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BREAST MILK COMPONENTS AND POTENTIAL INFLUENCE ON GROWTH

Maria Grunewald, Hans Demmelmair, Berthold Koletzko

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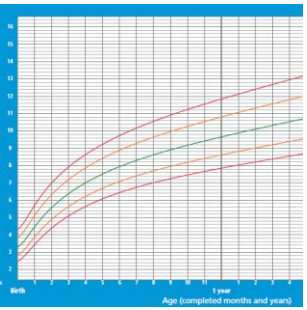

AGENDA

Breast Milk
Macronutrients in breast milk
- Carbohydrates
- Protein
- Lipids

Hormones
- Adiponectin
- Insulin

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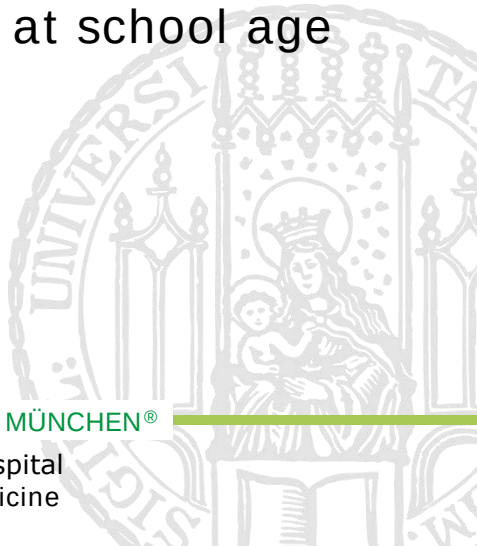
BREAST MILK

- exclusive breastfeeding widely recommended
  - optimal nutrition for health, growth and development
- a highly complex mixture of nutrients dissolved or emulsified in water
- human milk composition is influenced by:
  - genetic factors
  - term or preterm delivery
  - maternal nutrition
  - stage of lactation
  - time of day
  - foremilk or hindmilk
  - milk volume

BREASTFEEDING OR FORMULA FEEDING?

- first nutrition: choice between breast milk or formula

- Koletzko et al. 2005
  - breastfeeding is protective against later obesity
  - "growth acceleration hypothesis": early and rapid growth within first 2 years → programs metabolic profile → obesity risk
  - breastfeeding decreases the odds ratio for obesity at school age about 20%



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CASE: BABY M.D.

- healthy born male
  - birth weight: 4.5 kg
  - birth height: 54 cm
  - birth head circumference: 38 cm

