Technical updates of the guidelines on Integrated Management of Childhood Illness (IMCI)

Evidence and recommendations for further adaptations

IMCI

For further information please contact:

Department of Child and Adolescent Health and Development (CAH)

World Health Organization
20 Avenue Appia
1211 Geneva 27
Switzerland

Tel +41-22 791 3281
Fax +41-22 791 4853

e-mail cah@who.int
web site http://www.who.int/child-adolescent-health

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Abbreviations

ACT	Artemisinin based combination therapy
AOM	Acute otitis media
ARI	Acute Respiratory Infections
ARV	Antiretrovirals
AIDS	Acquired Immunodeficiency Deficiency Syndrome
APPIS	Amoxycillin Penicillin Pneumonia International Study
CAH	Department of Child and Adolescent Health and Development
CDD	Control of Diarrhoeal Diseases
CDS	Department of Communicable Diseases Surveillance and Response
CER	Cost-Effectiveness Ratio
CI	Confidence Interval
CPE	Department of Communicable Diseases Control, Prevention, and Eradication
CSOM	Chronic Suppurative Otitis Media
DALY	Disability Adjusted Life Year
FAO	Food and Agricultural Organization of the United Nations
FCH	Family and Community Health
HIV	Human Immunodeficiency Virus
IMCI	Integrated Management of Childhood Illness
kg	kilogram
MIC	Minimum Inhibitory Concentration
Mg	milligrams
n	number
NCHS	National Center for Health Statistics (US)
NHD	Department of Nutrition for Health and Development
OR	Odds ratio
ORS	Oral rehydration salts
p	p-values

PVC	Strategy Development and Monitoring for Parasitic Diseases and Vector Control
PNT	Post natal transmission
RBM	Roll Back Malaria
RHR	Department of Reproductive Health and Research
SP	sulfadoxine-pyrimethamine
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
UNU	United Nations University
WHA	World Health Assembly
WHO	World Health Organization

Executive Summary

It is over seven years since IMCI has been introduced and much has been learnt through the adaptation and implementation processes in countries. The Department of Child and Adolescent Health and Development (CAH) and other institutions have undertaken work to evaluate the evidence base for the technical guidelines of the IMCI strategy. Research results are emerging with potential implications for updating the technical guidelines of IMCI. The technical updates are provided for use by countries whenever there are opportunities to revise the country IMCI adaptations. It will be necessary to have a series of technical updates as new research findings become available. The current technical updates have compiled new evidence to inform countries immediately about IMCI adaptations and recommend adaptations in six areas shown below.

Antibiotic treatment of non-severe and severe pneumonia

For children 2 months up to 5 years with non-severe pneumonia in non-HIV countries three days in place of five days of antibiotic therapy with either oral amoxicillin or cotrimoxazole should be used. Where antimicrobial resistance to cotrimoxazole is high, oral amoxicillin is the better choice. Oral amoxicillin should be used twice daily instead of thrice daily. Injectable ampicillin plus an injection of gentamicin is preferable to injectable chloramphenicol for very severe pneumonia in children 2-59 months of age. For management of HIV-infected children, newly developed WHO draft treatment guidelines should be used. Children with wheeze and fast breathing and/or lower chest indrawing should be given a trial of rapid acting **inhaled bronchodilator**, before they are classified as having pneumonia and prescribed antibiotics.

Low osmolarity ORS and antibiotic treatment for bloody diarrhoea

Countries should now use and manufacture low osmolarity ORS for the management of dehydration in all children with diarrhoea but keep the same instructions for the preparation of the solution to avoid confusion. Ciprofloxacin is the most appropriate drug for the management of bloody diarrhoea in place of nalidixic acid which leads to rapid development of resistance. Along with increased fluids and continued feeding, all children with diarrhoea should be given zinc supplementation for 10-14 days.

Treatment of fever/malaria

The antimalarial drug policy in countries will vary and IMCI adaptations generally follow the national policy. In most countries, artemisinin-based combination therapies have been shown to improve treatment efficacy. The advantages of artemisinin-based combination therapy (ACT) relate to the unique properties and mode of action of the

artemisinin component, however, due to the very short half-life of artemisinin derivatives, their use requires combination of one of these drugs with a longer half-life "partner" antimalarial drug.

Treatment of ear infections

Oral amoxicillin is a better choice for the management of acute ear infection in countries where antimicrobial resistance to cotrimoxazole is high. Chronic ear infection should be treated with topical quinolone ear drops for at least two weeks in addition to dry ear-wicking.

Infant feeding

Exclusive breastfeeding should be promoted for six months rather than the previously recommended four to six months. The current IMCI guidelines for complementary feeding remain valid in developing countries. In areas where HIV is a public health problem all women should be encouraged to receive HIV testing and counselling. If a mother is HIV-infected and replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding is recommended. Otherwise, exclusive breastfeeding is recommended during the first months of life.

Treatment of helminthiasis

Albendazole and mebendazole have now been shown to be safe to use in children 12 months or older rather than from 24 months only. There is a paucity of safety data regarding the use of these drugs in infants under 12 months.

The new recommendations are predominantly based on the strength of the evidence supporting a change in current IMCI adaptations. Therefore emphasis has been on research findings from multicentre, randomized, controlled trials. Additional relevant information based on technical consultation has been included in some areas. Incorporation of summary recommendations into IMCI guidelines in countries should be considered when countries are reviewing and replanning or printing further materials for training. Suggested activities to facilitate this process include having orientation meetings with senior ministry of health and paediatric staff and addressing logistic issues and the role of IMCI programme managers associated with introduction of the new IMCI recommendations. Additional changes to IMCI pre-service education training courses and teaching materials may be necessary.

Introduction

It is over seven years since IMCI has been introduced and much has been learnt through the adaptation and implementation processes in countries. The Department of Child and Adolescent Health and Development (CAH) and other institutions have undertaken work to evaluate the evidence base for the technical guidelines of the IMCI strategy. Research results are emerging with potential implications for updating the technical guidelines of IMCI. In 2001 CAH, jointly with Roll Back Malaria, organized a technical consultation to examine the evidence base for the IMCI strategy for the management of malaria and other febrile illnesses including measles and dengue haemorrhagic disease. This international consultation came up with recommendations to improve the guidelines, as well as specific recommendations for operational research. Following the technical consultation, CAH held a series of meetings within the Department at HQ in addition to consultations with regional office staff where the updating process was discussed. In 2004 it was recommended that CAH finalize the IMCI updates on the basis of the best available evidence and country programme feedback, prioritizing those updates most likely to reduce child mortality.

The technical updates are considered necessary for the following reasons:

- New knowledge becomes available through research into clinical management of childhood diseases. Research results should be examined in a systematic manner to improve and update the IMCI guidelines.
- IMCI guidelines should be reviewed with regard to experiences and lessons learned through the adaptation and implementation process.
- Implementation of IMCI has identified problems and questions, some of which have been addressed through operational research in regions and countries.
- Since the development of the IMCI guidelines, the epidemiology of diseases has evolved and thus a revised version has to accommodate and reflect these changes. For example, the prevalence of HIV/AIDS has increased significantly over the last 10 years and specific aspects require updating in the context of IMCI.

The current technical updates have compiled new evidence and recommended adaptations in the following six areas:

- Antibiotic treatment of severe and non-severe pneumonia
- Low osmolarity ORS and antibiotic treatment for bloody diarrhoea
- Treatment of fever/malaria
- Treatment of ear infections
- Infant feeding
- Treatment of helminthiasis

This document presents evidence that is available to inform countries immediately about IMCI adaptations. New evidence for several IMCI-related conditions is emerging but cannot currently be recommended until results of further field testing becomes available. Additionally, research on some conditions is rapidly changing and detailed evidence and recommendations are presented in separate documents (HIV/AIDS, dengue fever, malaria).

Acute respiratory infections

Frequency of administration of amoxicillin treatment for non-severe pneumonia

TECHNICAL BASIS

For children with non-severe pneumonia, IMCI recommends oral amoxicillin (15 mg/kg of body weight/dose) thrice daily or oral cotrimoxazole (4 mg of trimethoprim/kg/dose) twice daily. The more frequent amoxicillin dosing may lead to compliance problems. A study compared the pharmacokinetics and levels of oral amoxicillin (15 mg/kg of body weight/dose) thrice daily with the 25 mg/kg/dose twice-daily regimen in 66 children aged 3 to 59 months with pneumonia. The pharmacokinetics study showed that amoxicillin twice daily is a feasible alternative to thrice-daily dosing (1).

A twice-daily dose is now also recommended by the American Academy of Paediatrics based on other studies supporting the recommendation (2).

A randomized, controlled, double-blind trial compared the clinical efficacy of twice daily oral cotrimoxazole with twice daily oral amoxicillin for treatment of childhood pneumonia in outpatient departments of seven hospitals and in one community health service in Pakistan. The study concluded that both amoxicillin and cotrimoxazole provided equally effective therapy for non-severe pneumonia (3).

