Food synergy: an operational concept for understanding nutrition

Food, not nutrients, is the fundamental unit in nutrition

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A strange claim for a pet food

Nutritional Nugget

What’s More Important – Ingredients Or Nutrients?

Pyramid of Essential Nutrients

- Vitamins
- Minerals
- Fat
- Protein
- Carbohydrates
- Water

Key Facts

- Ingredients should be selected for the nutrients they supply, and for their quality and taste.
- Nutrients are vital because the body absorbs nutrients, not ingredients.
- Ingredients are delivery vehicles for nutrients, and the presence or absence of a single ingredient doesn’t determine a pet food’s quality.
- A pet food is the sum of its parts. A balance of quality ingredients delivers protein, fat, fiber, carbohydrates, vitamins, and minerals to meet a pet’s nutritional needs.
- As ingredient quality increases, so does a pet’s ability to absorb and use the nutrients needed for optimum health.
- QUALITY PET FOOD requires a precise blend of ingredients to create a specific nutrient profile based on a pet’s lifestage, lifestyle or disease condition.
- Don’t assume a food is right for your pet simply by reading the ingredient list, because THE BODY NEEDS NUTRIENTS, NOT INGREDIENTS!
We all eat food, several times each day, in considerable variety

- Besides food, we consume purified substances
  - Intentional enrichment or fortification of the food
  - Unintentional contamination
  - Supplements
  - Drugs

- We *are composed of* these substances modulated by
  - Digestion and absorption
  - Synthesis of new compounds from intake
  - Genetic capability to process the ingested material
  - Pathologic changes

- All of this likely influences health
Nutrition = diet and health

- A fundamental feature of food is that the biological constituents are coordinated.
- Metaphors for lack of coordination
  - Put flour, sugar, egg, salt, and vanilla haphazardly in a bowl
  - Cook
  - A cake does not result
- OR:
  - Isolate protein, fat, CHO, vitamins, minerals, per Hill’s Nutrition Pyramid
  - Put haphazardly in dog’s bowl
  - Dog does not thrive
- The individual ingredients have to interact with each other in a specified way to turn into a cake or pet food.
The question of food vs. nutrients is central in nutrition

- Nutrient approach has enhanced understanding and set policy
  - Discovery of fundamental food constituents was astounding
  - Deficiency diseases exist and can be treated
  - Supplements and food energy combat malnutrition
  - Most diseases now are not deficiency conditions

- Reductionist tendency to oversimplification can stifle understanding/progress
  - Supposition: isolated nutrients = nutrients in food matrix
  - Diet supplement industry
  - Pharmaceutical-like products not well investigated
  - Clinical trials of supplements: most do not work as intended.
  - Macronutrient policies low total fat intake: don’t eat olives, nuts, and salmon.
The question of food vs. nutrients is central in nutrition.

In contrast to the nutrient approach, observational study link between Mediterranean dietary pattern and reduced rates of chronic diseases.

- Benefit of these dietary patterns not definable by the action of simple nutrients
- Implication: research and policy should be based on composite entities
- Foods rather than nutrients.
Ancel Keys and the scientific paradigm

● Science long series of feeding studies:
  \[ \Delta \text{Serum Cholesterol} = 1.35 \ (2\Delta S - \Delta P) \]

● Intuition and epidemiology:
  ● S. Europe: heart attacks in the rich, probably reflects Mediterranean Diet and serum cholesterol

● Later: Beyond fat, some plant foods lower serum cholesterol

● Reductionist solution precise, but incomplete
Studies of diet pattern are mostly observational

- Lyon Diet Heart Study very successful in people with heart disease, employed Mediterranean diet, also ALA supplement
- WHI healthy women, low fat diet, no effect
- WINS breast cancer survivors low fat diet, reduced risk
- WHEL breast cancer survivors low fat diet, emphasis on fruit/vegetables, no effect
NIH State-of-the-Science Conference Statement on Multivitamin/Mineral Supplements

