MANUAL of GYNECOLOGIC ONCOLOGY

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Accurate indications, adverse reactions, and dosage schedules for drugs are provided in this book, but it is possible that they may change. The reader is urged to review the package information data of the manufacturers of the medications mentioned.

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Preface

Our goal for the *Manual of Gynecologic Oncology* was for it to be compact and affordable. It is not intended to compete with the standard textbooks, but to be a handy pocket reference for physicians who treat women with gynecologic malignancies. The guidelines presented here are based on our experience and that of our mentors at The Johns Hopkins Hospital.

The manual contains twelve chapters and two appendices. Chapters 3, 4, and 5 are dedicated to each of the three most prevalent gynecologic malignancies: endometrial, cervical, and ovarian cancer. A brief summary of the clinical and epidemiologic features of each tumor is followed by a review of its histopathology. A detailed outline of the evaluation and management of patients with each of these malignancies is presented. Chapters 8, 9, and 10 are dedicated to three of the most common gynecologic oncology surgical procedures: radical hysterectomy, radical vulvectomy, and intracavitary irradiation; guidelines for the pre- and postoperative care of patients undergoing each of these procedures are described. Chapter 7, Chemotherapy, presents general guidelines, as well as a number of frequently used chemotherapy protocols. Since new protocols are constantly being developed and old ones frequently modified, the administration of chemotherapy should be under the supervision of a physician familiar with the drugs being used and the tumors being treated. The management of patients with cervical intraepithelial neoplasia and gestational trophoblastic neoplasia are described in Chapters 12 and 6, respectively. Nutritional support, blood component therapy, and the care of long-term venous catheters are covered in some detail in Chapters 1, 2, and 11; these topics are seldom covered in gynecology and gynecologic oncology textbooks.

A list of suggested readings follows each chapter. For in-depth coverage of the various gynecologic malignancies the reader is re-

ferred to these readings or to one of the many available standard textbooks (e.g., Gusberg, Shingleton, and Deppe's *Female Genital Cancer* and the third edition of Morrow and Townsend's *Synopsis of Gynecologic Oncology*).

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Contents

1

Nutritional Support of the Gynecologic Oncology Patient

Malnutrition is a frequent complication in the cancer patient. It can be secondary to the malignancy or to the therapy. Adequate nutrition is necessary for maintenance of body cell mass, metabolic processes, and tissue repair. Therefore, the gynecologic oncology patient should undergo periodic nutritional assessment and identification of any nutritional deficiencies that may need to be corrected.

NUTRITIONAL ASSESSMENT

SIMPLE MEASUREMENTS

The following simple measurements should be obtained from all gynecologic oncology patients.

Weight

Recent unintentional weight loss of 10% or greater may indicate malnutrition. Weighing less than 90% of ideal body weight may also indicate malnutrition.

Height

Height and frame size can be used to estimate the ideal body weight. An estimate of the female patient's ideal body weight can be obtained by allowing 100 pounds for the first 60 inches of height and adding 5 pounds for each additional inch. Subtract 10% for small frame. Add 10% for large frame. Frame size can be estimated

by asking the patient to place her index finger and thumb around her wrist. If the thumb and index finger do not touch, she has a large frame. If they just touch, she has a medium frame. If they pass each other, she has a small frame.

Total Lymphocyte Count

A decrease in total lymphocyte count is seen with decreased visceral protein. A total lymphocyte
indicate malnutrition.

Serum Albumin

A serum albumin concentration of less than 3.5 g/dl may indicate malnutrition.

ADDITIONAL MEASUREMENTS

If any of the above criteria is present, further measurements will help clarify the patient's nutritional status.

Skin Tests

A negative response to skin testing, for example, *Candida*, mumps, streptodornase-streptokinase, and purified protein derivative (PPD), indicates depressed cellular immunity and indirectly visceral protein status.

Serum Transferrin

Serum transferrin has a half-life of 8 days compared with 19 days for serum albumin. Therefore, serum transferrin will show decreased levels sooner in the presence of decreased visceral protein.

