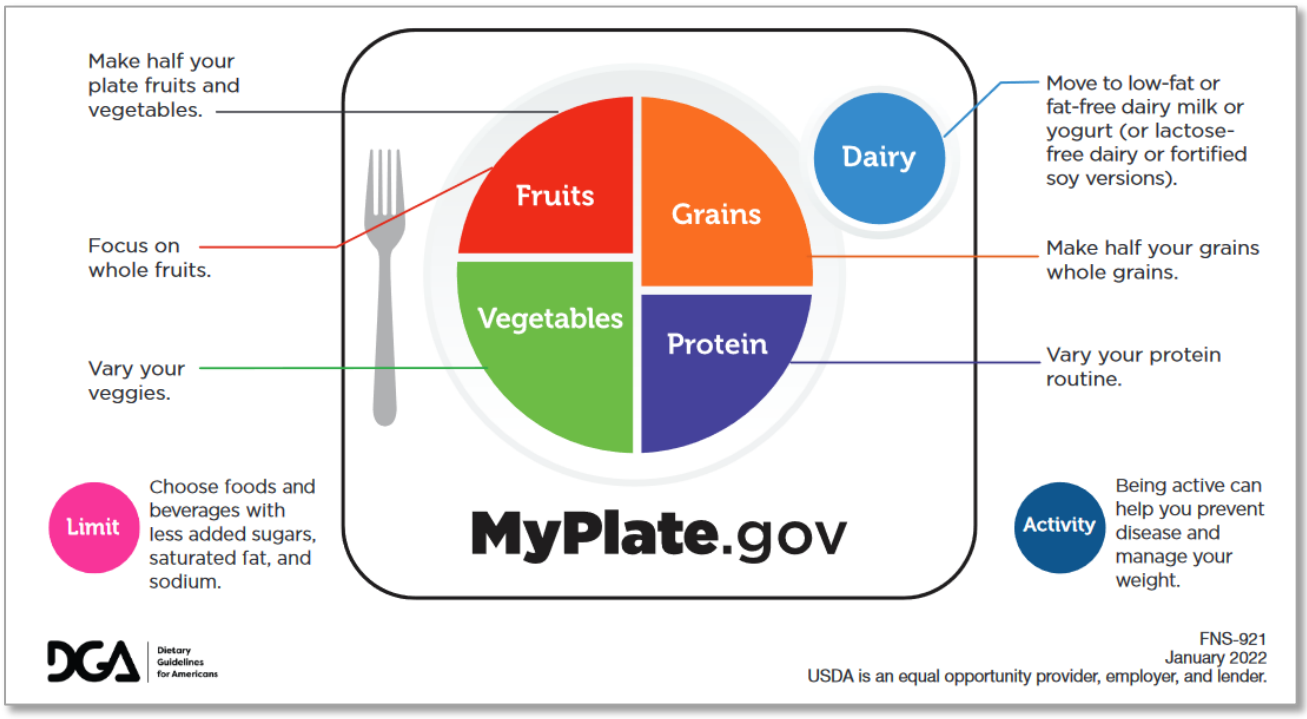
NUTRITIONAL ADVICE

for Persons with Porphyria

OVERVIEW

Good nutrition is important for all of us, including persons with porphyria. For the most part, persons with porphyria should follow the sensible and usual dietary advice of the U.S. Department of Agriculture and other responsible and reputable governmental agencies such as www.myplate.gov.

Because over-nutrition and obesity are such a great problem in the U.S. and other western countries, it is important that patients with porphyria do their best to avoid becoming obese or gaining weight beyond their ideal body weights. The acute porphyrias [acute intermittent porphyria, hereditary coproporphyria, variegate porphyria, and ALAD deficiency porphyria] may be made worse by prolonged fasting or crash dieting, because, in these forms of porphyria, glucose and other carbohydrates help to repress the activity of hepatic ALA synthase 1, the first enzyme of the heme synthetic pathway. In these forms of porphyria, uncontrolled up-regulation of ALA synthase 1 in the liver is a necessary component of the metabolic abnormalities that may give rise to acute attacks.



