Course report – questions and guide lines:

Supplementary questions:

1) Find and explain at least one MedLine scientific paper (animal or human study) that investigates an aspect (preferably related to nutrition) of your chosen organ/body function for newborns.
2) Find and explain at least one MedLine scientific paper (animal or human study) that investigates an aspect of your chosen nutrient group related to newborns.
3) What are the major physiological transitions that occur at birth?
4) Is gastrointestinal, muscle/fat proportion and nutrient metabolism immature at birth? What about other nutrient-relevant organs/tissues (e.g. kidneys, lungs, liver, immunology, endocrinology)?
5) How does colostrum differ from milk? What is special about milk proteins? Milk carbohydrate? Milk fats? Milk minerals? Milk vitamins? What else of neonatal health relevance is present in milk? Is milk components and contents similar among species? Does the digestibility (or bioavailability) of milk nutrients differ from that in vegetable diets? Breast milk versus cows milk or formula?
6) What are the major nutritional differences between mother´s milk and artificial milk replacers? Why is mothers milk particularly important for preterm/IUGR infants? Supplements needed? What is the optimal postnatal growth pattern for preterm/IUGR infants? How can it affect later disease risk?
7) How does breast-feeding, cardiovascular, lever, gastrointestinal factors affect neonatal jaundice?
8) Are there any known nutritional determinants of preterm labor? Of SGA (small for gestational age) infants? How does preterm/IUGR infants differ from normal infants regarding organ and body tissue development?
9) Why is parenteral nutrition not always an ideal solution for infants that do not tolerate oral nutrients? How is a parenteral nutrient solution constructed for preterms to optimize health outcome & growth?
10) How is the intestinal microflora important for neonatal nutrition? Is it diet-dependent? What is probiotics – and prebiotics? Can milk act as a pre- and probiotic diet? Does milk affect immunity?

Course report suggestions

Possible points to incllude in course report:

Organ systems/body functions:
a: Gastrointestinal (motility and passage of meconium, colic, jaundice problems, growth, development, colostrum versus milk versus formula, permeability, microbes, preterm, amniotic fluid ingestion)
b: Endocrine/Immunity (milk/colostrum endocrine factors, glucose tolerance, GLP-2 effects, Growth hormone/IGF-1 levels, immunoglobulin absorption, endogenous immunity, preterm/IUGR, cortisol)
c: Energy & nutrient metabolism (BMR changes, thermoregulation, method of birth, preterm metabolism, IUGR, energy needs, protein needs, growth rates, kidney function, liver function)
d: Liver/kidney (liver role in jaundice, bile secretion, gluconeogenesis role to stabilize blood glucose – especially in preterms, kidney problem in preterms fed high protein levels, gluconeogenesis in kidney cells)

Nutrient groups:
a: Protein (casein/whey/soy proteins, immunoglobulins, protein for growth, bone, muscle, preterm milk, preterm formulas, hydrolysis of large proteins, digestion, allergies, growth rate, use of protein for energy in sub-caloric preterms)
b: Carbohydrate (sugar versus fiber, lactose intolerance, fiber components, FOS, GOS, lactose in various diets, formula, breast milk, galactose liver problem,)
c: Fat (MCTs, hydrolysis, fat digestion, PUFAs for newborns, cholesterol, restriction of fat for newborns?, % energy from fat in various diets)
d: Bioactives (lactoferrin in milk, hormones in milk, oligosaccharides, immunological components)
e: Milk (breast versus formula, nutriensts, growth factors, immunology, microbiology, energy needs, protein levels, sub-fasting neonatal jaundice, colostrum versus mature milk, raw cows milk,)

Course report suggestions

Possible points to incllude in course report:

Organ systems/body functions:
a: Gastrointestinal (motility, growth, development, colostrum versus milk versus formula, permeability, microbes, preterm)
b: Endocrine/Immunity (milk/colostrum endocrine factors, glucose tolerance, GLP-2 effects, Growth hormone/IGF-1 levels, immunoglobulin absorption, endogenous immunity, preterm/IUGR, cortisol)
c: Energy & nutrient metabolism (BMR changes, thermoregulation, method of birth, preterm metabolism, IUGR)

Nutrient groups:
a: Protein (casein/whey/soy proteins, immunoglobulins, protein for growth, bone, muscle, preterm milk, preterm formulas)
b: Carbohydrate (sugar versus fiber, lactose intolerance, fiber components, FOS, GOS)
c: Fat (MCTs, PUFAs for newborns,)
d: Bioactives (lactoferrin in milk, hormones in milk, oligosaccharides, immunological components)

CASE study: Immature gut & nutrition

Following birth, preterm babies at Rigshospitalet have severe digestive problems. Use research to solve the problems. You have unlimited ressources to work with <u>pigs</u> as a model animal. Suggest 3 experiments to <u>understand</u> and/or <u>solve</u> the problem? Indicate specific questions/methods/expected results.


Nutrition of an immature gut?

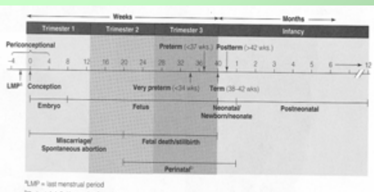
How to <u>understand</u> and/or <u>solve</u> the problem?

Q: Mode of birth?
Exp: Caesarean section versus vaginal birt
Anal: Hormonal levels, gut microbiology?


Lecture - overview

-Time line overview (Brown 4.1)
-Mortality (Table 4.1 + Fig 4.2, Table 4.2 Table 4.3 Brown)
- Famous preterms (own transparancy)
- Risk of multifetal pregnancies – just more of the same risks Table 5.14
- The fundamental changes in nutrient delivery that occurs at birth, the placenta, milk and the gut, microflora and lungs
- Colostrum, immunology, tissue growth, microbiasl protection,
- Delivery method
- Preterm deliveries
- Hypothermia in newborns
- Milk nutrient composition (Table 6.3). Compare with pig milk and colostrum (Sangild & Xu, 2004)
- Milk contents of various bioactives
- The special benefits of breast milk can be seen more clearly following preterm delivery
- Special metabolism in newborns (??, high metabolic rate, high proprtion of internal organs and muscle…) Old transp. Animal studies….
-Catch-up growth. Time frame and consequences (228)
-Table 9.1 Special concerns of preterms
-Table 9.2 Preterm and term formulas, Table 8.6 formulas versus milk.

Time and terms, pre- and postnatally



[a]LMP = last menstrual period
[b]Perinatal definition varies from 20 to 24 weeks gestation to 7 to 28 days after birth.

Illustration 4.1 Time-related terms before, during, and after pregnancy.

Infant mortality:

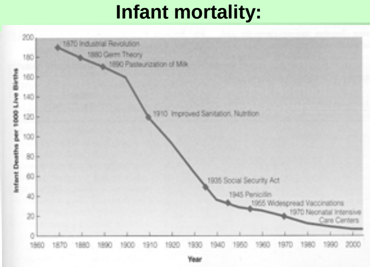


Illustration 4.2 Chronology of events related to declines in infant mortality in the United States.

Key Nutrition Concepts

- The dynamic growth experienced in infancy is the most rapid of any age.
- Inadequate nutrition in infancy, however, leads to consequences that may be lifelong, harming both future growth and development.