- Focused on 13 vitamins and 15 essential minerals
- History and scope of supplement use
  - Beginnings with James Lind’s studies of scurvy in the 1700s
  - Discovery of the first vitamin, thiamin, in 1913
  - Iodine added to table salt in 1924
  - Vitamin D to milk in 1933
  - Thiamin, riboflavin, niacin, and iron to flour in 1941
- In America, 20-30% of the population use a multivitamin daily
- The supplement industry reported annual sales of $23 billion in this 2006 report
- Many more Americans are effectively taking a multivitamin by eating fortified grain products
Many long term randomized clinical trials of supplements, mostly null

- Trials of vitamins or minerals, not containing herbs, hormones, or drugs
- Calcium+vitamin D increased bone mineral density and reduced fracture risk in postmenopausal women.
- Some evidence that selenium reduces risk for prostate, lung, and colorectal cancer
- Vitamin E may decrease cardiovascular deaths in women and prostate cancer incidence in male smokers
- Vitamin A+zinc may decrease risk for noncardia stomach cancer in rural China
- Otherwise, most findings were null
  - Niacin, folate, and B2, B6, and B12: no positive effect on chronic disease occurrence in the general population.
  - No evidence to recommend β–carotene; possible harm in smokers.
Meta-analyses of total mortality

- Vitamin D (mean dose 528 IU/day) reduced risk in almost all of 18 clinical trials
- Vitamin E doses in excess of 400 IU/day raised risk in 19 studies
Concerns about folate

- Flour supplemented with folic acid since 1998 to deliver folate to all potentially pregnant women and avoid neural tube defects
  - Risk reductions have been seen
- Worry about higher levels of folate leading to cancer progression
- Worry about higher folate in elderly masking B12 deficiency and leading to irreversible neuropathy
Do supplements only work in near deficiency state?

- Linxian General Population Trial and Dysplasia Trial saw reduction in cancer risk with multivitamin
  - Population had borderline deficiency at baseline
- WHI showed no reduction in 7 year colorectal cancer incidence with vitamin D and calcium
  - Neither nutrient was close to deficiency
1994 Dietary Supplement and Health Education Act (DSHEA)

- Difficult to monitor or evaluate supplemental nutrients consumed
  - Extensive enrichment/fortification of products
  - DSHEA allows manufacturers to label with minimum rather than actual amounts of nutrients contained in the supplements.
  - There is haphazard reporting of adverse events apparently related to supplement use.
- In most respects, despite their designation as Generally Regarded as Safe (GRAS), supplements are unregulated pharmaceuticals
NIH report recommendation

“The current level of public assurance of the safety and quality of multivitamins/multiminerals is inadequate, given the fact that manufacturers of these products are not required to report adverse events and the FDA has no regulatory authority to require labeling changes or to help inform the public of these issues and concerns. It is important that the FDA’s purview over these products be authorized and implemented.”
Is a multivitamin “insurance”?  

- Evidence for any benefit of multivitamins is sparse and inconsistent, perhaps with the exceptions of vitamin D and folate for neural tube defects  
- To ensure adequate intake of important nutrients, a nutrient-rich diet is preferred to taking supplements
Food Synergy

- Perspective that more information can be obtained by looking at foods than at single food components
- Food matrix = the composite of naturally occurring food components
- Organisms have coordinated constituents
- The cell is the director of the orchestra
- Isolated constituents formed outside of normal biological processes are not integrated
  - Intentional supplements
  - Unintentional contaminants
  - Compounds such as the trans fat formed in hydrogenation of vegetable oils
Food Synergy

- The composite nature of food, serving the life of the organism being eaten as well as the life of the eater, is central to the food synergy concept.
- Concept bolstered by lack of benefit in clinical trials of supplements.
- Viability of food synergy idea implies
  - Balance in the biochemical constituents of the organism being eaten
  - Pieces of this orchestration survive digestion to arrive
  - Coordinated constituents mutually affect human biology
Food matrix slows absorption

