

ESPGHAN Commentary

Preparation and Handling of Powdered Infant Formula: A Commentary by the ESPGHAN Committee on Nutrition

ESPGHAN Committee on Nutrition: *Carlo Agostoni, †Irene Axelsson, ‡Olivier Goulet, §Berthold Koletzko, ¶Kim F. Michaelsen, ||John W. L. Puntis, **Jacques Rigo, ††Raanan Shamir, ‡‡Hania Szajewska, §§Dominique Turck, ¶¶Yvan Vandenplas, and ||||Lawrence T. Weaver

*University of Milano, Milano, Italy; †University of Lund, Lund, Sweden; ‡Hôpital Necker Enfants-Malades, Paris, France; §Ludwig-Maximilians-University, Munich, Germany (committee chair); ¶The Royal Veterinary and Agricultural University, Frederiksberg, Denmark; ||University of Leeds, United Kingdom; **University of Liege, Liege, Belgium; ††Meyer Children's Hospital of Haifa, Israel; ‡‡The Medical University of Warsaw, Warsaw, Poland (committee secretary); §§University of Lille, Lille, France; ¶¶Free University of Brussels, Belgium (committee guest); ||||University of Glasgow, Glasgow, United Kingdom

ABSTRACT

Powdered infant formulae are not sterile and may contain pathogenic bacteria. In addition, milk products are excellent media for bacterial proliferation. Multiplication of *Enterobacter sakazakii* in prepared formula feeds can cause devastating sepsis, particularly in the first 2 months of life. In approximately 50 published case reports of severe infection, there are high rates of meningitis, brain abscesses and necrotizing enterocolitis, with an overall mortality from 33% to 80%. Breast feeding provides effective protection against infection, one of the many reasons why it deserves continued promotion and support. To minimize the risk of infection in infants not fully breastfed, recommendations are made for preparation and handling of powdered formulae for children younger than 2 months of age. In the home setting, powdered infant formulae should

be freshly prepared for each feed. Any milk remaining should be discarded rather than used in the following feed. Infant feeds should never be kept warm in bottle heaters or thermoses. In hospitals and other institutions written guidelines for preparation and handling of infant formulae should be established and their implementation monitored. If formula needs to be prepared in advance, it should be prepared on a daily basis and kept at 4°C or below. Manufacturers of infant formulae should make every effort to minimize bacterial contamination of powdered products.

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INTRODUCTION

Milk products are excellent media for multiplication of potentially pathogenic bacteria. Inadequate conditions of production, preparation and handling of formula milk may therefore pose a considerable risk to infants. A number of cases of serious and sometimes fatal *Enterobacter sakazakii* infection have been reported in formula

fed preterm and term infants. This has prompted the Committee on Nutrition to comment on the safe preparation and handling of infant formula.

Potentially Pathogenic Bacteria in Powdered Infant Formulae

Powdered infant formulae are not sterile but may contain coliform and other bacteria in low numbers. A study examining powdered infant formulae from 13 European countries found *Enterobacter spp.* in 53% of 141 samples (1). The gram-negative, rod-shaped bacteria *E. sakazakii* (previously called Yellow Pigmented *E. cloacae*), which appears to pose particularly serious risks,

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Address correspondence and reprint requests to Dr. Kim Fleischer Michaelsen, Department of Human Nutrition, The Royal Veterinary and Agricultural University, Rolighedsvej 30, DK-1958 Frederiksberg C, Denmark. (e-mail: kfm@kvl.dk).

was found in 14%. However, only low numbers of bacteria (<1 colony forming units [CFU]/g) were found, falling below the accepted maximal limit for powdered milk formulae of <3 CFU/g coliform organisms as defined by the Food and Agricultural Organization of the United Nations (FAO) (2). *E. sakazakii* was also frequently found in samples obtained from milk powder factories (21% positive) and household vacuum cleaners (31% positive) (3). The widespread occurrence of *E. sakazakii* may lead to frequent multiplication in prepared infant formula, which serves as a very good medium for bacterial multiplication, especially at temperatures of 25°C to 45°C (4).

Multiplication of *E. sakazakii* in prepared formula may yield an infectious dose that can cause severe invasive infections in preterm and term infants, particularly during the first weeks of life. Approximately 50 cases have been published, with very high rates of meningitis and brain abscesses, as well as necrotizing enterocolitis (1,4–11). Mortality of 33% to 80% has been reported in preterm infants affected by invasive *E. sakazakii* infection, with a high rate of neurologic impairment among the survivors (4,6,12–15).