Energy stores in newborn infants and animals

(Fletcher, 1992)

Species	Weight birth (kg)	Fat store (g/kg)	Muscle glycogen (g/kg)	Liver glycogen (g/kg)
Humans	3.5	160	7.5	3.8
Guinea P.	0.1	110	4.5	5.5
Rabbit	0.05	58	2.3	2.7
Sheep	4.5	30	8.8	2.2
Pig	1.3	11	20.9	2.1
Rat	0.005	11	1.8	5.8

Key Nutrition Concepts

- Early nutrition services and other interventions can improve long-term health and growth among infants born with a variety of conditions.
- The number of infants requiring specialized nutrition and health care is increasing due to the improved survival rates of small and sick newborns.
- Infants who are born preterm or who are sick early in life often require nutritional assessment and interventions that ensure they are meeting their nutritional needs for growth and development.

Benefits of Breastfeeding

- Benefits for mothers
- Benefits for infants
  - – nutritional benefits
  - – immunological benefits
  - – cognitive benefits
  - – reduced morbidity
  - – socioeconomic benefits
  - – analgesic effects

Key Nutrition Concepts

- Human milk is the best food for newborn infants for the first year of life or longer.
- Feeding infants early in the post delivery period whenever possible is important to successful breastfeeding.
- Maternal diet does not significantly alter the protein, carbohydrate, fat and major mineral composition of breast milk, but it does affect the fatty acid profile and the amounts of some vitamins and trace minerals.

Nutrient contents of colostrum/milk (pigs)

(Darragh & Moughan, The Lactating Sow)

Table 1.1. The major components of sow's colostrum and milk

Component	Colostrum[1]	Mature Milk[2]
Total Solids	24.8	18.7
Protein[4]	15.1	5.5
Non-protein Nitrogen	0.3	0.3
Lactose	3.4	5.3
Fat	5.9	7.6
Ash	0.7	0.9

[1] Taken immediately postpartum.
[2] Classified as milk samples collected between 14 and 21 days postpar

Table 1.2. The protein content of sow's colostrum and mature milk

	Colostrum[1]	Mature Milk[2]
Total Protein[4] (g/100 g milk)	15.14	5.47
Casein (g/100 g milk)	1.48	2.74
Whey (g/100 g milk)	14.75	2.22
Serum albumin (mg/ml milk)	15.79	4.61
IgG[5] (mg/ml milk)	95.6	0.9
IgA[6] (mg/ml milk)	21.2	5.3
IgM[7] (mg/ml milk)	9.1	1.4
Lactoferrin ((g/ml milk)	1200	<100

[1] Taken immediately postpartum.
[2] Classified as milk samples collected between 14 and 21 days postpartum.

Milk nutrients in different species: (Hand et al., 2000)

[illegible]

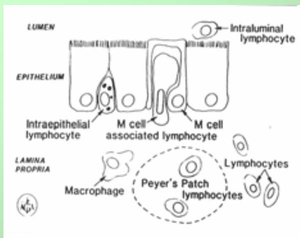
"Bioactive proteins" in milk (R. Zabielski, J.Anim.Feed Sci. 7 (suppl.), 1998)

Hormones	prolactin, somatostatin, growth hormone, growth hormone-releasing factor, calcitonin, insulin, thyroxin, oxytocin, melatonin, ANP, ET-1
Regulatory peptides	gastrin, bombesin, CCK, VIP, neurotensin, delta sleep inducing peptide
Growth factors	EGF-I and -II, IGF, nerve growth factor, TGF-α and -β, platelet-derived growth factor, CDGF
Mammary gland inhibitors	mammastatin, MDGI, MAF
Enzymes	amylase, serum-sensitive lipase
Immunoglobulins	IgA, IgG, IgM
Glycoproteins	lactoferrin, milk mucins (e.g., mannose containing glycoproteins), adhesion molecules
Protein precursors	bioactive substances resulting from the digestion of milk proteins
Casein	α and β-casein fragments – casomorphins, caseinophosphopeptides, immunopeptides, casokinins κ-casein fragments – casoxins, casoplatenins
Whey protein	α-lactoglobulin fragments – α-lactophorins β-lactoglobulin fragments – β-lactophorins
Lactoferrin	lactoferroxins
Lactoalbumins	lactorphins

Immune components in human milk

- Leucocytes
  - – B lymphocytes
  - – Macrophages
  - – Neutrofiles
  - – T lymphocytes*
- Secretory immunoglobulin A (SIgA)
- Oligosacharides
- Bifidus factor
- Lysozyme
- Lactoferrin
- Gamma-interferon*
- Nucleotides*
- Cytokines*

The intestinal immune system: (Shils et al.)



The biggest population of immune cells within the body

Breast milk & allergy/intolerance
(Brown, 188-189)

Allergy:
- Exaggerated immunological response to intact foreign food proteins
- Breast milk protective
- Interactions with resident microflora

Intolerance:
- Non-immunolocal negative response to food
- Spices, odors, oils
- Lactose

Lactase deficiency: (Shils et al)

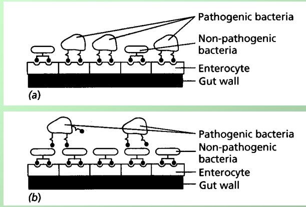
TABLE 74.3. PREVELANCE OF LACTASE NONPERSISTENCE IN VARIOUS ETHNIC GROUPS

GROUP	PREVALENCE (%)
Northern European	2–7
White (United States)	6–22
Central European	9–23
Indian (Indian subcontinent)	
Northern	20–30
Southern	60–70
Hispanic	50–80
Ashkenazi Jewish	60–80
African-American	60–80
Black African	70–95
Native American	80–100
Asian	85–100

Adapted from Srinivasan R, Minocha A. When to suspect lactose intolerance: symptomatic, ethnic, and laboratory clues. Postgrad Med 1998;104:109–23, with permission, copyright 1998 The McGraw-Hill Companies; data also from Sahi T. Genetics and epidemiology of adult-type hypolactasia. Scand J Gastroenterol 1994;29[Suppl 202]:7–20.

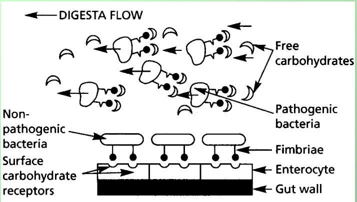
Classical ”nutri-genomics”

Probiotics – mode of action (McDonald et al., Fig.25.1)



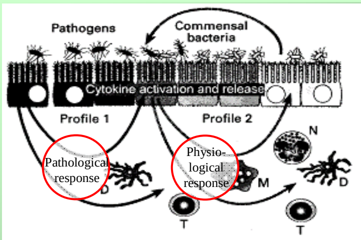
a) Blandet mikrobiel population med væsentlig tilhæftning af patogener
b) Patogeners tilhæftning er ”udkonkurreret” af ”kommensaler” (probiotika)

Pre-biotics – mode of action in the intestine
(McDonald et al. kap.25, Fig.25.3)



Oligosaccharides (FOS, TOS, MOS, GOS) may acts to bind microbial lectins and thus prevent mucosal colonization by pathogens, and/or enhance the growth of beneficial (commensal) bacteria (e.g. lactobacilli, bifidobacteria)

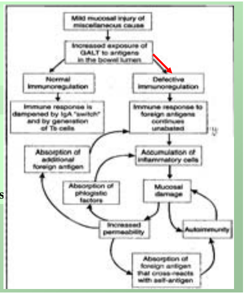
Gut bacteria and immune system ”cross-talk”
(Kelly & Coutts, 2000, Proc.Nutr.Soc. 59)



