BUNDESINSTITUT FÜR RISIKOBEWERTUNG

BfR
Risiken erkennen – Gesundheit schützen

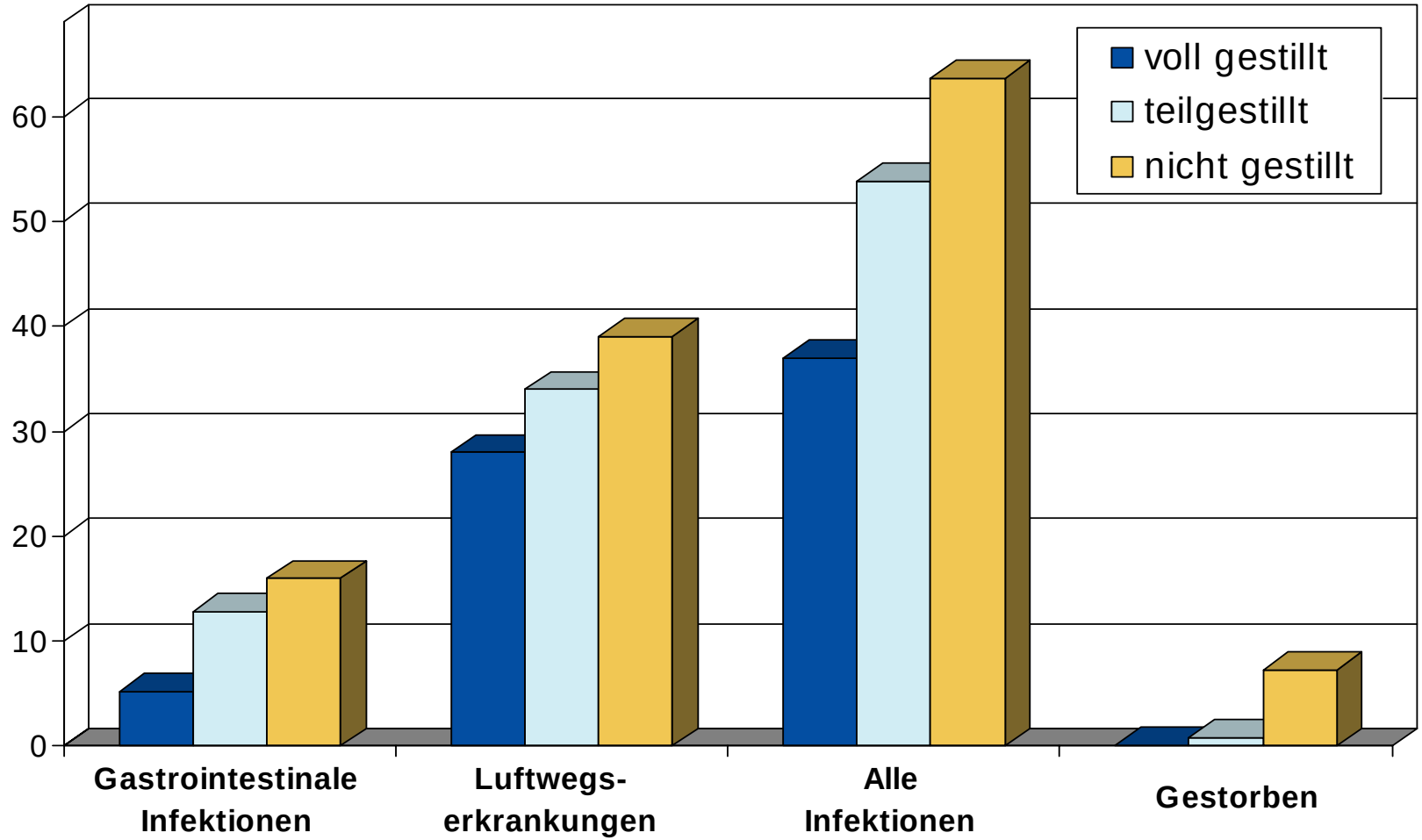
Welche wertvollen Inhaltsstoffe enthält die Muttermilch und welchen Nutzen haben gestillte Kinder?

Anke Weißenborn, BfR

Wert der Muttermilchernährung um 1900

TAFEL 62 AUS: LEO LANGSTEIN/FRITZ BOTT: ATLAS DER HYGIENE DES KINDES, BERLIN: PREUSSISCHE VERLAGSANSTALT 1918 CHROMOLITHOGRAPHIE; 35,2 X 49,8CM

Morbidität und Mortalität gestillter und nicht-gestillter Säuglinge bis zum Alter von 9 Monaten



Grulee et al. (1934) JAMA 103: 735-8

Wert der Muttermilchernährung heute

Gastrointestinale Infekte

- prospektive Kohorte
- 1900 Mutter-Kind-Paare
- Bayern
- Häufigkeit von Infektionen retrospektiv von Kinderärzten erfragt

Table 1 Adjusted ORs (95% CIs) for ≥1 episode of gastrointestinal infection(s) for infants from birth to month 9 (n = 1901)

Influencing factor*		Gastrointestinal infection OR (95% CI)	
Breastfeeding†			
Group A	**n=475 ≥ 6 Mo. full bf**	0.6 (0.44–0.82)‡	p < 0.01
Group B	**n=870 ≥ 4 Mo. full bf**	0.94 (0.74–1.21)	
Group C	**n=619 < 4 Mo./ no bf**	1	
Maternal age (y)			
<25		1.02 (0.64–1.62)	
25–34		0.87 (0.69–1.10)	
>34		1	
≥1 sibling in the household			
yes		1.49 (1.19–1.87)‡	p < 0.01
no		1	
daycare or child minder			
yes		2.17 (1.33–3.53)‡	p < 0.01
no		1	

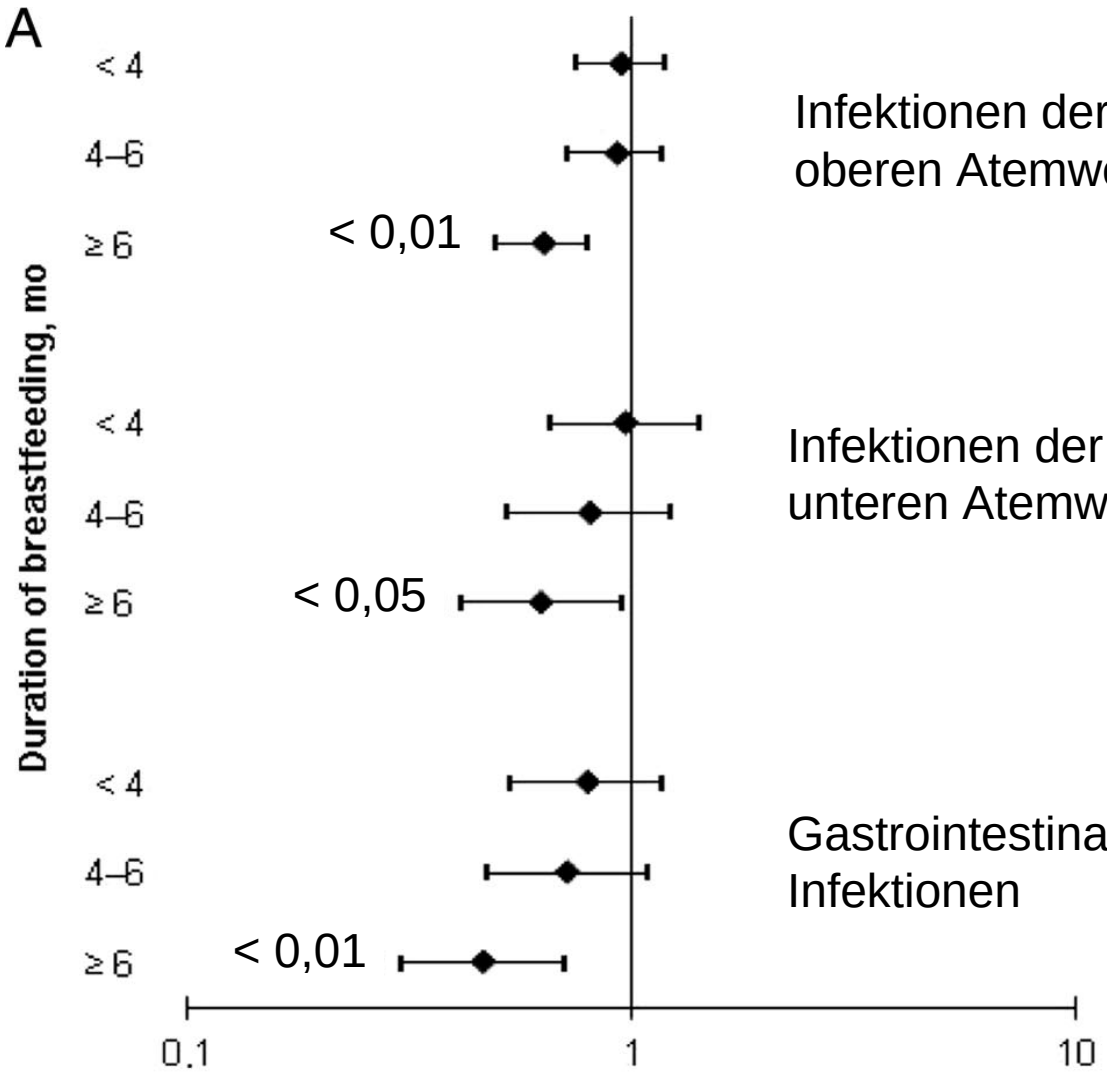
Rebhan et al., Acta Paediatr. 2009. 98(6):974-80.