  → 97th percentile

- 41st week of pregnancy, Cesarean section

- Parents: normal weight
- Mother: no gestational diabetes

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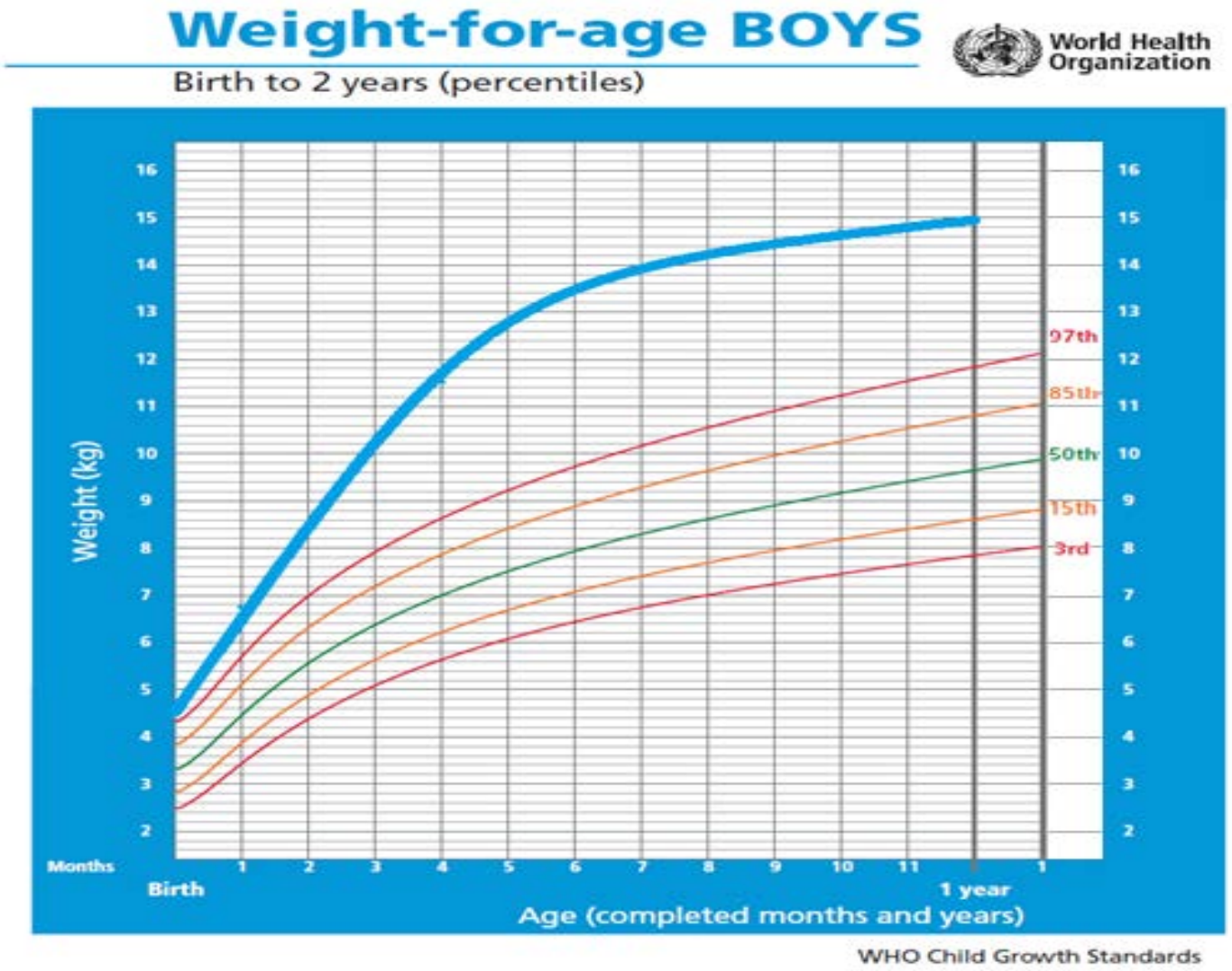
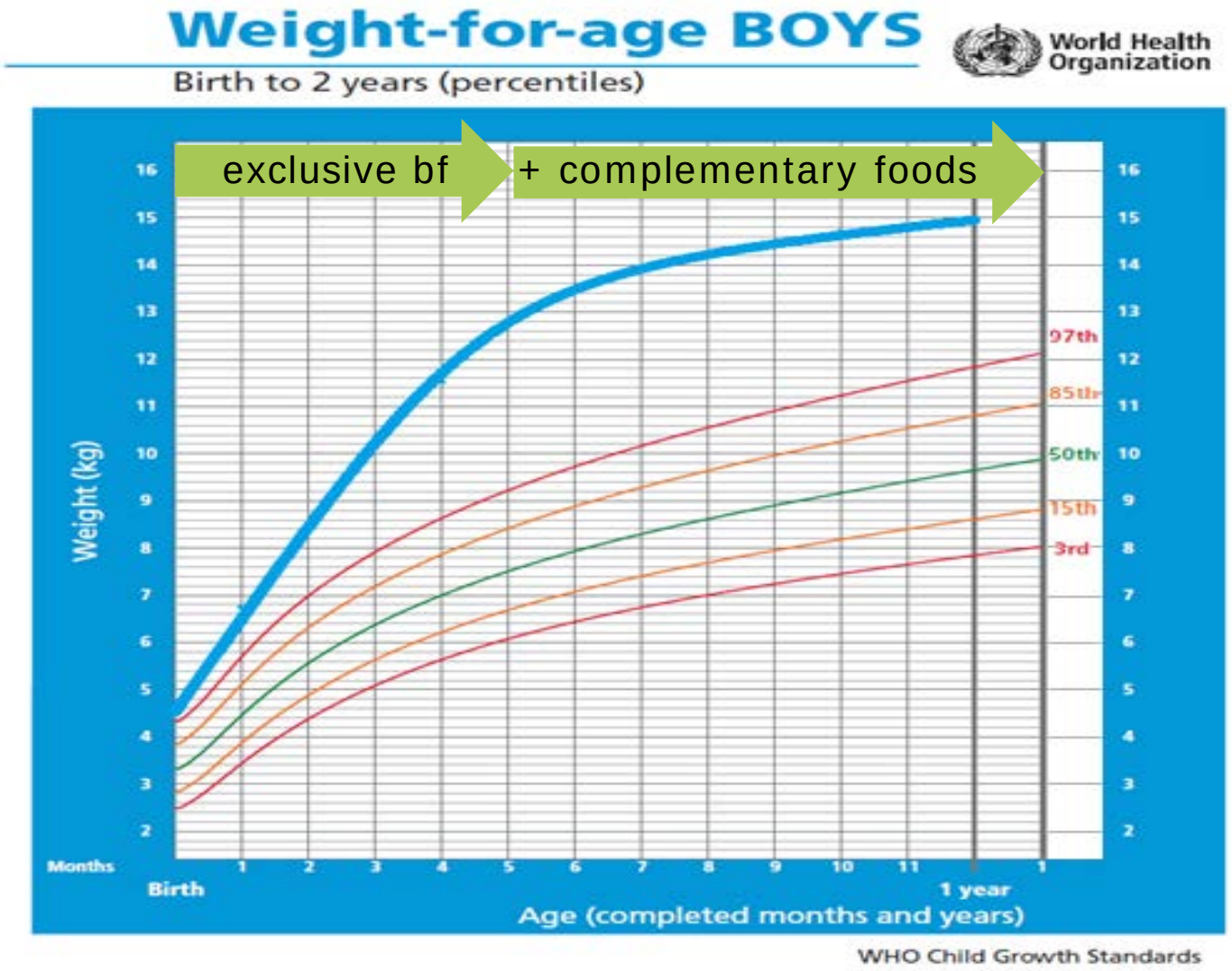

