DOCUMENT RESUME

ED 321 981 SE 051 489

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TITLE Nutrient and Drug Interactions. Nutrition in Primary Care Series, Number 3.
INSTITUTION Ohio State Univ., Columbus. Dept. of Family Medicine.
SPONS AGENCY Health Resources and Services Administration (DHHS/PHS), Rockville, MD. Bureau of Health Professions.
PUB DATE 80
CONTRACT 232-78-0194
NOTE 36p.; For related documents, see SE 051 486-502. See SE 051 503-512 for "Nutrition in Health Promotion" series.
PUB TYPE Guides - Classroom Use - Materials (For Learner) (051)

EDRS PRICE MF01/PC02 Plus Postage.
DESCRIPTORS Biochemistry; *Dietetics; Disease Control; *Drug Therapy; Drug Use; Health Education; *Independent Study; Interaction; *Medical Education; Medicine; *Nutrition; *Nutrition Instruction; Pharmacology; Physiology; Preventive Medicine; Science Education; Therapeutic Environment; Therapy

ABSTRACT

Nutrition is well-recognized as a necessary component of educational programs for physicians. This is to be valued in that of all factors affecting health in the United States, none is more important than nutrition. This can be argued from various perspectives, including health promotion, disease prevention, and therapeutic management. In all cases, serious consideration of nutrition related issues in the practice is seen to be one means to achieve cost-effective medical care. These modules were developed to provide more practical knowledge for health care providers, and in particular primary care physicians. The modules were written by dieticians and nutritionists working closely with physicians. The modules were field tested and reviewed by basic and clinical science faculty in a number and variety of educational programs. This module focuses on the complex interactions between drugs, food, and nutrients; specifically, the effect of drugs on absorption, metabolism, and excretion of nutrients; and the effect of food on the bioavailability and effectiveness of medications. Included are the learning goals and objectives, self-checks of achievement with regard to goals, tables, and references for the physician and for the physician to give to the patient. (CW)

3 Nutrient and Drug Interactions

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Nutrition in Primary Care

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The Nutrition in Primary Care Series Contains These Modules:

1. Nutrient Content of Foods, Nutritional Supplements, and Food Fallacies
2. Appraisal of Nutritional Status
3. Nutrient and Drug Interactions
4. Normal Diet: Age of Dependency
5. Normal Diet: Age of Parental Control
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12. Dietary Management in Hyperlipidemia
13. Dietary Management in Castrointestinal Diseases
14. Dietary Management for Alcoholic Patients
15. Nutritional Care of Deteriorating Patients
16. An Office Strategy for Nutrition-Related Patient Education and Compliance

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Contract Number 232-78-0194

U.S. Department of Health and Human Services
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Bureau of Health Professions · Division of Medicine

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A special note of appreciation is extended to persons in family practice residency programs and universities throughout Ohio for reviewing the materials, and to the faculty and residents where the materials were piloted:

Grant Hospital, Columbus, Ohio
Riverside Methodist Hospital, Columbus, Ohio
University Hospital, Columbus, Ohio

Production Assistants

Carol Ann McClish, Lynn Copley-Graves, Chris Bachman, Linda Farnsworth

Composition: Pony-X-Press, Columbus, Ohio
Camera Work: Printers' Service, Columbus, Ohio
Reproduction and Binding: PIP, Store 523, Columbus, Ohio

Library of Congress Catalog Card Number: 80-82859

3 Nutrient and Drug Interactions

Nutrition in Primary Care

Tables

Introduction

Interactions between drugs and nutrition are increasingly recognized as the source of some of the complications and side effects of drug therapy. It has been reported that 25% of patients' visits to physicians' offices are related to complaints about taking prescribed medications.[1] A study conducted at an outpatient clinic indicated that the drugs with the highest adverse drug reactions were penicillin, sulfonamides, codeine, and aspirin. Drugs used most frequently were aspirin, Librium, milk of magnesia, Maalox, Indocin, penicillin G, phenobarbital, tetracycline hydrochloride, and vitamin B_{12}. In addition, one-third of all drugs taken *were not* prescribed by physicians.[2]

Patients have long wondered whether it really mattered what they ate when taking medication, or whether the drug was best taken before or after a meal. As found so often in medicine and nutrition, there are traditions surrounding the proper regimen for taking medications with food. Many of the elderly in today's society were given stimulants or tonics before meals and were also told by physicians that drugs which might "irritate the stomach" should be taken after foods.

Although there was some rationale in these prescription practices, little has been known until recent years about how drugs can affect, and be affected by, nutrition.

With the proliferation of drugs, patients today increasingly need to know not only *when* to take a particular drug, but also what kinds of foods should or should not be consumed with the drug. The physician, in turn, may be unsure of how diet affects drugs and, conversely, how drugs affect food intake and nutrient utilization and requirements.

Examination of the complex interactions between drugs, food, and nutrients is the focus of this module. Specifically, this module has been designed to provide information for you with regard to (1) the effect of drugs on absorption, metabolism, and excretion of nutrients, and (2) the effect of food on the bioavailability and effectiveness of medications. With the knowledge of nutrient-drug interactions, practical suggestions for dietary manipulation are presented to aid you in the proper nutritional care of your patients who are receiving medications.

Goals

As a result of this unit of study, you should be able to:

1. *Identify five major classes of nutrient-drug interactions and identify the dietary modifications appropriate to each;*

2. *Describe the rationale for why some medications are taken with food and why others are not;*

3. *Describe the interrelationships between drugs typically used for various medical problems and nutrient absorption;*

4. *Identify the metabolic effects of drugs which adversely affect nutrient intake; and*

5. *Plan nutritional care and instruct patients on dietary modifications appropriate for the medications which they are receiving.*

Effect of Drugs on Absorption, Metabolism, and Excretion of Nutrients[3,9]

The drugs presented in Table 3–1 may affect the nutritional status of a patient by influencing the absorption, metabolism, and/or excretion of one or more nutrients. The clinical features of drug-induced malabsorption are similar to those of other malabsorption syndromes, including anemia, steatorrhea, and malnutrition. However, drug-induced malabsorption is reversible when the offending drug is removed.