Anthropometric Measurements

Muscle and fat wasting can be measured by the mid-arm muscle circumference and the triceps skinfold. These measurements are compared with that expected for age and sex and reported as percentage of normal.

DEFINITION OF MALNUTRITION

The severely malnourished woman will show obvious physical signs of protein malnutrition (kwashiorkor) or protein-calorie malnutrition (marasmus).

1. *Kwashiorkor:* The patient with severe protein malnutrition has changes in skin turgor, hair color, and consistency. There is edema, ascites, and enlargement of the liver and parotid gland.
2. *Marasmus:* The patient with severe protein-calorie malnutrition appears cachectic with muscle and fat wasting.

Most gynecologic oncology patients are not severely malnourished and do not present with obvious physical signs of malnutrition. Nevertheless, the patient should be strongly suspected of being malnourished if at least three of the following criteria are present:

1. Recent unintentional weight loss of 10% or greater
2. Total lymphocyte count below 1,500/mm^3
3. Serum albumin of less than 3.5 g/dl
4. Negative response to skin tests (anergy panel)
5. Serum transferrin of less than 200 mg/dl

DEGREE OF MALNUTRITION

An estimate of the degree of malnutrition can be obtained from the following table:

	Malnutrition		
Test	Mild	Moderate	Severe
Albumin (mg/dl)	3.0–3.5	2.5–2.9	<2.5
Transferrin (mg/dl)	180–200	160–179	<160
Lymphocytes (mm^3)	1,500–1,800	900–1,499	<900

NUTRITIONAL SUPPORT

Nutritional support of the malnourished patient is best accomplished via the gastrointestinal (GI) tract. If the GI tract cannot be used, peripheral parenteral nutrition (PPN) or total parenteral nu-

trition (TPN) through a central line should be considered as a viable option to provide caloric requirements and essential nutrients to promote anabolism.

CALORIC REQUIREMENTS

An average adult needs approximately 30 kcal/kg/day. This is a general guide. Other formulas are available, but they tend to overestimate. The above formula can be used and the caloric intake adjusted according to the patient's response.

To calculate the kilocalories (kcal) being delivered, the following formulas can be used:

kcal = grams of amino acids (protein) × 4
kcal = grams of carbohydrates × 3.4 (parenteral), or × 4 (enteral)
kcal = grams of fat × 9

The fat emulsion solutions (e.g., Intralipid 10%, Intralipid 20%) provide 1.1 or 2.0 kcal/ml of solution. The ratio of nonprotein calories to nitrogen should be 150–200:1. This may need to be lower (e.g., 100:1) in high-stress patients or higher (e.g., 300:1) in nitrogen-retaining states (e.g., acute renal failure, hepatic failure). It is recommended that no more than 60% of the total daily caloric intake be provided by fatty acids.

FLUID REQUIREMENTS

An average of 1,500 ml/m^2 of body surface area is needed per day. (The body surface area of a 66-inch tall, 140-pound woman is 1.5 m^2.) This woman will require 2,250 ml of fluids every 24 hours. The daily requirements for sodium and potassium are 60 mEq/m^2 and 30–40 mEq/m^2, respectively.

ENTERAL NUTRITION

The GI tract should be used whenever feasible. If the patient is eating, her diet can be supplemented with commercially available formulas. If the patient is not eating, tube feedings using a small-diameter (e.g., #8 Fr), soft, tungsten-tip feeding tube can be in-

stituted. In surgical patients whose return of gastric or colonic function is expected to be delayed, administration of an elemental diet through a catheter jejunostomy should be considered. Elemental formulas (e.g., Vivonex, Vital High Nitrogen) are absorbed in the small intestine. Only 100 cm of small intestine is required for absorption.

Enteral Formulas

A large number of formulas are commercially available. It is best to be familiar with the generic features of the formulas and to select one or two products in each group for clinical use.