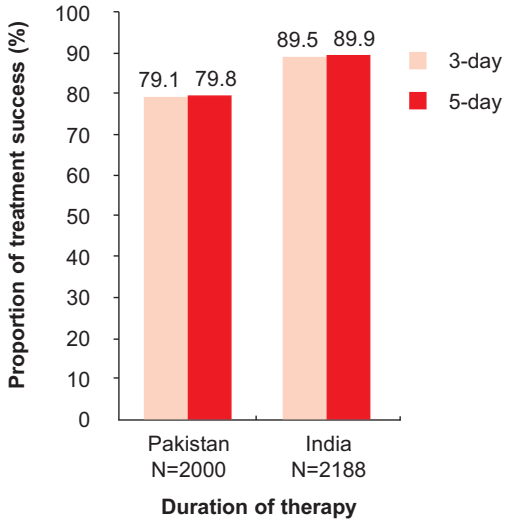
Oral amoxicillin should be used in 25 mg/kg/dose twice daily for the treatment of non-severe pneumonia.

Duration of amoxicillin treatment for non-severe pneumonia

TECHNICAL BASIS

The five-day duration of therapy for non-severe pneumonia is not based on empiric data. If shorter courses of antibiotics were found to be equally effective they could reduce the overall cost of treatment, in addition to improving the compliance and reducing the antimicrobial resistance in the community. Two double-blind randomized controlled trials in Pakistan and India compared the treatment outcome of three-day oral amoxicillin with that of the currently recommended five-day therapy for non-severe pneumonia in children 2-59 months of age. In the Pakistan study, 2000 children aged 2–59 months with non-severe pneumonia (WHO criteria) diagnosed in the outpatient department of seven hospitals were enrolled. Patients were randomly assigned to three days or five days of treatment with oral amoxicillin. The primary outcome was treatment failure. Analyses were by intention to treat. Treatment failed in 209 (21%) patients in the 3-day group, and 202 (20%)

Clinical outcomes of 3 versus 5 days of oral amoxicillin for non-severe pneumonia



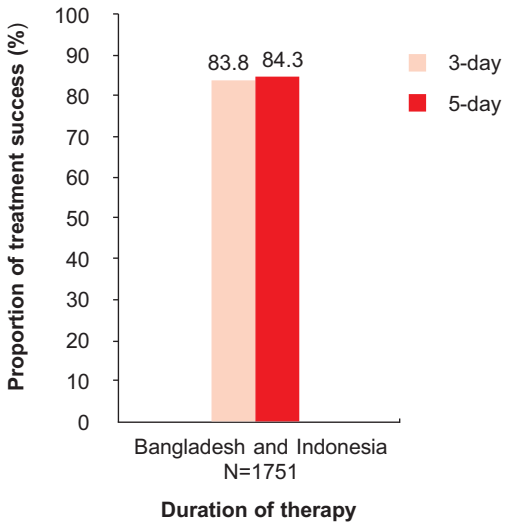
Pakistan: MASCOT Study Lancet 2002
India: ISCAP Study BMJ 2004

in the 5-day group (difference 0.7%; 95% CI 1.8-3.2). In 12 (1%) children in the 3-day group and in 13 (1%) in the 5-day group the disease relapsed (difference 0.1%; 0.6-0.8). Treatment was more likely to fail in children who did not adhere to treatment ($p<0.0001$), in those younger than 12 months ($p<0.0001$), in those whose illness lasted for three days or longer ($p=0.004$), in those whose respiratory rate was more than 10 breaths/min above the age-specific cut-off ($p=0.004$), and in those with vomiting ($p=0.009$). Non-adherence was also associated with failure of treatment in the 5-day group ($p<0.0001$) (4, 5).

The Indian study was conducted in ambulatory care settings in seven referral hospitals and included children aged 2-59 months with WHO-defined non-severe pneumonia. They received oral amoxicillin, 30-45 mg/kg/day, in three divided doses for the first three days and then either continued on an active drug or placebo for the next two days. The primary outcome was clinical cure. 2188 cases were randomized, 1095 to 3-day and 1093 to 5-day treatment with amoxicillin. Clinical cure was achieved in 980 (89.5%) and 983 (89.9%) patients on 3-day and 5-day treatment respectively (difference 0.4, 95% CI 2.1-3.0). Adherence assessed on day 3 and day 5 follow-up was 94% and 85.2%, respectively. Loss to follow-up was 5.4% by day 5. There were no deaths, 41 hospitalizations and 36 minor adverse reactions. Overall, there were 225 (10.28%) clinical failures and 106 relapses (5.3 %) and these rates were similar in both groups (6,7).

Oral amoxicillin should be given for three days for non-severe pneumonia in children 2-59 months of age.

Clinical outcomes of 3 versus 5 days of oral cotrimoxazole for non-severe pneumonia



WHO. Consultative Meeting ARI Research, 2003 Geneva, WHO/FCH/CAH/04.2

Duration of oral cotrimoxazole therapy for non-severe pneumonia

TECHNICAL BASIS

A double-blind, randomized, placebo-controlled multicentre equivalence trial was carried out at two sites in Indonesia and Bangladesh in which three days versus five days oral cotrimoxazole for the treatment of non-severe pneumonia, and their effect on antimicrobial resistance in nasopharyngeal *S. pneumoniae* and *H. influenzae* isolates was compared. All children were followed up for 15 days. Overall, 84.3% (735/872) children in the 5-day group and 83.8% (737/879) in the 3-day group were cured 15 days after enrolment. At enrolment cotrimoxazole non-susceptible *S. pneumoniae* were 54.7% (359/656) and 51.3% (329/641) in the 5-day and 3-day groups, which became 64.1% (262/409) and 61.5% (266/432) on day 15, in that order (P=0.50). In the case of *H. influenzae* prevalence of non-susceptible strains on 0 and 15 day were 44.6% vs. 61.9% and 41.7% vs. 53.7% in the 5-day and 3-day groups respectively (P=0.06) (8). This shows that with a shorter course of antibiotics, there is less likelihood of resistance.

Oral cotrimoxazole should be given for three days for non-severe pneumonia in children 2-59 months of age in low HIV prevalent countries.

Use of oral amoxicillin versus injectable penicillin in children with severe pneumonia

TECHNICAL BASIS

Some data exist that oral amoxicillin may be effective against WHO-defined severe pneumonia (9). If oral antibiotic treatment is shown to be as effective as currently recommended injectable therapy for the treatment of severe pneumonia it would become relatively easy to manage on an outpatient basis. Data from the Amoxicillin Penicillin Pneumonia International Study (APPIS), a multinational, multicentre trial conducted in eight countries comparing injectable penicillin (n=857) with oral amoxicillin (n=845), showed treatment failed in 187 (21.8%) patients in the injectable penicillin group, and 185 (21.8%) in the oral amoxicillin group. In 26 (3.0%) children in the injectable penicillin group and in 39 (4.6%) in the oral amoxicillin group the disease relapsed. The results showed that the clinical outcome with oral amoxicillin was comparable to injectable penicillin in hospitalized children with severe pneumonia (10).

Where referral is difficult and injection is not available, oral amoxicillin in 45 mg/kg/dose twice daily should be given to children with severe pneumonia for five days.

Gentamicin plus ampicillin versus chloramphenicol for very severe pneumonia

TECHNICAL BASIS

WHO currently recommends chloramphenicol for the treatment of very severe pneumonia. Up to 20% of children receiving chloramphenicol for very severe pneumonia fail treatment. An alternative to chloramphenicol at similar costs could be injectable penicillin plus an amino-glycoside. Both treatment options will have a good cover in the blood or the lungs against sensitive strains of *S. pneumoniae* and *H. influenzae*. Some patients with severe pneumonia may have meningitis, which may not be clinically evident at presentation. Chloramphenicol penetrates the blood brain barrier effectively whereas gentamicin does not. *Staphylococcus aureus* may be a common pathogen causing treatment-unresponsive severe pneumonia, and may be more susceptible to chloramphenicol than to gentamicin. On the other hand a major advantage of a penicillin-amino glycoside combination is that it is likely to provide superior treatment of enteric gram negative bacilli.

An open randomized clinical trial in Papua New Guinea aimed to establish whether the combination of benzylpenicillin and gentamicin or chloramphenicol would be better as first-line treatment in children with very severe pneumonia (11). 1116 children aged 1 month to 5 years of age were enrolled who fulfilled the WHO criteria for very severe pneumonia.

