

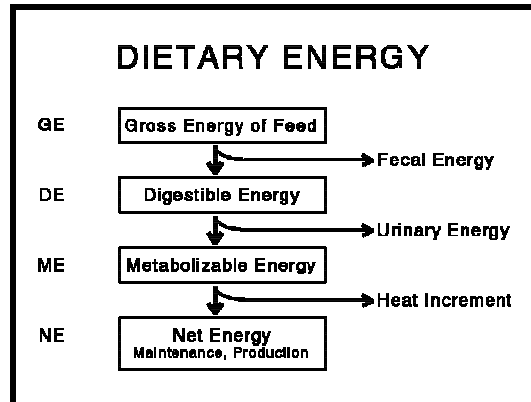
ENERGY METABOLISM AND VITAMINS/MINERAL

ENERGY SYSTEMS

1. Various Systems

A. Based on the quantity needed, energy is required in the highest amounts in an animal's diet.

- 1) Feeding standards used for formulating diets for all species are based on some form/measure of energy.
- 2) And, additional needs for protein or amino acids, essential fatty acids, vitamins, and minerals.



B.. Partition of dietary energy: [Redrawn from Wiseman & Cole, 1985. In: Cole & Haresign (Ed.)]

1) Energy:

- a) Defined as the capacity to do work, and it is the amount of heat produced when completely oxidized in the body, or loss of energy from the body.
- b) European countries use the joule, but calorie (cal), kilocalorie (kcal), and megacalorie (Mcal) are commonly used in animal nutrition in the US.
- c) One calorie is the heat required to raise the temperature of 1 gram (g) of water 1°C (= 4.1855 joules). A kilocalorie equals 1,000 cal, and a megacalorie (or therm) equals 1,000 kcal or 1,000,000 cal.

2) Gross Energy (GE):

- a) Refers to the heat generated when a feed is completely oxidized/burnt.
- b) To measure, a known amount of sample is placed a bomb calorimeter, and then oxygen is used to fill the chamber so that the sample will be completely oxidized.
- c) The GE content of a feed has little correlation with the portion of the energy that is available to an animal.

3) Digestible Energy (DE):

- a) The amount of energy apparently absorbed from a feed.
- b) Obtained by subtracting fecal energy from GE - Not strictly a measure of absorbed energy because some fecal energy is derived from sloughed off tissues lining the digestive tract rather than from undigested food.

- c) Can be determined relatively easily by a digestion trial, and DE values have been developed for quite a number of species & feedstuffs and are widely used.
- 4) Metabolizable Energy (ME):
 - a) Determined by subtracting energy losses in urine and combustible gases from DE consumed - Must collect feces, urine, and gaseous losses.
 - b) Slightly more accurate than DE in terms of estimating the available energy, but more expensive to determine.
 - 5) Net Energy (NE):
 - a) Determined by subtracting energy losses due to rumen fermentation and tissue metabolism from ME.
 - b) Most accurately predicts the available energy for the animal - Also, specifically for maintenance (NEm), gain (NEg) and milk production (NEl).
 - c) Have been determined on only a few feedstuffs, and many available values have been calculated using equations, but widely being used in formulating diets for various ruminant species.
- C. Total Digestible Nutrients (TDN):
- 1) A method used for many years for estimating the energy content of a feed - Sums all the fractions that are digestible.
 - 2) $\text{TDN} = \text{digestible crude protein} + \text{digestible crude fiber} + \text{digestible nitrogen-free extract (starch and sugars)} + 2.25 \text{ digestible ether extract (fat)}$.
- [The ether extract is multiplied by 2.25 in an attempt to adjust its energy value to reflect its higher caloric density (fat = 9.1 cal/g and carbohydrates = 4.1 cal/g).]
- 3) Usefulness?
 - a) Based on many assumptions & approximations, and perhaps, many errors associated with each one of those assumptions or approximations?
 - b) Using the same weight for protein and carbohydrates.
 - c) To use the “calorie” system, must be converted to ME or DE.
 - 4) The TDN is very similar to DE, but DE and NE are more commonly used.
- E. DE, ME & TDN systems - The heat loss is ignored.
- F. NE system - Considers a heat loss, but it may vary with a source of energy & also with purposes:
- 1) ME utilization for energy gain & maintenance - e.g., 27% for wheat middlings, 69% for corn & 75% for soybean oil.

2) Efficiency of utilization of major nutrients for different purposes (ARC, 1981):

Item	Maintenance	Fat production
Carbohydrate	100	100
Fat	95	112
Protein	78	81

☛ The bottom line?

- 1) The NE system - Theoretically the best measure of available energy for maintenance & production . . . But, may not be practical to use!?
- 2) Also, from “GE to NE,” progressively the function of animals rather than the feed ingredient or diet, so . . . !?

2. Choosing the System

A. The system should be: 1) Precise, 2) simple to apply, and 3) easily estimated!

B. TDN - As indicated before:

- 1) Various assumptions/estimates are involved in its calculation, thus not “exact,” vs DE & ME, which can be measured directly.
 - 2) Must be converted to DE or ME when switching to the “calorie” system.
- ☛ Thus, the DE, ME or NE system is preferred by many!

C. DE or ME vs NE:

- 1) In evaluating feedstuffs:
 - a) Again, from “GE → DE → ME → NE” estimations, values are influenced more by animals, i.e., not the value of a feedstuff or diet *per se*.
 - b) “NE values” may be too sensitive for a practical use, i.e., may have to use different values according to age, sex, etc.
- 2) Estimation of NE:
 - a) Direct determination - Very complex since it requires a measurement of total energy exchange by the calorimetry.
 - b) Based on the prediction equations using N, EE, CF & NFE in both feed & feces - May not be precise!
- 3) Practical diets for nonruminant species (e.g., grain-protein supplement-based diets) - Usually less variations in relative contributions of energy from protein, CH₂O and

fat to the total digested energy, thus the relationships among various systems would be relatively similar?

☛ Thus, DE or ME values are commonly used for nonruminant species!

D. Relationships between DE and ME:

1) Some estimated relationships between ME & DE:

- a) $ME/DE = 0.957, 0.949, 0.947, 0.977, 0.963, 0.982, 0.970, 0.967, 0.972$, etc. with an average of “**0.965**.”
- b) The most commonly used/quoted assumption - “ME consists of 96% of DE!”

2) But, the quantity & quality of dietary protein can affect this relationship, ∴ adjustment factor(s) must be used:

- a) There are many equations to estimate ME values from DE!
- b) Most commonly used?

$$ME = DE \times [96 - (0.202 \times \% CP)] \text{ (Asplund and Harris, 1969; NRC, 1988).}$$

3) DE or ME to use?

- a) The loss of energy as combustible gases in pigs - Generally ignored because losses are negligible & difficult to measure (NRC, 1988).
- b) The variation in the relationship between DE & ME - More of a function of the animal rather than feed or ingredient itself?
- c) “Determined” DE values for most ingredients are available?

☛ Thus, preferable to use DE values? (See Chiba, 2000. In: Theodorou & France.)

ENERGY REQUIREMENT

1. Energy Requirement of Growing Animals (e.g. with Pigs)

- The sum of requirements for maintenance, protein retention, fat retention and cold thermogenesis:

$$DE = \sum (DE_m + DE_{pr} + DE_f + DEH_c) \text{ (NRC, 1988).}$$

A. Energy requirement for maintenance:

- 1) Influenced by environmental temperatures, activity, group size, stress, body composition, etc.