Wert der Muttermilchernährung heute

GI- URT- LRT- Infekte

N > 3000 Säuglinge

Ausschließliches Stillen



Infektionen der oberen Atemwege

aOR: 0,37 (0,18–0,74)
P < 0,01

Infektionen der unteren Atemwege

aOR: 0,33 (0,08–1,40)
P < 0,01

Gastrointestinale Infektionen

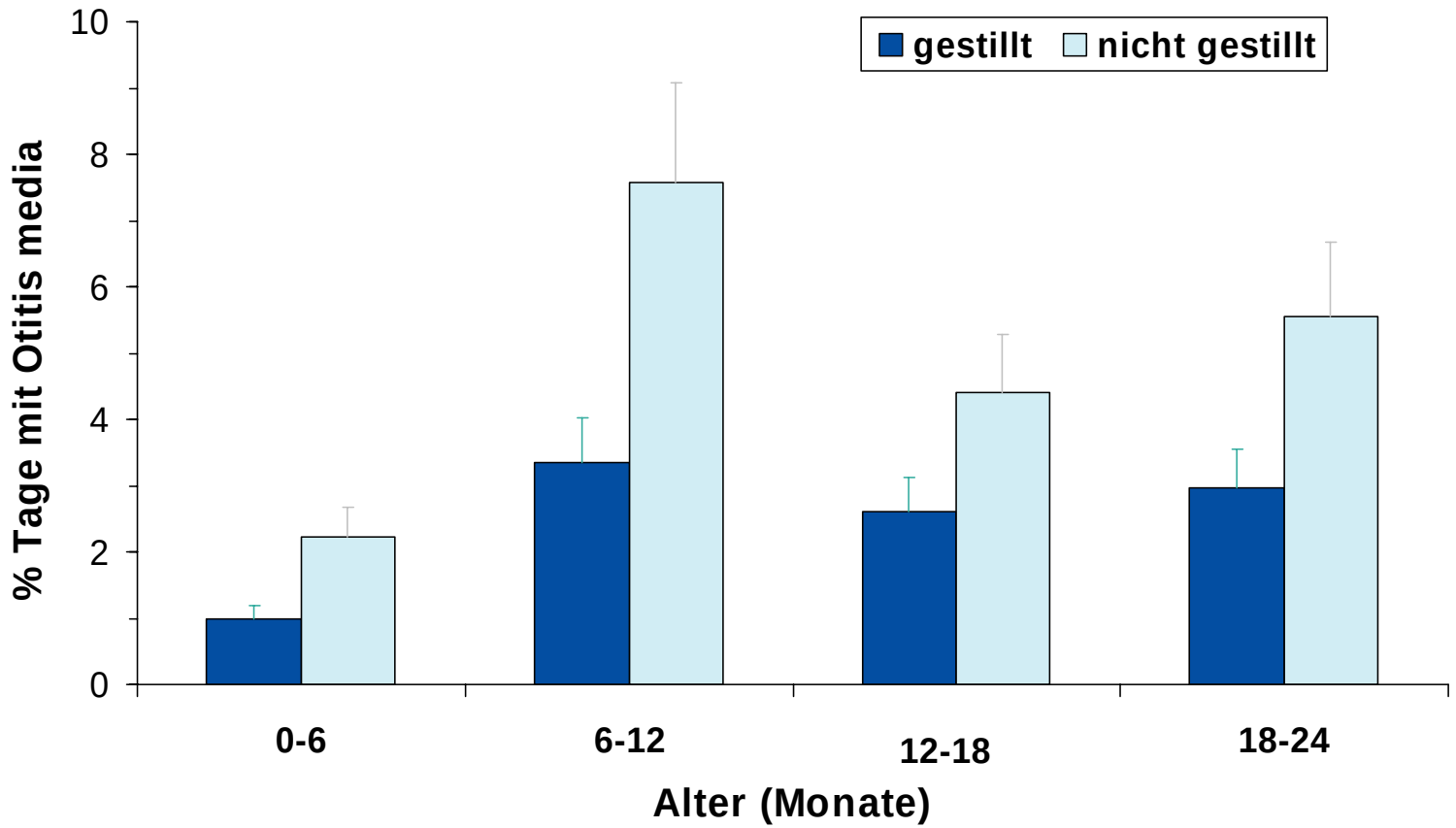
aOR: 0,46 (0,14–1,59)
P < 0,01

Duijts et al. Pediatrics 2010. 126;e18

Wert der Muttermilchernährung heute

Otitis media

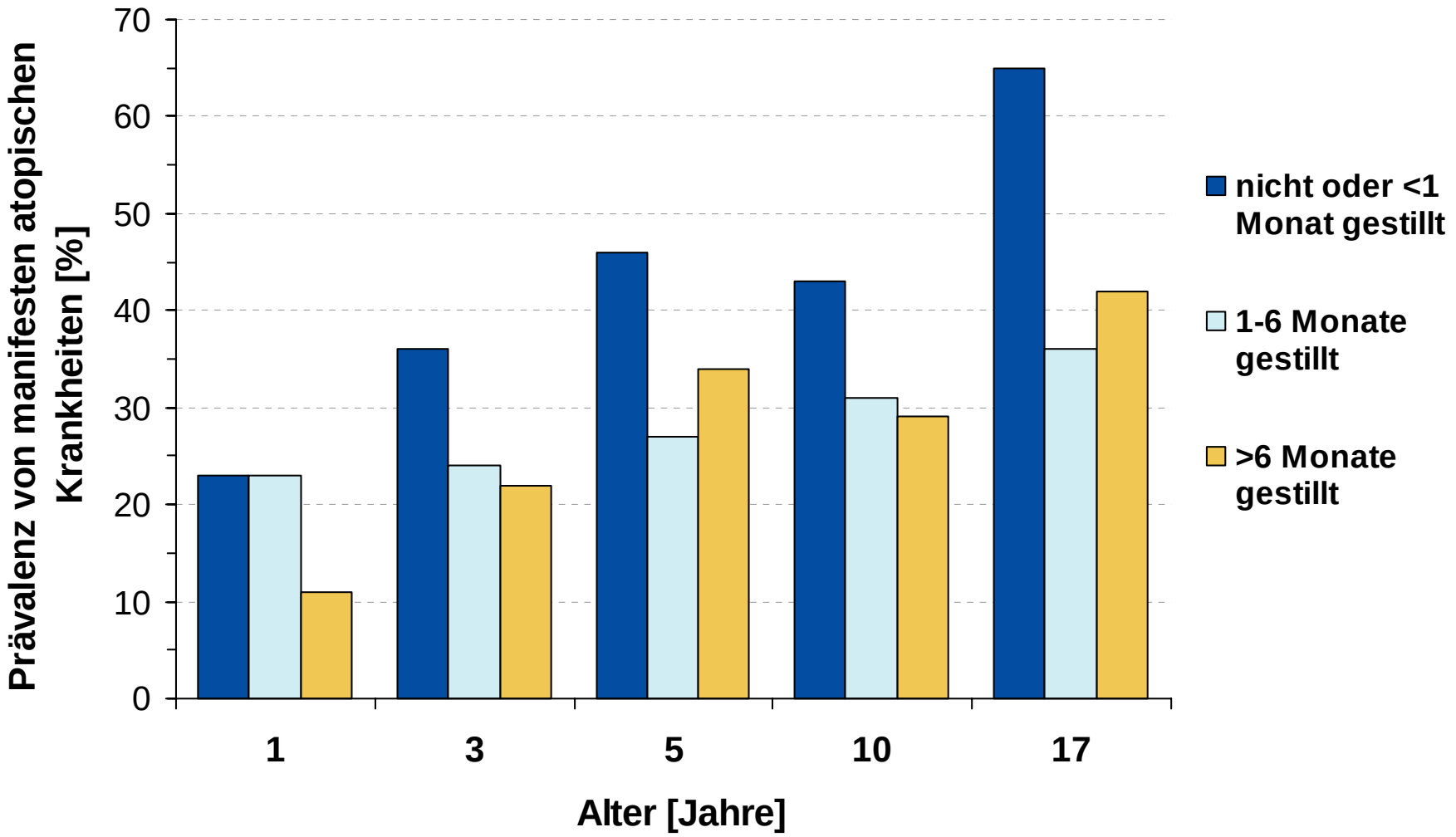
Vergleich: gestillte (n=45) und nicht gestillte (n=41) Säuglinge