Intact Nutrient Formulas

Intact nutrient formulas are used in patients with normal GI tract function. These polymeric mixtures contain proteins, fats, and carbohydrates. They are almost isosmolar (approximately 350 mOsm/L) and supply 1 kcal/ml with approximately 30% of the calories being provided by fat. We prefer the lactose-free formulas (e.g., Enrich, Isocal, Precision Isotonic). Enrich, Isocal, and Precision are unpalatable and are recommended for tube feeding only. For oral feedings (diet supplementation), Ensure or Resource are recommended.

Predigested Nutrient Formulas

Predigested nutrient formulas have been labeled elemental because they use amino acids as the nitrogen source and oligosaccharides as the carbohydrate source. Most contain little fat and no lactose (e.g., Vivonex T.E.N., Vital High Nitrogen). They are helpful in patients who have an abnormal GI tract. They are the preferred formulas for infusion through a needle-catheter jejunostomy because of their low viscosity. They frequently cause diarrhea because of their high osmolality (550–850 mOsm/L). A new semielemental formula of low viscosity, Reabilan, has an osmolality of 350 mOsm/L. The above formulas supply 1 kcal/ml and a calorie-to-nitrogen ratio of 150–200:1. Special formulas for patients with renal failure (e.g., Travasorb Renal, Amin-Aid), chronic hepatic

encephalopathy (e.g., Travasorb Hepatic, Hepatic-Aid) and for patients with respiratory insufficiency (Pulmocare) are available.

Tube Feedings

The continuous infusion is the simplest and safest way to administer tube feedings. It is the least time-consuming of all the tube-feeding techniques, resulting in maximum staff compliance. This method of nutrition allows for maximum control of the infusion rate and maximizes nutrient delivery. With the continuous infusion technique, there is the least chance for aspiration, nausea, gastric distention, cramping, and diarrhea. It requires a pump. This can result in limited ambulation if a battery-powered pump is not used. With this technique, the head of the bed needs to be elevated at least 30 degrees. A cyclic drip infusion can be used to allow the patient to have some time when she can be in bed without head elevation. Hyperosmolar medications (e.g., potassium chloride) should not be given through the tube, since they can cause diarrhea.

Infusion of enteral nutrient formulas through a nasogastric feeding tube is started at 50 ml/hr, using a lactose-free 1-kcal/ml formula, diluted to half-strength. Although intact nutrients formulas are almost isosmolar, some patients will develop diarrhea if the formula is started at full-strength. The half-strength dilution allows some time for GI adaptation to occur. On the second day, the infusion rate is increased to 100 ml/hr. If the half-strength formula is tolerated, a three-quarter strength formula is used on the third day, and a full-strength formula on the fourth day. When the patient is receiving the maximum tolerated concentration, the infusion rate is increased by 25 ml/hr every 8 hours until the desired rate is achieved.

Needle-Catheter Jejunostomy

Postoperative patients who receive a needle-catheter jejunostomy can start continuous infusion of a half-strength elemental formula in the recovery room at a rate of 50 ml/hr. On the second day of jejunostomy feeding, the rate is increased to 100 ml/hr. On the third day, the concentration of the formula is increased to three-quarters strength. If tolerated, it is increased to full-strength on the

TABLE 1-1. SUGGESTED FORMULATION FOR PERIPHERAL PARENTERAL NUTRITION

Component	Quantity
Dextrose 10%	500 ml
Travasol 5.5% with electrolytes	500 ml
Sodium	35 mEq/L
Chloride	35 mEq/L
Potassium	30 mEq/L
Phosphate	30 mEq/L
Magnesium	5 mEq/L
Acetate	50 mEq/L

fourth day. The infusion rate is then increased if necessary by 25 ml/hr every 24 hours, until the desired rate is achieved.

PERIPHERAL PARENTERAL NUTRITION

Peripheral parenteral nutrition can be used in patients needing nutritional support but who are not hypercatabolic and whose GI tract is expected to be functional within 5–7 days. It can also be used to supplement oral feedings in patients whose oral intake is inadequate.