Many of the drugs described in Table 3–1 may cause anorexia, nausea, vomiting, diarrhea, constipation, and gastrointestinal irritation. These in turn may result in decreased absorption and metabolism of minerals and vitamins, increased urinary excretion of minerals and vitamins, and significant weight loss. Dietary recommendations have been suggested which should be considered in counseling patients regarding dietary intake when receiving medications.

Table 3–1 Effect of Drugs on Absorption, Metabolism, and Excretion of Nutrients

Drug	Effect on Nutrients	Dietary Recommendations
Alcohol		
Note: The extensive effects of a diet containing alcohol include malabsorption of nutrients from the alcohol-altered gastrointestinal tract, changes in absorption of numerous medications, and interactions affecting metabolism of many drugs.		
Chronic Usage (in excess of 20% caloric intake)	Decreases absorption of folic acid, thiamin, B_{12}, B_6, magnesium, zinc, and other trace minerals, lipids; causes general decreased intake of foods.	Vitamin/mineral capsule to supply 100% of daily RDA. Increase kilocalorie level with a variety of foods. Provide a high caloric and high protein diet if individual is underweight. Prohibit alcohol intake.

Drugs which have special coatings that are soluble in alcohol may be released quicker than desired and are therefore hazardous when taken with alcohol. For example, antihistamines when combined with alcohol result in a fast antihistamine release. Drugs that are known to react with alcohol are listed as follows:

Table 3-1 (continued)

Ethyl Alcohol

Combined with	Consequence	Combined with	Consequence
Amitryptyline (Elavil) Antihistamines Barbiturates Chloral hydrate Chlordiazepoxide (Librium) Codeine Desipramine (Norpramin) Diazepam (Valium) Hydroxyzine (Atarax, Vistaril) Imipramine (Tofranil) MAO inhibitors Phenelzine (Nardil) Tranylcypromine (Parnate) Meprobamate (Equanil, Miltown) Morphine Nortriptyline (Aventyl) Phenothiazine tranquilizers Chlorpromazine (Thorazine) Prochlorperazine (Compazine) Thioridazine (Mellaril)	Increased central nervous system depression	Disulfiram (Antabuse) Metronidazole (Flagyl) Nitrofurans Furazolidone (Furoxone) Nitrofurantoin (Furadantin) Quinacrine (Atabrine) Sulfonylureas Chlorpropamide (Diabinese) Acetohexamide (Dymelor) Tolbutamide (Orinase)	Abdominal cramps, flushing, vomiting, malaise due to interference in detoxification of alcohol
		Insulin	Higher doses required
		Methyldopa (Aldomet) Nitrates, nitrites Nitroglycerin Mecamylamine (Inversine)	Increased hypotensive effect

From Asperheim, M K and Eisenhauer, L A *The Pharmacologic Basis of Patient Care*, 3rd ed. Philadelphia, W B. Saunders Co , 1977, p. 90. Used with permission of W.B. Saunders Co., © 1977, Philadelphia, PA

Table 3-1 (continued)

Drug	Effect on Nutrients	Dietary Recommendations
Analgesics		
Aspirin	Decreases absorption of ascorbic acid and folic acid. Patients receiving 12 aspirin tablets daily have significantly decreased platelet aggregation and plasma ascorbic acid levels[11]	Increase use of foods high in ascorbic acid. Example: consume at least 1 cup of orange juice, 1 cup tomato juice, 1/2 melon, or 1 medium baked potato daily
Barbiturates	Decrease absorption of folic acid	
Morphine and Narcotics	Decrease gastric and pancreatic secretions and appetite	Supplement with vitamin/mineral capsule to meet 100% daily RDA
Antacids		
Antacids are used for patients suffering from hyperchlorhydria associated with peptic ulcer disease, gastritis, peptic esophagitis, hiatus hernia, and heartburn.		
Maalox	Decreases absorption of iron if gastric content is not kept acidic	Iron supplementation if given for two weeks or longer
Aluminum hydroxide	Destroys thiamin	Give multivitamin capsule that will provide 100% of the Recommended Dietary Allowances (RDA)
	Phosphate depletion may occur if the patient is on a low phosphorus diet	Binding of phosphate is generally not a significant problem as the patient's diet is usually high in phosphorus
Note: Antacids plus Tetracycline	Antacids tend to precipitate tetracycline in the gastrointestinal tract, which decreases drug absorption rate; calcium carbonate antacids may form insoluble calcium soaps and produce steatorrhea	

Table 3-1 (continued)

Drug	Effect on Nutrients	Dietary Recommendations
Anticonvulsants		
Phenytoin sodium	Decreases absorption of calcium, folic acid, B_{12}, B_6, vitamin D, vitamin K	Supplement with a multivitamin and mineral tablet meeting 100% RDA daily
Phenobarbital	Decreases absorption of folic acid, B_{12}, B_6, vitamin D, vitamin K	
Anti-Inflammatory		
Colchicine	Decreases absorption of protein, fat, lactose, carotene, B_{12}, sodium, potassium, and bile acids	Low-fat diet with low whole milk intake. Encourage low fat cheese, yogurt and buttermilk
Salicylazosulfapyridine	Decreases serum folic acid level	Supplementary folic acid
Corticosteroids	Increases protein catabolism and sodium retention, decreases glucose tolerance, increases urinary loss of zinc, calcium, and potassium, causes fat mobilization and redistribution, increases metabolic need for B_6, ascorbic acid, and vitamin D	May need diet low in sodium (2 to 4 grams), high in protein, bland, and restricted in simple sugar. Vitamin/mineral capsule to meet 100% of the RDA. Avoid excess weight gain due to increased appetite.
Antimicrobials		
Cycloserine	Decreases absorption of calcium, magnesium, B_6, B_{12}, and folic acid	Supplementation of diet with vitamins and minerals if used for a long period of time. Supplement should supply 100% RDA.
Neomycin	Decreases absorption of fat, lactose, sucrose, nitrogen, sodium, potassium, iron, calcium, B_{12}, and carotene	
Tetracyclines	Decreases absorption of iron, calcium, magnesium, amino acids, fats, fat-soluble vitamins	

Table 3-1 (continued)

Drug	Effect on Nutrients	Dietary Recommendations
Antimitotics		
Methotrexate and other cytotoxic medications	Inhibits folic acid utilization. Decreases absorption of B_{12}. Increases excretion of nucleic acid metabolites	Supplement with vitamin/mineral capsule to supply 100% of RDA. Folic acid level should be 0.1 to 0.5 mg daily as excessive amounts alter methotrexate response

Note:
Cancer patients with a high kilocalorie, nutritionally-balanced diet have a better chance of successful chemotherapy, radiation therapy, and surgery than if a low kilocalorie, poorly-balanced diet is consumed. Cancer patients frequently lose interest in eating due to taste impairment plus depression of appetite secondary to toxic effects of chemotherapy and radiation therapy. You should be aware of this problem and adjust the patient's diet accordingly. High kilocalorie and high protein milk shakes and eggnogs, as well as soft foods like puddings, cottage cheese, yogurt, sherbet, and ice creams, may be used with success in improving kilocalorie intake. Foods may be chopped or pureed to insure ease in swallowing.