Dewey et al.: J. Pediatr. 126 (1995) 696-702

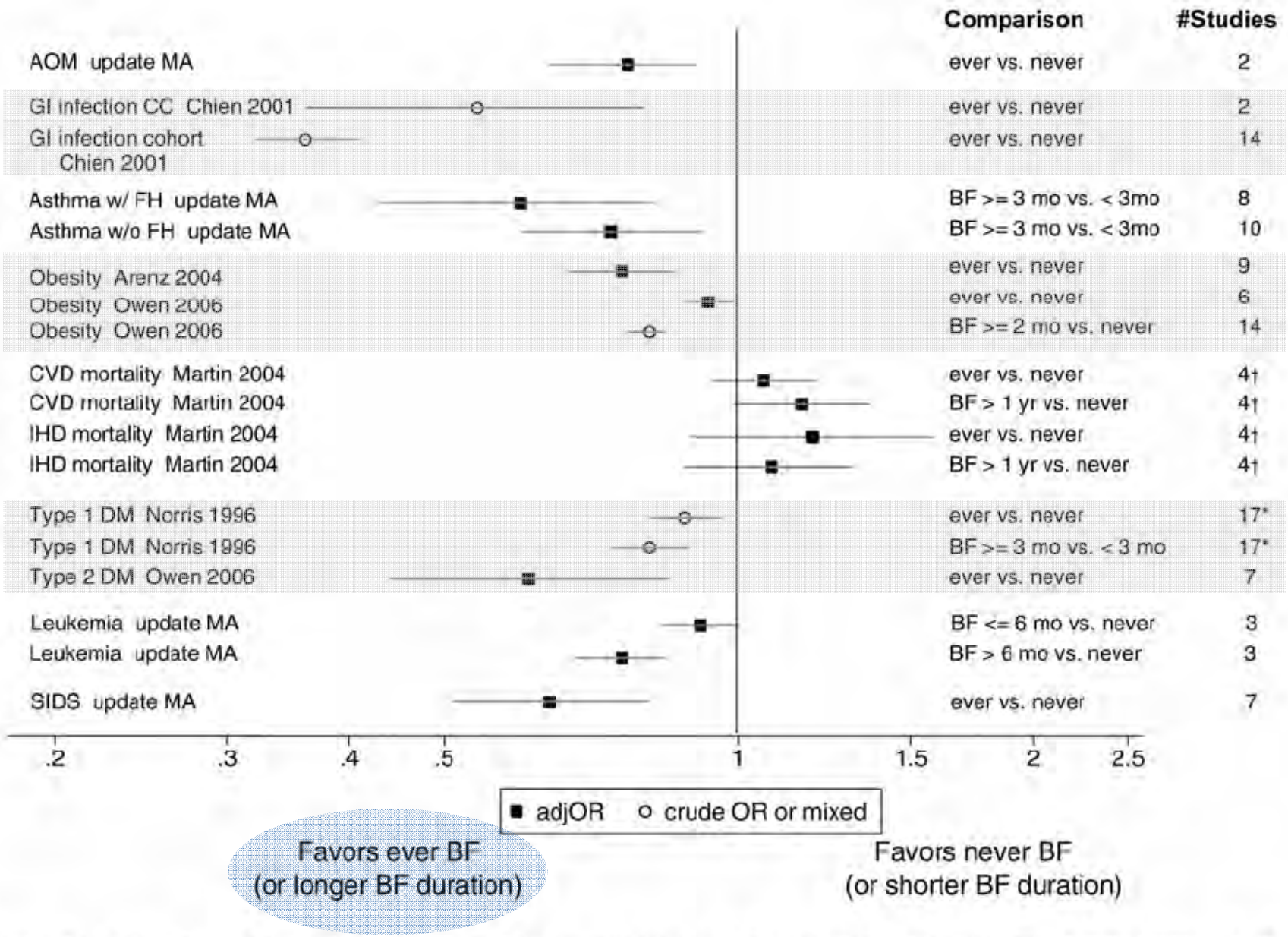
Wert der Muttermilchernährung heute

manifeste atopische Krankheiten



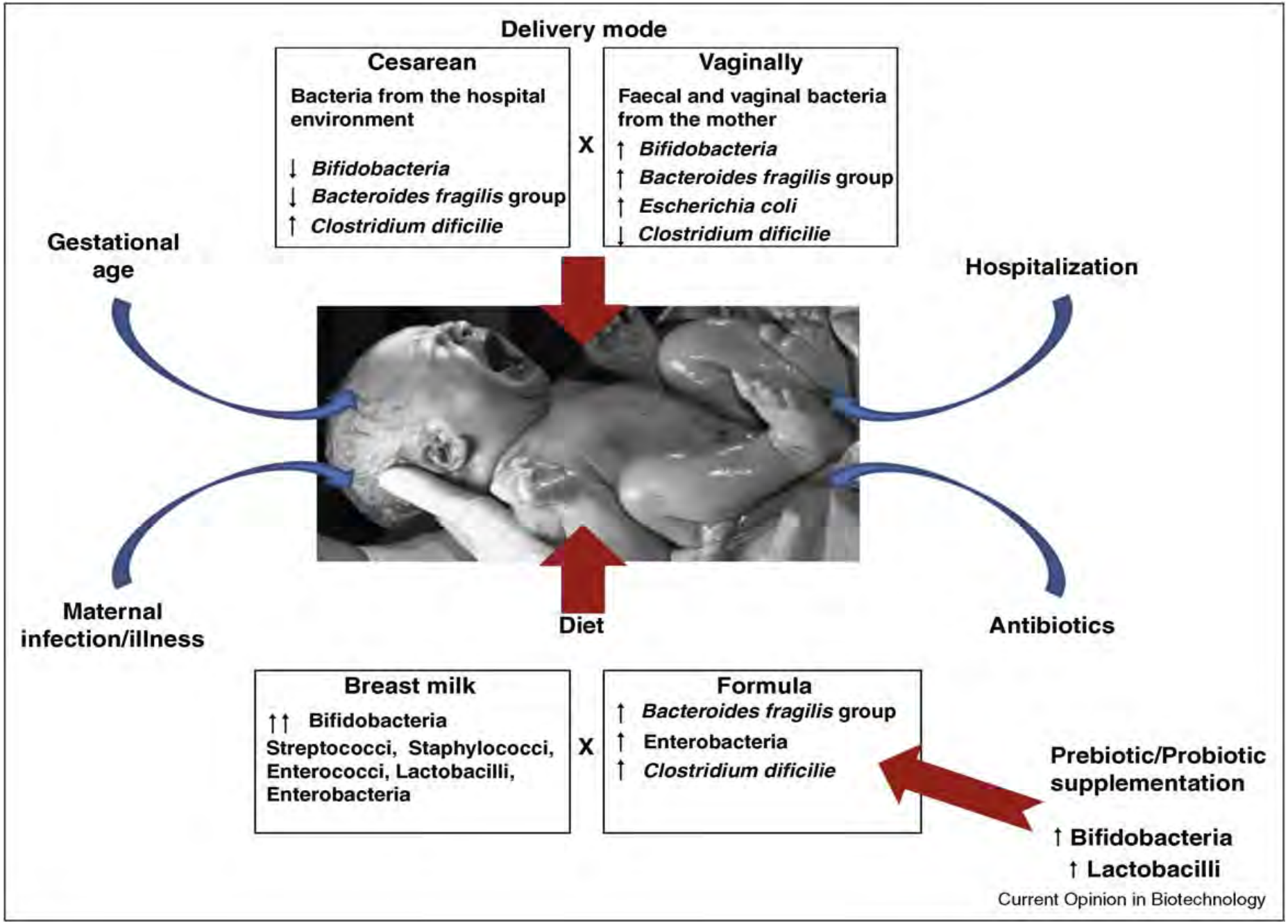
Saarinen und Kajosaari, Lancet 346 (1995) 1065-1069

