

# **WHY INFANT FORMULA CAUSES DEATHS DUE TO DIARRHOEA IN EMERGENCIES**

## **WHAT CAUSES DIARRHOEAL ILLNESS?**

Diarrhoeal disease is the leading infectious cause of death in young children, accounting for 22% of the 10 million annual worldwide deaths of children under 5 years.<sup>[1]</sup> Up to 90% of deaths in emergency situations are due to diarrhoea.<sup>[2]</sup> The symptoms of diarrhoea are an increase in the water content and usually the number and volume of stools<sup>[3]</sup> causing loss of water and salts from the body, which can result in dehydration. Vital organs cannot function without a certain level of water and if dehydration or the salt imbalance is severe enough, the body organs begin to shut down and the individual dies.<sup>[4]</sup> A baby can die of dehydration due to diarrhoea within a few days of becoming ill.

Infectious diarrhoea is caused by a bacterial, viral or parasitic infection in the small intestine. The inner surface of the small intestine is lined with specialised cells called enterocytes that are responsible for secretion and adsorption during the process of digestion.<sup>[4]</sup> When the intestine fails to absorb water or there is an increase in fluid secreted into the intestine, the amount of water in stools increases and the individual has diarrhoea.<sup>[4]</sup>

Infection of an infant by a diarrhoea-causing pathogen begins when the organism is swallowed by the baby. In order to cause diarrhoea, the pathogen must survive the stomach and then colonise the small intestine. The first step of colonisation involves pathogens sticking to a receptor on the enterocyte cells of the small intestine. If pathogens do not attach to and infect enterocytes then they cannot colonise the baby but will harmlessly pass out within stools and the infant will remain well.

Secretory diarrhoea occurs when pathogens stimulate infected enterocytes to secrete water and salts into the small intestine. If enough cells are affected, the intestine cannot reabsorb all of the fluid secreted and the individual develops diarrhoea.<sup>[4]</sup> Invasive diarrhoea occurs when pathogens kill enterocytes, reducing the surface area available for adsorption of water so reducing the ability of the intestine to absorb water and causing diarrhoea.<sup>[4]</sup> Organisms that cause diarrhoea include the bacteria *Vibrio cholerae*, *Escherichia coli*, *Shigella spp*, *Salmonella enteritidis*; the viruses rotavirus and norovirus; and the parasites *Cryptosporidium parvum*, *Entamoeba histolytica*, *Cyclospora cayetanensis*, *Isoospora belli* and *Giardia Lamblia*.<sup>[3]</sup>

## **THE IMPORTANCE OF BREASTMILK IN PREVENTING DIARRHOEAL ILLNESS**

Human milk is an incredibly complex fluid containing literally thousands of ingredients. Scientists have yet to discover the role that all of these ingredients play in supporting the normal health, growth and development of infants. Nonetheless, to detail all of the *known* ways in which breastmilk prevents and combats diarrhoeal illness would result in many pages of description. Thus, this article will detail just a few mechanisms by which

breastmilk prevents diarrhoea and briefly mention some of the anti-infective action of breastmilk ingredients.

### **Antibodies and ‘white cells’ in breastmilk actively fight infection**

Most people have heard that breastmilk contains antibodies that help babies to fight infection and this is indeed the case. Human milk contains antibodies that the mother produces in direct response to pathogens that she encounters in her environment.<sup>[5, 6]</sup> The active immunity that infants receive from their mothers is extremely important since babies’ immune systems are quite immature at birth and they have a limited ability to produce their own antibodies<sup>[7]</sup>. Antibodies in breastmilk bind to pathogens that enter the baby’s gut and so prevent them from attaching to the enterocytes in the small intestine and colonising the baby<sup>[7]</sup>.

