Human milk is the preferred feeding for all infants, including premature and sick newborns, with rare exceptions.

When direct breastfeeding is not possible, expressed human milk, fortified when necessary for the premature infant, should be provided.
The Committee advocates the use of human milk for preterm infants as standard practice, provided it is fortified with added nutrients where necessary to meet requirements.

Human milk is the preferred milk in preterm infant feeding.

The Milky Way
Peter Paul Rubens, Prado Museum, Madrid, Spain
Food for VLBW infants: Biological hierarchy

1. Fresh mother’s milk by direct breastfeeding
2. Fresh mother’s milk expressed from the breast
3. Donor’s human milk
4. Preterm formula

AAP-Policy Statement
Section on Breastfeeding
*Pediatrics; February 2005*

Human milk-fed premature infants receive significant benefits with respect to host protection and improved developmental outcomes compared with formula-fed premature infants.
Human milk & the premature infant

Special Advantages

Recent evidence shows that preterm infants fed HM have:

- Lower rates of NEC
- Lower rates of infections
- Improved feeding tolerance
- Improved mother-infant relation
- Improved neurodevelopmental outcomes
- Lower rates of arterial HT, CV risk

Hylander MA. Pediatrics 1998; 102 (2)
Vohr BR, Pediatrics 2006;118:e115-123.
Systematic Reviews

**SYSTEMATIC REVIEW**

Donor human milk versus formula for preventing necrotising enterocolitis in preterm infants: systematic review

W McGuire, M Y Anthony

Arch Dis Child Fetal Neonatal Ed 2003;88: F11-14

Donor breast milk versus infant formula for preterm infants: systematic review and meta-analysis

Catherine A Boyd, Maria A Quigley, Peter Brocklehurst


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**Figure 2** Individual and combined estimates of risk ratio of confirmed NEC for sole DMM versus sole formula milk.

Risk reduction in preterm infants fed exclusive bank human milk vs formula

Catherine A Boyd, Maria A Quigley and Peter Brocklehurst

Donor breast milk versus infant formula for preterm infants: systematic review and meta-analysis
Catherine A Boyd, Maria A Quigley, Peter Brocklehurst

Feeding intolerance

Significantly fewer episodes of feeding intolerance (including NEC) and diarrhoea in the donor milk group compared with the formula group

tolerated full enteral feeds earlier, significantly fewer withdrawals due to feeding intolerance
Human milk is better “tolerated” than formula

- **Faster gastric emptying** = shorter gastric half-emptying time
  - Cavell et al., 1981: HM 48 min vs Form 78 min
  - Ewer et al., 1994: HM 36 min vs Form 72 min
  - Van den Driessche et al., 1999: HM 47 min vs Form 65 min

- “Full feeds reached more quickly”  
  *(Simmer et al., 1997)*

- Less GE reflux with HM than formula  
  *(Peter et al., 2002)*

**CLINICAL STUDIES: Long term benefits**

Human milk promotes

- Cardiovascular and metabolic advantages
- Better neurocognitive outcome
LONG-TERM HEALTH BENEFITS
HM vs Formula

A representative subset (n=216) was evaluated at age 13–16 years for key cardiovascular risk factors:

- Arterial blood pressure [37]: mean arterial blood pressure was lower in adolescents who had been randomized to donor milk than those given preterm formula. The proportion of enteral intake as HM in the neonatal period was inversely related to later mean arterial blood pressure.
- Lipoprotein profile [26]: Adolescents who had been randomized to donor milk had a lower ratio of low-density to high-density lipoprotein cholesterol (LDL to HDL) than those fed preterm formula. A greater proportion of HM intake was associated with lower ratios of LDL to HDL and apoB to apoA-1. This “dose-response” association, together with the experimental design of the study, supports a causal link between HM feeding and the lipoprotein profile later in life.

• Singhal A. Lancet 2001
• Singhal A. Lancet 2004

Human milk and the premature infant

Neurocognitive development

Lucas et al., 1990, 1998, 2005    HM advantage
Horwood et al., 2001    HM advantage
Vohr et al., 2007    HM advantage
The nutritional quality of donor breast milk may be compromised by pasteurization.