Wert der Muttermilchernährung heute



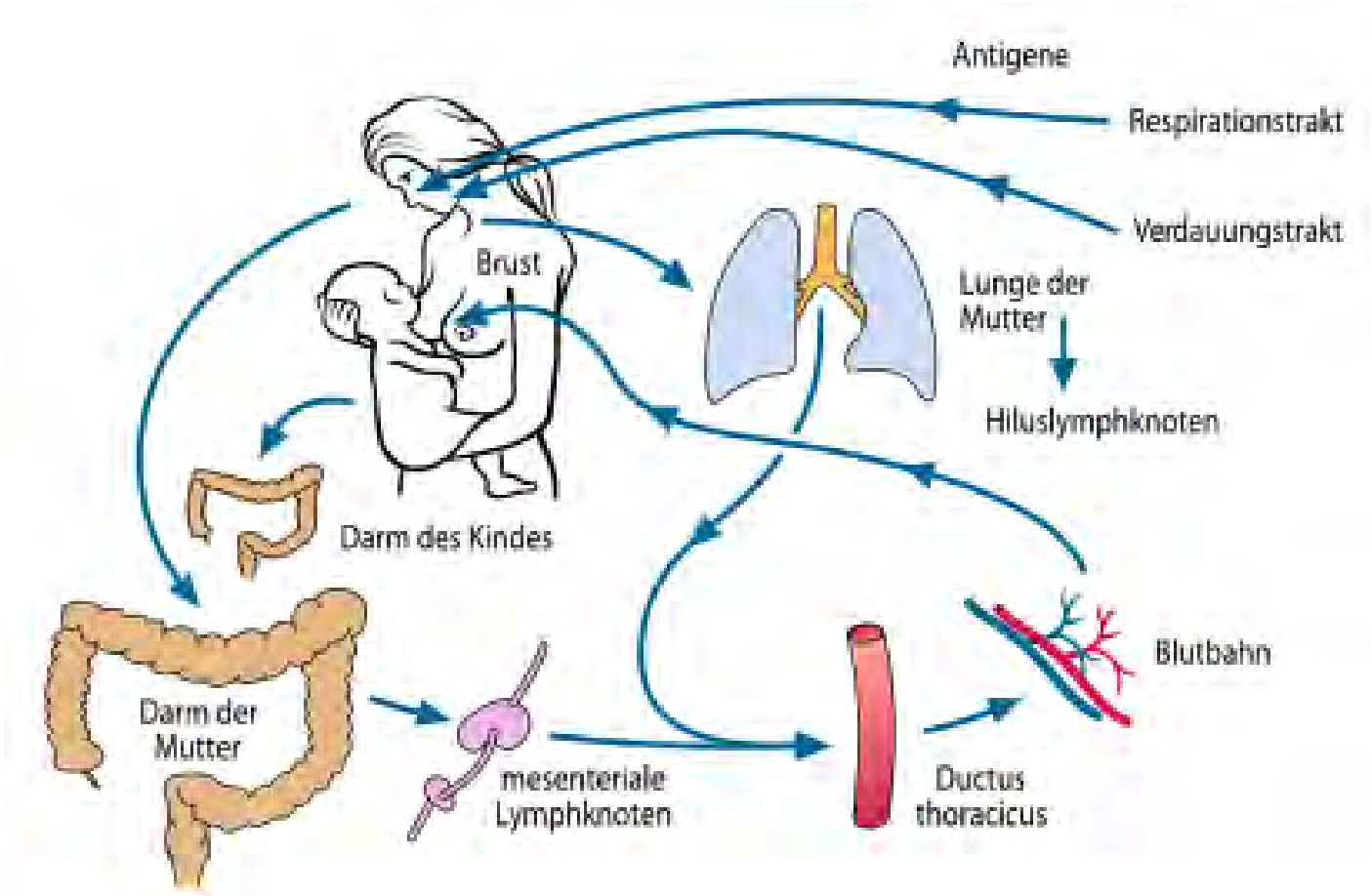
MA, meta-analysis; AOM, acute otitis media; GI, gastrointestinal; CC, case-control studies; FH, family history; CVD, cardiovascular disease; IHD, ischemic heart disease; DM, diabetes; adj, adjusted

Ip et al,, 2007; 2009



Marques et al. Current Opinion in Biotechnology. 2010, 21:149-56

Enterobronchomammäres System



Koletzko, Kinder- und Jugendmedizin, 13. Auflage

Substanzen mit immunologischen Effekten in Frauenmilch

Antimikrobielle Substanzen

Immunoglobuline: sIgA, sIgG, sIgM
Laktoferrin, Laktoferrizin B + H
Lysozym
Laktoperoxidase
Nukleotid-hydrolysierende AK
κ-Kasein und α-Laktalbumin
Haptocorrin
Muzine
Laktadherin
Freie sekretorische Komponente
Oligosaccharide
Fettsäuren
Mütterliche Leukozyten + Zytokine
sCD14
Komplement + Komplement-Rezeptoren
β-Defensin-1
Toll-like Rezeptoren
Bifidusfaktor

Toleranzerzeugende Substanzen

Zytokine: IL-10 + TGFβ
Anti-idiotypische Antikörper

Immunsystementwicklung

Makrophagen
Neutrophile
Lymphozyten
Zytokine
Wachstumsfaktoren
Hormone
Milchpeptide
LC-PUFA
Nukleotide
Adhäsionsmoleküle

Antientzündliche Substanzen

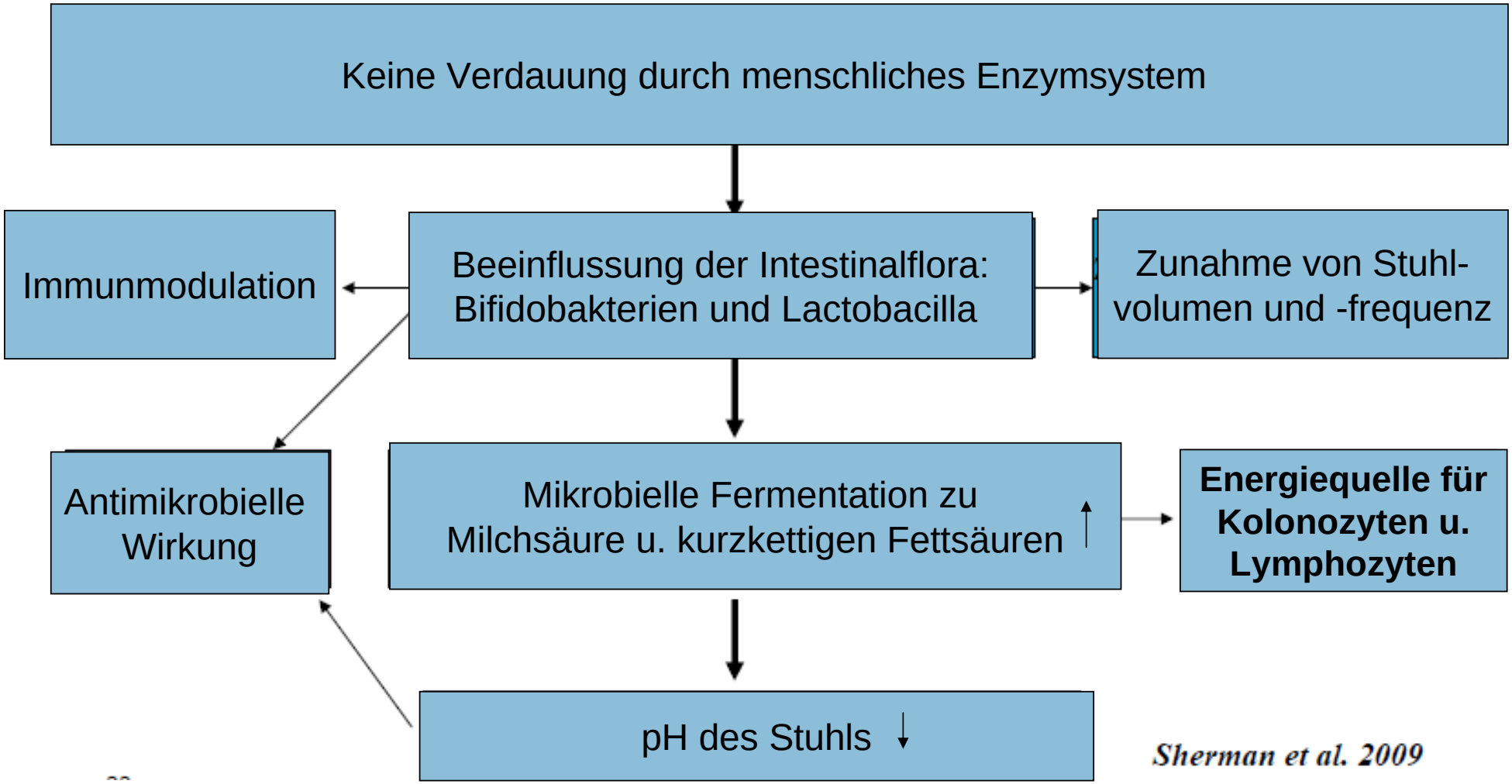
Zytokine: IL-10 und TGFβ
IL-1 Rezeptorantagonist
TNF-α und IL-6 Rezeptoren
sCD14
Adhäsionsmoleküle
LC-PUFA
Hormone und Wachstumsfaktoren
Osteoprotegerin
Laktoferrin