- 2) Can be estimated from: [Close & Fowler (1985) in Cole & Hersign]
- Measurements from fasting metabolism.
 - Linear regressions relating energy retention (ER) to ME intake & calculating ME_m where $ER = 0$.
 - The relationships between ME intake and protein & fat accretion rates, and determining ME_m as the intercept of the multiple regression analysis.
- 3) Live weights and maintenance requirements:
- e.g., Estimates based on two separate equations: [ARC, 1981; Close & Fowler (1985) in Cole & Haresign]

Weight, kg	ME, MJ/day	
	$ME_m = 0.719W^{0.63}$	$ME_m = 0.458W^{0.75}$
5	1.98	1.53
10	3.07	2.58
20	4.75	4.33
30	6.13	5.87
40	7.35	7.28
50	8.45	8.61
60	9.48	9.87
70	10.45	11.08
80	11.37	12.25
90	12.24	13.38

- The most commonly used estimate is ≈ 110 kcal/kg BW^{.75}.

B. Energy requirements for protein and fat retention:

- Chemical composition of growing pigs (% of body weight): [Kotarbinska, 1969. (Cited by ARC, 1981)]

Weight, kg	Protein	Fat	Water
2.5	15.6	5.0	77.3
8.5	16.7	6.1	75.3
20.7	16.2	9.6	71.0
30.2	16.4	12.4	67.8
60.6	16.6	20.5	59.9
90.4	15.9	26.3	55.1

- Considerable variations among reported estimates on the cost of protein or fat retention - One example (Tess et al., 1984. J. Anim. Sci. 58:111):

- a) Protein - 7.1 to 14.6 Mcal DE/kg with an average of 12.6 Mcal DE/kg protein.
- b) Fat - 9.5 to 16.3 Mcal DE/kg with an average of 12.5 Mcal DE/kg fat.

C. "Below" critical temperatures & energy requirement:

- 1) Equation to estimate the cold thermogenesis:

$$DEH_c \text{ (kcal DE/day)} = 0.326W + 23.65 (T_c - T) \text{ [where } W = \text{weight in kg and } T \text{ (ambient temperature) \& } T_c \text{ (critical temperature) in } ^\circ\text{C.]}$$

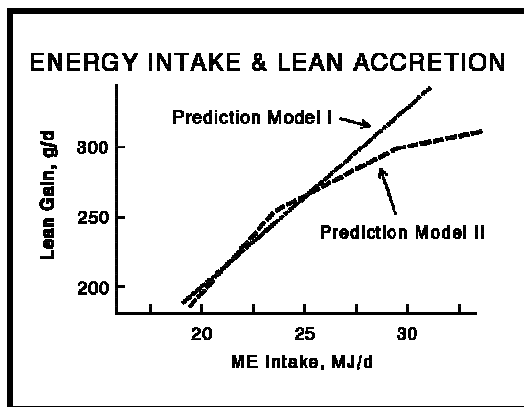
- 2) According to one estimate, need additional 25 g (80 kcal ME) of feed/day to compensate for each 1°C below T_c in 25- to 60-kg pigs.

D. Energy requirements: (e.g, NRC, 1988)

Body wt., kg	DE, kcal/d	ME, kcal/d
1-5	850	805
5-10	1,560	1,490
10-20	3,220	3,090
20-50	6,460	6,200
50-110	10,570	10,185

E. Energy intake & growth rate of lean tissues: [ARC, 1981; Close & Fowler, 1985. In: Cole & Haresign (Ed.)]

- 1) Presented only two regression lines covering a range of most ME intakes.
- 2) Assuming that N intake is not limiting!
- 3) Considerable variations in responses.
- 4) Young pigs tend to show a linear response, whereas a response tends to be curvilinear with older/larger pigs & higher energy intakes.



2. Energy Requirement of Breeding Animals (e.g. With Swine)

A. During pregnancy:

- 1) Should be gaining ≈ 25 kg (. . . more like 10 to 15 kg in net weight?) during gestation for the first 4-5 parities, plus ≈ 20 kg for placenta & products of conception, thus a total of ≈ 45 kg?!
- 2) Estimation of energy requirements (similar to growing swine):
 - a) Estimate the maintenance requirement.

- b) Consider the rate and efficiency of both uterine (all ♀) & net maternal tissue accretions (gilts & young sows).
- 3) Maintenance, maternal & conceptus gains:
- a) DE_m - 96 to 167 Mcal DE with an average of 110 kcal DE/kg $BW^{.75}$ /day.
- b) Maternal protein and fat gains (assuming maternal gains = 25% fat & 15% protein) - \approx 12.5 Mcal DE/kg of gain with 40% efficiency, thus, 5 Mcal DE/kg of maternal gains.
- c) Conceptus gain - Assuming 1% fat & 9% protein with 10% efficiency, thus, 1.3 Mcal DE/kg!
- d) Intrauterine deposition^a: (Noblet et al., 1990. J. Anim. Sci. 68:562)

	Weight, kg	DM, g	Protein, g	Energy, Mcal
Fetus	13.8 (61)	2444 (73)	1368 (68)	11.1 (72)
Placenta	4.3 (19)	387 (12)	272 (13)	1.9 (12)
Fluids	2.1 (9)	173 (5)	108 (5)	0.7 (5)
Uterus	2.3 (10)	350 (10)	276 (14)	1.7 (11)
Total	22.1 (100)	3365 (100)	2153 (100)	15.6 (100)

^aDetermined at d 110 of pregnancy & determinations are based on 12 fetuses; () = %; Uterus = empty uterus.

B. During lactation - Need energy for maintenance & milk production.

- 1) $DE_m = 110 \text{ kcal}/BW^{0.75}/\text{day}$.
- 2) Milk production - 2 Mcal DE/kg milk (assuming GE content of milk = 1.3 Mcal/kg & efficiency of utilization = 65%.)

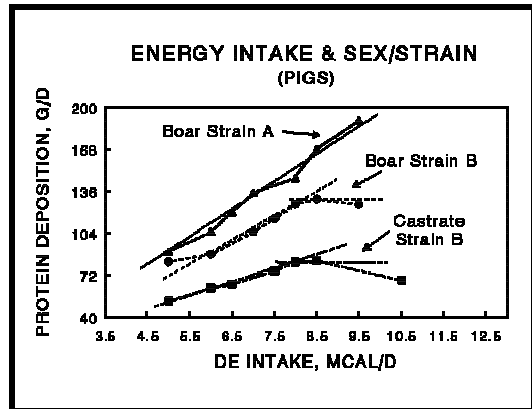
C. Requirements for sows:

Weight, kg:	
Weight at breeding time	140
Pre-farrowing	185
Post-farrowing	165
Gestation:	
Mean gestation wt, kg	162.5
Energy requirement, Mcal DE/d:	
Maintenance ($110 \times Wt^{.75}$)	5.00
Maternal gain ($25 \text{ kg} \times 5 \text{ Mcal/kg} \div 114$)	1.10
Conceptus gain ($20 \text{ kg} \times 1.3 \text{ Mcal/kg} \div 114$)	.23
Total	6.33
Lactation:	
Milk yield, kg/d	6.25
Energy requirement, Mcal DE/d:	
Maintenance ($110 \times \text{post-farrowing } wt^{.75}$)	5.1
Milk production [$(1.3 \text{ Mcal/kg} \div .65) \times 6.25$]	12.5
Total	17.6