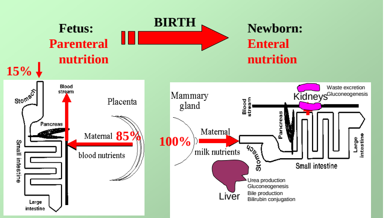
Gut atrophy: effects on absorption & immunology
(Hand et al., 2000, Ch.22)

GALT
(gut-associated lymphoid tissue)

After injury there is a lack of GALT to control immunological responses

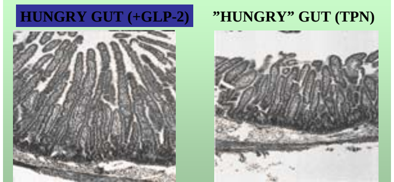


The nutritional transition at birth:



The newborn intestine depends on nutrition

HUNGRY GUT (+GLP-2) ”HUNGRY” GUT (TPN)



American Journal of Physiology 279, 2000

Infants at Risk

- Low birthweight infants
- Preterm infants born before 34 weeks of gestation
- Infants born with consequences of abnormal development
- Infants at risk for chronic health problems
- Families of infants with special health care needs

Weight, age at birth and mortality

Table 4.3 Range of birthweights by gestational age, U.S.[1]

BIRTHWEIGHT Pounds (lb) and Ounces (oz)	BIRTHWEIGHT Grams	WEEKS GESTATION	INFANT MORTALITY RATE
<1 lb 2 oz	<500	<22	846
1 lb 2 oz–2 lb 3 oz	500–999	22–27	316
2 lb 3 oz–3 lb 5 oz	1000–1499	27–29	62
3 lb 5 oz–4 lb 6 oz	1500–1999	29–31	28
4 lb 6 oz–5 lb 8 oz	2000–2499	31–33	12
5 lb 8 oz–6 lb 10 oz	2500–2999	33–36	4.6
6 lb 10 oz–7 lb 11 oz	3000–3499	36–40	2.4
7 lb 11 oz–8 lb 13 oz	3500–3999	40+	1.7
8 lb 13 oz–9 lb 14 oz	4000–4499	40+	1.5
9 lb 14 oz–11 lb	4500–4999	40+	2.5
>11 lb	5000+	40+	—

Good prospects - beyond 28 weeks, beyond 1 kg.

Diseases and low birth weight:

Table 4.14 Diseases and other conditions in adults related to smallness or thinness at birth[26,47]

Allergies	Mood disorders
Autoimmune diseases	Obesity
Bronchitis	Ovarian cancer
Cardiovascular disease	Polycystic ovary syndrome
Decreased bone mineral content	Schizophrenia
Gestational diabetes	Short stature
Hypertension	Stroke
Kidney disease	Subfertility in males
Metabolic syndrome	Suicide
	Type 2 diabetes

"Developmental Origins of Adult Disease" – "Barker Hypothesis"

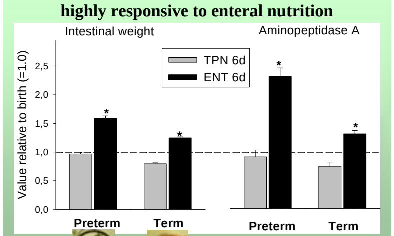
Perinatal problems in famous people

(TNK Raju, Neonatal & Perinatal Medicine, 1983)

Navn	Fødsel årstal	Problem v/fødsel	IQ ca.
Johannes Kepler	1571	7 mdr. graviditet	160
Isaac Newton	1642	Vægt: 1,5 kg	170
F.M. de Voltaire	1694	Ingen vejrtrækning	180
Johann Goethe	1749	Tilsynelad. dødfødt	200
Winston Churchill	1874	7½ mdr. graviditet	-
Pablo Picasso	1881	Tilsynelad. dødfødt	-

Perinatal problems do not always lead to poor mental/intellectual skills!

The preterm pig intestine is highly responsive to enteral nutrition



(J. Nutr. 132, 2673-2681, 2002)

Key Nutrition Concepts

- Nutrient requirements of term newborns have to be modified for preterm infants.
- Knowing the needs of sick and small newborns results in greater understanding of the complex nutritional needs of all newborns and infants.
- Changing feeding practices, such as the care of infants outside the home and the early introduction of foods, markedly affect nutritional status of infants.

Key Nutrition Concepts

- Human milk is the preferred feeding for all premature and sick newborns with rare exceptions.
- Breastfeeding women need consistent, informed, and individualized care in the hospital and at home after discharge.

Preterm & term milk – differences?

Table 8.6 How infant formulas are modified compared to breast milk

MACRONUTRIENTS	BREAST MILK	COW'S-MILK-BASED FORMULA	SOYBEAN-BASED FORMULA
Protein	7% of calories	9–12%	11–13%
Carbohydrates	38% of calories	41–43%	39–45%
Fats	55% of calories	48–50%	45–49%

OTHER WAYS INFANT FORMULAS ARE MODIFIED COMPARED TO BREAST MILK

What Is Modified	How It Is Modified	Examples from Two Major Manufacturers
Caloric level	[illegible]	[illegible]
Form of protein	[illegible]	[illegible]
Type of sugar	[illegible]	[illegible]
Type of fat	[illegible]	[illegible]
Allergy/intolerance	[illegible]	[illegible]
Micronutrients	[illegible]	[illegible]
Thickness	[illegible]	[illegible]
Age of infant	[illegible]	[illegible]

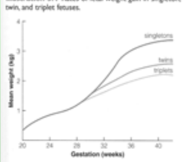
Multi-fetus pregnancies:

Table 5.14 Risks to mother and fetuses with multifetal pregnancy[84]

Pregnant Women
- Preeclampsia
- Iron-deficiency anemia
- Gestational diabetes
- Hyperemesis gravidarum
- Placenta previa
- Kidney disease
- Fetal loss
- Preterm delivery
- Cesarean delivery

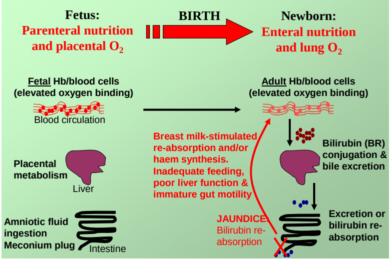
Newborns
- Neonatal death
- Congenital abnormalities
- Respiratory distress syndrome
- Intraventricular hemorrhage
- Cerebral palsy

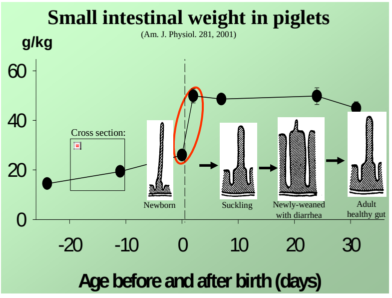
Illustration 5.4 Rates of fetal weight gain in singleton, twin, and triplet fetuses.