- Holder pasteurization (62.5 °C x 30 min) assures the safety of human milk.
- However, heat can destroy important nutritional biomolecules:
  - Nutritional quality
  - Growth factors
  - Immunological factors
## WHAT WE KNOW IS...

Tully BD. J Hum Lactation 2001  
Goelz R. Ped Research 2009  
Silvestre D. Acta Paediatrica 2008  
Czank C. Pediatric Research 2009  
Arslanoglu S, Moro G. J Perinatal Med 2010

### Holder Pasteurization

<table>
<thead>
<tr>
<th>DESTROYS</th>
<th>REDUCES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pathogens in milk, including:</strong></td>
<td><strong>B and T cells</strong></td>
</tr>
<tr>
<td>- S. aureus</td>
<td><strong>IgA, IgG, SIgA (20-30 %)</strong></td>
</tr>
<tr>
<td>- E. coli</td>
<td><strong>Lactoferrin /iron binding capacity</strong></td>
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<td>- Pseudomonas aeruginosa</td>
<td><strong>Lysozyme</strong></td>
</tr>
<tr>
<td>- M. tuberculosis</td>
<td><strong>IgM and Complement (destroyed)</strong></td>
</tr>
<tr>
<td>- Bacillus cereus</td>
<td><strong>IL 10</strong></td>
</tr>
<tr>
<td><strong>Viruses:</strong></td>
<td><strong>EPO</strong></td>
</tr>
<tr>
<td>- HIV</td>
<td><strong>Growth factors</strong></td>
</tr>
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<td>- HTLV 1-2</td>
<td><strong>Antioxidant capacity</strong></td>
</tr>
<tr>
<td>- CMV</td>
<td><strong>Lipases</strong></td>
</tr>
<tr>
<td>- Herpes simplex</td>
<td></td>
</tr>
<tr>
<td>- Rubella</td>
<td></td>
</tr>
<tr>
<td><strong>These results can not be achieved constantly with the treatment at a temperature of 56°C</strong></td>
<td></td>
</tr>
</tbody>
</table>
• How does pasteurization affect human milk oligosaccharides.

...WHAT ABOUT THE EFFECTS OF HOLDER PASTEURIZATION ON HUMAN MILK OLIGOSACCHARIDES?

Bertino, Coppa, Coscio, Fabris et Al
Int J Immunopathol Pharmacol 2008
Chromatographic pattern
24 oligosaccharides

Before pasteurization
After pasteurization

Persistence of the biological value of oligosaccharides after pasteurization!

Bertino, Coppa, Coscia, Fabris et al.
Int J Immunopathol Pharmacol 2008
• How does pasteurization affect milk protein pattern, from both a qualitative and a quantitative point of view.
IMPACT OF PASTEURIZATION TECHNIQUES ON THE PROTEIN PROFILE OF HUMAN MILK


AIM

Evaluate the impact of 2 different pasteurization techniques on the protein profile of human milk

To find out the best method that retains the protein quality
METHODS

• Holder pasteurization
• Short term high-temperature pasteurization

Dhar J J Food Sciences 1996
Hamprecht K Ped Res 2004
Silvestre J Hum Lact 2008

Heat treatment of human milk
Effects on protein structure

Direct effect
Maillard reaction
non enzymatic glycolization of proteins lactose binds to the proteins

Indirect effect
Lipid peroxidation
formation of HNE (4-hydroxy2nonenal) binds to proteins

Changes in protein structure

Consecutive biological changes
Heat treatment of human milk
Effects on protein structure

Direct effect
Maillard reaction
non enzymatic glycolization of proteins lactose binds to the proteins

Indirect effect
Lipid oxidation
formation of HNE (4-hydroxy2nonenal) binds to proteins

Changes in protein structure
- Formation of protein carbonilates
- Formation of molecular aggregates

Consecutive biological changes
- Possible loss in nutritional value
  Lysine, cistein and histidine residues are blocked (Finot 1990)
  Reduction of digestibility and enzymatic inhibition (Friedman 1996)
ANALYSIS PERFORMED

Characterization of protein pattern and degree of carbonylation

Identification of modified proteins

Lipase activity

Available lysine quantity

PROTEIN PATTERN

Homogenous SDS PAGE: Raw milk and flash milk have the similar protein pattern, whereas the density of the Bands A,B,C are reduced with Holder.
Flash milk protein pattern appeared to be very similar to raw milk, while it was modified by Holder pasteurization method.