Chemotherapeutic Agents and Causes of Anorexia

	Causes of Anorexia											
	stomatitis	nausea	vomiting	diarrhea	oral ulcerations	constipation	ulceration of buccal mucosa	gingivitis	metallic taste	prolonged anorexia	abdominal pain	glossitis
actinomycin D	X	X	X	X	X							
bleomycin	X	X	X									
cyclophosphamide		X	X									
cytarabine		X	X	X	X							
doxorubicin	X	X	X	X								
5-fluorouracil	X	X	X	X	X							
hydroxyurea	X	X	X	X			X	X				
melphalan		X	X									
6-mercaptopurine	X	X	X									
methotrexate	X	X	X	X	X		X					
nitrogen mustard		X	X	X					X			
nitrosoureas		X	X							X		
vinblastine	X	X	X	X		X					X	X
vincristine		X	X			X					X	

Table 3-1 (continued)

Drug	Effect on Nutrients	Dietary Recommendations
Cardiac Glycosides		
Digitalis	Intravascular potassium depletion may be induced by (1) administration of diuretics which increases potassium excretion, (2) corticosteroid administration or large amounts of ingested carbohydrates or infused glucose and insulin which cause intracellular shift of potassium with resultant decrease in serum potassium, or (3) prolonged nasogastric suction or diarrhea or persistent vomiting which precipitates digitalis toxicity and may also cause decreased serum potassium.	Patients should eat and/or drink fruits or juices high in potassium, equivalent to at least 60 mEq daily. An example supplying this amount is: 1 medium baked potato (13 mEq), 1 medium banana (10 mEq), 1 cup strawberries (6 mEq), 2 cups of orange juice (11 mEq), and 7 oz meat (21 mEq). (See Module 11 on hypertension.) The average American diet contains 60 to 100 mEq potassium daily.
Digoxin	Increases serum calcium levels and may produce arrhythmias.	
Digitoxin	Decreases glucose absorption.	
Diuretics		
Furosemide	Increases urinary excretion of ascorbic acid, calcium, potassium, magnesium, and sodium.	Increase dietary intake of potassium with orange or grapefruit juice, dried fruits or bananas. (See Module 11 on hypertension for a list of foods containing potassium).
Mercurials	Increases urinary excretion of calcium, potassium, thiamin, magnesium, and sodium.	
Thiazides	Increases urinary excretion of sodium, potassium, magnesium, zinc, and riboflavin. Decreases carbohydrate tolerance.	
Triamterene	Impairs utilization of folic acid. Increases loss of calcium.	

Table 3-1 (continued)

Drug	Effect on Nutrients	Dietary Recommendations
Hypocholesterolemics		
Cholestyramine	Decreases absorption of vitamins A, D, K, B_{12}, carotene, and folic acid, fat, medium-chain triglycerides, sugar, iron, and calcium	Supplement dietary intake with fat-soluble vitamins and B_{12}
Clofibrate	Decreases absorption of glucose, carotene, and B_{12}, and potentiates sodium warfarin drugs	
Laxatives		
Bisacodyl (chronic use)	Steatorrhea, protein-losing enteropathy, potassium loss; decreases glucose absorption	Potassium supplement. Increased protein and carbohydrate intake
Milk of Magnesia	Decreases absorption of calcium and potassium; causes steatorrhea	Potassium and calcium supplements
Mineral Oil	Decreases absorption of carotene, vitamins A, D, and K	Do not use in food preparation or give at meal time or close to meal time
Phenolphthalein	Decreases absorption of vitamin D and calcium, causes electrolyte losses and steatorrhea. and decreases glucose absorption	Drink at least 3 glasses of milk daily or use milk products. If lactose intolerant give fermented dairy products. If patient refuses dairy products, give 400 International Units (I.U.) vitamin D and 800 mg calcium daily.

Table 3-1 (continued)

Drug	Effect on Nutrients	Dietary Recommendations
Oral Contraceptive Agents	Decrease absorption of B_{12}, ascorbic acid, folic acid, B_6, riboflavin, magnesium, and zinc; impair glucose tolerance. Increase iron and calcium absorption	Regular diet. Some women seem to benefit from supplements of B_6 and folic acid. Avoid excessive weight gain

Note: Estrogens increase the rate of conversion of tryptophan to niacin, thereby altering tryptophan metabolism. Although oral contraceptives seem to alter absorption and metabolism of many nutrients, there is little accompanying evidence that women using this medication require increased amounts of nutrients to prevent nutritional deficiencies. If, however, a dietary evaluation reveals the patient's diet is marginal, malnutrition may occur. Give one multivitamin-mineral supplement equal to 100% RDA unless the diet can be improved.

Table 3–2 Drugs to Be Taken on an Empty Stomach

Ampicillin	Phenmetrazine hydrochloride
Bisacodyl	Lincomycin
Cloxacillin	Sulfonamides
Dipyridamole	Tetracyclines (except doxycycline)
Erythromycin	
Penicillin	

Table 3–3 Drugs to Be Taken One-Half Hour Before Meals

Atropine sulfate	Methscopolamine bromide
Belladonna	Propantheline bromide
Chlordiazepoxide	

Effect of Food on Drugs[3,6-9,13-16]

The presence of food in the digestive tract may delay gastric emptying time and thus slow intestinal absorption of many drugs. Food in the stomach increases pH of the gastric contents and may cause alteration in the rate and quantity of medication absorption. Stability and solubility of the drug also may be affected. Therefore, whether the drug should be taken before, during, or after meals is an important point to discuss with patients.