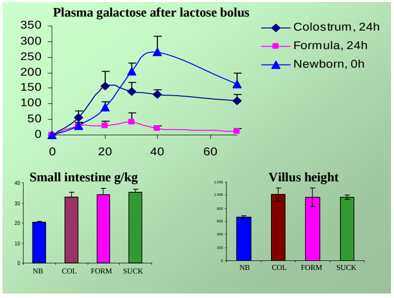


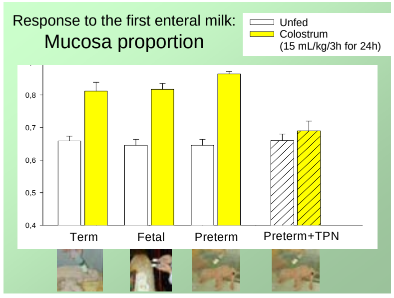
Increased late gestation problems

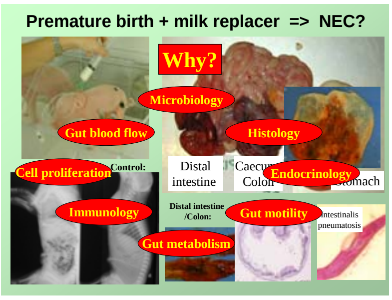
Haemodynamics & jaundice (Brown p. 184-187)

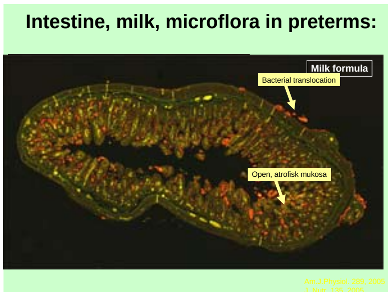


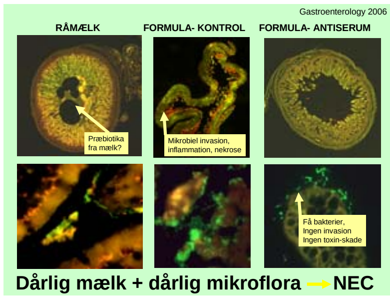

Small intestinal weight in piglets
(Am. J. Physiol. 281, 2001)
g/kg
Cross section:
Newborn
Suckling
Newly-weaned with diarrhea
Adult healthy gut
Age before and after birth (days)

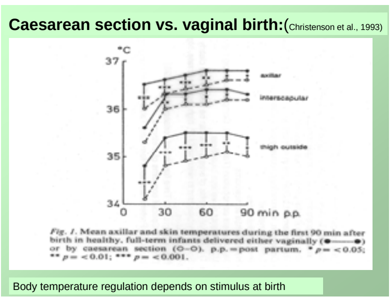

Plasma galactose after lactose bolus
Colostrum, 24h
Formula, 24h
Newborn, 0h
Small intestine g/kg
Villus height
NB
COL
FORM
SUCK

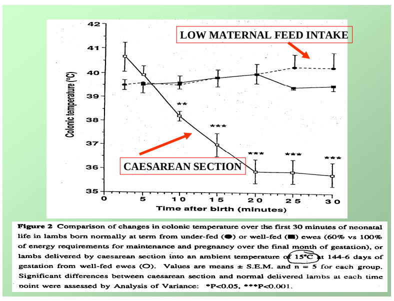

Response to the first enteral milk:
Mucosa proportion
Unfed
Colostrum
(15 mL/kg/3h for 24h)
Term
Fetal
Preterm
Preterm+TPN

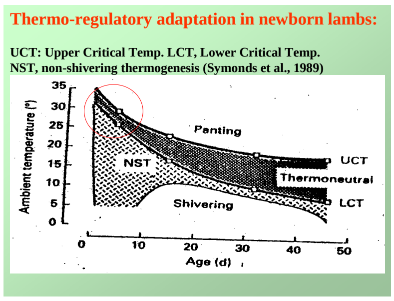

Premature birth + milk replacer => NEC?
Why?
Microbiology
Gut blood flow
Histology
Cell proliferation
Endocrinology
Immunology
Gut motility
Gut metabolism
Distal intestine
Distal intestine /Colon:

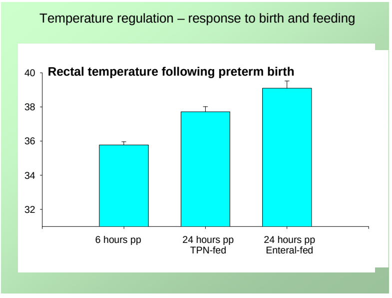

Intestine, milk, microflora in preterms:
Milk formula
Bacterial translocation
Open, atrofisk mukosa

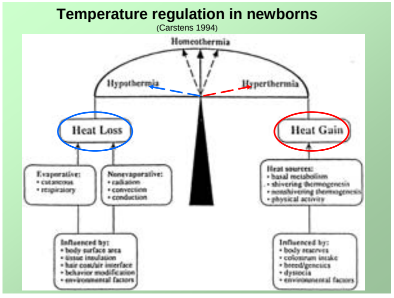

Gastroenterology 2006
RÅMÆLK
FORMULA- KONTROL
FORMULA- ANTISERUM
Præbiotika fra mælk?
Mikrobiel invasion, inflammation, nekrose
Få bakterier, Ingen invasion Ingen toxin-skade
Dårlig mælk + dårlig mikroflora → NEC


Caesarean section vs. vaginal birth:(Christenson et al., 1993)
°C
axillar
interscapular
thigh outside
min p.p.
Fig. 1. Mean axillar and skin temperatures during the first 90 min after birth in healthy, full-term infants delivered either vaginally (●—●) or by caesarean section (○-○). p.p.=post partum. * p=<0.05; ** p=<0.01; *** p=<0.001.
Body temperature regulation depends on stimulus at birth


LOW MATERNAL FEED INTAKE
Colonic temperature (°C)
CAESAREAN SECTION
Time after birth (minutes)
Figure 2 Comparison of changes in colonic temperature over the first 30 minutes of neonatal life in lambs born normally at term from under-fed (●) or well-fed (■) ewes (60% vs 100% of energy requirements for maintenance and pregnancy over the final month of gestation), or lambs delivered by caesarean section into an ambient temperature of 15°C at 144-6 days of gestation from well-fed ewes (○). Values are means ± S.E.M. and n = 5 for each group. Significant differences between caesarean section and normal delivered lambs at each time point were assessed by Analysis of Variance: *P<0.05, ***P<0.001.


Thermo-regulatory adaptation in newborn lambs:
UCT: Upper Critical Temp. LCT, Lower Critical Temp.
NST, non-shivering thermogenesis (Symonds et al., 1989)
Ambient temperature (°)
Panting
NST
UCT
Thermoneutral
Shivering
LCT
Age (d)





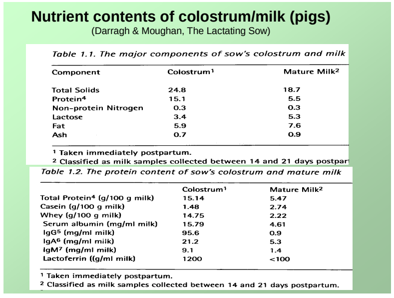


Table 1.1. The major components of sow's colostrum and milk

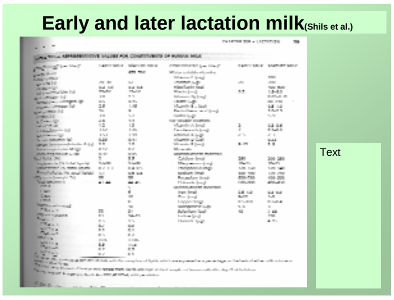
Component	Colostrum[1]	Mature Milk[2]
Total Solids	24.8	18.7
Protein[4]	15.1	5.5
Non-protein Nitrogen	0.3	0.3
Lactose	3.4	5.3
Fat	5.9	7.6
Ash	0.7	0.9

