CHAPTER 13

DELIVERING RESEARCH DIETS

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Many investigators believe that the best way to ensure dietary control in research studies is to house the research participants and carefully control their food intake. This is an ever less feasible option because it is very expensive for the investigators and burdensome for the participants. However, research studies can be carried out quite successfully with free-living participants. For some studies, free-living participants are required to eat all (or most) meals at the feeding facility. In other studies, participants may eat all (or most) meals away from the facility.

Although some degree of control is lost when the dietary staff does not directly observe the participants' food consumption, careful attention to compliance can yield good results. An advantage of using free-living participants is that the recruitment pool can be broadened to include those bound by geography or physical limitations, the elderly, and members of religious communities.

This chapter addresses how to ''deliver'' research diets to study participants. (Techniques for managing the delivery of diets for multiple concurrent studies are discussed in Chapter 20, ''Staffing Needs for Research Diet Studies.'') Topics include: methods for serving meals eaten at feeding facilities as well as for distributing food eaten away from the study site; practical ways to maintain masked study designs; eating techniques particular to controlled diet studies; and management approaches for problem situations that could affect compliance or nutrient intake. The discussion finishes with some ''true tales'' of mishaps.

FOODSERVICE AND DISTRIBUTION TECHNIQUES

On-Site Delivery

With the ''prepared-tray'' delivery system, trays are assembled by the kitchen staff and delivered to the dining room or to residents' rooms. This delivery method is popular in small facilities because it requires less space than the ''cafeteria style'' of service. The labor involved in tray assembly is not extensive if the number of study participants is small.

In many larger units, food is delivered in a cafeteria style. Participants collect designated foods, item by item, as they move down a cafeteria line. Food items are typically weighed, but in some circumstances ad libitum (ad lib) service may be appropriate. With this method, the labor involved in tray assembly is shifted from staff members to study participants.

For both methods, a quality control checklist should be used before the tray is released to the participant. (An example of a checklist is shown in Chapter 18, ''Documentation, Record Keeping, and Recipes.'' Menus also can be used as checklists.) A foodservice supervisor or the research dietitian checks the trays to ensure that each food item is present at the appropriate calorie level and for the appropriate dietary treatment. After marking each item on the checklist against the food items on the tray, the person checking trays will easily spot missing or duplicated food items. When more than one person checks trays, it is advised that they initial the checklists to indicate responsibility for the accuracy of the corresponding tray; this allows mistakes to be traced. Empty trays should be returned to the cafeteria window and checked to be certain all foods and beverages have been completely consumed.

If there are any leftovers, the participants should be reminded of their obligation to eat all of each food item. If there are extenuating circumstances, and food or beverages are refused, the kitchen staff must weigh the returned items and enter the weight data into the computer by participant name or code number. Thus the participant's dietary record is amended by subtracting the weights of refused items from the total for that day. In rare circumstances, the food refusals may be chemically analyzed for adjusting nutrient intake records. It is important that the investigator be notified immediately when food is not consumed, especially if the volunteer is sick.

Occasionally, extra portions of food remain on the serving line after participants have eaten; this occurs when a subject drops out of the study or is absent, or when extra servings are inadvertently portioned. Although it can be tempting to keep these items. it is prudent to discard any leftover, portioned food at the end of the day. This control point prevents an unintended food item from being served on a subsequent day.

The following example demonstrates how one facility successfully combined the prepared tray and the modified cafeteria style of service to meet study needs (1–3). The goal of the study was to determine which foods, and the amount of each food, that participants would select when given several food items to choose among.

Example: The prepared-tray method of food delivery is used to deliver foods to participants for ''skeleton meals'' served at 8:00 AM, noon, and 5:00 PM in the dining room. Each participant receives a tray, marked with his or her name, containing certain food items. These items, which include milk, tossed salads, fruits, and condiments, are served to each participant at appropriate meals to supply needed nutrients and to increase palatability. On the breakfast tray, all participants are given a vitamin-mineral supplement to compensate for the unlikely possibility of nutritional deficiencies arising during the study.

In addition, participants select among six isocaloric food items offered in unlimited quantity at each meal. Food choices are placed on a large tray in the dining room to simulate a cafeteria style of foodservice. Each of the food items is preweighed into small containers, covered, and labeled for easy identification. Participants may eat as many portions of each food item as desired. The research kitchen staff brings more food items to the tray when any food choice is low. In this particular protocol, the same food items are served at each breakfast, lunch, and dinner throughout the study.

A microwave oven near the table is available to warm food. Noncaloric beverages such as black coffee, tea, decaffeinated coffee, and herbal tea are available. In this study of food selection, carbonated beverages are not allowed because they tend to induce a sensation of fullness that may prevent participants from eating all their food. Sugar-free lemonade is provided to each participant in a thermos between meals.

Participants are instructed to not share food, to report spillage, and to leave food choice containers, empty or with refusals, on their own tray. After each meal, the research kitchen staff collects the individual trays, counts and records the containers by checking the food identification number on the bottom of the containers (eg, B2 denotes a food coded 2 that is served at breakfast), and weighs any refusals. This information is entered into the daily meal record sheet, and the nutrient intake is calculated.

Off-Site Delivery

Food Safety Considerations

Food hygiene and safety are primary concerns when food is to be eaten away from the controlled environment of the study facility. It is the responsibility of the research dietitian to ensure that volunteers understand the importance of proper food handling and storage. During the screening interview, the dietitian should discuss issues of food safety, including safe temperatures for foods; special care of milk, meats, and other perishables; the amount of refrigerator and freezer space that will be needed at home to store food; and special cooking required. In some centers, issues of food storage and the facility's liability are addressed in the consent form document to ensure that participants understand the importance of proper food handling.

Containers for carrying foods home can vary depending on the length of time the subject travels before the food can be refrigerated and on the ease of transport. Paper or plastic shopping bags should have carrying handles and can be purchased in colors to differentiate among diets. This is advantageous for the participant and the foodservice worker retrieving the bags from the refrigerator. They should not be used, however, when the subject's travel time is more than

an hour. For longer travel times and large storage needs, a food cooler used with reusable ''blue ice'' packs is the better alternative. Temperature-sensitive strips are available for monitoring food temperatures (MonitorMark®, 3M Packaging System Division, St Paul, Minn). A checklist (an example is shown in Chapter 18, ''Documentation, Record Keeping, and Recipes'') should be attached to show that all items are in the cooler and to identify when each item is to be eaten. The checklist includes instructions for food preparation and a phone number to call if problems arise. It is advisable to have a 24-hour hot line for participants to call regarding food problems. After hours and on weekends, the dietitian on duty can carry a beeper to ensure that calls are received.

Weekend Meals and Take-out Meals

Many protocols allow for take-out meals for all or some of the study. Any type of research diet can be prepared for take-out, but the more rigorous research diets are the most difficult for outpatient studies and require more work for the kitchen staff and the study participant. The usual strict quality control standards must be applied, and the food must be packaged in containers that will not leak or spill. The kitchen staff needs extra time to pack food for take-out. Participants have additional responsibility because they must heat meals and may be required to consume them at the specified times. Also, participants have the added temptation to consume unauthorized foods and beverages when away from the study facility.

Consumption of All Foods Away from the Feeding Facility

Delivering a Week's Food Supply

If subjects are particularly hard to recruit for a given study, this plan may be given as an option to individuals who are otherwise discouraged from participating. This delivery plan is practical for use in studies of homebound or frail individuals as well as participants who, because of geography or other daily commitments, are inconvenienced by the daily or twice-weekly visits to the feeding facility.

