Putting the priorities first: medicines for maternal and child health

Suzanne R Hill[a]

In recent years, there has been much work done due to increasing recognition that children need better medicines. The United States of America[1,2] and the European Union[3] have adopted regulations to encourage research and development of medicines for children; the World Health Organization (WHO) has been promoting "Make medicines child size"; and researchers and academics are starting to respond to the many unanswered questions about medicines for children, through research and international collaboration.

Countries that are working to meet the United Nations Millennium Development Goals related to maternal and child survival, however, need additional support to ensure access to medicines that will help achieve the specified targets. Fragile medicine supply systems, out-of-pocket payments and poor quality products are a particular challenge. These countries need urgent action to improve the quality, availability, supply and price of a small set of vital medicines.

The burden of disease data published by WHO list the major causes of maternal and child mortality.[4] Effective medicines exist for the major causes of mortality in children: pneumonia, neonatal infections, malaria, human immunodeficiency virus (HIV), diarrhoea and tuberculosis. However, data from country surveys show that less than 50% of 20 medicines[5] needed to treat priority conditions are available in health facilities. If these data are generally applicable to medicines for children, it is hardly surprising that child mortality is a problem. The availability of medicines that are needed for treating the causes of maternal death is less well known but, in general, availability of medicines in resource-limited settings is problematic.[6]

What are the priority products in addition to contraceptives and vaccines that might make a difference? WHO, the United Nations Children's Fund and the United Nations Population Fund have identified a list of the top 30 medicines based on burden of disease and evidence of benefit, as recommended in current WHO treatment guidelines. These diseases/conditions and medicines are listed in Table 1. These medicines need to be made available as appropriately packaged, affordable quality products, for use throughout the health system – especially in first-line facilities in the community.

Table 2 is the "wish list" of products that could make a difference, if they were available. For some medicines, what is needed is a commercialized product – perhaps a dispersible tablet – in a pack size that is designed to provide a full treatment course. The evidence for the optimal dosage regimen for some products and indications is new, and therefore regulatory approval may be required to allow supply. And for some products, what is needed is development of packaging that allows delivery of a month's supply on the back of a bicycle – so no more bulky bottles or liquids.

The bigger challenges are the formulations that do not yet exist. For tuberculosis, there is a need for a fixed-dose combination product that contains all of the medicines needed for first-line treatment, in sufficient doses, without an unreasonable pill load and in a palatable form. As well, there are products currently used in facilities, which may need to be repackaged to make them safe in community settings. Injections of a single dose of the antibiotic ceftriaxone may save a child with severe pneumonia or sepsis from dying – IF the injection can be given safely by a health worker. Preparations, such as single-use preloaded syringes would be an advance, if sufficiently stable and the price was affordable to procurement agencies and donors.

But one of the simplest developments is also the one that needs the most significant shift in expectations. Carers, patients and health workers currently expect medicines for children to be syrups. Yet liquid formulations – syrups, suspensions and mixtures – are more expensive than solid formulations, are less stable, harder to ship and transport and may need cold-chain facilities – all of which make them a problem for low-resource settings. Replacing syrups with flexible solid oral dosage forms, which could be given as liquids at the point of administration, would potentially be a huge advance in the provision of medicines for children – IF the end user will accept them. In the rollout of a dispersible antimalarial especially formulated for children there have been barriers to acceptance, simply because end users are not confident to use this dosage form in children.

So what would make a difference? The aim of publishing a priority list is to focus global attention on a package of interventions that can produce results, if implemented consistently. Manufacturers should ensure that the quality products are available for sale and international and national procurement organizations should prioritize these medicines for purchase. Health professionals should know how and when to use them. Community organizations should ensure that they ask for the medicines that work. And by strengthening health-care systems to deliver these medicines consistently, there should be progress – in availability, access and, ultimately, in survival. ■

Competing interests: Since writing this paper, the author has left WHO and is now chair of the Pharmaceutical Benefits Advisory Committee in Australia.

[a] Department of Essential Medicines and Pharmaceutical Policies, World Health Organization, avenue Appia 20, 1211 Geneva 27, Switzerland.
Correspondence to Suzanne R Hill (e-mail: suzannerhill@gmail.com).
(*Submitted: 13 July 2011 – Accepted: 7 September 2011 – Published online: 5 December 2011*)