Children were randomly assigned to receive chloramphenicol (25 mg/kg 6 hourly) or benzylpenicillin (50 mg/kg 6 hourly) plus gentamicin (7.5 mg/kg daily) by intramuscular injection. The primary outcome measure was a good or an adverse outcome. 559 children were treated with chloramphenicol and 557 with benzylpenicillin and gentamicin. At presentation the median haemoglobin oxygen saturation was 71% (IQR 57-77) for those allocated chloramphenicol and 69% (55-77) for those allocated penicillin and gentamicin. 147 (26%) children treated with chloramphenicol and 123 (22%) treated with penicillin and gentamicin had adverse outcomes (p=0.11). Thirty-six children treated with chloramphenicol and 29 treated with penicillin and gentamicin

died. More children treated with chloramphenicol than penicillin and gentamicin represented with severe pneumonia within one month of hospital discharge (p=0.03). They concluded that for children with severe pneumonia in less-developed countries the probability of a good outcome is similar if treated with chloramphenicol or with the combination of benzylpenicillin and gentamicin.

Injectable ampicillin plus injectable gentamicin is a better choice than injectable chloramphenicol for very severe pneumonia in children 2-59 months of age. A pre-referral dose of 7.5 mg/kg intramuscular injection gentamicin and 50 mg/kg injection ampicillin can be used.

Another multicentre randomized clinical study was conducted in eight sites in seven countries to compare the efficacy of chloramphenicol with that of ampicillin plus gentamicin in children aged 2 to 59 months with very severe pneumonia (12). 958 children were randomized, of which 122 (12.7%) patients failed treatment by day 6 (primary outcome). Treatment failure was higher in the chloramphenicol group, the relative risk being 1.5 (1.1-2.1). The common reasons for treatment failure by day 6 were death (n=44), development of septic shock (n=29) or persistence of very severe pneumonia (n=21). Treatment failure was checked at 48 hours, 10 and 30 days as secondary outcomes and found 82 (8.6 %) patients had treatment failure by 48 hours; constituting about 51% of all treatment failure. The cumulative treatment failures on day 10 and 30 remained higher in the chloramphenicol group and the distribution of treatment failure categories remained the same as seen on day 6. Forty-four deaths were recorded as the reason for treatment failure, of which 21 deaths occurred after changes of antibiotics and after the patients were categorized as treatment failure. Overall more deaths occurred in the chloramphenicol group than the ampicillin and gentamicin group by day 30 (RR=1.6; 95% CI 0.99-2.6). Most (74%) deaths occurred within 48 hours. Based on these results the use of gentamicin plus ampicillin for the management of very severe pneumonia is warranted.

OTHER ISSUES

During a consultative meeting to review evidence and research priorities in the management of acute respiratory infections (8), the following points were also made during the discussion of the possibility of a switch-over to a 3-day therapy with first-line antibiotics for non-severe pneumonia:

- Concern regarding 3-day antibiotic therapy being effective in children with non-severe pneumonia in HIV-endemic areas, where similar data are not yet available. It was clarified that in HIV-endemic areas this would not be recommended.
- Concern regarding using 3-day regimen in children less than six months of age, due to the safety issue. It was clarified that data showed that 2-6 month old children had an equal chance of responding to either 3-day therapy or 5-day therapy but that this would not be recommended for children less than two months of age.
- Criticism for the switch-over from cotrimoxazole to amoxicillin in malaria-endemic regions was that amoxicillin would not be effective against malaria. It was pointed out that cotrimoxazole was not recommended as a first-line anti-malarial in any country. Therefore, the switch-over would not affect the treatment of malaria.

Trial of rapid acting bronchodilators in children with wheeze and fast breathing and/or lower chest wall indrawing

There is concern that children with wheeze are not being managed properly using current WHO ARI case management guidelines. Most of the children with non-recurrent wheeze probably have a viral infection and hence will not benefit from the use of an antibiotic. Some of these children will benefit from the use of bronchodilators. The children with wheeze and fast breathing are being classified as pneumonia according to the current WHO ARI case management guidelines. It has long been felt that more information is needed for children who present with wheeze.

TECHNICAL BASIS

WHO has supported studies on "The assessment and management of wheeze in children 1-59 months of age presenting with cough and/or difficult breathing" in several countries. Results are now available from Pakistan (13) and Thailand (8). In this multicentre prospective study, children 1-59 months of age with auscultatory/audible wheeze with fast breathing and/or lower chest indrawing were screened and their response to up to three cycles of inhaled rapid acting bronchodilator (salbutamol) was recorded. The responders were enrolled and sent home on inhaled bronchodilators and followed up on days 3 and 5. In Pakistan, 1622 children with wheeze were screened, of which 1004 (61.8%) had WHO defined non-severe and 618 (38.2%) severe pneumonia. Wheeze was audible in only 595 (36.7%) of children. Of 1004 non-severe pneumonia children, 621 (61.8%) responded to up to three cycles of inhaled bronchodilator. Of 618 severe pneumonia children only 166 (26.8%) responded. Among responders, 93 (14.9%) children in non-severe and 63 (37.9%) in the severe pneumonia group showed subsequent deterioration on follow-ups. No family history of wheeze, temperature more than 100°F (37.7°C) and severe pneumonia at the time of screening were identified as independent predictors of subsequent deterioration.

In Thailand, 521 children with wheeze were screened, of which 256 (49.1%) had WHO defined non-severe and 265 (50.9%) severe pneumonia. Wheeze was audible in only 48 (9.2%) children. Of 256 non-severe pneumonia children, 217 (84.8%) responded to up to three cycles of bronchodilator. Of 265 severe pneumonia children 189 (71.3%) responded. Among responders, 14 (6.4%) children in non-severe and 24 (12.7%) in the severe pneumonia group showed subsequent deterioration on follow-ups. A body temperature more than 100°F (37.7°C) and severe pneumonia were identified as independent predictors of subsequent deterioration.

These data show that a large number of children with wheeze are being classified as pneumonia and are being prescribed antibiotics unnecessarily. Bronchodilators are being underutilized in children with wheeze. The results also showed that a great majority of children with wheeze who respond to a trial of inhaled bronchodilators continue to do well when sent home without an antibiotic.

Children with wheeze and fast breathing and/or lower chest indrawing should be given a trial of rapid-acting inhaled bronchodilator (up to three cycles) before they are classified as pneumonia and prescribed antibiotics. 0.5 ml salbutamol diluted in 2.0 ml of sterile water per dose nebulization should be used.

SUMMARY RECOMMENDATIONS

Non-severe pneumonia	• In low HIV prevalent countries three days of antibiotic therapy (oral amoxicillin or cotrimoxazole) should be used in children 2 months up to 5 years • Where antimicrobial resistance to cotrimoxazole is high oral amoxicillin is the better choice • Oral amoxicillin should be used twice daily at a dose of 25 mg/kg per dose
Severe pneumonia	• For management of HIV-infected children, newly developed WHO draft treatment guidelines should be used (14) • Children with wheeze and fast breathing and/or lower chest indrawing should be given a trial of rapid-acting inhaled bronchodilator before they are classified as pneumonia and prescribed antibiotics • Where referral is difficult and injection is not available, oral amoxicillin could be given to children with severe pneumonia
Very severe pneumonia	• Injectable ampicillin plus injection gentamicin is a better choice than injectable chloramphenicol for very severe pneumonia in children 2-59 months of age

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Diarrhoeal diseases

Use of low osmolarity ORS [1-3]

TECHNICAL BASIS

After 20 years of research to improve oral rehydration salts (ORS), a new formula has been developed and is now recommended by the World Health Organization (WHO) and the United Nations International Children's Emergency Fund (UNICEF). The new formula, which contains slightly less sodium and glucose than previously not only decreases the volume of diarrhoea and vomiting in children presenting acute non-cholera-related diarrhoea but also, and above all, significantly reduces the need for intravenous fluid treatment. This new low osmolarity ORS has been included in the WHO model list of essential medicines.

Studies have shown that the efficacy of ORS solution for treatment of children with acute non-cholera diarrhoea is improved by reducing its sodium concentration to 75 mEq/l, its glucose concentration to 75 mmol/l, and its total osmolarity to 245 mOsm/l. The need for unscheduled supplemental IV therapy in children given this solution is reduced by 33%, stool output is reduced by about 20% and the incidence of vomiting by about 30%.

Countries should now use and manufacture the low sodium ORS for all diarrhoeic children but keep the same instructions for the preparation of the solution.

For children with cholera, reduced osmolarity ORS solutions were at least as effective as standard ORS and safety data, while limited, are reassuring though further studies will soon be available. Because of the improved effectiveness of reduced osmolarity ORS solution, WHO and UNICEF now recommend that countries use and manufacture the low osmolarity ORS in place of the previously recommended ORS solution with a total osmolarity of 311 mOsm/l.

The new osmolarity ORS can still be called "ORS" to avoid any confusion and revision is required only in manufacturing and procurement of the drug.

Antibiotics in the management of bloody diarrhoea (*Shigella* dysentery) [4-10]

Shigellosis is increasingly becoming an important public health problem because of the development of multiple antimicrobial resistances, resulting in frequent treatment failure leading to complications and deaths. The use of an effective antimicrobial in shigellosis alleviates the dysenteric syndrome, fever and abdominal cramps, reduces the duration of pathogen excretion, interrupts disease transmission and reduces the risk of potential complications. In ideal situations, a stool or rectal swab sample should be taken for laboratory confirmation of diagnosis and drug sensitivity testing before institution of antimicrobial therapy. However, this is rarely possible and empiric antimicrobial therapy is instituted based on the knowledge of the antimicrobial resistance pattern of *Shigella* strains circulating locally.

