced Diagnostic Laboratories does not bill patients directly or third-party health insurance. Visit njlabs.org or call for details.			☐ Same as Billing Address		
			Client ID		
5. THERAPEUTIC DRUG MONITORING					
Please provide 2 mL serum per test. The number of hours after the dose to collect "peak" concentrations is shown in parentheses after each drug name, if applicable. To test for delayed drug absorption, a second sample may be collected 4 hours after the "peak". Trough concentrations (prior to next dose) are recommended for the anti-HIV and anti-fungal drugs.					
☐ PKAMX	Amoxicillin	☐ PKEMB	Ethambutol (2-3h)	☐ PKPDK	6 hr Prednisolone
☐ PKAZM	Azithromycin (2-3h)	☐ PKETA	Ethionamide (2h)	☐ PKPZA	Pyrazinamide (2h)
☐ PKCFZ	Clofazamine (2-3h)	☐ PKINH	Isoniazid (1-2h)	☐ PKRFB	Rifabutin (3h)
☐ PKCLR	Clarithromycin (2-3h)	☐ PKLVX	Levofloxacin (2h)	☐ PKRIF	Rifampin (2h)
☐ PKCRT	Cortisol (random)	☐ PKLZD	Linezolid (2h)	☐ PKSM	Streptomycin (1-2h)
☐ PKSTM	Cortisol Adrenal Stimulation	☐ PKMPK	12 hr Methylprednisolone Study	☐ PKTRX	Trikafta
☐ PKCSH	Cycloserine (2-3h)	☐ PKMXF	Moxifloxacin (2h)		
☐ PKDRV	Darunavir (2-4h)	☐ PKCPX	12 hr Prednisolone Study		
6. SPECIAL INSTRUCTIONS					
Please list additional medications patient is currently taking here.					
Sample preparation and shipment: Collect in a plain red top, 8-10 ml tube. Separate serum from cells immediately by centrifugation and aliquot into a labeled polypropylene or similar plastic tube. Use a separate tube for each test ordered. Allow room for expansion of sample inside tube. Freeze at -70°C if possible (otherwise -20°C.) Ship on ≥ 3 lbs. dry ice via overnight transport. SHIP SAMPLES TO BE RECEIVED MONDAY THROUGH FRIDAY. DO NOT SHIP ON FRIDAY OR SATURDAY.					

Step 4: Await results

IDPL @ UF Health

- No specific turnaround times specified on website
- Recommend overnight shipping and must arrive on a weekday

ADL @ National Jewish Health

- “Within 10 business days” listed for turnaround time on most levels within catalogue
- Recommend overnight shipping and must arrive on a weekday

Polling Question – Patient Case 2



KB is a 15-year-old female (45 kg) diagnosed with rifampin-resistant / fluoroquinolone-susceptible pulmonary TB. She was started on bedaquiline 400mg PO daily (2wk lead in), pretomanid 200mg PO daily, linezolid 600mg PO daily, and moxifloxacin 400mg PO daily last week.

- KB is scheduled for a linezolid trough; which of these are correct?
 - A. Draw the sample immediately before the next scheduled dose (within ~30 minutes prior), not after a dose.
 - B. Confirm the drug will be at steady state at the time of the scheduled draw.
 - C. Record the exact time of the last dose and the exact draw time and label clearly as a trough.
 - D. All of the above

Questions and Answers





Thank you