Weight-for-age BOYS
Birth to 2 years (percentiles)
World Health Organization
Weight (kg)
97th
85th
50th
15th
3rd
Months
Birth
1 year
Age (completed months and years)
WHO Child Growth Standards

CASE: BABY M.D.


Weight-for-age BOYS
Birth to 2 years (percentiles)
World Health Organization
exclusive bf
+ complementary foods
97th
85th
50th
15th
3rd
Weight (kg)
Months
Birth
1 year
Age (completed months and years)
WHO Child Growth Standards

DID HIS MOTHER'S BREAST MILK LEAD TO THE EXCESSIVE WEIGHT GAIN DURING THE FIRST MONTHS OF BABY M.D.?

WHICH COMPONENTS IN MILK DO PLAY A ROLE IN REGULATING GROWTH, DEVELOPMENT AND RISK OF OBESITY?

MACRONUTRIENTS IN BREAST MILK

Carbohydrates
Protein
Lipids

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BREAST MILK
COMPOSITION OF 100 ML MILK

nutrient	mature milk	changes one year postpartum*	M.D. (hindmilk, one year postpartum)
calories [kcal]	50 - 115	-	69
fat [g]	1.84 – 8.9	-	4.0
carbohydrates [g]	6.42 – 7.65	-	6.1
protein [g]	0.63 – 1.43	decrease	1.4

Handbook of milk composition (adapted from Michaelsen et al. 1991)

*Mitoulas et al. 2002, Shehadeh et al. 2006

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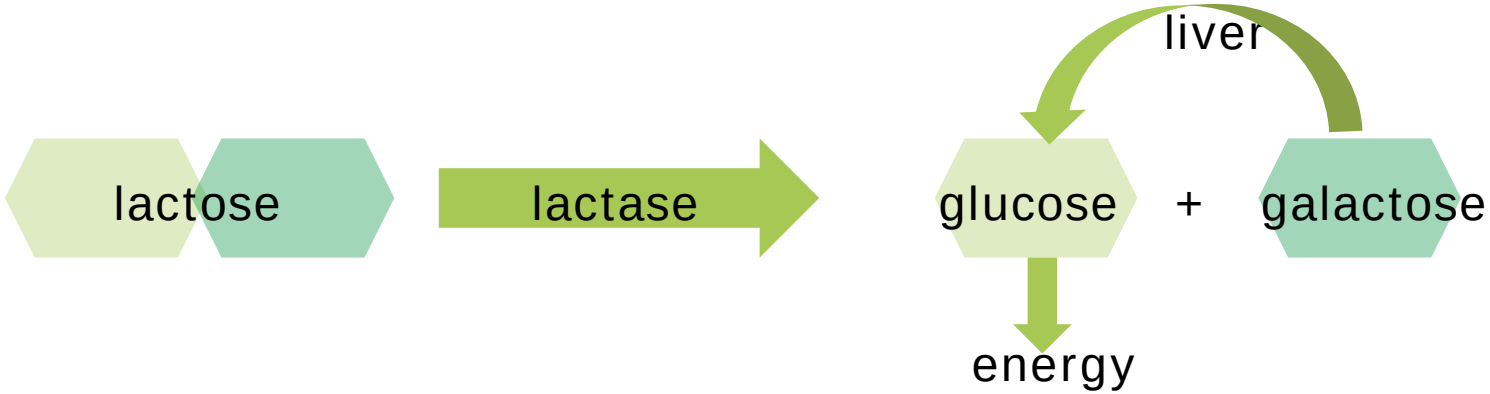
CARBOHYDRATES