ANTIBIOTICS USED SO FAR

The choice of antimicrobials effective in treating shigellosis has become very limited. Tetracycline, ampicillin, and cotrimoxazole, once used as first line antimicrobials, are no longer effective. *Shigella* strains are often sensitive *in vitro* to some antimicrobials such as furazolidone, gentamicin, early generation cephalosporin and amoxicillin. However, these antibiotics, including gentamicin if given orally, are not clinically effective against *Shigella* and therefore should not be recommended or used. At present, nalidixic acid is widely used as the first-line antimicrobial against *Shigella* in many countries. However, it is becoming increasingly ineffective in many parts of the world.

Nalidixic acid and ciprofloxacin both belong to a group of antimicrobials called "quinolones", nalidixic acid being the first antimicrobial agent developed in this family of antibiotics. In a few clinical trials conducted in the 70s and 80s, nalidixic acid was shown to be effective clinically against *Shigella*. Therefore, when resistance against the commonly used antibiotics (ampicillin, cotrimoxazole) became increasingly prevalent in the 80s, nalidixic acid became the drug of choice for treating shigellosis in spite of the failure of nalidixic acid to terminate rapidly faecal excretion of *Shigella*.

TECHNICAL BASIS

The newer quinolones, such as ciprofloxacin, have been shown to have some significant advantages over nalidixic acid. Firstly, their activity against *Enterobacteriacae* is several thousand-fold greater than that of nalidixic acid. Secondly, ciprofloxacin is 100 to 1000-fold less prone than nalidixic acid to selection of single-step spontaneous highly resistant organisms. Thirdly, simplified treatment regimens (2 doses per day for three days instead of 4 doses per day for five days with nalidixic acid) have been shown to be very effective against all species of *Shigella*.

In countries where nalidixic acid is still effective against shigellosis, ciprofloxacin is often used as a second-line antimicrobial for treating strains resistant to nalidixic acid. However, belonging to the same antibiotic family, it is not surprising that strains resistant to nalidixic acid show some degree of cross-resistance to ciprofloxacin and other newer quinolones. In fact, the Minimum Inhibitory Concentration (MIC) of ciprofloxacin is increased in strains already resistant to nalidixic acid, and the appearance of full resistance to ciprofloxacin is very likely hastened when this antibiotic is used as a second-line treatment of strains already resistant to nalidixic acid.

Based on these findings, experts met in Bangladesh in February 2004 and recommended that nalidixic acid should no longer be recommended for the management of *Shigella* infection and that ciprofloxacin should become the first-line antibiotic to treat shigellosis.

Two major concerns were considered by the experts when making this recommendation: (i) the safety of ciprofloxacin in children and (ii) the cost of this antibiotic compared to previously recommended treatment.

- **Safety** - Concern about the safety of quinolones came from results of studies showing that both nalidixic acid and the newer quinolones could cause arthropathy in young animals. However, in developed countries nalidixic acid has been used in children for more than 30 years to treat urinary tract infections,

sometimes for prolonged periods, with no reports of resultant arthropathy. In developing countries, nalidixic acid has been the recommended first line treatment for shigellosis for years, and has been used routinely to treat children, again without reports of arthropathy. Extensive use of the newer quinolones in children during the last few years has also confirmed the remarkable safety of these antibiotics, including the lack of reported arthropathies. There is, thus, no reason to consider the potential toxicity of newer quinolones to be any greater than that of nalidixic acid.

Ciprofloxacin is the most appropriate drug in place of nalidixic acid which leads to rapid development of resistance.

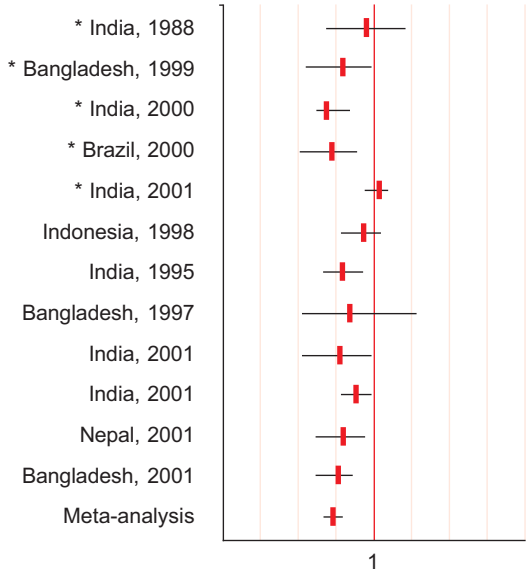
- **Cost** – The cost of treatment with ciprofloxacin was an issue a few years ago when the drug was still under patent. However, the cost of ciprofloxacin has significantly dropped since the patent expired and the drug became available as a generic. In fact, the cost of treatment with ciprofloxacin is now about one third of the cost of treatment with nalidixic acid. For example, a 5-day course of treatment with nalidixic acid for a 15 kg child costs about US$0.34, while treatment of the same child for three days with ciprofloxacin costs about US$0.10.

Based on its safety, efficacy and reduced cost, ciprofloxacin is now the recommended first-line antibiotic for shigellosis. The use of nalidixic acid should be discontinued, even in areas where it is still effective against *Shigella*.

Zinc in the management of diarrhoea [11-15]

A review of all clinical trials evaluating the impact of zinc supplementation on the clinical course of acute diarrhoea was performed during a meeting held in New Delhi in May 2001. This review concluded that zinc supplementation given during an episode of acute diarrhoea reduced the duration and severity of the episode. Before that, a meta-analysis of studies evaluating the impact of zinc supplementation to prevent diarrhoea had concluded that zinc supplementation given for 10-14 days lowered the incidence of diarrhoea in the following 2-3 months. It was also estimated that the inclusion of zinc in the management of diarrhoea could prevent 300 000 children from dying each year. Based on these findings, WHO and UNICEF have issued a joint statement on the clinical management of diarrhoea that recommends that, along with increased fluids and continued feeding, all diarrhoeic children be given 20 mg per day of zinc supplementation for 10-14 days (10 mg per day for infants below six months of age).

Effect of zinc supplementation on duration of acute diarrhoea/time to recovery



* Difference in mean and 95% CI
Relative Hazards and 95% CI

A recently published study analyzes the cost-effectiveness of zinc as adjunct therapy for acute childhood diarrhoea in developing countries. In this study, using data collected in Tanzania, the mean Cost-Effectiveness Ratio (CER)

was found to be reduced by more than one third when ORS was combined with zinc for the treatment of all children with acute diarrhoea, from US$113 to US$73 per Disability Adjusted Life Year (DALY) averted.

Pilot studies have been conducted recently in a number of countries (Brazil, Egypt, Ethiopia, India, Mali, Pakistan and the Philippines) prior to the implementation of large community-based studies to introduce zinc in the management of acute diarrhoea. Preliminary results of these studies show two interesting observations: (i) ORS use rates increase, and (ii) antidiarrhoeals and antimicrobial use rates significantly decrease when zinc is prescribed with ORS solution (O. Fontaine, personal communication). Large community-based studies are about to start in three countries (India, Mali and Pakistan) to investigate further these findings.

Along with increased fluids and continued feeding, all children with diarrhoea should be given zinc supplementation for 10-14 days.

SUMMARY RECOMMENDATIONS

Low osmolarity ORS	• Countries should now use and manufacture the low osmolarity ORS for all children with diarrhoea but keep the same instructions for the preparation of the solution.
Treatment of bloody diarrhoea	• Ciprofloxacin is the most appropriate drug in place of nalidixic acid which leads to rapid development of resistance. Ciprofloxacin is given in a dose of 15 mg/kg two times per day for three days by mouth.
Zinc in the management of diarrhoea	• Along with increased fluids and continued feeding, all children with diarrhoea should be given zinc supplementation for 10-14 days.

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Fever/Malaria

Malaria case management has been greatly affected by the emergence and spread of chloroquine resistance. This was reported from almost all malaria endemic countries of Africa. Sulfadoxine-pyrimethamine (SP) was, until recently, seen as the obvious successor to chloroquine. However, resistance to SP is developing quickly even with its current use, thus reducing the useful therapeutic life of this drug. Chloroquine and SP were the first-line and second-line antimalarial drugs recommended in the IMCI guidelines of many countries.

Antimalarials for treatment of malaria

TECHNICAL BASIS

Artemisinin-based combination therapies have been shown to improve treatment efficacy. The advantages of artemisinin-based combination therapy (ACT) relate to the unique properties and mode of action of the artemisinin component, which include rapid substantial reduction of the parasite biomass and rapid resolution of clinical symptoms. Due to the very short half-life of artemisinin derivatives, their use as monotherapy requires a multiple dose seven-day regimen. Combination of one of these drugs with a longer half-life "partner" antimalarial drug allows a reduction in the duration of artemisinin treatment, while at the same time enhancing efficacy and reducing the likelihood of resistance development to the partner drug. Artesunate used in combination therapy has been shown to delay the development of resistance to its partner drug (mefloquine) in low malaria transmission areas in South-East Asia.

