ENERGY METABOLISM AND VITAMINS AND MINERAL

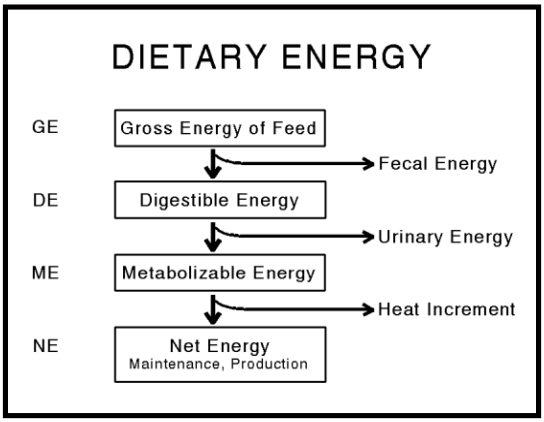
ENERGY SYSTEMS

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) TDN = digestible crude protein + digestible crude fiber + digestible nitrogen-free extract (starch and sugars) + 2.25 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, CH_2O 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 x [96 - (0.202 x % CP)] (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:

$DE = \sum(DE_m + DE_{pr} + DE_f + DEH_c)$ (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 & Heresign]

a) Measurements from fasting metabolism.
b) Linear regressions relating energy retention (ER) to ME intake & calculating ME_m where ER = 0.

c) 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:

a) e.g., Estimates based on two separate equations: [ARC, 1981; Close & Fowler (1985) in Cole & Haresign]

	ME, MJ/day	
Weight, kg	$ME_m=0.719W^{0.63}$	$ME_m=0.458W^{0.75}$
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

b) The most commonly used estimate is ≈ **110 kcal/kg $BW^{.75}$**.

B. Energy requirements for protein and fat retention:

1) 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

2) 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 (kcal DE/day) = 0.326W + 23.65 (T_c - T) [where W = weight in kg and T (ambient temperature) & T_c (critical temperature) in °C.]

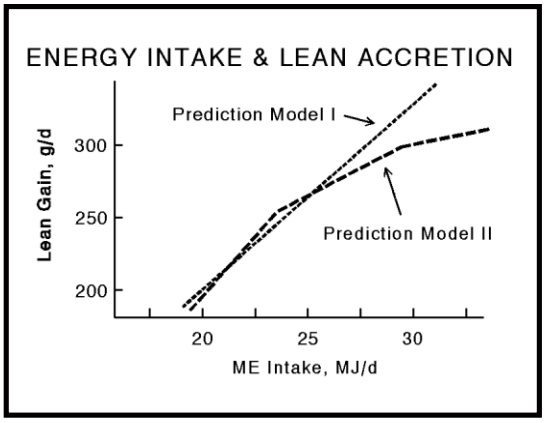
2) According to one estimate, need additional 25 g (80 kcal ME) of feed/day to compensate for each 1°C below T_c in 25- to 60-kg pigs.

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, and conceptus gain:

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) – Approximately 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)

[a]Determined 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 kcal/$BW^{0.75}$/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:

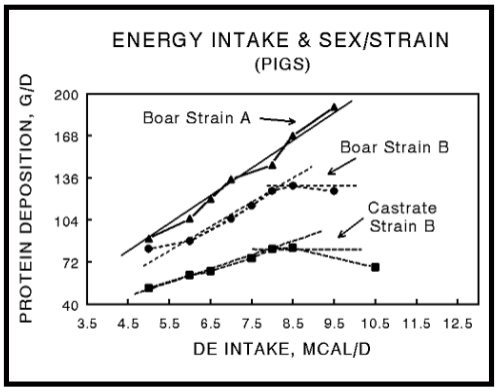
Weight, kg:	
Weight at breeding time	140
Pre-farrowing	185
Post-farrowing	165
Gestation:	
Mean gestation wt, kg	162.5
Energy requirement, Mcal DE/d:	
Maintenance (110 x $Wt^{.75}$)	5.00
Maternal gain (25 kg x 5 Mcal/kg ÷ 114)	1.10
Conceptus gain (20 kg x 1.3 Mcal/kg ÷ 114)	.23
Total	**6.33**
Lactation: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

GROWING ANIMALS AND ENERGY (EXAMPLES WITH PIGS)

1. Energy Intake & Body Component Deposition

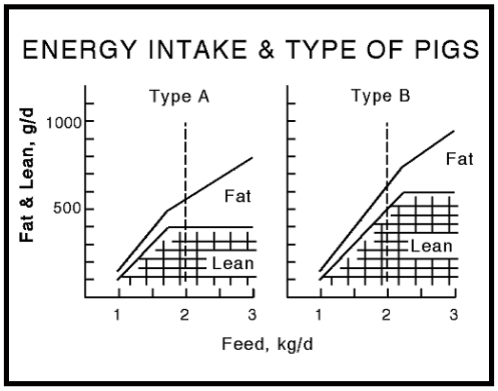
A. Effects of energy intake & sex/strain of pigs on protein deposition - Adapted & redrawn from Campbell and Taverner, 1988. J. Anim. Sci. 66:676.

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?

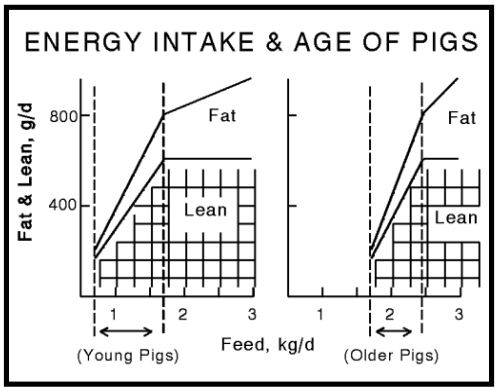
    1) No response in lean growth to additional energy once pigs consumed adequate energy for a maximum protein accretion! The potential for lean growth is determined by age, sex, breeds, strains, use of repartitioning agents, etc.
    2) Excess energy consumed can be partitioned into fat deposition, thus 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	0.798	0.686	0.573
Gain:feed	0.402	0.402	0.373
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	0.856	0.668
Gain:feed	0.297	0.308	0.286
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	0.773	0.693	0.546
Gain:feed	0.205	0.219	0.208
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	0.848	0.745	0.586
ADFI, kg	2.99	2.50	2.11
Gain:feed	.281	.295	.273

[a]Nutrient levels were adjusted to achieve similar daily intakes.

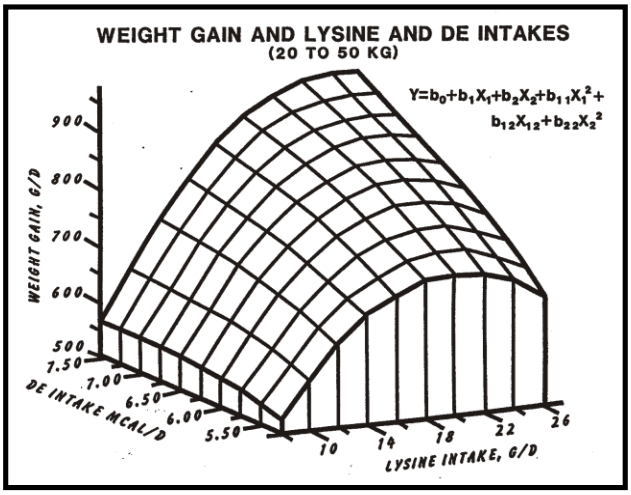
1) Carcass quality can be improved, but a limit-feeding ↑ days to market because of ↓ weight gain, thus need some incentive programs (premiums) to produce leaner pigs!
2) Presently, no practical means or feeding methods to ensure an adequate individual daily feed intake (i.e., in the group housing/feeding 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

[a]Involving 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.

