Microbial colonization in the newborn

- Mammals deliver next to the mother’s anus for the offspring to pick up a normal gut microflora.

- The immune system of the human neonate is very small.

- The gut microflora
  - is the main stimulus to its growth
  - and its education to develop tolerance

- The gut microflora continues to be added to from mother, family, surrounding.
Bacterial colonization of the gut

- **Aerobic bacteria**

- **Anaerobic bacteria**

Graph showing the bacterial colonization of the gut. The y-axis represents bacteria per gram of stool, ranging from $10^8$ to $10^{11}$. The x-axis represents developmental stages: Infant and Adult. The graph illustrates a comparison between Anaerobic and Aerobic bacteria colonization during infant and adult stages.
The immune system defends us but may also cause disease.

**Innate**

- Neutrophils
- Monocytes/macrophages

Cytokines: IL-1β, TNF, IL-6 - cause symptoms

**Adaptive**

- Dendritic cell

Antigen presentation
The immune system defends us but may also cause disease.

- **T helper cell**
  - **IL-12**
  - **IL-4**

- **Cytotoxic T cells**
  - Destroys cells infected with virus, Listeria etc.

- **B lymphocyte**
  - Antibodies in blood, tissues and on mucous membranes

- **NK-cells**
  - Can kill

- **Macrophages**
  - Can kill

- **IFN-γ**
The immune system has two parts

- **Antibodies** and **lymphocytes** in blood, secretions and tissues.
  
  They defend by activating leukocytes and inducing **inflammation** via the signals of the immune system: the **cytokines**. They cause the symptoms of infection, require much energy and cause **tissue damage**.

- **The secretory IgA antibodies** are present on all mucosal membranes and stop microbes from entering tissues.
  Therefore:  
  - No symptom,  
  - No energy loss and  
  - No tissue damage

The SIgA antibodies make up a main defence provided by breastfeeding
Breastfeeding protects especially via secretory IgA antibodies.

Mother’s gut

Blood

bacteria, viruses, foods etc

Peyer’s patch

lymph

Lymphocytes

SIgA antibodies

Mammary glands

Salivary glands
Lactoferrin protects without inflammation

- **Lactoferrin** (LF) is a major milk protein: 1 - 3 g/l

- LF and its proteolytic fragments can kill **bacteria**, **viruses**, and **fungi**

- LF is strongly **anti-inflammatory and anti-infectious**

  LF blocks the transcription factor NF kappa B in leucocytes, preventing production of pro-inflammatory cytokines (IL-1β, TNF-α, IL-6)

  - LF prevents inflammation in experimental colitis, reducing IL-1β, TNF-α in blood and CD4+ lymphocytes in mucosa

  - LF protects against experimental urinary tract infections
Oligosaccharides and certain glycoconjugates in human milk act as receptor analogues preventing microbes from attaching to mucosal epithelium. Thus preventing infections like otitis media, respiratory tract infections and diarrhoea.
AF may prevent mastitis in man

- A double blind pilot study of Swedish healthy mothers, started 3-7 days after delivery.

- 12 mothers received malted cereal daily for 4-5 weeks. The same cereal, untreated, was given to 17 control mothers.

- The frequency of mastitis in the test group was significantly less than in the control group p=0.0086
AF in milk from mothers in the experimental and the control group.
Proportion of children with acute and prolonged diarrhoea showing success or failure after 3 days of treatment with AF and Non AF

<table>
<thead>
<tr>
<th></th>
<th>Acute diarrhoea</th>
<th>Prolonged diarrhoea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful</td>
<td>AF: 82.8%</td>
<td>AF: 90.9%</td>
</tr>
<tr>
<td></td>
<td>Non AF: 54.4%</td>
<td>Non AF: 63.2%</td>
</tr>
<tr>
<td>Failure</td>
<td>AF: 10.9%</td>
<td>AF: 9.1%</td>
</tr>
<tr>
<td></td>
<td>Non AF: 36.8%</td>
<td>Non AF: 28%</td>
</tr>
<tr>
<td>Inconclusive</td>
<td>AF: 6.25%</td>
<td>AF: 8.8%</td>
</tr>
<tr>
<td></td>
<td>Non AF: 8.8%</td>
<td>Non AF: 0%</td>
</tr>
</tbody>
</table>

p=0.0001 (Acute diarrhoea)  p=0.0003 (Prolonged diarrhoea)
**α-lactalbumin - ”HAMLET”**
*(Human Alfa-lactalbumin Made LEthal to Tumor cells)*