Formula for Peripheral Parenteral Nutrition

A suggested formula for PPN is 500 ml Travasol 5.5% with electrolytes plus 500 ml 10% dextrose (Table 1-1). This will result in 1 L of solution containing 27.5 g of amino acids and 50 g of dextrose. It also contains 35 mEq/L of sodium and chloride, 30 mEq/L of potassium and phosphate, 5 mEq/L of magnesium, and 50 mEq/L of acetate. This solution has an osmolality of approximately 530 mOsm/L and contains 280 kcal/L. Infusing 2 L of this solution and 1 L of Intralipid 10% (1.1 kcal/ml) provides 1,660 kcal in 24 hours. Higher concentrations of dextrose (e.g., 10%) or amino acids (e.g., 4.25%) will universally cause phlebitis within 36–48 hours. The addition of 500 U of heparin and 5 mg of hydrocortisone sodium succinate (Solu-Cortef) to each liter of solution decreases

TABLE 1-2. MULTIVITAMINS

Vitamin	Quantity
M.V.I.-12 (to be added to 1 L/day)	
Vial 1	5 ml
Ascorbic acid (vitamin C)	100 mg
Retinol (vitamin A)	1 mg
Ergocalciferol (vitamin D)	5 μg
Thiamine (vitamin B_1)	3 mg
Riboflavin (vitamin B_2)	3.6 mg
Pyridoxine (vitamin B_6)	4 mg
Niacinamide	40 mg
Dexpanthenol	15 mg
Vitamin E	10 mg
Vial 2	5 ml
Biotin	60 μg
Folic acid	400 μg
Cyanocobalamin (vitamin B_{12})	5 μg

the risk of phlebitis. The simultaneous infusion of lipids and the hypertonic dextrose/amino acids solution through a Y-connector reduces the osmolality of the final infusate and reduces the incidence of phlebitis. The lack of a lipid free interval may promote intense hyperlipedemia.

Additional Additives

Multivitamins (e.g., M.V.I.-12) are added to one of the liters of parenteral nutrition solution once daily (Table 1-2). One ml of multiple trace metals is added to 1 L of solution every 24 hours (Table 1-3). Electrolytes can be supplemented as necessary by the addition of sodium chloride, sodium acetate, or sodium phosphate, potassium chloride, potassium acetate, or potassium phosphate, mag-

TABLE 1-3. TRACE ELEMENTS

Elements	Quantity
Multitrace 5	1 ml
Zinc	1 mg
Copper	0.4 mg
Manganese	0.1 mg
Chromium	4.0 μg
Selenium	20 μg

nesium sulfate, and calcium gluconate. The chloride salts are used in the presence of metabolic alkalosis and the acetate salts in patients with metabolic acidosis.

Administration

Peripheral parenteral nutrition should be delivered through an infusion pump (e.g., IMED, IVAC). Parenteral nutrition solutions (dextrose/amino acids) should not hang for more than 24 hours. The fat emulsion solutions should not hang for more than 12 hours. The IV site used for parenteral nutrition should not be used for other purposes (e.g., antibiotics, chemotherapy). It should be routinely changed every 72 hours.

Severe allergy to eggs is a contraindication to the administration of fat emulsions (e.g., Intralipid). Lipid infusions can cause altered clotting function and decreased pulmonary function. The initial infusion rate should be 1 ml/min for the first 15 minutes. If no adverse reaction is observed, the infusion rate is increased to deliver 500 ml over 4 hours. Only 500 ml of fat emulsion is infused the first day. As a general rule, no more than 2.5 g of lipids per kg of body weight is given daily. The lipid infusion should provide no more than 60% of the total calories.

TOTAL PARENTERAL NUTRITION

Total parenteral nutrition provides enough calories to support a malnourished hypercatabolic patient with a defective GI tract. The osmolality of the total parenteral nutrition solutions is high (1,900 mOsm/L), necessitating a central venous line.