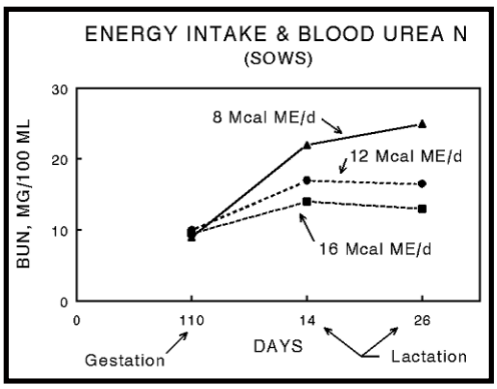
2. Energy Intake During Lactation

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 (unknown source).
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. Vitamins and Energy Metabolism?

A. Important vitamins in energy metabolism?

- Thiamin (B_1), riboflavin (B_2), niacin, pantothenic acid, and biotin!

B. Discovery of B vitamins?

1) A specific dietary factor essential for the prevention of beriberi & polyneuritis became known as a water-soluble B, and later simply as a "vitamin B."
2) Also, the scientists recognized that this factor was essential for growth and other physiological functions.
3) Further studies (1925-1930) revealed that a vitamin B actually consisted of two factors differing in the chemical nature & physiological effects, thus, the name vitamin B was changed to a "vitamin B complex."
4) The term vitamin B (or B_1) was reserved for an antineuritic factor, and the name "*thiamin(e)*" was introduced.
5) Many believed that other effects of vitamin B complex were result of an another single factor, thus, designated B_2 (or G by some). The other factor is now known as "*riboflavin*."
6) Then, they realized that there are more than two, and, possibly, several factors in the complex, which eventually led to identification of *pantothenic acid*, *niacin*, [pyridoxine, B_6], *biotin*, [cobalamin, B_{12}] & [folic acid].

THIAMIN (VITAMIN B_1)

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

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):

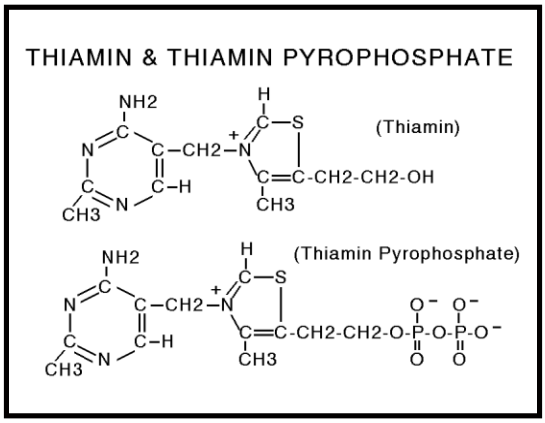
a) Obtained a potent anti-beriberi substance from rice bran (discovery of thiamin).
b) The substance had characteristics of amine, thus, coined the term "vitamin(e)" (vital amine).

- Found later that many vitamins are not amines, thus theterm was changed t "vitamin!"

6) The vitamin (thiamin) was crystallized in 1926 by Jansen & Donath, and chemically synthesized in 1936 by Williams et al.

2. Structure, Properties, and Analysis

A. Thiamin and thiamin pyrophosphate (TPP) – Redrawn from Martin et al., 1983.



B. Properties & antagonists:

1) Has a sulfurous odor & slightly bitter taste.
2) Soluble in water & slightly soluble in alcohol, but insoluble in fat solvents.
3) Very sensitive to alkali, and a thiazole ring opens at a room temperature when the pH is > 7.
4) In a dry state, stable to heat (several hours at 100℃), but moisture ↑ the rate of destruction.
5) Substances with an anti-thiamin activity are fairly common in nature, and also several synthetic compounds are available (e.g., amprolium , which is being used as a "coccidiostat").
6) Thiaminase can be found in some raw fish and others, and it can splits a thiamin molecule into two components, thus, making it inactive.

C. Analysis:

1) "Biological" - based on:

a) Ability of the vitamin to cure polyneuritis in pigeons & bradycardia in rats.
b) Also, based on the growth of the chick, pigeon & rat.

2) "Microbiological" - very rapid, inexpensive & sensitive, but some microorganisms lack a specificity for the vitamin.
3) "Chemical" - based on oxidation to thiochrome, which show a characteristic, blue fluorescence in the UV light. (Most widely used!)

3. Metabolism

A. Digestion/transport:

1) Thiamin seems to be readily digested & released from natural sources.
2) An adequate production of gastric HCl is important for digestion/absorption.
3) Readily absorbed in the duodenum area, and also free thiamin (but, not bound form) can be absorbed from the rumen.
4) Absorbed by both the active transport mechanism & simple diffusion depending on concentrations.
5) Transported to the liver with a plasma carrier protein.

B. Phosphorylation/excretion:

1) Phosphorylation takes place in most of the tissues, but especially in the liver (≈ 4/5 of thiamin):

   a) ≈ 80% of the total is TPP.
   b) ≈ 10% as thiamin triphosphate (TTP).
   c) The remainder as thiamin monophosphate (TMP) & free thiamin.

2) Preferentially retained in organs that have high metabolic activity (e.g., heart, brain, liver & kidneys), but the storage is very low:

   a) Intakes in excess of the current needs are readily excreted, ∴ the body needs a regular supply.
   b) For unknown reasons, pigs contain several times higher levels of thiamin vs other species, ∴ they may be able to tolerate a deficient diet up to 2 mo.

3) Excreted in both the urine & feces, with small amounts in sweat.

4. 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 + CO_2
   2) α-Ketoglutaric acid → succinyl-CoA + CO_2

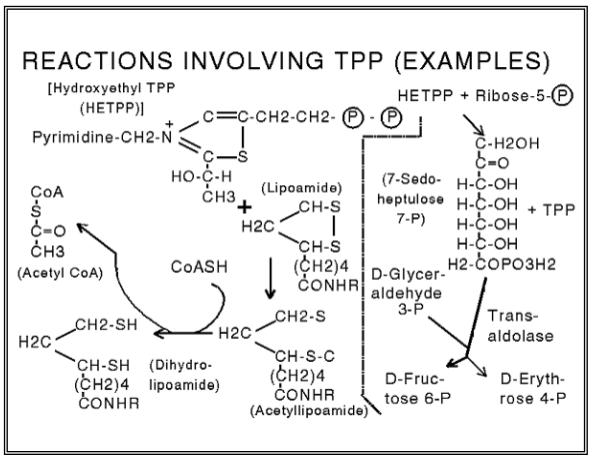
C. Transketolase reaction (pentose pathway) - catalyzes transfer of C2 fragments:

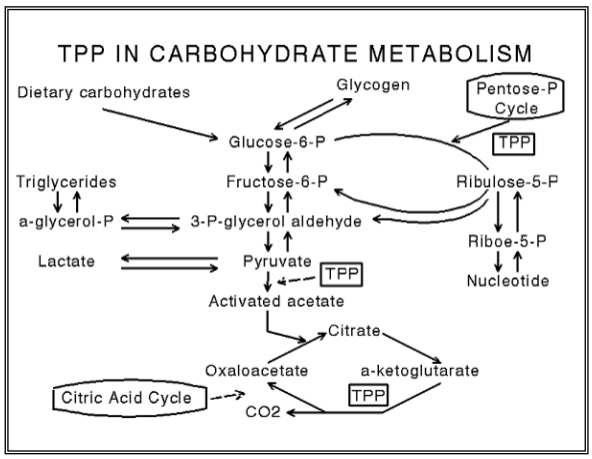
   1) Ribulose 5-P serves as a donor & ribose 5-P as an acceptor → sedoheptulose 7-P & triose P → nucleotide formation.
   2) Also, results in the formation of NADPH, which is essential for reducing intermediates from carbohydrate metabolism in the process of FA synthesis.

D. Neurophysiology: (Little is known!)

   1) A deficiency results in the ↓ synthesis of FA & cholesterol, which affects the membrane integrity & function.
   2) Involved in the synthesis of acetylcholine.
   3) Involved in the passive transport of Na (excitable membranes).
   4) A deficiency results in impairments of FA synthesis & CH_2O metabolism in the nervous system.