- Human milk is rich in α-lactalbumin
- α-lactalbumin → low pH in infant’s stomach → re-structures the molecule and makes it bind oleic acid
- α-lactalbumin has become ”HAMLET” and kills tumor cells (>40 human cell lines tested) - also it protects in *in vivo* experiments
- HAMLET may kill premalignant cells in the gut?
- Can HAMLET explain that breastfeeding may protect against leukemia in childhood and against breast cancer?

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Components in milk, which may actively affect the infant’s immune system

- **Cytokines**
  
  **Immunomodulating and anti-inflammatory:**
  - Interleukin-10 (IL-10)
  - Transforming Growth Factor-β (TGF-β)

  **Pro-inflammatory:**
  - IL-1β
  - IL-2
  - IL-6
  - IL-12
  - IFN-α
  - TNF-α
  - Interferon-γ (IFN-γ)

- **Chemokines**
  
  - Macrophage Migration Inhibitory Factor (MIF)
  - Colony Stimulating Factor (M-CSF)
  - Granulocyte Colony Stimulating Factor (G-CSF)
  - IL-18, IL-7
  - RANTES
  - Leptin
Breastfeeding and the central organ of the immune system: the thymus

- Exclusive breastfeeding doubles the size of the thymus

- Partial breastfeeding also increases the size of the thymus, where the key cells of the immune system, the T(thymus) lymphocytes mature

- Probably this is due to the cytokine IL-7 in the milk

- IL-7 make special gut organs: the cryptopatches develop. There special T lymphocytes develop (T\(\gamma\delta\))
Breastfeeding and vaccination

Breastfeeding can **increase responses** to some vaccines:
- BCG
- Hib vaccine
- Tetanus
- Diphteria
- Live poliovirus vaccine

**Not always effective for:**
- certain pneumococcal vaccine components
- rotavirus
- Hib vaccine
- Tetanus toxoid

**Note!** Do not breastfeed immediately before or after giving live oral poliovirus vaccine. Milk
BREASTFEEDING PROTECTS AGAINST CERTAIN INFECTIONS
(Quite good evidence from several studies)

- Reduction of infant mortality
- Neonatal sepsis and meningitis
- Necrotizing enterocolitis
- Diarrhea
- Otitis media and pneumonia
- Urinary tract infections

(in red: long-lasting effects suggested)
BREASTFEEDING AND PROTECTION AGAINST VARIOUS DISEASES
(Suggestive evidence)

- Sudden death in infancy
- Upper respiratory infections
- Celiac disease (gluten intolerance)
- Overweight, obesity, insulin resistance
- Crohn’s disease, ulcerative colitis, MS
- Diabetes types 1 and 2, arteriosclerosis
- Rheumatoid arthritis
- Lymphoblast. leukemia, Hodgkin, Neuroblastoma
Breastfeeding (BF) and postneonatal mortality (28 days-1 year) in USA

- BF ever reduced postneonatal deaths by 21 % (0.79, 95 % CI: 0.67-0.93) compared to non-BF in all USA
- Longer BF gave lower risk
- Promotion of BF in USA may save about 720 infants/year

A Chen and WJ Rogan. Pediatrics 113: 435-9, 2004
BREASTFEEDING AND ALLERGY

- ALLERGY: group of common genetic, immunological diseases: eczema, hayfever, asthma
- Variable outcomes of very many studies, some show increased, others decreased risk from breastfeeding
- The effects, positive or negative, are not strong
- More good studies show some protection rather than increased risk
The role of breast-feeding (BF)

- **BF** is a rich biological gift from the mother to her infant:

- **BF** provides numerous components which protect the infant against infections without causing inflammation, symptoms and damage.

- **BF** provides many signals to the infant supporting short and long term protection against infections and certain diseases, enhancing optimal development.