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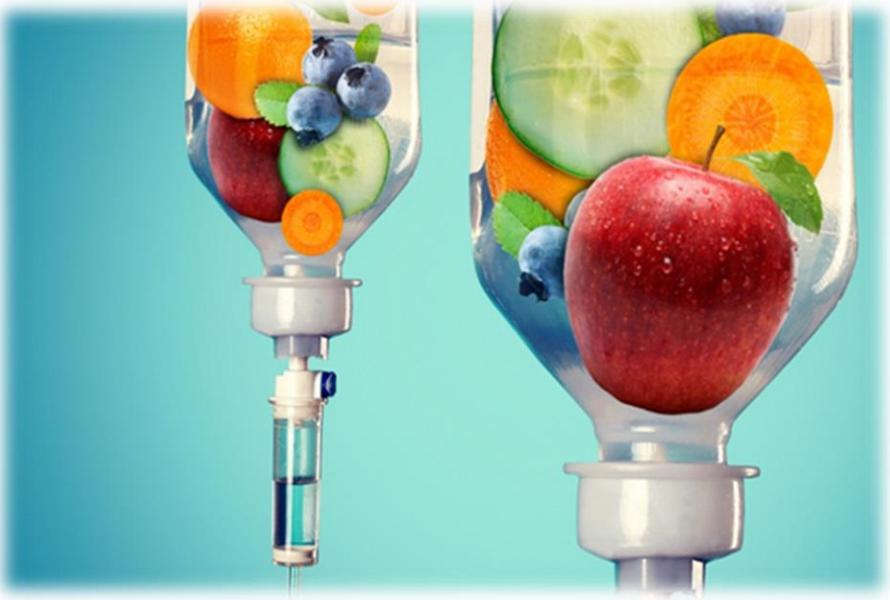
Quick Review of Clinical Nutrition

A Complete Handbook



Reviewed By:
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Preface

Malnutrition in all its forms remains a global concern, particularly affecting highly vulnerable populations in several regions of the world. Ambitious global targets and sustainable development goals have been set to address this problem. The UN General Assembly declared on April 1, 2016, the UN Decade of Action on Nutrition for the period 2016–2025.The Decade of Action reaffirms the call to end all forms of malnutrition as anchored in the ICN2 (The Second International Conference on Nutrition) Rome Declaration and in the 2030 Agenda for Sustainable Development. It provides a unique avenue for a sustained global push on nutrition.

Dietary factors have been implicated in at least four of the ten leading causes of death (heart disease, cancer, diabetes, and stroke). Nevertheless, physicians frequently receive inadequate training in nutrition to properly counsel their patients

Anyone interested in providing optimal nutrition support to their patients knows that it is essential that knowledge, judgment, proficiency, and competency must prevail in choosing the best nutrient constituents of a feeding regimen and in deciding how these formulations might best be provided for the maximal benefit and safety of the patient under virtually any condition or in any adverse situation. Not to have knowledge, experience, or proficiency with every tool in our clinical tool box detracts from our education and training; our trust, competence, and professionalism; and our morals, ethics, and obligations.

Practitioners who always treat their patients with enteral nutrition and those who always treat their patients with parenteral nutrition are both likely to be practicing less than optimal nutrition support. The most appropriate feeding modality in every conceivable clinical situation requires extensive versatility, experience, judgment, proficiency, wisdom, and equanimity. It bodes well for practitioners of nutrition support to appraise a given clinical situation comprehensively in order to identify and define the goals of nutrition support, and to choose and use the most appropriate nutrition support tools proficiently in the overall comprehensive management of the patient.

A primary goal of this text is to provide with information backed by nutritional science, and with a variety of resources that use scientific evidence to optimize health and prevent disease. There are many conditions and deadly diseases that can be prevented by good nutrition.

This book will facilitate the medical students, general practitioners, interns, dieticians, nurses, pharmacists and all others who are associated with the medical profession on daily basis to find the answers to their questions and enhance use of nutrition care in their daily practices. However, this booklet is not a substitute for the standard textbooks and references should be made to them, whenever appropriate.

Medical Department
Otsuka Pakistan Limited
2nd February 2019

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Section I: Nutrients and Metabolism

Chapter 1: Overview of Nutrition

Nutrition is a young science. A science that studies nutrients and other substances in foods and in the body and the way those nutrients relate to health and disease. **Nutrients** are the nourishing substances in food that provide energy and promote the growth and maintenance of the body. In addition, nutrients aid in regulating body processes such as heart rate and digestion and in supporting the body's optimum health. **Diet** is the food and beverages you normally eat and drink.

Our choice of diet strongly influences whether we will get certain diseases, such as heart disease, cancer, and stroke—the three biggest killers around the Globe. Indeed, high costs are associated with poor eating patterns. In 2014, the Centers for Disease Control and Prevention observed that diseases like heart disease and stroke around the Globe are among the top 5 causes of Deaths. Such diseases are associated with Bad eating habit. No doubt eating right contributes to health and quality of life, and this is reflected in growing consumer awareness of eating healthy.

Characteristics of a nutritious diet

A nutritious diet has four characteristics:

1. **ADEQUATE DIET-** A diet that provides enough energy, essential nutrients, and fiber to keep a person healthy.
2. **MODERATE DIET-** A diet that avoids excessive amounts of energy or any particular food or nutrient.
3. **BALANCED DIET-** A diet in which foods are chosen to provide energy, essential nutrients, and fiber in the right proportions.
4. **VARIED DIET-** A diet in which you eat a wide selection of foods to get necessary nutrients.

You've heard the term "nutrition" all your life. The food-fitness connection is what it's all about. In a nutshell, nutrition is how food nourishes your body. The intake of food you choose to eat determine which nutrients your body will receive and in what quantities, considered in relation to the body's dietary needs.

Today, we define nutrition as the sum of all processes involved in how organisms obtain nutrients, metabolize them, and use them to support all of life's processes.

The investigation of how an organism is nourished, and how nourishment affects personal health, population health, and planetary health is called Nutritional Science.

Today, nutrition advice, with the consensus of nutrition experts, is supported by solid scientific evidence. So unlike the ancients, you have a valid basis for choosing food for health. It's up to you to apply nutrition principles and advice for your own well-being.

Chapter 2: Body Composition

The human body is made up of different types of tissues including muscles, bones, fats and organs. The total percentage of these tissues describes the total composition of your body. Various factors involves to this body composition are heredity, age, healthy lifestyles (such as physical activity and eating habits) and maturation. Many of these factors are uncontrollable but two factors that can be controlled are physical activity and nutrition.

Body composition refers to the division of total body weight (mass) into components; most commonly fat mass and fat-free mass. The proportion of total body weight that is fat (referred to as percent body fat) is an important health-related indicator because high levels of body fatness are associated with increased risk of coronary heart disease, stroke, and diabetes.

Body fat is one important component of the body composition. Neither too much nor too less body fat is of benefit to the human body composition. The ideal situation is to be in the healthy fitness zone for body fatness. Essential fat is the minimum amount of fat necessary for good health. Fat is stored in the form of energy which can be utilized for the provision of fuel to carry out necessary physical activities. This source of energy is useful in case of longer starvation periods.

Body composition includes more than just muscle and fat; it also includes bones, organs, tendons and ligaments. Health wise, body composition typically measures body fat vs. lean body mass. **Lean body mass** not only includes your muscle but also organs, bones, tendons and ligaments. There are a number of tools used to measure body fat, including calipers, bioelectric impedance and underwater weighing. But according to Steven Heymsfield, author of "Human Body Composition," muscle mass testing is limited and based on cadaver dissection studies. While you may be able to determine your exact body fat percentage, determining your muscle mass is a little less precise.

Estimating Muscle Mass

When determining muscle mass, you want to know how much skeletal muscle you have, and this includes those muscles you're working out at the

gym. According to Heymsfield, 30 to 40 percent of a healthy person's body mass is made up of skeletal muscle. A study from 2000 published in the Journal of Applied Physiology found through whole body MRI testing that women tend to have less muscle mass, closer to 30 percent of their body weights, than men, who have closer to 40 percent. Based on this information, a 200-pound man has about 80 pounds of muscle mass.

Muscle mass is not the same for everyone, however, and may vary depending on age and fitness level. The amount of muscle you have in your body, according to the authors of the 2000 study in the Journal of Applied Physiology, decreases as you age and dramatically after age 45. And according to a classic study in the Journal of Sports Sciences, fitness and type of activity make a difference in muscle mass, with bodybuilders having a greater percentage of muscle than endurance athletes.

Body Fat and Its Distribution

Water, organs, bone tissue, fat, and muscle tissue make up a person's weight. Having more fat mass may be indicative of disease risk, but fat mass also varies with sex, age, and physical activity level. Females have more fat mass, which is needed for reproduction and, in part, is a consequence of different levels of hormones. The optimal fat content of a female is between 20 and 30 percent of her total weight and for a male is between 12 and 20 percent.

Methods to measure Fat mass

Fat mass can be measured in a variety of ways. The simplest and lowest-cost way is the skin-fold test. A health professional uses a caliper to measure the thickness of skin on the back, arm, and other parts of the body and compares it to standards to assess body fatness. It is a noninvasive and fairly accurate method of measuring fat mass. Other methods of measuring fat mass are more expensive and more technically challenging. They include:

- **Underwater weighing -** This technique requires a chamber full of water big enough for the whole body can fit in. First, a person is weighed outside the chamber and then weighed again while immersed in water. Bone and muscle weigh more than water, but fat does not—therefore

a person with a higher muscle and bone mass will weigh more when in water than a person with less bone and muscle mass.

- **Bioelectric Impedance Analysis (BIA) -** This device is based on the fact that fat slows down the passage of electricity through the body. When a small amount of electricity is passed through the body, the rate at which it travels is used to determine body composition. These devices are also sold for home use and commonly called body composition scales.
- **Dual-energy x-ray absorptiometry** - This technique can be used to measure bone density. It also can determine fat content via the same method, which directs two low-dose x-ray beams through the body and determines the amount of the energy absorbed from the beams. The amount of energy absorbed is dependent on the body's content of bone, lean tissue mass, and fat mass. Using standard mathematical formulas, fat content can be accurately estimated.

Body mass index (BMI) is calculated using height and weight measurements and is more predictive of body fatness than weight alone. BMI measurements are used to indicate whether an individual may be underweight, overweight or obese. High BMI measurements can be warning signs of health hazards ahead, such as cardiovascular disease, Type 2 diabetes, and other chronic diseases. BMI-associated health risks vary by race. Asians face greater health risks for the same BMI than Caucasians, and Caucasians face greater health risks for the same BMI than African Americans.

To calculate your BMI, multiply your weight in pounds by 703 (conversion factor for converting to metric units) and then divide the product by your height in inches, squared.

$\text{BMI} = \frac{[\text{weight (lb)} \times 703]}{\text{height (in)}^2}$ Or

$\text{BMI} = \frac{[\text{weight (kg)}]}{\text{height (m)}^2}$

Categories	BMI
Underweight	< 18.5
Normal weight	18.5–24.9
Overweight	25–29.9
Obese	> 30.0

Chapter 3: Classification of Nutrients

Nutrients are categorized into two major groups: Macronutrients and Micronutrients

Macronutrients

Nutrients needed in larger quantities (in grams) are called Macronutrients. These include carbohydrates, fat and proteins. Macronutrients are also known as **energy-providing nutrients.** Energy is measured in calories. It is required for the body to grow, repair and develop new tissues, conduct nerve impulses and regulate life process.

Micronutrients

Micronutrients are nutrients that are required by the body in minute quantity. These include *minerals* and *vitamins*. Both micro and macro nutrients are extremely significant to perform the basic functions of the body. Their key function is to facilitate the chemical reactions in the body. Micronutrients do not fulfill the function of energy.

Water is not classified as a macronutrient or micronutrient, but is essential for health and life. Water makes up a large part of our body weight and is the main component of our body fluids. The body needs more water every day than any other nutrient. Water carries nutrients throughout the body, provides lubricants and cushions for the joints and the eyes, eliminates wastes, and helps maintain body temperature and regulate many body processes. We lose water every day and our bodies do not store extra water, so we need to replenish water through the foods and liquids we eat and drink.

The energy nutrients are carbohydrate, protein, and fat; the non-energy nutrients are water, vitamins, and minerals.

Nutrient	Primary Functions
Protein	Builds new tissues, antibodies, enzymes, hormones, and other compounds
Carbohydrate	Provides energy
Fat	Provides long-term energy, insulation and protection
Vitamins	Facilitate use of other nutrients; involved in regulating growth and manufacturing hormones
Minerals	Help build bones and teeth; aid in muscle function and nervous system activity

Chapter 4: Functional Anatomy of GIT

Digestion

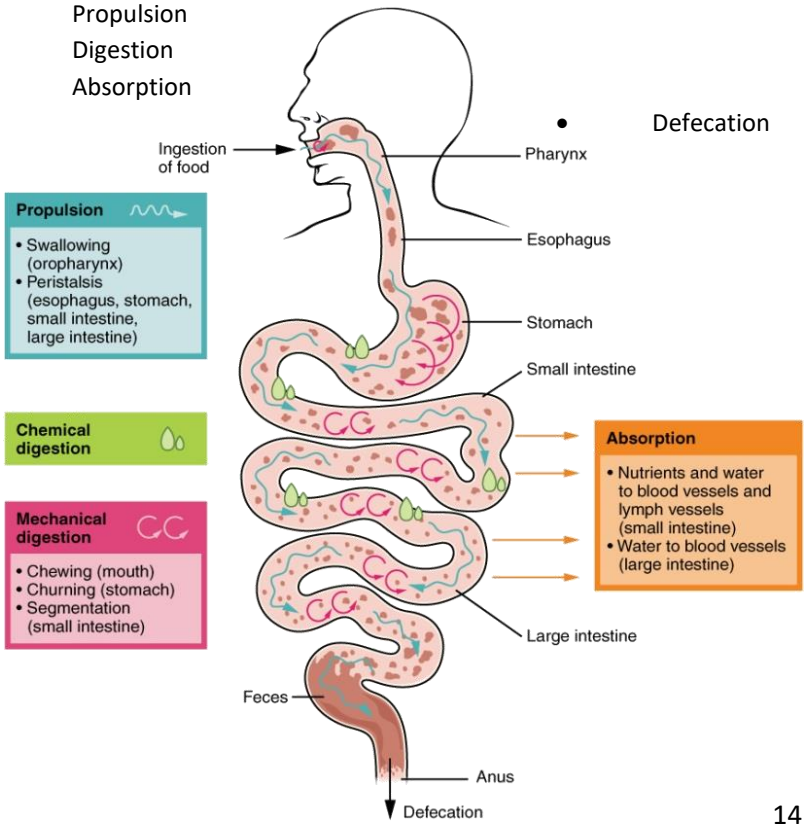
Digestion is the process by which food is broken down into molecules that are small enough to be absorbed into the circulation.

E.g. Ingested proteins are first reduced to polypeptides and then further degraded to small peptides and amino acids that can be absorbed.

Digestive Processes

The activities in the digestive system can be grouped under five main headings:

- Ingestion
- Propulsion
- Digestion
- Absorption
- Defecation



The first of these processes, **ingestion**, refers to the entry of food into the alimentary canal through the mouth. There, the food is chewed and mixed with saliva, which contains enzymes that begin breaking down the carbohydrates in the food plus some lipid digestion via lingual lipase. Chewing increases the surface area of the food and allows an appropriately sized bolus to be produced.

Food leaves the mouth when the tongue and pharyngeal muscles propel it into the esophagus. This act of swallowing, the last voluntary act until defecation, is an example of **propulsion**, which refers to the movement of food through the digestive tract. It includes both the voluntary process of swallowing and the involuntary process of peristalsis. **Peristalsis** consists of sequential, alternating waves of contraction and relaxation of alimentary wall smooth muscles, which act to propel food along. These waves also play a role in mixing food with digestive juices.

Digestion includes both mechanical and chemical processes. **Mechanical digestion** is a purely physical process that does not change the chemical nature of the food. Instead, it makes the food smaller to increase both surface area and mobility. It includes **mastication**, or chewing, as well as tongue movements that help break food into smaller bits and mix food with saliva. The mechanical churning of food in the stomach serves to further break it apart and expose more of its surface area to digestive juices, creating an acidic "soup" called **chyme**. **Segmentation**, which occurs mainly in the small intestine, consists of localized contractions of circular muscle of the muscularis layer of the alimentary canal.

In **chemical digestion**, starting in the mouth, digestive secretions break down complex food molecules into their chemical building blocks (for example, proteins into separate amino acids). These secretions vary in composition, but typically contain water, various enzymes, acids, and salts. The process is completed in the small intestine.

Food that has been broken down is of no value to the body unless it enters the bloodstream and its nutrients are put to work. This occurs through the process of **absorption**, which takes place primarily within the small intestine. There, most nutrients are absorbed from the lumen of the alimentary canal into the bloodstream through the epithelial cells that

make up the mucosa. Lipids are absorbed into lacteals and are transported via the lymphatic vessels to the bloodstream.

In **defecation**, the final step in digestion, undigested materials are removed from the body as feces.

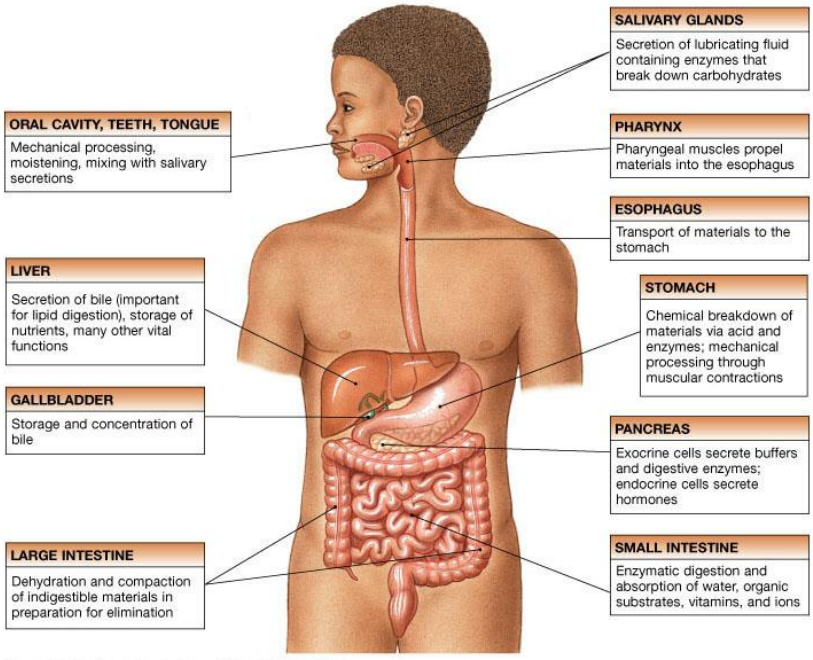
Digestive System Organs:

The easiest way to understand the digestive system is to divide its organs into two main categories. The first group is the organs that make up the alimentary canal. Accessory digestive organs comprise the second group and are critical for orchestrating the breakdown of food and the assimilation of its nutrients into the body. Accessory digestive organs, despite their name, are critical to the function of the digestive system.

