Treating children

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Baby M

Mom 36 years old

- Failing 1st line TDF/FDC/EFV
  - CD4: 26 cells/mm^3
  - VL Log 5.3 HIV RNA copies/mm^3
- Switched to LPV/r-based 2nd line regimen at 37 weeks gestation
- New TB diagnosis made 3 days prior to delivery
- Choosing to breastfeed

Baby 1.8 kg

- Term but very small for gestation
- Ongoing HIV exposure through breast feeding
  - PEP and PrEP
- Exposed to tuberculosis
  - Needs prevention
- **Confirmed HIV infection**
  - **PCR +ve on day 2**
- **Presumptive diagnosis of TB at 3 weeks of age**

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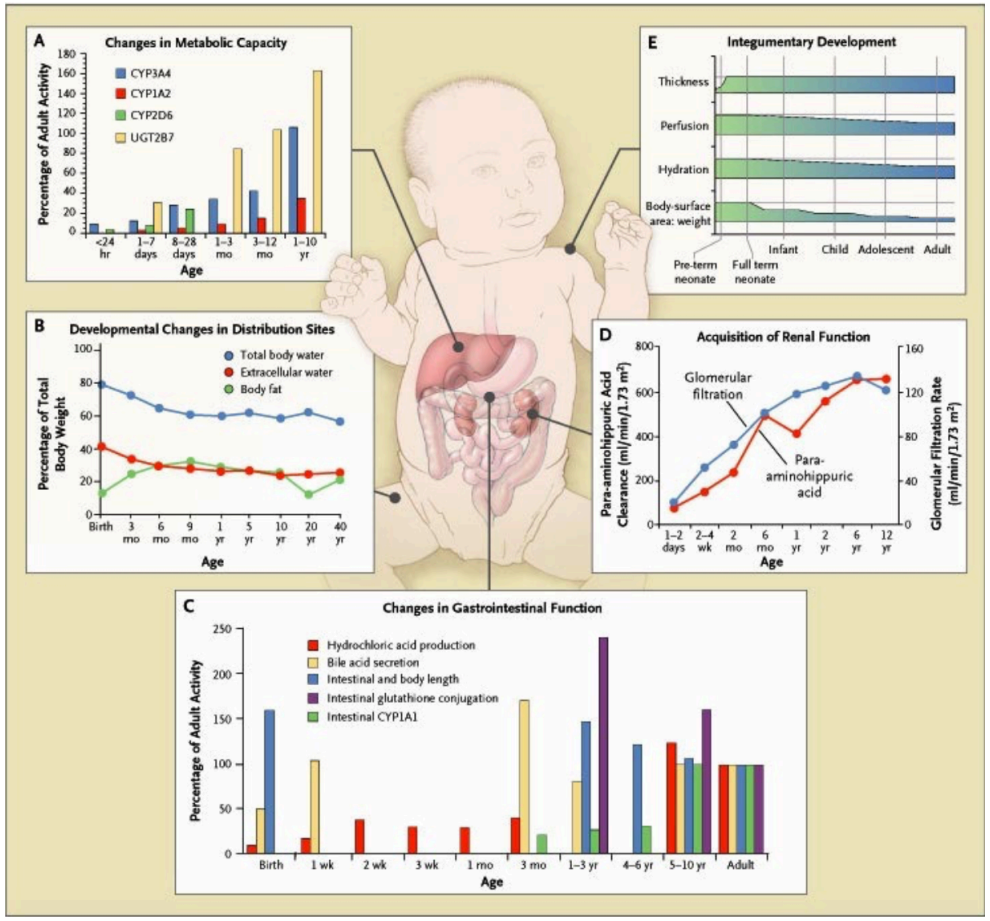
Dose and formulations for all ages needed



- Size - algometric scaling
- Physiology – age and gestation
- Formulations are not “equal”
  - Liquids vs dispersible tablets

Kearns NEJM 2003

Traditional study process

Adult compound
Safe and effective

Processes to ensure children are studied

Develop pediatric study → Develop weight band dosing → Develop the FDC → Study FDC → To Market with FDC

- Descending age cohort
- Bio-equivalence of formulations

- Issues around co-formulating medications

9 years later

To market with single drug formulations for all ages

Adapted from Penazzato CID 2017

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What can we use to manage children?

