

Setting standards for essential children's medicines

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The WHO Model List of Essential Medicines, used by many countries to guide drug procurement and supply, has been a global standard for 30 years. Although this list has included some paediatric medicines, a children's list has not been systematically developed until now. To address this shortcoming, a subcommittee of the WHO Expert Committee on Selection and Use of Essential Medicines met in July 2007, to develop a list of essential medicines for children.

In May 2007, the 60th World Health Assembly passed a resolution on Better Medicines for Children (WHA60.20) that described several strategies to improve access to essential medicines of adequate quality for children. As has been described in several reviews,^{1,2} the main causes of mortality in children can be treated by essential medicines such as antibiotics for infections or oral rehydration solution and zinc for diarrhoea. To apply this knowledge effectively requires that these medicines be available; yet suitable zinc tablets, for example, are still not included in many national essential medicines lists.

Children with chronic disease, such as HIV, will be taking medicines for many years, and if treatment is to be effective the medicines have to be of a shape, size and form that enhances adherence. A treatment regimen that requires several doses daily of four unpleasant-tasting syrups discourages adherence. For pharmaceutical reasons, oral liquid medications sometimes contain inappropriate ingredients, including alcohol; they also may be less stable, and often cost more, than the equivalent solid dosage forms.³

Children of different ages have different needs. Neonates are a vulnerable group for many reasons. They also

metabolize medicines differently from older children and adults. Doses of medicines for neonates need adjustment to take account of this difference. Where the available dosage form, such as the standard concentration in a morphine ampoule, is designed to deliver an adult dose, there is a risk of inadvertent overdose. Medicines for children may exist, but they are not always available where they are needed or may be inappropriate for the use required.

The WHO Model List has been used as a policy and advocacy tool to promote access to essential medicines, so the development of a global children's list is a timely standard for countries to consider. This list has been developed using the same procedures that are used to update the main list. Selection of medicines as essential is based on public health need and evidence of their efficacy and safety. In selecting essential medicines for children, one of the first difficulties encountered was the relative paucity of evidence about medicines used to treat children with "neglected" diseases such as leishmaniasis. The meeting report⁴ lists medicines for which further evidence is required to confidently assess the benefits and harms of their use in children. Some questions might be answered by systematic reviews of existing information, but others require more research and drug development. Novel approaches are needed for clinical research towards drug development, for example using population modelling, to estimate pharmacokinetic parameters of medicines in children that can then be tested in relatively small clinical studies.

The choice of dosage form presents a problem. Liquid forms may be essential for neonates but are undesirable for children who can swallow solid or semi-solid forms for the reasons noted above.

It is clear that an innovative approach to provide flexible dosage forms is needed. For children, doses need to be titrated more precisely for different age groups than for adults: they need dosage forms that are stable, titratable, suitable for different ages and affordable. Microencapsulated granules that can be measured precisely or dispensed in appropriate quantities are one option. Another is simple-to-administer fixed-dose combination products structured to provide appropriate paediatric doses across a wide range of age groups.

The proposed first list is only the beginning of a substantial programme of work. Although it includes about 200 medicines in about 450 dosage forms, many are marked as needing further review, or have age restrictions on their use because of lack of data. We hope that this list's publication will promote discussion on how to improve essential medicines for children, and that countries will use the list to review their essential paediatric medicines programmes. ■

References

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