1. Gastrointestinal (GI) tract or alimentary canal – mouth, most of pharynx, esophagus, stomach, small intestine, and large intestine.
2. Accessory digestive organs – teeth, tongue, salivary glands, liver, gallbladder, and pancreas.

Alimentary Canal Organs

Also called the gastrointestinal (GI) tract or gut, the alimentary canal (aliment- = "to nourish") is a one-way tube about 7.62 meters (25 feet) in length during life and closer to 10.67 meters (35 feet) in length when measured after death, once smooth muscle tone is lost. The main function of the organs of the alimentary canal is to nourish the body. This tube begins at the mouth and terminates at the anus. Between those two points, the canal is modified as the pharynx, esophagus, stomach, and small and large intestines to fit the functional needs of the body. Both the mouth and anus are open to the external environment; thus, food and wastes within the alimentary canal are technically considered to be outside the body. Only through the process of absorption do the nutrients in food enter into and nourish the body's "inner space."

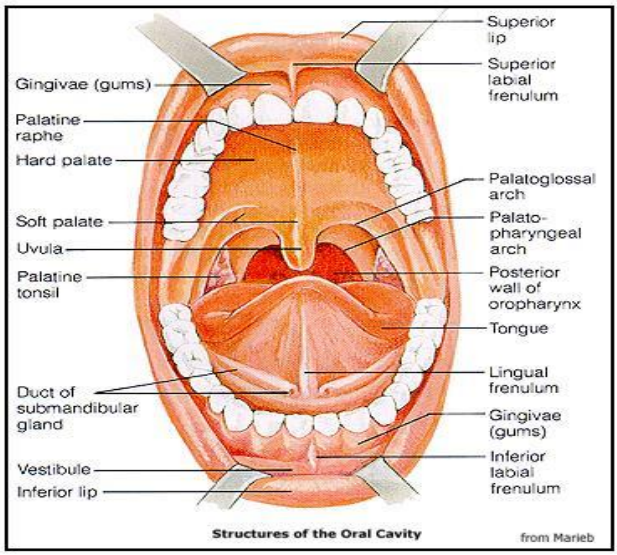


1. The Mouth

The cheeks, tongue, and palate frame the mouth, which is also called the **oral cavity** (or buccal cavity). At the entrance to the mouth are the lips, or **labia** (singular = labium). Lips are very vascular with a thin layer of keratin; hence, the reason they are "red." The lips cover the orbicularis oris muscle, which regulates what comes in and goes out of the mouth. The cheeks make up the oral cavity's sidewalls. While their outer covering is skin, their inner covering is mucous membrane.

The pocket-like part of the mouth that is framed on the inside by the gums and teeth, and on the outside by the cheeks and lips is called the **oral vestibule**. Moving farther into the mouth, the opening between the oral cavity and throat (oropharynx) is called the **fauces** (like the kitchen "faucet").

When you are chewing, you do not find it difficult to breathe simultaneously. The next time you have food in your mouth, notice how the arched shape of the roof of your mouth allows you to handle both digestion and respiration at the same time. This arch is called the palate. The anterior region of the palate serves as a wall (or septum) between the oral and nasal cavities as well as a rigid shelf against which the tongue can push food. It is created by the maxillary and palatine bones of the skull and, given its bony structure, is known as the hard palate. If you run your tongue along the roof of your mouth, you'll notice that the hard palate ends in the posterior oral cavity, and the tissue becomes fleshier. This part of the palate, known as the **soft palate**, is composed mainly of skeletal muscle. You can therefore manipulate, subconsciously, the soft palate—for instance, to yawn, swallow, or sing.

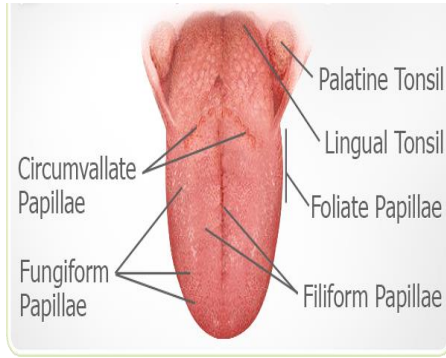


A fleshy bead of tissue called the uvula drops down from the center of the posterior edge of the soft palate. Although some have suggested that the uvula is a vestigial organ, it serves an important purpose. When you swallow, the soft palate and uvula move upward, helping to keep foods and liquid from entering the nasal cavity. Unfortunately, it can also contribute

to the sound produced by snoring. The lingual tonsils are located at the base of the tongue.

2. The Tongue

The **tongue** is the strongest muscle in the body. Although it is difficult to quantify the relative strength of different muscles, it remains indisputable that the tongue is a workhorse, facilitating ingestion, mechanical digestion, chemical digestion (lingual lipase), sensation (of taste, texture, and temperature of food), swallowing, and vocalization.



The tongue is attached to the mandible, the styloid processes of the temporal bones, and the hyoid bone. The tongue is positioned over the floor of the oral cavity.

The intrinsic muscles allow you to change the size and shape of your tongue, as well as to stick it out, if you wish. Having such a flexible tongue facilitates both swallowing and speech.

The extrinsic muscles of the tongue originate outside the tongue and insert into connective tissues within the tongue. The mylohyoid is responsible for raising the tongue, the hyoglossus pulls it down and back, the styloglossus pulls it up and back, and the genioglossus pulls it forward.

Working in concert, these muscles perform three important digestive functions in the mouth:

1) Position food for optimal chewing,
2) Gather food into a **bolus** (rounded mass),
3) Position food so it can be swallowed.

Fungiform papillae contain taste buds, and **filiform papillae** have touch receptors that help the tongue move food around in the mouth. Lingual

glands in the lamina propria of the tongue secrete mucus and a watery serous fluid that contains the enzyme **lingual lipase**, which plays a minor role in breaking down triglycerides but does not begin working until it is activated in the stomach. A fold of mucous membrane on the underside of the tongue, the **lingual frenulum**, tethers the tongue to the floor of the mouth.

3. The Salivary Glands

Many small salivary glands are housed within the mucous membranes of the mouth and tongue. These minor exocrine glands are constantly secreting saliva, either directly into the oral cavity or indirectly through ducts, even while you sleep. In fact, an average of 1 to 1.5 liters of saliva is secreted each day. Usually just enough saliva is present to moisten the mouth and teeth. Secretion increases when you eat, because saliva is essential to moisten food and initiate the chemical breakdown of carbohydrates. Small amounts of saliva are also secreted by the labial glands in the lips. In addition, the buccal glands in the cheeks, palatal glands in the palate, and lingual glands in the tongue help ensure that all areas of the mouth are supplied with adequate saliva.

The Major Salivary Glands

Outside the oral mucosa are three pairs of major salivary glands, which secrete the majority of saliva into ducts that open into the mouth:

- The **submandibular glands**, which are in the floor of the mouth, secrete saliva into the mouth through the submandibular ducts. They have cells similar to those of the parotid glands, as well as mucus-secreting cells. Therefore, saliva secreted by the submandibular glands also contains amylase but in a liquid thickened with mucus.
- The **sublingual glands**, which lie below the tongue, use the lesser sublingual ducts to secrete saliva into the oral cavity. They contain mostly mucous cells, and they secrete the thickest saliva with the least amount of salivary amylase.
- The **parotid glands** lie between the skin and the masseter muscle, near the ears. They secrete a watery solution that contains salivary amylase

into the mouth through the parotid duct, which is located near the second upper molar tooth.

Saliva

Saliva is essentially (95.5 percent) water. The remaining 4.5 percent is a complex mixture of ions, glycoproteins, enzymes, growth factors, and waste products. Perhaps the most important ingredient in saliva from the perspective of digestion is the enzyme **salivary amylase**, which initiates the breakdown of carbohydrates. Food does not spend enough time in the mouth to allow all the carbohydrates to break down, but salivary amylase continues acting until it is inactivated by stomach acids. Bicarbonate and phosphate ions function as chemical buffers, maintaining saliva at a pH between 6.35 and 6.85. Salivary mucus helps lubricate food, facilitating movement in the mouth, bolus formation, and swallowing. Saliva contains immunoglobulin A, which prevents microbes from penetrating the epithelium, and lysozyme, which makes saliva antimicrobial.

4. The Teeth

The teeth, or dentes (singular = dens), are organs similar to bones that you use to tear, grind, and otherwise mechanically break down food.

Types of Teeth

During the course of your lifetime, you have two sets of teeth (one set of teeth is a **dentition**). Your **20 deciduous teeth**, or baby teeth, first begin to appear at about 6 months of age. Between approximately age 6 and 12, these teeth are replaced by **32 permanent teeth**. Moving from the center of the mouth toward the side, these are as follows:

- The eight **incisors**, four top and four bottom, are the sharp front teeth you use for biting into food.
- The four **cuspids** (or canines) flank the incisors and have a pointed edge (cusp) to tear up food. These fang-like teeth are superb for piercing tough or fleshy foods.

- Posterior to the cuspids are the eight **premolars** (or bicuspids), which have an overall flatter shape with two rounded cusps useful for mashing foods.
- The most posterior and largest are the 12 **molars**, which have several pointed cusps used to crush food so it is ready for swallowing. The third members of each set of three molars, top and bottom, are commonly referred to as the wisdom teeth, because their eruption is commonly delayed until early adulthood. It is not uncommon for wisdom teeth to fail to erupt; that is, they remain impacted. In these cases, the teeth are typically removed by orthodontic surgery.

Digestive Functions of the Mouth

Structure	Action	Outcome
Lips and cheeks	Confine food between teeth	Food is chewed evenly during mastication
Salivary glands	Secrete saliva	Moisten and lubricate the lining of the mouth and pharynx Moisten, soften, and dissolve food Clean the mouth and teeth Salivary amylase breaks down starch
Tongue's extrinsic muscles	Move tongue sideways, and in and out	Manipulate food for chewing Shape food into a bolus Manipulate food for swallowing
Tongue's intrinsic muscles	Change tongue shape	Manipulate food for swallowing
Taste buds	Sense food in mouth and sense taste	Nerve impulses from taste buds are conducted to salivary nuclei in the brain stem and then to salivary glands, stimulating saliva secretion

Lingual glands	Secrete lingual lipase	Activated in the stomach Break down triglycerides into fatty acids and diglycerides
Teeth	Shred and crush food	Break down solid food into smaller particles for deglutition

5. The Pharynx

The pharynx (throat) is involved in both digestion and respiration. It receives food and air from the mouth, and air from the nasal cavities. When food enters the pharynx, involuntary muscle contractions close off the air passageways.

A short tube of skeletal muscle lined with a mucous membrane, the pharynx runs from the posterior oral and nasal cavities to the opening of the esophagus and larynx. It has three subdivisions.

- The most superior, the nasopharynx, is involved only in breathing and speech.
- The other two subdivisions, the oropharynx and the laryngopharynx, are used for both breathing and digestion.
- The oropharynx begins inferior to the nasopharynx and is continuous below with the laryngopharynx. The inferior border of the laryngopharynx connects to the esophagus, whereas the anterior portion connects to the larynx, allowing air to flow into the bronchial tree.

Usually during swallowing, the soft palate and uvula rise reflexively to close off the entrance to the nasopharynx. At the same time, the larynx is pulled superiorly and the cartilaginous epiglottis, its most superior structure, folds inferiorly, covering the glottis (the opening to the larynx); this process effectively blocks access to the trachea and bronchi. When the food "goes down the wrong way," it goes into the trachea. When food enters the trachea, the reaction is to cough, which usually forces the food up and out of the trachea, and back into the pharynx.

6. The Esophagus

The esophagus is a muscular tube that connects the pharynx to the stomach. It is approximately 25.4 cm (10 in) in length, located posterior to the trachea, and remains in a collapsed form when not engaged in swallowing. The esophagus runs a mainly straight route through the mediastinum of the thorax. To enter the abdomen, the esophagus penetrates the diaphragm through an opening called the esophageal hiatus.

Passage of Food through the Esophagus

The upper esophageal sphincter, which is continuous with the inferior pharyngeal constrictor, controls the movement of food from the pharynx into the esophagus. Rhythmic waves of peristalsis, which begin in the upper esophagus, propel the bolus of food toward the stomach. Meanwhile, secretions from the esophageal mucosa lubricate the esophagus and food. Food passes from the esophagus into the stomach at the lower esophageal sphincter (also called the gastro esophageal or cardiac sphincter). The lower esophageal sphincter relaxes to let food pass into the stomach, and then contracts to prevent stomach acids from backing up into the esophagus.

Surrounding this sphincter is the muscular diaphragm, which helps close off the sphincter when no food is being swallowed.

When the lower esophageal sphincter does not completely close, the stomach's contents can reflux (that is, back up into the esophagus), causing heartburn or gastro esophageal reflux disease (GERD).

7. Stomach

Although a minimal amount of carbohydrate digestion occurs in the mouth, chemical digestion really gets underway in the stomach. The stomach plays several important roles in chemical digestion, including the continued digestion of carbohydrates and the initial digestion of proteins and triglycerides. The stomach has four major regions: the **cardia, fundus, body**, and **pylorus**. The addition of an inner oblique smooth muscle layer gives the muscularis the ability to vigorously churn and mix food.

The stomach wall is adapted for the functions of the stomach. In the epithelium, gastric pits lead to gastric glands that secrete gastric juice. The gastric glands contain different types of cells that secrete a variety of enzymes, including hydrochloride acid, which activates the protein-digesting enzyme **pepsin**.

The glands of the cardia and pylorus are composed primarily of mucus-secreting cells. Cells that make up the pyloric antrum secrete mucus and a number of hormones, including the majority of the stimulatory hormone, **gastrin**. The much larger glands of the fundus and body of the stomach, the site of most chemical digestion, produce most of the gastric secretions. These glands are made up of a variety of secretory cells. These include:

- **Parietal cells**—Located primarily in the middle region of the gastric glands are parietal cells, which are among the most highly differentiated of the body's epithelial cells. These relatively large cells produce both hydrochloric acid (HCl) and intrinsic factor. HCl is responsible for the high acidity (pH 1.5 to 3.5) of the stomach contents and is needed to activate the protein-digesting enzyme, pepsin. The acidity also kills much of the bacteria you ingest with food and helps to denature proteins, making them more available for enzymatic digestion. Intrinsic factor is a glycoprotein necessary for the absorption of vitamin B12 in the small intestine.
- **Chief cells**—Located primarily in the basal regions of gastric glands are chief cells, which secrete pepsinogen, the inactive proenzyme form of pepsin. HCl is necessary for the conversion of pepsinogen to pepsin.
- **Mucous neck cells**—Gastric glands in the upper part of the stomach contain mucous neck cells that secrete thin, acidic mucus that is much different from the mucus secreted by the goblet cells of the surface epithelium.
- **Enteroendocrine cells**—finally, enteroendocrine cells found in the gastric glands secrete various hormones into the interstitial fluid of the lamina propria. These include gastrin, which is released mainly by enteroendocrine G cells.

8. The Small Intestine

Chyme released from the stomach enters the small intestine, which is the primary digestive organ in the body. Not only is this where most digestion occurs, it is also where practically all absorption occurs. The coiled tube of the small intestine is subdivided into three regions. From proximal (at the stomach) to distal, these are the **duodenum, jejunum, and ileum.** The longest part of the alimentary canal, the small intestine is about 3.05 meters (10 feet) long in a living person (but about twice as long in a cadaver due to the loss of muscle tone). Since this makes it about five times longer than the large intestine, you might wonder why it is called "small."

In fact, its name derives from its relatively smaller diameter of only about 2.54 cm (1 in), compared with 7.62 cm (3 in) for the large intestine. In addition to its length, the folds and projections of the lining of the small intestine work to give it an enormous surface area, which is approximately $200m^2$, more than 100 times the surface area of your skin. This large surface area is necessary for complex processes of digestion and absorption that occur within it.

The wall of the small intestine is composed of the same four layers typically present in the alimentary system. However, three features of the mucosa and submucosa are unique. These features, which increase the absorptive surface area of the small intestine more than 600-fold, include **circular folds, villi, and microvilli.** These adaptations are most abundant in the proximal two-thirds of the small intestine, where the majority of absorption occurs.

9. The Large Intestine

The large intestine is the terminal part of the alimentary canal. The primary function of this organ is to finish absorption of nutrients and water, synthesize certain vitamins, form feces, and eliminate feces from the body. The large intestine is subdivided into four main regions**: the cecum, the colon, the rectum, and the anus.** The ileocecal valve, located at the opening between the ileum and the large intestine, controls the flow of chyme from the small intestine to the large intestine.

Absorption, Feces Formation, and Defecation

The small intestine absorbs about 90 percent of the water you ingest (either as liquid or within solid food). The large intestine absorbs most of the remaining water, a process that converts the liquid chyme residue into semisolid feces ("stool"). Feces is composed of undigested food residues, unabsorbed digested substances, millions of bacteria, old epithelial cells from the GI mucosa, inorganic salts, and enough water to let it pass smoothly out of the body. Of every 500mL (17 ounces) of food residue that enters the cecum each day, about 150mL (5 ounces) become feces.

Feces are eliminated through contractions of the rectal muscles. You help this process by a voluntary procedure called **Valsalva's maneuver**, in which you increase intra-abdominal pressure by contracting your diaphragm and abdominal wall muscles, and closing your glottis.