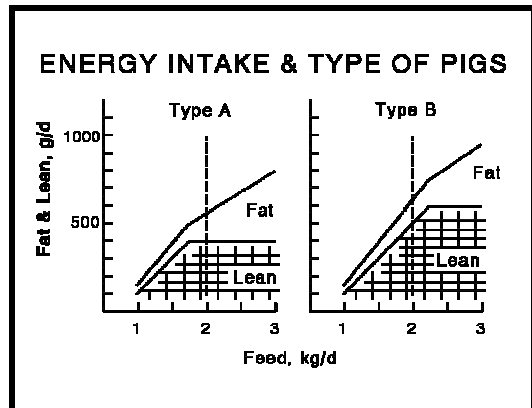
GROWING ANIMALS AND ENERGY (EXAMPLES WITH PIGS)

1. Energy Intake & Body Component Deposition

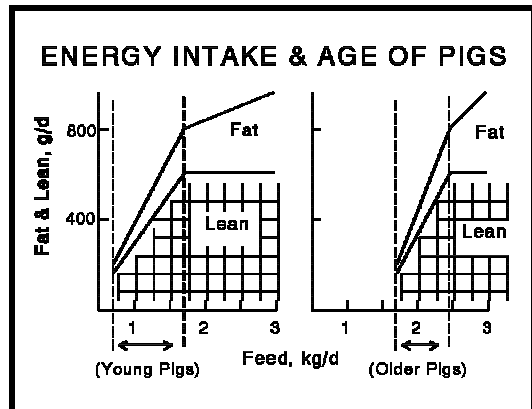
A. Effects of energy intake & sex/strain of pigs on protein deposition - Adapted & redrawn from Campbell and Taverner, 1988. *J. Anim. Sci.* 66:676.



B. Effects of energy intake and type of pigs on lean/fatty tissue growth - Whittemore, 1985. In: Haresign & Cole.



C. Effects of energy intake and age on lean/fatty tissue growth - Whittemore, 1985. In: Haresign & Cole.



☛ The bottom line?

- 1) No response in lean growth to additional energy once pigs consumed adequate energy for a maximum protein accretion! The potential for lean growth is determined by age, sex, breeds, strains, use of repartitioning agents, etc.
- 2) Excess energy consumed can be partitioned into fat deposition, thus increasing fat to lean ratio.

2. Restricting Energy Intake or Limit-Feeding

- A. Finisher pigs tend to consume energy in excess of that needed for maximum protein or lean deposition.
- B. Thus, energy intake can be restricted (usually ↓ by 10-15%) without adversely affecting performance.
- C. A limit feeding is very popular in many countries possibly because:
 - 1) Pigs are sold on carcass basis (discounts for fat carcasses).
 - 2) Availability & cost of feed ingredients.
 - 3) Possibly, lower labor costs.

D. Energy intake and pig performance^a: (Haydon et al., 1989. J. Anim. Sci. 67:1916)

Item	Ad libitum	85%	70%
20-50 kg:			
ADG, kg	.798	.686	.573
Gain:feed	.402	.402	.373
Avg. backfat, cm	2.14	1.78	1.51
Loin muscle, cm ²	23.97	25.61	24.09
Lean cut, %	65.12	66.11	68.32
50-80 kg:			
ADG, kg	1.015	.856	.668
Gain:feed	.297	.308	.286
Avg. backfat, cm	3.23	3.21	2.97
Loin muscle, cm ²	29.40	28.02	31.36
Lean cut, %	60.45	61.58	63.24
80-110 kg:			
ADG, kg	.773	.693	.546
Gain:feed	.205	.219	.208
Avg. backfat, cm	4.00	3.22	2.78
Loin muscle, cm ²	34.31	34.73	40.28
Lean cut, %	58.31	60.71	61.53
Overall:			
ADG, kg	.848	.745	.586
ADFI, kg	2.99	2.50	2.11
Gain:feed	.281	.295	.273

^aNutrient levels were adjusted to achieve similar daily intakes.

- 1) Carcass quality can be improved, but a limit-feeding ↑ days to market because of ↓ weight gain, thus need some incentive programs (premiums) to produce leaner pigs!
- 2) Presently, no practical means or feeding methods to ensure an adequate individual daily feed intake (i.e., in the group housing/feeding situation).
- 3) Probably, will not be accepted in the US (at least not in the near future) because:
 - a) Most pigs are sold on a live weight basis.
 - b) Feed ingredients are abundant and cheap.

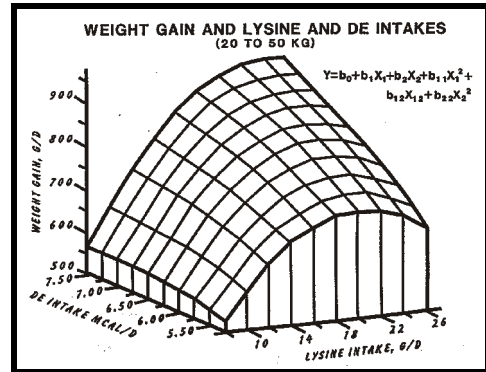
c) Pigs have been selected based on ad libitum feeding.

3. Interaction of Energy and Amino Acids

A. Effects of amino acid & energy intakes on weight gain - Chiba et al., 1991. J. Anim. Sci. 69:708)

B. When AA intake is inadequate:

- 1) ↑ AA intake results in a concomitant ↑ in protein deposition to a point.
- 2) ↑ energy intake has little beneficial effects on protein metabolism, and excess energy may be used for fat deposition!



C. When energy intake is limited:

- 1) ↑ energy supply ↑ protein deposition to a point, and excess energy may be used for fat deposition!
- 2) ↑ AA intake has little beneficial effects on protein metabolism, and some AA may be utilized for energetic purposes.

☛ For optimum growth/nutrient utilization - Must supply energy & AA in the correct proportion!

BREEDING ANIMALS AND ENERGY (EXAMPLES WITH SWINE)

1. Energy Intake During Gestation

A. Effect of additional feed during the late gestation on reproductive performance^a: [Cromwell et al., 1989. J. Anim. Sci. 67(1):3]

Item	Contr.	+ 1.36 kg/d
Gestation wt gain, kg	39.0	48.7
Weight change during lactation (from d 110 to d 21), kg	- 16.4	- 21.3
Total pigs born	10.42	10.77
Pigs born alive	9.71	10.05
No. of pigs at 21 d	8.06	8.35
Birth wt, kg	1.44	1.48
Weight at 21 d, kg	5.20	5.37
Return to estrus, d	5.81	5.70

^aInvolving 1,080 litters at 8 Exp. Stations (S-145); Additional feed offered during the last 23 d of gestation.

B. The bottom line?

- 1) Additional feed in the late gestation can improve reproductive performance of SOWS.

- 2) Benefits (0.3 more pig/litter at weaning & 2.6 kg more total litter weaning wt) can offset additional feed costs.