Breastmilk is also a living fluid and contains ‘white cells’ including mast cells, phagocytes and natural killer cells. These ‘white cells’ attack and kill pathogens by phagocytosis (engulfing and absorbing them) or by producing substances that are harmful to them.<sup>[8]</sup> ‘White cells’ are non-specific attackers and do not require that the mother has previously had contact with a pathogen in order to attack it.<sup>[7]</sup>

### **Glycans in breastmilk act as ‘decoys’ for pathogens**

The enterocytes in the intestine have structures on their surface called glycans.<sup>[9]</sup> Pathogens recognise intestinal enterocytes by these glycans and it is to these glycans that they attach themselves when they colonise the individual.<sup>[10]</sup> Human milk also contains glycans which have a similar structure to the glycans on the surface of enterocyte cells.<sup>[11]</sup> Human milk glycans act as ‘decoys’ for enterocyte glycans and pathogens bind to them instead of to the enterocyte glycans.<sup>[10]</sup> Once attached to the milk glycan ‘decoy’ the pathogen is harmless and is excreted.<sup>[10]</sup> Specific protection against diarrhoea-causing pathogens including *Vibrio cholerae*, *Campylobacter jejuni*, Enterotoxigenic *E. coli*, Enteropathogenic *E. coli*, *Shigella spp*, *Giardia lamblia*, rotavirus and norovirus by the ‘decoy’ action of human milk glycans has been demonstrated.<sup>[5]</sup>

### **Oligosaccharides and lactose in human milk encourage the growth of beneficial bacteria**

Many of the diarrhoea-causing pathogens are bacteria. Pathogenic bacteria compete for colonisation of the gut with the non-pathogenic, beneficial bacteria *Bifidobacteria spp* and *Lactobacillus spp*.<sup>[12]</sup> Lactose and oligosaccharides in human milk encourage the growth of these beneficial bacteria so that they predominate in the intestine of exclusively breastfed infants.<sup>[5, 12]</sup> *Bifidobacteria* and *Lactobacillus* are beneficial for several reasons including that they:

- Acidify the environment suppressing the growth of pathogenic bacteria<sup>[13]</sup>
- Excrete substances that inhibit the growth of pathogens<sup>[13, 14]</sup>
- Out-compete pathogens for nutrients and for adhesion sites on the wall of the intestine<sup>[15]</sup>
- Produce compounds that encourage the growth of the protective mucous layer in the intestine making pathogenic colonisation more difficult<sup>[16]</sup>
- Assist in the development of the infant’s immune system<sup>[16]</sup>

### **Components of human milk act directly and indirectly to prevent illness**

As mentioned, it is not possible to detail here all of the ways in which human milk helps to prevent and treat diarrhoea. However, some of the illness-fighting mechanisms include:

- A component of human milk called lactoferrin inhibits bacterial growth by depriving pathogenic bacteria of iron;<sup>[17]</sup> diminishing bacterial virulence by disrupting the integrity of the outer membrane of bacteria<sup>[18]</sup> and assisting in intestinal maturation and in the recovery of the intestine from injury<sup>[19]</sup>
- A protein in human milk called lysozyme kills pathogenic bacteria such as *E. coli* and *Salmonella* by disrupting their cell walls<sup>[17]</sup>
- Digestion of fat in human milk creates free fatty acids and monoglycerides that have anti-protozoal action including against the diarrhoea-causing parasite *Giardia lamblia*<sup>[7]</sup>
- Epidermal growth factor and other growth factors in human milk foster the growth and maturation of the lining of the intestine (including enterocytes and the protective mucous layer) making colonisation by pathogens more difficult<sup>[19]</sup>
- Peptides that are present pre- and post-digestion of human milk suppress bacterial growth<sup>[6]</sup>
- Fatty acids and monoglycerides that are released by the digestion of human milk have antibacterial, antiviral, and antiparasitic properties<sup>[6]</sup>
- Human milk supports the normal development of the infant's own immune system<sup>[19]</sup>

### **HOW INFANT FORMULA MAKES INFANTS VULNERABLE TO DIARRHOEA**

There are a number of ways in which the use of infant formula makes babies vulnerable to developing diarrhoea.

#### **Infant formula and feeding implements can be contaminated with pathogens**

In emergency situations, water supplies are often contaminated with faecal material containing diarrhoea-causing pathogens.<sup>[2]</sup> Contamination happens in different ways depending on the type of emergency. Earthquakes can rupture sewage pipes resulting in the flow of sewage into water supplies. Storms, tsunamis and flooding similarly can wash human and animal faecal material into water supplies.<sup>[20]</sup> Water supply systems can also be damaged by events such as earthquakes and floods resulting in the necessity of obtaining water from poor quality and potentially contaminated sources.<sup>[20]</sup> In addition, when large numbers of people are homeless, sanitary services may be makeshift and inadequate which creates an environment where water supplies are easily contaminated. Since the use of infant formula requires water to both make up the formula and to clean feeding implements, formula feeding is often a direct source of infection.