FOR NEONATES

AZT	Term & preterm infants
3TC	Term infants
FTC	Term infants
RAL	Term Infants
NVP	Term -2 Weeks
LPV/r	Term - 2 Weeks (42 completed weeks)

+

1 MONTH TO 3 YEARS

ABC	3 Months
TDF	2 Years
ATV	3 Months + 5Kg

+

OLDER THAN 3 YEARS

TAF	> 35Kg
EFV	10Kg
RIL	12Years, 35Kg
ETR	6 Years, 16 Kg
DTG	30Kg
EVT	35Kg
DRV	10Kg

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Regimens recommended by WHO till July 2018

Dosing & regimen in neonates separate

No FDC

	Preferred First regimen	Second regimen	Third regimen
Adolescents	TDF + 3TC/FTC + EFV	2 NRTIs +ATV/r or LPV/r 2 NRTIs +DTG	DTG + 2 NRTIs DRV/r + 2 NRTIs DRV/r + DTG + 1-2 NRTIs
Children ≧ 3	ABC + 3TC + EFV	2 NRTIs +ATV/r or LPV/r	
Children < 3	ABC + 3TC + LPV/r AZT + 3TC + LPV/r	<3 years: 2 NRTIs + RAL >3 years: 2 NRTIs + EFV or RAL	

Poor harmonization between
- Children
- Adults, adolescents and children
- Countries

No FDC
Solid LPV/r only now rolled out

Regimens currently recommended by WHO

	Preferred First regimen	Alternative
Neonates	AZT+3TC+RAL	AZT+3TC+NVP LPV – special circumstance
Children	ABC + 3TC +DTV	2 NRTIs +ATV/r or LPV/r

Better harmonization between
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culosis
n

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2

gnosis of TB at 3

- Dose in creases
  - Weight
- Formulation changes
  - Liquid to solid
  - All not equal
- Simplification
  - New drugs and formulations, weight increases
- Toxicity
  - Acute / chronic
- Failure
- The un forseen

What do we need to think about when we switch?

- Why?
- Age
- Weight
- Co-morbidity – In particular TB
- Viral load?
- Formulations available
- **Ease of use**
- **Drug interactions**

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

ANTIRETROVIRAL DRUG DOSING CHART FOR CHILDREN 2013

Compiled by the Child and Adolescent Committee of the SA HIV Clinicians Society in collaboration with the Department of Health

SOUTHERN AFRICAN HIV CLINICIANS SOCIETY

	Abacavir (ABC)		Lamivudine (3TC)		Efavirenz (EFV)	Lopinavir/ritonavir (LPV/rtv)	Ritonavir boosting (RTV)	Stavudine (d4T)	Didanosine (ddI)	Nevirapine (NVP)	Zidovudine (AZT)	
Target Dose	8mg/kg TWICE daily **OR** **≥10kg:** 16mg/kg ONCE daily		4mg/kg TWICE daily **OR** **≥10kg:** 8mg/kg ONCE daily		By weight band **ONCE** daily	300/75mg/m²/dose LPV/rtv **TWICE** daily	ONLY as booster for LPV/rtv when on Rifampicin **TWICE** daily (0.75xLPV dose bd)	1mg/kg/dose **TWICE** daily	180-240mg/m²/dose **ONCE** daily	160-200 mg/m²/dose **TWICE** daily (after once daily lead-in x 2 wks)	180-240mg/m²/dose **TWICE** daily	**Target Dose**
Available Formulations	Sol 20mg/ml Tabs 60mg (scored dispersible), 300mg (not scored), ABC/3TC 600/300mg		Sol. 10mg/ml Tabs 150mg (scored), 300mg, ABC/3TC 600/300mg		Caps 50,200mg Tabs 50,200, 600mg (not scored)	Sol. 80/20mg/ml Adult Tabs 200/50mg, Paeds Tabs 100/25mg	Sol. 80mg/ml	Sol. 1mg/ml Caps 15,20,30mg	Tabs 25,50,100mg (dispersible in 30ml water) Caps 250mg EC	Sol. 10mg/ml Tabs 200mg (scored)	Sol. 10mg/ml Caps 100mg Tabs 300mg (not scored), AZT/3TC 300/150mg	**Available Formulations**
Wt. (kg)	**Currently available tablet formulations of abacavir (except 60mg), efavirenz, LPV/rtv and AZT must be swallowed whole and NOT chewed, divided or crushed**											**Wt. (kg)**
<3	**Consult with a clinician experienced in paediatric ARV prescribing for neonates (<28 days of age) and infants weighing <3kg**											**<3**
3-3.9	2ml bd		2ml bd		**Avoid using when <10kg or <3 years:** dosing not established	*1ml bd	1ml bd	6ml	Avoid	5ml bd	6ml bd	**3-3.9**
4-4.9												**4-4.9**
5-5.9	3ml bd		3ml bd			*1.5ml bd	1.5ml bd	**7.5mg bd:** open 15mg capsule into 5ml water: give 2.5ml	100mg od: *(2x50mg tabs)*			**5-5.9**
6-6.9									125mg od: *(1x100mg + 1x25mg tabs)*	8ml bd	9ml bd	**6-6.9**
7-7.9	4ml bd		4ml bd					**10mg bd:** open 20mg capsule into 5ml water: give 2.5ml				**7-7.9**
8-8.9											1 cap bd OR 12ml bd	**8-8.9**
9-9.9												**9-9.9**
10-10.9	Choose only one option: 6ml bd OR 2x60mg tabs bd	12ml od OR 4x60mg tabs od	Choose only one option: 6ml bd	12ml od	200mg nocte *(1x200mg cap/tab)*	2ml bd	1.5ml bd	**15mg bd:** open 15mg capsule into 5ml water	150mg od: *(1x100mg +1x50mg tabs)*	10ml bd		**10-10.9**
11-13.9												**11-13.9**
14-16.9	8ml bd OR 2.5x60mg tabs bd	5x60mg tabs od OR 1x300mg tab od OR 15ml od	½ x150mg tab bd OR 8ml bd	1x150mg tab od OR 15ml od	300mg nocte: *(200mg cap/tab + 2x50mg cap/tab)*	Choose one option: -2.5ml bd -100/25mg **paeds tabs:** 2 bd -200/50mg **adult tabs:** 1 bd	2ml bd	**20mg bd:** open 20mg capsule into 5ml water (if the child is unable to swallow a capsule)	175mg od: *(1x100mg + 1x50mg + 1x25mg)*	1 tab am ½ tab pm OR 15ml bd	2 caps am 1 cap pm OR 15ml bd	**14-16.9**
17-19.9												**17-19.9**
20-22.9	10ml bd OR 3x60mg tabs bd	1x300mg tab + 1x60mg tab od	1x150mg tab bd OR 15ml bd	2x150mg tab od OR 1x300mg tab od OR 30ml od		Choose one option: -3ml bd - 100/25mg **paeds tabs:** 2 bd - 200/50mg **adult tabs:** 1 bd	2.5ml bd		200mg od: *(2x100mg tabs)*		2 caps bd OR 20ml bd	**20-22.9**
23-24.9		1x300mg tab + 2x60mg tabs od										**23-24.9**
25-29.9	1x300mg tab bd	2x300mg tabs od OR 1xABC/3TC 600/300mg tab od	1x150mg tab bd	2x150mg tabs od OR 1x300mg tab od OR 1xABC/3TC 600/300mg tab od	400mg nocte: *(2x200mg caps/ tabs)*	Choose one option: - 3.5ml bd - 100/25mg **paeds tabs:** 3 bd - #200/50mg **adult tabs:** 1 bd + 100/25mg **paeds tabs:** 1 bd	3ml bd	**30mg bd**	250mg od: *(2x100mg + 1x50mg tab)* OR 1x250mg EC cap od	1 tab bd	1x300mg tab bd OR 1xAZT/3TC 300/150mg tab bd	**25-29.9**
30-34.9						Choose one option: - 4ml bd - 100/25mg **paeds tabs:** 3 bd - #200/50mg **adult tabs:** 1 bd + 100/25mg **paeds tabs:** 1 bd						**30-34.9**
35-39.9						Choose one option: - 5ml bd - 200/50mg **adult tabs:** 2 bd	4ml bd					**35-39.9**
>40					600mg tab nocte							**>40**