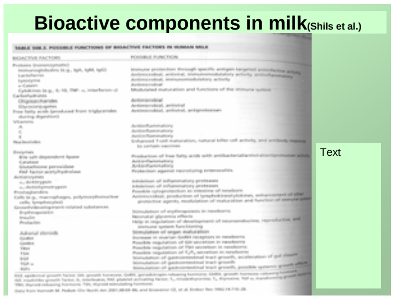
[1] Taken immediately postpartum.
[2] Classified as milk samples collected between 14 and 21 days postpart

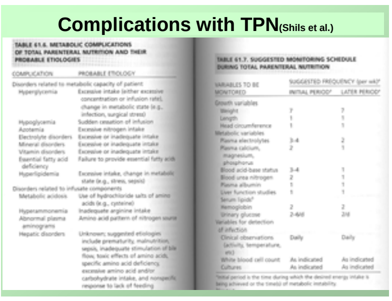
Table 1.2. The protein content of sow's colostrum and mature milk

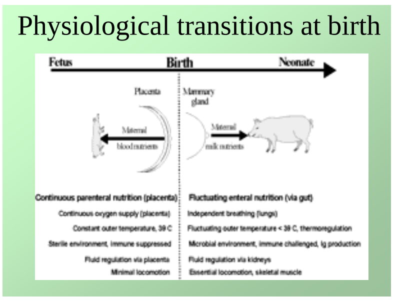
	Colostrum[1]	Mature Milk[2]
Total Protein[4] (g/100 g milk)	15.14	5.47
Casein (g/100 g milk)	1.48	2.74
Whey (g/100 g milk)	14.75	2.22
Serum albumin (mg/ml milk)	15.79	4.61
IgG[5] (mg/ml milk)	95.6	0.9
IgA[6] (mg/ml milk)	21.2	5.3
IgM[7] (mg/ml milk)	9.1	1.4
Lactoferrin ((g/ml milk)	1200	<100

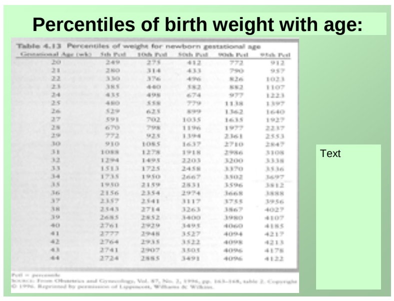
[1] Taken immediately postpartum.
[2] Classified as milk samples collected between 14 and 21 days postpartum.











Nutrition concerns for infants:

Table 9.1 Nutrition concerns in infants with special health care needs

Growth	Slow rate of weight gain
	Fast rate of weight gain
	Slow rate of gain in length
	Disproportionate rate of weight to height gain
	Unusual growth pattern with plateau in weight or length gain
	Altered body composition that decreases or increases muscle size or activity
	Altered brain size that decreases or increases muscle size or activity
	Altered size of organs or skeleton, such as an enlarged liver or shortened leg length
Nutritional adequacy	Calorie needs are higher or lower
	Nutrient requirements higher or lower overall
	Specific nutrients, such as protein or sodium, are required in higher or lower amounts
	Vitamins, minerals, or cofactors (such as carnitine) are required in higher or lower amounts
Feeding	Disruption of the delivery of nutrients as a result of:
	• Structure or functioning of the mouth or oral cavity
	• Structure or functioning of the gastrointestinal tract, including diarrhea, vomiting, and constipation
	• Appetite suppression by constipation or medications
	• Disrupted interaction of the infant with the parent, such as infant cues being so subtle that parent responses are delayed
	• Posture or position promotes or interferes during meal times
	• Timing of nursing, meals, and snacks throughout the day
	• Inappropriate food choices or methods of preparation
	• Interruptions in adequate shelter for feeding and sleeping
	• Instructions were unclear or too complicated for the parent to follow

Text

Titel:

Text

Human Milk Composition

- Colostrum
- Water
- Energy
- Lipids
  - effect of maternal diet on fat composition
  - DHA
  - cholesterol

- Protein
  - casein
  - whey proteins
  - nonprotein nitrogen
- Milk carbohydrates
- Fat-soluble vitamins
  - vitamin A
  - vitamin D
  - vitamin E
  - vitamin K

- Water-soluble vitamins
  - vitamin B_{12} and folic acid
- Minerals in human milk
  - bioavailability
  - zinc
  - trace minerals
- Taste of human milk

Key Nutrition Concepts

- Most medications, including over-the-counter as well as prescription drugs, drugs of abuse, alcohol, nicotine and herbal remedies taken by nursing mothers are excreted in breast milk.
- Twins and other multiples can be successfully breastfed without formula supplementation.

Other Concerns

- Breastfeeding multiples
- Infant allergies
- Food intolerance
- Near-term infants
- Human milk and preterm infants
- Medical contraindications to breastfeeding
- Breastfeeding and HIV infection

Assessing Newborn Health

- Birthweight as an outcome
- Infant mortality
- Combating infant mortality
- Standard newborn growth assessment

Infant Development

- Motor development
- Critical periods
- Cognitive development
- Digestive system development
- Parenting

Energy and Nutrient Needs

- Caloric needs
- Protein needs
- Fats
- Metabolic rate, calories, fats and protein—how do they all tie together?

- Other nutrients and non-nutrients
  - fluoride
  - vitamin D
  - sodium
  - fiber
  - lead

Feeding in Early Infancy

- Breast milk and formula
- Cow's milk during infancy

Energy and Nutrient Needs

- Energy needs
- Protein requirements
  - form of protein
- Fats
- Vitamins and minerals

Common Nutritional Problems

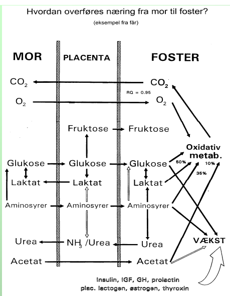
- Nutrition risks to development
- Developmental delay
- Down syndrome

Severe Preterm Birth and Nutrition

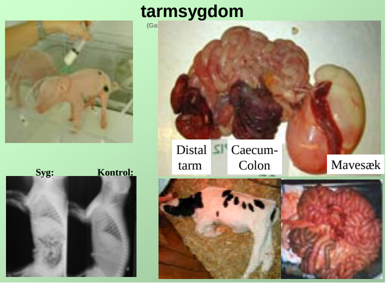
- How sick babies are fed
  - food safety
- What to feed preterm infants
- Preterm infants and feeding
  - fatigue
  - low tolerance of volume
  - "disorganized feeding"

Congenital Abnormalities and Chronic Illness

- GI tract disorders
  - diaphragmatic hernia
  - tracheoesophageal atresia
- Cleft lip and palate
- Genetic disorders
  - maple syrup urine disease
  - DiGeorge syndrome



tarmsygdom



KONKLUSION:

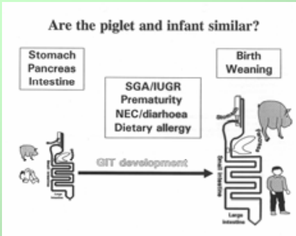
Tarmen i umodne og/eller små nyfødte er ekstremt følsom overfor ernæring
- men virkningen afhænger af:

- Diæt type
- Modenhed

DYREART?

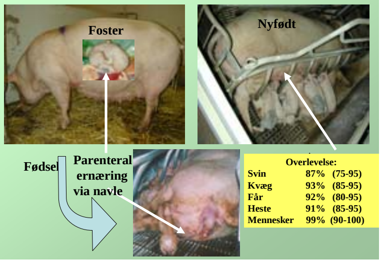
- blod vs. enteral ernæring
- Fødselstype

Animal models in infant nutrition?