Drugs to Be Taken On an Empty Stomach

The drugs listed in Table 3–2 are destroyed by gastric acidity; they should be given when there is the *least acid* present and the *shortest gastric emptying time*, therefore on an empty stomach. These drugs should be taken 1 hour before meals or 2 hours after meals.

Drugs to Be Taken One-half Hour Before Meals

The anticholinergic medications listed in Table 3–3 should be taken one-half hour before meals, as they decrease gastric secretions and motility immediately upon eating.

Drugs to Be Taken At Mealtime or With Food

Many drugs, such as those shown in Table 3–4, irritate the gastrointestinal tract and should be taken with meals or snacks.

Table 3–4 Drugs to Be Taken at Mealtime or With Food

Aminophylline
Aminosalicyclic acid
Aspirin-phenacetin-caffeine (APC)
Aspirin
Chlorpromazine
Chlorpropamide
Ferrous gluconate
Ferrous salts (lactate, fumarate, sulfate)
Hydrochlorothiazide
Hydrocortisone
Indomethacin
Isoniazid
Metronidazole
Nalidixic acid
Potassium salts (chloride gluconate, bicarbonate)
Prednisolone
Prednisone
Procyclidine
Reserpine
Sulfinpyrazone
Tolbutamide
Triamterene
Trihexyphenidyl
Trimeprazine

Visconti, J.A *Nutrition in Disease. Drug-Food Interactions* Columbus, OH, Ross Laboratories, 1977, p 16

Table 3–5 Drugs Not to Be Taken with Milk or Milk Products

Bisacodyl: Milk or antacids cause dissolution of enteric coating with release of drug resulting in gastric irritation.

Ferrous compounds: Milk forms iron complexes and interferes with iron absorption. Encourage patients to take iron with meals but not to drink milk 1 to 2 hours before or after iron ingestion.

Tetracyclines (except doxycycline): Calcium present in milk, cottage cheese, and other milk products is chelated by tetracycline preventing drug absorption from the gastrointestinal tract.

Note, however, that sometimes drugs are mixed with foods to mask the taste or smell. You must be careful in recommending such administration, since many beverages and juices are acidic and may affect acid-labile drugs such as ampicillin, erythromycin, and penicillin. Coca-Cola syrup is sometimes used to mix with vitamin B-complex supplements to disguise the taste. The syrup contains sugar, so diabetics should not use it for taking the supplement. Sustained-release tablet and capsule formulations should not be broken or crunched and mixed with food.

Drugs Not to Be Taken With Milk or Milk Products

Nutrients in milk may have an adverse effect on the absorption of several medications as described in Table 3–5.

Specific Nutrients Affecting Drug Utilization

Patient use of multivitamin and multimineral preparations may have an effect on drug effectiveness, as shown in Table 3–6.

Foods That Contain Tyramine

The foods in Tables 3–7 and 3–8 should be eliminated on the tyramine-free diet in patients receiving MAO inhibitors.

Table 3–6 Nutrients Which Affect Drug Utilization

Drug	Nutrient(s) Interference
Coumadin (Sodium warfarin)	High doses of vitamin K in foods and as supplements affect prothrombin time. Foods with high vitamin K content are: cabbage, spinach, kale, lettuce, cauliflower, tomatoes, wheat bran, cheese, egg yolk, and liver.
Levodopa	5 mg or more of pyridoxine may reverse the effects of levodopa. Multivitamins and fortified cereals should be checked for pyridoxine content. Protein intake should be 0.5 gm protein per kilogram body weight as excessive protein inhibits levodopa effects.
Phenytoin sodium	Folic acid excess may lead to decreased absorption of the drug. If megaloblastic anemia develops, folic acid (0.1 to 1 mg/day) may be prescribed as a supplement.
Tetracycline	Ferrous and calcium salts interfere with absorption.
Methotrexate	Vitamin/mineral supplements may include folic acid (or its derivatives) which decreases methotrexate response. If megaloblastic anemia develops, folic acid (0.1 to 1 mg daily) may be prescribed as a supplement.
Griseofulvin	Dietary fat stimulates bile which makes the drug more water soluble.
Propoxyphene hydrochloride	High protein diet depresses blood levels of this drug.

Table 3-6 (continued)

Drug	Nutrient(s) Interference
Monoamine Oxidase Inhibitors	(neurotransmitter, hormone) monoamines. Thus, MAO maintains norepinephrine in nerve endings. MAO inhibitors block MAO, thus allowing norepinephrine, dopamine, and serotonin to accumulate in the brain contributing to an improved mood. TYRAMINE has the ability to release norepinephrine and epinephrine. Normally MAO blocks absorption of tyramine and the norepinephrine released is quickly inactivated. MAO inhibitors impair this mechanism allowing tyramine in the general circulation to cause a hypertensive crisis. See the list of tyramine-containing foods. (Table 3-7). Patients on MAO inhibitors must also avoid amphetamines, sympathomimetic drugs, levodopa, reserpine, and most cough and cold remedies. MAO inhibitors may potentiate action of insulin and hypoglycemic drugs.

Table 3-7 Tyramine Content of Selected Foods

Food	Tyramine Content µg/gm
Cheeses	
Camembert	86
Stilton	466
Brie	180
Ementhal	225
New York State Cheddar	1,416
Gruyère	516
Processed American	50
Yeast	ND
Yogurt	ND
Beer	1.8-4.4
Chianti Wine	25.4
Sherry	3.6
Riesling	0.6
Sauterne	0.4
Port	ND

From Horowitz, D et al. "Monoamine Oxidase Inhibitors, Tyramine and Cheese." *Journal of the American Medical Association*, 188:1108, 1964. Used with permission of the American Medical Association, © 1964, Chicago, IL.

Table 3-8 Other Foods Containing Tyramine

Avocados	Raisins
Bananas	Licorice
Bologna	Soy sauce
Canned figs	Meat tenderizers
Caffeine beverages	Pickled or kippered herring
Chocolate	Other cheeses: Gouda
Cream, sour	Mozzarella
Broad bean pods	Parmesan
Dried fish	Provolone
Herring	Romano
Cod	Roquefort
Caplin	
Dates	Vanilla
Nuts	
Pepperoni	Liver and pâtés
Salami	
Sausage	

See *American Family Physician* July, 1978, for MAO inhibitor therapy and dietary implications.
From Sen, J.P.: "Analysis and Significance of Tyramine in Food" *Journal of Food Science*, 34.22, 1969.