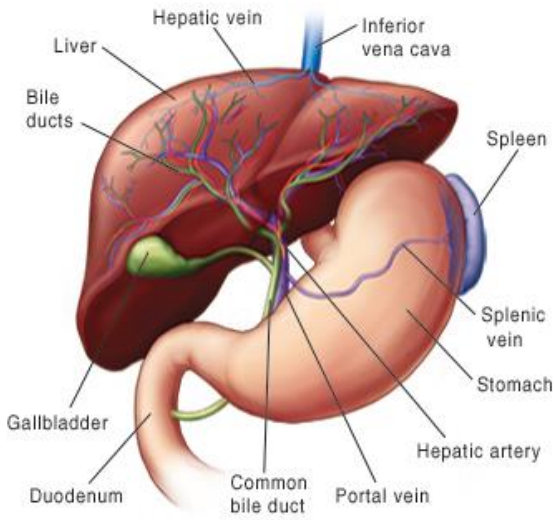
Accessory Structures

Each accessory digestive organ aids in the breakdown of food. Within the mouth, the teeth and tongue begin mechanical digestion, whereas the salivary glands begin chemical digestion. Once food products enter the small intestine, the gallbladder, liver, and pancreas release secretions—such as bile and enzymes—essential for digestion to continue. Together, these are called accessory organs because they sprout from the lining cells of the developing gut (mucosa) and augment its function; indeed, you could not live without their vital contributions, and many significant diseases result from their malfunction. Even after development is complete, they maintain a connection to the gut by way of ducts.

1. The Liver

The liver is the largest gland in the body, weighing about three pounds in an adult. It is also one of the most important organs. In addition to being an accessory digestive organ, it plays a number of roles in metabolism and regulation. The liver lies inferior to the diaphragm in the right upper quadrant of the abdominal cavity and receives protection from the surrounding ribs.

Bile is a mixture secreted by the liver to accomplish the emulsification of lipids in the small intestine. Hepatocytes secrete about one liter of bile each day. A yellow-brown or yellow-green alkaline solution (pH 7.6 to 8.6), bile is a mixture of water, bile salts, bile pigments, phospholipids (such as lecithin), electrolytes, cholesterol, and triglycerides. Bile salts act as emulsifying agents, so they are also important for the absorption of digested lipids. While most constituents of bile are eliminated in feces, bile salts are reclaimed by the enterohepatic circulation. Once bile salts reach the ileum, they are absorbed and returned to the liver in the hepatic portal blood. The hepatocytes then excrete the bile salts into newly formed bile. Thus, this precious resource is recycle**Bilirubin**, the main bile pigment, is a waste



product produced when the spleen removes old or damaged red blood cells from the circulation. These breakdown products, including proteins, iron, and toxic bilirubin, are transported to the liver via the splenic vein of the hepatic portal system. In the liver, proteins and iron are recycled, whereas bilirubin is excreted in the bile. It accounts for the green color of bile. Bilirubin is eventually transformed by intestinal bacteria into **stercobilin**, a brown pigment that gives your stool its characteristic color.

2. The Pancreas

The soft, oblong, glandular pancreas lies transversely in the retro peritoneum behind the stomach. Its head is nestled into the "c-shaped" curvature of the duodenum with the body extending to the left about 15.2 cm (6 in) and ending as a tapering tail in the hilum of the spleen. It is a curious mix of exocrine (secreting digestive enzymes) and endocrine (releasing hormones into the blood) functions.

Scattered through the sea of exocrine acini are small islands of endocrine cells, **the islets of Langerhans**. These vital cells produce the hormones pancreatic polypeptide, insulin, glucagon, and somatostatin.

Pancreatic Juice

The pancreas produces over a liter of pancreatic juice each day. Unlike bile, it is clear and composed mostly of water along with some salts, sodium bicarbonate, and several digestive enzymes. Sodium bicarbonate is responsible for the slight alkalinity of pancreatic juice (pH 7.1 to 8.2), which serves to buffer the acidic gastric juice in chyme, inactivate pepsin from the stomach, and create an optimal environment for the activity of pH-sensitive digestive enzymes in the small intestine. Usually, the pancreas secretes just enough bicarbonate to counterbalance the amount of HCl produced in the stomach. Regulation of pancreatic secretion is the job of hormones and the parasympathetic nervous system.

3. The Gallbladder

The gallbladder is 8–10 cm (~3–4 in) long and is nested in a shallow area on the posterior aspect of the right lobe of the liver. This muscular sac stores, concentrates, and, when stimulated, propels the bile into the duodenum via the common bile duct.

Chapter 5: Carbohydrates and their Importance

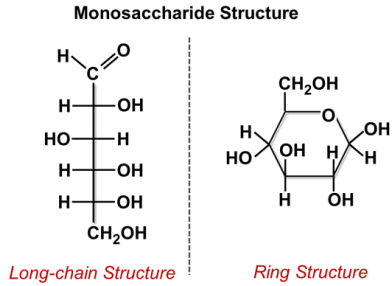
Carbohydrates contain carbon, hydrogen and oxygen in the ratio of $C_n:H_{2n}:O_n$. The family of carbohydrates includes both simple and complex sugars.

Monosaccharide (sugar molecule) is the basic unit of carbohydrates.

The classification of carbohydrates:

Dietary carbohydrates can be classified in two main groups:

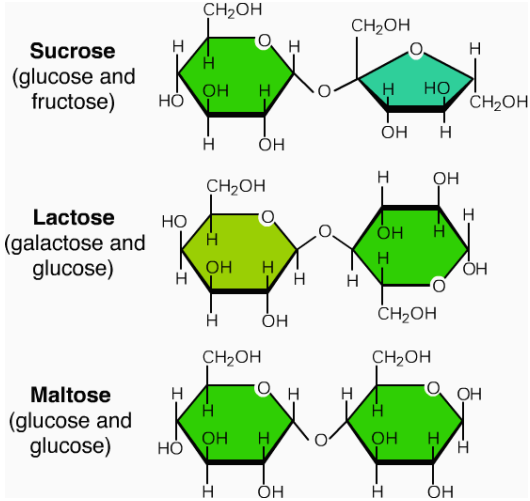
- Sugars
  - Monosaccharide
  - Disaccharide
  - Oligosaccharide
- Polysaccharides
  - Starch Polysaccharide
  - Non-starch polysaccharides



The simplest type of sugar is a monosaccharide – a single sugar unit.

Disaccharides are formed by condensation between two monosaccharides to form a glycoside bond.

Oligosaccharides are linked by glycoside bonds and consists of three or four monosaccharide units (trisaccharides and tetrasaccharides), and sometimes more.



The Functions of Carbohydrates in the Body:

There are five most important functions of carbohydrates in the human body. They are energy production, energy storage, building macromolecules, sparing protein and assisting in lipid metabolism.

Energy Production

The primary role of carbohydrates is to supply energy to all cells in the body. Many cells prefer glucose as a source of energy versus other compounds like fatty acids. About 70 percent of the glucose entering the body from digestion is redistributed (by the liver) back into the blood for use by other tissues. Cells that require energy remove the glucose from the blood with a transport protein in their membranes.

Energy Storage

If the body already has enough energy to support its functions, the excess glucose is stored as glycogen. The molecule of glycogen may contain in excess of fifty thousand single glucose units and is highly branched, allowing for the rapid dissemination of glucose when it is needed to make cellular energy

Building Macromolecules

Although most absorbed glucose is used to make energy, some glucose is converted to ribose and deoxyribose, which are essential building blocks of important macromolecules, such as RNA, DNA, and ATP. If all of the energy, glycogen-storing capacity, and building needs of the body are met, excess glucose can be used to make fat. This is why a diet too high in carbohydrates and calories can add on the fat pounds.

Sparing Protein

In a situation where there is not enough glucose to meet the body's needs, glucose is synthesized from amino acids. Because there is no storage molecule of amino acids, this process requires the destruction of proteins, primarily from muscle tissue. The presence of adequate glucose basically spares the breakdown of proteins from being used to make glucose needed by the body.

Lipid Metabolism

As blood-glucose levels rise, the use of lipids as an energy source is inhibited. Thus, glucose additionally has a “fat-sparing” effect. This is because an increase in blood glucose stimulates release of the hormone insulin, which tells cells to use glucose (instead of lipids) to make energy.

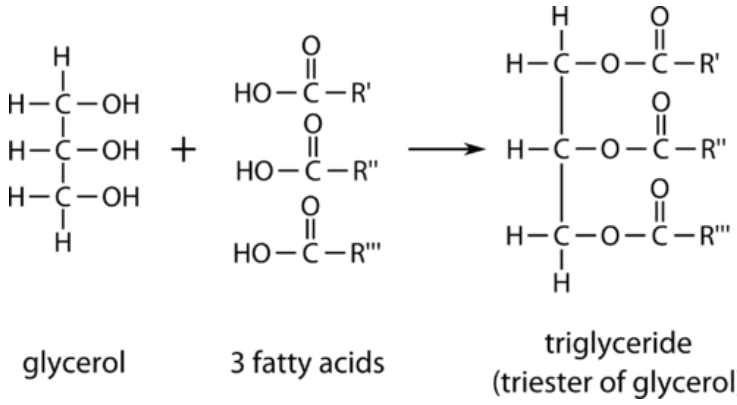
In addition, extreme amount of glucose turn into triglycerides at liver. It’s the reason of fatty liver during parenteral nutrition without lipid emulsion products.

Chapter 6: Lipids and their Role

Lipids are a family of organic compounds that are mostly insoluble in water. Composed of fats and oils, lipids are molecules that yield high energy and have a chemical composition mainly of carbon, hydrogen, and oxygen.

The three main types of lipids are triacylglycerol, phospholipids, and sterols.

- We commonly call the **triacylglycerol** in our food "fats" and "oils." Fats are lipids that are solid at room temperature, whereas oils are liquid.
- **Phospholipids** make up only about 2 percent of dietary lipids. They are water soluble and crucial for building the protective barrier, or membrane, around your body's cells. Phospholipids are synthesized in the body to form cell and organelle membranes. In blood and body fluids, phospholipids form structures in which fat is enclosed and transported throughout the bloodstream.
- **Sterols** are the least common type of lipid. Cholesterol is perhaps the best well known sterol. Though cholesterol has a notorious reputation, the body gets only a small amount of its cholesterol through food—the body produces most of it. Cholesterol is an important component of the cell membrane and is required for the synthesis of sex hormones, vitamin D, and bile salts.



Role of Lipids in Human Body:

Lipids perform three primary biological functions within the body:

- They serve as structural components of cell membranes
- Function as energy storehouses
- Function as important signaling molecules

Storing Energy

The excess energy from the food we eat is digested and incorporated into adipose tissue or fatty tissue. Most of the energy required by the human body is provided by carbohydrates and lipids. Fats are packed together tightly without water and store far greater amounts of energy in a reduced space. A fat gram is densely concentrated with energy—it contains more than double the amount of energy than a gram of carbohydrate. Fat cells are specialized for fat storage and are able to expand almost indefinitely in size. A serious impact of excess fat is the accumulation of too much cholesterol in the arterial wall, which can thicken the walls of arteries and lead to cardiovascular disease.

Regulating and Signaling

Triacylglycerol control the body's internal climate, maintaining constant temperature. Those who don't have enough fat in their bodies tend to feel cold sooner, are often fatigued, and have pressure sores on their skin from fatty acid deficiency. Triacylglycerol also help the body produce and regulate hormones. Lipids transport fat-soluble nutrients and phytochemicals and promote bioavailability of these compounds.

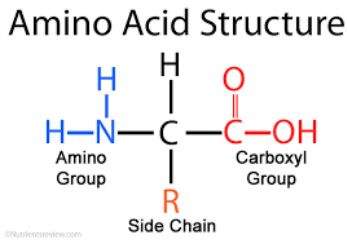
Essential fatty acids provide eicosanoids for regulating the inflammation etc.

Insulating and Protecting

The composition of the brain is outstandingly 60 percent fats, demonstrating the major structural role that fat serves within the body. You may be most familiar with subcutaneous fat, or fat underneath the skin. This blanket layer of tissue insulates the body from extreme temperatures and helps keep the internal climate under control. It pads our hands and buttocks and prevents friction, as these areas frequently come in contact with hard surfaces.

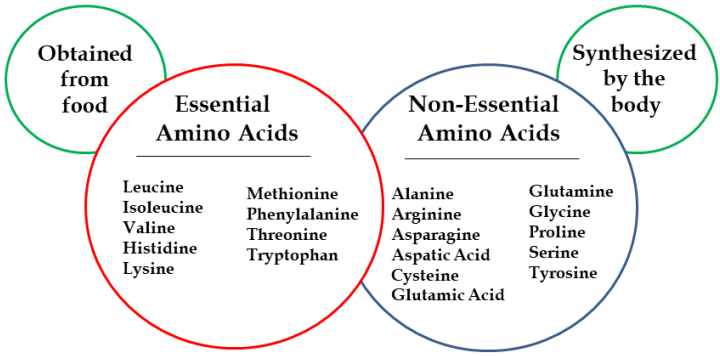
Chapter 7: Proteins in Nutrition

Proteins are called the workhorses of life as they provide the body with structure and perform a vast array of functions. Proteins are necessary for proper immune system function, digestion, and hair and nail growth, and are involved in numerous other body functions. Proteins are macromolecules composed of amino acids. Amino acids are commonly called protein's building blocks. They are simple monomers composed of the elements carbon, oxygen, hydrogen, and nitrogen.



Essential and Non-essential Amino Acids

Amino acids are further classified based on nutritional aspects. There are a total of 20 different amino acids. 11 amino acids are **Non-essential Amino acids** that can be manufactured by the body in sufficient quantities and therefore do not need to be consumed regularly in our diet. Whereas 9 of them are called **Essential Amino Acids** which are not produced by the body or not produced in sufficient amounts so that they must be obtained from food.



Under some conditions, a nonessential amino acid can become an essential amino acid. In this case, the amino acid is called a conditionally essential amino acid. Consider what occurs in the disease known as phenylketonuria (PKU).

Someone with PKU cannot metabolize phenylalanine (an essential amino acid). Normally, the body uses phenylalanine to produce the nonessential amino acid tyrosine, so the inability to metabolize phenylalanine results in failure to make tyrosine. If PKU is not diagnosed immediately after birth, it results in irreversible brain damage. In this situation, tyrosine becomes a conditionally essential amino acid that must be provided by the diet. Other conditionally essential amino acids include arginine, cysteine, and glutamine.

The Functions of Proteins in the Body:

Proteins are crucial for the nourishment, renewal, and continuance of life. Some of the numerous functions of proteins are:

Proteins Contribute to Cell Growth, Repair and Maintenance
The proteins in the body are dynamic, meaning that they are constantly being broken down, repaired, and replaced. When proteins are broken down, many amino acids are recycled into new proteins. The constant turnover of proteins from our diet is essential for such cell growth, repair, and maintenance.

Proteins Act as Enzymes and Hormones

Enzymes are small chemicals, usually proteins that speed up chemical reactions, without being changed by the chemical reaction themselves. Enzymes can act to bind substances together or break them apart and can transform one substance into another. Proteins act as enzymes. Enzymes facilitate chemical reactions such as joining two compounds together. **Hormones** are special chemical messengers in the body that are created in the endocrine glands. These messengers control most major bodily functions, from simple basic needs like hunger to complex systems like reproduction, and even the emotions and mood. Some hormones are made from amino acids, whereas others are made from lipids.

Proteins Help Maintain Fluid and Electrolyte Balance

Electrolytes are electrically charged particles that assist in maintaining fluid balance. Proteins attract fluids, and the proteins that are in the bloodstream, in the cells, and in the spaces surrounding the cells work together to keep fluids moving across these spaces in the proper quantities to maintain fluid balance and blood pressure. Conduction of nerve signals and contraction of muscles depend on a proper balance of electrolytes. If protein intake is deficient, we lose our ability to maintain these functions, resulting in potentially fatal changes in the rhythm of the heart.

Proteins Help Maintain Acid–Base Balance

The body's cellular processes result in the constant production of acids and bases. The human body maintains very tight control over the pH, or the acid–base balance of the blood. The body goes into a state called acidosis when the blood becomes too acidic. Alkalosis results if the blood becomes too basic. Proteins are excellent buffers, meaning they help maintain proper acid–base balance. By buffering acids and bases, proteins maintain acid–base balance and blood pH.

Proteins Help Maintain a Strong Immune System

Antibodies are special proteins that are critical components of the immune system. When a foreign substance attacks the body, the immune system produces antibodies to defend against it. Adequate protein is necessary to support the increased production of antibodies that occurs in response to a cold, flu, or allergic reaction. If we do not consume enough protein, our resistance to illnesses and disease is weakened.

Proteins Serve as an Energy Source

Proteins do not have a specialized storage form for energy. When proteins need to be used for energy, they are taken from the blood and body tissues such as the liver and skeletal muscle. Body proteins can be broken down and converted into glucose to provide needed energy to the brain.

Proteins Assist in the Transport and Storage of Nutrients

Proteins act as carriers for many important nutrients in the body. Lipoproteins contain lipids bound to proteins, which allows the transport of hydrophobic lipids through the watery medium of blood. Another example of a transport protein is transferrin, which carries iron in the blood. Ferritin,

in contrast, is an example of a storage protein: it is the compound in which iron is stored in the liver.

Recommended Dietary Allowance for Protein

The RDA for protein is **0.8 g** per kilogram of body weight per day. The RDA for protein for most non-pregnant, non-lactating, non-vegetarian adults is 0.8 g per kg body weight. Children, pregnant women, nursing mothers, vegetarians, and active people need slightly more. Good sources of protein include meats, eggs, dairy products, soy products, legumes, whole grains, and nuts.

Chapter 8: Vitamins, Minerals and Phytochemicals

Vitamins, minerals, and phytonutrients: your body needs them—perhaps more of them— for your good health. Today's nutrition breakthroughs focus less on cures and more on the roles of nutrients, phytonutrients, and other food components in health promotion and in protection from cancer, heart disease, and osteoporosis, among other health concerns.

Vitamins – are essential for normal metabolism, growth and development, and regulation of cell function. They work together with enzymes and other substances that are necessary for a healthy life. Vitamins are either fat-soluble or water-soluble. Fat soluble Vitamins can be stored in the fatty tissues in the body when in excess. Water soluble vitamins are excreted in urine when in excess and so need to be taken daily. Water soluble vitamins include Vitamin B and C. Green leafy vegetables are rich in Vitamin B, whereas Vitamin C is found abundantly in citrus fruits. Fat soluble vitamins are Vitamin A, D, E and K. Green leafy vegetables, milk and dairy products and plant oils provide these vitamins.