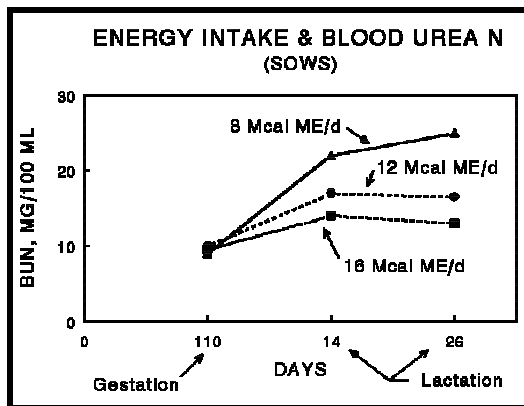
2. Energy Intake During Lactation

A. Effect of energy intake during lactation on reproductive performance: (Reese et al., 1982. J. Anim. Sci. 55:590) [Provided 8, 12 or 16 Mcal ME/d during lactation.]

- 1) Sow & pig performance:

Item	8 Mcal/d	12 Mcal/d	16 Mcal/d
Sow wt change (lact.), kg	- 25.7	- 13.3	- 3.3
Sow BF change (lact.), mm	- 8.4	- 4.6	- 1.8
Return to estrus (≤ 7 d), %	65.2	91.3	95.7
Avg. pig weaning wt, kg	6.6	6.7	7.0

- 2) Energy intake & changes in blood urea N - Figure on the right.
- 3) An inadequate energy intake may increase the rate of protein catabolism (tissues and dietary sources) to support lactation.
- 4) An adequate energy intake is important in minimizing weight and backfat losses of lactating sows.
- 5) An excessive wt loss is likely to have adverse effects on early return to estrus & others.



B. Effects of a source of energy during lactation:

- 1) Effect of tallow or cornstarch on reproductive performance (restricted to 8 Mcal ME/d): (Nelssen et al., 1985. J. Anim. Sci. 60:171)

Item	Tallow	Cornstarch
Lactation wt change, kg	- 27.5	- 24.3
Lact. backfat change, mm	- 10.0	- 9.6
Return to estrus (%):		
≤ 7 d	68.2	56.5
≤ 14 d	79.5	73.9
Pig wt at d 28, kg	6.7	6.5
No. of pigs at d 28	8.5	8.9

- 2) Other research:

- a) Addition of 2.5% sucrose - No effect. (NCR-89, 1990. J. Anim. Sci. 68:3498.)
- b) Addition of fructose - No effect. (Campbell et al., 1990. J. Anim. Sci. 68:1378.)

☛ The bottom line? - *“For optimum reproductive performance, ensuring an adequate energy intake during lactation is more important than the source of energy!”*

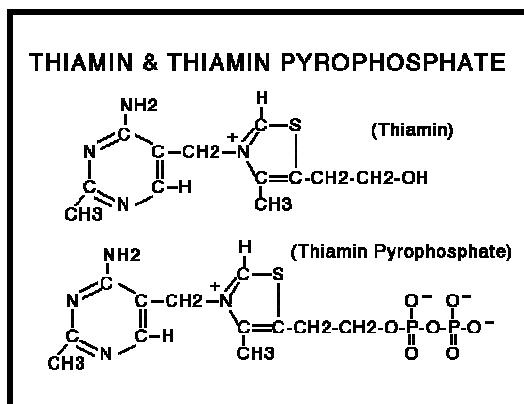
3. **Some Important Vitamins in Energy Metabolism?** - Thiamin (B₁), Riboflavin (B₂), Niacin, Pantothenic acid, and Biotin!

THIAMIN (VITAMIN B₁)

1. General

A. Considered to be the oldest vitamin:

- 1) The first “water-soluble” vitamin to be discovered from so called a “growth factor.”
- 2) The deficiency disease, beriberi, is probably the earliest documented disorder. (Recorded in China as early as 2,600 B.C.).



B. Beriberi in general: [Please see Maynard et al. (1979), McDowell (1989) & others]

- 1). The major health problem observed in the Far East for a long time, and the problem persisted until fairly recently - e.g., Even as recently as 1940's, the mortality rate from beriberi in Philippine was 132/100,000 (1947).
- 2) Usually both cardiac and nervous functions are disturbed:
 - a) Signs include edema (ankles), puffiness of face, anorexia, digestive disturbances, heart enlargement, tachycardia, lassitude & muscle weakness, loss of knee & ankle reflex, etc.
 - b) Beriberi patients are unable to rise from a squatting position, indicating the neurological damages.
- 3) In the early 1880s - A physician in the Japanese Navy substituted some of polished rice with other foods, and was able to ↓ the incidence of beriberi, and incorrectly thought that added protein was responsible for preventing beriberi.
- 4) In the 1890s:
 - a) Eijkman discovered polyneuritis in chickens & symptoms were similar to beriberi.

- b) Rice bran was effective in curing & preventing beriberi, and also it had similar effects on polyneuritis.
 - c) Incorrectly assumed that polished rice produced a toxin.
- 5) Casmir Funk (1910s) obtained a potent anti-beriberi substance from rice bran (discovery of thiamin), and a substance had characteristics of amine, thus coined the term “vitamin(e)” (vital amine). (Found later that many vitamins are not amines!)
2. **Structure** - See the figure on thiamin and thiamin pyrophosphate (TPP; Martin et al., 1983).
3. **Functions**
- A. Along with riboflavin and niacin, plays important roles in the citric acid cycle.
 - B. TPP is responsible for decarboxylation:
 - 1) Pyruvate → acetyl-CoA + CO₂
 - 2) α-Ketoglutaric acid → succinyl-CoA + CO₂
 - C. TPP is also involved in transketolase reaction (pentose pathway/synthesis of ribose).
 - D. In nervous tissues - Little is known, but involved in:
 - 1) The synthesis of acetylcholine - Transmission of neural impulses.
 - 2) A passive transport of Na (excitable membranes) - Transmission of impulses.
4. **Deficiency**
- A. Signs in poultry - Loss of appetite & weight, weakness in leg/muscular, bradycardia (from 300 to 90-100/min), edema, diarrhea, vomiting, . . . & death.
 - B. Signs in pigs - Loss of appetite & weight, weakness, premature birth, high mortality, slow pulse, heart failure, edema, hemorrhages, diarrhea, vomiting & sudden death.
 - C. Fish:
 - 1) Signs include poor appetite, muscle atrophy, convulsions, instability & loss of equilibrium, edema & poor growth.
 - 2) Thiaminase - Found in tissues of most fish, and can destroy thiamin:
 - a) Can split the vitamin into two component ring structures in non-living tissues.
 - b) Thiaminase in unheated fish or fish viscera can destroy the vitamin prior to ingestion - e.g., Channel catfish can develop a deficiency by feeding diets containing 40% unheated fish viscera for 10 wk.
5. **Requirements and Sources**
- A. Thiamin (B₁) requirements: (Also see appropriate “Nutrition & Feeding” sections)
-
-

Animal	mg/kg
Poultry (NRC, 1994):	
Immature chickens	0.8-1.0
Laying	0.60-0.88
Broilers	1.80
Turkeys, all classes	2.0
Swine (NRC, 1998):	
3-120 kg	1.0-1.5
Adults	1.0
Horses (NRC, 1989):	
Horses & ponies (DM)	3.0-5.0
Also via	Microbial synthesis?
Fish (NRC, 1993):	
Channel catfish & rainbow trout	1.0
Pacific salmon	No dietary requirement?
Common carp	.5
Tilapia	Not tested

☛ Usually, can be met by natural ingredients!