Field (2005) J Nutr 135:1-4

Muttermilch…

- …ist in ihrer Zusammensetzung auf die Nährstoffbedürfnisse des Säuglings abgestimmt
- …mikrobiologisch einwandfrei
- …enthält Faktoren, die das Immunsystem beeinflussen, wie z, B, Immunglobuline, Enzyme, Wachstumsfaktoren, Oligosaccahride
- … variiert in der Zusammensetzung
    - von Mutter zu Mutter
    - im Verlauf des Tages und von einzelnen Mahlzeiten
    - im Laufe der Stillzeit
    - in Abhängigkeit von der mütterlichen Ernährung

Oligosaccharide als Präbiotika

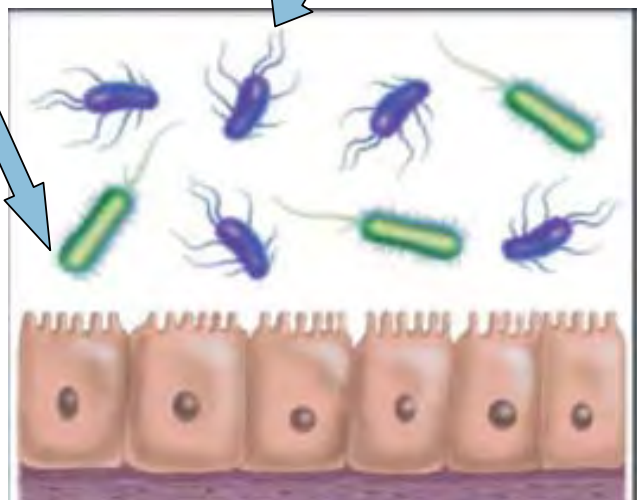


Sherman et al. 2009

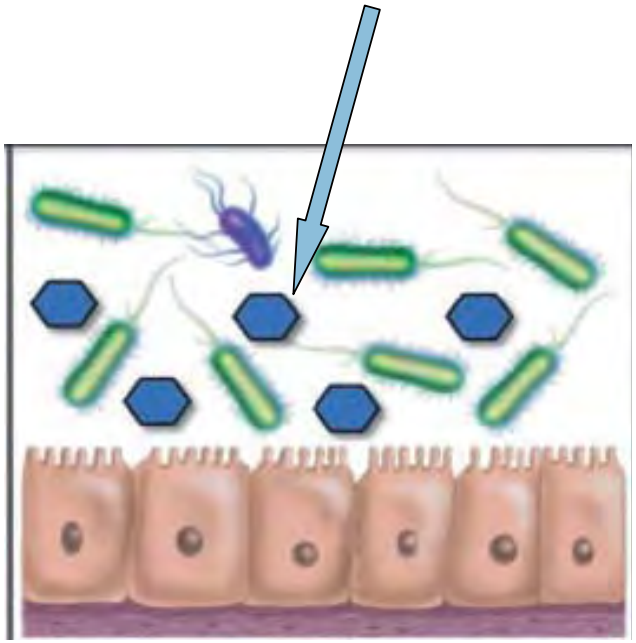
Oligosaccharide als Präbiotika

unerwünschte Bakterien

Milchsäure- und Bifidobakterien



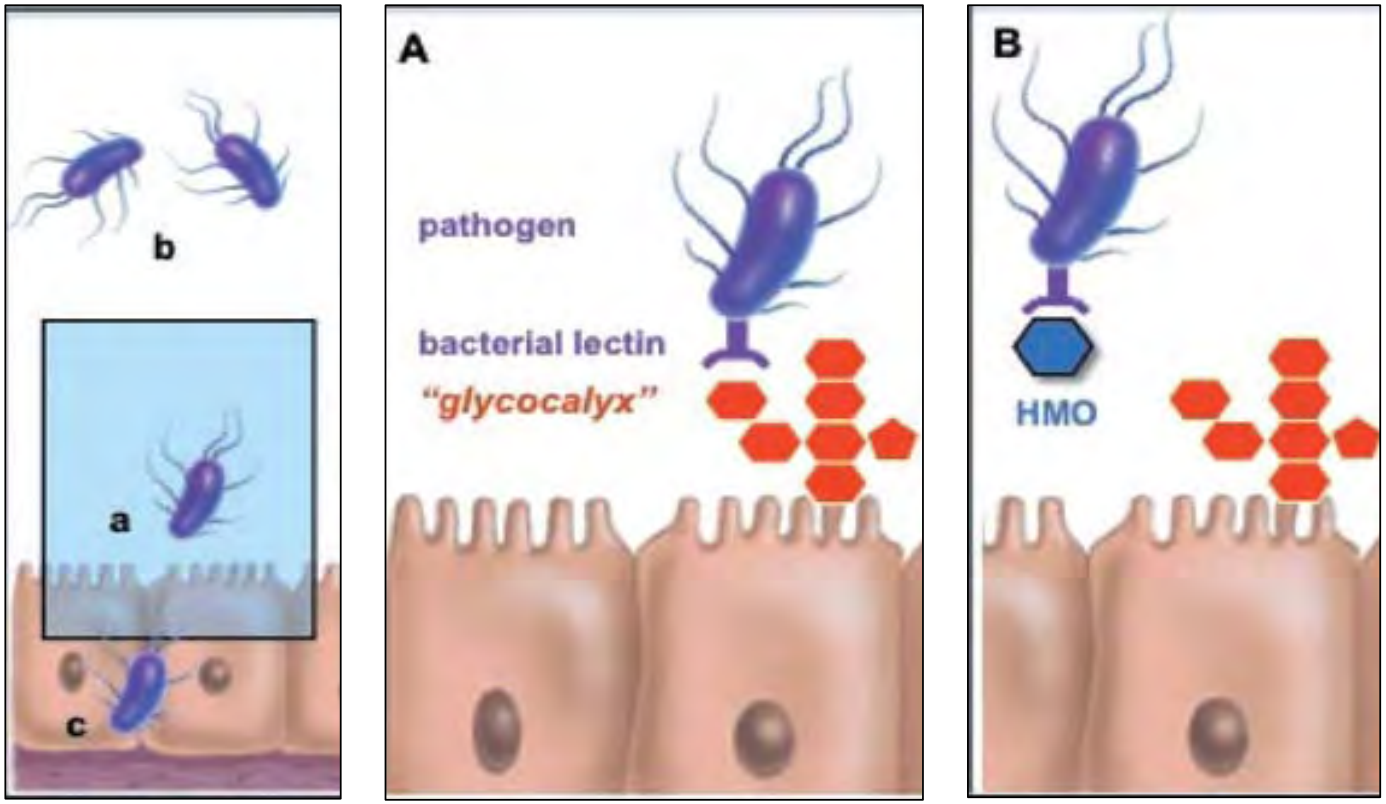
Muttermilch-Oligosaccharide



Steigerung der Anzahl oder Aktivität der Milchsäure- und Bifidobakterien

Bode. *Nutrition Reviews® Vol. 67(Suppl. 2):S183–S191*

Oligosaccharide als Rezeptoranaloga



Bode. 2009. *Nutrition Reviews® Vol. 67(Suppl. 2):S183–S191*

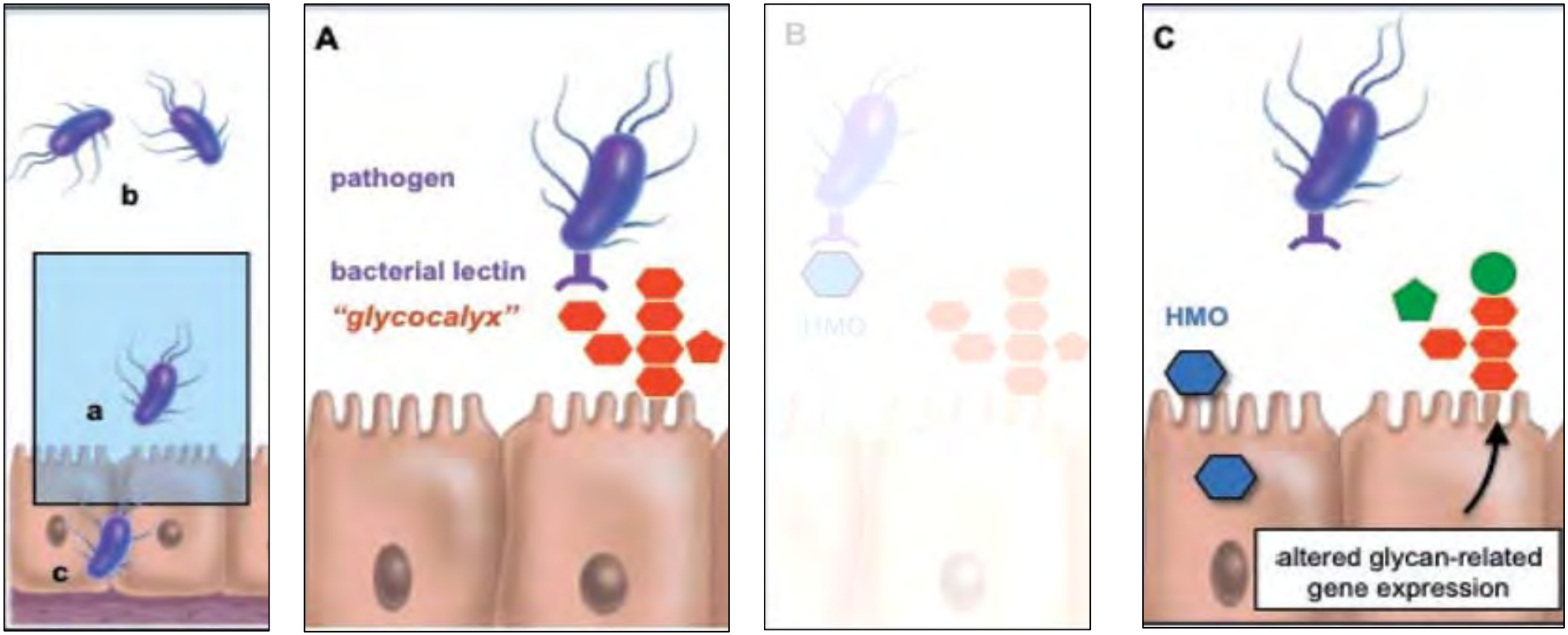
Oligosaccharide als Rezeptoranaloga

Receptors	Microorganisms