od = once a day
(usually at night)
bd = twice a day

* Avoid LPV/rtv solution in any full term infant <14 days of age and any premature infant <14 days after their due date of delivery (40 weeks post conception) or obtain expert advice.
# Children 25-34.9kg may also be dosed with LPV/rtv 200/50mg adult tabs: 2 tabs am; 1 tab pm

Weight (kg)	**3-4.9**	**5-9.9**	**10-13.9**	**14-29.9**	**≥30**
Cotrimoxazole Dose	2.5ml od	5ml od	5ml od	10ml or 1 tab od	2 tabs od
Multivitamin Dose	2.5ml od	2.5ml od	5ml od	5ml od	10ml or 1 tab od

For baby M

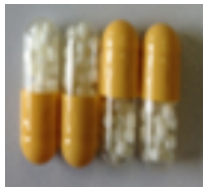
1. AZT,3TC, NVP (RAL) The initial regimen for most young infants. Dosing age-based and weight-based
2. AZT, 3TC, LPV/r (RAL) At 42 completed weeks we can start LPV/r
3. ABC, 3TC, LPV/r (RAL) We can start ABC?

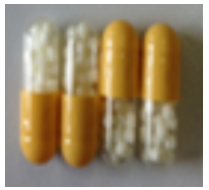
   Children still require rifampicin-based TB therapy with ART
4.

Solids are coming

A 10 kg toddler needs:

- LPV/r: **4** capsules x2/day
- ABC/3TC 60/30mg: **4** /day





Can we get to daily dosing using **preferred** agents?

It will not be 1 pill for most children before they reach 25Kg

Other switches

- Class switch for simplification – make sure patient is suppressed
- Drug switch for simplification – LPV/r to atazanavir – Consider resistance
- Remember the basic rules
  - Even if you are 14 you may not weigh 40!
  - **No unboosted PI to children**
- New(er) drugs
  - Dolutegravir
  - TAF
  - Etc etc