B. Sources:

- 1) Cereal grains (seed coats & germs) & their by-products, oil extraction residues - relatively rich sources (\approx 3-12 mg/kg).
- 2) Brewer's yeast is the richest known natural source (95.2 mg/kg).

C. Thiamin in pork:

- 1) For some unknown reason, pigs' tissue contains high levels of thiamin vs other species (several times higher).
- 2) Thus, pork is an excellent source of thiamin (0.87 mg/3 oz of broiled chop vs RDA of 1-2 mg/day).

D. Factors affecting the requirement:

- 1) Heat processing - Cooking, pelleting, etc. (Thiamin is relatively heat-stable, but it's not stable in a moist-heat!)
- 2) Presence of thiaminases - e.g., Moldy grains/feeds (microbes can produce thiaminases).

RIBOFLAVIN (VITAMIN B₂)

1. General [Please see Maynard et al. (1979), McDowell (1989) & others]

- A. "Water-soluble" factor or factors promoted growth & prevented beriberi.
- B. Heating destroyed anti-beriberi effect more rapidly than growth-promoting effect.
- C. Water-soluble fractions consisted of two essential factors:

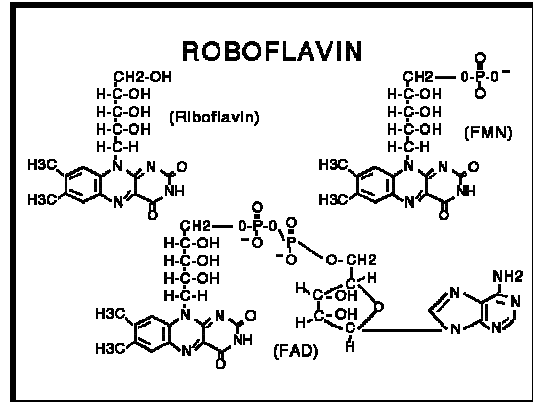
- 1) Less heat stable factor - Thiamin.
- 2) Heat stable factor - Riboflavin.

D. Warburg & Christian (1932) - Isolated an oxidative enzyme from yeast, which showed "yellow" color with green fluorescence (∴ "Old Yellow Enzyme!"), and able to split it into a protein- & nonprotein (pigment)-fraction.

☛ Perhaps, this was the first identification of a "prosthetic" group of the enzyme!?

E. Kuhn (1933) - Isolated a yellow pigment from egg white with oxidative properties & suggested the name "flavin."

- 1) e.g., Ovoflavin - isolated from eggs, lactoflavin - isolated from milk, hepatoflavin - isolated from liver, & uroflavin - isolated from urine.
- 2) Crystalline compounds contained a ribose, thus the name, "riboflavin!"

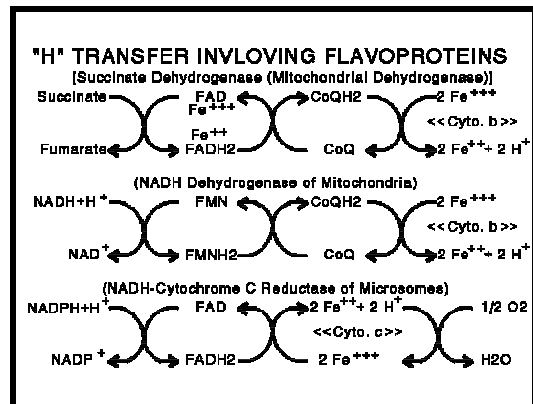


2. **Structure** - Redrawn from Martin et al. (1983).

3. Functions

- A. A component of FMN and FAD - A prosthetic group for active enzymes, flavoproteins. (Most flavoproteins contain FAD.)
- B. Involved in a transfer of electrons in biological oxidation-reduction reactions.
- C. About 40 flavoprotein enzymes participate in the electron transfer:

- a) Some examples - "Hydrogen transfer involving flavoproteins:" (Adapted & redrawn from McDowell, 1989)
- b) Aerobic dehydrogenases (no metal) - D- & L-AA oxidase, glucose oxidase, etc.
- c) Oxidases (Cu, Fe or Mo) - Cuproflavoprotein in butyryl-CoA-dehydrogenase, xanthin oxidase, etc.
- d) Anaerobic dehydrogenases - acyl-CoA dehydrogenases & electron-transferring flavoprotein, succinic dehydrogenase, fumaric reductase, etc.
- e) Others - Choline dehydrogenase, α -glycerophosphate dehydrogenase, L-lactate dehydrogenase, D-lactate cytochrome reductase, etc.



4. Deficiency

- A. Poultry - A characteristic sign, curled-toe paralysis, is a reflection of degenerative changes in myelin sheaths in sciatic & brachial nerves; other signs include retarded growth, diarrhea, high mortality, reduced hatchability, reduced egg production, etc.
- B. Swine - Signs include anorexia, slow growth, rough hair coat, dermatitis, unsteady gait, scours, reproductive & digestive tracts disorders, vomiting, cataracts, light sensitivity, etc.
- C. Fish - Signs include cloudy lens, hemorrhagic eyes & other organs, photophobia, dim vision, incoordination, abnormal pigmentation of iris, striated constriction of abdominal wall, dark coloration, poor appetite, anemia, poor growth, etc.

5. Requirements and Sources

- A. Riboflavin requirements: (Also, see appropriate “Nutrition & Feeding” sections)

Animal	mg/kg
Poultry (NRC, 1994):	
Immature chickens	1.7-3.6
Laying hens	2.1-3.1
Broilers	3.0-3.6
Turkeys	2.5-4.0
Swine (NRC, 1998):	
3-120 kg	2.0-4.0
Adults	3.75
Horses (NRC, 1978):	2.0
Fish (NRC, 1993):	
Channel catfish	9.0
Rainbow trout	4
Pacific salmon & common carp	7
Tilapia	6

- ☛ One of the vitamins most likely to be deficient in nonruminant species, and also in humans!

- B. Sources:

- 1) Cereal grains, their by-products & soybean meal are rather low (e.g., corn, 1.4 mg & SBM, 3.2 mg/kg DM) - Corn-soy diets are borderline to deficient, thus must be supplemented!
- 2) Green, leafy vegetables, yeast & forages are good sources - e.g., Sun cured alfalfa leaves contain 23.1 mg/kg.

- ☛ For humans, milk, eggs, liver, heart & muscle are rich sources!

- C. Factors affecting the requirement:

- 1) Heating will destroy some vitamin (little more stable than thiamin though).
- 2) A free-form (produced by microbes or by chemical synthesis) is sensitive to light.
- 3) Divalent heavy metals (Cu, Fe, Mn, Zn, Cd) bind the vitamin & make it unavailable.