- most constant macronutrient in milk
- mainly lactose, very low levels of glucose, galactose



- human milk oligosaccharides (HMOs)
  - 3-32 sugars, very heterogenic
  - prebiotic → promote growth for probiotic bacteria in child‘s gut (Dai et al., 2000)

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NITROGENOUS COMPOUNDS

- protein (whey and casein fraction)
- NPN fraction (~20-25%), like urea, creatine, amino acids, carnitine
- Early High Protein hypothesis: (Koletzko et al. 2005)

Protein

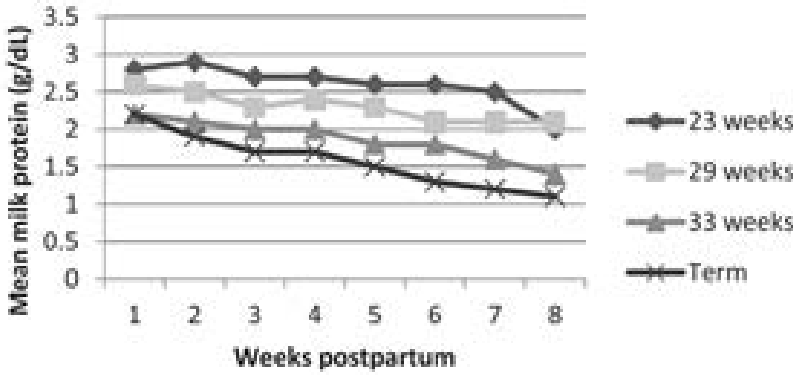
↓

Insulin, IGF-I

↙ ↘

Early growth (first 2 years) | Adipogenic activity (adipocyte differentiation)

- milk of preterm mothers has higher protein content:



Milk protein concentrations, comparing mothers who delivered preterm and term, by gestational age at delivery and weeks postpartum (Ballard et al., 2013)

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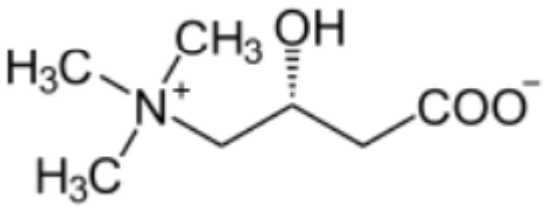
CARNITINE



- function: transports long chain FA across mitochondrial membrane for FA oxidation
- content in breast milk: highest values after 2 weeks postpartum (98.2 µmol/l), than decrease (4 months: 62.3 µmol/l)
- important for newborns because of limited endogenous carnitine synthesis (low gamma butyrobetaine hydroxilase)

µmol/l	Range (1-10m pp) (Mitchell et al., 1991)	M.D. Foremilk	M.D. Hindmilk
total	28.01 – 72.18	49.3	31.5
free	22.68 – 56.25	39.2	22.3

LIPIDS AND FATTY ACID COMPOSITION

- 98% of the milk fat as TAG
- crucial for the newborn: up to 55% of the calories are supplied as fat
- most variable milk component:
  - hindmilk: significant higher fat content (Mitoulas et al. 2002)
  - lower content in night/morning than in afternoon/evening milk
- perinatal LC-PUFA status may influence neurological development, immune system

fatty acid (%)	12 m postpartum (mean ± SEM, adapted from Mitoulas et al. 2003)	M.D.
C10:0	1.14 ± 0.026	1.39
C12:0	6.53 ± 0.169	7.89
C14:0	9.27 ± 0.220	8.96
C16:0	24.15 ± 0.222	21.77
C16:1n-7	2.32 ± 0.073	1.47
C18:0	8.43 ± 0.267	7.51
C18:1*n*-7	1.45 ± 0.043	1.47
C18:1*n*-9	30.21 ± 0.261	31.77
C18:2*n*-6	9.28 ± 0.345	13.15
C18:3*n*-3	0.79 ± 0.031	0.93
C20:0	0.66 ± 0.014	0.21
C20:4*n*-6 (AA)	0.34 ± 0.006	0.44
C22:6*n*-3 (DHA)	0.18 ± 0.005	0.20

