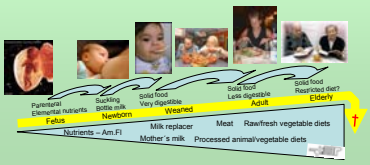
Nutrition, growth and development 2009

Friday 11.9: Aud 3-13

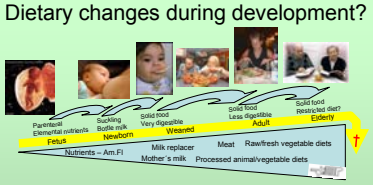
09.00-10.15: Lecture: Nutrition of the fetus.
10.25-11.00: Lecture: Fetal nutritional insults – does it matter?
11.15-12.00: Lecture: Nutritional physiology of the newborn.



General:
Course Literature:
Nutrition through the life cycle. 3d.ed. Judith E. Brown et al. 2007 Thomson Wadsworth, USA. Selected literature and articles. Nordic Nutrition Recommendations 2004 Chapter 1 (Nutrient req. across life stages).

Developmental nutrition/programming.
Primary literature:
Brown et al., Ch 4 p 97 - 99.
The origin of the developmental origins theory, DJP Barker J Int Med 2007 412-417. Epidemiology, genes and---. JG Eriksson. J Int Med 2007 418-425.

Dietary changes during development?



Why?

- Changes in organ anatomy/physiology (e.g. GIT, liver, pancreas)
- Altered growth of tissues/organs
- Altered function of tissues/organs
- Altered disease sensitivity of tissues/organs

Developmental nutrition research - difficult?

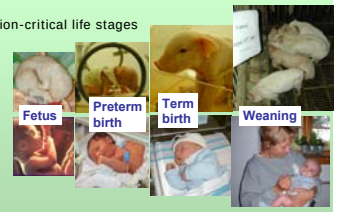
LONG TERM STUDIES:

- **It takes too long to investigate (PhD programs are 3 years!)**
- **The long time factor makes experiment uncontrollable**
- **Cell function changes over the course of an experiment**

RESULT: Nutritional advice based on epidemiology and tradition

Important supplement: Animal model developmental studies

Nutrition-critical life stages

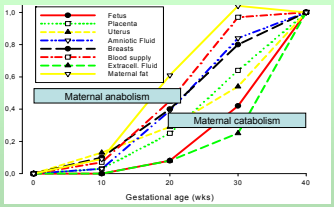


Topics of ongoing PhD projects (children/piglets):

- Colostrum or mature milk for preterm newborns?
- Optimal lipid and protein in preterm formulas?
- Enteral nutrition of children after gut resection?
- Antibiotics or probiotics to prevent gut disease?
- Can milk bioactives prevent preterm gut disease?
- Enteral versus parenteral nutrition in preterms?
- Stimulation of fetal development before birth?
- Nutrition for children with leukaemia?
- What is the role of amniotic fluid before birth?
- Is lactose goood or bad in infant formula?

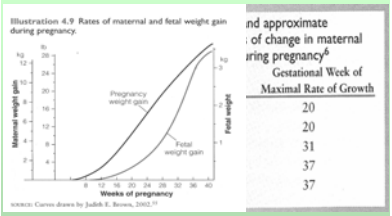
Nutrition and development of the fetus

Maternal & fetal tissue changes: (Brown 4.17)



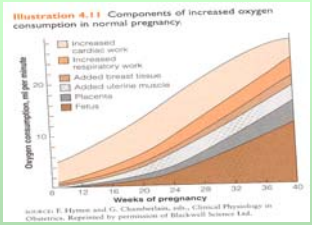
Blood supply + Maternal fat – early gestation
Extracellular Fluid + Fetus – late gestation

Fetal & maternal tissue growth:



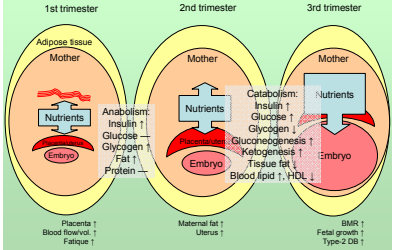
Time: Placenta → Maternal weight & blood volume → Fetal protein → Fetal fat

Maternal & fetal tissue changes: (Brown 4.11)



1) What does oxygen consumption illustrate? 2) What are the trends throughout gestation?
3) Do these metabolism trends have any implications for maternal nutrient recommendations?