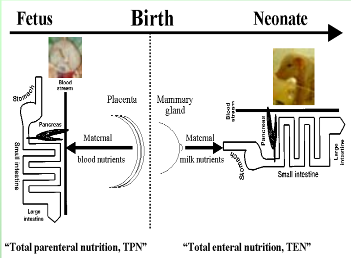


Text

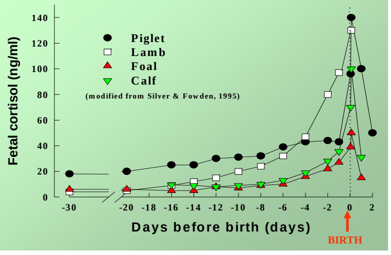
Skift i ernæringsforhold ved fødsel:



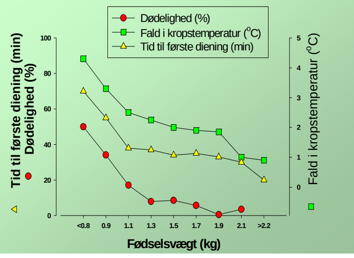
Nutritional transition at birth



Development of blood cortisol before birth



Fødselsvægt og vitalitet hos grise (Hoy & Bauer, 1998)



Grise fødes relativt små og med lille depot

(Fletcher, 1992)

- Så hurtigt forsvinder depoterne:

	Fødsel	24t faste varmt	
Plasma glukose (mM)	5.28	5.17	
Lever glykogen (g/kg)	472	283	
Muskel glykogen (µmol/g)	400	333	

Grise fødes relativt små og med lille depot

(Fletcher, 1992)

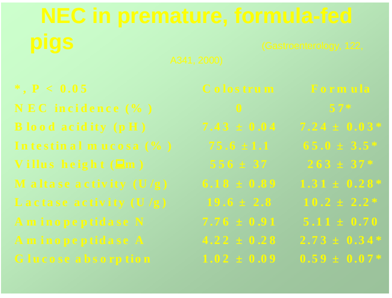
- Så hurtigt forsvinder depoterne:

	Fødsel	24t faste varmt	24t faste køligt
Plasma glukose (mM)	5.28	5.17	0.78
Lever glykogen (g/kg)	472	283	55
Muskel glykogen (µmol/g)	400	333	22

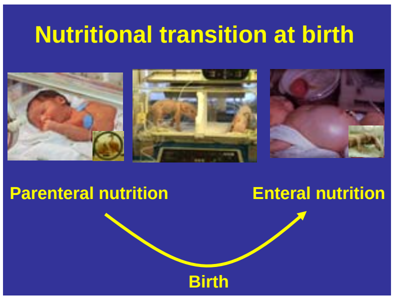
Transmission of passive immunity in different species:

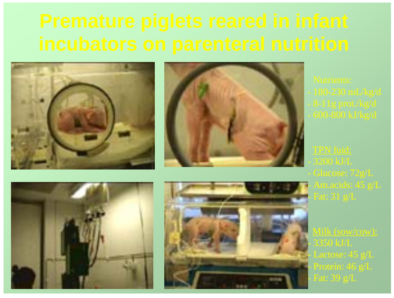
(0, no transfer; +, variable degrees of transfer, m.f. Brambell, 1970)

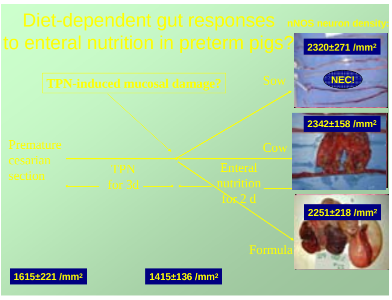
Species	Before birth (parenteral via placenta)	After birth (oral via gut)
Horse	0	+++ (24h)
Pig	0	+++ (24h)
Ox,goat,sheep	0	+++ (24h)
Wallaby	0	+++ (180d)
Dog, cat	+	++ (1-2d)
Fowl	++	++ (<5d)
Hedgehog	+	++ (40d)
Mouse	+	++ (16 d)
Rat	+	++ (20d)
Guinea Pig	+++	0
Rabbit	+++	0
Man, monkey	+++	0

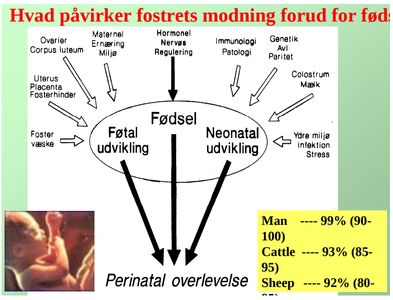


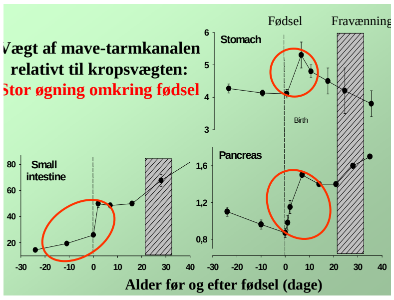
*, P < 0.05	Colostrum	Formula
NEC incidence (%)	0	57*
Blood acidity (pH)	7.43 ± 0.04	7.24 ± 0.03*
Intestinal mucosa (%)	75.6 ± 1.1	65.0 ± 3.5*
Villus height (µm)	556 ± 37	263 ± 37*
Maltase activity (U/g)	6.18 ± 0.89	1.31 ± 0.28*
Lactase activity (U/g)	19.6 ± 2.8	10.2 ± 2.2*
Aminopeptidase N	7.76 ± 0.91	5.11 ± 0.70
Aminopeptidase A	4.22 ± 0.28	2.73 ± 0.34*
Glucose absorption	1.02 ± 0.09	0.59 ± 0.07*