- Supplements are delivered as a bolus
  - 14 mg iron = 1 tablet
  - 14 mg iron = 670 g roast beef, 875 g spinach, or 209 g cornflakes
- The same nutrient in food will be eaten over several meals
- The food matrix itself will slow absorption
- Digesta reaching the large bowel may enhance the health of microbiota there
Mixtures, Chemical, and Biological Incorporation

- Orange juice with added calcium is a mixture that does not contain any substance that naturally balances the biologic action of the calcium.
- Trans fat resulting from hydrogenation of vegetable oils is probably a mixture with no biological function, while the trans conjugated linoleic acid may have benefit.
- Minerals naturally occurring may be chemically bound in proteins, such as selenoproteins.
- Antioxidants in the cereal germ are biologically close to the fatty acids that they protect.
Biological balance clearly exists

- Many biologic systems are in homeostasis
  - Glucose
  - Lipid type and distribution
- Plant protection from pests
  - Plants must contain pesticide compounds and must protect against these compounds damaging themselves, e.g. by signalling or antidote compounds
  - Polyphenolics may play this kind of role
Do such systems survive digestion?

- Many food constituents are degraded during digestion
  - Proteins into amino acids: proteases
  - Carbohydrates: maltase, lactase, and sucrase
- Other constituents do survive digestion, particularly fats and small molecules such as phenolic acids and flavonoids, especially if they are fat soluble
- The cell is the great integrator in all organisms
  - Many regulatory systems and ways to pick and choose among available constituents
Do such systems survive digestion?

- Small molecules and their association with fat molecules are relevant to health because the cell has the ability to be responsive to different compounds.
  - Cancer only emerges after numerous cell cycles in which cell replication was not exactly right.
  - Small compounds that survive digestion are active throughout remodeling of the cell, especially dependent on how much fat the cell is exposed to, if the particular process happens to be fat dependent.
Hydroxycinnamic acids in coffee survive to be found in LDL particles

Natella et al fed a single cup of coffee after 2 days of avoiding phenolic rich foods and an overnight fast.

Caffeic p-Coumaric Ferulic

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<td>LDL before</td>
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<td>post consumption</td>
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Am J Clin Nutr 2007
Coffee phenolics inhibit LDL oxidation

- Natella et al found reduced LDL oxidation
  - Ex vivo (blood drawn after coffee consumption)
  - In vitro (LDL particles tested after test tube incubation with artificial mixture of phenolics resembling those in coffee)

Am J Clin Nutr 2007
Examples of food synergy

- Jacobs and Tapsell provided examples of food synergy involving grain, apples, tomatoes, pomegranates and broccoli
  - Whole food typically affected mortality, cell proliferation, drug induced mammary tumor in a rat model, prostate tissue health, or biochemical reaction more than parts of the food or an equivalent cocktail of compounds

Nutr Reviews 2007
Harmful food synergy

- Jacobs and Tapsell provided an example of peanut allergy that only occurred with exposure to the whole peanut, not the allergenic proteins in isolation.
- Humans have identified safe foods by trial and error:
  - Don’t eat
  - Eat only small amounts and tolerate the poison
  - Prepare in special ways to break down the toxin

Nutr Reviews 2007
Food synergy is a viable concept that can help understand nutrition and in making food policy.
The idea “think foods first” whether doing research or helping to formulate a diet postulates that the structure and life of the organism eaten matters to the health of the human eater.
By focusing on balance and orchestration for life in the organism eaten, the whole food and food patterns as valid nutritional units, identifying blocks of constituents that should be considered together, and joint functionality of the different food constituents it should be possible to get new insights into diet and health.
Implications of food synergy

- The principle does not recommend or condemn a food
- It does imply that supplements and post-life amendments of food content, such as addition of trans fat, should be regarded and tested in the same way as pharmaceuticals
- It provides a method for studying whole foods and food patterns and learning more completely about the biological and health action of components of the food
- It does support the idea of variety in diet and of selecting nutrient-rich foods, among which plant foods are prominent
- The more we understand our own biology and the parallel biologies of food, the better our understanding and consequent dietary policy will be