Sodium Content of Selected Medications

Patients with cardiovascular disease are frequently seen by primary care physicians. Medications such as antibiotics and some over-the-counter medications vary in sodium content and, in some instances, may negate the low-sodium diet that you have prescribed for the patient.

A 2- to 4-gram sodium diet, depending upon the severity of fluid accumulation and hypertension, may be used for the management of these symptoms. (You may wish to see Module 11 on hypertension for the sodium content of selected foods.) Table 3–9 shows the sodium content of certain drugs.

Table 3–9 Sodium Content of Selected Prescription Drugs

Drug	Dosage	Sodium Content mg	mEq
Ampicillin	1 gram	65	2.8
Carbenicillin	382 mg tablet	22	1.0
Cephalothin	1 gram vial	62	2.7
Cephalothin	4 gram vial	249	10.8
Chloramphenicol	1 gram vial	52	2.3
Cloxacillin	250 mg vial	13	0.6
Dicloxacillin	63 mg/5 ml	27	1.2
Erythromycin	250 mg	70	3.0
Methicillin	1 gram vial	55	2.4
Nafcillin	1 gram vial	73	3.2

Visconti, J.A.: *Nutrition in Disease. Drug-Food Interactions* Columbus, OH, Ross Laboratories, 1977, p 19

Table 3–10 Sodium Content of Selected Over-the-Counter Medications

Medication	Sodium Content mg	Per Average Dose
Bisodol Powders	1,540	1 packet
Alka Seltzer (blue)	1,064	2 tablets
Sal Hepatica	1,000	1 rounded teaspoon
Bromo Seltzer	717	1.25 grams
Metamucil instant mix	250	1 packet
Sodium bicarbonate (baking soda)	178	2 tablets
Rolaids	100	2 tablets
Creamalin tablets	50	2 tablets
Tums	40	2 tablets
Phosphaljel suspension	39	15 milliliters
Titralac liquid	37.5	15 milliliters
Milk of Magnesia	36	30 milliliters
Basaljel suspension	27	15 milliliters
Gelusil liquid	21	15 milliliters
Kolantyl tablets	20	2 tablets
Mylanta II liquid	20	10 milliliters
Maalox suspension	18	15 milliliters
Riopan tablets	2	3 tablets

Remember that the milliequivalents of sodium per dose may be obtained by dividing the amount in milligrams by 23.

From Lipman, A.G. "Sodium Content of Frequently Used Analgesic and Gastrointestinal Drugs." *Modern Medicine*, 45:59-60, 1977. Used with permission of *Modern Medicine*, © 1977, New York, NY.

Note: Riopan has an extremely low sodium content. The recommended dosage is 400 to 800 mg 4 times daily. A 400 mg dose contains 0.7 mg of sodium. If used for a patient on a 500 mg sodium diet, the recommended dose would provide a low 2.8 mg sodium daily, as compared with the other antacids which supply well above this amount and would therefore be unacceptable on a 500 mg sodium diet.

Medications Affecting Appetite

Medications are *not* the answer to weight reduction. Many pills, tablets, and candies are claimed to provide a quick way to lose weight. Most of these products are costly and a waste of money. The best way to lose weight is to reduce kilocalorie

Table 3–11 Medications Depressing the Appetite

1. Diethylpropion (use with hypertensive patients).
2. Fenfluramine (should not be used with patients with a history of depression; best choice for diabetics).
3. Mazindol (use with hypertensive patients).
4. Phentermine.

intake and to increase physical activity under the direction of a physician and a dietitian (see Module 9 on obesity).

Medications Decreasing Appetite

If appetite-suppressing drugs are used in conjunction with a weight-reduction diet, thought must be given to their abuse potential. The drugs in Table 3-11 have a low abuse potential and may be used with the types of patients listed with them.

Medications Stimulating the Appetite

The medications shown in Table 3-12 stimulate the appetite and cause weight gain as described in the table.

Table 3-12 Medications Stimulating the Appetite

Drug	Effect
Chlorpromazine	May cause a weight gain of 1 to 2 pounds per week, usually leveling off when 20 pounds have been gained. This weight gain could in part be due to fluid retention, as well as increased appetite and deposition of fat. Weight may decline when use of the drug is discontinued.[6]
Lithium Carbonate	Taken over a period of months, this drug has been shown to cause weight gain; cause of weight gain is not understood.[6]
Corticosteroids	Contributes to an increased weight gain, fluid retention, and fat redistribution, particularly to the truncal area.
Cyproheptadine hydrochloride	Stimulates appetite, perhaps by activating the hypothalamic appetite-regulating center.
Butazolidin	Accelerates the degradation of digitoxin by induction of the hepatic microsomal drug-metabolizing system. Patients receiving digitalis may gain up to 10 pounds which may occur rather quickly due to fluid retention. Cardiac decompensation and acute pulmonary edema may result. Weight will return to normal when medication is stopped.

Medications Altering Taste Sensitivity

Many medications can alter taste sensitivity, reduce taste acuity, and/or leave an unpleasant aftertaste. Other medications cause nausea and vomiting, diarrhea and thus loss of appetite, examples of such medications are narcotics, cytotoxic agents, and cholinergic drugs. Some liquid medications that are unpleasant to take due to taste are chloral hydrate, potassium chloride, paraldehyde, and the B vitamins. Table 3–13 lists the medications that can alter taste sensitivity and explains in what ways they do it.