A drawback to this plan is the lack of frequent contact between participants and investigators or other staff members. (However, meetings with participants can be scheduled for purposes other than picking up food.) Another drawback is the effect on participant morale if some participants are perceived to have special privileges. It must be stressed that although this system of food delivery is appropriate for many studies of total diet composition (ie, macronutrient studies), it may not be appropriate for precise nutrient balance studies.

This plan is not so radical a departure from on-site feeding of free-living participants as it may seem. Feeding arrangements for free-living participants are structured in various ways, wherein volunteers may come in daily or Monday through Friday, consume one or more meals at the facility, and take home the remainder of the day's meals or snacks, as allowed. Additional data and sample collections (24-hour urine and stool specimens, daily weights and blood pressures) may make daily visits necessary. Other visit schedules may entail two or three trips to the research facility each week. Sometimes the entire week's food is packaged for home consumption and is disbursed to the participant at one weekly visit.

The monitoring of a volunteer's progress on a study is a crucial part of the success of any research study. However, daily visits sometimes focus on obtaining food at the expense of time for visiting with study personnel. If the volunteer designates one day for pickup of the week's food, other visits could be set aside for reviewing any compliance questions or for reviewing lab values. Because the purpose of such visits focuses on an exchange of information between the participant and the study's professional staff, this could be a more ''caring'' approach to a volunteer's participation.

The logistics of the food delivery system depend on the type of food offered. Typically, most food items (and particularly those food items needing the most precise measurements) are portioned at the feeding facility. The main dishes, foods that are difficult to portion, and foods that contain key nutrients for the study should be weighed precisely. Preweighed food items or entire meals can be sent home frozen, with instructions for cooking. Some items can be sent home in bulk. Directions for measuring these foods in household units can be provided, and volunteers can portion many items, including lettuce, milk, rice, and bread.

The alternative to daily visits to the test facility is beneficial in many ways. Food preparation is less dictated by a daily or a three times per week food pickup, and food preparation and staffing patterns can be more flexible. Volunteers can pick up food with one trip to the feeding facility and take the food directly home, thereby eliminating the possible inadequacy of refrigeration of food at the participant's job site, for example. Sending bulk food items reduces leakage and spillage that is common when items are individually portioned. Additionally, this lightens the workload associated with portioning foods; the kitchen staff can spend more time with the participants, thus adding an extra dimension to their jobs.

It is important to teach the participants appropriate techniques for measuring and preparing food items. These instructions are commonly included in an orientation workshop that is held during the first week of the study. It should also be mandatory for each volunteer to come to the facility every day of the first week of the research study to verify the appropriate energy level for weight stabilization as well as to review all food preparation techniques.

Courier Service

A courier service can be effectively used to deliver research diets to home-based participants. Dietary staff packages food items in three boxes for each study participant: (1) dry

goods, (2) refrigerated goods (4°C) (bread, fruit, vegetables, dairy, etc), and (3) frozen goods (–20°C). All boxes are labeled with the participant's full name, address, and telephone number (conveniently printed on a sticker) together with a clearly visible courier delivery number. Boxes should also be labeled (eg, A, B, and C), and the courier should know the number of boxes to deliver to each participant. To avoid potential confusion, the number of boxes should be standard for all participants, if possible, regardless of caloric intake.

The courier should be instructed on the most convenient time for participants to receive delivery (nothing annoys participants more than being roused from bed to accept a delivery, and nothing frustrates the courier more than to be refused admission to an apartment because the occupant is not at home). A courier service once trained should be retained for further studies. The courier service can also be used for the retrieval of fecal and urine samples.

The courier system of food delivery has appeal in studies when special groups of participants are recruited; for example, patients with specific diseases or specific genetic characteristics. These individuals may be working full time and unable to visit a feeding facility on a daily basis. When the courier system is used, it is advisable that the participant always be in possession of an extra two days' supply of food to be kept for emergencies such as snow or floods that may prevent the courier from getting through.

Vending Machine Feeding Systems

Vending machines have been successfully used in studies of food intake regulation (1–3).

Example: Ten isocaloric food choices were made available to study participants through refrigerated vending machines. Food items were prepared, portioned, and wrapped with plastic wrap, then stocked into the individual slots of a vending machine. Items were restocked at least twice a day by the research kitchen staff so that items were consistently available to participants. Participants obtained any one of the food choices by entering their code number on the keypad attached to the machine. A microcomputer connected to the vending machine recorded the identity of the participant, the item of food removed, and the time that food was obtained.

Participants immediately consumed the whole portion upon its removal from the vending machine. If they could not finish the whole food portion at that time, they reported this to the staff. Participants had access to the vending machine 24 hours a day.

Considerations in Designing Vending Machine Feeding Systems

- Select food items tailored to the study population and the study hypothesis.
- Offer a variety of selections. Include at each meal food items that can be heated as well as those that can be eaten cold and provide microwave ovens and ice machines as needed.
- Assess the availability of the food items to be used. Manufacturers change their recipes and packaging sizes, so it is advisable to check the projected availability of the product.
- Consider each food choice with respect to the physical facility, operating system, staffing pattern, and storage space requirements. Making food items from original recipes is a good option if staffing for food preparation is adequate but storage space is limited. Otherwise, commercially prepared and packaged food items are recommended. (Note that composition of foods must be verified.)
- Select food items that can be weighed and portioned in advance and stored in a freezer or refrigerator. This saves time and avoids last-minute rushes that can cause errors.
- Devise recipes that can be produced in large quantity, then measure them into smaller portions.
- Identify packaging that is suitable for each food item (heat-sealable containers can be useful). Avoid using poor quality paper containers. They tend to absorb liquid or fat and can also affect the appearance of foods.
- Avoid foods that change in color or texture after being refrigerated. For foods that require warming, avoid items that develop an odd texture when heated in a microwave oven.
- Avoid food items with easily separated components; for example, a bagel and cream cheese. Participants may remove the cream cheese, thus altering the intended calorie level and nutrient content of the meal.

Unit Foods

Unit foods are food items such as muffins and cookies that mimic the nutrient content of a dietary treatment. Unit foods are typically used to adjust calories in a research study. For example, in a long-term feeding study examining the effect of a low-fat diet (25% fat, 15% protein, 60% carbohydrate) on serum lipoproteins, a muffin was designed to approximate this particular diet composition. When calories were needed, this muffin, portioned into 100-calorie units, was used. Examples of recipes for unit food items are given in Chapter 18, ''Documentation, Record Keeping, and Recipes.''

Masking or Blinding Dietary Treatments

General Considerations

The technique of *masking* (sometimes called *blinding*) is frequently used in human research studies. The goal of masking is to prevent bias on the part of study participants or the data collector (the investigator measuring the clinical or cognitive parameter of interest). If the identity of the dietary treatment is withheld from both the participant and the data collector, the study is considered ''double-blinded.'' A study is

''single-blinded'' when the identity of the treatment is withheld from either the participant or the data collector, but not both. In single-blinded studies, it is typically the participant rather than the data collector who is blinded, but occasionally the reverse is true. For example, study participants taking fish oil supplements may know whether they are receiving active treatment because of the supplements' smell and taste, but the treatment could be blinded to the data collector.

Masking is a valuable tool that adds credibility to diet studies, and it is a desirable study trait to employ when possible. Masking of participants prevents variation in compliance based on knowledge of the treatment. When participants provide data (eg, questionnaires evaluating emotional or cognitive parameters), masking prevents bias in responses. Masking of the data collector prevents bias in measurements.