Holder reduced the intensity of bands A, B, C, J, K, O, Q.
ANALYSIS PERFORMED

Characterization of protein pattern and degree of carbonylation

Identification of modified proteins

SDA-PAGE + Blotting + Immuno-staining

Tandem Mass Spectrometry

<table>
<thead>
<tr>
<th>Band</th>
<th>Description</th>
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<tbody>
<tr>
<td>B</td>
<td>bile salt-stimulated lipase</td>
</tr>
<tr>
<td>C</td>
<td>human lactoferrin</td>
</tr>
<tr>
<td>J,K</td>
<td>Ig λ-light chain variable region, MHC class I antigen</td>
</tr>
<tr>
<td>O,Q</td>
<td>IgA</td>
</tr>
</tbody>
</table>
The increase in lysine quantity by Holder pasteurization: increased digestibility of protein.

But loss in lipase and some immunologically active components...

IgA, lactoferrine, lipase, lipase activity are preserved.

Protein profile does not seem to alter with Flash pasteurization.

Carbonylation is not induced.

IgA, lactoferrine, lipase, lipase activity are preserved.
The preliminary results are in favor of Flash pasteurization.

**Holder Pasteurization**

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Optimizing pasteurization method would enhance the protein quality and biological functions of pasteurized donor human milk.
Heat Treatment of Human Milk

Currently, Holder pasteurization (+62.5°C) is the most studied and recommended method for the heat treatment of donor human milk.

The Holder method affects some of the nutritional and biological properties of HM, and decreases its nutritional value.

To overcome these limitations of Holder pasteurization, different methodologies of HM treatment are at the moment under investigation.
Heat Treatment of Human Milk

1. Rapid Pasteurization
2. Thermoultrasound
3. High Pressure Processing
4. Ohmic Heating

1. **Rapid Pasteurization**
   (HTST: 72 °C for 5 - 15 sec)

**Advantages:** This method seems superior to Holder pasteurization, reaching a better compromise between microbiological safety and nutritional and biological quality of the milk

**Disadvantages:** It requires technological investment and presently is available only at industrial level
2. Thermoultrasound
(combination of ultrasound and heat)

**Advantages:** It is an emerging food preservation technique that retains higher quantities of bioactive components.

**Disadvantages:** The present experimental system is limited to small volumes and scale-up studies would need to be undertaken.

Further experimental evaluation is necessary.

3. High Pressure Processing
(HPP: 400 MPa, < 30 °C)

**Advantages:** Recent studies found that total IgA, immuno and lysozyme activity were significantly higher in HPP human milk compared with pasteurized HM (100% of IgA preserved vs 72%).

The method results in a product of improved nutritional quality.

It is faster and perhaps more convenient than Holder pasteurization.

**Disadvantages:** Protein denaturation. Increase rate of lipid oxidation. Enzymes inactivation.
4. Ohmic Heating  
(heat treatment with electricity)

OH is an advanced thermal processing method where the food material, which serves as an electric resistor, is heated by passing electricity through it. Electrical energy is dissipated into heat, which results in rapid and uniform heating. With conventional thermal processing significant product quality damage can occur due to slow conduction and conventional heat transfer.

Advantages:
- Rapid and uniform heating.
- First trials: no modification of the protein pattern of HM at 72°C, small changes at 78°C, and significant changes at 85°C.

Disadvantages:
- Preliminary data. More studies are necessary to evaluate the theoretical advantages of this new technology in heating human milk.
2nd International Congress of the European Milk Bank Association (EMBA)

ISTANBUL, 8th-9th November 2013

Donor Milk: So precious we keep it in a bank!

www.europeanmilkbanking.com