GENERAL ADVICE

There is no special or particular diet required OR recommended for persons with porphyria. Rather, the principles of good and sensible nutrition apply. These principles call for a varied and balanced diet, particularly with avoidance of over-nutrition or under-nutrition. Consumption of too many calories, in excess of daily needs for calorie and energy consumption, has emerged as a major public and personal health problem not only in The Americas, but across the globe. The growing problem of obesity is present in much of the world, not just in North America.

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The graphic on the previous page is based on the Dietary Guidelines for Americans, as developed by the U.S. Department of Agriculture. Such advice should be followed by persons with porphyria, as well as those without. The keys are adherence to a varied and balanced diet with moderate consumption of carbohydrates, protein, and fats. The fats should include little or no trans-fats and preferably include a substantial proportion as unsaturated fatty acids [such as olive oil, safflower oil], rather than saturated fatty acids [such as animal fat]. The protein may be in the form of animal or vegetable protein. The carbohydrates should preferably not include large amounts of refined sugars or high fructose corn syrup, although oral or intravenous carbohydrate in the form of dextrose may be prescribed for therapy of acute attacks of porphyria. However, day in and day out, even persons with one of the acute porphyrias should not be consuming large amounts of dextrose (sugar) or fructose.

NUTRITIONAL ADVICE FOR PERSONS WITH PORPHYRIA

The acute or inducible porphyrias include acute intermittent porphyria (AIP), hereditary coproporphyria (HCP), variegate porphyria (VP), and porphyria due to severe deficiency of ALA dehydratase (ALADP). Most persons that have one of these forms of porphyria, all of which are due to inherited deficiencies in one of the enzymes of heme biosynthesis, have no symptoms or signs of porphyria most of the time. They may, however, occasionally develop acute attacks, usually characterized by severe bouts of abdominal pain with variable increases in blood pressure and pulse rate and with severe constipation. Sometimes, the pain may be in the chest, back or extremities instead of, or in addition to, the abdomen [belly]. Such attacks are characterized by a marked up-regulation of an enzyme in the liver called delta-aminolevulinic acid synthase 1 (ALAS1). This up-regulation leads to a marked over production and urinary over-excretion of delta-aminolevulinic acid (ALA) and porphobilinogen (PBG), which are the biochemical hallmarks of acute porphyric attacks. Although the precise pathogenesis of acute porphyric attacks remains incompletely understood, most of the evidence points at an excess of ALA as being a key factor. Thus, efforts to down-regulate the high expression of ALA synthase-1 are of paramount importance in treating and preventing acute porphyric attacks.

During such acute attacks, the usual therapeutic recommendations by experienced physicians are for the daily intake of dextrose or other metabolizable carbohydrates to be approximately 300 grams per day.

The treatment of acute attacks is focused on controlling the severe pain, on decreasing systemic arterial hypertension and tachycardia, when present, on decreasing nausea and vomiting, and on decreasing the up-regulation of hepatic ALAS1. This is done by the administration of sugar [dextrose] and by the administration of heme, which must be given intravenously. During acute attacks, patients often have nausea and vomiting, as well as disturbances of normal gastrointestinal function, so that it is often necessary for the dextrose to be administered intravenously, as well. If the attacks are less severe, however, patients may be able to take in dextrose orally, such as by adding sugar to orange juice, by sucking on hard candies, etc. ***During such acute attacks, the usual therapeutic recommendations by experienced physicians are for the daily intake of dextrose or other metabolizable carbohydrates to be approximately 300 grams per day.***

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It is also important for persons with one of the acute porphyrias to avoid drugs or other factors that are known to be able to trigger acute attacks. Chief among these are estrogen and especially progesterone. Thus, some menstruating women unfortunately experience monthly symptoms during the middle of their menstrual cycles, around the time of ovulation, when their endogenous production of progesterone is at a peak. Such women may benefit from drugs such as gonadotropin-releasing hormone antagonists [leuprolide] or low doses of oral contraceptives, which interrupt
their normal monthly hormonal cycles. Some benefit from receiving prophylactic infusions of IV heme on once weekly or twice or thrice monthly basis, typically administered shortly before the time of the month when they ovulate [mid-menstrual cycle].