Tissue growth & nutrition in pregnancy



Anabolic & catabolic pregnancy phases

Table 4.6 Summary of maternal anabolic and catabolic phases of pregnancy[7,8,11]

Maternal Anabolic Phase 0–20 Weeks	Maternal Catabolic Phase 20+ Weeks
Blood volume expansion, increased cardiac output	Mobilization of fat and nutrient stores
Buildup of fat, nutrient, and liver glycogen stores	Increased production and blood levels of glucose, triglycerides, and fatty acids; decreased liver glycogen stores
Growth of some maternal organs	Accelerated fasting metabolism
Increased appetite, food intake (positive caloric balance)	Increased appetite and food intake decline somewhat near term
Decreased exercise tolerance	Increased exercise tolerance
Increased levels of anabolic hormones	Increased levels of catabolic hormones

Despite increasing body weight the physiological state is catabolic

Maternal and fetal weight gain:

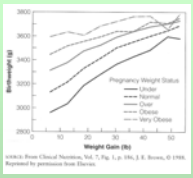


Table 4.16 Pregnancy weight gain recommendations[11]

Prepregnancy Weight Status	Recommended Gain*
Underweight, BMI <19.8	28-40 lb (12.7-18.2 kg)
Normal weight, BMI 19.8-26.0	25-35 lb (11.4-15.9 kg)
Overweight, BMI >26.0-29.0	15-25 lb (6.8-11.4 kg)
Obese, BMI >29.0	15 lb (6.8 kg) at least
Twin pregnancy	35-45 lb (15.9-20.5 kg)

*Young adolescents should achieve gains at the upper end of ranges, short women at the lower end.

Low maternal gain in underweight mothers → lower birth weight → higher perinatal morbidity/mortality

Placental nutrient transfer:

Table 4.10 Mechanisms of nutrient transport across the placenta[11,21]

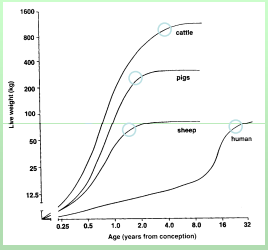
MECHANISM	EXAMPLES OF NUTRIENTS
Passive diffusion (also called *simple diffusion*) Nutrients transferred from blood with higher concentration levels to blood with lower concentration levels	Water, some amino acids and glucose, free fatty acids, ketones, vitamins E and K,* some minerals (sodium, chloride), gases
Facilitated diffusion Receptors ("carriers") on cell membranes increase the rate of nutrient transfer	Some glucose, iron, vitamins A and D
Active transport Energy (from ATP) and cell membrane receptors	Water-soluble vitamins, some minerals (calcium, zinc, iron, potassium) and amino acids required for transfer
Endocytosis (also called *pinocytosis*) Nutrients and other molecules are engulfed by placenta membrane and released into fetal blood supply	Immunoglobulins, albumin

Well-controlled and selective nutrient transfer – "the intestine of the fetus"

Key Nutrition Concepts - Fetus

- Periods of rapid growth and development of fetal organs and tissues occur during specific times during pregnancy.
- Essential nutrients must be available in required amounts during these times for fetal growth and development to proceed optimally.
- The (human) fetus is not a "parasite"

Body weight increase across species:



Sigmoid curves

Age at adult weight:
- Similar among breeds
- differs among species

Birth weight and infant mortality:

Table 4.1 Natality statistics: Rates, definitions, and trends in the rates in the United States[1]