Unfortunately, some experimental variables cannot readily be masked because of their taste (artificial sweeteners), smell (fish oils, thiamin), or texture (some dietary fibers). Others cannot be masked because of physiological effects; for example, the altered mental state produced by alcohol, the distinctive yellow color of urine after riboflavin ingestion, and some orange skin discoloration associated with long-term use of beta-carotene supplements.

Ethical issues to consider in masking subjects to treatments include the subject's ''right to know'' and safeguarding the well-being of the subject. Prior to committing to a research study, potential participants are typically informed of the study protocol, including dietary treatments, both verbally (at an information meeting) and in writing (as part of the informed consent document). At this time participants are also told whether the treatments are to be masked. Most participants accept this arrangement as fair, especially in conjunction with a crossover or Latin square design in which every participant cycles through every treatment.

Some investigators believe that the participant always has the right to know which treatment he or she is receiving and will tell the participant if asked. Others do not share this concern. If participants have been adequately informed about the diets and the masking procedures prior to the study, they rarely ask about the treatment codes. Dietitians and investigators need to share an understanding about when and how to break the code to participants. In addition, it is prudent, and in some studies essential, to establish procedures for monitoring treatment effects to ensure safety of the study participants. The criteria by which an individual investigator or a protocol oversight committee might ''unmask'' the study to ensure safety also should be developed before the study begins.

Practical Approaches

Masking is difficult in dietary fiber studies and in studies comparing the effects of different protein sources (eg, dairy vs red meat). In fiber studies, purified fibers or fiber supplements may be masked to participants by incorporating the fiber into standard foods such as breakfast cereals; the required technology usually necessitates help from industrial collaborators. Similarly, in highly flavored dishes such as chili or burgers, it is possible to use different protein sources (eg, vegetable proteins) in exchange for animal protein. Sometimes masking is not possible because the nature of the fiber or protein is to be assessed in terms of whole foods. In these cases, control foods should be chosen for similar macronutrient content and dietary function (eg, milk vs milk analogues) in the diet in order not to distort the meal pattern or alter the palatability or acceptability of the diet.

To mask dietary treatments in fat substitution studies, it is advisable to avoid food items with obvious changes in ''mouth feel.'' For example, the flavor and mouth feel of butter as opposed to margarine or whole milk compared with skim milk are likely to be detected by participants, whereas these differences are less easily detected in baked products, particularly when the product is highly flavored (eg, through use of flavoring extracts).

Certain foods are particularly useful vehicles for adding fats or oils without compromising taste, texture, or masking. These include mashed potatoes; tuna salad; chicken salad; salad dressings; meatloaf; chili; spaghetti sauce; other mixed casseroles and rice dishes; and baked products such as muffins, quick breads, and cookies. (See also Chapter 18, ''Documentation, Record Keeping, and Recipes.'') Preparing portions in individual baking tins allows for participant-specific addition of ingredients. This strategy for individualization also works well in the case of preparation of individual pizzas, which can be baked with varying amounts of cheeses and pizza sauces prepared with differing amounts of oils or hard fats.

Coding diets by color, number, or letter is an effective way to mask dietary treatments. With this system, each dietary treatment is assigned a different code and references to specific diets are by code rather than by description of the dietary treatment. The topic of masking should be discussed with the foodservice workers. Like dietitians, they are not likely to be masked to dietary treatments, and they should be cautioned not to interpret codes for study participants.

In the following example, color coding is used in conjunction with the cafeteria style approach to foodservice. Note that although the calorie levels and gram amounts of each food item are displayed on the participants' menus in this example, participants are blinded to this information in many studies. (See the discussion of bar codes in Chapter 12, ''Producing Research Diets.'')

Example: As study participants enter the cafeteria line they pick up their menus from assigned slots in an accordion folder. This menu is used by the participants to identify food items to gather from the cafeteria line. The menu is printed on green or yellow paper with the color green corresponding to a diet high in monounsaturated fats and the color yellow to a diet high in saturated fats. Food items on the cafeteria line are also color coded, each bearing a green or yellow label. (See Chapter 12, ''Producing Research Diets.'') This

label helps the participants to locate their food items on the serving line and facilitates the dietitian in checking their trays.

Exhibit 13-1 shows a ''master menu'' from which participants' menus are printed onto colored paper. As a precautionary measure, the word *green* is printed in the upper left corner of the menu. This ensures that the monounsaturated diets corresponding to ''green'' are not mistakenly copied onto the yellow paper. It should be noted that use of color codes is problematic if colors are similar or if any staff member or study participant is color blind.

Another caveat about masking treatments is that the description of food items should be limited on participants' menus. Exhibit 13-2 is a kitchen menu or production sheet (refer to Chapter 18, ''Documentation, Record Keeping, and Recipes'') used to portion food items by calorie levels. The detailed description of food items that appear on the kitchen menu is not present on the participants' menus. In contrast to the dietary staff, the participants only need to know which foods to gather; the fat content of the items is masked.

Thus, in this example, a salad dressing is listed as a single item on the participants' menu, whereas the two fat sources that are added directly to the salad dressing are detailed on the kitchen menu. On the participants' menu the two asterisks after ''salad dressing'' indicate that the code 31 dressing was modified by the addition of two ingredients. Notice also that the kitchen menu bears not only the color code and full description of menu items but, unlike the participants' menus, also bears the identification of the dietary treatment (monounsaturated).

In the study from which this example was drawn, the dietary treatments were masked to both the participants and the data collector. The primary investigator, the study coordinator, and the dietary staff were not masked; their knowledge of the treatments was necessary to ensure accurate delivery of test meals. Data were sent directly from the analytical laboratory (the data collector) to an independent statistician without passing through the primary investigator. The statistician, who had assigned the participant codes during the design of the study, received the data and conducted statistical analyses as designated in the study protocol. This system ensured that the resulting data could not be influenced by potentially biased parties (the data collector to whom treatments were masked and the primary investigator to whom treatments were not masked).

Eating Techniques

Thorough instructions detailing how study participants should consume their food are instrumental to the accuracy of tightly controlled feeding studies. Verbal instructions given by the dietitian or investigator enable the rationale and techniques to be explained to and discussed with the participant. This also affords staff the opportunity to assess participant comprehension and potential compliance. Written instructions should then be given to the participant to keep.

Most controlled feeding studies require participants to eat ''all'' of each food item given to them, but ''all'' can imply different degrees of thoroughness depending on the nutrients under investigation and the outcome variables to be assessed. The word can also mean different things to different participants.

The *scrape and wash technique* is used in metabolic balance studies in which a high degree of control is required, such as vitamin, mineral, and nitrogen balance studies. Although this eating technique breaks the rules for good table manners, it is employed to ensure that participants consume every morsel of food and liquid they are served. The following specific techniques are suggested:

- Participants should use a small, five-inch ''icing spatula'' (eg, Revere® or Corning®) to scrape up any particles of food remaining on the plate or dish, and eat the scrapings.
- Participants should save a piece of bread and use it to absorb any liquid remaining on the serving plate or dishes, and eat the bread.
- Participants should save a portion of allotted drinking water (distilled) and use it to rinse all beverage glasses, and drink it.
- Staff should use weighed salt, pepper, pectin, etc, very carefully so as not to lose a grain. If it is to be consumed in total, provide the participant with a cotton tipped swab to clean out the shaker at the last meal of the day or have it added to the food directly by the technician responsible for distributing the research diet. (When mineral intake is critical, the minerals, such as NaCl or $KHCO_3$, may be mixed in a weighed amount of deionized water at a specific concentration and distributed on the meal tray.)