Mannose-containing glycoproteins	*Escherichia coli* (type 1 fimbriae)
Fucosylated oligosaccharides	*E. coli* (heat-stable enterotoxin)
Fucosylated tetra- and pentasaccharides	*E. coli*
Sialyl(α2-3)lactose and glycoproteins	*E. coli* (S-fimbriae)
Sialyl(α2-3)galactosides in mucins	*E. coli* (S-fimbriae)
Neutral oligosaccharides (LNT, neo-LNT)	*Streptococcus pneumoniae*
Gal(ß1-4)GlcNAc or Gal(ß1-3)GlcNAc	*Pseudomonas aeruginosa*
Fucα1-2Gal epitopes	*Candida albicans*
Sialyl-lactose	*Helicobacter pylori*
Sialyl-lactose	*Streptococcus sanguis*
Sialyl-lactose and sialylated glycoproteins	*H. pylori*
Sialylated glycoproteins (α2-3-linked)	*Mycoplasma pneumoniae*
Sialylated poly-*N*-acetyllactosamine	*M. pneumoniae*
Sialylated (α2-3)poly-*N*-acetylactosaminoglycans	*Streptococcus suis*
Sialyl(α2-6)lactose	Influenzavirus A
Sialyl(α2-3)lactose	Influenzavirus B
9-O-Ac of NeuAc(α2-3)R	Influenzavirus C

[a]For References, see 47.

Kunz et al. Annu. Rev. Nutr. 2000. 20:699–722

Oligosaccharide als Glykom- modifizierende Stoffe



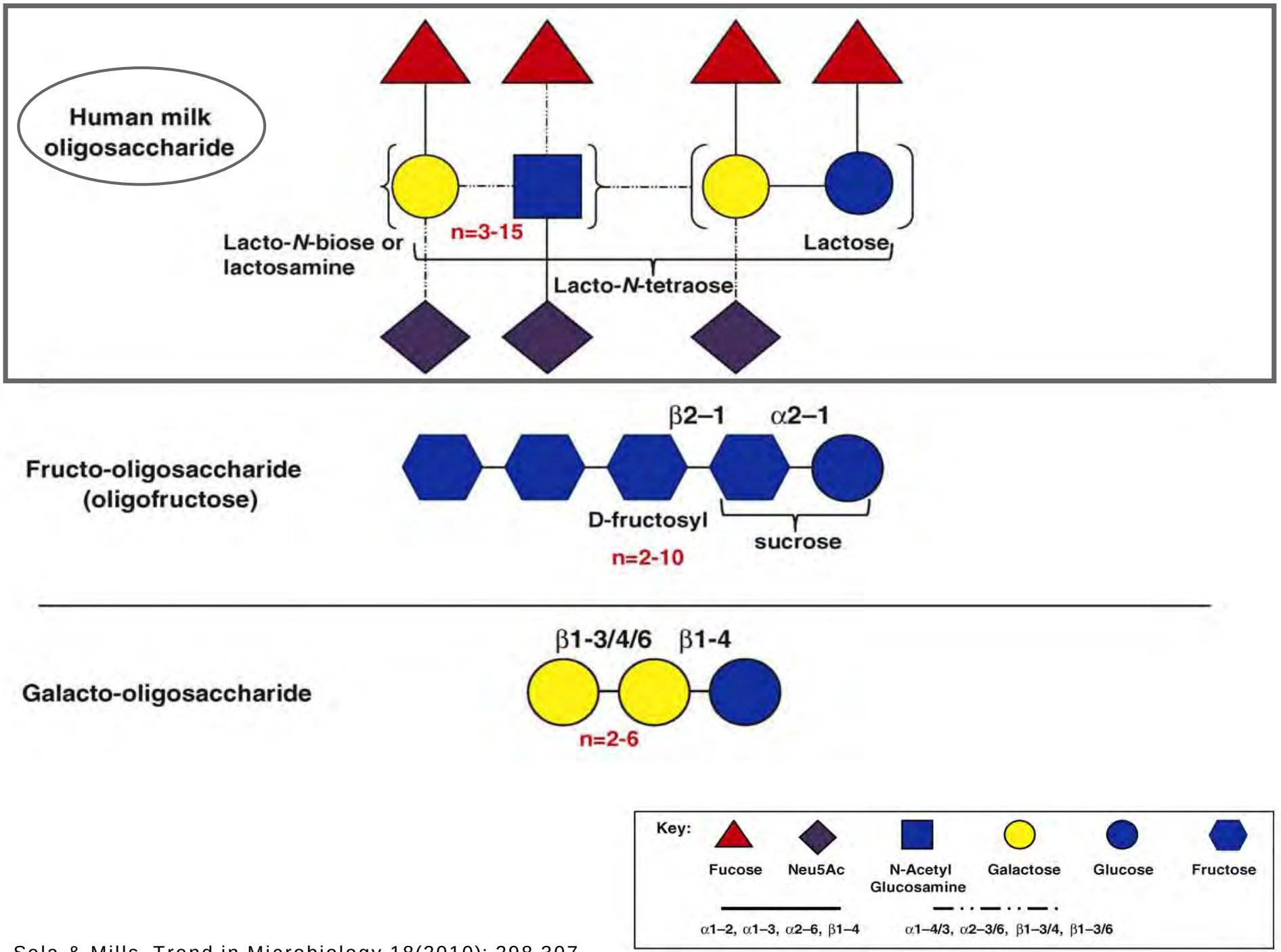
Bode. 2009. *Nutrition Reviews® Vol. 67(Suppl. 2):S183–S191*