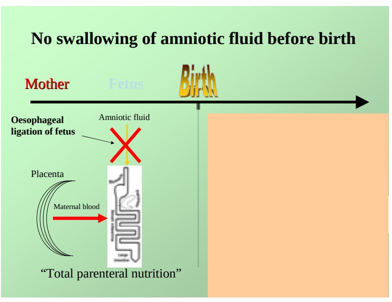


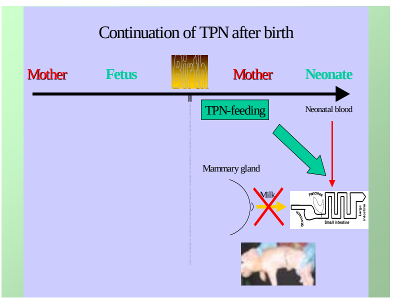


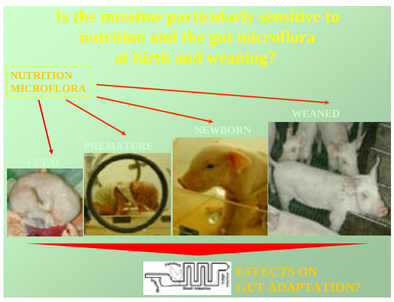


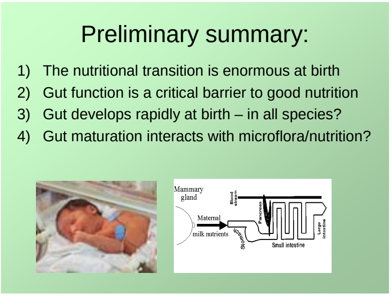




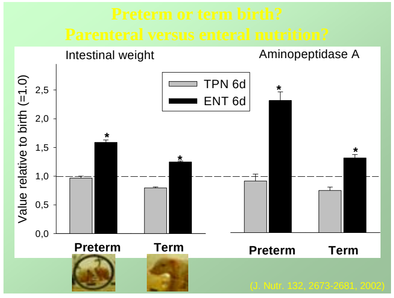


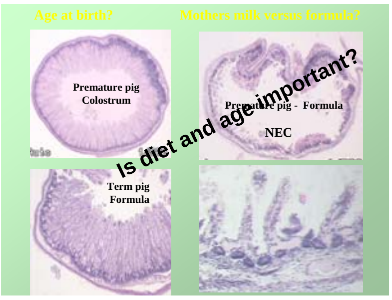


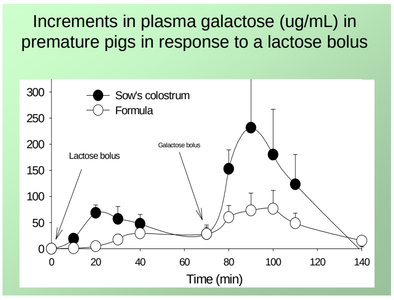


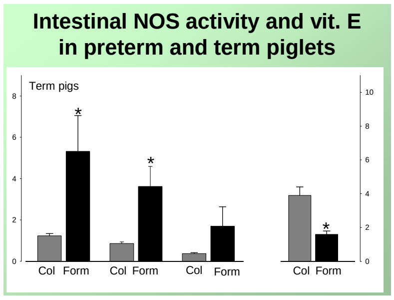

Preliminary summary:
1) The nutritional transition is enormous at birth
2) Gut function is a critical barrier to good nutrition
3) Gut develops rapidly at birth – in all species?
4) Gut maturation interacts with microflora/nutrition?
Mammary gland
Maternal milk nutrients
Small intestine

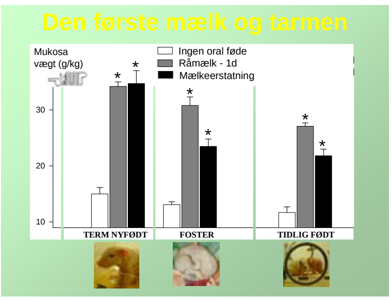

Premature piglets reared in infant incubators on parenteral nutrition
Physiology:
Does physiology relate to infants?
Can reasons/treatments be found?
Philosophical?
Why should we save newborns?
OK to kill piglets but not infants?
Nutrients:
- 180-230 mL/kg/d
- 8-11g prot./kg/d
- 600-800 kJ/kg/d
TPN fuid:
- 3200 kJ/L
- Glucose: 72g/L
- Am.acids: 45 g/L
- Fat: 31 g/L
Milk (sow/cow):
- 3350 kJ/L
- Lactose: 45 g/L
- Protein: 46 g/L
- Fat: 39 g/L


Preterm or term birth?
Parenteral versus enteral nutrition?
Intestinal weight
Aminopeptidase A
TPN 6d
ENT 6d
Value relative to birth (=1.0)
2,5
2,0
1,5
1,0
0,5
0,0
Preterm
Term
Preterm
Term
(J. Nutr. 132, 2673-2681, 2002)

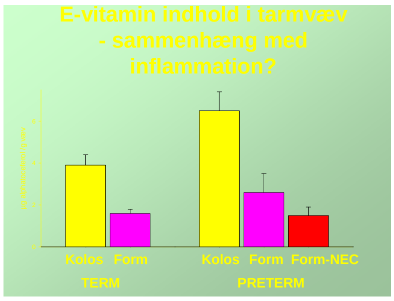

Age at birth?
Mothers milk versus formula?
Premature pig
Colostrum
Premature pig - Formula
NEC
Term pig
Formula
Is diet and age important?

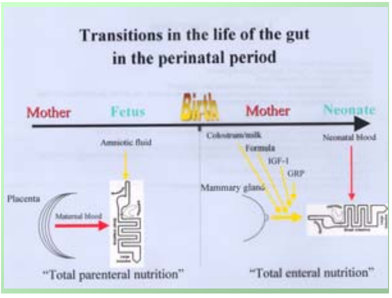

Increments in plasma galactose (ug/mL) in premature pigs in response to a lactose bolus
Sow's colostrum
Formula
Lactose bolus
Galactose bolus
300
250
200
150
100
50
0
0
20
40
60
80
100
120
140
Time (min)

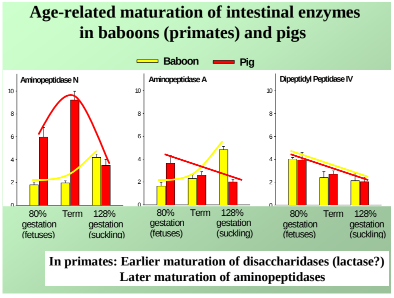

Intestinal NOS activity and vit. E in preterm and term piglets
Term pigs
Col
Form
Col
Form
Col
Form
Col
Form

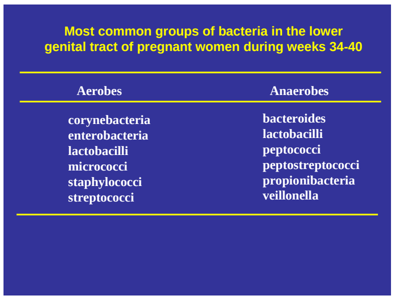

Den første mælk og tarmen
Mukosa vægt (g/kg)
Ingen oral føde
Råmælk - 1d
Mælkeerstatning
30
20
10
TERM NYFØDT
FOSTER
TIDLIG FØDT

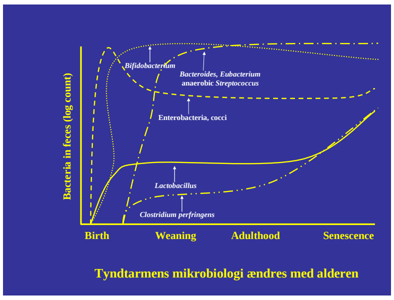

Does nutrition interact with the gut microflora?
Mother´s milk
Infant formula

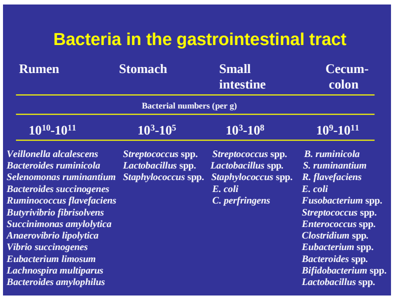

E-vitamin indhold i tarmvæv
- sammenhæng med inflammation?
µg alphatocoferol /g væv
6
4
2
0
Kolos
Form
Kolos
Form
Form-NEC
TERM
PRETERM

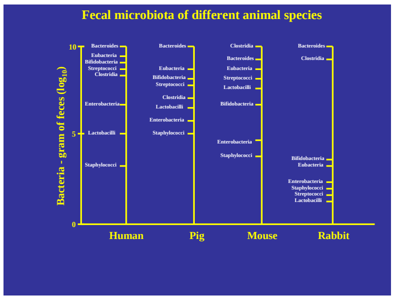

Transitions in the life of the gut
in the perinatal period
Mother
Fetus
Birth
Mother
Neonate
Amniotic fluid
Colostrum/milk
Formula
IGF-I
GRP
Neonatal blood
Placenta
Maternal blood
Mammary gland
"Total parenteral nutrition"
"Total enteral nutrition"