A number of drugs and chemicals are capable of up-regulating hepatic ALAS1 and are thus best avoided by persons with acute porphyria. Such drugs include barbiturates, such as phenobarbital, hydantoins such as phenytoin and carbamazepine. Any drugs that are inducers or that cause destruction of the heme of cytochromes P-450 have the proclivity to cause or to exacerbate acute porphyric attacks. Another factor that is capable of triggering acute porphyric attacks is excess intake of alcoholic beverages. Thus, persons with acute porphyria should avoid any binge drinking. ***Good general advice is that men should drink either not at all or not more than two drinks of alcohol per day and women should drink not all or not more than one drink of alcohol per day.***

There is no convincing clinical or scientific evidence that any particular foods (with the exception of alcoholic beverages, as described above) are capable of triggering or worsening acute porphyric attacks.

Any acute stress such as an acute illness or severe emotional or psychological stress or exhaustion may also trigger acute porphyric attacks. Therefore, patients with acute porphyria should receive vaccinations to protect them from preventable acute infections, including annual flu shots, Pneumovax, vaccinations to protect against diphtheria pertussis and tetanus, with booster shots for tetanus at least every ten years, vaccinations to protect against hepatitis A or hepatitis B infection, and for those who have had chicken pox, the vaccination to protect against development of shingles (Shingrix).

There is no convincing clinical or scientific evidence that any particular foods (with the exception of alcoholic beverages, as described above) are capable of triggering or worsening acute porphyric attacks. There are, however, some foods that have been shown to contain chemical substances that, in large amounts, can up-regulate hepatic ALA synthase 1. Such foods include charcoal-broiled meats, cabbage, and Brussels sprouts. The amounts of such foods that would need to be eaten in order to produce induction of hepatic ALA synthase 1 have not been carefully studied, but are probably far above the amounts that would be eaten as part of reasonable, well balanced diets. Probably, none of these foods needs to be avoided completely by persons with acute porphyria. ***Moderation in all things is the best course of action.*** The **Appendix** lists suggested meal plans for persons with acute porphyria who are of normal weight and with normal daily needs for energy [~30-35 Kcal/kg BW/d].

DIETING IN ACUTE PORPHYRIA

It is important that persons with acute porphyria avoid crash diets with extreme decreases in daily carbohydrate and caloric intakes. However, it is also important that they avoid obesity. If they already are obese, they should gradually lose weight. This should be done with a formal diet plan and under the supervision of an experienced physician and nutritionist.

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SULFUR CONTAINING AMINO ACIDS & ESSENTIAL AMINO ACIDS

Our normal diets contain proteins. In fact, regular and adequate intakes of protein are essential to normal growth and health. Proteins are found in both vegetable and animal sources of foods. The building blocks of proteins are called amino acids. Some of these amino acids, such as methionine and cysteine, contain sulfur. Such amino acids are not the same thing as "sulfa drugs". They are not contraindicated for patients with acute porphyria. In fact, methionine is one of the nine **essential amino acids**: if adequate amounts of these nine amino acids [histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine] are not consumed regularly, deficiencies will develop that can lead to malnutrition and disease. The reason is that humans are unable to make these amino acids and must take them in regularly, in order to achieve and maintain adequate levels to permit their bodies to make the hundreds of thousands of proteins that are essential for good health.

PORPHYRIA CUTANEA TARDA [PCT]

The major risk factors for the development of porphyria cutanea tarda are excess alcohol intake, increased iron, certain chronic viral infections, especially hepatitis C virus and human immunodeficiency virus, and estrogens. About 20 to 25% of persons with PCT also have a genetic predisposition in the form of an inherited partial deficiency of an enzyme called uroporphyrinogen decarboxylase. Genetic mutations that lead to iron overload, such as those that occur in hereditary hemochromatosis [HFE gene mutations—C282Y, H63D, S65C] may also contribute to hepatic iron overload, which is a risk factor.

The principal dietary advice for persons with porphyria cutanea tarda is to avoid all alcohol in any form.