- Examples of reactions involving TPP (Adapted & redrawn from Sullivan, Univ. of Nebraska, Lincoln) & TPP in CH_2O metabolism (Adapted & redrawn from McDowell, 1989):





5. Deficiency

A. General:

1) Classic diseases, "beriberi & polyneuritis," represent a late stage of the deficiency resulting from a peripheral neuritis - probably due to accumulation of intermediates of CH_2O metabolism?
2) Other main disorders involve damages to the cardiovascular system - e.g., bradycardia, enlarged heart & edema.

B. Signs in poultry - Loss of appetite & weight, weakness in leg/muscular, bradycardia (from 300 to 90-100/min), edema, diarrhea, vomiting, . . . & death.

C. Signs in pigs - Loss of appetite & weight, weakness, premature birth, high mortality, slow pulse, heart failure, edema, hemorrhages, diarrhea, vomiting & sudden death.

D. 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, Supplementation, and Sources

A. Thiamin (B_1) requirements:

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, microbial synthesis?)
Fish (NRC, 1993):	
Channel catfish & rainbow trout	1.0
Pacific salmon	No dietary requirement?
Common carp	0.5
Tilapia	Not tested
Adult cattle, sheep, goat, horse	Microbial synthesis
Dairy calf, µg/kg	65
Adult cat	5.00
Growing dog	0.75
Rat	4.00
Humans, mg/d: (RDA)	
Infants	0.30-0.40
Children	0.70-1.00
Males	1.20-1.50
Females	1.00-1.10
Pregnant/lactating	1.50-1.60

B. Supplementation:

1) Although concentrations differ widely, the thiamin content of most common feeds should be 3-4 times greater than the requirement for most species.
2) For swine & poultry, thiamin is one of the least likely to be deficient in practical diets.
3) For ruminants, a deficiency should not occur in the young or adult under normal feeding and management conditions.

- But, a supplementation may be a low-cost insurance for swine & poultry, and also for ruminants consuming high-concentrate diets? (Not only for an insurance against a possible inadequacy, but also against a presence of anti-thiamin substances such as thiaminase in moldy feeds!?)

C. Sources:

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

D. 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).

E. 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 B_2)

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

A. By 1915, it's known that “water-soluble” factor or factors promoted growth of rats and prevented beriberi in rats.
B. In 1920, it's found that 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):"

1) Isolated an oxidative enzyme from yeast that was yellow with green fluorescence (∴ "Old Yellow Enzyme").
2) were able to split it into a protein and a nonprotein (pigment) fraction.

a) This was the first identification/recognition of a "prosthetic" or activating group of an enzyme!
b) Also, a coenzyme of riboflavin was discovered before it was found in free from.

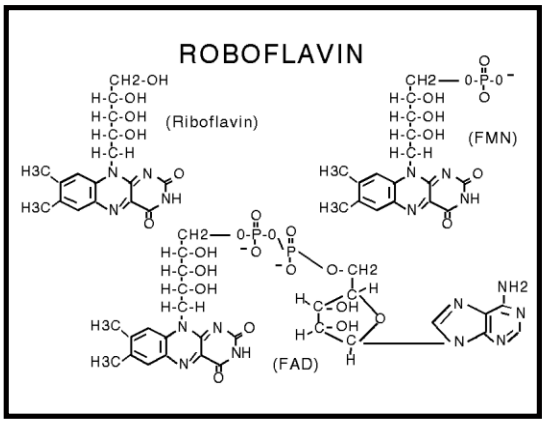
E. Kuhn (1933) - Isolated a yellow pigment from egg white with oxidative properties & suggested the name “flavin.”

1) e.g., Ovoflavin - isolated from eggs, lactoflavin - isolated from milk, hepatoflavin - isolated from liver, & uroflavin - isolated from urine.
2) Pure crystalline compounds were found to contain a ribose, thus the name, “riboflavin” became popular.

F. In 1935:

1) Kuhn (Germany) and Karrer (Switzerland) independently synthesized riboflavin.
2) Szent-Györgi demonstrated that both synthetic & natural vitamins had the same biological activity.

2. Structure, Properties, and Analysis



A. Structures of riboflavin, flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD) - Adapted & redrawn from Martin et al., 1983.

- Coenzyme derivatives are synthesized sequentially from riboflavin:

a) Riboflavin reacts with ATP to form FMN - catalyzed by flavokinase.
b) FMN combines with the second APT to form FAD - catalyzed by FAD pyrophosphorylase.

B. Properties:

1) An odorless, bitter, orange-yellow compound with a melting point of ≈ 280°C – Thus, very little is lost during the cooking.
2) Slightly soluble in water, but readily soluble in dilute basic or strong acid solutions.
3) Aqueous solutions are unstable to visible & UV light (↑ instability when combined with heat & alkalinity).

C. "Analysis" - chemical & microbiological assays are more commonly used in recent years:

1) "Microbiological" - growth & production of lactate by L. casei are dependent on presence of riboflavin in the medium. (Read turbidity from the growth of bacteria in a colorimeter after 16-24 h incubation at 37°C.)
2) "Fluorometric method" - effective because of unique properties of the vitamin (e.g., stable to heat, acid & oxidizing agents, gives off an intense greenish fluorescence, etc.), but operations must been done under a dim light or amber or red glassware.

3. Digestion-Transport & Distribution-Excretion

A. Digestion-transport:

1) Found in feeds as FAD, FMN & free riboflavin:

a) FAD & FMN are hydrolyzed by phosphatase in the upper GI tract.
b) Bound riboflavin is released by proteolytic enzymes before absorption.

2) Free riboflavin is probably absorbed in all parts of the SI (equally?) by an active carrier-mediated process in low concentrations & a passive diffusion at high concentrations.
3) After absorption:

a) Riboflavin is phosphorylated to FMN in mucosal cells.

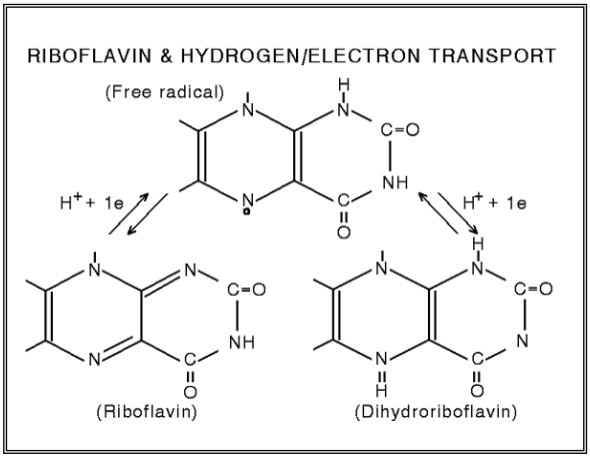
b) FMN enters the portal system, where it is bound to plasma albumin.
c) Transported to the liver, where it is converted to FAD.

B. Distribution-excretion:

1) The storage of riboflavin in the body is rather limited.
2) Relatively high in the liver (≈ ⅓ of the total), kidney & heart, with 70 to 90% in the form of FAD < 5% as free riboflavin.
3) An excess is rapidly excreted in the urine (primarily as free riboflavin), and small amounts of absorbed riboflavin are excreted in the feces, bile & sweat.