Oligosaccharide in Frauenmilch und Kuhmilch

Component	Amount (g/liter)	
	Human milk[a]	Cow's milk[b]
Lactose	55–70	40–50
Oligosaccharides		
Lacto-*N*-tetraose	0.5–1.5	Traces
Lacto-*N*-fucopentaose I	1.2–1.7	—
Lacto-*N*-fucopentaose II	0.3–1.0	—
Lacto-*N*-fucopentaose III	0.01–0.2	—
Lacto-*N*-difucohexaose I	0.1–0.2	—
NeuAc(α2-6)lactose	0.3–0.5	0.03–0.06
NeuAc(α2-3)lactose	0.1–0.3	
NeuAc-lacto-*N*-tetraose a	0.03–0.2	Traces
NeuAc-lacto-*N*-tetraose c	0.1–0.6	Traces
$NeuAc_2$-lacto-*N*-tetraose	0.2–0.6	Traces
Oligosaccharides (total)	5.0–8.0	Traces

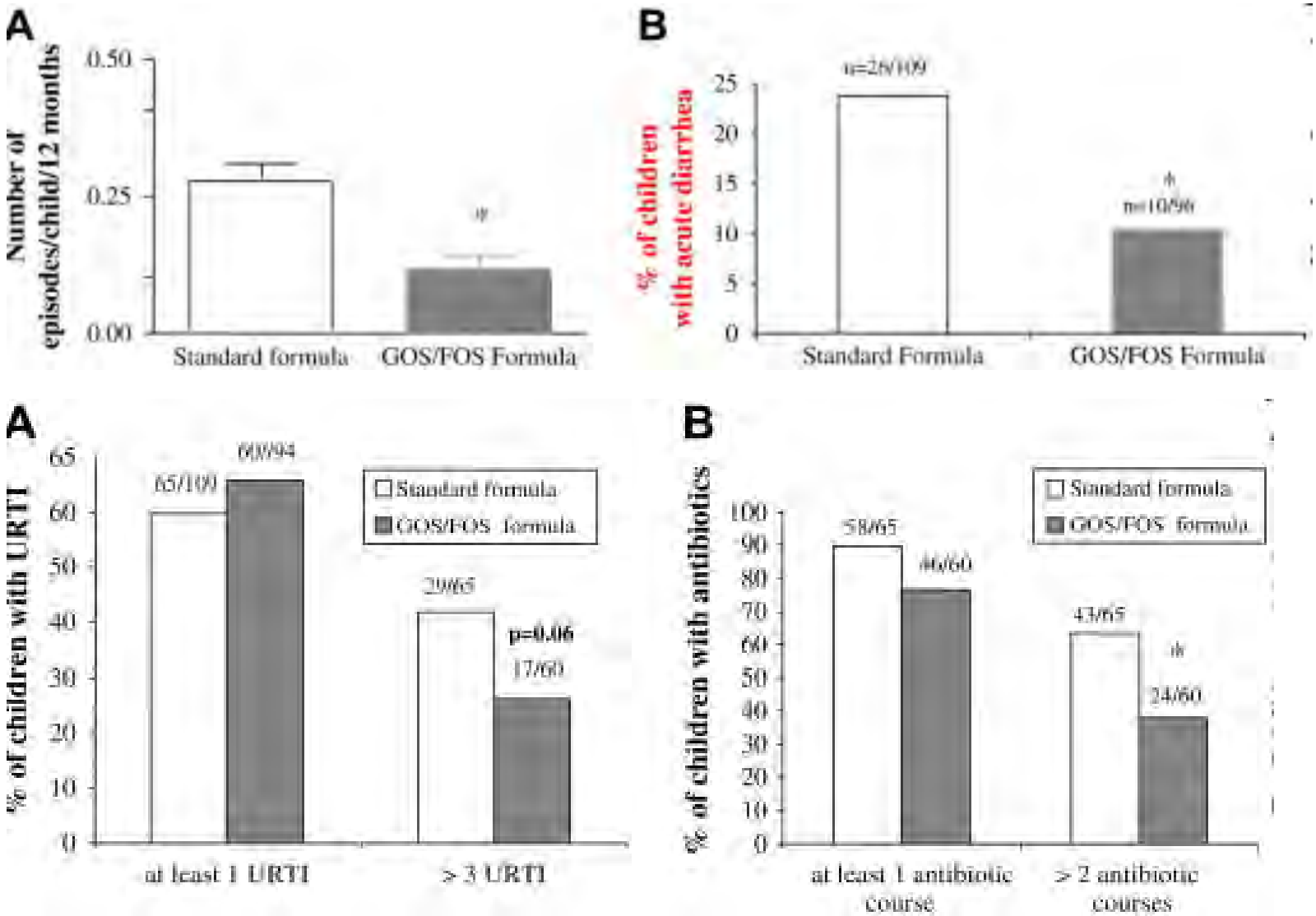
[a]Data are obtained from References 17 and 31.
[b]Data are obtained from A Kobata (1972, *Methods Enzymol.* 28:262) and J Parkkinen & J Finne (1987, *Methods, Enzymol.* 138:289).

Kunz et al,, 2000



Sela & Mills, Trend in Microbiology 18(2010): 298-307.

Wirkung von GOS/FOS-angereicherter Säuglingsnahrung auf die Häufigkeit von gastrointestinalen Infektionen und Atemwegsinfektionen bei nicht gestillten Säuglingen (n = 342)



E. Bruzzese et al. / Clinical Nutrition 28 (2009) 156–161

Prebiotic Supplementation in Full-term Neonates

A Systematic Review of Randomized Controlled Trials

Shripada Rao, MD, DM, FRACP; Ravisha Srinivasjois, FRACP; Sanjay Patole, DrPH, FRACP

Objective: To systematically review randomized controlled trials evaluating the efficacy and safety of prebiotic supplementation in full-term neonates.

Data Sources: Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, and CINAHL databases and proceedings of relevant conferences.

Study Selection: Eleven of 24 identified trials (n=1459) were eligible for inclusion.

Intervention: Trials comparing formula milk supplemented with or without prebiotics, commenced at or before age 28 days and continued for 2 weeks or longer.

Main Outcome Measures: Stool colony counts (bifidobacteria, lactobacilli, and pathogens), pH, consistency, frequency, anthropometry, and symptoms of intolerance.

Results: Six trials reported significant increases and 2 reported a trend toward increases in bifidobacteria counts after supplementation. Meta-analysis estimated significant reduction in stool pH in infants who received prebiotic supplementation (weighted mean difference, –0.65; 95% confidence interval, –0.76 to –0.54; 6 trials). Infants who receive a supplement had slightly better weight gain than did controls (weighted mean difference, 1.07 g; 95% confidence interval, 0.14-1.99; 4 trials) with softer and frequent stools similar to breastfed infants. All but 1 trial reported that prebiotic supplementation was well tolerated. In that trial, diarrhea (18% vs 4%; $P=.008$), irritability (16% vs 4%; $P=.03$), and eczema (18% vs 7%; $P=.046$) were reported more frequently by parents of infants who received prebiotic supplements.

Conclusions: Prebiotic-supplemented formula is well tolerated by full-term infants. It increases stool colony counts of bifidobacteria and lactobacilli and results in stools similar to those of breastfed neonates without affecting weight gain. Larger trials with long-term follow-up are needed to determine whether these short-term benefits are sustained.

Arch Pediatr Adolesc Med. 2009;163(8):755-764

Prebiotics in infants for prevention of allergic disease and food hypersensitivity (Review)

Osborn DA, Sinn JKH

THE COCHRANE COLLABORATION®

Objectives

To determine the effect of prebiotics given to infants for the prevention of allergic disease or food hypersensitivity.

Main results

Seven studies were eligible for inclusion. Only two studies reported an allergic disease outcome for 432 infants. Meta-analysis of the two studies found no significant difference in eczema, but significant heterogeneity was detected. Differences were potentially attributable to differences in infant risk, prebiotic formulation or measurement of eczema. Analysis of five studies reporting measures of infant growth found no consistent adverse effects.

Authors' conclusions

There is insufficient evidence to determine the role of prebiotic supplementation of infant formula for prevention of allergic disease and food hypersensitivity.

One small trial of prebiotic oligosaccharides with excess losses reported a reduction in eczema in high risk formula fed infants.

Osborn DA, Sinn JKH. Prebiotics in infants for prevention of allergic disease and food hypersensitivity. *Cochrane Database of Systematic Reviews* 2007, Issue 4. Art. No.: CD006474. DOI: 10.1002/14651858.CD006474.pub2.

