Comment

Problems with the WHO guidelines for management of childhood pneumonia

Global child mortality has fallen substantially in the past 25 years. Available data and modelled estimates indicate that pneumonia mortality has fallen to a greater extent.¹ Although improved community development and immunisation have no doubt contributed to this decline, improved management of cases is also a major factor. For virtually all high-mortality settings, the WHO case management strategy implemented as a component of the Integrated Management of Childhood Illness (IMCI) algorithm has formed the basis for pneumonia management. The algorithm for pneumonia management had not changed for 24 years until 2013 when the key physical sign previously used to identify severe pneumonia cases (lower chest wall indrawing) was downgraded to become a sign of nonsevere pneumonia, to be managed with oral antibiotics at home.²

In The Lancet Global Health, Ambrose Agweyu and colleagues³ report a large, retrospective study of pneumonia admissions among 16031 Kenyan children admitted to 14 Kenyan hospitals. At the time, Kenya was using both Haemophilus influenzae type b and pneumococcal conjugate vaccines. 832 fatal cases (5%) were reported. This case fatality rate might seem high, but it is probably typical for much of sub-Saharan Africa. Of the children who died, at least 322 (39%) would have been classified by WHO as having nonsevere pneumonia requiring home treatment by the 2013 revision. These children actually did die despite inpatient treatment, but the fact that the WHO IMCI revision would have sent them home raises very serious questions. Review of the children who were likely misclassified as non-severe pneumonia (due to their fatal outcome) showed that risk of mortality is associated with malnutrition (frequently unrecognised) and pallor. The latter might indicate some diagnostic confusion between malaria and pneumonia, although Agweyu and colleagues state that this risk factor held even in the non-malarious areas. Clearly, recognition of severe malnutrition remains an important issue. Of great concern is the strong association between lower chest wall indrawing and mortality in this group. Specifically, children classified as having non-severe pneumonia by the new definition, who had indrawing (and were admitted to hospital) had a case fatality rate of 3.2% (95% Cl 2.7-3.7). Under the pre-2013 system these children would have been classified as having severe pneumonia in need of hospital care; under the current system they would have been sent home.

This study is not the only one to identify lower chest wall indrawing as an important sign of potentially fatal pneumonia. In South Africa, chest wall indrawing was a strong indicator of a fatal outcome in both HIVpositive and HIV-negative children with pneumonia.4 However, lower chest wall indrawing is a confusing sign. Wheezing children will often demonstrate the sign with moderately severe illness due to the reduced lung compliance associated with wheezing, so in areas where asthma prevalence is increasing this has led to problems with over-referral of children not deemed to be severely ill.⁵ Indrawing is also a sign that can be very subtle, and is easy to overcall. Not surprisingly then, a prospective study of Pakistani children, presenting as outpatients with acute respiratory infections and indrawing, enrolled a large number of children, most with wheezing illness with extremely low mortality.⁶ In such a group, clinical failures will occur, but will usually be due to viral infections such as respiratory syncytial virus (RSV) that can typically produce symptoms for 7-10 days. Management at home with amoxicillin and daily review can be expected to have a similar failure rate to inpatient management, as was found.

It is extraordinary then that the study by Hazir and colleagues,⁶ supported by a non-randomised multi-country study that enrolled only 873 of the 6582 "severe pneumonia" cases screened,⁷ with a case fatality rate of zero, should be used as the basis to revise the WHO algorithm for identification of severe pneumonia.⁸ African countries with high pneumonia mortality are now in the process of introducing this revised IMCI strategy. The study by Agweyu and colleagues³ gives some indication of the potentially serious consequences of this policy change. It has been argued that the use of pulse oximetry at community level could identify the cases that are truly in need of hospital care. This could certainly improve



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the identification of severe cases; what proportion of potentially fatal cases could be identified by oximetry is an important area of current field research.

The study by Agweyu and colleagues³ also highlights the fact that, with current hospital care, about 5% of children with pneumonia in many African hospitals will die. Some of these will have very severe disease and cannot be saved, but this is probably a small group. Some children could be saved by ventilation or use of the much simpler bubble continuous positive airways pressure approach,⁹ but sadly there is also likely to be a substantial number of deaths that could be avoided by paying attention to basic clinical care, including nutrition, careful management of intravenous fluids (or avoiding the use of intravenous fluids), prevention of hypothermia, and prevention of nosocomial infections.

An urgent need exists for the WHO/IMCI pneumonia case management strategy to be reviewed and probably revised. What the world needs is a safe and effective system for the management of childhood pneumonia, re-examining the importance of chest wall indrawing, improving recognition of malnutrition, and taking note of the important role of anaemia, especially in malarious settings. Pulse oximetry at the primary care level should be the future, and future technological developments might add respiratory rate and work of breathing to the parameters measured by oximetry. However, for the foreseeable future, especially in the most difficult settings, simple clinical signs will be the means of identifying the most severe cases, so it is essential that we get this right.

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I declare no competing interests.

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- GBD 2016 Causes of Death Collaborators. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017; 390: 1151–210.
- Izadnegahdar R, Cohen A, Klugman K, Qazi SA. Childhood pneumonia in developing countries. *Lancet Respir Med* 2013; **1:** 574–84.
- 3 Agweyu A, Lilford RJ, English M, et al. Appropriateness of clinical severity classification of new WHO childhood pneumonia guidance: a multi-hospital, retrospective, cohort study. *Lancet Glob Health* 2018; 6: e74–83.
- 4 Reed C, Madhi SA, Klugman KP, et al. Development of the Respiratory Index of Severity in Children (RISC) score among young children with respiratory infections in South Africa. PLoS One 2012; 7: e27793.
- 5 Mulholland EK, Olinsky A, Shann FA. Clinical findings and severity of acute bronchiolitis. *Lancet* 1990; **335:** 1259–61.
- 6 Hazir T, Fox LM, Nisar YB, et al. Ambulatory short-course high dose oral amoxicillin for treatment of severe pneumonia in children: a randomized equivalency trial. *Lancet* 2008; **371**: 49–56.
- 7 Addo-Yobo E, Anh DA, El-Sayed HF, et al. Outpatient treatment of children with severe pneumonia with oral amoxicillin in four countries: the MASS study. Trop Med Int Health 2011; 16: 995–1006.
- 8 Mulholland K, Carlin JB, Duke T, Weber M. The challenges of trials of antibiotics for pneumonia in low-income countries. *Lancet Respir Med* 2014; 2: 952–54.
- 9 Chisti MJ, Salam MA, Smith JH, et al. Bubble continuous positive airway pressure for children with severe pneumonia and hypoxaemia in Bangladesh: an open, randomised controlled trial. *Lancet* 2015; **386**: 1057–65.