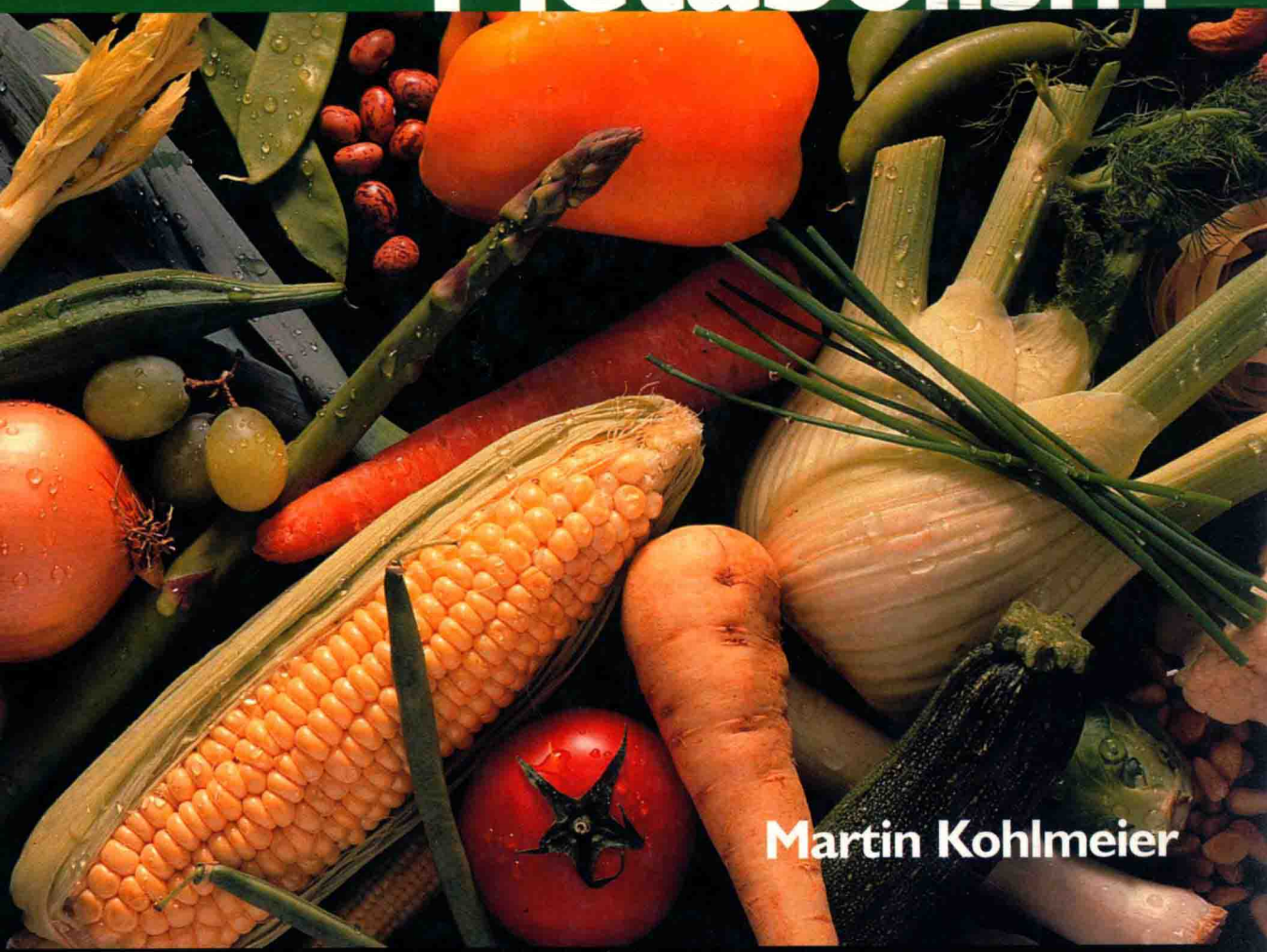
Nutrient Metabolism



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Nutrient Metabolism

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Foreword

It is likely that an understanding of nutrient metabolism will become increasingly valuable as it becomes more necessary to translate from molecular events, to whole body metabolism, to behaviors. This text, providing an excellent systematic overview of nutrient metabolism, provides an outstanding avenue for learning the fundamentals of this important area. Of course it will be useful for nutrition students and professionals, but also for other biologists who work at the interface with nutrition and need to have a concise reference on metabolism.