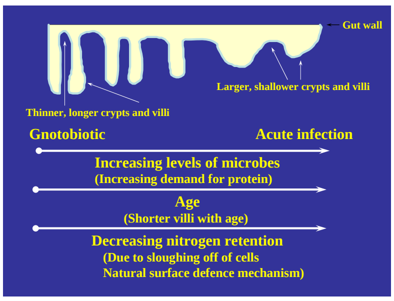

Age-related maturation of intestinal enzymes
in baboons (primates) and pigs
Baboon
Pig
Aminopeptidase N
Aminopeptidase A
Dipeptidyl Peptidase IV
80% gestation (fetuses)
Term
128% gestation (suckling)
In primates: Earlier maturation of disaccharidases (lactase?)
Later maturation of aminopeptidases

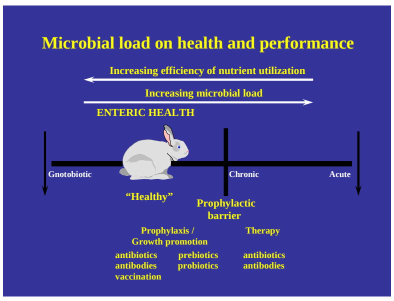

Most common groups of bacteria in the lower
genital tract of pregnant women during weeks 34-40
Aerobes
Anaerobes
corynebacteria
enterobacteria
lactobacilli
micrococci
staphylococci
streptococci
bacteroides
lactobacilli
peptococci
peptostreptococci
propionibacteria
veillonella

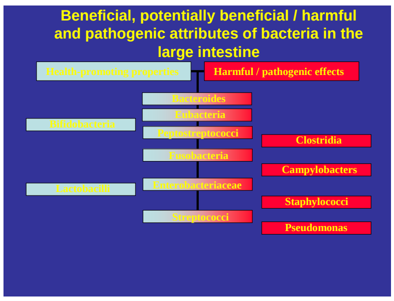

Bacteria in feces (log count)
Bifidobacterium
Bacteroides, Eubacterium
anaerobic Streptococcus
Enterobacteria, cocci
Lactobacillus
Clostridium perfringens
Birth
Weaning
Adulthood
Senescence
Tyndtarmens mikrobiologi ændres med alderen


Bacteria in the gastrointestinal tract
Rumen
Stomach
Small intestine
Cecum-colon
Bacterial numbers (per g)
10¹⁰-10¹¹
10³-10⁵
10³-10⁸
10⁹-10¹¹
Veillonella alcalescens
Bacteroides ruminicola
Selenomonas ruminantium
Bacteroides succinogenes
Ruminococcus flavefaciens
Butyrivibrio fibrisolvens
Succinimonas amylolytica
Anaerovibrio lipolytica
Vibrio succinogenes
Eubacterium limosum
Lachnospira multiparus
Bacteroides amylophilus
Streptococcus spp.
Lactobacillus spp.
Staphylococcus spp.
Streptococcus spp.
Lactobacillus spp.
Staphylococcus spp.
E. coli
C. perfringens
B. ruminicola
S. ruminantium
R. flavefaciens
E. coli
Fusobacterium spp.
Streptococcus spp.
Enterococcus spp.
Clostridium spp.
Eubacterium spp.
Bacteroides spp.
Bifidobacterium spp.
Lactobacillus spp.


Fecal microbiota of different animal species
Bacteria - gram of feces (log10)
10
5
0
Bacteroides
Eubacteria
Bifidobacteria
Streptococci
Clostridia
Enterobacteria
Lactobacilli
Staphylococci
Bacteroides
Eubacteria
Bifidobacteria
Streptococci
Clostridia
Lactobacilli
Enterobacteria
Staphylococci
Clostridia
Bacteroides
Eubacteria
Streptococci
Lactobacilli
Bifidobacteria
Enterobacteria
Staphylococci
Bacteroides
Clostridia
Bifidobacteria
Eubacteria
Enterobacteria
Staphylococci
Streptococci
Lactobacilli
Human
Pig
Mouse
Rabbit

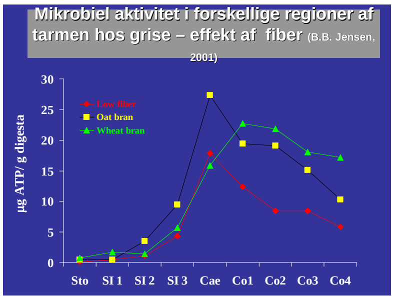

Gut wall
Larger, shallower crypts and villi
Thinner, longer crypts and villi
Gnotobiotic
Acute infection
Increasing levels of microbes
(Increasing demand for protein)
Age
(Shorter villi with age)
Decreasing nitrogen retention
(Due to sloughing off of cells
Natural surface defence mechanism)

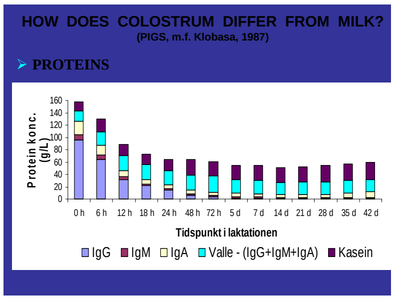

Microbial load on health and performance
Increasing efficiency of nutrient utilization
Increasing microbial load
ENTERIC HEALTH
Gnotobiotic
Chronic
Acute
"Healthy"
Prophylactic
barrier
Prophylaxis /
Growth promotion
Therapy
antibiotics
antibodies
vaccination
prebiotics
probiotics
antibiotics
antibodies

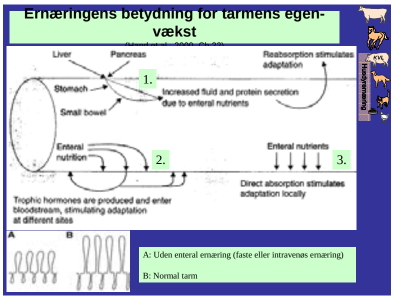

Beneficial, potentially beneficial / harmful
and pathogenic attributes of bacteria in the
large intestine
Health-promoting properties
Harmful / pathogenic effects
Bacteroides
Eubacteria
Bifidobacteria
Peptostreptococci
Clostridia
Fusobacteria
Campylobacters
Lactobacilli
Enterobacteriaceae
Staphylococci
Streptococci
Pseudomonas

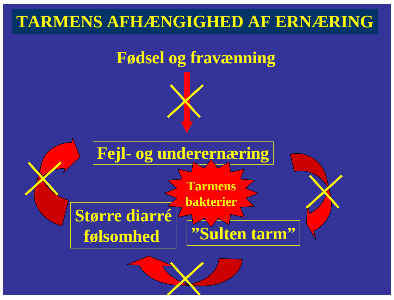
Birth mode & bacterial colonization

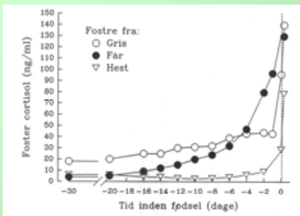
- The intestinal flora depends on the mode of delivery up to at least 12 months after delivery
- Children delivered by ceasarian are more likely to develop allergic disease











Figur 3. Typiske prænatale ændringer i plasma kortisol for føtale lam, grise og føl. Der har været indlagt vaskulære katetre i fostrene sidst i drægtigheden for at tage blodprøver til og med fødselstidspunktet (data fra Silver & Fowden, 1988).

Tabel 2. Koncentration af kortisol og adrenalin ved henholdsvis 95% drægtighedsalder