NIACIN

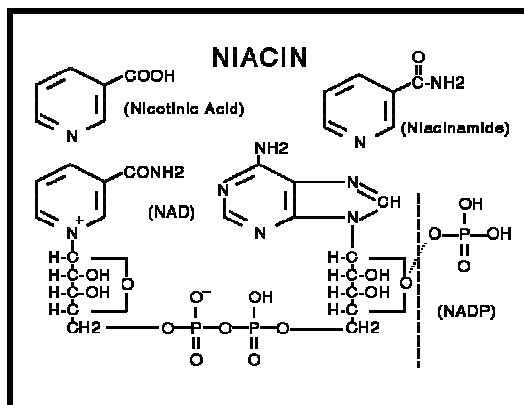
1. **General** [Please see Maynard et al. (1979), McDowell (1989) & others]
 - A. Niacin has been known to organic chemists since 1867, a long before its importance as an essential nutrient was discovered.
 - B. Funk (1911-1913) isolated niacin from yeast & rice polishing.
 - C. The interest in niacin was lost because of its ineffectiveness in curing beriberi.
 - D. Warburg et al. (1935) reported that niacin functioned as part of a hydrogen transport system.
 - E. Third vitamin to be discovered from the “vitamin B complex,” i.e., thiamin first, riboflavin second & then niacin.

2. **Pellagra in General**
 - A. A niacin deficiency in humans - Means a rough skin (dermatitis).
 - B. May also involve Trp, thiamin, riboflavin and pyridoxine.
 - C. A condition common in the corn-eating population - Appeared in Europe in the 1730s when corn from the New World became the major staple foodstuff.
 - D. Most cases occurred in a low-income group - Diets associated with the disease were referred to as three **M**'s:
 - **M**eal (corn), **M**eat (back fat) and **M**olasses. (+ **p**overty!)
 - E. In the US (especially in the south), it's common for 20,000 deaths/year from pellagra around the turn of the century.
 - F. Clinical signs & mortality are referred to as the **four D**'s:
 - **D**ermatitis of the area exposed to sun, **D**iarrhea, **D**ementia [a mental disorder - depression & schizophrenia (indifference, withdrawal, hallucination, illusion of persecution and omnipotence)], and **D**eath.

3. Structure (Redrawn from McDowell, 1989)

4. Functions

- A. Component of 2 important coenzymes, NAD (formally called DPN) & NADP (formally called TPN), which are involved in biological oxidation-reduction systems.
- B. Important reactions catalyzed by NAD & NADP:



- 1) CH_2O metabolism - Glycolysis (anaerobic & aerobic oxidation of glucose) & citric acid cycle.

- 2) Lipid metabolism - Glycerol synthesis and breakdown, fatty acid oxidation and synthesis & steroid synthesis.
- 3) Protein metabolism - Degradation and synthesis of amino acids & oxidation of carbon chains via citric acid cycle.
- 4) Others - Photosynthesis & rhodopsin synthesis.

5. Deficiency

- A. Poultry - Black tongue (inflammation of the tongue, mouth cavity, & esophagus), ↓ appetite & growth or weight loss, reduced egg production and hatchability, etc.
- B. Swine - Poor appetite & weight gain, dermatitis, hair loss, diarrhea, inflammation & necrosis of the GI tracts, etc.
- C. Fish - Loss of appetite, lesions in colon, jerky or difficult motion, weakness, edema of stomach & colon, muscle spasms, poor growth, anemia, fin lesions, etc.

6. Requirements and Sources

- A. Niacin requirements: (Also, see appropriate “Nutrition & Feeding” sections.)

Animal	mg/kg
Poultry (NRC, 1994):	
Immature chickens	10.3-27.0
Laying hens	8.3-12.5
Broilers	25-35
Turkeys	40-60
Swine (NRC, 1998): (Available)	
3-120 kg	7-20
Adult	10
Horses (1978):	Microbial synthesis
Fish (NRC, 1993):	
Channel catfish	14
Rainbow trout	10
Pacific salmon	Required, but not determined
Common carp	28
Tilapia	Not tested

- Usually, diets are supplemented!

- B. Sources:

- 1) Grains (corn, sorghum, wheat & oats) are low in niacin, and it exits 1° as a bound form (85 to 90%) & not available to animals.
- 2) Soybean meal (31 mg/kg DM) - 100% available based on a chick assay.
- 3) Wheat bran (268 mg) & brewer’s yeast (482 mg/kg DM) are good sources.

7. Trp & Niacin Requirement

- A. Animals can synthesize niacin from Trp, but there are wide variations in their ability to synthesize this vitamin.

- B. Trp levels in the diet may affect niacin requirements: (e.g. in pigs)
 - 1) ≈ 50 mg Trp $\rightarrow \approx 1$ mg niacin - i.e., Every 0.01% Trp above the requirement (or 100 mg/kg), pigs can synthesize 2 mg niacin/kg of diet.
 - 2) Thus, for high-protein diets, probably no need for niacin supplementation.

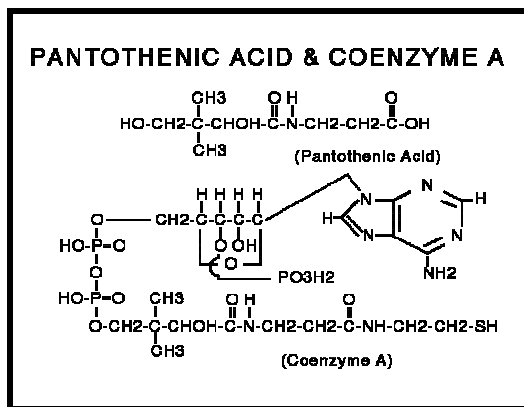
PANTOTHENIC ACID

1. **Introduction** [Please see Maynard et al. (1979), McDowell (1989) & others]

- A. Isolated during the 1930s from the vitamin B₂ complex along with pyridoxine.
- B. Previously called a chick anti-dermatitis factor.
- C. The name pantothenic acid was derived from the Greek word “*Pantos*,” meaning found everywhere.
- D. Found in two enzymes, coenzyme A and acyl carrier protein, which are involved in many reactions in CH₂O, fat & protein metabolism.

2. **Structure** (Adapted & redrawn from McDowell, 1989)

- A. Found in feeds in both bound (as coenzyme A) & free forms.
- B. A free form is unstable & easily degraded by heat, acids & bases.



3. **Functions**

- A. A constituent of coenzyme A and acyl carrier protein.
- B. The most important function of coenzyme A is probably its role as a carrier of carboxylic acids.
- C. Some biochemical reactions involving pantothenic acid: (McDowell, 1989)

Enzyme	Derivative	Reactant	Product	Site
Pyruvate dehydrogenase	CoA	Pyruvate	Acetyl CoA	Mitochondria
α -ketoglutarate dehydrogenase	CoA	CoA	α -ketoglutarate	Succinyl CoA
Fatty acid oxidase	CoA	Palmitate	Acetyl CoA	Mitochondria
Fatty acid synthetase	Acyl carrier protein	Acetyl CoA, malonyl CoA	Palmitate	Microsomes
Propionyl CoA carboxylase	CoA	Propionyl CoA, CO ₂	Methylmalonyl CoA	Microsomes
Acyl CoA synthetase	Phospho-pantetheine	Succinyl CoA, GDP + Pi	Succinate, GTP + CoA	Mitochondria

4. **Deficiency**

- A. Poultry - Signs include severe dermatitis, broken feathers (become brittle & fall-off), perosis, poor growth, reduced egg production & hatchability, mortality, etc.
- B. Swine - Signs include anorexia, poor growth, diarrhea, rough hair coat, brown exudates around eyes, anemia, "goose stepping" (resulting from sciatic nerve damages), etc.
- C. Fish - Signs include clubbed gills, prostration, loss of appetite, necrosis & scarring, cellular atrophy, gill exudate, sluggishness, poor growth, anemia, etc.