During the past 20 years, powerful new molecular techniques have generated incredible insights about human biology by identifying the molecules involved in biological events and examining them in purified form or simple systems. Most basic life science disciplines converged, though they were once based on metabolic and nutritional biochemistry, and evolved during the 1980s and 1990s so that they focused almost exclusively on molecular events. As a result, the reservoir of knowledge that this book contains (nutritional/metabolic biochemistry), knowledge that used to be at the core of such research, is often not part of the training of biologists. Though nutrient metabolism was not fully valued during the ascendance of the reductionist approach, there is now growing recognition that these skills will be essential for the next phase of biological science.

As we rapidly approach the time when the entire human genome is sequenced, a pressing need arises for scientific integrationism; an increased focus on nutrient metabolism is the next step in this process. Today we are faced with difficult questions dealing with the complex interactions that determine phenotype. Basic science disciplines are becoming increasingly aware that an understanding of metabolism and metabolic regulation is central to the understanding of how molecular events result in life itself. How do you explain phenotype once you know genotype? What are the complex effects on metabolism of deleting or changing expression of a gene? This new text on nutrient metabolism will be an invaluable tool for scientists who wish to address these questions.

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Contents

Introduction

1

Nutrients

What nutrients are

We depend for sustenance on what we consume, but fortunately we are not what we eat! The foods that we eat and drink are broken down by grinding and digestion, sorted by selective absorption, and changed in metabolic reactions. The ultimate fate of an absorbed compound in the body depends on how quickly it is metabolized for energy production or excreted with bile or urine. Most ingested compounds leave again after a short time – which is for the better. Some of those that insist on staying on (pesticides, toxic heavy metals, too much fat) are unwelcome guests that make us wish for more short-term visitors like vitamin C (ascorbic acid) that cheerfully do their job and leave again in a timely manner.

Nutrients are compounds from foods and bacterial production in the gut that the body uses for its normal (physiological) functions. This broad definition includes compounds that are utilized directly for energy production (ethanol), to aid in metabolism (coenzymes), to build body structures (cholesterol), or to serve in a specific cellular function (bromine for the oxidative burst of eosinophils). A nutrient has been considered essential in short-lived organisms if its lack prevents the organism from completing its life cycle and if the compound is directly involved in the function of the organism (Epstein, 1994). This definition has some obvious shortcoming for humans, because many of current concerns are about health long beyond reproductive age. Indeed, more than half of healthy people's life span is spent after cessation of reproduction (Blurton Jones *et al.*, 2002). Prevention of cardiovascular disease, cancer and dementia has come to the forefront of today's healthcare efforts. The significance of an individual's exposure to particular food compounds for a span of nearly a hundred years is just beginning to come into focus.

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Essential building blocks

At least 26 different elements are used to build the human body and keep it functioning, and possibly a few more. Fourteen of them are usually found in quantities of at least a gram or more in a young 70 kg man. Fluorine (as fluoride) strengthens and protects teeth, possibly also bones, but is not considered essential. Additional elements, including tin, rubidium, germanium, and lithium, are consumed in small, but significant amounts with foods and are regularly present in the body. It is uncertain, however, whether these are truly needed at any stage in life or provide any health benefit (Nielsen, 2001).