Table 3–13 Medications Altering Taste Sensitivity

Drug	Effect
Amphetamines	May decrease sweet sensitivity and increase bitter sensitivity
Anesthetics	
Cocaine, Eucaine, Amydricaine	Decreased bitter and sweet sensitivity
Amylocaine	Decreased bitter sensitivity, and loss of salt sensitivity with high drug intake
Isococaine and tropacocaine	Decreased sweet sensitivity
Benzocaine	Increased sour sensitivity
Amethocaine	Increased bitter sensitivity and decreased sweet sensitivity
Lidocaine	Decreased salt and sweet sensitivity
Acetyl sulfosalicylic acid	Decreased sensitivity
Clofibrate	Decreased sensitivity
Dinitrophenol	Loss of salt taste; general hypogeusia
D-Penicillamine	General decrease in overall taste sensitivity
5-Fluorouracil	Some alterations in bitter and sour sensitivity
Griseofulvin	Decreased sensitivity
Insulin	Decreased sweet and salt sensitivity with prolonged use
Lithium carbonate	Strange, unpleasant taste
Phenindione	Decreased sensitivity
Phenytoin	Decreased sensitivity

Adapted from Carson, J.A.S. and Gormican, A.. Disease-Medication Relationships in Altered Taste Sensitivity. *Journal of the American Dietetic Association*, 68:550, 1976.

Alteration of Urinary pH

The effectiveness of food in altering the pH of the urine is questionable. Cranberries, prunes, and plums increase urine acidity as hippuric acid is excreted. However, excessive quantities of cranberry juice (up to 4 liters per day) create only a transient change in urine pH.[19] The effect of urinary pH on drug excretion is shown in Table 3–14. The use of ammonium chloride or ascorbic acid (2 to 3 grams) to acidify the urine and acetazolamide or sodium bicarbonate to alkalinize the urine achieves results more rapidly than using food to shift the urinary pH.

Special Nutrient Considerations of Specific Drugs

Several medications have a specialized effect on nutrient intake. These are listed and explained in Table 3–15.

Table 3–14 Effect of Urinary pH on Drug Excretion

Drugs	Drug Excretion	
	In Acid Urine	In Alkaline Urine
Weak Acids (pKa 3.0-7.5)		
Coumarins Nalidixic acid Phenobarbital Phenylbutazone Salicylic acid Streptomycin Sulfonamides	Decreased	Increased
Weak Bases (pKa 7.5-10.5)		
Amitriptyline Amphetamines Antihistamines Antipyrine Chloroquine Imipramine Mecamylamine Meperidine Methenamine Nicotine Quinine Theophylline	Increased	Decreased

From Carmichael, B.L. "Some Aspects of Diet and Its Relationship to Drug Therapy." *Canadian Journal of Hospital Pharmacy*, 26 202-209, 1973 Used with permission of the *Canadian Journal of Hospital Pharmacy*, © 1973, Saskatoon, Saskatchewan.

Megavitamin Therapy

There are those who advocate excessive doses of vitamins to cure a multitude of physical and psychological problems. Many patients ask, "If a little is good, why isn't a lot better?" The reason is simple. Vitamins function as coenzymes. They are absorbed from the diet and carried in the blood to cells whose function depends upon them. After entering the cell, the vitamins combine with enzymes, called apoenzymes, and become synthesized in the cells resulting in a holoenzyme that catalyzes reactions inside the cell. The quantity of apoenzymes is limited. The apoenzyme is usually saturated by the amounts of vitamins suggested in the RDA. Thus, excessive amounts of vitamins serve no nutritional purpose and may have a pharmacologic and/or toxic effect. If one eats a variety of fruits, vegetables, meats, milk and milk products, eggs, and whole grain products daily in

Table 3–15 Special Nutrient Considerations of Specific Drugs

Drugs	Effect
Quinidine	Quinidine intoxication may occur if a patient takes excessive antacids and drinks 1 quart or more of fruit juice (which contributes about 40 mEq of bicarbonate ion); alkalinization of the urine decreases excretion of quinidine and may cause quinidine toxicity.
Methenamine hippurate Methenamine mandelate	These medications are most effective when fluid intake is 1,200 to 1,500 ml per day and urinary pH is kept at 5.5 or below. Supplementary urinary acidification if required may be achieved by using ascorbic acid, ammonium chloride, or sodium acid phosphate which helps to keep calcium in solution.
Methocrexate	Up to 90 percent of this drug is cleared by the kidneys. In the presence of hyperuricemia, fluid intake should be 2,000 ml per 24 hours to dilute the hyperuricemic state.
Acetazolamide	Can be used in treatment of edema due to congestive heart failure, glaucoma, and drug-induced edema. Acetazolamide causes a loss of bicarbonate ion which increases the excretion of sodium, water, and potassium. Alkalinization of the urine and promotion of diuresis are thus affected.

quantities meeting The Daily Food Guide recommendations, vitamin supplementation is not necessary and toxicities will not occur.

Although megavitamin therapy poses a risk of toxicity, malabsorption syndromes and some inborn errors of metabolism may be corrected or alleviated by large doses of specific vitamins. Malabsorption syndrome patients will benefit from vitamin therapy in the amounts suggested by Hodges in Table 3–16. The amounts listed are generally well tolerated, at least for a few weeks. Care should be exercised in the administration of the doses of vitamins A and D for a prolonged period of time.

A list of the more common vitamin-dependent syndromes and their recommended therapeutic dose of vitamin supplementation is found in Table 3–17. Caution must be exercised in giving large doses of vitamin D for long periods of time.

You should ask patients if they are taking vitamin supplements on their own and, if so, how frequently and of what strength. The elderly are particularly prey to food quacks and often take large amounts of vitamins and minerals to "ward off" or "cure" disease. If toxic symptoms should appear from excessive intake, immediate withdrawal of the offending vitamin is necessary with the exception of vitamin C, which should be tapered over a 2 to 3 day period.

Table 3–16 Appropriate Oral Doses of Vitamins* and Minerals for Patients With Any Type of Malabsorption Syndrome

I. Water-Soluble Vitamins (In Divided Doses)	
Ascorbic acid	150–300 mg daily
Thiamin	5–15 mg daily
Riboflavin	5–15 mg daily
Niacin	30–60 mg daily
Folic Acid	15–30 mg daily
Vitamin B_{12}	100–300 µg daily
Vitamin B_6	5–15 mg daily
II. Fat-Soluble Vitamins	
Vitamin A (as Retinyl palmitate)	30,000–60,000 IU daily
Vitamin D (as vitamin D_2)	30,000 IU daily
Vitamin E	30 mg daily
Vitamin K	15 mg daily
Essential Fatty Acids (as linoleic)	15 gm daily
III. Minerals	
Calcium (as calcium gluconate)	1.5 gm calcium daily
Magnesium (as magnesium sulfate)	600 mg magnesium daily
Iron (as $FeSO_4$)	300 mg daily
Other trace minerals (as indicated by plasma levels or clinical status)	

*Doses for adults. For children give ¼ to ½ depending on age.