5. Requirements and Sources

- A. Pantothenic acid requirements: (Also, see appropriate "Nutrition & Feeding" section.)

Animal	mg/kg
Poultry (NRC, 1994):	
Immature chickens	9.4-10.0
Laying hens	1.7-2.5
Broilers	10.0
Swine (NRC, 1998):	
3-120kg	7-12
Adults	12
Horses (NRC, 1978):	Microbial synthesis
Fish (NRC, 1993):	
Channel catfish	15
Rainbow trout	20
Pacific salmon	20
Common carp	30
Tilapia	Not tested

- B. Sources:

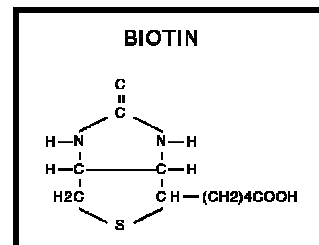
- 1) Corn (6.6 mg) & SBM (18.2 mg/kg DM) based diets tend to be deficient in pantothenic acid, ∴ diets are usually supplemented.
- 2) Milling by-products such as rice bran (25.2 mg) & wheat bran (33.5 mg/kg DM) are good sources.

BIOTIN

1. **General** [Please see, e.g., Maynard et al. (1979), McDowell (1989)]

- A. Different lines of investigations led to the discovery of biotin:

- 1) Coenzyme R - Required for legume nodule bacteria.
- 2) Biotin - Isolated from egg yolk, which was necessary for yeast growth.
- 3) Factor H or vitamin H - A factor present in certain foods (especially in the liver & kidney) that protected egg-white injury (dermatitis).



- B. Szent-György et al. (1940) found that all three were the same substance.

- C. Generally believed for many years that supplemental biotin is not necessary for swine & poultry because biotin is widely distributed in nature/feedstuffs & it is synthesized by many different microorganisms in the GI tract.
 - D. But in the mid 1970s, several field cases of deficiency signs were observed, and animals responded to a supplemental biotin, which led to re-evaluation of the role of biotin in animal diets.
2. **Structure** (Adapted and Redrawn from Martin et al., 1983 - See the box)
3. **Functions**
- Serves as a prosthetic group for a number of enzymes (carboxylases, transcarboxylases & decarboxylases), and biotin moiety functions as a mobile carboxyl carrier.
- A. Carbohydrate metabolism:
- 1) Carboxylation of pyruvic acid to oxaloacetic acid.
 - 2) Conversion of malic acid to pyruvic acid.
 - 3) Interconversion of succinic acid and propionic acid.
 - 4) Conversion of oxalosuccinic acid to α -ketoglutaric acid, etc.
- B. Protein metabolism:
- 1) Protein synthesis.
 - 2) Amino acid deamination.
 - 3) Purine synthesis & nucleic acid metabolism, etc.
- C. Lipid metabolism:
- 1) Conversion of acetyl-CoA to malonyl-CoA (the first reaction in FA synthesis).
 - 2) Essential FA metabolism, etc.
4. **Deficiency**
- A. Poultry - Signs include reduced performance, broken feathers, dermatitis, leg & beak deformities, increased embryonic mortality & reduced viability after hatching, etc.
 - B. Swine - Signs include reduced performance, loss of hair, dermatitis (dry & rough), brownish exudate, ulceration of skin, inflammation of the mouth mucosa, cracking of soles & top of hooves, etc.
 - C. Fish - Signs include loss of appetite, lesions in colon, coloration, muscle atrophy, spastic convulsion, fragmentation of erythrocytes, skin lesions, poor growth, etc.
5. **Requirements and Sources**

A. Requirements: (Also, see appropriate "Nutrition and Feeding" sections.)

Animal	mg/kg
Poultry (NRC, 1994):	
Immature chickens	0.09-0.15
Laying hens	0.08-0.13
Broilers	0.12-0.15
Turkeys	0.10-0.25
Swine (NRC, 1998):	
3-120 kg	0.05-0.08
Adults	0.20
Horses (NRC, 1978)	Microbial synthesis?
Fish (NRC, 1993):	
Channel catfish	Required, but not determined
Rainbow trout	.15
Pacific salmon	Required, but not determined
Common carp	1.0
Tilapia	Not tested

B. Sources:

- 1) Exists in both bound (unavailable) & free forms - e.g., > ½ of biotin in various feedstuffs is in the bound form & biologically unavailable.
- 2) Contents in cereal grains are influenced by variety, season, yield, storage conditions, etc.
- 3) Corn (.07 mg/kg) and SBM (.32 mg/kg DM) are highly available sources, but the availability in wheat, barley & milo is very low.

C. Avidin (antivitamin):

- 1) Present in raw eggs, which is denatured by moist heat.
- 2) Secreted by mucosa of oviduct of the hen into egg white, and combines with biotin in "1:1 ratio" (the bound biotin is not available).
- 3) Dietary avidin < biotin - Cures/prevent deficiency symptoms.

6. Biotin Supplementation (e.g. with Swine)

A. In general, no improvement in performance of growing pigs with biotin supplementation.

B. In sows, inconsistent responses:

- 1) Observed improved hoof hardness/strength, improved skin & hair coat condition, reduced hoof cracks & footpad lesions in some investigations.
- 2) Also observed improved reproductive performance (litter size, weaning wt, days to return to estrus, etc.) in some studies.

C. Recent data:

A. Biotin and reproductive performance of sows: (Watkins et al., 1991. J. Anim. Sci. 69:201)

Item	Basal	+ Biotin
Foot score	7.16	6.48
Hair score	1.68	1.58
Soundness score	2.38	2.23
Rebreeding interval, d	4.98	5.25
No. of pigs born	11.41	10.66
% born alive	78.8	81.9
Pig birth wt, kg	1.58	1.45
No. of pigs at 21 d	7.42	7.56
% alive at 21 d	89.0	85.8
Pig 21-d wt, kg ^a	5.15	4.73

^aBiotin effect, $P < 0.03$.

B. Biotin and foot lesions: (Lewis et al., 1991. J. Anim. Sci. 69:207)

Item	0	330 µg/kg	<i>P</i>
Kentucky:			
No. of lesions ^a	2.59	2.40	0.59
Overall lesion score ^b	1.20	1.07	0.24
Minnesota & Nebraska:			
No. of horn crack ^a	3.04	3.19	0.68
Severity of horn cracks ^c	0.91	0.98	0.51
No. of heal cracks ^a	2.86	3.03	0.58
Severity of heal cracks ^c	1.19	1.14	0.72
No. sidewall cracks ^a	3.57	4.57	0.08 ^d
Severity of sidewall cracks ^c	1.27	1.44	0.19
No. of bruises ^a	0.87	1.40	0.01
Severity of bruises ^c	0.52	0.93	0.01

^aTotal No. of lesions for all four feet; ^bBased on overall condition of the feet where 0 represents no lesions & 5 represents many lesions; ^cBased on the system where each lesion was given severity score ranging from 1 (a very small lesion) to 5 (a very large severe lesion); ^dStation x treatment, $P < .05$.

- Biotin has no effect on cracks & bruises on the feet of sows.