	RATES 1995	2001	Definition
Maternal mortality	7.1	7.1	Deaths/100,000 live births
Fetal deaths (stillbirths)	7.0	6.6	Deaths/1000 pregnancies over 20 weeks gestation
Perinatal mortality	7.6	7.0	Deaths/1000 deliveries over 20 weeks gestation to 7 days after birth
Neonatal mortality	4.9	4.6	Deaths from delivery to 28 days/1000 live births
Postneonatal mortality	2.7	2.3	Deaths from 28 days after birth to 1 year/1000 live births
Infant mortality	7.6	6.8	Deaths from birth to age 1 year/1000 live births
Preterm	11.0	11.8	Births <37 weeks gestation/100 live births
Very preterm	1.9	1.9	Births <34 weeks gestation/100 live births
Low birthweight	7.3	7.8	Newborn weights <2500 g (5 lb 8 oz)/100 live births
Very low birthweight	1.4	1.5	Newborn weights <1500 g (3 lb 4 oz)/100 live births
Multifetal pregnancies			
Twins	1 in 40	1 in 34	Number of twin births/total live births
Triplets+	1 in 784	1 in 555	Number of triplets plus higher-order multiple births/total live births
Adolescent pregnancies	56.8	45.9	Births /1000 females aged 15 to 19 years

Neonatal mortality and morbidity is high and is related to birth weight

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"

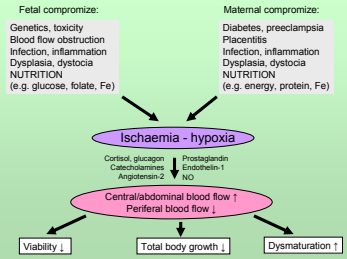
Birth weight & cardiovascular disease

Table 4.15 Association of birthweight with the risk of cardiovascular disease in the U.S. Nurses Study[49]

BIRTHWEIGHT	RELATIVE RISK OF:	
	Heart Disease	Stroke
<5 lb (2240 g)	1.5	2.3
5–5½ lb (2240–2500 g)	1.3	1.4
5½–7 lb (2500–3136 g)	1.1	1.3
7–8½ lb (3136–3808 g)	1.0	1.0
8½–10 lb (3808–4480 g)	1.0	1.0
>10 lb (>4480 g)	0.7	0.7

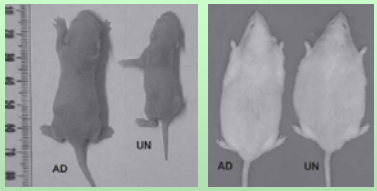
Low birth weight → 50-100% greater risk of heart disease/stroke

Under-weight or immature fetuses – mechanisms?



Fetal undernutrition – later obesity and type-2 diabetes

(AD: Ad libitum fed mothers; UN: Undernourished mothers)

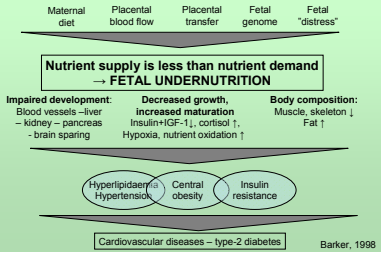


1) How critical are specific nutritients/foods for development at specific life stages?

2) What are the organs/tissues that are affected short-term/long-term?

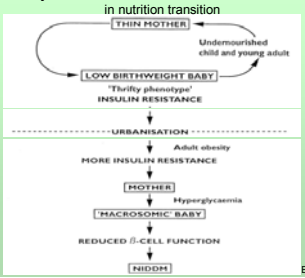
Breier, Krechowec & Vickers, 2006: Programming of Obesity – Experimental evidence. In Early Life Origins of Health and Disease, Wintour & Owen, eds.