Based on available safety and efficacy data, the following therapeutic options are available and have potential for deployment (in prioritized order) if costs are not an issue:

- artemether-lumefantrine (CoartemTM)
- artesunate (3 days) plus amodiaquine
- artesunate (3 days) plus SP in areas where SP efficacy remains high
- SP plus amodiaquine in areas where efficacy of both amodiaquine and SP remain high. This is mainly limited to countries in West Africa.

These combination options need continued documentation of safety and efficacy as part of any potential implementation process, especially among very young children, pregnant women, and breastfeeding mothers and their babies.

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Ear infections

Chronic suppurative otitis media

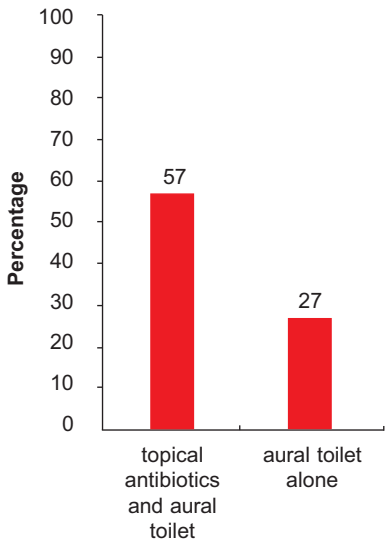
TECHNICAL BASIS

A systematic review of randomized controlled trials (RCTs) published in the Cochrane Library and further RCT retrieved by the staff of the ENT Disorders Review Group based in Oxford, UK has attempted to summarize the results of best available evidence on the management of chronic suppurative otitis media (1).

From the Cochrane review, aural toilet combined with antimicrobial treatment is more effective than aural toilet alone (OR 0.31, 95% CI 0.23-0.43). The studies reviewed used various topical and oral antibiotics. Oral antibiotics were found to be better than aural toilet alone. A trial comparing various oral antibiotics with aural toilet alone reported a higher otorrhoea resolution rate in the antibiotic treated group (OR 0.35, 95% CI 0.14-0.87). There was no clear indication of which oral antibiotic was superior.

Topical antibiotics were found to be better than aural toilet alone. The addition of topical antibiotics to aural toilet was associated with a 57% rate of otorrhoea resolution, compared to 27% with aural toilet alone (OR 0.31, 95% CI 0.19-0.49). The topical antibiotics used were framycetin, gramicidin, ciprofloxacin, tobramycin, gentamicin and chloramphenicol.

Topical antibiotics and aural toilet versus aural toilet alone in otorrhoea resolution



Additionally topical antibiotics were found to be better than systemic antibiotics. The Cochrane review found that topical antibiotics were more effective than systemic antibiotics in resolving otorrhoea and eradicating middle ear bacteria (OR 0.46, 95% CI 0.30-0.68). Again various topical antibiotics were used. In general, topical quinolones were found to be better than topical non-quinolones. The Cochrane review showed that in 5 studies topical ofloxacin or ciprofloxacin was more effective than intramuscular gentamicin, topical gentamicin, tobramycin or neomycin-polymyxin in resolving otorrhoea (OR 0.36, 95% CI 0.22-0.59) and in eradicating bacteria (OR 0.34, 95% CI 0.20-0.57). Five additional RCTs have shown similar results. Finally combined topical and systemic antibiotics are no better than topical antibiotics alone. The safety of topical quinolones in children has been well documented without good evidence of a risk of ototoxicity. The concentrations of these drugs are highest in otorrhoea, the main route of exit from the ear, and lowest in the serum (1).

Daily instillation of topical antiseptics or topical antibiotics after meticulous aural toilet for at least two weeks is the most cost-effective treatment for the short-term resolution of otorrhoea. Intravenous antibiotics, particularly the anti-pseudomonal drugs, are highly effective but too expensive (1).

Chronic ear infection should be treated with topical quinolone ear drops for at least two weeks in addition to dry ear wicking.

Oral amoxicillin is a better choice for the management of acute ear infection in countries where antimicrobial resistance to cotrimoxazole is high.

Acute otitis media

TECHNICAL BASIS

A recent consultative meeting recommended the use of oral amoxicillin as the better choice for the management of acute ear infection in countries where antimicrobial resistance to cotrimoxazole is high. Even though antibiotics may provide a small benefit for acute ear infection in children as most resolve spontaneously, oral amoxicillin plays an important role in reducing the risk of mastoiditis in populations where it is more common (2,3).

SUMMARY RECOMMENDATIONS

CHRONIC EAR INFECTION	• Chronic ear infection should be treated with topical quinolone ear drops for at least two weeks in addition to dry ear wicking
ACUTE EAR INFECTION	• Oral amoxicillin is a better choice for the management of suppurative otitis media in countries where antimicrobial resistance to cotrimoxazole is high

References for ear infections

1. *Chronic suppurative otitis media: Burden of illness and management options*. Geneva, World Health Organization, 2004.

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Infant feeding

Exclusive breastfeeding

TECHNICAL BASIS

A systematic review of current scientific evidence on the optimal duration of exclusive breastfeeding identified and summarized studies comparing exclusive breastfeeding for four to six months, versus six months, in terms of growth, infant iron status, morbidity, atopic disease, motor development, postpartum weight loss and amenorrhoea. The evidence did not suggest an adverse effect of exclusive breastfeeding for six months on infant growth on an overall population basis. The available data suggested that exclusive breastfeeding for six months has a protective effect against gastrointestinal infection in developing and developed countries, and confers an advantage to the mother in prolonging the duration of lactational amenorrhoea (1).

In 2001, an expert consultation on the optimal duration of exclusive breastfeeding, considering the results of the systematic review, concluded that exclusive breastfeeding for six months confers several benefits to the infant and mother (2). In 2002, the World Health Assembly endorsed the recommendation of exclusive breastfeeding for six months with the introduction of complementary foods and continued breastfeeding thereafter (3).

Studies that assessed the effect of not breastfeeding on the risk of death due to infectious diseases in Brazil, The Gambia, Ghana, Pakistan, the Philippines and Senegal were analysed. Protection provided by breast milk declined steadily with age during infancy [pooled odds ratios: 5.8 (95% CI 3.4-9.8) for infants <2 months of age, 4.1 (95% CI 2.7-6.4) for 2-3 months of age, 2.6 (95% CI 1.6-3.9) for 4-5 months of age, 1.8 (95% CI 1.2-2.8) for 6-8 months of age, and 1.4 (95% CI 0.8-2.6) for 9-11 months of age]. In the first six months of life, protection against diarrhoea was substantially greater (odds ratio 6.1) than against deaths due to acute respiratory infections (odds ratio 1.4) (4).

A research study in India included eight communities randomized to either receive an intervention in training/counselling on breastfeeding or no intervention. 1115 infants were enrolled, 552 in the intervention and 473 in control communities. At three months, exclusive breastfeeding rates were 79% in the intervention and 48% in control communities (OR 4.0, 95% CI 3.01-5.38, p<0·0001). The 7-day diarrhoea prevalence was lower in the intervention than in the control communities at three months (0.64, 95% CI 0.44-0.95, p=0.028) and six months (0.85, 95% CI 0.72-0.99, p=0.04). The mean weights and lengths, and the proportion with weight-for-height or height for-age *Z* scores of 2 or less, at age three months and six months did not differ much between groups (5).

The Promotion of Breastfeeding Intervention Trial (PROBIT) was a cluster randomized trial including 31 maternity hospitals and polyclinics in the Republic of Belarus and a total of 17 046 mother-infant pairs, 16 491 (96.7%) of which completed the entire 12 months of follow-up. Sites were randomly assigned to receive an experimental intervention (n=16) modelled on the Baby-Friendly Hospital Initiative or a control intervention (n=15) of continuing usual infant feeding practices and policies. Infants from the intervention sites were significantly more likely than control infants to be breastfed to any degree at 12 months (19.7% versus 11.4%; adjusted OR 0.47 95% CI 0.32-0.69), were more likely to be exclusively breastfed at three months (43.3% versus 6.4%; p<0.001) and at six months (7.9% versus 0.6%; p=0.01), and had a significant reduction in the risk of one or more gastrointestinal tract infections (9.1% versus 13.2%; adjusted OR 0.60 95% CI 0.40-0.91) and of atopic eczema (3.3% versus 6.3%; adjusted OR 0.54 95% CI 0.31-0.95), but no significant reduction in respiratory tract infection (intervention group, 39.2%; control group, 39.4%; adjusted OR 0.87 95% CI 0.59-1.28) (6).