Supplementation of Infant Formula With Probiotics and/or Prebiotics: A Systematic Review and Comment by the ESPGHAN Committee on Nutrition

*ESPGHAN Committee on Nutrition: *Christian Braegger, [+3]Anna Chmielewska, [†]Tamas Decsi, [‡]Sanja Kolacek, [‡‡]Walter Mihatsch, [§]Luis Moreno, [+3]Małgorzata Pieścik, [‖]John Puntis, [¶1]Raanan Shamir, [#]Hania Szajewska, [++2]Dominique Turck, and [††]Johannes van Goudoever*

Summary and interpretation of data on stool pH: Compared with controls, prebiotic supplementation of infant formula has the potential to reduce faecal pH.
The Committee notes that **whether this reduction in faecal pH per se is of benefit to the infants is currently not established.**

Summary and interpretation of data on stool frequency Limited available data suggest that prebiotic supplementation of infant formula has the potential to increase stool frequency.
However, **the clinical significance of this finding is unclear.**

Summary and interpretation of data on stool consistency Limited available data suggest that prebiotic supplementation of infant formula has the potential to soften stools.
However, **the clinical significance of this finding is unclear.**

JPGN 2011;52: 238–250)

Lactoferrin

Kuhmilch:	20 - 200mg/ L
Reife Frauenmilch:	1 - 2 g/ L

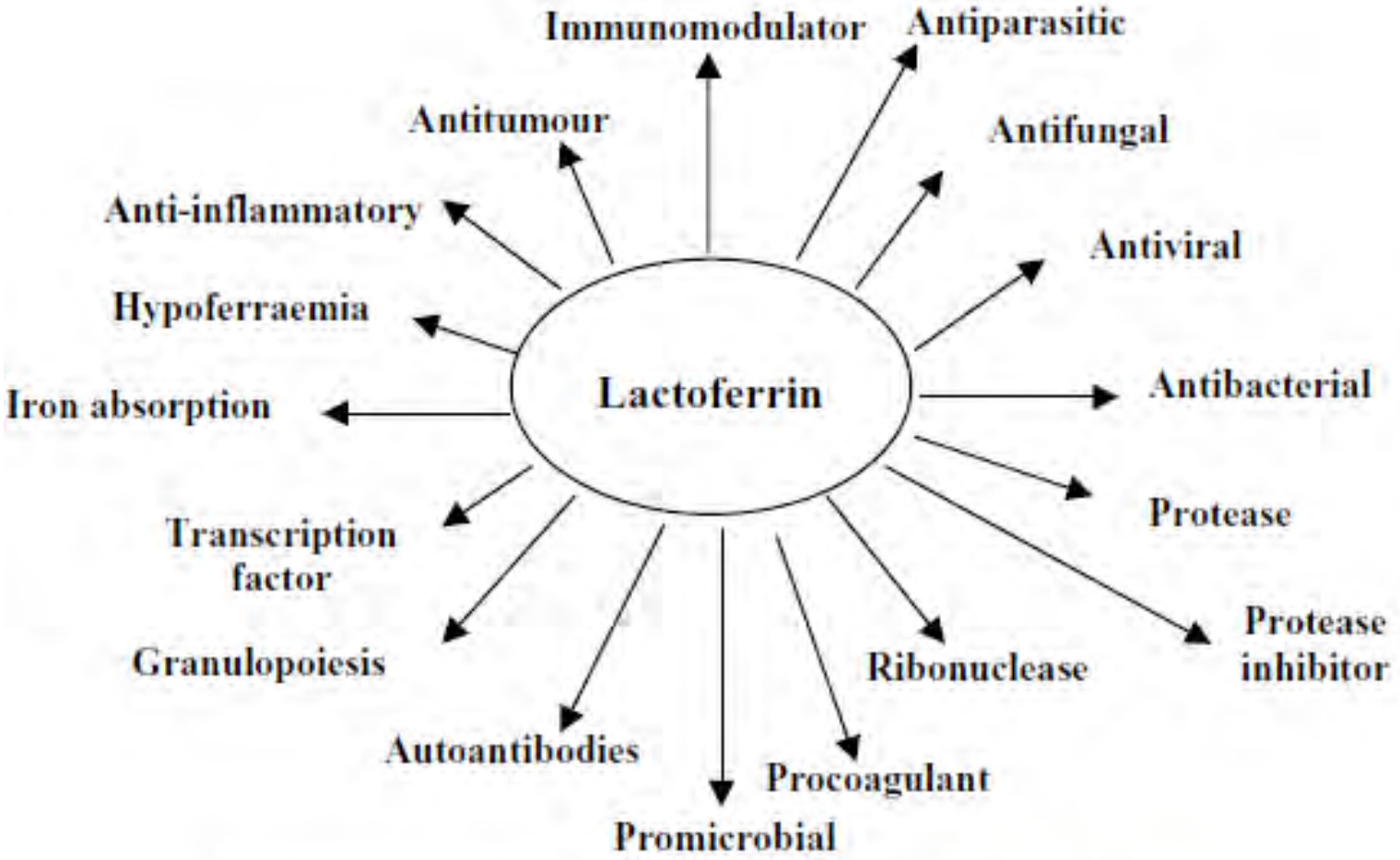


Fig. 2. Proposed roles of lactoferrin. Adapted from Brock (2002).

Fanoud & Evans, Molecular Immunology 40 (2003) 395–405

Wirkung von bovinem Lactoferrin auf die Infektionshäufigkeit bei nicht gestillten Säuglingen

Type of illness	**Interventionsgruppe** Episodes/infant-year	**Kontrollgruppe** Control Episodes/infant-year	
Diarrhea/gastroenteritis	1.31 (0–5)	1.35 (0–4)	
URI	3.92 (2–10)	4.00 (2–9)	
AOM	0.92 (0–3)	0.92 (0–3)	
LRTI	0.15* (0–1)	0.5* (0–2)	**(*P* < 0,05)**
Other	0.73 (0–2)	0.69 (0–5)	
Colic	1 (0–1)	2 (0–2)	

Laboratory test	Data at 9 mo Treatment	Control
Hemoglobin, g/dL*	12.1 (8.9–14.2) (n = 17)	11.8 (9.7–15.2) (n = 21)
Hematocrit, %*	37.1† (33.9–40.9) (n = 18)	35.4 (32.1–41.6) (n = 22)
MCV, fL*	79.8 (67–88) (n = 16)	77.9 (65–86) (n = 20)
Diphtheria, IU/Ml§	2.2 (0.1–11.2) (n = 26)	4.2 (0–18.8) (n = 26)
Tetanus, IU/mL§	3.6 (0.6–6.6) (n = 26)	3.4 (0.1–7.1) (n = 26)
H influenzae b, μg/mL§	15.6 (0.2–80) (n = 26)	18.1 (0.2–64) (n = 26)
Hepatitis B, 10 mIU/mL‖		

King et al. JPGN 44:245–251, 2007.

[Intervention Review]

Oral lactoferrin for the prevention of sepsis and necrotizing enterocolitis in preterm infants

Mohan Pammi[1], Steven A Abrams[2]

THE COCHRANE COLLABORATION®

Objectives

To assess the safety and effectiveness of oral lactoferrin in the prevention of sepsis and NEC in preterm neonates.

Reults

This review found one study conducted in Italy that used lactoferrin to prevent sepsis and NEC in preterm infants.

In this study, supplementing lactoferrin in the milk of infants weighing less than 1500 g reduced infection after 72 hours of life, but not NEC.

We recommend that the findings of this study be confirmed in future studies with respect to safety, dosing, duration and type of lactoferrin in preventing infections and NEC in the preterm babies.

PammiM, Abrams SA. *Cochrane Database of Systematic Reviews* 2011, Issue 10. Art. No.: CD007137.

Gestillte Säuglinge haben im Vergleich zu nicht gestillten…

- seltener Infektionen (gastrointenstinale und akute Mittelohrentzündung)
- ein geringeres Risiko für Zöliakie und atopische Erkrankungen
- ein geringeres Risiko für Diabetes Typ 1

- ein geringeres Risiko für die Entstehung von Übergewicht
- ein geringeres Risiko für Diabetes Typ 2

- niedrigeren Blutdruck ?
- geringere LDL- und Cholesterolkonzentrationen ?
- bessere kognitive Fähigkeiten ?

- Stillen fördert die emotionale Bindung zwischen Mutter und Kind

„Die beste Verbesserung der künstlichen Ernährung ist der Ersatz durch die natürliche Ernährung.“ (Keller, 1909)

BUNDESINSTITUT FÜR RISIKOBEWERTUNG

Risiken erkennen – Gesundheit schützen

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