Fat-soluble Vitamins

Vitamin and alternative name	Sources	RDA	Function	Problems associated with deficiency
A retinal or β-carotene	Yellow and orange fruits and vegetables, dark green leafy vegetables, eggs, milk, liver	700–900 µg	Eye and bone development, immune function	Night blindness, epithelial changes, immune system deficiency
D cholecalciferol	Dairy products, egg yolks; also synthesized in the skin from exposure to sunlight	5–15 µg	Aids in calcium absorption, promoting bone growth	Rickets, bone pain, muscle weakness, increased risk of death from cardiovascular disease, cognitive impairment, asthma in children, cancer
E tocopherols	Seeds, nuts, vegetable oils, avocados, wheat germ	15 mg	Antioxidant	Abetalipoproteinemia an inherited disorder of fat metabolism that results in poor absorption of dietary fat and vitamin E.
K phylloquinone	Dark green leafy vegetables, broccoli, Brussels sprouts, cabbage	90–120 µg	Blood clotting, bone health	Hemorrhagic disease of newborn in infants; uncommon in adults

Water-soluble Vitamins

Vitamin and alternative name	Sources	Recommended daily allowanc	Function	Problems deficiency
B_1 thiamine	Whole grains, enriched bread and cereals, milk, meat	1.1–1.2 mg	Carbohydrate metabolism	Beriberi, Wernicke-Korsikoff syndrome
B_2 riboflavin	Brewer's yeast, almonds, milk, organ meats, legumes, enriched breads and cereals, broccoli, asparagus	1.1–1.3 mg	Synthesis of FAD for metabolism, production of red blood cells	Fatigue, slowed growth, digestive problems, light sensitivity, epithelial problems like cracks in the corners of the mouth
B_3 niacin	Meat, fish, poultry, enriched breads and cereals, peanuts	14–16 mg	Synthesis of NAD, nerve function, cholesterol production	Cracked, scaly skin; dementia; diarrhea; also known as pellagra
B_5 pantothenic acid	Meat, poultry, potatoes, oats, enriched breads and cereals, tomatoes	5 mg	Synthesis of coenzyme A in fatty acid metabolism	Rare: symptoms may include fatigue, insomnia, depression, irritability
B_6 pyridoxine	Potatoes, bananas, beans, seeds, nuts, meat, poultry, fish, eggs, dark green leafy vegetables, soy, organ meats	1.3–1.5 mg	Sodium and potassium balance, red blood cell synthesis, protein metabolism	Confusion, irritability, depression, mouth and tongue sores

B_7 biotin	Liver, fruits, meats	30 μg	Cell growth, metabolism of fatty acids, production of blood cells	Rare in developed countries; symptoms include dermatitis, hair loss, loss of muscular coordination
B_9 folic acid	Liver, legumes, dark green leafy vegetables, enriched breads and cereals, citrus fruits	400 μg	DNA/protein synthesis	Poor growth, gingivitis, appetite loss, shortness of breath, gastrointestinal problems, mental deficits
B_{12} cyano-cobalamin	Fish, meat, poultry, dairy products, eggs	2.4 μg	Fatty acid oxidation, nerve cell function, red blood cell production	Pernicious anemia, leading to nerve cell damage
C ascorbic acid	Citrus fruits, red berries, peppers, tomatoes, broccoli, dark green leafy vegetables	75–90 mg	Necessary to produce collagen for formation of connective tissue and teeth, and for wound healing	Dry hair, gingivitis, bleeding gums, dry and scaly skin, slow wound healing, easy bruising, compromised immunity; can lead to scurvy

Minerals – are found in ionized form in the body. They are further classified into macrominerals and microminerals (or trace minerals). Macrominerals present in the body include Calcium, Potassium, Iron, Sodium and Magnesium to name a few. Iron is a constituent of Hemoglobin which is present in blood. Macrominerals are needed in more amounts, as compared to microminerals. Microminerals include Copper, Zinc, Cobalt, Chromium and Fluoride. They are mostly co-factors, and are necessary for the function of enzymes in the body, but are needed only in minor quantities. Approximately 4% of the body's mass consists of minerals.

Major Minerals

Mineral	Sources	Recommended daily allowance	Function	Problems associated with deficiency
Potassium	Meats, some fish, fruits, vegetables, legumes, dairy products	4700 mg	Nerve and muscle function; acts as an electrolyte	Hypokalemia: weakness, fatigue, muscle cramping, gastrointestinal problems, cardiac problems
Sodium	Table salt, milk, beets, celery, processed foods	2300 mg	Blood pressure, blood volume, muscle and nerve function	hyponatremia
Calcium	Dairy products, dark green leafy vegetables, blackstrap molasses, nuts, brewer's yeast, some fish	1000 mg	Bone structure and health; nerve and muscle functions, especially cardiac function	Slow growth, weak and brittle bones

Phosphorous	Meat, milk	700 mg	Bone formation, metabolism, ATP production	Refeeding syndrome
Magnesium	Whole grains, nuts, leafy green vegetables	310–420 mg	Enzyme activation, production of energy, regulation of other nutrients	Agitation, anxiety, sleep problems, nausea and vomiting, abnormal heart rhythms, low blood pressure, muscular problems
Chloride	Most foods, salt, vegetables, especially seaweed, tomatoes, lettuce, celery, olives	2300 mg	Balance of body fluids, digestion	Loss of appetite, muscle cramps

Trace minerals: Your body needs just small amounts—fewer than 20 milligrams daily—for each of the trace minerals, or trace elements: chromium, copper, fluoride, iodine, iron, manganese, molybdenum, selenium, and zinc.

Phytochemicals- Besides nutrients, plant-based foods (legumes, vegetables, fruits, whole grains, nuts, seeds, and teas as well as herbs and spices) have another "crop" of naturally occurring compounds with potential health benefits. Collectively they're called phytonutrients, or phytochemicals, meaning plant chemicals.

Neither vitamins nor minerals, phytonutrients are substances that plants produce naturally to protect themselves against viruses, bacteria, and fungi, as well as insects, drought, and even the sun. Beyond that, they provide the color, aroma, texture, and flavor that give food so much sensual appeal.

Phytonutrients are bioactive compounds in food that promote your health by helping to slow the aging process or reducing the risk for many diseases. These are among the ways that phytonutrients might work:

- Serve as antioxidants
- Enhance immunity
- Enhance communication among body cells
- Cause cancer cells to die
- Detoxify carcinogens
- Repair damage to DNA that's caused by smoking and other toxins

FUNCTIONAL NUTRITION: A QUICK LOOK AT KEY PHYTONUTRIENTS

A HANDFUL OF PHYTONUTRIENTS	WHAT TH EY APPEAR TO DO	WHERE THEY'RE FOUND (SOME FOOD SOURCES)
Carotenoids Beta carotene	As an antioxidant, neutralizes free radicals that may damage cells Bolsters antioxidant defenses in cells	Yellow-orange fruits and vegetables such as apricots, cantaloupes, papayas, carrots, pumpkins, sweet potatoes, winter squash, Green vegetables such as broccoli, spinach, kale
Lutein	May contribute to maintaining healthy vision	Green vegetables such as kale, spinach, collard greens, Swiss chard, Romaine lettuce, broccoli, Brussels sprouts: 1. Kiwifruit 2. Egg yolks
Lycopene	May reduce risk of prostate cancer	Most red fruits and vegetables such as tomatoes, processed tomato products, pink grapefruit, guava, watermelon (The red pigment in red peppers is from keto carotenoids, not lycopene.)
Zeaxanthin	May contribute to maintaining healthy vision	Corn, spinach, winter squash, green vegetables, citrus fruits (Eggs have a small amount of zeaxanthin, too.)

Flavonoids Anthocyanidins	As an antioxidant, neutralizes free radicals that may damage cells May contribute to maintaining brain function May contribute to maintenance of healthy immune function	Blueberries, blackberries, cranberries, cherries, strawberries, kiwifruit, plums, red grapes, red cabbage, eggplant (skin)
Flavanols: catechins, epicatechins, procyanidins	May contribute to maintaining heart health	Apples, chocolate, cocoa,grapes, tea (black, oolong, or green), wine
Flavanones: hesperetin, naringenin	Neutralizes free radicals that may damage cells Bolsters antioxidant defenses in cells	Citrus fruit
Flavonols (quercetin)	Neutralize free radicals that may damage cells Bolster antioxidant defenses in cells	Apples, broccoli, onions, tea
Proanthocyanidins	May contribute to maintaining urinary tract health and heart health	Apples, cinnamon, cocoa, cranberries, grapes, peanuts, strawberries, wine
Resveratrol	May contribute to maintaining heart health Bolster antioxidant defenses in cells	Red grapes, red grape juice, red wine, peanuts
Isothiocyanates Sulphoraphane	As an antioxidant, neutralizes free radicals that may damage cells May aid in detoxification of undesirable compounds Bolsters antioxidant defenses in cells	Cruciferous vegetables, such as bok choy, broccoli, broccoli sprouts, cabbage, cauliflower, collard greens, kale, turnips, turnip greens
Phenols Caffeic acid, ferulic acid	May bolster cellular antioxidant defenses May contribute to maintaining healthy vision and heart health	Fruits, including apples, citrus, pears, some vegetables
Ellagic acid	Neutralize free radicals that may damage cells Bolster antioxidant defenses in cells	Berries, red grapes, kiwifruit
Polyols Sugar alcohols: lactitol, mannitol, sorbitol, xylitol	May reduce risk of dental caries	Some chewing gums Other food applications

Phytoestrogens Isoflavones: daidzein, genestein	May reduce menopause symptoms, such as hot flashes May contribute to maintenance of bone health May contribute to healthy brain function and immune function	Soybeans, soy-based foods
Lignans	May contribute to heart health and healthy immune function	Flaxseed (not flaxseed oil unless hull remains), rye, wheat bran, oatmeal, barley, vegetables
Phytic acid	May contribute to maintaining normal blood sugar levels and maintaining heart health Neutralizes free radicals that may damage cells Bolsters antioxidant defenses in cells	Cereal grains, nuts, seeds
Prebiotics and probiotics Inulin, fructo-oligosaccharides, polydextrose	May improve gastrointestinal health May improve calcium absorption	Whole grains, onions, some fruits, garlic, honey, leeks, fortified foods and beverages
Lactobacilli, bifidobacteria	May improve gastrointestinal health and systemic immunity	Yogurt, other dairy and nondairy applications
Soy protein Soy protein	May reduce risk for coronary heart disease (CHD)	Soybeans, soy-based foods
Sulfides/Thiols Allyl methyl trisulfide, diallyl sulfide	May help maintain heart health May help maintain a healthy immune system May aid in detoxification of undesirable compounds	Chives, garlic, onions, leeks, scallions
Dithiolthiones	Contributes to maintenance of healthy immune function	Cruciferous vegetables

Chapter: 9 Fluids and Electrolytes in Human Nutrition

Body Water Content

A human body is made up of mostly water. An adult consists of about 37 to 42 liters of water, or about eighty pounds. Newborns are approximately 70 percent water. Adult males typically are composed of about 60 percent water and females are about 55 percent water. Dehydration accelerates the aging process whereas keeping hydrated decreases headaches, muscle aches, and kidney stones.

Fluid and Electrolyte Balance

Although water makes up the largest percentage of body volume, it is not actually pure water but rather a mixture of cells, proteins, glucose, lipoproteins, electrolytes, and other substances. **Electrolytes** are substances that, when dissolved in water, disassociate into charged ions. Positively charged electrolytes are called cations and negatively charged electrolytes are called anions.

Solutes refers to all dissolved substances in a fluid, which may be charged, such as sodium (Na^+), or uncharged, such as glucose.

Fluid Compartments

Body fluids can be discussed in terms of their specific fluid compartment, a location that is largely separate from another compartment by some form of a physical barrier. In the human body, water and solutes are distributed into two compartments:

1. Intracellular Fluid (ICF) is the system that includes all fluid enclosed in cells by their plasma membranes. The ICF lies within cells and is the principal component of the cytosol/cytoplasm. It makes up about 60 percent of the total water in the human body.

2. Extracellular fluid (ECF) surrounds all cells in the body. The ECF accounts for the other one-third of the body's water content. Approximately 20 percent of the ECF is found in plasma.

The extracellular water compartment is subdivided into the spaces between cells (interstitial), blood plasma, and other bodily fluids (such as cerebrospinal fluid which surrounds and protects the brain and spinal cord).

Composition of Body Fluids

The compositions of the two components of the ECF (plasma and Interstitial Fluid) are more similar to each other than either is to the ICF. Blood plasma has high concentrations of sodium, chloride, bicarbonate, and protein. The IF has high concentrations of sodium, chloride, and bicarbonate, but a relatively lower concentration of protein. In contrast, the ICF has elevated amounts of potassium, phosphate, magnesium, and protein. Overall, the ICF contains high concentrations of potassium and phosphate (HPO4 2 −), whereas both plasma and the ECF contain high concentrations of sodium and chloride.

Movement between Compartments

One of the essential homeostatic functions of the body is to maintain fluid balance and the differences in solute composition between cells and their surrounding environment.

Osmoregulation is the control of fluid balance and composition in the body. The processes involved keep fluids from becoming too dilute or too concentrated. Fluid compartments are separated by selectively permeable membranes, which allow some things, such as water, to move through while other substances require special transport proteins, channels, and often energy. The movement of water between fluid compartments happens by **osmosis.**

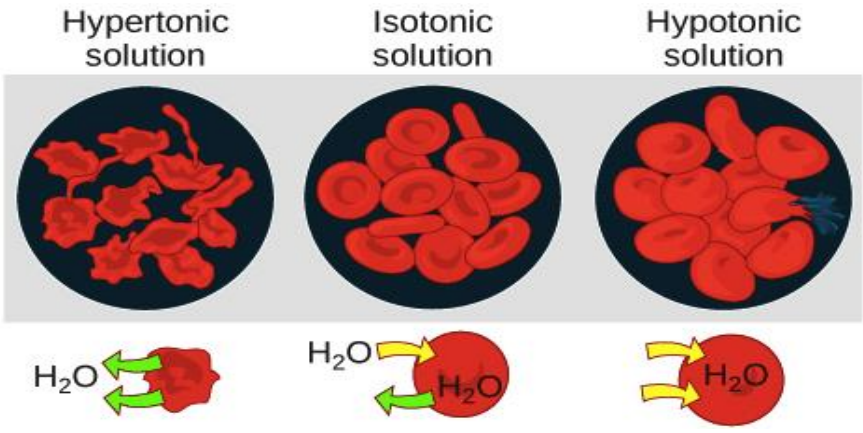
Tonicity

The ability of an extracellular solution to make water move into or out of a cell by osmosis is known as its **tonicity**. A solution's tonicity is related to its **Osmolarity**, which is the total concentration of all solutes in the solution.

- If the extracellular fluid has lower osmolarity than the fluid inside the cell, it’s said to be hypotonic—hypo means less than—to the cell, and the net flow of water will be into the cell.

- In the reverse case, if the extracellular fluid has a higher osmolarity than the cell's cytoplasm, it's said to be hypertonic—hyper means greater than—to the cell, and water will move out of the cell to the region of higher solute concentration.

- In an isotonic solution—iso means the same—the extracellular fluid has the same osmolarity as the cell, and there will be no net movement of water into or out of the cell.



Role of Electrolyte

The body contains a large variety of ions, or electrolytes, which perform a variety of functions. Some ions assist in the transmission of electrical impulses along cell membranes in neurons and muscles. Other ions help to stabilize protein structures in enzymes. In terms of body functioning, six electrolytes are most important: sodium, potassium, chloride, bicarbonate, calcium, and phosphate. These six ions aid in nerve excitability, endocrine secretion, membrane permeability, buffering body fluids, and controlling the movement of fluids between compartments.

1. Sodium

Sodium is the major cation of the extracellular fluid. It is responsible for one-half of the osmotic pressure gradient that exists between the interior of cells and their surrounding environment. The excess sodium appears to

be a major factor in hypertension (high blood pressure) in some people. Excretion of sodium is accomplished primarily by the kidneys. Sodium is freely filtered through the glomerular capillaries of the kidneys, and although much of the filtered sodium is reabsorbed in the proximal convoluted tubule, some remains in the filtrate and urine, and is normally excreted.

Electrolyte and Ion Reference Values

Name	Chemical symbol	Plasma	CSF	Urine
Sodium	Na^+	136.00–146.00 (mM)	138.00–150.00 (mM)	40.00–220.00 (mM)
Potassium	K^+	3.50–5.00 (mM)	0.35–3.5 (mM)	25.00–125.00 (mM)
Chloride	Cl^-	98.00–107.00 (mM)	118.00–132.00 (mM)	110.00–250.00 (mM)
Bicarbonate	HCO_3^-	22.00–29.00 (mM)	------	------
Calcium	Ca^{++}	2.15–2.55 (mmol/day)	------	Up to 7.49 (mmol/day)
Phosphate	HPO_4^{2-}	0.81–1.45 (mmol/day)	------	12.90–42.00 (mmol/day)

Hyponatremia is a lower-than-normal concentration of sodium, usually associated with excess water accumulation in the body, which dilutes the sodium. It is generally defined as a sodium concentration of less than 135 mmol/L (135 mEq/L), with severe hyponatremia being below 120 mEq/L. An absolute loss of sodium may be due to a decreased intake of the ion coupled with its continual excretion in the urine. An abnormal loss of sodium from the body can result from several conditions, including excessive sweating, vomiting, or diarrhea; the use of diuretics; excessive production of urine, which can occur in diabetes; and acidosis, either metabolic acidosis or diabetic ketoacidosis.

Hypernatremia is an abnormal increase of blood sodium a rise in serum sodium concentration to a value exceeding 145 mmol/L. It is strictly defined as a hyperosmolar condition caused by a decrease in total body water (TBW) relative to electrolyte content.. It can result from water loss from the blood, resulting in the hemoconcentration of all blood constituents. Hormonal imbalances involving ADH and aldosterone may also result in higher-than-normal sodium values.

Potassium Potassium is the major intracellular cation. It helps establish the resting membrane potential in neurons and muscle fibers after membrane depolarization and action potentials. In contrast to sodium, potassium has very little effect on osmotic pressure. The low levels of potassium in blood and CSF are due to the sodium-potassium pumps in cell membranes, which maintain the normal potassium concentration gradients between the ICF and ECF. The recommendation for daily intake/consumption of potassium is 4700 mg. Potassium is excreted, both actively and passively, through the renal tubules, especially the distal convoluted tubule and collecting ducts.