The principal dietary advice for persons with porphyria cutanea tarda is to avoid all alcohol in any form. In addition, adherence to a low iron diet with avoidance of any medicinal iron and with ingestion of limited amounts of liver or red meat, is recommended, at least until remission of active PCT has been achieved. Remissions are achieved by the removal of iron, usually by therapeutic phlebotomy, which is the removal of one unit of blood every week or two. This is continued until an iron reduced state has been achieved. Patients with active PCT typically require the removal of eight to twelve pints of blood, although this number is variable. The progress of iron removal is best followed with serial measurements of serum ferritin. The ideal serum ferritin is 50 to 100 ng per ml. Typically, removal of one pint of blood will lead to a decrease in serum ferritin of about 30 ng per ml.

Person with PCT and chronic hepatitis C are usually cured of both conditions with a brief 6-12 week course of highly active direct-acting antiviral medications, such as Epclusa, Harvoni, or Mavyret.

ERYTHROPOIETIC PROTOPORPHYRIA [EPP/XLP]

In EPP or the phenotypically identical XLP there is excess production of protoporphyrin by developing red blood cells in the bone marrow. This is due usually to an inherited deficiency in an enzyme called ferrochelatase or heme synthase, the final enzyme in the heme synthetic pathway. A less common form called X-linked protoporphyria, is caused by an increase in activity of the erythroid form of ALA synthase [ALAS2], the first enzyme of the heme synthetic pathway in red blood cells. The gene for this enzyme is on the X chromosome, hence the name XLP.

Many persons with EPP have a mild degree of anemia with measures of iron that suggest iron deficiency. Such persons with XLP appear to benefit from iron administration with improvements in blood hemoglobin, serum

iron and serum ferritin. In contrast for still unclear reasons, persons with EPP have seemed to worsen with iron administration, especially if high doses of iron are administered intravenously. Thus, we recommend that patients with EPP and iron deficiency not receive IV iron, but rather that they take iron once per day or once every other day and in the form of iron carbonyl + vitamin C, which has been better tolerated than ferrous sulfate or gluconate.

There also have been a few reports that intake of glucose has led to an improvement in EPP.

For the most part, there is no particular special diet recommended for patients with EPP. A varied well balanced diet with avoidance of excess calories and with assurance of adequate intakes of iron and other minerals and vitamins is recommended.

RARE CUTANEOUS FORMS OF PORPHYRIA
CONGENITAL ERYTHROPOIETIC PORPHYRIA [CEP]

CEP is a rare genetic disorder characterized by deficient activity of an enzyme called uroporphyrinogen 3 synthase (also sometimes called uroporphyrinogen co-synthase). It is characterized by severe over-production of uroporphyrin 1, which is manifest at birth and in the neonatal period. There is no particular diet that is indicated or recommended for persons with CEP. Recent evidence has suggested that removal of iron by phlebotomies is of benefit for patients with CEP. Cure of CEP requires bone marrow transplantation. **Hepato erythropoietic porphyria [HEP]**, which presents in the new born period, as does CEP, is due to severe deficiency of uroporphyrinogen decarboxylase (homozygous or compound heterozygous deficiency). There is no special diet that is known for persons with HEP.

ADVICE ABOUT VITAMINS & MINERALS

For most persons who are consuming mixed, well-balanced diets, there is no need for routine use of vitamin or mineral supplements. Persons who consume few dairy products [milk, yogurt, cheese, etc.] and older persons, especially women, and those with little exposure to sunlight are prone to develop deficiencies of vitamin D and to have inadequate intake of calcium. Thus, they should have their serum levels of 25-hydroxy vitamin D checked and should seek advice of a well-trained physician or nutritionist regarding supplements of vitamin D and calcium. There is potential harm from the excessive intake of vitamin D or calcium, or of excessive intakes of other fat-soluble vitamins [vitamins A and E]. Thus, moderation in intake is best. There is little harm, but also little likelihood of benefit, in the intake of water-soluble vitamins [vitamins B and C]. Iron may trigger or worsen porphyria cutanea tarda, and it may also increase levels of hepatic ALA synthase 1. Thus, it should not be taken in medicinal form unless there is evidence of iron deficiency. There is little reason for anyone with porphyria [or most without porphyria] to take in supplemental copper, zinc, selenium, chromium, silver, gold, or other metals.