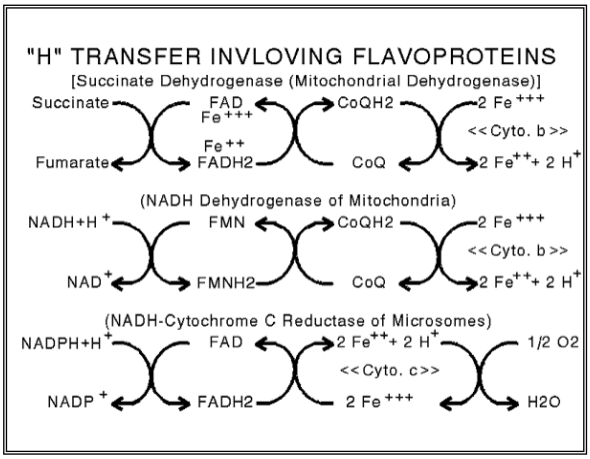
4. Functions

A. A component of FMN and FAD - A prosthetic group for active enzymes, flavoproteins. Most flavoproteins contain FAD and involved in a transfer of electrons in biological oxidation-reduction reactions. (Aapted & redrawn from Sullivan, Univ. of Nebraska)



B. 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/Supplementation

A. General:

1) Riboflavin is one of the vitamins most likely to be deficient in nonruminant species (i.e., usually a borderline to deficient) & also in human diets.
2) Young ruminants (< 2 mo of age?) weaned early or dependent on milk replacer may have a dietary need for riboflavin.
3) Because of its roles in the release of energy & assimilation of nutrients, it is almost impossible to define specific deficiency signs.
4) ↓ rate of growth & feed efficiency are common among all species, and also clinical signs often involve the eye, skin & nervous system.
5) A deficiency would not be expected in young nursing animals because milk is a rich source of the vitamin.

B. 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.
C. Swine - Signs include anorexia, slow growth, rough hair coat, dermatitis, unsteady gait, scours, reproductive & digestive tracts disorders, vomiting, cataracts, light sensitivity, etc.
D. 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.
E. Ruminants:

1) No dietary requirement for adult ruminants because of the ruminal synthesis of the vitamin by the microorganism.
2) Signs in young ruminants include redness of buccal mucosa, lesions in the corner of the mouth, loss of hairs, excessive saliva production, anorexia, diarrhea, ↓ growth, etc.

F. Humans:

1) The deficiency may retard the growth.
2) Signs include dermatitis around the nose & mouth, soreness & burning of the lips, mouth & tongue, photophobia, burning & itching of the eyes, superficial vascularization of the cornea, neuropathy, anemia, etc.

5. Requirements and Sources

A. Riboflavin requirements:

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
Adult cattle, goat & sheep	Microbial synthesis
Dairy calf, liquid feed	0.65
Growing cat	1
Growing dog	2-4
Rat	2-4
Humans, mg/d: (RDA)	
Infants	0.40-0.50
Children	0.80-1.20
Males	1.40-1.80
Females	1.20-1.30
Pregnant/lactating	1.60-1.80

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.
3) Human foods such as milk, eggs, liver, organ meats, green leafy vegetables, wheat germ, whole grains, and legumes 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. General:

1) Niacin was the third vitamin to be identified from the "vitamin B complex."
2) Niacin has been known to organic chemist since 1867, a long before its importance as an essential nutrient was established.
3) As early as 1911 to 1913, Funk had isolated "niacin" from yeast & rice polishings in his attempt to identify the antiberiberi vitamin.

   - Obviously, the interest in niacin was lost because of its ineffectiveness in curing beriberi.

4) Warburg et al. (1935) first demonstrated the biochemical function of niacin as a part of the hydrogen transport system.
5) Elvehjem et al. (1937) isolated nicotinamide from liver that cured blacktongue in dogs, which is a pellagra-like disease.
6) In 1945, Krehl & others found that Trp was as effective as niacin in the treatment of pellagra.

- 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. (+ **poverty**!)

E. In the US (especially in the south):

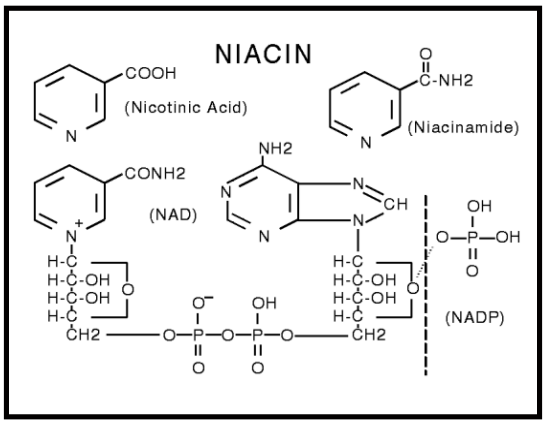
a) It's common for 20,000 deaths/year from pellagra around the turn of the century.
b) Even in 1941 (5 yr after the discovery of the cause), 2,000 deaths were reported.

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 – Analysis

A. Nicotinic acid, nicotinamide, NAD & NADP: (Adapted & redrawn from McDowell, 1989)



1) One of the simplest vitamins.
2) The term niacin is a generic descriptor of pyridine 3-carboxylic acid & derivatives exhibiting the same qualitative biological activity of nicotinamide.
3) White, odorless, crystalline solids, which are soluble in water & alcohol.
4) Resistant to heat, air, light, alkali & oxidizing agents, but destroyed by a high temperature in the alkaline medium.
5) Readily forms salts with Al, Ca, Cu & Na, and also readily forms other compounds (e.g., nicotinic acid·HCl & carboxylic acid salts).

B. Analysis:

1) The most sensitive method is "microbiological assay," but the vitamin must be released from bound forms by acid hydrolysis before assay:

   a) Leuconostoc mesenteroides responds to nicotinic acid only.
   b) Lactobacillus plantarum responds to both forms.

2) "Chemical methods" - less sensitive & generally require more extensive extraction procedures.
3) "Bioassay:"

   a) One difficulty associated with the bioassay is the conversion of Trp to niacin!
   b) Also, the variation in the intestinal synthesis by bacteria.

4. Metabolism

A. Absorption-excretion:

1) Readily absorbed by diffusion at either physiological or pharmacological doses.
2) Absorbed equally well from both the stomach and upper small intestine in humans.
3) Niacin & nicotinamide transport:

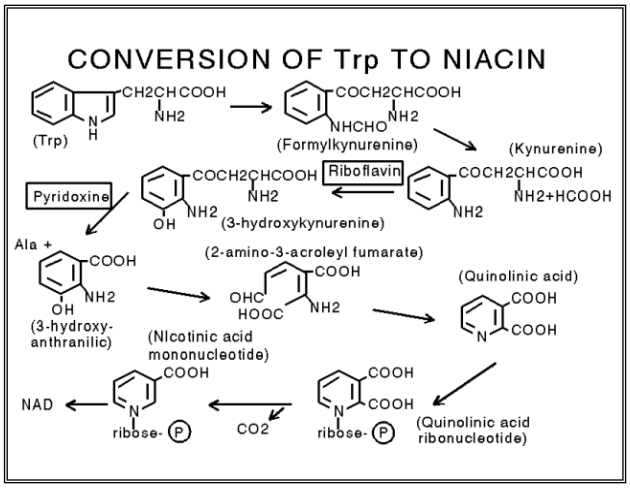
   a) Has not been studied extensively, but there seems to be a continual transport of the two via bloodstream (primarily with red blood cells).
   b) Rapidly leaves the circulation & enters kidneys, liver and adipose tissues.

4) Although niacin coenzymes are widely distributed in the body (the highest in the liver), the amount stored is very small & no true storage occurs.
5) "Excretion" - the urine is the 1° pathway for absorbed niacin & its metabolites:

   a) In humans, dogs, rats & pigs, 1° excretory products are N'-methylnicotinamide & its oxidation products (4-pyridone or 6-pyridone).
   b) Herbivores excrete large amounts unchanged, i.e., not metabolized via methylation.
   c) In chickens, nicotinic acid is conjugated with ornithine as either α- or δ-nicotinyl ornithine or dinicotinyl ornithine.

B. Trp-niacin conversion: (Adapted & redrawn from McDowell, 1989)

1) Can take place in the intestine, and also in the developing chick embryo.



2) Contributions to the animal's' requirement?

   a) Probably depends on dietary Trp & the efficiency of conversion.
   b) e.g., conversion rate is high at low Trp intake, and also high among the pregnant ♀.