Hypokalemia is an abnormally low potassium blood level. Blood potassium level is 3.6 to 5.2 millimoles per liter (mmol/L). A very low potassium level (less than 2.5mmol/L) can be life-threatening and requires urgent medical attention. It can occur because of either an absolute reduction of potassium in the body or a relative reduction of potassium in the blood due to the redistribution of potassium. An absolute loss of potassium can arise from decreased intake, frequently related to starvation. It can also come about from vomiting, diarrhea, or alkalosis.

Hyperkalemia, an elevated potassium blood level, also can impair the function of skeletal muscles, the nervous system, and the heart. Blood potassium level is normally 3.6 to 5.2 millimoles per liter (mmol/L). Having a blood potassium level higher than 6.0 mmol/L can be dangerous and usually requires immediate treatment. Hyperkalemia can result from increased dietary intake of potassium. In such a situation, potassium from the blood ends up in the ECF in abnormally high concentrations. This can result in a partial depolarization (excitation) of the plasma membrane of skeletal muscle fibers, neurons, and cardiac cells of the heart, and can also lead to an inability of cells to repolarize. For the heart, this means that it won't relax after a contraction, and will effectively "seize" and stop pumping blood, which is fatal within minutes.

2. Chloride

Chloride is a major contributor to the osmotic pressure gradient between the ICF and ECF, and plays an important role in maintaining proper hydration. Chloride functions to balance cations in the ECF, maintaining the electrical neutrality of this fluid. The paths of secretion and reabsorption of

chloride ions in the renal system follow the paths of sodium ions. The normal serum range for chloride is 97 to 107 mEq/L.

Hypochloremia, or lower-than-normal blood chloride levels, can occur because of defective renal tubular absorption. Vomiting, diarrhea, and metabolic acidosis can also lead to Hypochloremia. **Hyperchloremia**, or higher-than-normal blood chloride levels, can occur due to dehydration, excessive intake of dietary salt (NaCl) or swallowing of sea water, aspirin intoxication, congestive heart failure, and the hereditary, chronic lung disease, cystic fibrosis.

3. Bicarbonate

Bicarbonate is the second most abundant anion in the blood. Its principal function is to maintain your body's acid-base balance by being part of buffer systems. Bicarbonate ions result from a chemical reaction that starts with carbon dioxide (CO_2) and water, two molecules that are produced at the end of aerobic metabolism. Only a small amount of CO_2 can be dissolved in body fluids. Thus, over 90 percent of the CO_2 is converted into bicarbonate ions, HCO_3 –, through the following reactions:

$$\mathbf{CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+}$$

The bidirectional arrows indicate that the reactions can go in either direction, depending on the concentrations of the reactants and products.

4. Calcium

About two pounds of calcium in your body are bound up in bone, which provides hardness to the bone and serves as a mineral reserve for calcium and its salts for the rest of the tissues. Teeth also have a high concentration of calcium within them. A little more than one-half of blood calcium is bound to proteins, leaving the rest in its ionized form. Calcium ions, Ca^{2+}, are necessary for muscle contraction, enzyme activity, and blood coagulation. In addition, calcium helps to stabilize cell membranes and is essential for the release of neurotransmitters from neurons and of hormones from endocrine glands. Calcium is absorbed through the intestines under the influence of activated vitamin D. A deficiency of vitamin D leads to a decrease in absorbed calcium and, eventually, a depletion of calcium stores from the skeletal system, potentially leading to

rickets in children and osteomalacia in adults, contributing to osteoporosis. The normal adult value for calcium is 4.5-5.5 mEq/L.

Hypocalcaemia, or abnormally low calcium blood levels, is seen in hypoparathyroidism, which may follow the removal of the thyroid gland, because the four nodules of the parathyroid gland are embedded in it. **Hypercalcaemia**, or abnormally high calcium blood levels, is seen in primary hyperparathyroidism.

5. Phosphate

Phosphate is present in the body in three ionic forms: H_2PO_{4-}, HPO_4^{2-}, and PO_4^{3-}. The most common form is HPO_4^{2-}. Bone and teeth bind up 85 percent of the body's phosphate as part of calcium-phosphate salts. Phosphate is found in phospholipids, such as those that make up the cell membrane, and in ATP, nucleotides, and buffers.

Hypophosphatemia, or abnormally low phosphate blood levels, occurs with heavy use of antacids, during alcohol withdrawal, and during malnourishment. In the face of phosphate depletion, the kidneys usually conserve phosphate, but during starvation, this conservation is impaired greatly.

Refeeding syndrome can be defined as the potentially fatal shifts in fluids and electrolytes that may occur in malnourished patients receiving artificial refeeding (whether enterally or parenterally). These shifts result from hormonal and metabolic changes and may cause serious clinical complications. The hallmark biochemical feature of refeeding syndrome is hypophosphataemia. However, the syndrome is complex and may also feature abnormal sodium and fluid balance; changes in glucose, protein, and fat metabolism; thiamine deficiency; hypokalaemia; and hypomagnesaemia.

In refeeding syndrome, chronic whole body depletion of phosphorus occurs. Also, the insulin surge causes a greatly increased uptake and use of phosphate in the cells. These changes lead to a deficit in intracellular as well as extracellular phosphorus. In this environment, even small decreases in serum phosphorus may lead to widespread dysfunction of cellular processes affecting almost every physiological system

Hyperphosphatemia, or abnormally increased levels of phosphates in the blood, occurs if there is decreased renal function or in cases of acute lymphocytic leukemia. Additionally, because phosphate is a major constituent of the ICF, any significant destruction of cells can result in dumping of phosphate into the ECF.

Chapter 10: Malnutrition Revisited

For many, the word "**malnutrition**" produces an image of a child in a third-world country with a bloated belly, and skinny arms and legs. However, this image alone is not an accurate representation of the state of malnutrition.

Malnutrition refers to one not receiving proper nutrition and does not distinguish between the consequences of too many nutrients or the lack of nutrients, both of which impair overall health. **Undernutrition** is characterized by a lack of nutrients and insufficient energy supply, whereas **overnutrition** is characterized by excessive nutrient and energy intake. Overnutrition can result in **obesity**, a growing global health threat. Obesity is defined as a metabolic disorder that leads to an over accumulation of fat tissue.

A person living in a food-insecure household may suffer from malnutrition, which results from a failure to meet nutrient requirements. This can occur as a result of consuming too little food or not enough key nutrients. There are two basic types of malnutrition. The first is macronutrient deficiency and relates to the lack of adequate protein, which is required for cell growth, maintenance, and repair. The second type of malnutrition is micronutrient deficiency and relates to inadequate vitamin and mineral intake.

Who is at Risk?

Worldwide, the groups those are most at risk of hunger:

- **The rural poor** in developing nations who also lack access to electricity and safe drinking water.
- **The urban poor** who live in expanding cities and lack the means to buy food.
- **The victims** of earthquakes, hurricanes, and other natural and man-made catastrophes.
- **Senior citizens** are also a major at-risk group. Many elderly people are frail and isolated, which affects their ability to meet their dietary requirements.
- One of the groups that struggle with hunger is the millions of **homeless people** across North America. Hunger and homelessness often go

hand-in hand as homeless families and adults turn to soup kitchens or food pantries or resort to begging for food.

- In **Children** hunger delays growth and development and affects their educational progress because it is more difficult for hungry or malnourished students to concentrate in school. In addition, children who are undernourished are more susceptible to contracting diseases, such as measles and pneumonia.

Function, Deficiency, Efficiency, and Toxicity of Vitamins and Trace Elements			
	Function/Source/Comments	**Deficiency State**	**Toxicity**
Fat-Soluble Vitamins			
Vitamin A	• Sources: carrots and dark-green leafy vegetables • Group of compounds called retinoids • Integral component of rhodopsin and iodopsins, lightsensitive proteins in retinal rod and cone cells • Essential for vision, growth, cellular differentiation and proliferation, reproduction, and the integrity of the immune system • Patients (pts) at risk of deficiency: GI dysfunction—diarrhea or fat malabsorption Chronic alcoholics Impaired vitamin A transport—protein or zinc deficiency increase needs or losses—burns, major trauma or surgery, fever, or infection	• Night blindness* • Follicular • hyperkeratosis* • Xerosis or xerophthalmia • Irreversible corneal lesions • Anorexia • Immunodepression • Metaplasia of respiratory, GI, GU epithelial cells * Early signs of vitamin A deficiency	• Acute (>150,000 mcg) Increased intracranial pressure Headache Nausea/vomiting Vertigo Blurred vision Muscular incoordination • Chronic (>30,000 mcg/d) Bone malformations and fractures Dermatitis Alopecia Ataxia Muscle pain Cheilitis Membrane dryness Skin disorders and pruritus Vision disorders Pseudotumor cerebri/HA Hepatocellular necrosis Hyperlipidemia Inhibits vitamin K • Early pregnancy (>7800 mcg/d)—teratogenic with spontaneous abortions, birth defects, and learning disabilities
Vitamin D	• Sources (2 forms): Vitamin D2 (ergocalciferol)—consumed in diet (eggs, butter, and fortified milk and margarine) Vitamin D3 (cholecalciferol)—synthesized in skin	• Childhood—rickets that result in deformation of the skeleton • Adults—osteomalacia and osteopenia that can result in fractures • Hypocalcemia	• Hypercalcemia—anorexia, nausea, vomiting, headache, weakness, fatigue, diarrhea, confusion, psychosis, tremor • Hypercalcinuria—renal stones

	during exposure to solar or artificial ultraviolet light • Requires hydroxylation in the liver to 25-OH-D followed by hydroxylation in the kidneys to its active form of 1,25-(OH)2-D • Maintains intra- and extracellular calcium and phosphorous levels by enhancing GI absorption and promoting mobilization from bone mineral • Also involved with growth and maturation of other cells, including immune and hematopoietic cells • Pts at risk for deficiency: Elderly or very young with inadequate oral intake of vitamin D Pts with regional enteritis (Crohn's disease), celiac disease, cystic fibrosis, cholestatic liver disease, pancreatic insufficiency, gastric resection, or jejunoileal bypass surgery Pts with liver dysfunction or renal failure Certain drugs—anticonvulsants, cimetidine, isoniazid	• Bone pain and tenderness • Hypophosphatemia	• Metastatic calcifications with irreversible renal damage, altered mentation, and cardiovascular damage

Vitamin E	• Sources: vegetable oils (olive, soy, and corn oils, including margarine and shortening), wheat germ, nuts, green leafy vegetables, sunflower and cotton seeds • Group of compounds called tocopherols • Antioxidant and free radical scavenger • Found in cell membranes of all tissues throughout the body and protects the cells from free radical formation from oxidation reactions • Pts at risk for deficiency: Pts with prolonged steatorrhea, pancreatitis, cystic fibrosis, short bowel syndrome, or cholestasis Premature infants and infants with severe malnutrition, liver dysfunction, or abetalipoproteinemia Pts with mechanical ventilation and on high oxygen concentration Pts supplemented with ω-3 fatty acids	• Hemolytic anemia (only significant in infants) • Increased platelet aggregation • Axonal neuropathy involving peripheral nerves, posterior column fibers, and gracillus nuclei causing ataxia and weakness • Causes retinal dysfunction, resulting in tunnel vision • Decreased serum creatinine due to excessive urinary losses • Skeletal lesions similar to muscular dystrophy	• Very uncommon even with large doses (3200 International Units/d) • Liver impairment with depressed levels of vitamin K–dependent coagulation factors potentiating bleeding if pt has a coagulopathy or is on oral anticoagulants and can increase incidence of hemorrhagic stroke in these situations • Impaired leukocyte function • Preterm infants may be more susceptible to liver damage
Vitamin K	• Sources (2 forms): Vitamin K_1 (phylloquinone)—oral intake with green leafy vegetables with smaller amounts in milk, dairy products, meats, eggs, cereal, fruits, and other vegetables Vitamin K_2 (menaquinone)—synthesized by gut bacterial flora in colon but poorly absorbed • Functions in the	• Coagulopathy with excessive bleeding Fetal intracranial hemorrhage Easy bruisability Mucosal bleeding Splinter hemorrhages Melena Hematuria • Rare in healthy adults • Common in newborns due to	• Rare • Rapid IV infusion can cause anaphylactoid reaction with dyspnea, flushing, and cardiovascular collapse Pregnant woman taking large dose of vitamin K may deliver infants with hemolytic anemia, hyperbilirubinemia, and kernicterus

	posttranslational γ-carboxylation of the clotting factors II (prothrombin), VII, IX, and X as well as proteins C and S, all of which are vital in the clotting cascade and normal blood clotting • Required for the synthesis of other proteins in the plasma, bone, and kidney • Pts at risk for deficiency: Breast-fed newborns Pts with malabsorption syndromes, cystic fibrosis, tropical sprue, celiac disease, ulcerative colitis, regional enteritis (Crohn's disease), or short bowel syndrome Pts with cholestasis, biliary obstruction, liver disease, or renal failure Pts on certain medications such as large doses of salicylates, broad-spectrum antibiotics, megadoses of vitamin A and E, cholestyramine Pts on long-term PN	immature liver, low vitamin K in breast milk, sterile gut, and poor placental transfer of vitamin K • Fetal skeletal deformities (chondrodysplasia)	
Water-Soluble Vitamins			
Thiamin [also spelled thiamine] (vitamin B1)	• Sources: enriched and fortified grains, cereals, and bakery products; organ meats (liver, kidney, and heart); lean cuts of pork; legumes; and seeds/nuts • Coenzyme required for oxidative decarboxylation of α-keto acids (eg, pyruvate → coenzyme A [CoA] to link glycolysis to Krebs cycle and the	• Dry beriberi—causes peripheral neuropathy resulting in paresthesias, anesthesia, and weakness, mostly of the lower extremities • Hypothermia • Wet beriberi—causes cardiovascular symptoms such as cardiomyopathy, edema, tachycardia,	• Rare • Easily cleared from the kidney so toxicities are rare and have never been reported from oral thiamine alone • No toxicity reported

	conversion of α-ketoglutarate → succinyl CoA within the Krebs cycle) and for the activity of transketolase in the pentose phosphate pathway • Inadequate thiamin availability results in inadequate ATP synthesis and abnormal carbohydrate metabolism • High carbohydrate intake increases thiamin requirements • Pts at risk for deficiency: Underdeveloped countries—thiamin-poor diets or diets containing thiamin antagonists Alcoholics Refeeding syndrome PN without thiamine supplementation Pts with ñ needs—fever, infection, trauma, burns, hyperparathyroidism, pregnancy, lactation, strenuous exertion, adolescent growth Pts with ñ losses—dialysis, diuresis, malabsorption, prolonged antacid tx	dyspnea, hepatomegaly, oliguria, metabolic lactic acidosis • Wernicke-Korsakoff syndrome Wernicke's disease—ophthalmoplegia, nystagmus, and ataxia Korsakoff psychosis—shortterm memory loss and confabulation but otherwise normal cognition	

Riboflavin (vitamin B2)	• Sources: enriched and fortified grains, cereals, and bakery products; meats; poultry; fish; and dairy products • Component of 2 flavin coenzymes Flavin mononucleotide (FMN) Flavin adenine dinucleotide (FAD) Catalyzes many oxidative-reduction reactions in the body such as the conversion of tryptophan to niacin and functions in xanthine oxidase, succinic dehydrogenase, and glutathione reductase oxidative enzyme systems • Essential for proper functioning of vitamin B_6 and niacin • Pts at risk for deficiency: Pts with malabsorption (celiac disease, short bowel syndrome, etc), thyroid dysfunction, diabetes, or alcoholism Pregnancy and lactation Pts with surgery, trauma, burns, or fractures Pts on psychotropic drugs, tricyclic antidepressants, or barbiturates Pts with anorexia nervosa or who avoid dairy products	• Oral-buccal lesions such as cheilosis, glossitis, and angular stomatitis • Seborrheic dermatitis Scrotal and vaginal skin changes • Ocular disturbances such as itching, burning, dryness, corneal inflammation, and photophobia • Normochromic, normocytic anemia • Frequently accompanied by vitamin B_6 and niacin deficiency with their associated symptoms	• No toxicity reported

Niacin (vitamin B3)	• Sources: meat and tryptophan-containing foods such as milk and eggs (niacin is unique among vitamins in that it can be formed in the body from dietary tryptophan) • Niacin includes nicotinic acid and nicotinamide • Nicotinamide functions in 2 coenzyme systems, NAD and NADP • These coenzymes are present in all cells and are essential in many metabolic processes, including glycolysis, fatty acid metabolism, and tissue respiration • Pts at risk for deficiency: Pts with malabsorption, thyroid dysfunction, cancer, burns, or alcoholism Pts on isoniazid therapy for tuberculosis Pts with carcinoid syndrome (tryptophan is metabolized to 5-OH tryptophan and serotonin instead of nicotinic acid) Hartnup's disease—autosomal recessive congenital disorder that interferes with absorption of tryptophan	• Pellagra—"4 Ds" Dermatitis (also, glossitis, stomatitis, vaginitis) Diarrhea (also vomiting) Dementia—headaches, dizziness, insomnia, irritability, depression, disorientation, delusions, catatonia Death • Seen also in carcinoid syndrome in which tryptophan is diverted to other synthetic pathways	• Nicotinamide has no reported toxicity • Nicotinic acid in high doses (3–9 g/d) can cause: Flushing Nausea and vomiting Liver toxicity Blurred vision Impaired glucose tolerance

Pantothenic acid (vitamin B5)	• Sources: meat, whole grain cereals, and legumes • Component of CoA (involved in gluconeogenesis, synthesis of heme and sterols, and release of energy from carbohydrate, fat, and ketogenic amino acids) and acyl carrier protein (necessary for fat synthesis) • Pts at risk for deficiency: Chronically malnourished Alcoholics	• Rare and usually in combination with other vitamin B deficiencies • Growth retardation • Infertility • Abortion and neonatal death • Listlessness and fatigue Abnormalities of skin and hair • Abdominal pain, vomiting, and diarrhea • Impaired mentation and insomnia • Paresthesias • Poor wound healing • Increased susceptibility to infection • Adrenal cortical failure • Sudden death	• Rare High doses (10–20 g/d) have been reported to cause diarrhea and fluid retention