ADVICE ABOUT HERBAL REMEDIES & DIETARY SUPPLEMENTS

Herbal remedies and dietary supplements (HDS) have become popular in the USA and in many other parts of the world. In fact, there is widespread irrational enthusiasm for taking such supplements. We recommend against their use because the composition and purity of them are uncertain. They are unregulated by the US Food and Drug Administration, and they have not been shown to be safe and effective. Many of them probably contain chemicals that are capable of up-regulating hepatic ALAS1 and thus of triggering or exacerbating acute porphyria. In addition, they often are adulterated with potentially toxic substances, such as heavy metals.

Contact the UPA with questions any time at 1-800-868-1292 or info@porphyria.org.

Note: There is no special or particular diet required or recommended for persons with porphyria. Rather, the principles of good and sensible nutrition apply. These principles call for a varied and balanced diet, particularly with avoidance of over-nutrition or under-nutrition

SAMPLE MENUS
for Persons with Porphyria

WEEK 1 Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Breakfast 1 large banana 1 c cereal 1½ c skim milk	Breakfast 1 slice rye bread w/ 1 tbsp fruit spread ¾ c oat-type cereal, ¾ c skim milk 1 c melon, raw ½ c grapefruit juice	Breakfast ½ bagel, sesame seed 1 tbsp cream cheese, low fat 1 c oatmeal ½ c skim milk ½ c peaches, canned, light	Breakfast 1 slice wheat bread w/ 2 tsp margarine 1 fried egg, 1 link (about 1½ oz) sausage, lean or turkey 1 orange 1 c milk, skim	Breakfast 2 Belgian Waffles 2 tbsp pancake syrup, low calorie 1 c skim milk ½ c strawberries	Breakfast 1 c corn flakes cereal 1 c skim milk 1 slice wheat bread w/ 1 tbsp creamy peanut butter 1 pear	Breakfast ¾ c Raisin Bran cereal 1 c skim milk ½ bagel, cinnamon & raisin 1 tbsp peanut butter, plain 1 kiwifruit
Snack 1 slice wheat bread 1 tbsp peanut butter	Snack 1 c chicken gumbo soup 1½ c salad with 2 tbsp light dressing 1 slice bread	Snack 10 pretzel twists 1 c orange juice, calcium fortified	Snack 1 wheat tortilla 1 tbsp jelly or honey ½ grapefruit or 1 apple	Snack Smoothie ½ c low-fat yogurt 1 c fruit juice ½ c-1c fruit, fresh, frozen or canned, sweetener as desired	Snack 1 orange or fresh fruit	Snack 6 oz apple-grape-raspberry Cocktail juice drink Sports bar or fruit/oat bar