Fetal undernutrition and adult disease:



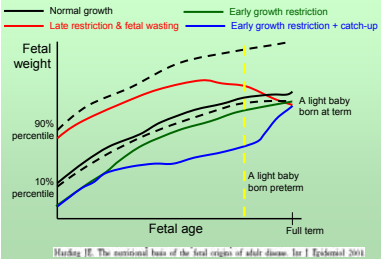
Barker, 1998

Early malnourishment and later diabetes risk in nutrition transition



Barker, 1998

Growth trajectories in fetal life?



Harding JE. The nutritional basis of the fetal origins of adult disease. Int J Epidemiol 2001

Body Growth and Development

(Brown ch. 4)

- Critical periods
  - hyperplasia
  - hyperplasia and hypertrophy
  - hypertrophy
  - maturation
- Body composition
  - Differential increases in fat, protein minerals

Growth/cell proliferation in different tissues:

- No stop during the life time – intestinal/skin epithelia
- Growth arrest – but ability to re-adapt (liver, muscle, heart)
- Complete stop of growth (skeleton, nervous system)

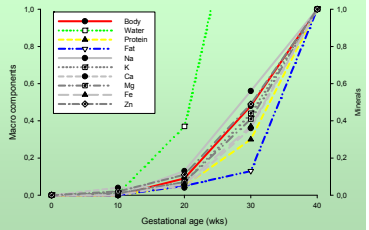
Chemical change during fetal life:

Table 4.12 Estimated changes in body composition of the fetus by time in pregnancy[11,29]

Component	10 Weeks	20 Weeks	30 Weeks	40 Weeks
Body weight, g	10	300	1667	3450
Water, g	<9	263	1364	700
Protein, g	<1	22	134	446
Fat, g	<1	26	66	525
Sodium, meq	<1	32	136	243
Potassium, meq	<1	12	75	170
Calcium, g	<1	1	10	28
Magnesium, mg	<1	5	31	76
Iron, mg	<1	17	104	278
Zinc, mg	<1	6	26	53

Skeleton development → Muscle development → Fat development

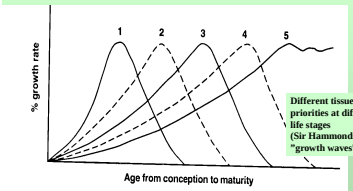
Chemical change during fetal life:



Skeleton development → Muscle development → Fat development (Brown Table 4.12)

Tissue growth rate during development

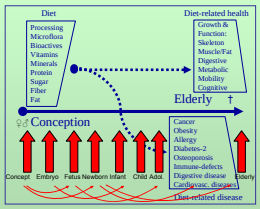
(Reeds et al., in Growth of the Pig, ed. GR Hollis)



Different tissue priorities at different life stages (Sir Hammonds "growth waves")

Fig. 6.2. Waves of growth: 1 = nervous tissue; 2 = bone; 3 = muscle; 4 = fat; 5 = daily feed intake. When all the tissues reach mature size daily intake may have declined from its maximum value and often fluctuates on a seasonal basis.

Early Nutrition – Later disease:



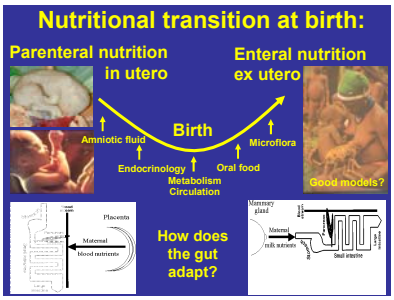
Under-weight or immature fetuses – how to help?

Early delivery – postnatal catch-up	Delivery delay - maturation
In utero intra-amniotic feeding?	Ex utero feeding of "fetal" diets?
Prenatal growth hormones?	Prenatal maturation hormones?
Nutrient-enriched milk formulas	Parenteral or elemental diets
Postnatal growth hormones?	Postnatal maturation hormones?