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Fat-Soluble Vitamins

Vitamin A

Vitamin A toxicity is seen most frequently in children and adolescents.[4] The toxicity of the vitamin depends upon age, dosage,and duration of administration. The following amounts have been suggested as toxic levels for individuals:

- infants less than 1 year of age = 18,000–60,000 IU daily (13 to 43 times the RDA)
- children age 1 to 5 years = 80,000–500,000 IU daily (40 to 250 times the RDA)
- adults = 200,000–275,000 IU daily (40 to 55 times the RDA)

On the basis of available data, ingestion of vitamin A in amounts greater than 5 to 10 times the RDA should not occur without special reason and close supervision by a nutritionist or physician.

Hypervitaminosis A in humans is characterized by anorexia, headache, blurred vision, hair loss, dry and flaky skin, irritability, reddened gingiva, nosebleeds, bone pain, enlarged spleen and liver, anemia, and a high plasma or serum vitamin A level performed on a fasting blood sample.

Carotene-rich foods such as carrots can be ingested in large amounts without producing hypervitaminosis A; however, a yellowing of the skin, but not of the sclera, does occur. Hypervitaminosis A does not occur from food sources alone,

Table 3–17 Some Vitamin-Dependent Syndromes

Name	Common Findings	Vitamin Involved	Daily Amount RDA*	Daily Amount Therapeutic Dose
B_6-dependent syndrome	Convulsions	Vitamin B_6	0.5 mg	20 mg
Sideroblastic anemia	Microcytic hypochromic anemia	Vitamin B_6	1–2 mg	10 mg
Xanthurenic aciduria	Mental retardation	Vitamin B_6	1–2 mg	10 mg
Homocystinuria	Mental retardation Vascular occlusions	Vitamin B_6 (or folic acid)	1–2 mg 100 µg	500 mg 20 mg
Hartnup's disease	Mental retardation Cerebellar ataxia	Niacin	5–20 mg	200 mg
Methylmalonic aciduria	Mental retardation Ketoacidosis	Vitamin B_{12}	>0.3 µg	1 mg
Hypophosphatemic rickets	Bony deformities	Vitamin D	400 IU	50,000–200,000 IU

*RDA-Recommended Dietary Allowances

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except if polar bear liver is consumed; instead, it occurs only with massive vitamin A supplementation. To calculate retinol equivalents (RE), divide international units (IU) by 5. RDA of 5,000 IU vitamin A = 1,000 RE.

Vitamin D

There is great variation in the amount of vitamin D that causes toxic reactions. As little as 1,800 IU can be toxic to children, and doses in excess of 100,000 IU may be necessary to cause toxicity in adults.[22] On the basis of available information, it appears that 4 to 5 times the RDA for vitamin D (RDA = 400 IU) is safe for children and adults. There is no evidence that normal, healthy persons are benefited by intakes greater than the RDA.

Vitamin D is formed through the action of sunlight on the precursors in the skin (a variable and undependable source) and is found in vitamin D-fortified milk, butter and margarine, eggs, cheese, and fish. Vitamin D fortification of milk is set at 400 IU per quart.

Excessive doses of vitamin D are sometimes given by parents to children and are frequently taken by adults who have rheumatoid arthritis in the belief that vitamin D will be of benefit. Some symptoms of hypervitaminosis D include hypercalcemia, renal stones, calcium deposits in soft tissues, anorexia, vomiting, renal insufficiency, hypertension, systolic heart murmur, and an elevated blood vitamin D level.

Vitamin E

Evidence is lacking that excessive doses of vitamin E affect physical endurance, enhance sexual potency, prevent or cure heart attacks, or increase longevity in individuals.[22] Herbert[23] reports that insufficient research has been done on the toxicity of vitamin E and that doses of 300 mg daily for several months have been given to patients without negative effects. It has been suggested, however, that an unbalanced ratio between vitamin E and vitamin K can lead to impaired blood coagulation.

The richest sources of vitamin E are vegetable oils, margarines or shortenings made from them, and whole cereal grains. The vitamin E requirement increases as polyunsaturated oil ingestion increases. Polyunsaturated oils are rich sources of vitamin E.

Vitamin K

Excessive ingestion of vitamin K has been observed to result in hemolytic anemia, hyperbilirubinemia, and kernicterus in infants. Vitamin K_1 administered orally is less toxic in large amounts than the water-soluble derivatives of menadione.

The daily requirement for vitamin K is 1 to 2 mcg per kilogram body weight per day; the ordinary mixed diet may provide as much as 400 mcg per day. Even with complete biliary obstruction, stores of vitamin K in the adult are sufficient to maintain blood coagulability for several weeks. Therefore, there is no need for self-medication with vitamin K. Vitamin K occurs in leafy green vegetables as well as in a variety of other foods. Supplementation of the newborn with vitamin K should be determined by the physician.

Water-Soluble Vitamins

Orthomolecular psychiatry, promulgated initially by Hoffer and Osmund in the 1950s, involves the use of megavitamin therapy (ascorbic acid, B_6, B_{12}, niacin) and conventional therapy in the treatment of schizophrenia. A task force of the American Psychiatric Association[24] reviewed the uses of megavitamins and concluded that the results of such therapy have not been confirmed, as the proponents have not performed controlled experiments or reported their results satisfactorily. Massive doses of vitamin B_6 may produce liver disease[25], and excessive folic acid antagonizes the protective effect of dilantin against convulsions in patients with epilepsy. Intravenous administration of 14 mg of folic acid may induce seizures in some subjects; others may tolerate 5 to 10 times this amount.[26]

Ascorbic Acid[25]

Benefits of megadoses of ascorbic acid are unproven. Ascorbic acid (RDA equals 60 mg daily for adults) is necessary for synthesis and maintenance of collagen and intercellular ground substance necessary for wound healing; it prevents scurvy and enhances absorption of iron. Large doses of ascorbic acid are poorly absorbed and may produce osmotic diarrhea; this mechanism is one reason why ascorbic acid toxicity is not common. Intake of large doses of ascorbic acid increases the rate of ascorbic acid excretion, which

also has a blood-lowering effect on ascorbic acid.