CHROMIUM

1. Essentiality

A. Glucose Tolerance Factor (GTF): (Bosco, 1989)

- 1) In 1955, researchers found that rats maintained on a diet of torula yeast (not brewer's yeast) had impaired glucose tolerance (unable to handle large doses of sugar).
- 2) No other nutrients could overcome this, ∴ they concluded that something was missing from torula yeast, and named this mystery substance "*Glucose Tolerance Factor* (GTF)."

- 3) Subsequently, GTF was found to exist in brewer's yeast, and the active component was identified to be a trivalent chromium. The GTF also contains nicotinic acid, Gly, Glu & Cys, but exact structure is not yet known.
- 4) Further studies revealed that a severe Cr deficiency can impair glucose tolerance as serious as mild diabetes.
 - ▶ Most animal products contain much of their total Cr in the form of GTF, and GTF organic complex is 50 times more active than inorganic Cr.
 - ▶ The GTF may qualify as a vitamin!?! (An organic compound containing Cr, and has a greater biological activity than inorganic Cr . . . similar to vitamin B₁₂!)

B. Other research:

- 1) In rats & mice, 5 ppm Cr supplementation in drinking water ↑ growth rate over controls for both sexes, and ↓ mortality rate in ♂ (Schroeder et al., 1963a,b. J. Nutr. 80:39 & 48).
- 2) In humans, Cr had beneficial effects on malnourished children, i.e., restored glucose tolerance (Mertz, 1974. In: Proc. 2nd Int. Symp. Trace Elem. Metab. p 185).
- 3) In birds, 10 ppm Cr as CrCl₃ improved interior egg quality as measured by Haugh units (Jensen et al., 1978. Fed. Proc. 37:404).
- 4) In ruminants, supplementation of Cr as GTF to stressed calves improved weight gain and efficiency [Chang et al., 1991. JAS 69(Suppl. 1):212].

C. The deficiency is characterized by impaired growth, impaired glucose tolerance, ↑ serum cholesterol & triglycerides, ↑ incidence of aortic plaques, ↓ fertility and sperm count and shortened life-expectancy.

D. The function seems to be to potentiate the action of insulin:

- 1) According to Mertz et al. (1974. Fed. Proc. 33:2275), Cr may form a complex between insulin & insulin receptor, ∴ facilitating the insulin-tissue interaction.
- 2) Effects of Cr on the metabolism?
 - a) "Glucose" - a Cr deficiency can cause a syndrome resembling diabetes mellitus with hyperglycemia. (Cr & action of insulin?)
 - b) "Lipids" - Cr has effects on serum cholesterol homeostasis. (↓ serum levels?)
 - c) "Protein" - Cr ↑ incorporation of AA (Gly, Ser, Met) into heart muscle. (via the action of insulin?)

2. Toxicity

A. General:

- 1) Chromic oxide (Cr₂O₃) has been used as a fecal marker for several wk at levels as high as 3,000 ppm without adverse effects.
- 2) The rat can tolerate 100 mg/kg, whereas cats can tolerate 1,000 mg/kg.

- 3) Chicks were not adversely affected by feeding 1,000 ppm Cr, but ↓ growth rate with 2,000 ppm.
- 4) A single oral dose of 700 mg or 30-40 mg Cr/kg BW resulted in acute toxicity in mature cattle & young calves, respectively.

B. Toxicity signs:

- 1) "Industrial exposure (humans)" - allergic dermatitis, skin ulcers & ↑ incidence of bronchogenic carcinoma.
- 2) "Animals" - skin-contact dermatitis, irritation of respiratory passages, ulceration & perforation of the nasal septum & lung cancer.
- 3) "Acute toxicosis in ruminants" - inflammation & congestion of the stomach & ulceration of the rumen & abomasum.

C. Maximum tolerable dietary level - 3,000 ppm Cr as oxide & 1,000 ppm as Cl for domestic animals (NRC, 1980).

D. "Adequate" & "safe" intake levels in humans: (RDA, 1989)

- 1) 10-60 for infants, 30-120 for children (> 6 yr) & 50-200 µg/d for others.
- 2) The upper levels should not be habitually exceeded.

3. Cr & Heart Disease

A. Leading cause of death among diabetics is cardiovascular disease:

- 1) Diabetics suffer the lesions of atherosclerosis, and people with atherosclerosis also have impaired glucose tolerance.
- 2) People dying from atherosclerosis have lower (or absent) Cr levels than people dying from other causes such as accidents.
- 3) People with heart disease had consistently lower Cr, while none of people with blood Cr of ≥ 5.5 µg/L had the disease. The link is very clear in animals, i.e., Cr-deficient animals have impaired glucose tolerance & atherosclerotic plaques in their aortas.

B. ↑ scientific evidence that when Cr is added to the diet, blood cholesterol ↓ and incidence of atherosclerosis ↓.

C. Although the requirement is not well established, probably quite few people are not getting enough Cr. (One USDA study found that 90% of the diets examined did not supply 50 µg/d!)

4. Chromium & Metabolism (NRC, 1997)

A. Carbohydrate:

- 1) Cr potentiates the action of insulin via the GTF (contains nicotinic acid, glycine, glutamic acid, and cysteine, as well as Cr . . . but the exact structure of the native complex has not been determined).
- 2) Increase glucose uptake, glucose use for lipogenesis, glucose oxidation to carbon dioxide, and glycogenesis with the addition of Cr to animal tissues.
- 3) Normalization of glucose metabolism in humans afflicted with a variety of disorders (e.g., diabetes-like symptoms) with Cr supplementation.
- 4) A decreased sensitivity of peripheral tissues to insulin may be the primary biochemical lesions in Cr deficiency.
- 5) Cr can potentiate the activity of insulin, but does not substitute!

B. Lipids:

- 1) Cr may be necessary for normal lipid metabolism and for minimizing rates of atherogenesis because rats & rabbits fed low-Cr diets had greater concentrations of serum cholesterol and aortic lipids and exhibited greater plaque formation . . . Cr supplementation reduced cholesterol concentrations.
- 2) With Cr supplementation, increases in HDL cholesterol, decreases in total cholesterol, LDLP cholesterol, and triacylglycerols in humans have been observed . . . But not very consistent!

C. Protein:

- 1) Because of the role of insulin in amino acid uptake by animal tissues, Cr is predicted to have an effect on protein metabolism.
- 2) One report indicated that Cr supplementation increased amino acid incorporation into heart proteins and uptake into tissues of rats.

D. Nucleic acids:

- 1) Cr in trivalent state seems to be involved in structural integrity and expression of genetic information in animals.
- 2) Cr protects RNA against heat denaturation.
- 3) Cr seems to be concentrated in the nuclei of animal cells, and has been shown to enhance RNA synthesis in mice in vitro and in vivo.

E. Stress:

- 1) Cr status seems to be influenced by physiological, pathological, and nutritional stresses.
- 2) For instance, exercise and trauma can increase urinary Cr in humans, thus contributing to Cr deficiency.
- 3) Symptoms of Cr deficiency can be aggravated by a low-protein diet, exercise, blood loss, and infection.

- 4) Supplemental Cr may increase longevity and retards aging by improving immune function and enhancing resistance to infectious diseases . . . e.g., supplemental Cr for market-transit-stressed feedlot calves and periparturient and early-lactation dairy cows improved immune status and health.