Epidemic outbreaks of *E. sakazakii* infection have occurred on neonatal wards. Repeatedly, identical *E. sakazakii* strains have been isolated from the powdered milk used for feeding and the blood or cerebrospinal fluid of infected infants (5,6,8,9,16,17). *E. sakazakii* infection in infants has also resulted from contaminated utensils used for feed preparation, such as blenders and spoons, as well as prolonged storage of feed in bottle warmers that effectively promote bacterial multiplication (7,18,19).

The risk of infection with *E. sakazakii* appears to be particularly high in preterm and low birthweight infants, in term infants during the first one to two months of life and in children with impaired immune defenses (14). For these at-risk groups in particular, the conditions of production, preparation and handling of infant formulae must be such that the content of potentially pathogenic bacteria is kept to a minimum. *E. sakazakii* is relatively resistant to heat so that inactivation in infant formula will occur only at or higher than 60°C (4,20). Heating of prepared milk to 80°C to 90°C kills most microorganisms (21) but may detract from its nutritional value and therefore can not be recommended.

Bacteria rapidly multiply in milk kept at or above room temperature. Therefore, it is recommended that feeds prepared from both powdered and liquid formulae should not be kept at room temperature for more than 4 hours (22). *Enterobacter spp.* cultivated from infant formulae did not grow at temperatures below 5.5°C but began to multiply at temperatures between 5.5°C and 8°C (4). Average generation times were 5 hours at 10°C and only 40 minutes at 23°C (4). On a practical level, it may take a long time for formula prepared with hot water to cool down after being placed in a refrigerator. An additional concern is that refrigerators opened frequently

(for example, in busy hospital wards) may have temperatures considerably higher than 4°C.

The FAO and WHO recently convened an expert meeting on *E. sakazakii* and other microorganisms in powdered infant formulae (23). One of their recommendations was that whenever possible, sterile liquid formula or reconstituted powder formula that has undergone an effective decontamination step (such as mixing with boiled water or heating) should be used for high-risk infants. The ESPGHAN Committee on Nutrition disagrees with the use of boiling water and of heating of reconstituted formula to temperatures close to the boiling point because of possible adverse effects on nutrients such as vitamins.

In maternity units where more mature infants are looked after for short periods of time, liquid formulae appear to be a suitable alternative to powder formulae to reduce the risk of milk-borne infections. However, even liquid formulae may pose infectious risks if handling after opening is not appropriate. The use of liquid formula in small preterm infants is still controversial, and a more detailed evaluation of the nutritional and safety aspects of current formulations appears desirable. For example, depending on the degree and conditions of heat treatment, the formation of Maillard reaction products may reduce the biologic value of the nitrogen source, and with very extensive heat treatment the bioavailability of micronutrients such as copper may also be markedly reduced (24,25). Further disadvantages of liquid infant formulae include greater expense and more limited scope for modifying feed density.

If milk preparation is in a central facility and in accordance with strict criteria including immediate cooling and storage below 4°C, the Committee finds it reasonable that powdered infant formula is only prepared once a day. Even in these circumstances infant formula should not be used more than 30 hours after reconstitution.

In the home setting it is unlikely that similarly strict criteria can be applied when making feeds. For this reason, the Committee recommends that powdered infant formula should be prepared fresh for each feed during the first 2 months of life, when risk from severe infection with *E. Sakazakii* is at its highest (14). For convenience, preparation of feeds during the night and when away from home can be done with warm water kept in a thermos at feeding temperature. The importance of thorough cleaning of bottles and teats between feeds should be emphasized to parents.

Recommendations

Breast feeding provides effective protection against infection, which is one of many reasons why it deserves continued promotion and support. For infants that are not fully breastfed the Committee makes the following recommendations on preparation and handling of infant for-

mulae during the first 2 months of life, when the risk of milk-borne infection appears to be at its highest. We emphasize that these recommendations, although based on our current best knowledge, do not represent evidence-based guidelines owing to the limitations of available information.

Home Settings

- If powdered infant formulae are used they should be prepared fresh for each meal.
- Remnants of feed should be discarded and not used as part of the following feed.
- Infant formula should never be kept warm in bottle heaters or thermoses. As an alternative, warm water may be kept in a thermos and mixed with powdered formula before feeding.

Institutional Settings

- Written guidelines for preparation and handling of infant formula should be established for hospitals and other institutions, and their implementation should be monitored.
- The use of sterile liquid formula is encouraged for healthy newborn infants in maternity wards.
- If formula needs to be prepared in advance, it should be prepared on a daily basis and should be kept at 4°C or below for not more than 30 hours. The storage temperature should be monitored. Formula should only be warmed immediately before feeding.
- If formula needs to be kept at room temperature for a prolonged period (e.g. for continuous tube feeding), the maximum accepted hang time is 4 hours.

Formula Manufacturers

- Manufacturers of infant formulae should continue to make rigorous efforts to minimize bacterial contamination of powdered products.

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