The body can use several elements only when they are ingested as part of particular compounds. Carbon has to be supplied mainly as digestible carbohydrate, alcohol, fat or protein. Nitrogen has to be consumed as protein; small amounts of ammonia and some

Table 1.1 Elements of the body

	Intake body content (g/day)	(g/70kg)	
Oxygen	2000	45 000	Estimated
Carbon	305	16 000	Estimated
Hydrogen	275	4000	Estimated
Nitrogen	10	4000	Estimated
Calcium	1	700	Food and Nutrition Board, 1997
Phosphorus	1	450	Aloia *et al.*, 1984
Sulfur	0.3	200	Estimated
Potassium	3	140	Larsson *et al.*, 2003
Sodium	3	100	Forbes, 1987
Chloride	6	95	Forbes, 1987
Magnesium	0.3	25	Elin, 1987; Rude, 2000
Fluorine	0.002	6	Whitford, 2000
Iron	0.008	3	
Zinc	0.011	2	King and Keen, 1994
Copper	0.0009	0.1	
Manganese	0.0002	0.1	
Iodine	0.00015	0.02	
Selenium	0.000055	0.017	Schroeder *et al.*, 1970
Molybdenum	0.000045		
Chromium	0.000020		
Cobalt	–		
Bromine	–		
Boron	–		
Silicon	–		
Arsenic	–		
Vanadium	–		
Nickel	–		
Tin	–		
Rubidium			
Germanium			
Lithium			
Aluminum			
Cadmium			
Lead			

nitrogen compounds can also be utilized. Hydrogen comes with water and smaller amounts with nutrients. Sulfur has to come with methionine, cysteine, and sulfate. Phosphorus can be utilized only in the form of phosphate salts.

Essential nutrients

Only 24 complex nutrients are absolutely essential, because they cannot be adequately produced from precursors. Precursors can provide for a small percentage of the requirements for water (oxidation of macronutrients) and niacin (metabolism of tryptophan), but most has to come from the outside.

Some of the nutrients are only essential for humans and possibly a few other species. Thus, most mammals can synthesize ascorbic acid from glucose and produce daily amounts equivalent to several grams per 70 kg body weight. Humans, like the other primates, have lost their ability to synthesize vitamin C from L-gulonate, because their gene for L-gulonolactone oxidase (EC1.1.3.8) is riddled with crippling mutations. Other nutrients that cannot be synthesized at all by humans include nine amino acids, the omega-3 and omega-6 fatty acids, eleven vitamins, and queuine. Queuine appears to be important, since a dedicated human enzyme inserts this nucleotide-like compound into specific DNA sequences that promote colonocyte stability and function.

Vitamin D is not on this list of essential nutrients, since vitamin D is synthesized in the body from a precursor and people can thrive without any intake. If anything, the ultraviolet light that is needed for vitamin D production in skin might be considered essential. Under some conditions, especially in children and older people living at high latitudes and staying too much indoors, dietary intakes become important for optimal health. This is not different from arginine, which is also of critical importance for health and needs to be partially supplied with the diet, if vitamin B6 and niacin status is inadequate, especially during times of high need. Food compounds such as phytate (Heim *et al.*, 2002) may still turn out to be important, if not essential, as new evidence sheds light on their role in human metabolism.

The list of essential nutrients may serve as a reminder that only a few of them are actually nutrients of concern in an affluent society. Many essential nutrients are harmful if consumed in excess. The bottom line is that for every nutrient, optimal intake levels need to be determined, and that too much is usually as problematic as too little.

Non-essential organic micronutrients

Some compounds can be synthesized by humans, but production may not always cover needs, especially at certain times in the life cycle. Thus, food sources have to augment endogenous synthesis of arginine, cysteine, taurine, and docosahexaenic acid (an omega-3 fatty acid) to meet the needs of very young infants. Severe injury, infections, chronic diseases or other temporary circumstances also may increase needs beyond the capacity of endogenous synthesis. On the other hand, dietary intakes of specific non-essential nutrients may become more important when genetic variants create a bottleneck in the synthesis of a particular compound, such as carnitine. Vitamin D provides