Some studies are well-controlled but require less stringent eating techniques. Examples follow:

- A protocol to study the effect of the type or amount of dietary fat may not require the scrape and wash technique because trace amounts of fat, rather than gram amounts, are left behind on the plate.
- If a participant left the crust of a meal's bread uneaten, he or she would be asked to eat it to comply with caloric intake requirements; however, a normal scattering of bread crumbs might be considered inconsequential.
- Small quantities of such foods as carrots or celery might be provided as ''free items'' in a lipid study because of their low caloric content and lack of fat; of course, this would not be appropriate in studies of fiber or carotenoids.
- Because the ideal quantity of lettuce for consuming a given amount of salad dressing is a matter of individual preference, participants might be given a generous serving of lettuce to ensure that all of the salad dressing is consumed. In many lipid studies, uneaten lettuce (without dressing) would not be challenged, because lettuce is not supplying critical nutrients, including calories. However, participants would be asked to eat all visible traces of salad dressing and margarine by picking up traces of these fat

EXHIBIT 13-1

Master Menu for a Participant Menu

This master menu is from a study using color coding to mask dietary treatments. The master menu is copied onto green paper and distributed to all participants eating the diet coded by the color green. As part of the masking procedure, this menu describes foods generically. The participants collect preweighed food items at their assigned calorie levels according to the food items designated on the menu. The calorie levels displayed on the menu typically include at least one level above and below the expected use (here, from 1,400 kcal to 4,400 kcal). The amount of each food item is shown in the body of the exhibit for incremental calorie levels. Amounts are in grams unless otherwise indicated. Amounts of milk are number of cartons plus number of grams.

Name		**DIET = 07 GREEN**								**Date:**				
SECTION	CODE	FOOD DESCRIPTION	1,400	1,600	1,800	2,000	2,200	2,400	2,800	3,200	3,600	4,000	4,400	EXTRAS:
		BREAKFAST												
1100	503	ORANGE JUICE	96	109	123	137	150	164	191	219	246	273	301	CUCUMBERS:
7	7064	SAUSAGE	16	18	20	23	25	27	32	36	41	45	50	CARROTS:
1100	242	BLUEBERRY MUFFIN	54	61	69	77	84	92	107	123	138	153	169	CELERY:
100	1149.1	JELLY. PKT	1 pkt	1 pkt	1 pkt	1 pkt	1 pkt	1 pkt	2 pkt	2 pkt	2 pkt	3 pkt	3 pkt	ONION PACKETS:
1100	34	SPREAD	8.9	10.1	11.4	12.7	13.9	15.2	17.7	20.3	22.8	25.3	27.9	PICKLE RELISH:
1	1079	MILK	1 + 0	1 + 26	1 + 59	1 + 92	1 + 125	1 + 158	2 + 0	2 + 53	2 + 118	2 + 184	3 + 0	KETCHUP:
		LUNCH												
10	1013	HAM	42	48	54	60	66	72	84	96	108	120	132	*Record extra amounts eaten
1100	104	RYE BREAD	23	27	30	33	37	40	47	53	60	67	73	
		MUSTARD, 2												
11	1125	LETTUCE	12	13	15	17	18	20	23	27	30	33	37	
11	1152	TOMATOES	21	24	27	30	33	36	42	48	54	60	66	
1100	542	OATMEAL BAR	35	40	45	50	55	60	70	80	90	100	110	
		DINNER												
5	5064	CHICKEN BREAST	70	80	90	100	110	120	140	160	180	200	220	
1100	629	CHICKEN GRAVY	9	11	12	13	15	16	19	21	24	27	29	
11	1167	BAKED POTATOES	117	133	150	167	183	200	233	267	300	333	367	
11	11095	BROCCOLI	28	32	36	40	44	48	56	64	72	80	88	
11	1125	LETTUCE	26	29	33	37	40	44	51	59	66	73	81	
11	1152	TOMATOES	21	24	27	30	33	36	42	48	54	60	66	
1	1125	EGG YOLK	2	3	3	3	4	4	5	5	6	7	7	
1100	31	SALAD DRESSING**	6.5	7.5	8.4	9.3	10.3	11.2	13.1	14.9	16.8	18.7	20.5	
1100	100	WHEAT BREAD	30	35	39	43	48	52	61	69	78	87	95	
1100	34	SPREAD	7.0	8.0	9.0	10.0	11.0	12.0	14.0	16.0	18.0	20.0	22.0	
1	1079	MILK	0 + 115	0 + 131	0 + 148	0 + 164	0 + 180	0 + 197	1 + 0	1 + 26	1 + 59	1 + 92	1 + 125	
300	2230	EXTRAS:												
9	9003	APPLE WITH SKIN	85	95	110	120	130	145	165	190	215	240	265	
100	2230	SUGAR, PKT	2	2	2	3	3	3	4	4	5	5	6	

Source: "Well-Controlled Diet Studies in Humans, A Practical Guide to Design and Management", American Dietetic Association, © 1999.

EXHIBIT 13-2

Master Menu for a Kitchen Menu

This master menu is an example of a kitchen menu (or production sheet) that is used by the kitchen staff to portion individual food items for the calorie levels designated. The calorie levels displayed on the menu typically include at least one level above and below the expected use (here, from 1,400 kcal to 4,400 kcal). Note that in contrast to the participants' menu, where the goal is to mask dietary treatments, the kitchen menu displays the identification of the dietary treatment and the full description of food items (eg saturated margarine vs spread). The full description of the salad dressing is also displayed.

MONOUNSAT		**DIET = 07 GREEN ENSUS**								**Date:**				
SECTION	CODE	FOOD DESCRIPTION	1,400	1,600	1,800	2,000	2,200	2,400	2,800	3,200	3,600	4,000	4,400	EXTRAS:
		BREAKFAST												
1100	503	ORANGE JUICE, W/CALCIUM	96	109	123	137	150	164	191	219	246	273	301	CUCUMBERS:
7	7064	SAUSAGE PORK LINK, CKD	16	18	20	23	25	27	32	36	41	45	50	CARROTS:
1100	242	BLUEBERRY MUFFIN. W/CANOLA OIL (CODE 42)	54	61	69	77	84	92	107	123	138	153	169	CELERY:
100	1149.1	JELLY. PKT	1 pkt	1 pkt	1 pkt	1 pkt	1 pkt	1 pkt	2 pkt	2 pkt	2 pkt	3 pkt	3 pkt	ONION PACKETS:
1100	34	MARGARINE, SATURATED	8.9	10.1	11.4	12.7	13.9	15.2	17.7	20.3	22.8	25.3	27.9	PICKLE RELISH:
1	1079	MILK, 2%	1 + 0	1 + 26	1 + 59	1 + 92	1 + 125	1 + 158	2 + 0	2 + 53	2 + 118	2 + 184	3 + 0	KETCHUP:
		LUNCH												
10	10135	HAM	42	48	54	60	66	72	84	96	108	120	132	
1100	104	RYE BREAD	23	27	30	33	37	40	47	53	60	67	73	
		MUSTARD, 2 PACKETS (OPTIONAL)												
11	11252	LETTUCE	12	13	15	17	18	20	23	27	30	33	37	
11	11529	TOMATOES	21	24	27	30	33	36	42	48	54	60	66	
1100	542	OATMEAL BAR COOKIES W/CANOLA OIL (CODE 42)	35	40	45	50	55	60	70	80	90	100	110	

Source: "Well-Controlled Diet Studies in Humans, A Practical Guide to Design and Management", American Dietetic Association, © 1999.