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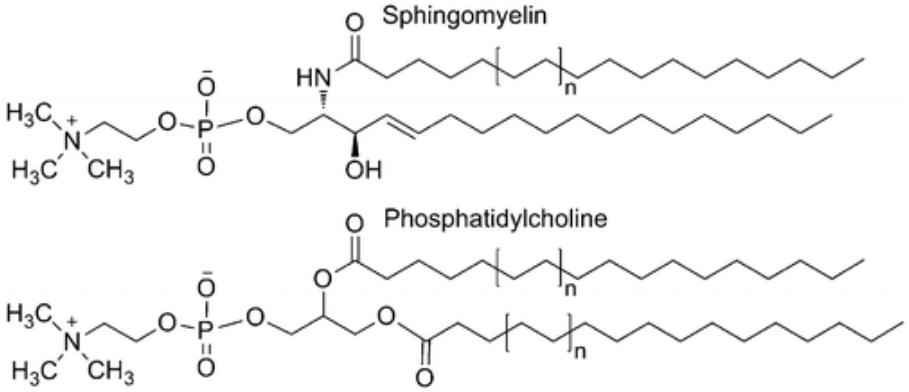
PHOSPHOLIPIDS

- Sphingomyelin, Phosphatidylcholine
  - Membrane constituent
  - Regulation of cell growth, differentiation, apoptosis
  - neonatal gut maturation



µmol/l	PC	PC M.D.	SM	SM M.D.
foremilk	**115.7 ± 5.5**	**65.7**	**163.4 ± 11.3**	**63.3**
hindmilk	**179.5 ± 10.0**	**133.4**	**206.4 ± 9.4**	**147.0**

(mean ± SEM, Data adapted from Zeisel et al. 1986)

HORMONES IN BREAST MILK

Adiponectin
Insulin

ADIPONECTIN

- reduced serum levels in **obese** adults (although produced by adipose tissue)

- functions:
  - regulates lipid and glucose metabolism
  - improves insulin sensitivity
  - increases fatty acid oxidation
  - anti-inflammatory

- Mouse: adiponectin receptor 1 in small intestine → absorption of breast milk adiponectin into blood (Zhou et al. 2005)

ADIPONECTIN

- breast milk adiponectin:
  range between 0.8-110 ng/ml
  (Ozarda et al. 2012)
- higher concentration than other milk adipokines

- average after one year:
  25.7 ± 1.4 ng/ml (Bronsky et al. 2011)

- M.D.:
  adiponectin content 35 ng/ml

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- Woo et al. 2009:
- breast milk adiponectin is associated with lower infant weight-for-age and WA Z-score during the first six months of life

- Weyermann et al. 2007:
- high levels of breast milk adiponectin were associated with higher risk for overweight at 2 years of age

→ different results

INSULIN

- key hormone in blood glucose homeostasis

- orally administered breast milk insulin promotes gut maturation (Shehadeh et al. 2003)
- breast milk insulin is increased in obese and overweight mothers (pre-pregnancy BMI) (Ahuja et al. 2011; Ley et al. 2012)

- Insulin mean ± SEM: 15.64 mU/l ± 1.03 (Whitmore et al 2012)
- M.D.: 16.65 mU/l

INSULIN

- Fields et al. 2012
- breast milk insulin is negatively associated with infant weight and lean mass (not fat mass)

- Plageman et al. 2002
- increased concentration of breast milk glucose and breast milk insulin of diabetic mother predict obesity in adulthood

→ different results

CONCLUSION

- for many milk components the influence on growth and development is still not surely known
- sometimes the studies lead to contrary results

- M.D. was growing very fast – just because high protein?
  - influence of higher adiponectin?
  - influence of lower saturated FA, polar lipids?

→single case does not say enough about the potential influence growth

→more information is needed

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PREVENTCD STUDY

- European research project to prevent coeliac disease, startet January 2007
- more than 1000 children in 10 study centers from 7 countries
- Intervention study: influence of dietary history in prevention of CD

- 600 breast milk samples from 5 countries from M1-3 and M4
- 250 matching serum samples

- available growth data up to 6 years of age

- analysis of milk components

ACKNOWLEDGEMENTS

EARLYNUTRITION
Long-term effects of early nutrition on later health

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