Vitamin B6	• Sources: chicken, fish, kidney, liver, pork, eggs, rice, soy beans, oats, whole wheat, peanuts, and walnuts • Comprises 3 forms: pyridoxine, pyridoxal, and pyridoxamine • Liver, erythrocytes, and other tissues convert these forms into pyridoxal phosphate and pyridoxamine phosphate, which are essential coenzymes in transamination and decarboxylation reactions • These reactions are important in the transformation of certain amino acids and in the metabolism of lipids and nucleic acid, as well as conversion of tryptophan to niacin • These coenzymes are also essential for glycogen phosphorylase • Pts at risk for deficiency: Usually seen in conjunction with other B vitamin deficiencies Certain medications inhibit vitamin B_6 metabolism such as isoniazid, cycloserine, penicillamine, ethanol, and theophylline	• Usually accompanies deficiencies of other B vitamins • Stomatitis, angular cheilosis, and glossitis • Irritability, depression, and confusion • Convulsions • Dermatitis • Normochromic, normocytic, sideroblastic anemia • In infants, various neurologic symptoms and abdominal distress	• Acute toxicity is rare • However, if taken in high doses for a prolonged period of time (treatment of PMS or certain mental disorders), it can cause ataxia, peripheral neuropathies, and severe sensory neuropathy with photosensitivity

Vitamin B12 (cobalamin)	• Sources: fish, eggs, and milk • Must be converted to one of its coenzyme forms, methylcobalamin or 5'-deoxyadenosylcobalamin • Adequate absorption depends on: Dietary intake Acid-pepsin in stomach to liberate B_{12} from food sources Pancreatic proteases to free B_{12} from binding with R factors Secretion of IF by gastric parietal cells to bind to B_{12} Ileal B_{12}-IF receptors • Functions: Coenzyme that shifts hydrogen atoms from one carbon to another (eg, converts methylmalonyl CoA to succinyl CoA, which is vital in lipid and carbohydrate metabolism) Coenzymes that transfer methyl groups (eg, convert methyl folate back to tetrahydrofolic acid [THFA], the metabolically active form of folic acid, which has numerous functions, including synthesis of thymidylate and DNA) Coenzymes also convert homocysteine to methionine, which is needed to myelin formation for nerves • Pts at risk for deficiency: Total vegetarians decrease absorption—	• Megaloblastic anemia • Peripheral nerve, spinal cord, and/or cerebral damage Peripheral neuropathy (paresthesias of the hands and feet) Impaired vibration and position sense Unsteadiness Confusion Depression Impaired mentation and memory Delusion Psychosis Visional disturbances • Leukopenia • Thrombocytopenia	• No toxicity reported

	pernicious anemia, total gastrectomy, tropical sprue, celiac disease, resection of terminal ileum, gastric bypass surgery, intestinal parasites increase requirements—pregnancy, lactation, infancy, hyperthyroidism, alcoholism, megadoses of vitamin C Pts on ethanol, neomycin, colchicine, potassium, aminosalicylic acid, metformin, proton pump inhibitors		

Folate	• Sources: liver, yeast, leafy vegetables, legumes, some fruits (as much as 50% of folate in food destroyed with cooking) • Folate and folacin are generic descriptors for compounds that have nutrition properties and chemical structures similar to those of folic acid (pteroylglutamate, PTE-Glu_n) • Folic acid must be converted to its active form, THFA • Functions as coenzymes that transport single carbon fragments from one compound to another in amino acid metabolism and synthesis of purines and pyrimidines, which are essential in DNA • Deficiency leads to impaired cell division and alterations in protein synthesis • Pts at risk for deficiency: Chronic alcoholics Malabsorption—celiac disease, inflammatory bowel disease, and short bowel syndrome increase cell division/metabolism—trauma, burns, infections, cancer, chronic hemolytic anemia, hyperthyroidism, pregnancy, lactation, and early infancy	• Megaloblastic anemia • Neural tube defects (anencephaly and spina bifida) in newborns of mothers not taking folate supplement • Glossitis • Diarrhea • Weight loss • Impaired cell-mediated immunity • Dementia	• Folic acid and the anticonvulsant phenytoin inhibit uptake of each other in the GI tract and possibly at the brain cell membrane, so large doses of folic acid (>400 mcg) can precipitate seizures in epileptics on phenytoin
Vitamin C (ascorbic acid)	• Sources: fruits (especially citrus fruits) and vegetables with smaller amounts in meat, fish, poultry, eggs,	• Mild deficiency Anorexia Fatigue Muscle pain Increased	• Rare • Doses >500 mg/d can cause nausea and diarrhea • Withdrawal from high

	and dairy products • Antioxidant and free radical scavenger • Necessary for: Collagen synthesis via hydroxylation of proline and lysine Carnitine biosynthesis and neurotransmitter synthesis and metabolism Enhanced intestinal absorption of nonheme iron Hepatic microsomal hydroxylation of cholesterol required for its excretion in bile acids Reduction of toxic transition metals Reductive protection of folic acid and vitamin E Immune-mediated and antibacterial functions of white blood cells • Pts at risk for deficiency: Smokers Pregnancy and lactation Pts with major surgeries, trauma, burns, cancer Pts on PN	susceptibility to stress and infection • Severe deficiency Scurvy Weakening of the collagenous structures (bone cartilage, teeth, and connective tissue) Bleeding gums Petechiae and ecchymosis Perifollicular hemorrhage Impaired wound healing Anemia Joint effusions with arthralgia Fatigue Depression	chronic doses should be gradual to avoid "rebound scurvy" • Pts with renal failure, kidney stones, or iron overload disease should avoid large doses of vitamin C • Large amounts of vitamin C can cause falsepositive fecal occult blood and glycosuria testing and may hinder heparin or coumarin anticoagulation therapy

Biotin	• Sources: liver, egg yolk, soy flour, cereals, and yeast • Sulfur-containing water-soluble vitamin, which can also be synthesized by intestinal bacteria • Magnesium and ATP required for conversion of biotin to its active coenzymes • Biotin functions as a component of 4 enzymes that transport carboxyl units to various substrates as follows: acetyl CoA carboxylase (required for fatty acid synthesis), pyruvate carboxylase (required for gluconeogenesis), propionyl CoA carboxylase (for propionate metabolism), and 3-methylcrotonyl CoA carboxylase (required for catabolism of branched-chain amino acids) • Pts at risk for deficiency: Avidin, a biotin-binding glycoprotein, is found only in raw eggs and consumption of large amounts of raw eggs can cause biotin deficiency Pregnancy and lactation Alcoholics Pts with partial or total gastrectomy or burns	• Dry scaly dermatitis • Anorexia • Pallor • Glossitis • Nausea and vomiting • Impaired mentation • Hyperesthesias • Muscle pain • Hair loss • Elevated serum cholesterol and bile pigments	• No toxicity reported
Trace Elements			

Chromium	• Sources: chromium value of many foods unknown but yeast, calf's liver, American cheese, and wheat germ have high bioavailability of chromium • Enhances the ability of insulin to bind to insulin receptors on the cell surface and thereby participates in metabolism of carbohydrates, protein, and fat • Pts at risk of deficiency: Burns, trauma, short bowel syndrome PN pts without chromium supplementation	• Very rare and only reported in 3 long-term PN patients • Hyperglycemia and glucosuria refractory to insulin • Peripheral neuropathy • Encephalopathy • Hyperlipidemia	• No toxicity reported from dietary chromium • Toxic levels of airborne chromium Allergic dermatitis Skin ulcers Bronchogenic carcinoma
Copper	• Sources: liver, seafood (especially shellfish), nuts, legumes, and seeds • Incorporated into metalloenzymes that are involved with connective tissue formation; metabolism of iron (ceruloplasmin), cholesterol, and glucose; myelin synthesis; conversion of dopamine to norepinephrine in the brain, serotonin synthesis, melanin pigment formation; and antioxidant participating in the immune system • Pts at risk of deficiency: Low birth weight infants PN pts without copper supplementation Chronic peritoneal dialysis	• Hypochromic, microcytic anemia • Neutropenia • Osteopenia • Depigmentation of skin and hair • Skeletal abnormalities • Neurologic abnormalities	• Acute (rare): nausea, vomiting, diarrhea, epigastric abdominal pain, coma, oliguria, acute renal failure, hepatic necrosis, vascular collapse, and death • Chronic: accumulates in liver (hepatic necrosis and cirrhosis), kidneys (renal failure), brain (neurologic disorders), and corneas • Wilson's disease—hereditary condition of copper toxicity

Fluoride	• Sources: fluorinated water and tea • Assists in enamel formation of teeth and helps avoids caries, especially during maximal tooth formation (first 8 years of life); however, older children and adults continue to benefit from consumption of fluoridated water • Pts at risk of deficiency: Infants and children who drink non-fluoridated water	• Contributes to dental caries	• Acute, high dose (5–10 g)—death • Chronic (years of 20–80 mg/d)—mottling of teeth, calcification of tendons and ligaments, exostoses, and increased brittleness of bones
Iodine	• Sources: seafood, iodized table salt, and certain baked breads and dairy products • Essential nutrient that is incorporated into thyroid hormones, thyroxine (T4) and tri-iodothyronine (T3), which modulate resting energy expenditure and are important in growth and development	• Newborns—spontaneous abortions, stillbirths, congenital abnormalities, hypothyroidism, dwarfism, deafness and severe mental retardation (cretinism), increased perinatal and infant mortality • Adults—thyroid goiter and hypothyroidism, impaired mentation	• Chronic ingestion of large quantities can lead to hypothyroidism with goiter or hyperthyroidism
Iron	• Sources: meat, eggs, vegetables, fortified cereals • Forms of iron in body Present in hemoglobin (60% of iron in body) Myoglobin (4% of iron in body) Iron-containing enzymes (5%–15% of iron in body) Remaining iron is as storage iron (hemosidum) in liver, spleen, bone marrow,	• Most common nutrient deficiency in U.S. • Microcytic, hypochromic anemia (causing tachycardia, fatigue, pallor, and altered mental and motor development) • Glossitis • Impaired temperature regulation in the cold	• Hemosiderosis or siderosis—excessive total body iron that accumulates in iron stores and RE system, little consequence • Hemochromatosis • Hereditary or acquired (chronic hemosiderosis) • Classic triad Cirrhosis Diabetes mellitus Hyperpigmentation

	and circulating iron bound to carrier protein transferrin • Ionic forms of iron: Ferric (Fe3+) Ferrous (Fe2+) • Functions: Involved in transport and storage of oxygen by its incorporation in hemoglobin and myoglobin Incorporated into nonheme metalloenzymes that are involved in energy release from oxidative phosphorylation and ATP generation; detoxifying drugs, carcinogens, and pesticides; biosynthesis of aldosterone, glucocorticoids, and sex hormones; and synthesis of DNA, unsaturated fatty acids, carnitine, collagen, and neurotransmitters • Lab tests—serum iron, serum ferritin, TIBC, transferrin saturation • Pts at risk for deficiency: Growing children Women in childbearing ages Chronic blood loss	• Decreased resistance to infection	(gray tinge) of the skin Other Fatigue Testicular atrophy and sterility Arthropathy Cardiac arrhythmias Hypothyroidism
Manganese	• Sources: whole grains and cereals and, to a lesser extent, fruits and vegetables • Incorporated into metalloenzymes involved with energy release, fatty acid and cholesterol synthesis,	• Deficiency states not well documented but some reports of dermatitis and hypocholesterolemia	• Neurotoxicity (primarily associated with oversupply associated with chronic PN)

	and release of lipids from the liver		
Molybdenum	• Sources: milk, beans, breads, and cereals • Incorporated into several enzymes, including aldehyde oxidase, xanthine oxidase, and sulfite oxidase • Pts at risk for deficiency: Deficient in copper intake or have dysfunction in copper metabolism	• Deficiency rare but was reported in a long-term PN patient causing amino acid intolerance, irritability, visual field defects, coma; patient also noted to have hypermethioninemia, increased urinary excretion of xanthine and sulfite, and decreased serum uric acid	• Excess of 10–15 g/d can cause gout-like syndrome with elevated serum molybdenum, uric acid, and xanthine oxidase • Even moderate doses of molybdenum can cause increased urinary excretion of copper and possible copper deficiency
Selenium	• Sources: seafood, kidney, liver and some meats Incorporated at the active site of glutathione peroxidase, an enzyme that catalyzes the breakdown of hydroperoxides and has metabolic interrelationships with vitamin E, an antioxidant • Participates in enzymatic conversion of thyroxine to its more active metabolite, tri-iodothyronine • Cofactor for protein and DNA synthesis	• Deficiency state not well characterized but in 3 longterm PN patients with low serum selenium levels, muscular discomfort or weakness • Cardiomyopathy has also occurred in PN patients with low selenium levels • Anemia	• Garlic smell to breath (from ñ production of dimethylselenide in body and release from the lungs) • Nausea and vomiting • Abdominal pain • Loss of hair and nails • Tenderness and loss of fingernails • Diarrhea • Peripheral neuropathy • Fatigue • Irritability and altered mental status

Zinc	• Sources: meat, liver, eggs, and seafood (especially oysters) • Essential nutrient participating in multiple metalloenzyme involving zinc in most central metabolic pathways, including metabolism of protein, fat, and carbohydrates; DNA binding; gene regulation; transcription of DNA to RNA; synthesis of heme, long-chain fatty acids, and prostaglandins; cholesterol transport; stabilization of cell membrane lipids; sexual maturation and reproduction; and immune function • Pts at risk for deficiency: Chronic PN without zinc supplementation Pts with severe diarrhea, inflammatory bowel disease, malabsorptive disorders, pregnancy, starvation, alcoholic cirrhosis, diabetes mellitus	• Alopecia • Skin rash of face, groins, hands, and feet • Growth retardation • Delayed sexual development • Impaired wound healing and immune function • Diarrhea • Blunting of taste and smell	• Acute (>200 mg orally): Epigastric abdominal pain Nausea and vomiting Diarrhea • Chronic (>20 mg/d orally) Decreased serum copper levels (hypocupremia) Microcytosis and neutropenia Reduced HDL cholesterol Impaired immune function

ATP, adenosine triphosphate; CoA, coenzyme A; GI, gastrointestinal; GU, genitourinary; HA, headache; HDL, high-density lipoprotein; IF, intrinsic factor; IV, intravenous; NAD, nicotinamide adenine dinucleotide; NADP, nicotinamide adenine dinucleotide phosphate; PMS, premenstrual syndrome; PN, parenteral nutrition; Pts, patients; RE, reticuloendothelial; THFA, tetrahydrofolic acid; TIBC, total iron binding capacity; tx, treatment.

Chapter 11: Nutrition and Energy Metabolism

Certain micronutrients we consume in our diet assist us in generating energy from the carbohydrates, lipids, and proteins we eat along with them. Although vitamins and minerals do not contain calories and thus do not directly provide energy, the body is unable to generate energy from the macronutrients without them. The B-vitamins are particularly important in assisting energy metabolism and include thiamin, riboflavin, vitamin B_6, niacin, folate, vitamin B_{12}, pantothenic acid, and biotin. Except for vitamin B_{12}, these water-soluble vitamins need to be consumed regularly, because the body has no storage reservoir for them. Conversely, excess amounts of these vitamins, either from food or supplementation, are easily lost in the urine.

The primary role of the B-vitamins is to act as coenzymes in a number of metabolic processes. A coenzyme is a molecule that combines with an enzyme to activate it and help it do its job. Six of them (thiamin, riboflavin, vitamin B_6, niacin, pantothenic acid, and biotin) function primarily in energy metabolism, whereas the other two (folate and vitamin B_{12}) function primarily in cell regeneration and the synthesis of red blood cells.

Some Micronutrients Assist with Nutrient Transport and Hormone Production

Some micronutrients promote energy metabolism by facilitating the transport of nutrients into the cells. For instance, the mineral chromium helps improve glucose uptake into cells. Other micronutrients assist in the production of hormones that regulate metabolic processes; the mineral iodine, for example, is necessary for synthesis of thyroid hormones, which regulate our metabolic rate and promote growth and development.

A Profile of Nutrients Involved in Energy Metabolism

The primary function of the B-vitamins, except for folate and B_{12}, is to facilitate the production of energy in the body. Other nutrients involved in energy metabolism include a vitamin-like substance called choline and the minerals iodine, chromium, manganese, and sulfur.

1. Thiamin (Vitamin B_1)

Thiamin was the first B-vitamin discovered, hence its designation as vitamin B1.

Functions: Thiamin is required for the formation of its coenzyme thiamin pyrophosphate, or TPP. Dietary thiamin is converted to TPP by the body. Thiamin is important in a number of energy-producing metabolic pathways within the body. As a part of TPP, thiamin plays a critical role in the breakdown of glucose for energy. Thus, when dietary thiamin is inadequate, the body's ability to metabolize carbohydrate is diminished.

Another primary role of TPP is to act as a coenzyme in the metabolism of the branched-chain amino acids, which include leucine, isoleucine, and valine. TPP is a coenzyme for two α-keto acid dehydrogenase complexes. One of these enzyme complexes helps convert the carbon skeletons of the branched-chain amino acids into products that can enter the TCA cycle. The highest concentrations of the branched-chain amino acids are found in the muscle, where they make up approximately 25% of the content of the average protein. Thus, these amino acids play a significant role in providing fuel for the working muscle, especially during high-intensity exercise.

TPP also assists in the production of DNA and RNA, making it important for cell regeneration and protein synthesis. Finally, it plays a role in the synthesis of neurotransmitters— chemicals that transmit messages throughout the central nervous system.

Nutrient	Recommended Intake
Thiamin (Vitamin B_1)	RDA for 19 years and older: Women = 1.1 mg/day Men = 1.2 mg/day
Riboflavin (Vitamin B_2)	RDA for 19 years and older: Women = 1.1 mg/day Men = 1.3 mg/day
Niacin (Nicotinamide and nicotinic acid)	RDA for 19 years and older: Women = 14 mg/day Men = 16 mg/day
Pyridoxidine (Vitamin B_6)	RDA for 19 to 50 years of age: Women and men = 1.3 mg/day RDA for 51 years and older: Women = 1.5 mg/day Men = 1.7 mg/day
Folate (folic acid)	RDA for 19 years and older: Women and men = 400 µg/day
Vitamin B_{12} (Cobalamin)	RDA for 19 years and older: Women and men = 2.4 µg/day
Pantothenic acid	AI for 19 years and older: Women and men = 5 mg/day
Biotin	AI for 19 years and older: Women and men = 30 µg/day
Choline	AI for 19 years and older: Women = 425 mg/day Men = 550 mg/day

Food Sources: Sunflower seeds, beans, oat bran, mixed dishes that contain whole or enriched grains and meat, tuna fish, soy milk, and soy-based meat substitutes are good sources of thiamin. Enriched and wholegrain foods, including fortified ready-to-eat cereals, are rich in several B-vitamins, including thiamin.

