Paediatric ARV Formulations and Regimes : Still more to do

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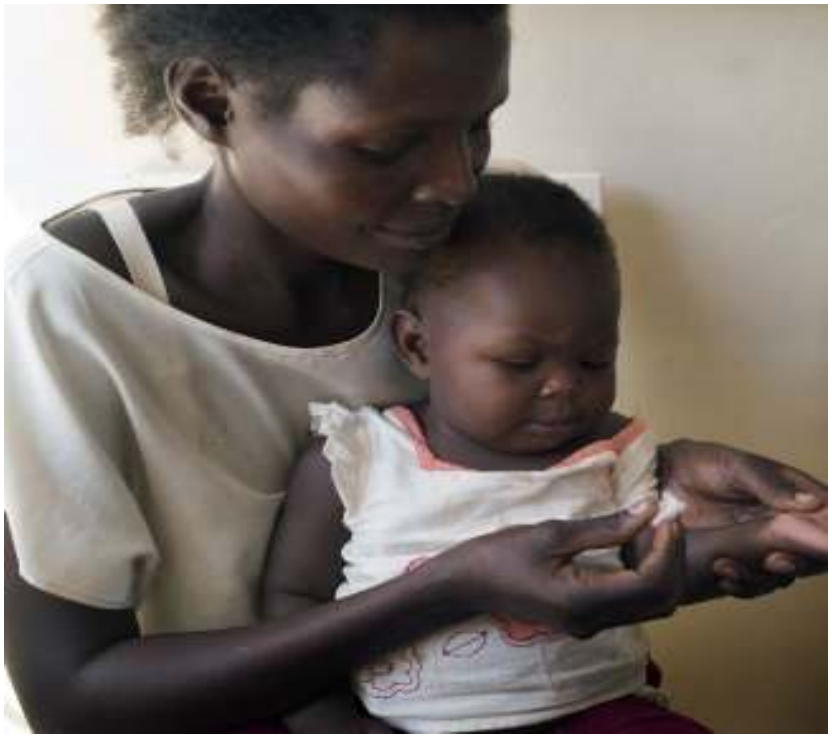
CAMPAIGN FOR ACCESS TO ESSENTIAL MEDICINES

MEDECINS SANS FRONTIERES

Overview

- Global Challenges
- ARV availability for children
- Adaptability of formulations
- Development of fixed dose combinations for children
- Challenges of treatment