Table 1.2 Essential nutrients

Water	Aqueous environment, protons, hydroxide ions
Sugars	Energy production, synthesis of most organics
Amino groups	Protein, mediator synthesis
Leucine	Protein and beta-leucine synthesis
Valine	Protein synthesis
Isoleucine	Protein synthesis
Lysine	Protein synthesis
Tryptophan	Protein, niacin, and mediator synthesis
Phenylalanine	Protein, tyrosine, mediator, and pigment synthesis
Methionine	Protein and cysteine synthesis, methyl donor
Threonine	Protein and glycine synthesis
Histidine	Protein synthesis
Omega-3 fatty acids	Eicosanoid synthesis
Omega-6 fatty acids	Eicosanoid synthesis
Vitamin A	Regulator of numerous genes
Vitamin E	Antioxidant
Vitamin C	Antioxidant, cofactor of numerous enzymes
Riboflavin	Cofactor of numerous enzymes
Niacin	Cofactor of several hundred enzymes
Pantothenate	Cofactor of numerous enzymes
Folic acid	Cofactor of numerous enzymes
Vitamin B6	Cofactor of several hundred enzymes
Vitamin K	Cofactor of one enzyme that modifies 14 proteins
Thiamin	Cofactor of 5 enzymes, neuronal action
Biotin	Cofactor of 4 enzymes, additional actions
Vitamin B12	Cofactor of 3 enzymes
Queuine	Stabilizes specific tRNAs in colon
Sodium	Osmolyte, enzyme cofactor, cotransport
Potassium	Signal transduction, enzyme cofactor
Chloride	Osmolyte, cotransport, digestion, immune defense
Iron	Cofactor of numerous enzymes and proteins
Zinc	Cofactor of numerous enzymes
Copper	Cofactor of numerous enzymes and proteins
Manganese	Cofactor of numerous enzymes
Iodine	Constituent of thyroid hormones
Selenium	Cofactor of 13 enzymes and proteins
Molybdenum	4 enzymes, additional actions
Chromium	Chromomodulin, interaction with DNA
Cobalt	Vitamin B12, methionine aminopeptidase
Bromine	Halogenating oxidant of eosinophils
Boron	Unknown
Silicon	Unknown
Arsenic	Unknown
Vanadium	Unknown
Nickel	Unknown
Tin	Unknown
Rubidium	Unknown
Germanium	Unknown
Lithium	Unknown
Aluminum	Unknown
Cadmium	Unknown
Lead	Unknown

Table 1.3 Conditionally essential nutrients

Vitamin D	Regulates numerous genes
Choline	Phospholipid synthesis, methyl-group donor
Arginine	Protein, creatine, nitrous oxide synthesis
Tyrosine	Protein, mediator, pigment synthesis
Cysteine	Glutathione synthesis, conjugation
Taurine	Constituent of bile acids, osmolyte
Choline	Constituent of phospholipids, methyl group donor
Lipoic acid	Antioxidant, cofactor of 4 enzymes
Ubiquinone	Cofactor of oxidative phosphorylation
Carnitine	Cofactor of fatty acid translocation
DHA	High need for brain growth

Table 1.4 Non-essential nutrients conferring health benefits

Fluorine	Fluoride stabilizes tooth minerals
Flavonoids	Antioxidants, phytoestrogens
Carotenoids	Antioxidants

another illustration of an endogenously synthesized compound that can be conditionally essential. Humans can produce large amounts of cholecalciferol (vitamin D3) as long as their skin is exposed long enough to sufficiently intense sunlight. Only life at higher latitudes (especially during winter months) or indoors, or prevention of skin exposure to sun by clothing or sun-screen lotion makes any dietary intake of this misnamed nutrient (cholecalciferol is not even an amine, much less a vitamin) necessary. Decreased availability (for instance of lipoic acid), when production by intestinal bacteria is disturbed, should also be mentioned.

Undoubtedly, there are numerous further dietary compounds that promote health, sometimes to a very significant extent. Examples include a wide range of polysaccharides, flavonoids, phytosterols, saponins, and other constituents of plant-derived foods that have shown some promise for the prevention of atherosclerosis, cancer, or other debilitating disease. The real question about such nutrient-like compounds is how much can be safely consumed and whether higher than typical consumption with foods provides any worthwhile health benefit.

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