Table 1. **Priority medicines for mothers and children**

Indication	Medicine
For mothers	
Postpartum haemorrhage:	
treatment	Oxytocin: 10 IU in 1-ml ampoule
	Sodium chloride: injectable solution 0.9% isotonic *or* Sodium lactate compound solution – injectable (Ringer's lactate)
prevention	Misoprostol: tablet 200 µg
Severe pre-eclampsia and eclampsia	Magnesium sulfate: injection 500 mg/ml in a 2-ml ampoule, 500 mg/ml in a 10-ml ampoule
	Calcium gluconate injection (for treatment of magnesium toxicity): 100 mg/ml in a 10-ml ampoule
Maternal sepsis:	
treatment of infection due to sepsis	Ampicillin: powder for injection 500 mg; 1 g (as a sodium salt) in vial
	Gentamicin: injection 10 mg; 40 mg/ml in a 2-ml vial
	Metronidazole: injection 500 mg in a 100-ml vial
treatment incomplete miscarriage	Misoprostol: tablet 200 µg
Chlamydia	Azithromycin: capsule 250 mg; 500 mg or oral liquid 200 mg/5 ml
Gonorrhoea	Cefixime: capsule 400 mg
Syphilis	Benzathine benzylpenicillin: powder for injection 900 mg benzylpenicillin in a 5-ml vial; 1.44 g benzylpenicillin in a 5-ml vial
Prevention of early labour	Betamethasone: injection 5.7 mg/ml as betamethasone sodium phosphate 3.9 mg (in solution) or betamethasone acetate 3 mg (in suspension) in an aqueous vehicle *or* Dexamethasone – injection 4 mg dexamethasone phosphate (as disodium salt) in 1-ml ampoule
	Nifedipine: immediate release capsule 10 mg
For children aged less than 5 years	
Pneumonia	Amoxicillin: dispersible, scored tablets 250 mg and 500 mg *or* equivalent flexible oral solid dosage form, in blister packs of 10
	Ampicillin: powder for injection 500 mg and 1 g
	Ceftriaxone: powder for injection 250 mg and 1 g
	Gentamicin: injection 20 mg/ml
	Procaine benzylpenicillin: powder for injection 1 g and 3 g
	Oxygen: medicinal gas
Diarrhoea	Oral Rehydration Salts (ORS): sachets of 200 ml; 500 ml and 1 litre, appropriate flavour
	Zinc: 20 mg scored dispersible tablet or equivalent flexible oral solid dosage form
Malaria	Artemisinin combination therapy (ACT): strengths and combinations according to WHO treatment guidelines 2010, dispersible tablet or flexible oral solid dosage form and dose-optimized
	Artesunate: rectal and injection dosage forms 50–200 mg
Neonatal sepsis	Ceftriaxone: powder for injection 250 mg and 1 g
	Gentamicin: injection 20 mg/ml
	Procaine benzylpenicillin: powder for injection 1 g and 3 g
Standard regimen for first-line antiretroviral treatment for HIV/AIDS	1 non-nucleoside reverse transcriptase inhibitor plus 2 nucleoside reverse transcriptase inhibitors (such as the fixed-dose combination of lamivudine + nevirapine + zidovudine)
Measles/vitamin A deficiency	Vitamin A: capsule 100 000 IU strength; 200 000 IU strength
Palliative care and pain	Paracetamol: variable flexible oral solid dosage forms
Palliative care and pain	Morphine: granules 20 mg, 30 mg, 60 mg, 100 mg, 200 mg, injection 10 mg/ml, oral liquid 10 mg/5 ml, variable flexible oral solid dosage forms

Table 2. **"Wish list" of priority medicines for mothers and children**

Type of product needed	Optimal dosage regimen
Tuberculosis: development of a product that will deliver these doses when given in 0.5 to 2.0 tablets per day over the weight range 5–30kg. For example, a fixed-dose combination containing rifampicin 250 mg, isoniazid 150 mg, pyrazinamide 400 mg and ethambutol 250 mg.	Ethambutol: 20 mg/kg/day (15 mg–25 mg/kg/day) Rifampicin: 15 mg/kg/day (10–20 mg/kg/day) Isoniazid: 10 mg/kg/day (10–15 mg/kg/day) Pyrazinamide: 35 mg/kg/day (30–40 mg/kg/day)
HIV, TB prophylaxis, *Pneumocystis carinii* pneumonia: development of a fixed-dose combination product of appropriate strength.	Isoniazid/co-trimoxazole
Neonatal care:	
apnoea: availability of a fully commercialized quality product in more countries; determination of the regulatory pathway; and dissemination of information on use.	Caffeine citrate: liquid 20mg/ml
cord care: availability of a fully commercialized quality product in more countries; determination of the regulatory pathway; establishment of optimal product types.	Chlorhexidine digluconate: solution, 4%
vitamin K deficiency: identification of optimal dose and strength of injection.	Vitamin K

References

1. Best Pharmaceuticals For Children Act, January 4 2002 (Public Law 107–109). Silver Spring: United States Food and Drug Administration; 2002.
2. Pediatric Research Equity Act of 2003, December 3 2003 (Public Law 108–155). Silver Spring: United States Food and Drug Administration; 2003.
3. Regulation (EC) no 1901/2006 of the European Parliament and of the Council on medicinal products for paediatric use. Brussels: European Commission; 2006.
4. *World health statistics 2011*. Geneva: World Health Organization; 2011.
5. Robertson J, Forte G, Trapsida JM, Hill S. What essential medicines for children are on the shelf? *Bull World Health Organ* 2009;87:231–7. doi:10.2471/BLT.08.053645 PMID:19377720
6. Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R. Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. *Lancet* 2009;373(Issue 9659):240–9. doi:10.1016/S0140-6736(08)61762-6 PMID:19042012