		DINNER											
5	5064	CHICKEN BREAST	70	80	90	100	110	120	140	160	180	200	220	
1100	629	CHICKEN GRAVY + FAT. W/MOD OLEIC MAYO (CODE 29)	9	11	12	13	15	16	19	21	24	27	29	
11	11674	BAKED POTATOES WITH SKINS	117	133	150	167	183	200	233	267	300	333	367	
11	11095	BROCCOLI, SPEARS CKD	28	32	36	40	44	48	56	64	72	80	88	
11	11252	LETTUCE	26	29	33	37	40	44	51	59	66	73	81	
11	11529	TOMATOES	21	24	27	30	33	36	42	48	54	60	66	
1	1125	EGG YOLK	2	3	3	3	4	4	5	5	6	7	7	
1100	31	SALAD DRESSING, HIGH OLEIC POURABLE	6.5	7.5	8.4	9.3	10.3	11.2	13.1	14.9	16.8	18.7	20.5	
1100	29	MAYONNAISE, MOD OLEIC (ADD TO DRESSING)	4.7	5.3	6.0	6.7	7.3	8.0	9.3	10.7	12.0	13.3	14.7	ADD MAYO TO DRESSING
110041		COCONUT OIL (ADD TO DRESSING)	2.8	3.2	3.6	4.0	4.4	4.8	5.6	6.4	7.2	8.0	8.8	ADD OIL TO DRESSING
1100	100	CRACKED WHEAT BREAD	30	35	39	43	48	52	61	69	78	87	95	
1100	34	MARGARINE, SATURATED	7.0	8.0	9.0	10.0	11.0	12.0	14.0	16.0	18.0	20.0	22.0	
1	1079	MILK, 2%	0 + 115	0 + 131	0 + 148	0 + 164	0 + 180	0 + 197	1 + 0	1 + 26	1 + 59	1 + 92	1 + 125	
100	2230	EXTRAS:												
9	9003	APPLE WITH SKIN	85	95	110	120	130	145	165	190	215	240	265	
100	2230	SUGAR, PKT	2	2	2	3	3	3	4	4	5	5	6	

Source: "Well-Controlled Diet Studies in Humans, A Practical Guide to Design and Management", American Dietetic Association, © 1999.

sources with bread. The use of distilled water would not be necessary nor would a water allotment be given.
- Coffee, tea, and diet beverages might be allowed free choice, within a given limit, as well as selected spices, including salt. Caution should be used that the spices allowed do not influence the outcome variables to be measured.

In studies of free-living participants, it is prudent to ensure that the foods that are vehicles for critical nutrients are wholly or primarily incorporated into those meals that are eaten at the facility. Most facilities discourage participants from taking out foods that are intended for consumption at the facility. When participants are allowed to take home foods ordinarily eaten at the facility, they may be required to record the items taken out (eg, by listing the items on the back of the menu). Participants should understand that this is not a simple issue of trust between the participant and the investigator but rather is one aspect by which the scientific community will assess the quality of the study.

Regardless of which eating technique is used in a study, it is important that the technique is applied consistently across all treatments, all dietary periods, and all volunteers. Participants' attention to the details of the eating technique can lapse during the course of the study. The research dietitian whose approach focuses on encouraging and reminding participants about eating techniques, rather than monitoring and scolding, is likely to have better cooperation.

Common Problems of Study Participants Eating Research Diets

Too Full, Too Hungry

Feeling either too full or too hungry is a frequent complaint of study participants, even though research diets usually are designed to maintain body weight. These symptoms are most likely to occur during the first days of the study—a time of adjustment both psychologically and physiologically. For some individuals, a study diet consisting of three meals a day may replace a habitual diet that was more calorically dense (fewer fruits and vegetables; more fats or candy). This change is likely to cause a too-full feeling. However, a premature decrease in the participant's energy intake may cause subsequent hunger and weight loss. On the other hand, if the distribution of calories among meals is markedly different from a participant's habitual diet, the participant may experience hunger between light and heavy meals.

A bloated or too-full feeling without weight gain can often be solved by allowing foods from heavier meals to be eaten at other times during the day. Similarly, the problem of hunger without weight loss is commonly solved by providing snacks between meals and by redistributing foods among meals. Adding foods with bulk may also help alleviate the feeling of hunger. The research dietitian should be vigilant to follow up on complaints of hunger. Not only is this unpleasant for the participant, but a hungry participant will be tempted to eat unauthorized foods. If a participant is losing weight and complains of hunger, the dietitian and study investigator should consider increasing the calorie level, even if the weight loss does not meet the criteria for a calorie increase. (See Chapter 17, ''Energy Needs and Weight Maintenance in Controlled Diet Studies,'' for information on setting calorie levels.)

Depending on the diet composition and the study objective, these side effects may be inevitable. For example, some types of dietary fiber may cause discomfort from a too-full feeling, whereas a study designed to produce weight loss may cause hunger. During the planning phase of the protocol, criteria should be established for changing calorie levels, allowing food to be eaten between meal times, and acceptable use of medications for an upset stomach or constipation. During the orientation or screening interview, participants should be told that feelings of hunger or fullness may occur until diet adjustments have been made. This will ease anxiety of participants and reassure them that what they are experiencing is normal.

Food Refusal

Reasons that volunteers in a research study refuse to consume food are numerous. They include illness, food allergies, inadequate preparation of meals, poor meal quality, monotony, and dislike. In any event, incidents of food omission should be communicated to the investigator, and a decision should be made as to how to replace the food or whether to dismiss the participant from the study.

Food refusals should always be documented. The study records should be amended with an account of what food was not consumed, the weight of the refused food, and a recalculation of the day's intake. The participant's explanation for refusal is useful for documenting volunteer compliance, for assessing risk management issues in the case of food allergies or foodborne illnesses, and as a rationale for improving food quality or cooking procedures.

Displeasure with Calorie Changes

Weight gain and loss during nutrition research studies are variables that must be recognized either as needing to be controlled or of no consequence, depending on the objective of the study. Issues concerning body weight must be addressed with study participants during the recruitment phase. Unfortunately, many potential volunteers will think that a ''diet study'' is actually a ''weight-loss study.'' If a study requires weight maintenance and a volunteer is expecting to lose weight while in the study, this can be distressing, particularly if the calorie level is increased because of weight loss. During the recruitment as well as the first few days of a study, the body weight range acceptable for each volunteer

should be discussed privately with each participant. In studies in which weight is controlled by adding or deleting specific food items, choices should be offered to the participants so that they feel that they have a say in the matter. If a study is designed deliberately to provide excess calories, this should be clearly stated in the study protocol, the consent form, and verbally at the initial interview. Additionally, for participants who gain weight, provision should be made to offer optional dietary counseling to lose weight once the study is completed.

When a participant's calorie intake must be changed because of a change in body weight, it is advisable for the investigator or research dietitian to discuss the change with the participant in advance. Some participants will welcome the change because they felt the amount of food was too much or too little. However, it can be upsetting for a participant to unexpectedly find a change (particularly an increase) in his or her calorie level, especially if coupled with other life events that the participant cannot control. With an explanation of the anticipated change and a day's advance notice, most participants accept the change easily.