3) Conversion rate:

   a) Need ≈ 60 mg Trp for synthesis of 1 mg niacin in humans.
   b) Need ≈ 35-50 mg Trp for synthesis of 1 mg niacin in rats.

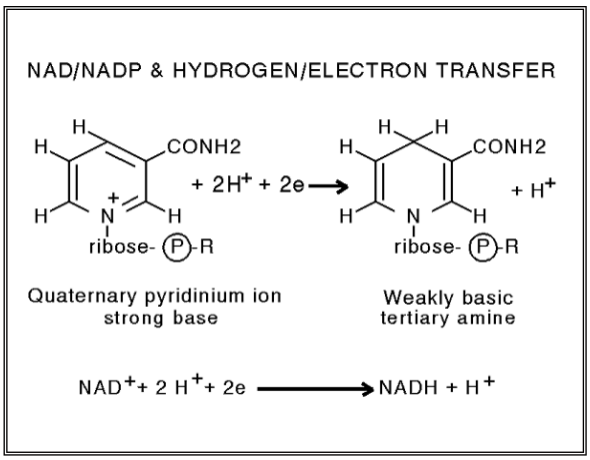
   • Cats cannot convert Trp to niacin, thus, they have the absolute requirement for this vitamin.

5. Functions

A. Niacin is a component of the two important coenzymes:

1) NAD (formally called DPN) & NADP (formally called TPN).
2) NAD- & NADP-containing enzymes are involved in biological oxidation-reduction systems.

• NAD & NADP in transfer of hydrogen & electron: (Adapted & redrawn from Sullivan, Univ. of Nebraska)



B. Important reactions catalyzed by NAD & NADP:

1) CH_2O metabolism:

   a) Glycolysis (anaerobic & aerobic oxidation of glucose).
   b) Citric acid cycle.

2) Lipid metabolism:

   a) Glycerol synthesis and breakdown.
   b) Fatty acid oxidation and synthesis.
   (c) Steroid synthesis.

3) Protein metabolism:

   a) Degradation and synthesis of amino acids.
   b) Oxidation of carbon chains via the citric acid cycle.

4) Others? - Rhodopsin synthesis (& photosynthesis).

C. Specific reactions of NAD & NADP:

1) Dehydration of primary & secondary alcohols:

$$R - CH2OH + NAD^+ \text{ or } NADP^+ \rightleftharpoons R - CHO + NADH + H^+$$

e.g., Alcohol dehydrogenase (NAD)

$$\begin{array}{l} R \\ | \\ CHOH + NAD^+ \text{ or } NADP^+ \\ | \\ R1 \end{array} \quad \rightleftharpoons \quad \begin{array}{l} R \\ | \\ C = O + NADH + H^+ \\ | \\ R1 \end{array}$$

e.g., Lactate dehydrogenase (NAD)
Malate dehydrogenase (NAD > NADP)
β-glycerophosphate dehydrogenase (NAD)
Isocitrate dehydrogenase (NAD, NADP)
β-hydroxy acyl CoA dehydrogenase (NAD)

2) Oxidative decarboxylation:

$$R{-}\overset{\overset{O}{\|}}{C}{-}COOH + NAD^+ + CoASH \xrightarrow[TPP]{\text{Lipoic acid}} R{-}\overset{\overset{O}{\|}}{C}{\sim}SCoA + NADH + H^+ + CO_2$$

e.g., Pyruvate dehydrogenase
α-ketoglutaric dehydrogenase

6. Deficiency/Supplementation

A. General:

1) A deficiency is characterized by severe metabolic disorders in the skin and digestive organs, and the first signs to appear are loss of appetite, retarded growth, weakness & diarrhea/digestive disorders.
2) A "dietary supplementation" must be considered as a "possibility" for all classes of animals, especially for swine & poultry.
3) Much of niacin in common feeds (plant sources) is in the bound form, which is not available to animals, thus niacin content in grains & their by-products generally has no value to swine & poultry.

B. Poultry:

1) Chickens (even embryos) can synthesize niacin, but the synthetic rate may not be adequate for optimum performance.
2) Deficiency signs:

    a) Main clinical signs in young poultry are enlargement of the hock joint and bowing of the legs, plus appetite loss & growth failure.
    b) Other signs include "blacktongue" (inflammation of the tongue & mouth cavity, and also esophagus), ↓ egg production & hatchability.

C. Swine:

1) Niacin is one of the B vitamins deficient in typical swine diets, especially in corn-based diets.
2) Wide variations among animals in the severity of deficiency signs, even with similar breeding & environmental conditions.
3) Signs include poor appetite & weight gain, anemia, dermatitis, hair loss, diarrhea, vomiting, inflammation & necrosis of GI tracts, etc.

D. Fish - Loss of appetite, lesions in colon, jerky or difficult motion, weakness, edema of stomach & colon, muscle spasms, poor growth, anemia, fin lesions, etc.

E. Ruminants:

1) Young ruminants are expected to suffer from niacin deficiency, but niacin-free diets have failed to produce a deficiency in earlier studies.
2) Dietary niacin requirements may not exist in ruminants if adequate Trp is provided in the diet.

    • But, positive responses to "niacin-supplementation" have been reported in both sheep & cattle!

3) Signs in young ruminants fed niacin-free, low-Trp diets include a sudden anorexia, severe diarrhea, & dehydration followed by a sudden death.

6. Requirements, Sources, and Toxicity

A. Niacin requirements:

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
Growing cat	40
Growing dog	450 µg/kg BW
Rat	20
Adult cattle, sheep, goat, horse	Microbial synthesis
Dairy calf	2.6 mg/L milk
Human, mg niacin, or 60 mg Trp/d: (RDA)	
Infants	5-6
Children	9-13
Males	15-20
Females	13-15
Pregnant/lactating	17-20

B. Sources:

1) The niacin content in corn, sorghum, wheat and oats is low, and mostly exist in the bound form (85 to 90%), ∴ totally unavailable.
2) Based on the chick assay, niacin in soybean meal (31 mg/kg DM) might be 100% available.
3) Rice bran (330 mg), wheat bran (268 mg) and brewer's yeast (482 mg/kg DM) are very good sources.

C. Trp & niacin requirement:

1) Animals can synthesize niacin from Trp, but the ability to synthesize the vitamin differs widely among the species (or even within a species).
2) Trp levels in the diet affect niacin requirement: (e.g., pigs)

   a) ≈ 50 mg Trp needed to synthesize 1 mg niacin.
   b) Thus, every 0.01% Trp (or 100 mg/kg) above the requirement can result in the synthesis of 2 mg niacin/kg of diet.

   • Thus, may not be necessary to supplement high-protein diets, but Trp can be one of the limiting amino acids for some animals, so . . . !?

D. Toxicity:

1) In humans, high levels such as 3 g/d can cause vasodilation, itching, nausea, vomiting, headaches & occasional skin lesions.
2) The level of 350 mg nicotinamide/kg BW/d may be safe, and nicotinic acid may be tolerated at intakes as much as four times this level.

7. Niacin Supplementation for Ruminants

A. Beef cattle in the feed lot: (Byers, 1981. Proc. Symp. Vitamins - The Life Essentials. ISU, Ames)

Item	Δ in ADG, %	Δ in FE, %
First 28-35 d:		
50-200 ppm	+9.7	+10.9
500 ppm	-3.5	-2.2
d 73 to 160:		
50 ppm	+2.4	+.6
100 ppm	+3.6	+3.7
150-250 ppm	+.9	+2.7
500 ppm	+2.0	+2.2

B Effect of oral nicotinic acid (12 g/d) on treating subclinical & clinical ketosis: (Fronk & Schultz, 1979. J. Dairy Sci. 62:1804.)