Birth and its complications

Growth & maturation – not the same:

Nutritional transition at birth:



CASE study: Immature gut & nutrition

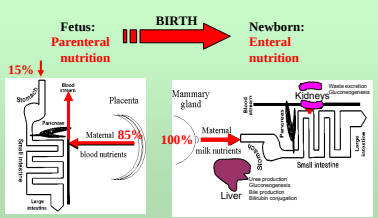
Following birth, preterm babies at Rigshospitalet have severe digestive problems. Use research to solve the problems. You have unlimited ressources to work with pigs as a model animal. Suggest 3 experiments to understand and/or solve the problem? Indicate specific questions/methods/expected results.

Nutrition of an immature gut?

How to understand and/or solve the problem?

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

The nutritional transition at birth:



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

Time and terms, pre- and postnatally

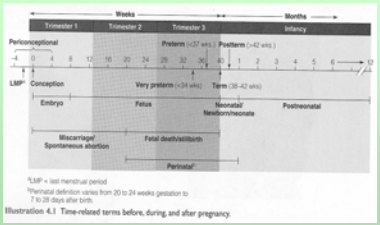


Illustration 4.1 Time-related terms before, during, and after pregnancy.

Infant mortality:

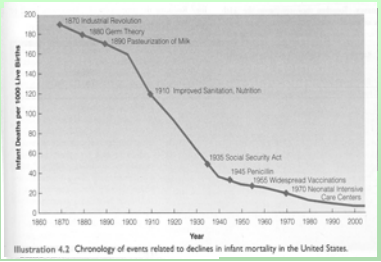


Illustration 4.2 Chronology of events related to declines in infant mortality in the United States.

Weight, age at birth and mortality

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

BIRTHWEIGHT		WEEKS GESTATION	INFANT MORTALITY RATE
Pounds (lb) and Ounces (oz)	Grams		
<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.

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

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!

Preterm & term milk – differences?

Milk and microflora in preterms:

Gastroenterology, 130, 2006
Am.J.Physiol. 289, 2005
J. Nutr. 135, 2005

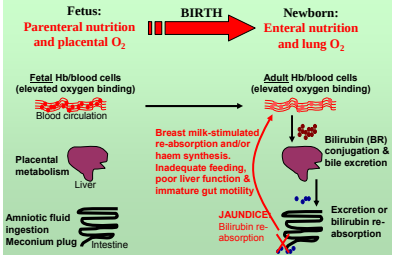
Key Nutrition Concepts

- 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.

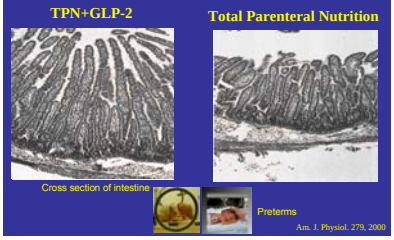
Key Nutrition Concepts

- 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.

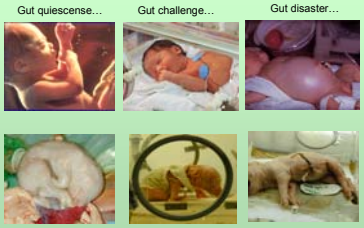
Haemodynamics & jaundice (Brown p. 184-187)



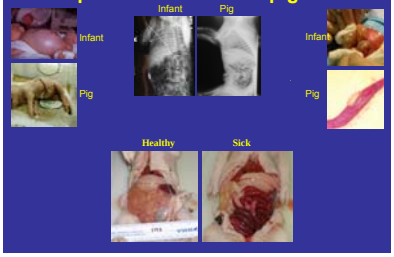
Villous growth, enteral food and GLP-2



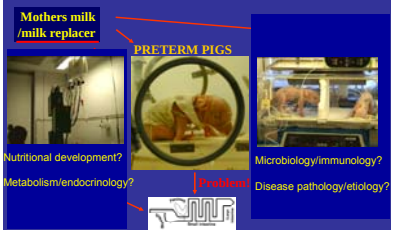
Preterm gut (mal)adaptation



Necrotizing enterocolitis (NEC) in preterm infants and piglets:



Gut responses to milk formula:



Catheterization of fetal pigs in utero