Lunch 1 apple, sliced, w/skin 1 c spaghetti, ½ c marinara sauce, ½ c beans 1 slice bread, 2 tsp margarine 1½ c salad: 1 c lettuce, tomato, carrot, cucumber green pepper & radishes, ½ c endive, 2 tbsp light creamy Italian salad dressing, 10 pretzel twists	Lunch Noodles w/ tuna & vegetables: 1¼ c egg noodles, cooked w/out salt, ⅓ c green peas, ½ c sweet red peppers, ¼ c tuna in water, 1 tbsp low fat mayonnaise 1 oz roll ½ c strawberries	Lunch 1 deli sandwich: 1 hard roll, 4 oz lean turkey or chicken breast, 1 oz cheddar cheese, low fat ¾ c lettuce, shredded 2 tomatoes, sliced ¾ c juice drink, mixed fruit 1 apple	Lunch 1½ c fresh fruit salad, w/ apples, bananas, grapes, oranges, pears roast beef sandwich: 2 slices bread, 3 oz lean meat 1 tbsp light mayo, lettuce 6 oz low fat yogurt	Lunch 1 piece cheese pizza (⅛ of 12 in pizza) 2 c tossed salad with lettuce, tomato, carrots, cucumber green pepper & radishes 2 tbsp vinegar & oil salad dressing 1 c asparagus 1 c apple juice	Lunch 2 slices multigrain bread 2 tbsp peanut butter 1 tbsp jelly 1c baby carrots 1 c skim milk 1 oatmeal cookie	Lunch: 1 wheat tortillas ¾ c refried beans 1-2 chopped tomatoes, lettuce 1 oz cheese ½ c rice 1 piece fruit 6 oz low fat or skim milk
Snack Sports bar	Snack 1 apple	Snack 1 banana 4 oz low fat yogurt	Snack ½-1 c low-sugar cereal 4 oz skim or low-fat milk	Snack 1 c mixed fruit ½ c applesauce	Snack 1 slice wheat bread, 1 oz deli sliced lean turkey, lettuce, mustard 1 fruit	Snack 10 pretzel twists 1 piece fruit
Dinner 1 burrito, large: 1 flour or wheat tortilla, ½ c pinto beans, 3 oz lean meat or chicken 1 oz cheddar cheese, reduced fat ½ c rice ½ c carrots ½ c low-fat ice cream	Dinner Baked potato w/ ½ c veggie chili or beef chili ¼ c onion 1 oz cheese 2 c salad: green lettuce, carrots, cucumbers, tomatoes, mushroom 2 tbsp low fat dressing ½ c low fat cottage cheese	Dinner 3 oz haddock, baked ½ c rice 2 Tbsp margarine 1 c squash, winter, mashed ½ c broccoli	Dinner grilled chicken salad: 1 c loose-leaf lettuce, ½ c garbanzo beans, 3 tbsp carrots, shredded, 3 oz grilled chicken, 2 tbsp lite dressing ½ c lima bean 1 wheat dinner rolls, small 2 tsp margarine	Dinner 1 c spaghetti, ½ c spaghetti sauce 2 tbsp parmesan cheese, grated 1 slice Italian Bread 2 tsp margarine, unsalted 1 c green beans, ½ c corn 8 oz skim or low-fat milk	Dinner 1 c mixed vegetables (broccoli, peppers, mushrooms) w/ 1 c linguini & 3 oz salmon 1 tbsp olive oil 2 sprigs parsley, chopped ¼ tsp sage, ground ½ c sweet potato	Dinner 3 oz pork chop, center loin, lean only, broiled ½ potato, boiled without skin ½ c winter squash, mashed ½ c green beans chopped, cooked 1 tbsp margarine
Snack 1 small peanut butter cookie ¾ c apple juice	Snack 4 graham cracker halves 1 tbsp peanut butter	Snack 1 c frozen dessert, low-fat ice cream or frozen yogurt	Snack 1 frozen fruit bar	Snack Ice cream sandwich	Snack 3 c popcorn, natural flavor, salt free 8 oz mixed juice	Snack Ice cream sundae with: ½-1 c low-fat ice cream, 1 tbsp dessert topping, strawberry, 1 tbsp nuts, non-fat chocolate sauce