Item	Day 0	Day 7
Milk, lb/d	66.2	75.0
Glucose, mg/100 mL	43.1	50.6
β-HBA, mg/100 mL	10.3	6.7
Free-FA, mg/100 mL	21.1	11.3

C. Effects of niacin (100 ppm) on growing lambs: (Shields & Perry, 1982. Purdue Univ., West Lafayette)

Item	SBM	SBM + niacin	Urea	Urea + niacin
DM intake, lb/d	2.25	2.73	2.34	2.09
ADG, lb/d	0.51	0.82	0.26	0.62
FE	4.41	3.33	9.00	3.37
N-digestibility, %	70.0	72.0	67.0	72.7
N-retention, g/d	2.4	7.9	2.8	4.9
N-retention, % N-intake	15.8	38.7	18.6	34.9

D. Research findings on niacin supplementation:

1) Improve performance of feedlot cattle, especially during the adaptation period - a 100 ppm may be most effective dose?
2) Small oral doses are effective in alleviating subclinical & clinical ketosis problems in cows - blood glucose & fat mobilization?
3) Improve milk production, especially in fresh cows vs. those in mid-lactation.
4) Increase microbial protein synthesis in cattle and sheep.
5) Improve protein digestion & nitrogen retention.

- **The bottom line?**

"Ruminants may synthesize [microbial and(or) conversion from Trp] adequate amounts of niacin to avoid a deficiency, but a supplementation may be necessary for optimum performance!"

PANTOTHENIC ACID

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

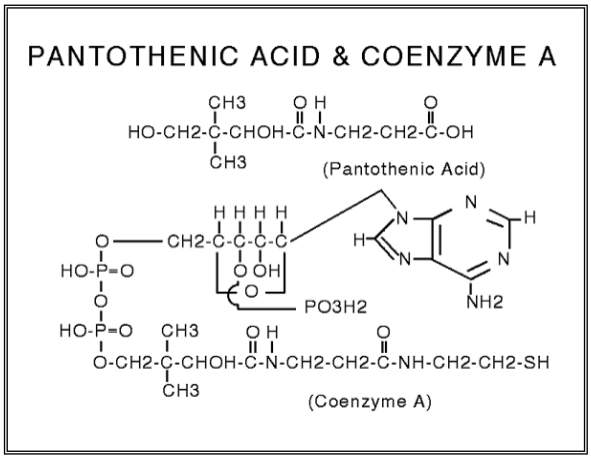
A. After isolating thiamin, riboflavin & niacin from the vitamin B complex, researchers realized that at least one more factor remained in the complex.
B. It was discovered in the 1930s from the "B2" complex along with pyridoxine:

    1) Pantothenic acid deficiency was first described in the chick by Norris & Ringrose (1930) as a "pellagra-like dermatitis" - the name, "chick anti-dermatitis factor," was given to a factor that cured this condition.
    2) Williams et al. (1933) fractionated "bios," a growth factor for yeast, and Snell et al. (1933) studied the nature of "an essential factor" for lactic acid bacteria.
    - All these factors were found to be "pantothenic acid."

C. The structure was determined, and the vitamin was synthesized in 1940.
D. Lippman (1946-47) determined the active form & biological functions.

2. Structure and Analysis

A. Pantothenic acid & coenzyme A:
(Adapted redrawn from McDowell, 1989)



    1) The vitamin is derivatized at carboxyl & alcoholic ends to form coenzyme A.
    2) Another metabolically active form is acyl carrier protein.
    3) Free acid of the vitamin is a viscous, pale yellow oil readily soluble in water & ethyl acetate.
    4) Extremely hygroscopic & easily destroyed by acids, bases & heat.
    5) Ca pantothenate is a pure form of the vitamin used in the commerce, and it is reasonably stable to the light and air.

B. Analysis:

    1) "Chick bioassays" - widely used & measure both bound- & free-vitamin.
    2) "Radioimmunoassay & automated fluorometric assay technique" - reported by some to be successful/useful.
    3) "Microbiological" - being used, but the vitamin must be freed from the coenzyme form first.

3. Metabolism

A. Found in feeds in both bound (primarily as coenzyme A) & free forms.
B. Little is known about digestion, absorption & transport of the vitamin:

    1) "Bound forms" - the vitamin must be released from the complex before absorption.

2) Salt & alcohol forms are absorbed from the GI tract probably by diffusion.
3) "Free vitamin" seems to be absorbed very efficiently by animals - e.g., 81-94% of oral dose in the dog.

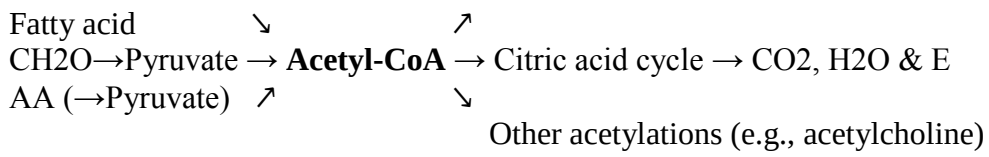
C. Availability in "typical" U.S. diets is 41 to 61% in adult men.
D. Urinary excretion is the 1° route, mostly as a free vitamin.
E. No appreciable storage of the vitamin in animals & humans, but higher concentrations in the liver & kidney vs other organs.

4. Functions

- A constituent of two important coenzyme, coenzyme A (CoA) and acyl carrier protein (ACP).

A. Coenzyme A:

1) One of the most important coenzymes for tissue metabolism.
2) The most important function of coenzyme A is to act as a carrier mechanism for carboxylic acids: (Adapted & redrawn from Marks, 1975. In: A Guide to Vitamins. Their Role in Health & Disease. Medical & Technical Publ., Lancaster, England)



B. Acyl carrier protein:

1) "ACP" is a protein with a sulfhydryl group covalently attached to acetyl, malonyl & intermediate-chain acyl groups.
2) ACP replaces CoA during the building of C chain in the synthesis of FA.
3) ACP & coenzyme A have similar acyl-binding sites.

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	α-ketoglutarate	Succinyl CoA	Mitochondria
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

5. Deficiency/Supplementation

A. General:

1) Deficiency signs & symptoms take many forms & differ from one species to another, but the followings are usually observed:

a) ↓ growth & feed efficiency.
b) Lesions of the skin & its appendages.
c) Disorders of the nervous & gastrointestinal systems.
d) Inhibition of the formation of antibodies & ↓ resistance to infections.
e) Impairment of the adrenal function.

2) Practical diets for nonruminant species usually contain a sufficient pantothenic acid, but it is routinely added because of a number of factors can influence the requirements.

- e.g., levels of other vitamins (e.g., vitamin B_{12}, folacin, biotin, and vitamin C), fat, protein, fiber, etc. + availability.

B. Poultry:

1) Primary deficiency signs involve the nervous system, adrenal cortex & skin.
2) Other signs include broken feathers (become brittle & fall), perosis, poor growth & efficiency, reduced egg production & hatchability, ↑ mortality (embryos & after hatching), etc.

C. Swine:

1) Many swine diets can be a borderline in pantothenic acid content.
2) Nonspecific signs include anorexia, poor growth & efficiency, diarrhea, rough hair coat, brown exudate around eyes, anemia, etc.
3) "Goose stepping" is a characteristic deficiency sign for swine:

a) Results of sciatic nerve damages → locomotor incoordinations.
b) First, the movement of back legs becomes stiff & jerky.
c) In the advanced stage, the back legs may touch the belly as the pig moves forward, and eventually a severe paralysis of the hind quarters.

D. Fish - Signs include clubbed gills, prostration, loss of appetite, necrosis & scarring, cellular atrophy, gill exudate, sluggishness, poor growth, anemia, etc.

E. Ruminants:

1) No dietary requirement for adult ruminants.
2) Deficiency signs in calves include anorexia, reduce growth, rough hair coat, dermatitis (around the eyes & muzzle is 1˚sign), diarrhea, weakness, convulsion & eventual death.

F. Humans:

1) A deficiency has not been observed under natural conditions (except in cases of severe malnutrition), possibly because of a widespread distribution of the vitamin.
2) The deficient diet alone may take ≈ 12 wk to produce recognizable symptoms such as fatigue, headaches, muscle weakness, cramps, GI tract disorders, impaired motor coordination, depression, impaired adrenal function, etc.