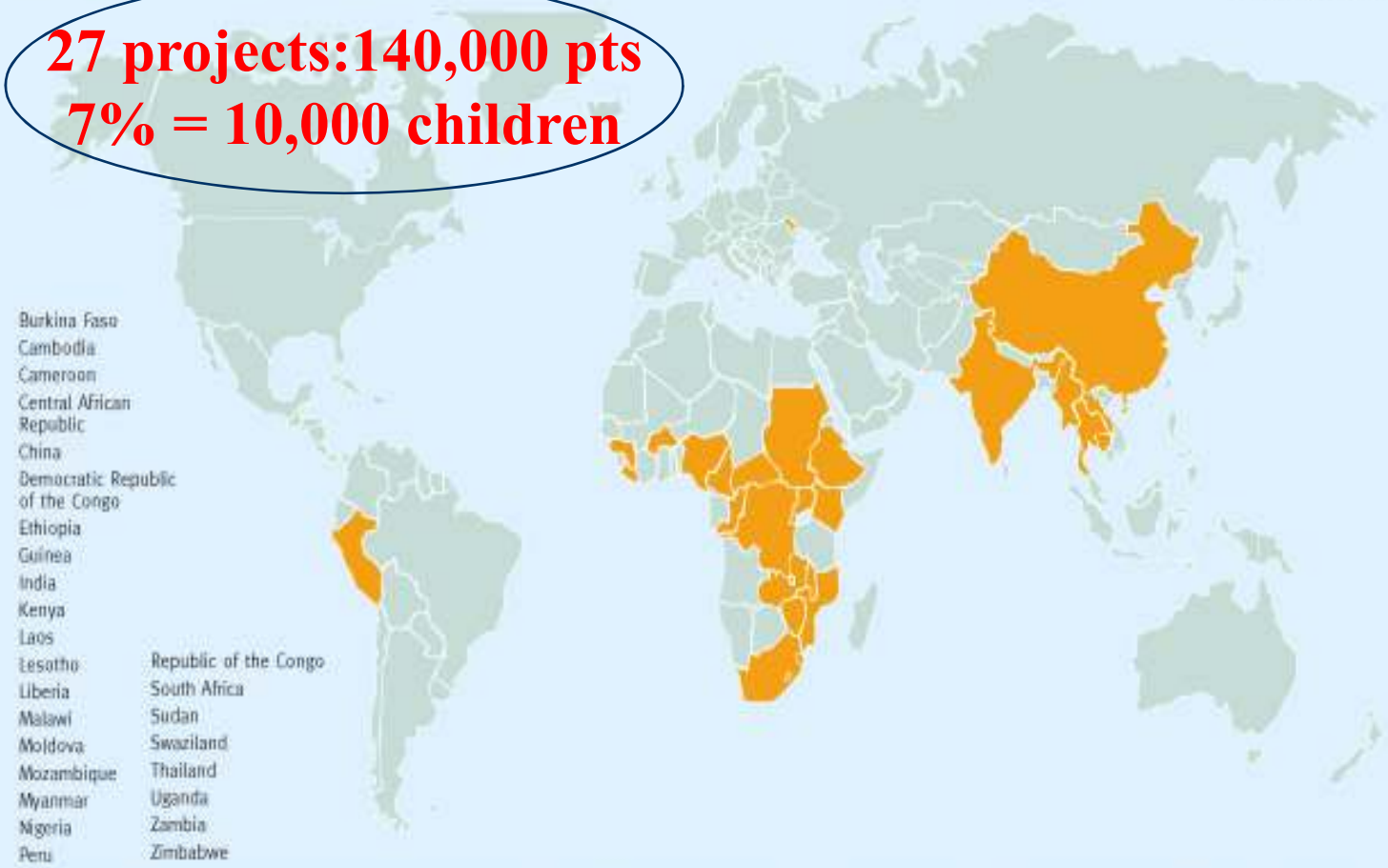
The situation today



In 2007 approx 1,150 new infections in children **each DAY.** This is more than 4.5 times the number of new infections in the US in **one YEAR**

MSF HIV/AIDS TREATMENT PROGRAMMES

27 projects:140,000 pts
7% = 10,000 children



Burkina Faso
Cambodia
Cameroon
Central African Republic
China
Democratic Republic of the Congo
Ethiopia
Guinea
India
Kenya
Laos
Lesotho
Liberia
Malawi
Moldova
Mozambique
Myanmar
Nigeria
Peru
Republic of the Congo
South Africa
Sudan
Swaziland
Thailand
Uganda
Zambia
Zimbabwe

MSF PROGRAMMES ARE CURRENTLY PROVIDING ANTIRETROVIRAL TREATMENT TO MORE THAN 140,000 PATIENTS (10,000 OF WHOM ARE CHILDREN) IN 27 COUNTRIES*

Global Challenges
(a pharmacist perspective)

- Lack of **safety and pharmacokinetic studies** in children, both in currently available ARVs and those in the pipeline.
- Lack of **quality-assured paediatric adapted formulations**, both single molecules and Fixed Dose Combinations (FDCs)
- **Limited choices** when regimes need to be changed due to treatment failure, side effects and interactions.

Antiretroviral Options Today

- 25 ARVs approved for use in adults
- 22 still on the market
  - zalcitabine, delviradine, amprenavir no longer marketed
- 14 approved for use in children
  - enfuvirtide (over 6), abacavir, didanosine, emtricitabine, lamivudine, stavudine, zidovudine, efavirenz (over 3), nevirapine, fosamprenavir, lopinavir/ritonavir, nelfinavir, ritonavir, tipranavir.
- 13 have paediatric formulations available
  - enfuvirtide has no paediatric formulation

Adaptability of formulations
(single ARV originator products)

- 2 products have paediatric tablet formulations and liquids available
  - ddI; chewable dispersable tablets + powder for reconstituiton
  - LPV/r; heat stable tablet + liquid
- 3 supplied as powder requiring reconstitution
- 3 stored between 2-8°C

Criteria for paediatric formulations

- Small tablets, scored for ease of splitting
- Should be able to be crushed, chewed or dispersed in water
- Palatable for children
- Stable in high humidity and high temperature
- Long shelf life
- Common regimes available in a FDCs

Quality-assured FDCs available Today

- 3TC/d4T/NVP 30/6/50mg (WHOPQ)
- 3TC/d4T/NVP 60/12/100mg (WHO PQ)
- 3TC/d4T 30/6mg (USFDA tent approval)
- 3TC/d4T 60/12mg (USFDA tent approval)
- LPV/r 100/25mg (WHO PQ)

Paediatric formulations in the Pipeline

- AZT/3TC/NVP 60/30/50mg
- AZT/3TC 60/30mg
- AZT/3TC/ABC 60/30/60mg
- ABC 60mg

Challenge of TB / HIV Coinfection

2 year old child on 1st line NVP based regime

- ARV treatment is available as a FDC
- TB Treatment includes rifampicin and is available in a FDC
- Interaction between NVP and rifampicin
  - Decreased blood levels of NVP

Options

- Change NVP to **EFV**
  - Not approved for children under 3 years
- Change NVP to **ABC**
  - Sub-optimal, triple NRTI regime
  - Combination of tablet and liquid

Challenges of TB/HIV Coinfection: Child from PMTCT program

- New WHO guidelines (April 2008)
  - Start on PI based regime if exposed to NVP
- ARV regime not available as FDC
  - Different tablets and liquids
  - LPV/r tablets cannot be crushed
  - LPV/r solution must be refrigerated
- Interaction between LPV/r and rifampicin
  - Decreased blood levels of LPV

Options

- use “super” boosted LPV/r + r
  - bad taste of ritonavir syrup
  - many tablets / liquids
  - Needs monitoring
- Change rifampicin to rifabutin
- Defer ARV treatment until TB treatment completed

Conclusion

- Children when put on treatment do respond well
- Scientific community & drug companies need to address the unanswered questions on interactions and safety of ARVs for pediatrics
- Resolve the patent barriers that will hinder development of paediatric ARVs
- Prioritisation of WHOPQ and stringent regulatory bodies in review of paediatric ARV dossiers
- Responsibility of all, to ensure that children have access to quality FDCs

Thank you