#### **Use of infant formula deprives babies of breastmilk**

Formula feeding deprives infants of the disease prevention and fighting action of breastmilk and retards the development of the immune system. Without the external immune support provided by breastmilk infants are effectively immunocompromised.<sup>[7]</sup>

This increases the risk of formula-fed infants developing diarrhoea and the risk that the illness will be more severe.

### **Formula fed babies are more susceptible to colonisation by pathogens**

The use of infant formula directly impacts the intestine of infants so that they are more vulnerable to infection and illness. This includes creating an environment that retards the growth of beneficial *Lactobacillus* and *Bifidobacteria* and encourages the growth of bacteria that may be pathogenic. Standard infant formula lacks the oligosaccharides that *Lactobacillus* and *Bifidobacteria* use as a food\* hindering their growth and ability to compete for colonisation of the intestine with pathogens. The lower population of these beneficial bacteria results in a higher pH in the intestine of formula-fed babies which encourages the growth of pathogenic bacteria.<sup>[13, 21]</sup> Formula fed babies have about one tenth of the population of *Lactobacillus* and *Bifidobacteria*<sup>[12]</sup> whilst having larger populations of potentially pathogenic enterobacteria, bacterioids and enterococci as compared to exclusively breastfed babies.<sup>[12]</sup>

Components of infant formula can also damage the protective mucous barrier in the small intestine. The mucosal membrane of a baby's developing intestine is very delicate. Ingestion of "foreign" protein such as cows' milk protein in infant formula can damage the mucous membrane of the intestine.<sup>[22, 23]</sup> The mucous membrane helps to protect the intestine from colonisation by pathogens and so damage to the membrane facilitates colonisation by pathogenic organisms.<sup>[8]</sup>

The intestine of newborn babies is quite permeable and vulnerable to infection. Over time the intestine becomes less permeable, however the use of infant formula delays this process.<sup>[24]</sup> The more permeable intestine makes formula fed infants more vulnerable to colonisation by diarrhoea-causing pathogens.<sup>[25]</sup>

### **Use of infant formula can lead to malnutrition and increased susceptibility to illness**

Diarrhoea is not always fatal however, babies who recover from it are physically weakened and may be malnourished. Such babies are more vulnerable to further infections.<sup>[25]</sup> Formula-fed babies are more likely to become infected with diarrhoea-causing pathogens, more likely to be malnourished and thus more likely to suffer from multiple bouts of more serious illness and eventually die.<sup>[26]</sup>

Food security is a serious issue in emergency situations. Continuity of supply of infant formula cannot always be guaranteed.<sup>[26]</sup> If infant formula is not available, then even poorer foods may be substituted leading to malnutrition. As discussed, malnourished babies are vulnerable to infection and more likely to die from diarrhoea.<sup>[3]</sup> Lack of food security is a significant risk factor associated with the use of infant formula in emergency situations.

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\* Specialty formulas may contain some oligosaccharides but they lack the concentration and variety of human milk; there are more than 1000 different type of oligosaccharides in human milk.<sup>[11]</sup> The oligosaccharides that are added to infant formula have not been shown to be equivalent in function to those in human milk.

### **Partial formula feeding dramatically increases the risk of illness**

Where donated infant formula is given to breastfeeding women, many will continue to breastfeed while also using the formula.<sup>[27]</sup> However, even supplementation with a small amount of infant formula can be problematic and dramatically increase the risk of illness. Use of a small amount of infant formula can still introduce pathogens via contaminated water. It also alters the bacterial composition of the intestine so that it has few beneficial bacteria and a greater population of potentially pathogenic bacteria like fully formula-fed babies.<sup>[28, 29]</sup> A small amount of infant formula can also damage the protective mucous layer in the intestine<sup>[23]</sup> making the baby more vulnerable to infection.

### **CONCLUSION**

The use of infant formula in emergencies causes illness and death in babies because it deprives infants of breastmilk, because it actively makes babies more susceptible to developing diarrhoea and because it introduces the pathogens that cause diarrhoeal illness. Maximising the number of babies exclusively breastfeeding and minimising the use of infant formula is required to protect infants in emergencies.

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