Deficiency:

The thiamin-deficiency disease is called **beriberi.** In this disease, the body's inability to metabolize energy leads to muscle wasting and nerve damage; in later stages, patients may be unable to move at all. The heart muscle may also be affected, and the patient may die of heart failure.

Thiamin deficiency is also seen in industrialized countries in people with chronic heavy alcohol consumption and limited food intake. This alcohol-related thiamin deficiency is called **Wernicke–Korsakoff syndrome.**

Lactic acidosis, the most common kind of metabolic acidosis, is characterized by reduced blood pH (usually <7.25) in association with marked increase in blood lactate (usually >5.0 mmol/L). Lactic acidosis has many possible causes but two broad etiological classes have been defined: type A (hypoxic) lactic acidosis and type B (non-hypoxic) lactic acidosis.

Of the two, type A lactic acidosis, i.e. lactic acidosis arising from reduced tissue perfusion and/or severe hypoxemia, is the more common. In the absence of an adequate oxygen supply, tissue cells must depend on less efficient anaerobic metabolism of glucose for its energy production, and this alternative metabolic pathway results in accumulation of lactic acid.

Type B lactic acidosis (i.e. lactic acidosis in the presence of adequate tissue perfusion and normal blood oxygenation) has many possible causes, including a range of medicinal drugs, liver failure, renal disease, diabetic ketoacidosis, hematological malignancy, and some inherited defects of metabolism.

Deficiency of vitamin B1 (thiamine) is a very rare cause of type B lactic acidosis that is highlighted in two recently published papers. The mechanism of lactic acidosis in vitamin B1 deficiency is explained by the fact that thiamine is an essential co-factor for the enzyme pyruvate dehydrogenase that allows oxidation of pyruvate to acetyl CoA.

This is a key step in the process that allows energy production, in the form of ATP, from glucose oxidation. In the absence of thiamine this reaction cannot proceed and instead, pyruvate is converted to lactate. The resulting accumulation of lactate causes lactic acidosis.

Thiamine deficiency may cause unspecific neurologic symptoms. Glucose administration or feeding may aggravate depletion. Thiamine deficiency is an underdiagnosed cause of lactic acidosis, although treatment is safe, inexpensive, and readily available. Current guidelines on parenteral nutrition recommend a daily intravenous dose of 100 to 300 mg of thiamine during the first 3 days in the intensive care unit when deficiency is a possibility (grade B). In conclusion, although its clinical significance has been known for decades, thiamine deficiency remains an under-recognized condition. Intensivists should have an increased awareness of this problem and a low threshold to infuse high-dose thiamine. Future prospective studies to define the optimal dose and duration of treatment are warranted.

2. Riboflavin (Vitamin B_2)

Riboflavin was the second B-vitamin discovered, thus, its designation as vitamin B_2.

Function: Riboflavin is an important component of two coenzymes that are involved in oxidation– reduction reactions occurring within the energy-producing metabolic pathways, including the electron transport chain. These coenzymes, flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD) are involved in the metabolism of carbohydrates, fatty acids, and amino acids for energy.

Food Sources: In addition to dairy products, foods considered good sources of riboflavin include eggs, meats, including organ meats; broccoli, enriched bread and grain products, and ready to- eat cereals. Milk is a good source of riboflavin and is stored in opaque containers to prevent the destruction of riboflavin by light.

Deficiency:

Riboflavin deficiency is referred to as **ariboflavinosis**. Symptoms of ariboflavinosis include sore throat; swelling of the mucous membranes in the mouth and throat; lips that are dry and scaly; a purple-colored tongue; and inflamed, irritated patches on the skin. Severe riboflavin deficiency can impair the metabolism of vitamin B6 (or pyridoxine) and niacin.

3. Niacin

Niacin is a generic name for two specific vitamin compounds, nicotinic acid and nicotinamide. Niacin was first established as an essential nutrient in the treatment of pellagra in 1937.

Function: The two forms of niacin, nicotinic acid and nicotinamide, are essential for the formation of the two coenzymes nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP). These coenzymes, like those formed from riboflavin and thiamin, are required for the oxidation–reduction reactions involved in the catabolism of carbohydrate, fat, and protein for energy.

Food Sources: Good food sources of niacin include meat, fish, poultry, enriched bread products, and ready-to-eat cereals; however, the availability of this niacin for absorption differs.

Deficiency:

Pellagra is a disease that results from severe niacin deficiency. Initial symptoms of pellagra include functional changes in the gastrointestinal tract that decrease the amount of HCl produced and the absorption of nutrients, and lesions in the central nervous system causing weakness, fatigue, and anorexia. These initial symptoms are followed by what have been identified as the classic “three Ds”—dermatitis, diarrhea, and dementia. The name pellagra literally means “rough skin”.

4. Vitamin B_6 (Pyridoxine)

Vitamin B_6 is actually a group of three related compounds: pyridoxine (PN), pyridoxal (PL), pyridoxamine (PM), and their phosphate forms.

Function: In the form of PLP, vitamin B_6 is a coenzyme for more than 100 enzymes involved in the metabolism of amino acids. It plays a critical role in transamination, which is the key process in making nonessential amino

acids; without adequate vitamin B_6, all amino acids become essential, as the body cannot make them in sufficient quantities.

Vitamin B_6 is also essential for gluconeogenesis and assists in several steps of glucose metabolism.

Vitamin B6 is also important, along with folate and vitamin B_{12}, for the metabolism of the amino acid homocysteine. It also plays a role in the synthesis of hemoglobin and in oxygen transport.

Food Sources: Good sources of vitamin B6 include meat, fish (especially tuna), poultry, and organ meats, which are also high in protein. Thus, protein and vitamin B_6 are provided together in the same food, which ensures adequate protein metabolism.

Deficiency:

If we don't get enough vitamin B_6 in the diet, the symptoms of vitamin B_6 deficiency can develop. These include anemia, convulsions, depression, confusion, and inflamed, irritated patches on the skin. Notice that the symptoms associated with vitamin B_6 deficiency involve three tissues: skin, blood, and nervous system.

5. Pantothenic acid

It is an essential vitamin that is metabolized into two major coenzymes: coenzyme A (CoA) and acyl carrier protein (ACP).

Function: Both of these are essential in the synthesis of fatty acids, while CoA is essential for fatty acid oxidation, ketone metabolism, and the metabolism of carbohydrate and protein.

Food Sources: Pantothenic acid is available from a variety of foods, including chicken, beef, egg yolk, potatoes, oat cereals, tomato products, whole grains, and organ meats.

Deficiency:

There are no known adverse effects from consuming excess amounts of pantothenic acid, and deficiencies of pantothenic acid are very rare.

6. Biotin

Biotin is a component of four carboxylase enzymes that are present in humans. These enzymes serve as the CO_2 (carbon dioxide) carrier and the carboxyl donor for substrates.

Function: The enzymes that require biotin as a coenzyme are involved in fatty acid synthesis (for example, lipogenesis), gluconeogenesis, and carbohydrate, fat, and protein metabolism.

Food Sources: The biotin content has been determined for very few foods, and these values are not reported in food composition tables or dietary analysis programs. In food, biotin exists as free biotin or bound to protein as biocytin, both of which appear to be widespread in foods.

Deficiency:

Biotin deficiencies are typically seen only in people who consume a large number of raw egg whites over long periods of time. This is because raw egg whites contain a protein that binds with biotin and prevents its absorption. Biotin deficiencies are also seen in people fed total parenteral nutrition (nutrients administered by a route other than the GI tract) that is not supplemented with biotin. Symptoms include thinning of hair; loss of hair color; development of a red, scaly rash around the eyes, nose, and mouth; depression; lethargy; and hallucinations.

7. Choline

Choline is a vitamin-like substance that is important for metabolism, the structural integrity of cell membranes, and neurotransmission. It is typically grouped with the B-vitamins because of its role in fat digestion and transport and homocysteine metabolism.

Function: Choline plays an important role in the metabolism and transport of fats and cholesterol. High amounts of the choline-containing compound phosphatidylcholine are found in bile, which aids fat digestion, and in the formation of lipoproteins, which transport endogenous and dietary fat and cholesterol in the blood to the cells.

Choline accelerates the synthesis and release of acetylcholine, a neurotransmitter that is involved in many functions, including muscle movement and memory storage.

Food Sources: Foods that are high in choline include milk, liver, eggs, and peanuts. Lecithin (another term for phosphatidylcholine) is added to foods during processing as an emulsifying agent, which also increases choline intakes in the diet.

Deficiency:

Inadequate intakes of choline can lead to increased fat accumulation in the liver, which eventually leads to liver damage.

8. Iodine:

Iodine is the heaviest trace element required for human health and a necessary component of the thyroid hormones, which help regulate human metabolism.

Function: Iodine is responsible for a single function within the body: the synthesis of thyroid hormones. Thyroid hormones regulate key metabolic reactions associated with body temperature, resting metabolic rate, macronutrient metabolism, and reproduction and growth.

Food Sources: Good food sources include saltwater fish, shrimp, seaweed, iodized salt, and white and whole-wheat breads made with iodized salt and bread conditioners. In addition, iodine is added to dairy cattle feed and used in sanitizing solutions in the dairy industry, making dairy foods an important source of iodine.

Deficiency:

A number of deficiency disorders are associated with low iodine intakes. Paradoxically, **goiter** is also the most classic disorder of iodine deficiency. An insufficient supply of iodine means there is less iodine for the production of thyroid hormones. The body responds by stimulating the thyroid gland, including increasing the size of the gland, in an attempt to capture more iodine from the blood.

If a woman experiences iodine deficiency during pregnancy, her infant has a high risk of being born with a unique form of mental retardation referred to as **cretinism**. In addition to mental retardation, these infants may suffer from stunted growth, deafness, and muteness.

Iodine deficiency can also cause **hypothyroidism** (low blood levels of thyroid hormone), which is characterized by decreased body temperature, inability to tolerate cold environmental temperatures, weight gain, fatigue, and sluggishness.

9. Chromium

Chromium is a trace mineral that plays an important role in carbohydrate metabolism.

Function: Chromium enhances the ability of insulin to transport glucose from the bloodstream into cells. Chromium also plays important roles in the metabolism of RNA and DNA, in immune function, and in growth.

Food Sources: Foods identified as good sources of chromium include mushrooms, prunes, dark chocolate, nuts, whole grains, cereals, asparagus, brewer's yeast, some beers, red wine, and meats, especially processed meats. Dairy products are typically poor sources of chromium.

Deficiency: When chromium deficiency is induced in a research setting, glucose uptake into the cells is inhibited, causing a rise in blood glucose and insulin levels. Chromium deficiency can also result in elevated blood lipid levels and in damage to the brain and nervous system.

10. Manganese

A trace mineral, manganese is a cofactor involved in protein, fat, and carbohydrate metabolism, gluconeogenesis, cholesterol synthesis, and the formation of urea, the primary component of urine.

Function: It assists in the synthesis of the protein matrix found in bone tissue and in building cartilage, a tissue supporting joints. Manganese is also an integral component of superoxide dismutase, an antioxidant enzyme. Thus, it assists in the conversion of free radicals to less damaging substances, protecting the body from oxidative damage.

Food Sources: Whole-grain foods such as oat bran, wheat flour, whole-wheat spaghetti, and brown rice are good sources of manganese. Other sources include pineapple, pine nuts, okra, spinach, and raspberries. Overall, grain products contribute approximately 37% of dietary manganese, and vegetables and beverages, primarily tea, contribute another 18% to 20%.

Deficiency: Manganese deficiency is rare in humans. Symptoms include impaired growth and reproductive function, reduced bone density and impaired skeletal growth, impaired glucose and lipid metabolism, and skin rash.

11. Sulfur

Sulfur is a major mineral and a component of the B-vitamins thiamin and biotin. As such, it is essential for macronutrient metabolism.

Function: As part of the amino acids methionine and cysteine, sulfur helps stabilize the three-dimensional shapes of proteins in the body. The liver requires sulfur to assist in the detoxification of alcohol and various drugs, and sulfur assists in maintaining acid–base balance.

Food Sources: The body is able to obtain ample sulfur from protein-containing foods; as a result, there is no DRI specifically for sulfur.

Deficiency: There are no known toxicity or deficiency symptoms associated with sulfur.

Section II: Nutrition and Lifecycle

According to the American Journal of Clinical Nutrition, the human life span, or the maximum length of time possible for human life, is 130 years. Human bodies change significantly over time, and food is the fuel for those changes. People of all ages need the same basic nutrients—essential amino acids, carbohydrates, essential fatty acids, and twenty-eight vitamins and minerals—to sustain life and health.

Throughout the human life cycle, the body constantly changes and goes through different periods known as stages. The major stages of the human life cycle are defined as follows:

- **Pregnancy-** The development of a zygote into an embryo and then into a fetus in preparation for childbirth.
- **Infancy**-The earliest part of childhood. It is the period from birth through age one.
- **Toddler years-** Occur during ages two and three and are the end of early childhood.
- **Childhood-** Takes place from age four to eight.
- **Puberty-** The period from ages nine to thirteen, which is the beginning of adolescence.
- **Older adolescence**- The stage that takes place between ages fourteen and eighteen.
- **Adulthood-** The period from adolescence to the end of life and begins at age nineteen.
- **Middle age-** The period of adulthood that stretches from age thirty-one to fifty.
- **Senior years, or old age**- Extend from age fifty-one until the end of life.

Changing Needs and Nutrition

Nutritional needs continue to change at each stage of life. It is important to adjust your diet and physical activity to meet these changing needs and ensure health and wellness throughout your life. Parents must continue to help their school-aged children and adolescents establish healthy eating

habits and attitudes toward food. Their primary role is to bring a wide variety of health-promoting foods into the home, so that their children can make good choices. As children become adults, they must be mindful of the choices they make and how those choices affect their health, not only in the present but also in the future.

Chapter 12: Nutrition in Pregnancy

At no stage of life is nutrition more crucial than during fetal development and infancy. From conception through the end of the first year of life, adequate nutrition is essential for tissue formation, neurologic development, and bone growth, modeling, and remodeling. The ability to reach peak physical and intellectual potential in adult life is in part determined by the nutrition received during fetal development and the first year of life.

Why Is Nutrition Important During Pregnancy?

A balanced, nourishing diet throughout pregnancy provides the nutrients needed to support fetal growth and development without depriving the mother of nutrients she needs to maintain her own health. It also minimizes the risks of excess energy intake.

- **First Trimester:** The first trimester (approximately weeks 1 through 13) begins when the ovum and sperm unite to form a single, fertilized cell called a **zygote**. Not only alcohol and illegal drugs but also prescription and over-the-counter medications, mega doses of supplements such as vitamin A, certain herbs, viruses, cigarette smoking, and radiation can interfere with embryonic development and cause birth defects. Because the formation of body limbs, eyes and ears, and organs occurs during the first trimester, nutrient deficiencies during this time can lead to irreversible structural or functional damage. During the first trimester, a pregnant woman has the same energy requirements as normal and should consume the same number of calories as usual—about 1,800 calories for a woman living a sedentary lifestyle, about 2,000 calories for a woman who is moderately active, and about 2,200 for a woman who is active. However, as the pregnancy progresses, a woman must increase her caloric intake.

- **Second Trimester:** During the second trimester (approximately weeks 14 to 27 of pregnancy), the fetus continues to grow and mature. In this phase, a pregnant woman should consume an additional 340 calories per day.

- **Third Trimester:** The third trimester (approximately weeks 28 to birth) is a time of remarkable growth for the fetus. Because of the intense growth and maturation of the fetus during the third trimester, it continues to be critical that the mother eat an adequate and balanced diet. An additional 450 calories per day should be consumed during the third trimester.
- Pregnant women must consume more calories and nutrients in the second and third trimesters than other adult women. However, the average recommended daily caloric intake can vary depending on activity level and the mother's normal weight. Also, pregnant women should choose a high-quality, diverse diet, consume fresh foods, and prepare nutrient-rich meals. Steaming is the best way to cook vegetables. Vitamins are destroyed by overcooking, whereas uncooked vegetables and fruits have the highest vitamin content. It is also standard for pregnant women to take prenatal supplements to ensure adequate intake of the needed micronutrients.

Carbohydrates- The recommended daily allowance, or RDA, of carbohydrates during pregnancy is about 175 to 265 grams per day to fuel fetal brain development. They also help to build the placenta and supply energy for the growth of the unborn baby.

Protein- During pregnancy, extra protein is needed for the synthesis of new maternal and fetal tissues. Protein builds muscle and other tissues, enzymes, antibodies, and hormones in both the mother and the unborn baby. Additional protein also supports increased blood volume and the production of amniotic fluid. The RDA of protein during pregnancy is 71 grams per day.

Fat- There are no specific recommendations for fats in pregnancy, apart from following normal dietary guidelines. Fats should make up 25 to 35 percent of daily calories, and those calories should come from healthy fats. Also, it is not recommended for pregnant women to be on a very low-fat diet, since it would be hard to meet the needs of essential fatty acids and fat-soluble vitamins. Fatty acids are important during pregnancy because they support the baby's brain and eye development. Fats can also help the placenta grow and may help to prevent premature birth and low birth weight.

Fiber- Ideally, a pregnant woman should eat 25 to 30 grams of dietary fiber per day. There are two types of fiber, and pregnant women should consume both.

Fluids- Fluid intake must also be monitored. Pregnant women should drink 2.3 liters (about 10 cups) of liquids per day to provide enough fluid for blood production. The combination of a high-fiber diet and lots of liquids also helps to eliminate waste.

Vitamins and Minerals- Pregnancy requires certain conditionally essential nutrients, which are nutrients that are supplied only under special conditions, such as stress, illness, or aging. The daily requirements for non-pregnant women change with the onset of a pregnancy. Taking a daily prenatal supplement or multivitamin helps to meet many nutritional needs. However, most of these requirements should be fulfilled with a healthy diet.