6. Requirements, Sources, and Toxicity

A. Pantothenic acid requirements:

Animal	mg/kg or others
Poultry (NRC, 1994):	
Immature chickens	9.4-10.0
Laying hens	1.7-2.5
Broilers	10.0
Swine (NRC, 1998):	
3-120 kg	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
Growing cat	5
Growing dog	400 µg/kg BW
Rat	8
Adult cattle, sheep, horse & goat	Microbial synthesis
Dairy calf	130 µg/kg BW
Human, mg/d[a]: (RDA)	
Infants	2-3
Children (< 10 yr)	3-5
Adults	4-7

aThe average intake in the US is 5-20 mg/d.

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.
3) d- & dl-Ca pantothenate are commercially available products for dietary supplementation.

C. Toxicity:

1) Has only limited pharmacological effects on humans or animals.

2) No upper safe levels have been established, but dietary levels of at least 20 g/kg can be tolerated by most species (NRC, 1987).

BIOTIN

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

A. General:

1) Has been believed for many years that supplemental biotin was not necessary for swine & poultry because of a wide distribution of the vitamin in feedstuffs & synthesis by the intestinal microflora.
2) In the mid 1970s:

a) Field cases of deficiency signs were reported.
b) Also, animals responded to biotin supplementation.

- Thus, began re-evaluation of the roles of biotin for animals!

B. History:

1) Different lines of the investigation led to the discovery of biotin:

a) Allison et al. (1933) discovered a growth factor that was required for legume nodule bacteria, and they named it "coenzyme R."
b) Kögl & Tönnis (1936) isolated a substance from egg yolk that was necessary for yeast growth, and they named it "biotin."
c) Szent-György (1937) studied a factor present in certain foods (especially in liver & kidney) that protected "egg-white injury" (dermatitis & hair loss), and he named it "vitamin H" (from the German word "haut," meaning skin).

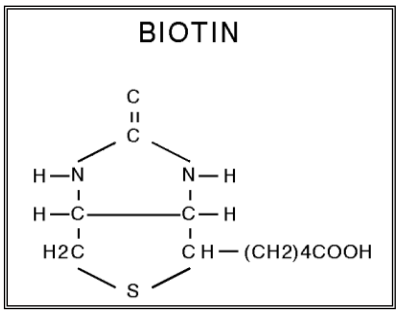
2) In 1940, Szent-György & others found that all three were the same substance.
3) The structure & properties of the vitamin were established between 1940 & 1943, and the vitamin was synthesized in 1945.

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, Properties, and analysis**

A. Structure: (Adapted and Redrawn from Martin et al., 1983)

B. Properties & antagonists:



1) Has rather "unique" structure, and contains three asymmetric carbonations, ∴ eight different isomers are possible - d-biotin has a vitamin activity, but l-biotin is inactive.
2) Crystallizes from water as long, white needles, and melting point is 232-233°C.
3) Soluble in dilute alkali and hot water, and practically insoluble in fat & organic solvents.
4) Quite stable, but destroyed by nitrous acid, other strong acids, strong bases & formaldehyde, and also gradually by the UV radiation.
5) Some analogs have varying degrees of vitamin activity (e.g., oxybiotin), whereas others have antibiotin activity (e.g., sulfone & norbiotin).

C. Analysis:

1) "Bioassays using animals (rats & chicks) and microorganisms" are easier methods for natural materials.
2) "Colorimetric, GC & polarographic methods" can be used, but not for estimating the amount available to animals.

3. Metabolism

A. Exists in natural materials in both protein-bound and free forms, and much of bound biotin is not available - e.g., < ½ of biotin in feedstuff is available for poultry.
B. Absorbed as an "intact" molecule in the first ⅓ to ½ of the SI.
C. Limited information on transport & deposition/storage:

1) May be transported as a free water-soluble component of plasma.
2) Taken up by cells via active transport & attached to its apoenzyme.
3) All cells contain biotin, but large amounts in the liver & kidneys.

D. Often the amount of biotin excreted in the urine & feces exceeds dietary intake, a indication of a considerable synthetic activity!

4. Functions

A. Serves as a prosthetic group for a number of enzymes (carboxylases, transcarboxylases, and decarboxylases), and biotin moiety functions as a mobile carboxyl carrier.
B. Overall importance of biotin in metabolism:

1) Carbohydrate metabolism:

a) Carboxylation of pyruvic acid to oxaloacetic acid.
b) Conversion of malic acid to pyruvic acid.

c) Interconversion of succinic acid and propionic acid.
d) Conversion of oxalosuccinic acid to α-ketoglutaric acid, etc.

2) Protein metabolism:

a) Protein synthesis.
b) Amino acid deamination.
c) Purine synthesis & nucleic acid metabolism, etc.

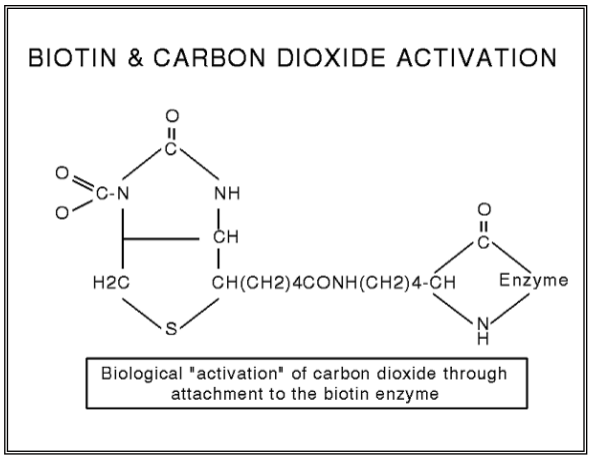
3) Lipid metabolism:

a) Conversion of acetyl-CoA to malonyl-CoA (the first reaction in FA synthesis).
b) Essential FA metabolism, etc.

C. Biological activation of carbon dioxide: (Adapted & redrawn from Sullivan, Univ. of Nebraska, Lincoln)

D. An essential coenzyme (functions as a mobile carboxyl carrier) for enzymes involved in carbohydrate, fat & protein metabolism:

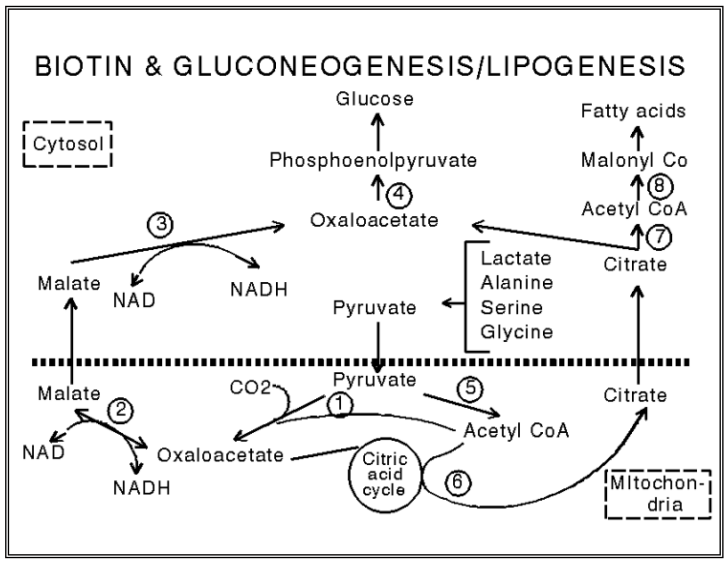
1) Conversion of carbohydrate to protein & vice versa.
2) Conversion of protein & carbohydrate to fat.
3) Maintaining a normal blood glucose level . . . , etc.