SAMPLE MENUS

for Persons with Porphyria

WEEK 2 Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Breakfast 1 c fortified bran flakes 1 c skim or soymilk (fat free) 1 medium banana ½ c egg substitute, scrambled	Breakfast 3 egg white omelet w/ 2 tbsp each of chopped green peppers, onion, tomato, 2 tbsp olive oil 1 c skim milk 1 whole wheat toast 1 tbsp almond butter ½ c cantaloupe	Breakfast 1 large cinnamon raisin bagel with 2 tbsp peanut butter 1 banana	Breakfast ¾ c cold cereal, bran flakes, high fiber 1 c low-fat milk, 1% 1 banana-medium 12 oz coffee	Breakfast 1½ c shredded wheat 1 c skim milk, 1 c blueberries ½ oz chopped almonds	Breakfast 2 scrambled eggs with 1 oz goat cheese, 1 c steamed spinach and ½ c mushrooms 1 whole wheat English muffin 12 oz orange juice	Breakfast 1 c whole grain cereal 1 c blueberries and strawberries 1 c fat free milk
Snack 1 c soy yogurt 2 tbsp granola ¼ c raisins	Snack ¼ c dried cranberries ¼ c cashews, unsalted	Snack 1 oz cheddar cheese 10 woven wheat crackers	Snack 1 apple, medium	Snack 6 oz yogurt with fruit, low-fat	Snack 1 c sliced strawberries 6 oz fat free yogurt 1 tbsp crunchy whole grain cereal	Snack Chocolate bar
Lunch 1 vegetarian fajita: 1 whole wheat tortilla, ¼ c each sliced red & green bell peppers, onion, cooked pinto beans, corn,1 tbsp olive oil, 2 tbsp guacamole, 2 tbsp tomato salsa 1 c fruit salad	Lunch 2 c spinach (raw) 2 oz baked skinless chicken breast 2 tbsp black bean & corn salsa 2 tbsp shredded cheese 1 sesame breadstick 1 c skim milk 1 orange	Lunch Burrito: whole wheat tortilla, ½ c black beans, ¼ c salsa, chopped romaine 1 oz baked tortilla chips	Lunch 2 slices whole wheat bread 1 slice cheddar cheese 2 tbsp mayo 3 oz turkey breast 1 c strawberry	Lunch 2 c whole wheat pasta 2 oz chicken breast 1 c broccoli ½ c marinara sauce	Lunch Sandwich: 3 oz deli turkey, 2 slices whole grain bread, spinach, ¼ avocado 1 c minestrone soup 1 oz pretzels	Lunch Salad: 1 grilled chicken breast, 1 oz feta cheese, 2 c chopped lettuce, cucumber and tomato, ½ apple, 2 tbsp black olives, 2 tbsp fat free salad dressing
Snack 1 c blueberries, fresh 5 whole wheat crackers	Snack 1 medium apple 8 whole wheat crackers 2 tbsp hummus	Snack 6 oz plain low-fat yogurt blended with 1 c strawberries and 1 tbsp honey	Snack PBJ sandwich: 2 slices multi-grain bread, 4 tsp jelly, 2 tbsp peanut butter	Snack ½ c hummus with cut up vegetables	Snack 2 oz low-sodium ham with crisp rye crackers and 1 oz Swiss cheese.	Snack 6 vanilla wafers 1 c 1% milk
Dinner ½ c whole wheat pasta ½ c regular pasta ½ c tomato sauce (low sodium) 1 tbsp garlic ¼ c fresh cilantro 6 soy 'meatballs' 1 small garden Salad (mixed lettuce, tomatoes, carrots) 2 tbsp fat-free salad dressing	Dinner 4 oz broiled salmon (wild) 1 c couscous ¾ c broccoli ¾ c carrots 1 c tomato slices ½ c low sodium mozzarella	Dinner 4 oz broiled salmon topped with tsp brown sugar, chili powder 1 medium baked sweet potato 10 asparagus spears roasted with 2 tsp olive oil	Dinner 4 oz chicken breast/white meat 1½ c brown rice (cooked) 4 tbsp Thousand Island reduced calorie dressing ¼ c croutons, plain 1 small garden salad (mixed lettuce, tomatoes, carrots, onion)	Dinner 4 oz lean turkey burger on a whole grain roll with tomato, ½ oz blue cheese and a small baked potato 4 oz grapes	Dinner 4 oz flank steak grilled 1 c onions and peppers, sautéed in 1 tbsp olive oil 1 c brown rice (cooked)	Dinner 6 oz shrimp with ½ c chopped onion, celery and garlic 1 tsp olive oil, 1 can (14.5 oz) diced tomatoes, 4 tbsp black olives, ½ c chopped artichoke hearts 2 oz whole wheat pasta w/ fresh basil
Snack 1 c light vanilla soymilk 2 whole low-fat graham crackers	Snack ¼ c tuna salad Crackers	Snack 1 c tomato soup 1 whole grain roll	Snack 4 peanut butter crackers	Snack Cashew nut Fruit shake	Snack 1 c vegetable soup	Snack 1 banana Light yogurt