A prospective observational study was conducted on a birth cohort of 1677 infants who were born in slum areas of Dhaka in Bangladesh and followed from birth to 12 months of age. Compared with exclusive breastfeeding in the first few months of life, partial or no breastfeeding was associated with a 2.23-fold higher risk of infant deaths resulting from all causes and 2.40 and 3.94-fold higher risk of deaths attributable to ARI and diarrhoea, respectively (7).

Exclusive breastfeeding for six months should be strongly promoted in all countries.

In Mexico, the body weight and length, feeding mode and morbidity of 170 healthy infants were assessed at 15-day intervals from birth to six months. At six months, the weight of breastfed infants reached to the weight of NCHS standards, while the weight of infants fed formula fell to around minus 1 NCHS-Z-score for weight and length. The cumulative six-month weight increments were negatively related to the number of episodes of diarrhoea, and positively to the duration of lactation (p=0.03, R^2 5 0.17). The six-month length gain was negatively related to infections but not to duration of lactation (p=0.004, R^2 5 0.19). Never-ill infants attained a better weight (p=0.04) and length (p=0.02) than infants who suffered one or more episodes of diarrhoea. Weight increments of 15 days were positively related to breastfeeding and negatively to introduction of solids (8).

A randomized controlled trial in Honduras found that introducing fluids or foods into the infant's diet from four to six months of age did not benefit infant growth or energy intake (9).

Complementary feeding

TECHNICAL BASIS

A global consultation on complementary feeding (2001) has resulted in updated guidelines (10). Ten guiding principles for complementary feeding of the breastfed child were summarized in a 2003 publication (11). Where countries are adapting the generic IMCI guidelines for complementary feeding after six months of age for the first time, these standards may be used to guide the adaptation. Evidence for some of these guiding principles is described below.

Following practising exclusive breastfeeding from birth to six months of age, complementary foods should be introduced at 6 months of age (180 days) while continuing to breastfeed (10,11). The guiding principles recommend continuing breastfeeding for up to two years or beyond. A cohort of 443 Senegalese children recruited from dispensaries at two months of age were visited in their homes at six-month intervals when they were 1.5 to 3 years of age. The mean duration of breastfeeding was 24.1 months. Height-for-age at the age of three years was negatively associated with age at weaning ($p<0.01$), but this association disappeared after adjustment for height-for-age in infancy. Length increments were significantly greater in both the second and third years of life in children breast-fed for longer durations ($p<0.05$) and tended to be greater in breast-fed than in weaned children in the second year of life ($p=0.05$). Growth in weight did not differ significantly according to breastfeeding (12).

In terms of the amount of complementary food needed, meal frequency and energy density, the latest estimated energy requirements for complementary foods, endorsed by a FAO/WHO/UNU consultation, are 200 kcal/day for infants aged 6-8 months, 300 kcal/day for infants aged 9-11 months, and 550 kcal/day for children aged 12-23 months (13). An infant receiving foods with energy density of 0.8 kcal/g and average breast milk intake will need 2-3 meals at 6-8 months, 3-4 meals at 9-23 months of age and additional nutritious snacks may be offered 1-2 a day as desired (13).

Recommended meal frequencies on a population basis, assuming a diet with energy density of 0.8 kcal per gram or above and low breast-milk intake, are: 2-3 meals for infants aged 6-8 months, 3-4 meals for infants aged 9-23 months and additional nutritious snacks may be offered 1-2 times a day as desired. Therefore the current IMCI guidelines for complementary feeding remain valid in developing countries.

Management of severe malnutrition where referral is not possible

If a child is classified as having severe malnutrition and referral is not possible, the guidelines should be adapted to include management at first-level facilities.

TECHNICAL BASIS

During the initial phase, if the child has a poor appetite, a modified milk diet is given. This is made of dried skimmed milk (DSM) sugar and oil. Start by mixing 25 g of dried skimmed milk, 70 g of sugar, 35 g of cereal flour and 27 g of oil and some water. Boil for 5-7 minutes. Allow to cool and then add 20 ml of WHO mineral vitamin mix for severe malnutrition and mix again. Make up the volume to 1000 ml of water. Feed for a few days 11 ml/kg every 2 hours.

Once appetite is restored, a diet with 80 g of dried skimmed milk, 50 g of sugar and 60 g of oil is prepared. Add water up to 1000 ml and 20 ml of WHO mineral and vitamin solution. Increase progressively the feeds up to 200 ml/kg/day given in 6 feeds (30 ml/kg every 4 hours adjusted to the child's appetite) (14,15).

Where a child is classified as having severe malnutrition and referral is not possible, the IMCI guidelines should be adapted to include management at first-level facilities.

HIV and infant feeding

TECHNICAL BASIS

A WHO Technical Consultation in October 2000 (16) reviewed the data on prevention of mother-to-child transmission of HIV and their policy implications, including implications on HIV and infant feeding. The recommendations from this consultation and a review of the evidence on transmission through breastfeeding (17) have formed the basis upon which further guidance related to HIV and infant feeding has been developed (18).

Mother-to-child transmission of HIV can occur through breastfeeding. A clinical trial in Nairobi (2000) (19), randomly allocated HIV-infected pregnant women to either breastfeeding (n=212) or artificial feeding (n=213). Compliance with the assigned feeding modality was 96% in the breastfeeding arm and 70% in the formula arm. Median duration of breastfeeding was 17 months though it is not clear if exclusive breastfeeding in early months occurred or not. The cumulative probability of HIV infection at 24 months of age in the breastfeeding and formula-feeding arms was, respectively, 36.7% and 20.5%. The estimated absolute rate of transmission through breastfeeding was therefore 16.2% at two years follow-up and in the breastfeeding arm, 44.1% of all mother-to-child transmission was attributable to breastfeeding.

HIV can be transmitted through breast milk at any point during lactation. There is strong evidence that the longer the duration of breastfeeding the greater the risk of transmission. There is no evidence to suggest that avoidance of colostrum would reduce the risk of breastfeeding transmission to the infant (17).

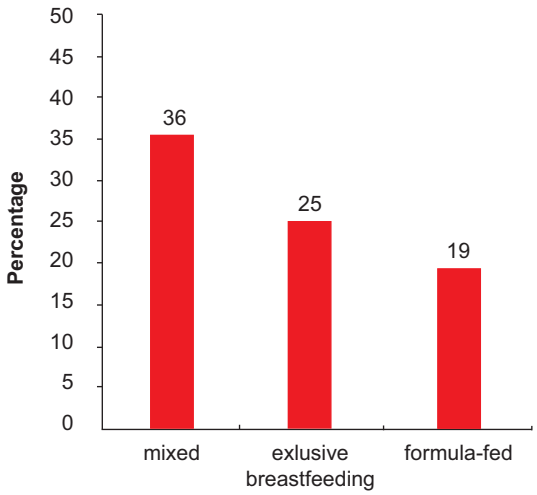
A recent meta-analysis in sub-Saharan Africa (17) of a large number of individual data on breastfeeding and post-natal transmission of HIV from randomized controlled trials of peripartum interventions included 4343 children that were breastfed and HIV-tested. The overall rate of transmission was 24%. Of the 993 infected children, the infection had occurred early in 314 (31.4%), late in 225 (23.1%), and at an unknown time in 454 (45.4%). The mean duration of breastfeeding was nearly seven months, and the median, four months. The risk of late postnatal transmission continued throughout the breastfeeding period and was more or less constant over time. The cumulative probability of becoming HIV-infected after age four weeks was 1.6% at three months, 4.2% at six months, 7.0% at 12 months, and 9.3% (95% CI 3.8-14.8) at 18 months. The contribution of late postnatal transmission (after four weeks) to overall transmission was estimated to be at least 23%, but possibly as much as 42%.

The risk of transmission through breastfeeding is probably strongly related to RNA levels in the milk, but the degree of risk has not yet been adequately determined. Low maternal CD4 counts in plasma close to the time of delivery and mastitis have also been associated with an increased transmission risk (17).

In a study in Durban, South Africa (20), 551 HIV-infected women were counselled and chose whether to breastfeed or formula-feed. Those who chose to breastfeed were encouraged to do so exclusively for three to six months. A total of 157 formula-fed from birth and never breastfed, 118 breastfed exclusively for three months or more, and 276 practised mixed breastfeeding. The three groups did not differ in any of the significant risk factors for transmission, and at birth the rate of infection in their infants had been similar at about 7%. Infants who received both breast milk and other feeds were significantly more likely to be infected by 15 months of age (36%) than those who had been exclusively breastfed (25%) or formula-fed (19%). Exclusive breastfeeding carried a significantly lower risk of HIV infection than mixed breastfeeding (Hazard ratio 0.56, 95% CI 0.32-0.98) and was similar in this respect to never breastfeeding (Hazard ratio 1.19, 95% CI 0.63-2.22).