E. Biotin & gluconeogenesis & lipogenesis: (Adapted & redrawn from Sullivan, Univ. of Nebraska, Lincoln)

- "Enzymes:" a) pyruvate carboxylase, b) mitochondrial malic dehydrogenase, c) cytosolic malic dehydrogenase, d) phosphoenolpyruvate carboxykinase, e) pyruvate dehydrogenase complex, f) citrate synthetase, g) citrate cleavage enzyme, and h) acetyl-CoA carboxylase.

F. Specific biotin-dependent enzymes:



1) Carboxylases:

   a) Pyruvate → oxaloacetate (gluconeogenesis, lipogenesis).
   b) Acetyl-CoA → malonyl CoA (FA biosynthesis).
   c) Propionyl-CoA → methylmalonyl CoA (propionate metabolism).
   d) 3-methylcrotonyl-CoA → 3-methylglutaconyl CoA (catabolism of Leu).
   e) Geranyl-CoA → carboxygeranyl CoA (microbial catabolism of isoprenoid compounds).
   f) Urea → N-carboxyurea (bacterial catabolism of urea that lack urease & grow on urea as sole source of N).

2) Transcarboxylase - "methylmalonyl-CoA carboxyltransferase:"

   • Methylmalonyl CoA + pyruvate → oxaloacetate + propionyl CoA (fermentation of CH2O to propionate in propionibacteria).

3) Decarboxylases:

   a) Methylmalonyl-CoA → propionyl CoA + CO_2 (the last step in lactate fermentation in Micrococcus lactylticus).
   b) Oxaloacetate → pyruvate + CO_2 (inducible enzyme in Aerobacter aerogenes challenged to grow on citrate as a source of C).

5. Deficiency/Supplementation

A. General:

1) Biotin is important for "normal function" of the thyroid gland, adrenal gland, the reproductive tract and the nervous system.
2) Effects of deficiency on the cutaneous system is most dramatic since severe dermatitis is the major obvious clinical sign observed in the poultry & livestock.
3) Of all vitamins considered for supplementation, biotin is the most expensive, ∴ has a great economical significance!
4) For many species fed typical diets, supplementation is probably not necessary, but ... factors that can affect the availability of biotin & microbial synthesis could have a great impact.

B. Poultry:

1) The requirement for the turkey is higher than the chick, i.e., more deficiency problems with turkeys have been reported.
2) Some deficiency signs include reduced performance, broken feathers, dermatitis, leg & beak deformities, increased embryonic mortality & reduced viability after hatching, etc.

C. Swine:

1) Borderline deficiency signs include ↓ growth & efficiency (possibly others).
2) Clinical signs include loss of hair (alopecia), dermatitis (dry & rough), brownish exudate, ulceration of the skin, inflammation of the mouth mucosa, transverse cracking of soles & tops of hooves, etc.
3) For reproducing swine, a biotin deficiency may have significant consequences on the productivity and longevity.

D. Fish - Signs include loss of appetite, lesions in colon, coloration, muscle atrophy, spastic convulsion, fragmentation of erythrocytes, skin lesions, poor growth, etc.

E. Ruminants:

1) No evidence for a deficiency in animals with functional rumens.
2) Even for preruminant calves and lambs, the need for supplementation is questionable.

F. Humans:

1) Except in infants, there is no evidence of spontaneous biotin deficiency.
2) Consumption of raw eggs & biotin deficiency, i.e., "egg-white injury":

a) In one study, feeding 200 g egg-white/d to human volunteers resulted in mild depression, hallucination, anxiety with muscle pain, anorexia, a striking grayish pallor with dermatitis & desquamation.
b) A disorder is caused by an antagonist, "avidin":

(1) Avidin is a glycoprotein secreted by mucosa of the oviduct, and found in egg-white.
(2) Combines stoichiometrically with biotin (1:1), and a complex is not degraded by proteolytic activity.
(3) If the level of biotin > avidin, it cures deficiency problems.
(4) Avidin can be denatured by moist heat.

6. Requirements, Sources, and Toxicity

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

Animal	mg/kg or others
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	0.15
Pacific salmon	Required, but not determined
Common carp	1.0
Tilapia	Not tested
Adult cattle, sheep, horse & goat	Microbial synthesis
Dairy calf	10 µg/kg BW
Cat	0.07
Human, µg/d: (RDA)	
< 10 yr	10-30
> 11 yr	30-100

B. Sources:

1) Exists in the bound & free forms, and the bound form is not available to animals, and < ½ of biotin in various feedstuffs may be biologically available.
2) The content in cereal grains is influenced by the variety, season, yield, storage conditions, etc.
3) Biotin in corn (0.07 mg/kg) and SBM (0.32 mg/kg DM) is highly available, but the vitamin in wheat, barley & milo is not readily available.
4) Biotin is commercially available as a 100% crystalline product or as dilutions.

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/prevents deficiency symptoms.

D. Toxicity - Biotin is generally non-toxic:

1) e.g., 5,000 to 10,000 times the requirement had no adverse effects on rats.
2) Safe tolerance levels of 4-10 times the requirement in swine & poultry, but a maximum tolerable level is probably considerably greater.

7. Biotin Supplementation (e.g., in Swine)

- Review? - "Kornegay, E. T. 1986. Biotin in swine production: A review. Livest. Prod. Sci. 14:65-89."

A. Growing pigs:

1) "Alleged" field cases of the vitamin deficiency were reported in the early 1970s.
2) Also, there were some reports indicating beneficial effects of biotin supplementation on growth rate.
3) Field trials involving a number of countries in the mid 1970s reported improved performance of growing pigs by supplemental biotin.

4) But, generally no response to biotin supplementation under "experimental conditions" when growing pigs were offered "natural ingredients."

B. Very inconsistent responses in sows:

1) Some investigators reported:

a) Improved hoof hardness & strength, and skin & hair coat conditions.
b) Reduced hoof cracks & footpad lesions.
c) Improved reproductive performance, i.e., ↑ litter size & weaning wt, and ↓ days to return to estrus, etc.

2) 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

[a]Biotin effect, $P < 0.03$.

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

Item	0	330 μg/kg	*P*-value
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

[a]Total No. of lesions for all four feet; [b]Based on overall condition of the feet where 0 represents no lesions & 5 represents many lesions; [c]Based on the system where each lesion was give severity score ranging from 1 (a very small lesion) to 5 (a very large severe lesion); [d]Station x treatment, $P < 0.05$.

- 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 B_{12}!)

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 $CrCl_3$ 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, and Met) into heart muscle (via the action of insulin?).

2. Toxicity

A. General:

1) Chromic oxide (Cr_2O_3) 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 $\geq$ 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. Increasing 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 triacylglycerol 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.

5. Cr for Growing-Finishing Pigs (Page et al., 1993. JAS 71:656)

A. Effects of 0 to 200 & 0 to 800 ppb (Cr picolinate):

Item	Basal	25	50	100	200
Gain, g/d	807	807	840	759	870
Cholesterol, mg/dL	82.0	84.7	83.9	73.1	73.3
Insulin, µIU/mL	13.1	14.8	12.7	19.8	12.5
LMA, cm^2	34.9	35.9	35.3	34.2	37.2

B. Effects of 0 to 800 ppb (Cr picolinate):

Item	Basal	100	200	400	800
Gain, g/d	910	899	904	854	827
Cholesterol, mg/dL	101.8	87.7	97.1	93.1	97.7
Insulin, µIU/mL	15.3	16.0	13.0	15.0	14.1
LMA, cm^2	34.0	40.4	39.9	41.7	40.3

C. Effect of picolinate (Pic), inorganic Cr, and Cr picolinate (CrPic) in ppb:

Item	Basal	200 Pic	Pic + 200 $CrCl_3$	100 $CrCl_3$	200 CrPic	CrPic
Gain, g/d	686	709	727	739	730	723
Cholesterol, mg/dL	101.0	103.5	101.1	101.7	103.9	98.6
Insulin, µIU/mL	19.5	20.5	20.6	17.7	22.3	22.5
LMA, cm^2	31.5	31.8	31.2	30.7	38.1	38.4