Calorie levels of diets can be masked to participants. (See the use of bar code labels for food items discussed in Chapter 12, ''Producing Research Diets.'') Blinding enables the investigator to alter a participant's energy intake without alienating the study participant. Although a participant may suspect that he or she is getting slightly more or less quantity of food items, the change may go unnoticed. Certainly the masked approach is more subtle than announcing the change. If calorie levels are to be masked, this, like other aspects of the diet, must be understood by participants before they commit to the study.

Take-out Meals

Requests for taking meals out—for work or weekends or beyond what the protocol permits—occur frequently. It is difficult to run a long-term study without allowing participants to occasionally take their food out on their request. If participants do not have this flexibility, there are likely to be problems in retention and future recruitment. Efforts should be made to accommodate the participants by packing some of their meals to take out. However, this step must be well-planned and managed; if not, control will be lost as an increasing number of meals are eaten away from the facility. If some participants are allowed to take meals out more often than others, this disparity will likely be noticed by participants and considered unfair.

When take-out is authorized, advanced notice should be given to the kitchen staff to allow for adequate time to pack meals; otherwise, transfer mistakes are likely to occur. Before permission is granted to the participant to take any meal out, certain assurances regarding the participant's eating techniques and habits should be obtained. Issues to be reviewed with the participant include compliance, food spillage, food safety, and appropriate reheating of food.

Emergency Meals

It is necessary to have contingency plans for keeping free-living participants on dietary treatments when it is not feasible for them to receive their meals in the usual way (eg, at a feeding facility or by courier). These events may include family emergencies, inclement weather (notably snow), lack of transportation, or errors of food omission. Providing one or two full days' meals for home storage can alleviate this potential break in a study protocol. Emergency meals are typically composed of foods that can be stored for a number of weeks without deterioration. Typically these include canned goods, frozen dinners, dry foods, and shelf-stable milk. In rare situations (death in the family, testing procedure conducted away from the facility), overnight air express may be the best means of providing study foods.

The research dietitian should ensure that each participant will have adequate storage space for frozen goods. Perishable items such as fresh fruits should not be included but may be listed on the emergency meal menu for optional use if they are available. If perishable foods are allowed, those approved foods should be listed along with the amounts to consume (in household measures). A research dietitian should contact participants to advise them of suitable substitutions.

Because emergency meals are tailored to the participant's dietary treatment, these meals must be distributed at the beginning of each treatment period. It is prudent to collect any unused emergency meals at the end of the dietary period. Otherwise, these meals may accumulate as participants switch over to different dietary treatments, and there is the potential for meals from different treatment phases to be confused with one another.

Studies Spanning Holidays

Studies are typically scheduled to avoid major holidays, particularly those associated with consumption of special foods and alcoholic beverages. When this is not possible, advance planning for these days is necessary. This may mean advance notice at the initial interview and again before the holiday that exceptions will not be made. Holidays are generally celebrated in dining facilities with appropriate decorations or party favors.

Commonly, some exceptions are made to the normal feeding procedure. For example, at Thanksgiving, participants may be allowed to eat specific foods at a traditional family dinner, whereas foods critical to the diet are provided from the feeding facility. In other situations, participants may be given a free meal on a holiday. Some investigators require that food records be maintained for any free-choice meal.

Holiday parties can be difficult for study participants, because celebrations are typically centered around food and, perhaps, alcohol. It is helpful if participants take approved snacks (those provided with their study diets) with them to

parties. If a holiday such as New Year's Eve falls in the early days of a study period, one or two alcoholic drinks may not compromise the study results. However, as with any exception, it is important to give detailed instructions to the participant concerning what is and is not acceptable, and to record deviations from protocol in the participant's dietary record.

Illnesses

The study investigator must determine, on a case-by-case basis, whether a participant's illness during the study will compromise the study results. In some cases, a study physician or medical expert should be consulted before this determination is made. Sometimes participants are dismissed from studies because of unanticipated illnesses; more commonly, the illness (a cold or the flu) does not require the participant's dismissal. However, a contagious illness can compromise a study if it affects a large proportion of the participants. For this reason, some study investigators ask that participants take flu shots prior to the study. (The timing of the shots may be important.) Additionally, it is useful to provide a setting at the feeding facility where participants who have a contagious illness can eat away from other participants. Frequently, meals are sent home to participants during brief illnesses.

Participants should be cautioned not to force themselves to eat if they feel nauseated. If, because of illness, a research participant cannot consume all or part of a day's food, this must be noted in the participant's diet record. In some situations the illness may occur in a phase of the diet study where the investigator can ''forgive'' noncompliance that occurs because of illness, and the individual's participation may still be viable. Participants should discuss use of medication for an illness with the study investigator. All medications should be approved prior to use and documented in the study record as to type, dosage, and length of treatment.

Adverse Food Reactions

Adverse food reaction is the general term referring to both food intolerances (nonimmunologic reactions to foods) and food allergies (an abnormal immunologic reaction). Food intolerances are far more common in the general population than are food allergies, although many people believe that they are allergic to certain foods. Food intolerance reactions can be caused by enzyme deficiencies, toxins, infectious organisms, accidental contaminants, or pharmacologic substances. Strong intolerances also may be rooted in psychologically based aversions.

The symptoms for allergic and nonallergic reactions are not distinguishable. These reactions may be manifested as systemic (eg, headaches, irritability), gastrointestinal (eg, nausea, abdominal pain, vomiting, diarrhea, flatulence), respiratory (eg, rhinitis, asthma), or dermatologic symptoms (eg, hives, eczema) (4–6).

Food Allergies

Food allergies are more prevalent in children than in adults. Up to 4% of children younger than 6 years of age have food allergies (4), whereas 1% to 2% percent of adults do (5). Food allergies are more common in children with asthma and in atopic adults. Most allergic reactions are caused by relatively few foods: cow's milk, eggs, fish, shellfish, soybeans, tree nuts, and peanuts (4, 5). People who are sensitive to certain nonfood allergens are more likely to be reactive to certain foods. For example, those who are sensitive to ragweed pollen as an antigen commonly react to bananas and melons (watermelon, cantaloupe, honeydew), and those sensitive to birch pollen are more likely to react to apple, carrot, and hazelnut (4, 5).

Food Intolerances

Food intolerances are often caused by enzyme deficiencies and by sensitivity to agents used as preservatives, flavors, or color enhancers such as sulfites, nitrite and nitrate, monosodium glutamate, and tartrazine yellow (6). However the single most common food intolerance encountered in human feeding studies is lactose maldigestion or lactose intolerance. Dietitians planning studies conducted primarily among groups with a high prevalence of lactose maldigestion such as African Americans or Asians should consider menus that minimize the use of milk products. However, lactose maldigestion is frequently encountered in other populations, and all potential study participants should be queried about their tolerance for milk products.

For most people with lactose maldigestion, lactase is effective in relieving symptoms of gas, bloating, and diarrhea. Lactase is sold in tablet form (eg, Lactaid®, Lactaid Inc, Pleasantville, NJ, or Dairy Ease®, Sterling Winthrop Inc, New York, NY) to be taken with milk or other dairy products. Lactase is also sold in a liquid form designed to be added directly to milk. In feeding facilities this is less convenient, because for best results the lactase must act on milk lactose for 24 hours. Lactaid milk is now available in 1%, 2%, and 4% fat from the manufacturer in quarts and half-pints.

Individuals vary in the amount of milk and milk products that they can tolerate. Additionally, milk products such as yogurt with live cultures may not produce problems in participants who have lactose maldigestion. However, aversions to milk are not always related to adverse food reactions. Some participants are accustomed to drinking less milk than is typically served in diet studies; others simply dislike the taste or texture of milk. Depending on the goal of the study, it may be possible to substitute other foods for milk. (See the discussion of substitutions in Chapter 11, ''Designing Research Diets.'')