Large doses of ascorbic acid have been shown to impair fertility and terminate pregnancy in guinea pigs and women. In susceptible individuals, large doses of ascorbic acid may precipitate oxalate renal stones by raising urinary oxalate levels, secondary to the degradation of ascorbic acid to oxalate. Vitamin C can also decrease the rate of uric acid excretion and precipitate gout in susceptible patients.

Ascorbic acid is a powerful antioxidant. Lowering the urine pH with large intakes of ascorbic acid (3 to 6 grams daily in normal adults does not affect urine pH) will cause false-negative tests for urinary glucose in the diabetic using the popular tape or dipstick method. Large amounts of vitamin C may also result in high-altitude hypoxia. There is also some evidence that large amounts of ascorbic acid can create false-negative tests for blood in stools of patients with intestinal bleeding. High amounts of ascorbic acid can destroy vitamin B_{12}, decrease white blood cell count, and cause acute erythrocyte hemolysis.

One hazard of megadose ascorbic acid ingestion is "rebound scurvy" in adults and newborn infants. Large doses cause an increase in degradation of this vitamin. This process continues when massive doses are decreased, and a transient case of scurvy may result if tapering occurs faster than 2 to 3 days. The same problem can occur in the newborn infant of a mother who has taken megadoses of vitamin C, thus creating a dangerous situation for the infant.

There is little evidence to support the concept that massive doses of vitamin C will prevent or be of therapeutic advantage in treating the common cold. If there is any beneficial effect, it may be that ascorbic acid has some antihistamine effect.

Summary

With new drugs becoming available at an increasing rate, it is important to recognize the immediate and long-term metabolic effects of all drugs. Drugs affect many nutrition-related factors such as appetite, gastrointestinal absorption, and nutrient and drug metabolism. When prescribing medications, you must consider the age of the patient, especially children and the elderly, because these two groups are particularly susceptible to adverse drug-nutrient interactions. If two or more medications are prescribed, consider the interactions that could influence nutrient intake. Physiological changes that occur in the elderly, such as alterations in taste, smell, appetite, and the gastrointestinal tract, may create compliance difficulties. Asking your patient "Are you taking any other medications?" and "What do you eat during the day and when do you take your medications?" may prevent medical complications.

Test Your Knowledge

Select the *ONE* best answer for each of the following statements:

1. Cancer chemotherapeutic agents may cause the following effects:
   a. Gingivitis
   b. Stomatitis
   c. Metallic taste
   d. None of the above
   e. All of the above
2. When prescribing diuretics, you should remind patients to drink fruit juices high in:
   a. Vitamin A
   b. Ascorbic acid
   c. Potassium
   d. Sodium
   e. B_{12}
3. Aspirin tends to decrease the absorption of:
   a. Vitamin A
   b. Ascorbic acid
   c. Thiamin
   d. Vitamin K
   e. Potassium
4. Antacids affect the absorption of:
   a. Iron and zinc
   b. Thiamin and ascorbic acid
   c. Calcium and magnesium
   d. Iron and thiamin
   e. Phosphorus and potassium
5. When a patient is receiving corticosteroids, the recommended diet should include:
   a. Sodium modification
   b. Potassium modification
   c. Calcium modification
   d. Zinc modification
   e. Iron modification
6. Drugs which increase the need for B_6 are:
   a. ACTH and L-Dopa
   b. Methotrexate and alcohol
   c. Oral contraceptives and penicillamine
   d. Hydralazine and aspirin
   e. Alcohol and thyroxine
7. If a woman is using an oral contraceptive agent, and her dietary intake is marginal, which of the following vitamins should be supplemented?
   a. Thiamin and riboflavin
   b. Riboflavin and B_6
   c. Vitamin A and vitamin K
   d. B_6 and thiamin
   e. Niacin and riboflavin

8. Alcohol interferes with the absorption of:
   a. Calcium
   b. Vitamin K
   c. Vitamin D
   d. Iron
   e. Folate
9. Which of the following medications will *not* cause malabsorption?
   a. Laxatives
   b. Clofibrate
   c. Tetracyclines
   d. Amphetamines
10. Monoamine oxidase inhibitors are potentiated by tyramine, significant amounts of which are contained in:
   a. Some beers
   b. Chianti wine
   c. Whiskey
   d. All of the above
   e. Only a and b
11. Corticosteroids affect nutrient intake because of their actions on:
   a. Fat metabolism
   b. Protein metabolism
   c. Carbohydrate metabolism
   d. All of the above
   e. Only b and c
12. The over-the-counter medication containing the least amount of sodium is:
   a. Metamucil Instant Mix
   b. Alka Seltzer
   c. Bisodol Powders
   d. Bromo Seltzer
   e. Riopan
13. A medication affecting the taste sensitivity is:
   a. Ampicillin
   b. Griseofulvin
   c. Maalox
   d. Salicylates
   e. Bisacodyl
14. A drug not to be taken with milk is:
   a. Penicillin
   b. Tetracycline
   c. Disulfiram
   d. Nitroglycerin
   e. Tolbutamide
15. Acid ash fruits include:
   a. Cranberries
   b. Prunes
   c. Plums
   d. All of the above

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Answers

1. e
2. c
3. b
4. d
5. a
6. c
7. b
8. e
9. d
10. e
11. d
12. e
13. b
14. b
15. d

Some Abbrevations Used in the Nutrition in Primary Care Series

ATP	adenosine triphosphate
c	cup
cc	cubic centimeter
CNS	central nervous system
FDA	Food and Drug Administration
gm	gram
IBW	ideal body weight
IU	International Units
kcal	kilocalorie
kg	kilogram
lb	pound
lg	large
MCV	mean corpuscular volume
MDR	minimum daily requirement
med	medium
mEq	milliequivalent
mg	milligram
MJ	megajoule
ml	milliliter
oz	ounce
RDA	Recommended Dietary Allowances
RE	retinol equivalents
sl	slice
sm	small
Tbsp	Tablespoon
TPN	total parenteral nutrition
tsp	teaspoon
USDA	United States Department of Agriculture