A recent randomized trial of postpartum vitamin A supplementation in Zimbabwe (21), that additionally provided education and counselling on infant feeding and HIV, included 4495 mothers who tested HIV-positive and with post-natal transmission (PNT) of 12.1%. Compared with exclusive breastfeeding, early mixed breastfeeding was associated with a 4.03 (95% CI 0.98-16.61), 3.79 (95% CI 1.40-10.29), and 2.60 (95% CI 1.21-5.55) greater risk of PNT at 6, 12 and 18 months, respectively. Predominant breastfeeding was associated with a 2.63 (95% CI 0.59-11.67), 2.69 (95% CI 0.95-7.63) and 1.61 (95% CI 0.72-3.64) trend towards greater PNT risk at 6, 12, and 18 months, compared with exclusive breastfeeding. The study concluded that exclusive breastfeeding might substantially reduce breastfeeding-associated HIV transmission when compared with mixed feeding.

HIV infected at 15 months by feeding type: Durban



No study has so far assessed the feasibility, mortality and morbidity risks of early cessation, but early and complete cessation reduces exposure and hence the risk of transmission through breastfeeding without eliminating the risk as the infant has been exposed for the first few months of life (17).

The review (17) reaffirmed the recommendation from the Technical Consultation (16), "when replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV-infected mothers is recommended. Otherwise, exclusive breastfeeding is recommended during the first months of life". All HIV-infected mothers should receive counselling, which includes provision of general information about the risks and benefits of various infant-feeding options, including risks associated with no breastfeeding in their circumstances (see breastfeeding section) and specific guidance in selecting the option most likely to be suitable for their situations.

If a young child is infected with HIV, or if clinical signs according to recommended clinical staging indicate that the infant is positive, and the mother is still breastfeeding, she should continue according to the recommendations for the general population.

If there is reason to believe that the mother may be HIV-infected, she should be referred for HIV testing and counselling. If she tests positive and is still breastfeeding, and the child is negative or the status unknown, a counsellor trained in HIV and infant-feeding, for example through the WHO/UNICEF/UNAIDS course (22), should provide information and guidance on the various infant feeding options and support the mother in her choice.

Guiding principles for feeding the non-breastfed child from 6 to 24 months are similar to those for the breastfed child when another milk source is available, but require more attention when this is not the case (23).

The potential role of infant and/or maternal ARV prophylaxis in preventing postnatal transmission of HIV is still being investigated. Until further evidence is available on this subject the current recommendations on HIV and infant feeding remain unchanged in women receiving ARV treatment (17).

In areas where HIV is a public health problem all women should be encouraged to receive HIV testing and counselling. If a woman is HIV-infected and replacement feeding is acceptable, feasible, affordable, sustainable and safe for her and her infant, avoidance of all breastfeeding is recommended. Otherwise, exclusive breastfeeding is recommended during the first months of life.

SUMMARY RECOMMENDATIONS

Exclusive breastfeeding up to 6 months (180 days) of age	• Breastfeed as often as the child wants, day and night, at least 8 times in 24 hours. • Breastfeed when the child shows signs of hunger: beginning to fuss, sucking fingers, or moving the lips. • Do not give other foods or fluids. • Only if the child is older than 4 months, and appears hungry after breastfeeding, and is not gaining weight adequately, add complementary foods (listed under 6 months up to 23 months). Give 1 or 2 tablespoons of these foods 1 or 2 times per day after breastfeeding.
Complementary feeding 6 months up to 23 months	• Breastfeed as often as the child wants. • Give adequate servings of complementary foods: 3 times per day if breastfed, with 1-2 nutritious snacks, as desired, from 9 to 23 months. • Give foods 5 times per day if not breastfed with 1 or 2 cups of milk. • Give small chewable items to eat with fingers. Let the child try to feed itself, but provide help.
Management of severe malnutrition where referral is not possible	• Where a child is classified as having severe malnutrition and referral is not possible, the IMCI guidelines should be adapted to include management at first-level facilities.
HIV and infant feeding	• In areas where HIV is a public health problem all women should be encouraged to receive HIV testing and counselling. • If a mother is HIV-infected and replacement feeding is acceptable, feasible, affordable, sustainable and safe for her and her infant, avoidance of all breastfeeding is recommended. Otherwise, exclusive breastfeeding is recommended during the first months of life. • The child of an HIV-infected mother who is not being breastfed should receive complementary foods as recommended above.

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Helminth infestations

Management of helminth infestations in children below 24 months

TECHNICAL BASIS

Data from studies in Africa, Asia and Latin America, that included children below the age of two years, was provided to an informal consultation (1). Albendazole was the drug chosen for the treatment in eight studies and mebendazole in two studies. In a recent study in Tanzania with children aged 6 to 59 months (212 were less than 24 months), mebendazole was the drug of treatment and parasitological, nutritional and cognitive variables were assessed. Mebendazole had a positive effect on motor and language development and comparison between the treated and placebo groups revealed no difference in the occurrence of adverse effects (fever, cough, diarrhoea, dysentery and acute respiratory illness) one week after intervention.

A recent consultation addressing the use of albendazole/mebendazole in children under 24 months stated that there was paucity of safety data regarding the use of these drugs in infants under 12 months.

A 500 mg dose of mebendazole is recommended for all children with anaemia age 12 months or older who live in an area with hookworm (*Ancylostoma* and *Necator*) or whipworm (*Trichuris*) and who have not been treated with mebendazole in the last six months. Mebendazole is also a very effective treatment of infection by roundworm (*Ascaris*), which contributes to malnutrition. Mebendazole is given without microscopic examination of the stool. As a general rule, these infections are transmitted in all tropical and sub-tropical areas. However, for infants below 12 months, such cases should be referred and managed on a case-by-case basis.

As a consequence of (i) the great distribution of the parasites; (ii) the safety of the drug; (iii) the low cost of the treatment (<0.017$ for one dose of mebendazole or albendazole); (iv) the relative high cost of diagnosis (need of microscope, lab material and training) in endemic areas, children who have not been dewormed in the previous six months should be offered deworming irrespective of the possibility of confirming their infectious status (2).

Albendazole and mebendazole can be safely used in children 12 months or older.

HELMINTH INFESTATIONS in children below 24 months	• Albendazole and mebendazole can be safely used in children 12 months or older.	SUMMARY RECOMMENDATION

References for helminth infestations

1. *Report of the WHO Informal Consultation on the use of praziquantel during pregnancy/lactation and albendazole/mebendazole in children under 24 months.* Geneva World Health Organization, 8-9 April, 2002. (WHO/CDS/CPE/PVC/2002.4).

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Suggested process for further adaptations of IMCI

The technical updates presented may be introduced to countries that are adapting IMCI for the first time or have already adapted and are currently implementing IMCI. In those countries adapting IMCI for the first time, this document may be used as a technical resource in addition to country specific data. For countries currently implementing IMCI, the summary recommendations may be introduced into existing IMCI or ARI and CDD guidelines at opportune times during IMCI review or re-planning meetings, when printing new materials or conducting re-adaptation meetings to include HIV, dengue or new malaria policy. The new evidence may be presented by medical officers from WHO or other UN or partner agencies. It is particularly important that the technical basis of the proposed recommendations are discussed and consensus is achieved. The technical update document may be used to develop a presentation with the key points highlighted.

Adaptations of these technical updates require extensive and multiple changes throughout the charts, modules, facilitator guides, and other training materials. These changes go well beyond filling in the blanks. The adaptation changes should also be made in pre-service training materials such as the model IMCI chapters, model textbooks, student assessment tools, etc.

For example, a change on the *Treat the child* chart could require changes in: the wall chart, chart booklet, throughout the text and exercises in the module, answer sheets for exercises, drills and other exercises in the facilitator's guide, and supply lists in the facilitator and director guides.

Policy changes

With the current technical updates, it is important to address availability of the recommended medicines, including low osmolarity ORS, ciprofloxacin, ACT combination antimalarials and topical quinolone ear drops. The adaptation changes should include change in policy of these medicines at first-level facilities.

To translate the new technical updates into policy changes, several steps are suggested:

- Initial discussions among senior decision-makers. This could be in a form of a seminar or a briefing. It should consist of reviewing the nature and scope of the technical updates and how they relate to the national country adaptations of IMCI.
- Endorsement of the technical updates and development/re-adaptation of the national IMCI policy accordingly.
- Setting up a small working group that takes the task of making further adaptations and dissemination.

- Logistical issues - Some new drugs and supplies (eg. zinc, low osmolarity ORS, ciprofloxacin, topical quinolones) may need to be added to the essential drug list and made available at all levels of health facilities.
- Role of IMCI programme managers - staff responsible for IMCI or ARI and CDD programmes in governments or partner organizations need to ensure that issues of logistics, costs, training and monitoring related to the new IMCI recommendations are discussed and appropriate action taken.

Developing re-adapted IMCI materials

In countries where there has been an initial adaptation of IMCI, further adaptation with the current technical updates should be organized taking advantage of any forthcoming opportunities:

A) NATIONAL IMCI REVIEW AND REPLANNING

If there is a plan to do a national IMCI review and re- planning meeting, this may be the best opportunity to introduce the current technical updates.