EXHIBIT 13-3

Sources of Information about Adverse Food Reactions

American Academy of Allergy, Asthma, and Immunology
611 East Wells Street
Milwaukee, WI 53202
800-882-2762
http://www.aaaai.org

Asthma and Allergy Foundation of America
1125 15th Street NW, Suite 502
Washington, DC 20005
800-727-8462
http://www.aafa.org

The American Dietetic Association
216 West Jackson Blvd
Suite 800
Chicago, IL 60606-6995
800-877-1600 (for dietitians)
http://www.eatright.org

The Food Allergy Network
10400 Eaton Place, Suite 107
Fairfax, VA 22030
800-929-4040
http://www.foodallergy.org

American College of Allergy, Asthma, and Immunology
85 West Algonquin Road, Suite 550
Arlington Heights, IL 60005
800-842-7777
http://allergy.mcg.edu

National Eczema Association
1221 SW Yamhill, Suite 303
Portland, OR 97205
800-818-7546
http://www.eczema-assn.org

National Institutes of Health
Food allergy
Information Center
National Institute of Allergy and Infectious Disease
Building 31, Room 7A50
Bethesda, MD 20892-2520
301-496-5717
http://www.niaid.nih.gov

Lactose intolerance
National Digestive Diseases Information Clearinghouse
2 Information Way
Bethesda, Md 20892-3570
301-496-3583
http://www.niddk.nih.gov

Controlling Extraneous Sources of Nutrients and Other Confounding Substances

In addition to providing a well-planned diet for human feeding studies, the research dietitian and the study investigator must consider the influence of other sources of nutrients or nonnutritive substances that may affect the outcome of their study. This section addresses a number of those extraneous variables.

Vitamin and Mineral Supplements

Added nutrients, such as vitamin and mineral supplements, if not recognized or accounted for within a study protocol, can adversely affect interpretation of results from research studies. Volunteers are typically questioned at the initial screening regarding supplement use. Extra queries may be required concerning habitual use of ''natural'' or ''alternative'' products and supplemented sports drinks or other beverages because participants may not view them as supplements. The principal investigator must determine whether any supplements will be allowed during the study and, additionally, must make it clear to the participant consuming the supplements when to discontinue them prior to participation. For some studies it is important that participants not take large doses of specific vitamins for a certain period of time prior to the admission date.

Supplements may need to be prescribed in conjunction with feeding studies, particularly when diets are designed to be low in certain nutrients. These preparations are generally tailor-made for the study specifications. If a commercial vitamin and mineral preparation is used for a research study, it is important to have it analyzed independently from its manufacturer. As part of a study protocol, a dietitian may be responsible for observing participants as they take supplements, thus adding an extra degree of control to the study.

Water and Seltzer Water

Controlling water source and quantity are important for mineral or electrolyte control/balance studies. Because the elec-

trolyte content of tap water may be subject to variability, the use of deionized or distilled water is recommended. In such studies, a constant source and quantity of water should be used throughout the study. Intake and output records should be kept for any fluid balance study. For macronutrient studies, tap water, seltzer water, and spring water may be allowed ad lib. A number of flavored seltzers are now available, which can be used to add variety to diets, but these calorie-free beverages must be distinguished from sugar-containing sodas. A comprehensive discussion of water intake can be found in Chapter 15, ''Meeting Requirements for Fluids.''

Coffee, Tea, and Soft Drinks

Black coffee, tea, and diet soft drinks usually are considered to be noncaloric beverages and are thus allowed free choice, or within established guidelines, in many studies. The amount of each beverage should be kept consistent throughout the study, or a record of consumption should be kept. The methylxanthines contained in coffee, tea, cocoa, and some soft drinks include caffeine, theophylline, and theobromine. These are known to stimulate metabolic processes and affect the metabolism of free fatty acids, catecholamines, and creatinine. These beverages should be carefully monitored or avoided in metabolic research studies.

Instant coffee may be processed with gelatins and gums. Instant teas can include lemon flavor and sugar, saccharin, or aspartame. Considerations for the use of diet soft drinks relate to the sweetener contained in the product and its effects on the outcome variables to be measured. (See the discussion of artificial sweeteners.)

Alcohol

Alcoholic beverages are commonly not allowed in research diets because of their high energy content and their effects on various metabolic processes. This prohibition should be discussed with potential volunteers before they commit to a study. To the dietitian, the statement that ''foods and beverages other than those provided by the study are not allowed'' clearly means that alcohol is not to be consumed. However, some study participants may not understand this to include alcoholic beverages unless this is directly stated.

When consumption of alcoholic beverages is allowed, the type and amount of the beverage should be recorded. In studies that span a holiday that is associated with consumption of alcoholic beverages (eg, New Year's Eve), some investigators allow a limited number of alcoholic drinks, depending on the outcome variables to be assessed. The participant and investigator must have a mutual agreement regarding consumption of alcoholic beverages as part of religious rituals; frequency and amount of alcohol consumed at religious ceremonies should be determined and recorded.

Garnishes

Plate or tray garnishes for controlled diet studies must be planned in the context of the experimental diet. Many edible garnishes, such as parsley, watercress, and orange slices, contain levels of vitamins and minerals that are sufficient to destroy dietary control. When edible garnishes are used, the research dietitian must include them in the meal plan and the nutrient analysis and must ensure that participants eat the garnishes. Inedible garnishes such as paper flowers are generally a preferred option for adding color and interest while keeping a tight control on nutrient intake.

Chewing Gum

Gum is typically allowed but monitored. Regular chewing gum contributes trace amounts of carbohydrate. Sugarless gum is generally allowed ad lib because the content of calories and macronutrients is negligible. Gum can be useful for a participant on a liquid formula diet because it provides the chewing action the volunteer may miss and helps eliminate any aftertaste of formula diets. Labels should be read for type of sweetener and other additives to assess whether or not the additive will introduce an extraneous variable to the study. For instance, the sodium content of sugarless gum may affect electrolyte balance studies.

Hard Candy and Sugar

Hard candy typically has negligible nutritive value other than energy. In some situations hard candy can be used ad lib if its composition is not expected to affect electrolytes or nutrients under study.

Sugar allotments are typically included in controlled diets, but in determining the amount of the allotment investigators should consider participants' dental health. It is difficult to include an amount that pleases everyone; those who use sugar in coffee may want more than is allotted, whereas others may want less. Hard candy or jelly beans can be exchanged isocalorically for all or part of participants' daily sugar allotment, thus adding a small but welcome degree of control for the participants. (See the discussion of tradeoffs in Chapter 11, ''Designing Research Diets.'') Hard candy is also often used to clear objectionable aftertastes, such as those experienced after taking fish oil capsules.

Artificial Sweeteners

The artificial sweeteners typically permitted in research diets are saccharin and aspartame. However, because many people do not care for the taste of artificial sweeteners, participants should be informed at recruitment whether these sweeteners are to be used. The safety and relative sweetness of promi-

nently used nutritive and nonnutritive sweeteners has been reviewed (7, 8). Saccharin is a nonnutritive synthetic sweetener that is 300 times sweeter than sucrose (7). It is heat stable and has a long shelf-life, but it has a slightly bitter aftertaste. Saccharin was used in most dietetic foods, liquid and solid form, prior to the approval of use of aspartame. Because it is a nonnutritive product and has little effect on the metabolism of most nutrients, saccharin-sweetened soft drinks, candy, and gum are allowed for most metabolic research studies.

