

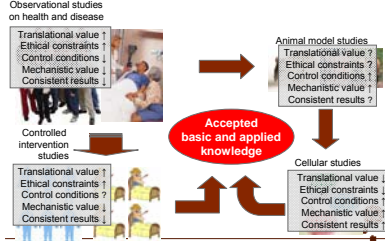
THEME course in Human Nutrition 2009

Evidence hierarchy

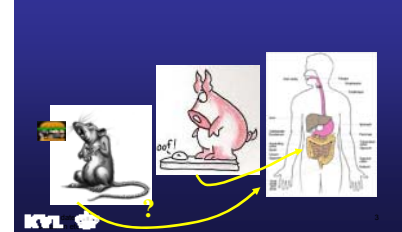
Animal Models



Nutrition science epistemology  
(- how do we know, that we know...)



Animal models  
in human nutrition research?



### Animal models in human nutrition research?

- 1) What is a good animal model?
- 2) What is a good nutritional animal model?
- 3) Animal models for nutrition related diseases - examples
- 4) Life Cycle Nutrition – comparison to animals?

KVL

### Animal model

- Something that accurately resembles something else  
- (Oxford English Dictionary)
- An animal model is a living organism in which normative biology or behaviour can be studied,
  - or in which a spontaneous or induced pathological process can be investigated,
  - and in which *the phenomenon in one or more respects resembles the same phenomenon in humans or other species of animal*  
- (Wessler, 1976)

KVL

### What is a good nutritional animal model?

- 1) Similarity in key nutrition-relevant organs/tissues?  
(gastrointestinal tract, liver, metabolism.....)
- 2) Similarity in natural dietary habits?  
(herbivore, omnivore, carnivore, meal pattern, seasonal changes....)
- 3) Spontaneous nutrition-related diseases  
(e.g. type-2, CHD, obesity, allergy, malabsorption, atherosclerosis...?)
- 4) Life cycle development & body composition  
(maturity at birth, life span, nutritional transitions.....)

KVL

### Animal nutrition versus human nutrition research - the classical differences:

Humans/ pet animals:	Production/ experimental animals:
Health - function	Growth - production
Micronutrients	Macronutrients
Qualitative nutrition	Quantitative nutrition
Variable standards	Exact standards
"Holistic nutrition"	Mechanical nutrition

Mutual benefit and interchange ?

KVL

### Animal models

- Spontaneous
  - The phenomenon occurs spontaneously
- Induced
  - The phenomenon is induced chemically or surgically.
- Negative
  - The phenomenon never occurs
  - Why ?

KVL

### Validity of Animal Models

- Predictive validity
  - Performance in the test predicts performance in modelled condition
- Face validity
  - Phenomenological analogy with modelled condition
- Construct validity
  - The model has a sound theoretical rationale

KVL

### Nutrition and the gut?

**Mucosa**

Nutrients → Blood circulation

- Picky eater of nutrients. "Bottle neck"
- Function essential for body health
- Populated with immunological /endocrine cells
- Large environmental surface area. Billions of bacteria.

KVL

### Gastrointestinal anatomy - a key factor for species-specific nutrition

**PIG (omnivore)**  
 High protein diet  
 High fiber diet  
**HORSE (herbivore)**  
 High fiber diet  
**MINK (carnivore)**  
 High protein diet  
 High fat diet

Similar tissue/cell metabolism

KVL

### Rodent gastrointestinal tract

Rat (*Rattus norvegicus*)  
Body Length: 17 cm

KVL

The graph below shows the development of the small intestine with age in piglets. You are now an MSc student at LIFE and must design 3 experiments that test whether nutrition is likely to play a role for gastrointestinal development in newborn infants. You have unlimited resources with pigs as infant models.

- Which experiments do you suggest?
- What are the main benefits relative to studies in infants?
- What are the main limitations for interpretation to infants?

Weight (kg body weight)

Age (days)

Place, date, unit, occasion etc.

13

### Fetal undernutrition – later obesity and type-2 diabetes

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

1) How critical are specific nutrients/foods for development at specific life stages?  
2) What are the organs/tissues that are affected short-term/long-term?

Place, date, unit, occasion etc.

14

### Gastrointestinal Ontogeny: Conception to Maturity

Conception Birth Weaning Maturity

- Human - 280 d gestation: 70-90% gestation (Early and slow...), 10-20 weeks (Intermediate...), 52 weeks (Late and rapid...)
- Pig - 115 d gestation: 90-95% gestation (Early and slow...), 3-6 weeks (Intermediate...), 12 weeks (Late and rapid...)
- Rat - 22 d gestation: 94-97% gestation (Early and slow...), 2-3 weeks (Intermediate...), 5 weeks (Late and rapid...)

Legend: ■ Preterm birth of piglets, occasional in newborn; ■ Birth cluster of GIT maturational changes; ■ Weaning cluster of maturational changes

Source: Exp. Biol. Medicine (2006)

### Preterm gut (mal)adaptation

Gut development... Gut challenge... Gut disaster...

Place, date, unit, occasion etc.

### Intestinal inflammatory response to diet:

Milk replacer

PRETERM pigs

OK Problem! OK

Place, date, unit, occasion etc.

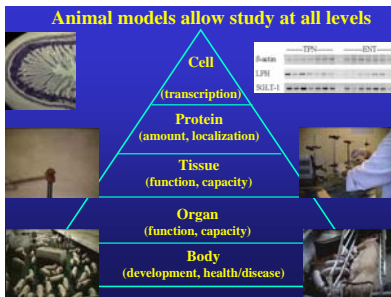
17

### Milk, microflora & gut inflammation:



Loss of muscle tone, Dilated vessels, Milk-replacer, Translocation of bacteria, Open, atrophic mucosa, Deep penetration of bacteria

Place, date, unit, occasion etc.

Gastroenterology 130 (2008) 1491-1498  
J. Nutr. 135, 2005




### Pig models – which pig?

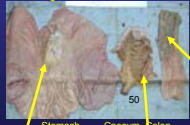

Mini pig	Conventional
 Slow growth Fat growth High viscera/body More herbivorous? More mature? Stress-resistant?	 Rapid growth Protein growth Low viscera/body More omnivorous? Less mature? Stress-sensitive?

KVL

### Nutrition-related gut disease in adults:

**DP Burkitt (1975):**  
 Big faeces → Small hospitals  
 Small faeces → Big hospitals



High fat–low fiber, 3 months:	Low fat–high fiber:
 Stomach Caecum Colon Keratinization and erosion (developing ulceration)	 Stomach Caecum Colon Red/brown/yellow inflammation Sticky food material with epithelial contact

### Does fat diet induce gut disease?

Location	FAT	FIBRE
STO	~6.8	~5.2
SIB	~8.2	~5.8
CAE	~8.5	~6.5
CO2	~7.8	~6.5

- Microbiology (more pathogens, changed fermentation)
- Pathology/histology (light inflammation, OK histology)
- Organ anatomy (less stomach, colon)
- Gene expression (lowered ClCa-1 mRNA, 90 others OK)
- Mucosal physiology (OK enzymes)