B) PRINTING NEW IMCI MATERIALS

New IMCI materials may need to be printed because they are out of stock or there are other reasons to print new IMCI materials. In this case, the opportunity should be used to update the materials.

C) INCLUSION OF NEW AREAS

Re-adaptation may be required for other reasons. A common reason for producing new materials may be that there is a change in the national policy on areas such as:

- IMCI HIV adaptation
- Adding first week of life
- Adaptation to include dengue fever
- Adaptation to incorporate the new ACT policy for anti-malarials, etc.

D) PLACING STICKERS ON EXISTING IMCI MATERIALS

There may be IMCI materials, including participant modules, chart booklets, facilitator guidelines and wall charts, already printed that do not have the new recommendations. As the changes are minor, it is suggested that during facilitators' meetings prior to first-level health worker courses, the changes be included in the existing materials by placing a sticker with the new recommendation over the previous text. This would require pre-planning and preparation of stickers with text.

E) IMCI PRE-SERVICE EDUCATION

Medical and nursing academic institutions will need to be aware of the new recommendations so that changes can be made to IMCI pre-service education training courses and teaching materials. Orientation of academic staff in the participating institutions in-country will assist this process.

F) OTHER OPPORTUNITIES

Countries may have to look for other opportunities to make the technical updates if necessary. For example, in some countries, there are computer-based programmes that could be used to make technical updates in the national IMCI guidelines.

Informing health workers about the IMCI technical updates

REFRESHER TRAINING COURSES

The information on the IMCI technical updates may be made available to health workers in different ways. If the technical updates are being introduced along with other "refresher" IMCI courses such as the HIV complementary course, then health workers should be trained in IMCI technical updates at the same time.

However, some countries may not have plans to do "refresher courses" and in this case several possible activities are suggested to update health workers who are implementing IMCI.

ORIENTATION MEETING

An orientation meeting should be conducted with senior ministry of health staff responsible for the child health programmes including IMCI, senior paediatric staff from academic and referral institutions and representatives of the paediatric associations and nongovernmental organizations. Again there must be a presentation of new recommendations, discussion and consensus achieved.

PRINTED INFORMATION

A flyer could be prepared by the regional office (with country office support if available) highlighting the new recommendations and then distributed to countries, particularly to government departments or partners responsible for IMCI or ARI and CDD programmes and senior paediatric staff.

Once the recommendations have been accepted in countries further dissemination may be achieved through:

- **Professional associations**
  Many countries have professional associations for paediatricians and academics responsible for pre-service education. These individuals, if provided with the appropriate information, are in a strong position to disseminate the new recommendations to all levels of health workers.

- **IMCI supervisory visits**
  Orientation in the new recommendations could be provided to senior health workers at provincial or district level during IMCI supervisory visits. Information could then be transmitted to previously IMCI-trained health workers during on-the-job training at first-level health facilities.

Adapting IMCI charts

Examples are given below to show where changes could be made in IMCI adaptations in countries. The change resulting from the recommendations in this document are shown in **red bold**.

EXAMPLE 1. Adaptation for cough or difficulty breathing

• Any general danger sign or • Chest indrawing or • Stridor in calm child	SEVERE PNEUMONIA OR VERY SEVERE DISEASE	• Give first dose of an appropriate antibiotic • Refer URGENTLY to hospital
• Fast breathing	PNEUMONIA	• **Give an appropriate antibiotic for 3 days** • Soothe the throat and relieve the cough with a safe remedy • Advise the mother when to return immediately • Follow-up in 2 days
No signs of pneumonia or very severe disease	NO PNEUMONIA: COUGH OR COLD	• If coughing more than 30 days, refer for assessment • Soothe the throat and relieve the cough with a safe remedy • Advise the mother when to return immediately • Follow-up in 5 days if not improving

EXAMPLE 2. Adaptation for including wheezing (wheezing added in the cough or difficult breathing box) *

• Any general danger sign or • Chest indrawing or • Stridor in calm child • Wheeze	SEVERE PNEUMONIA with WHEEZING OR VERY SEVERE DISEASE	• Give first dose of an appropriate antibiotic • **Give a trial of rapid acting inhaled bronchodilator up to 3 cycles before classified as pneumonia** • Refer URGENTLY to hospital
• Fast breathing with or without wheezing **(after trial of rapid-acting inhaled bronchodilator, up to 3 cycles)**	PNEUMONIA with WHEEZING	• **Give an appropriate antibiotic for 3 days** • **Give an inhaled or oral bronchodilator for 5 days** • Soothe the throat and relieve the cough with a safe remedy • Advise the mother when to return immediately • If recurrent wheezing refer for assessment if not done • Follow-up in 2 days
• Wheezing **(before or after trial of rapid-acting inhaled bronchodilator, up to 3 cycles)**	NO PNEUMONIA: WHEEZING	• Give an inhaled or oral bronchodilator for 5 days • If recurrent wheezing refer for assessment if not done • Advise the mother when to return immediately • Follow-up in 2 days if not improving

*** Another version could be where examples 1 and 2 are combined.**

EXAMPLE 3. Adaptation for including low osmolarity ORS and zinc

Two of the following signs: • Lethargic or unconscious • Sunken eyes • Not able to drink or drinking poorly • Skin pinch goes back very slowly	SEVERE DEHYDRATION	• If child has no other severe classification: Give fluid for severe dehydration (Plan C) or If child also has another severe classification: Refer URGENTLY to hospital with mother giving frequent sips of ORS on the way. Advise the mother to continue breastfeeding • If child is 2 years or older and there is cholera in your area, give antibiotic for cholera
Two of the following signs: • Restless, irritable • Sunken eyes • Drinks eagerly, thirsty • Skin pinch goes back slowly	SOME DEHYDRATION	• **Give ORS, zinc supplements and food for some dehydration (Plan B).** • If child also has a severe classification: Refer URGENTLY to hospital with mother giving frequent sips of ORS on the way. Advise the mother to continue breastfeeding • Advise mother when to return immediately
Not enough signs to classify as some or severe dehydration	NO DEHYDRATION	• **Give fluid, zinc supplements and food to treat diarrhoea at home (Plan A)** • Advise mother when to return immediately

part 1 of 2

EXAMPLE 3. Adaptation for including low osmolarity ORS and zinc		
• Dehydration present	SEVERE PERSISTENT DIARRHOEA	• Treat dehydration before referral unless the child has another severe classification • Refer to hospital
• No dehydration	PERSISTENT DIARRHOEA	• Advise the mother on feeding a child who has PERSISTENT DIARRHOEA • **Give multivitamin and minerals (including zinc) for 14 days** • Follow-up in 5 days
• Blood in the stool	BLOOD IN STOOL	• Treat for 3 days with ciprofloxacin. Treat dehydration and give zinc • Follow-up in 2 days

part 2 of 2

EXAMPLE 4. Plan A: Treat diarrhoea at home

Counsel the mother on the 4 rules of home treatment:
Give Extra Fluid, **Give Zinc Supplements**, Continue Feeding, When to Return

1. GIVE EXTRA FLUID (as much as the child will take)

- TELL THE MOTHER:
  - Breastfeed frequently and for longer at each feed.
  - If the child is exclusively breastfed, give ORS or clean water in addition to breastmilk.
  - If the child is not exclusively breastfed, give one or more of the following: ORS solution, food-based fluids (such as soup, rice water, and yoghurt drinks), or clean water.

  It is especially important to give ORS at home when:
  - the child has been treated with Plan B or Plan C during this visit.
  - the child cannot return to a clinic if the diarrhoea gets worse.
- TEACH THE MOTHER HOW TO MIX AND GIVE ORS. GIVE THE MOTHER 2 PACKETS OF ORS TO USE AT HOME.
- SHOW THE MOTHER HOW MUCH FLUID TO GIVE IN ADDITION TO THE USUAL FLUID INTAKE:

  Up to 2 years — 50 to 100 ml after each loose stool and between them
  2 years or more — 100 to 200 ml after each loose stool and between them

  Tell the mother to:
  - Give frequent small sips from a cup.
  - If the child vomits, wait 10 minutes. Then continue, but more slowly.
  - Continue giving extra fluid until the diarrhoea stops.

2. GIVE ZINC SUPPLEMENTS

- **TELL THE MOTHER HOW MUCH ZINC TO GIVE:**

  Up to 6 months — 1/2 tablet per day for 14 days
  6 months or more — 1 tablet per day for 14 days
- **SHOW THE MOTHER HOW TO GIVE ZINC SUPPLEMENTS**

  Infants — dissolve the tablet in a small amount of expressed breastmilk, ORS or clean water, in a small cup or spoon
  Older children — tablets can be chewed or dissolved in a small amount of clean water in a cup or spoon
- **REMIND THE MOTHER TO GIVE THE ZINC SUPPLEMENTS FOR THE FULL 14 DAYS**

3. CONTINUE FEEDING

4. WHEN TO RETURN