Aspartame is a synthetic sweetener that is a dipeptide, providing 4 calories per gram. It is 200 times as sweet as sucrose and tastes similar to sucrose. Aspartame is used in most low-calorie dietetic foods now on the market because of its preferred taste. However, aspartame is unstable in liquid systems resulting in a decrease in sweetness with time. Aspartame is not usually used in baked goods because it breaks down at high temperatures. Because aspartame is a dipeptide it has some effects on amino acids and neurotransmitter metabolism. Therefore, a careful evaluation is necessary prior to permitting any aspartame-containing beverage, candy, or gum to be included in a metabolic research study involving amino acids or neurotransmitters.

Nonprescription Medications

Study volunteers are carefully screened for their use of prescription medications; however, they should also be screened for use of nonprescription medications. Because many nonprescription medications are casually used, participants should be made aware of the nutritional and/or biochemical impact of common medications, including antacids, laxatives, fibers, analgesics, and cough medicines. During the study period, the use of nonprescription medications should be discouraged, but if they need to be used, the brand name, composition, and incidence of usage should be reported.

Contraceptive Hormones and Hormone Replacement Therapy

Hormones can have a confounding effect on many outcome variables. Some studies accept women who are using hormones, whereas others do not. (See Chapter 8, ''Women as Participants in Controlled Diet Studies.'') In studies in which women using hormones are accepted, these volunteers are typically paired and then randomly assigned to the dietary treatments. The type and the amount of hormone used are routinely monitored. (See the daily record form discussed in Chapter 18, ''Documentation, Record Keeping, and Recipes.'')

For most studies it is important that the type and dosage of the hormones not change during the course of the study. A participant may have to be discharged from the study if a change is necessary.

Toothpaste and Dentifrices

The commercial dentifrices vary greatly in composition and ingredients, and their use can have an effect on metabolic research studies. For instance, toothpastes with baking soda formulas should be eliminated for sodium balance studies. Research volunteers should be instructed not to swallow any toothpaste. In some studies, for consistency, one brand of toothpaste is used by all participants throughout the entire study. Special dentifrices can be formulated for the study if no compatible commercial preparations can be found (Table 13-1). (Also see Chapter 12, ''Producing Research Diets.'')

Tobacco and Nicotine

Nicotine and curing compounds found in tobacco affect metabolic processes. Tobacco chewing and smoke inhalation habits should be carefully screened and monitored during controlled feeding studies. If studies accept volunteers who smoke, it is generally important that smoking status not change during the course of the study. Participants should be questioned about the use of nicotine gum and patches.

Other Sources

Food eaten during religious practices (communion wafers, sacramental bread, and wine) must also be approved and recorded in the participant's file. Licking prepasted stamps or stickers should be controlled or avoided for volunteers in trace mineral studies. Potential participants should be questioned in a nonjudgmental way at recruitment to determine whether they have pica, an appetite for nonfood items.

TABLE 13-1

Formulas for Dentifrice[1,2]

Ingredient	Amount
Sodium lauryl sulfate	30 g
Urea	80 g
Cinnamon water	1,000 ml
or	
Cinnamon oil	0.8 ml
Saccharin (soluble)	0.4 g
Methyl cellulose	20 g
Amaranth solution	1 ml
or	
Amaranth solution 1%	5 ml
Distilled water to volume	4,000 ml

[1] Adapted from Jones E. *A Dietetic Manual for Metabolic Kitchen Units.* Washington, DC: US Government Printing Office; 1969.
[2] To avoid mold growth, rinse container with ethanol.

Conclusion: Tales from the Real World

Dinner with a group of research dietitians would lead to all sorts of stories about mistakes that were made and how problems were solved. What, for example, do you do when Bob has used Joe's salt shaker? This section relates some of those tales and tells how various mistakes or problems were handled. These are hints for avoiding the potholes of human nutrition research. (Fictitious names have been substituted for participants' actual names.)

> Ellen Stevens and Fred Stevens were unrelated subjects in a free-living diet study. Fred, who was assigned to the green (no *trans* fatty acid) diet, accidentally picked up Ellen's weekend meals. Ellen, who was assigned to the blue (*trans* fatty acid) diet, discovered the mistake when she looked for her weekend cooler. Luckily, Fred was located before he ate the weekend food; otherwise, he would have been dropped from the study. Now the color coded cards that this facility uses on coolers bear first names in addition to last names and subject numbers. Additionally, concurrent use of blue and green color codes is being reconsidered because these colors are difficult for some individuals to distinguish, especially when they have a similar hue.

> In portioning oranges for a study, the oranges were weighed with the peel attached and a refuse factor was used to determine the edible portion. The gram amounts displayed on the participants' food selection sheets indicated the weight of the orange with the peel for each calorie level and were therefore designated ''orange with peel.'' Jane Fox was a participant committed to thoroughly complying with study protocol. She ate the orange and the peel for two menu cycles before the error in communication was discovered. No harm was done, and the participant enjoyed telling her tale.

> A dinner tray was about to be delivered to an inpatient enrolled in a study that involved ascorbic acid depletion. The meal consisted of milk, chicken breast, rice, and canned corn, served on standard white hospital china. The cook, wanting to enliven the appearance of the meal and unaware of its high ascorbic acid content, added a sprig of parsley for color. Fortunately the tray was examined by a dietitian before service, and the parsley was removed. These research dietitians now recommend using paper garnishes.

> When the staff plan menus for emergency meals or for take-out meals for weekends, special care must be given to provide foods that are relatively resilient to mishandling by participants. With food safety in mind, dietitians planning for an upcoming study intended to provide frozen dinners as part of the weekend take-out meals. Additionally, the participants were to be given a frozen dinner as part of their emergency meals. However, during recruitment of participants and query about storage space for frozen foods, it was found that several potential participants had inadequate freezers for storing frozen meals for even short periods of time. One couple who wanted to participate did not have a home freezer; they lived on a boat and used a simple ice chest as a refrigerator. Many participants engage in recreational activities on weekends that do not lend themselves to using frozen dinners. It is advised that dietitians discuss these problems and issues of food safety individually with participants.

Sometimes it is less labor intensive to send two employees to the grocery store, so that one may guard the shopping cart:

> An employee picked up the 30 lb of specially ordered fish (Turbot) from the grocery store, but it was gone by the time she brought the van to the pick-up point. Another customer had made off with the next day's entree. Because this incident happened in a metropolitan area, it was possible to replace the Turbot. If it had not been recoverable, a readily available substitute would have been served and adjustments calculated for participants' diet records.

> An employee was sent to a large grocery store to purchase 50 loaves of bread and a box of tea. After carefully counting the loaves, the employee left the grocery cart to search for tea on another aisle. The employee was perplexed to find only 46 loaves when they were counted at the feeding facility. The problem was traced to a cost-conscious shopper. According to the grocery clerk, a customer demanded a lower price for 4 loaves of bread in the ''sale basket.''

Perhaps every dietitian has a prize real-life story of ''how the food item got away.'' Common ones include spilled or dropped items, or instances where the dog or the babysitter ate the food item. A favorite at one facility is from a participant who called to say that he would need to have his tuna replaced. He had left his lunch items on the window sill one November morning so that fellow employees would not take his food from a common refrigerator. A squirrel opened the Styrofoam container and ate the tuna, leaving behind peanuts, crackers, and other items more befitting a squirrel.

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