The micronutrients involved with building the skeleton—vitamin D, calcium, phosphorus, and magnesium—are crucial during pregnancy to support fetal bone development.

Chapter 13: Nutrition in Children

1. Infancy (Birth to Age one)

Healthy infants grow steadily, but not always at an even pace. Requirements for macronutrients and micronutrients on a per-kilogram basis are higher during infancy than at any other stage in the human life cycle. These needs are affected by the rapid cell division that occurs during growth, which requires energy and protein, along with the nutrients that are involved in DNA synthesis. Energy needs relative to size are much greater in an infant than an adult. A baby's resting metabolic rate is two times that of an adult.

The dietary recommendations for infants are based on the nutritional content of human breast milk. Carbohydrates make up about 45 to 65 percent of the caloric content in breast milk, which amounts to a RDA of about 130 grams. Almost all of the carbohydrate in human milk is lactose, which infants digest and tolerate well. In fact, lactose intolerance is practically nonexistent in infants. Protein makes up about 5 to 20 percent of the caloric content of breast milk, which amounts to 13 grams per day. About 30 to 40 percent of the caloric content in breast milk is made up of fat. A high-fat diet is necessary to encourage the development of neural pathways in the brain and other parts of the body.

Human milk is low in vitamin D, which is needed for calcium absorption and building bone, among other things. Therefore, breastfed children often need to take a vitamin D supplement in the form of drops. Breast milk is also low in vitamin K, which is required for blood clotting, and deficits could lead to bleeding or hemorrhagic disease. Babies are born with limited vitamin K, so supplementation may be needed. Also, breast milk is not high in iron, but the iron in breast milk is well absorbed by infants.

2. The Toddler Years (Ages Two to Three)

During this phase of human development, children are mobile and grow more slowly than infants, but are much more active. However, with the proper diet and guidance, toddlers can continue to grow and develop at a healthy rate. A toddler's serving sizes should be approximately one-quarter that of an adult's. The energy requirements for age's two to three are about

1,000 to 1,400 calories a day. Toddlers require small, frequent, nutritious snacks and meals to satisfy energy requirements. Calcium is necessary for children to promote optimal bone mass, which continues to accumulate until early adulthood. For toddlers, the Adequate Intake for calcium is 500 mg/day.

For carbohydrate intake, the Acceptable Macronutrient Distribution Range (AMDR) is 45 to 65 percent of daily calories. Toddlers' needs increase to support their body and brain development. The RDA of protein is 5 to 20 percent of daily calories. The AMDR for fat for toddlers is 30 to 40 percent of daily calories. Essential fatty acids are vital for the development of the eyes, along with nerve and other types of tissue. Toddlers and children of all ages need 600 international units of vitamin D per day. Vitamin D-fortified milk and cereals can help to meet this need.

3. Childhood

Early childhood encompasses infancy and the toddler years, from birth through age three. The remaining part of childhood is the period from ages four through eight and is the time when children enter school. A number of critical physiological and emotional changes take place during this life stage. The RDA for carbohydrate for children is 130 g/day, which is about 45% to 65% of total daily energy intake. Complex carbohydrates from whole grains, fruits, vegetables, and legumes should be emphasized. The RDA for protein is 0.95 g/kg body weight per day.

Chapter 14: Nutrition in Adults

1. Puberty

The onset of puberty is the beginning of adolescence, and is the bridge between the childhood years and young adulthood. Medically, adolescence is defined as the period between ages eleven and fourteen for girls and twelve to fifteen for boys. Some of the important physiological changes that take place during this stage include the development of primary sex characteristics, or the reproductive organs, along with the onset of menstruation in females. All of these changes, as well as the accompanying mental and emotional adjustments, should be supported with sound nutrition.

2. Adolescence

The Dietary Guidelines defines the next phase of the human life cycle, late adolescence, as the period from ages fourteen to eighteen. After puberty, the rate of physical growth slows down. As teenagers make more and more of their dietary decisions, parents or other caregivers and authority figures should guide them towards appropriate, nutritious choices. Adequate energy intake is necessary to maintain adolescents' health, support their dramatic growth and maturation, and fuel their physical activity.

The RDA for carbohydrate for adolescents is 130 g/day. As with adults, this amount of carbohydrate covers what is needed to supply adequate glucose to the brain, but it does not cover the amount of carbohydrate needed to support daily activities. Thus, it is recommended that adolescents consume more than the RDA, or about 45% to 65% of their total energy as carbohydrate, and most carbohydrate should come from complex carbohydrate sources. The RDA for protein for adolescents, at 0.85 g of protein per kilogram body weight per day, is similar to that of adults, which is 0.80 g per kilogram body weight.

Micronutrients of particular concern for adolescents include calcium, iron, and vitamin A. Adequate calcium intake is critical to achieve peak bone density, and the AI for calcium for adolescents is 1,300 mg/day. The iron needs of adolescents are relatively high; this is because iron is needed to replace the blood lost during menstruation in girls and to support the

growth of muscle mass in boys. The RDA for iron for boys is 11 mg/day, and the RDA for girls is 15 mg/day. Vitamin A is critical to support the rapid growth and development that occurs during adolescence. The RDA for vitamin A is 900 µg per day for boys and 700µg per day for girls.

3. Adulthood

The next phase, young adulthood, is the period from ages nineteen to thirty. It is a stable time compared to childhood and adolescence. Physical growth has been completed and all of the organs and body systems are fully developed. Proper nutrition and adequate physical activity at this stage not only promote wellness in the present, but also provide a solid foundation for the future.

Chapter 15: Nutrition in Elderly

1. Middle Age

The early period of this stage is very different from the end. For example, during the early years of middle age, many women experience pregnancy, childbirth, and lactation. In the latter part of this life stage, women face peri menopause, which is a transition period that leads up to menopause or the end of menstruation. A number of physical changes take place in the middle-aged years, including the loss of bone mass in women due to dropping levels of estrogen during menopause.

All of these are signs of aging, as the human body begins to change in subtle and not-so-subtle ways. However, a middle aged person can remain vital, healthy, and near his or her physical peak with proper diet and adequate exercise.

2. Old Age

The process of aging is natural and inevitable, influenced by genetic and environmental factors. Aging occurs at the molecular, cellular, and tissue levels. Some signs of aging, such as the graying of hair, do not impair function or health. Older adulthood is a time in which growth is complete and body systems begin to slow and degenerate. Older adults who regularly participate in strengthening exercises and aerobic-type activities reduce their risks for low bone mass and muscle atrophy and weakness, which in turn reduce their risk for falls.

The energy needs of older adults are lower than those of younger adults because loss of muscle mass and lean tissue results in a lower basal metabolic rate, and older adults have a less physically active lifestyle. It is estimated that total daily energy expenditure decreases approximately 10 kcal each year for men and 7 kcal each year for women ages 19 and older.

To reduce the risk for heart disease and other chronic diseases, it is recommended that total fat intake remain within 20% to 35% of total daily energy intake, with no more than 10% of total energy intake coming from saturated fat. Dietary sources of Trans fatty acids should be kept to a minimum. Micronutrients of concern for older adults include calcium, vitamin D, the B-vitamins, and the antioxidants. Older adults are at risk for

chronic dehydration and hypernatremia, so ample fluid intake should be encouraged.

Elderly adults may also need guidance from dietitians and health-care professionals to make the best dietary choices for this stage of life. Healthy nutritional choices can help to prevent or manage disability and chronic conditions.

Sarcopenia is a disease associated with the ageing process. Loss of muscle mass and strength, which in turn affects balance, gait and overall ability to perform tasks of daily living, are hallmark signs of this disease.

Scientists have long believed muscle loss and others signs associated with aging are an inevitable process. However, researchers are looking for ways in which we can slow the aging process, specifically in relation to loss of muscle mass and strength.

Aging-related sarcopenia means that muscle mass, strength, and physical performance tend to decline with age, and malnutrition is associated with sarcopenia. Therefore, nutritional interventions may make an important contribution to prevent the development of sarcopenia. Here I reviewed published articles about the effects of nutritional factors on sarcopenia in elderly people. A growing body of evidence suggests that metabolic factors associated with obesity and diabetes induce the progression of sarcopenia. However, the effectiveness and safety of caloric restriction for sarcopenia remained unclear. Protein intake and physical activity are the main anabolic stimuli for muscle protein synthesis.

As optimal dietary protein intake, 1.0 - 1.2 g/kg (body weight)/day with an optimal repartition over each daily meal or 25 - 30 g of high quality protein per meal were recommended to prevent sarcopenia, which was supported by some observational studies. Protein supplementation using cheese and milk protein, essential amino acids, leucine, beta-hydroxy-beta-methylbutyrate and vitamin D has been investigated as a potential supplement to improve muscle quality in sarcopenic elderly people.

Section III: Nutrition in Disease States

Chapter 16: Metabolic Response to Trauma and Surgery

Introduction

Metabolic and nutritional profiles of patients with major trauma are characterized by hypercatabolism. In the absence of exogenous provision of substrates, amino acids are "autocannibalized" from endogenous sources. Initially, skeletal muscle proteolysis is followed by erosion of visceral structural elements and circulating proteins. The resultant acute protein malnutrition is associated with cardiac, pulmonary, hepatic, gastrointestinal, and immunologic dysfunctions. Late infectious complications can prolong the hypermetabolic or hypercatabolic state, eventually resulting in multiple organ failure.

Pathophysiology of Trauma

The pathophysiology of trauma includes an immediate cardiovascular response, an inflammatory response occurring several hours after the injury, and finally a metabolic response.

Cardiovascular response

The cardiovascular response associates hemorrhage, tissue damage, pain and anxiety and has three phases:

- First, heart rate and total peripheral vascular resistance increase to maintain blood pressure.
- After a loss of a third of blood volume, blood pressure falls and is accompanied by bradycardia and syncope.
- Finally, when about 44% of blood is lost, heart rate increases again massively.

Metabolic response

Finally, the metabolic response consists mainly of hypermetabolism, mediated by the stimulation of catabolic hormones (glucagon, catecholamine and corticoids) and insulin resistance. Associated with

inadequate nutrition, the administration of drugs as glucocorticoids and physical immobilization, this neuroendocrine response leads to protein breakdown to amino acids which are used to produce de novo glucose in the liver.

Branched Chain Amino Acids

It is well documented that BCAAs may favorably influence protein metabolism by inhibiting muscle protein breakdown and promoting muscle and hepatic protein synthesis. It has been reported that supplying BCAAs to injured and septic animals and to stressed patients has beneficial effects.

BRANCHED-CHAIN AMINO ACIDS (BCAAs) (leucine, valine and isoleucine) are essential amino acids for humans, so they must be sourced from the diet. BCAAs account for approximately 35% of the essential amino acids and 14% of the total amount of amino acids in skeletal muscle. After a meal, BCAAs constitute at least 50% of the amino acid uptake by skeletal muscle. The mean requirement and population-safe level (upper limit of 95% confidence interval) of the total BCAA were 144 and 210 mg/(kg/ d), respectively.

Parentally administered BCAAs are used clinically in nutritional support for postoperative, traumatized, and septic patients, and the oral use of BCAAs suppresses whole-body proteolysis in tissues other than skeletal muscle in healthy men. Beside these strictly nutritional aspects of BCAAs, numerous studies suggest that these amino acids may also have a notable effect on cognitive functions. In clinical settings, orally administered or parentally infused BCAAs improved mental status, flapping, orientation, speech, and writing in patients with cirrhosis and chronic hepatic encephalopathy.

It is well documented that BCAAs, particularly leucine, are essential for the regulation of insulin production by pancreatic beta cells. When leucine was ingested with glucose, it attenuated the serum glucose response and strongly stimulated additional insulin secretion. Early studies found that leucine not only stimulates insulin release but also is the sole indispensable amino acid capable of inducing insulin secretion, even in the absence of glucose. Therefore, it goes without saying that BCAAs are most studied amino acids both experimentally and clinically. Recently, BCAAs had been reported to improve central fatigue and anorexia by competitively blocking

the influx of tryptophan (precursor of serotonin) into the CNS. Wu et al found the beneficial effect of BCAAs in relieving postoperative fatigue.

It is reasonable to believe that normalization of plasma concentrations of BCAAs may lead to increased BCAA provision to the brain. These amino acids may be used to produce energy and synthesize proteins in the central nervous system (CNS). Given that they are amino acids, BCAAs can enter the energy-producing oxidative pathway of the Krebs cycle so that higher amounts of adenosine 5'-triphosphate (ATP) can be formed. The finding that processed amino acids in the Krebs cycle make a very large contribution to CO_2 production of brain cells supports this BCAA supplementation mechanism of effect. An increase in brain ATP availability in Traumatic Brain Injury (TBI) may represent an important factor, contrasting the cascade of biochemical alterations caused by the injury. For instance, in severe brain injury, ATP depletion is responsible for alterations in ion pumps, which bring about a failure of cellular sodium, potassium, and calcium homeostasis. The loss of ion homeostasis contributes to the death of neurons in TBI. Therefore, BCAA supplementation might protect and restore the function of those neurons that are still viable although metabolically altered. The BCAAs, particularly leucine, play an important role in mediating amino acid–regulated steps of protein synthesis. To get an idea of the importance of active protein synthesis for the brain structures of TBI patients, it is sufficient to mention that de novo protein synthesis is essential for brain tissue repair, sprouting, and circuitry remodeling. BCAAs may also favor the recovery of cognition indirectly by an insulin-mediated action. This hypothesis is highly plausible, both because BCAAs induce insulin secretion and release and because this hormone crosses the blood-brain barrier, exerting profound effects on the CNS.

Chapter 17: Nutrition, Infection and Immunity

Immune System and its Functions:

A healthy immune system protects the body from infectious diseases; helps heal wounds, and guards against the development of cancers. Made up of cells and tissues throughout the body, the immune system acts as an integrated network to carry out surveillance against invaders and destroy them before they can cause significant tissue damage. Although immune cells communicate with one another extensively, each cell has a specialized protective function in either nonspecific or specific immunity.

Non-specific immune function is generalized body defense mechanisms that protect against the entry of foreign agents such as microorganisms and allergens; also called **innate immunity** while **specific immune function** is the strongest defense against pathogens. It requires adaptation of white blood cells that recognize antigens and that multiply to protect against the pathogens carrying those antigens. It is also called **adaptive immunity or acquired immunity.**

Types of Cells that Provide Specific Immunity

In specific immune responses, two primary types of immune cells are activated:

- **B cells** are a type of white blood cell. During a primary immune response, B cells differentiate into two types:
    i. **The memory cells**- White blood cells that recognize a particular antigen and circulate in the body, ready to respond if the antigen is encountered again. The purpose of vaccination is to create memory cells.
    ii. **The plasma cells**- produce thousands of antibodies, proteins that attach to recognized antigens on invaders and flag them for destruction.

- **T cells** are also white blood cells. They differentiate into several types, the most important of which are:
    i. **Cytotoxic T cells**- They are toxic to body cells harboring microbes or any other non-self-substances.
    ii. **Helper T cells**- They don't kill directly. Rather, they manufacture chemicals that activate B cells and cytotoxic T cells.

Immune System Malfunction Can Cause Chronic Inflammation and Infection

A malfunctioning immune system can damage body tissues or prevent resolution of infection. For example, during allergic reactions, harmless proteins in the environment or in food are mistaken for pathogens, producing a hypersensitivity immune response. Autoimmune responses occur when the body's own proteins are mistaken for pathogens. This occurs, for example, in rheumatoid arthritis and lupus and results in a chronic inflammatory state.

How Does Nutrition Affect the Immune System?

A nourishing diet provides all the nutrients the immune system needs to carry out its defense of the body. Single-nutrient deficiencies or subclinical deficiencies can cause subtle, but important, abnormalities in immune function, even in apparently healthy people. This type of malnutrition is common in hospitalized individuals and the elderly. Moreover, protein/ energy malnutrition and severe deficiencies of several micronutrients reduce immune function.

1) **Protein/Energy Malnutrition**
   Malnutrition and infection participate in a vicious cycle: Malnutrition increases the risk for infection; infection depresses appetite and often causes vomiting and diarrhea; decreased appetite, vomiting, and/or diarrhea cause malnutrition, which increases vulnerability to infection. Specifically, protein/energy malnutrition is known to severely diminish the ability of the immune system to respond to antigens.

2) Obesity

Obesity has become a public health issue much more recently than the problem of protein/energy malnutrition. Obesity has been associated with increased incidence of infection, delayed wound healing, and poor antibody response to vaccination.

3) Essential Fatty Acids

The essential fatty acids are precursors for important signaling molecules called **eicosanoids**. The immune system requires certain eicosanoids to respond appropriately to threatening agents. Experimental dietary deficiency of essential fatty acids impairs aspects of the immune response. On the other hand, excess amounts given by supplementation can also diminish immune function.

Chapter 18: Nutritional Metabolism in Chronic Liver Disease

Protein-calorie malnutrition (PCM) is a transversal condition to all stages of chronic liver disease (CLD) and maybe present in 65-90% of patients with advanced disease. Malnutrition develops at an early stage of liver disease and there is, almost, a direct relationship between the severity of liver disease and the degree of malnutrition. The presence of PCM is associated with an increased number of complications such as esophageal varices, hepatic-encephalopathy (HE), hepatorenal syndrome, impaired liver function and regeneration capacity and increased surgical morbidity and mortality.

Malnutrition is independent predictors of mortality in patients with CLD. Cirrhotic patients have a higher risk of micronutrient deficiency. Early recognition of micro or macronutrient deficiencies is essential, because the use of nutritional supplements has been proved to be associated with a reduced risk of infection, in-hospital mortality and improved liver function.

Multiple factors contribute to malnutrition in CLD, including anorexia, inefficient digestion/absorption, iatrogenic measures or impaired metabolism. Many patients with CLD have a decreased food intake, often due to HE and digestive symptoms such as anorexia, nausea, early satiety (sometimes related to micronutrients deficiencies, such as zinc or magnesium), gastroparesis, ascites or increased leptin levels.

In CLD there occurs a decrease in branched chain amino acids/aromatic amino acids (BCAA/AAA) ratio, as observed in sepsis or major trauma. Cirrhotic patients may also have an impaired digestion/absorption, often caused by the presence of portal hypertension that promotes changes in the intestinal mucosa, like increased permeability, contributing to an increased loss of proteins.

Main micronutrient deficits in chronic liver disease and its etiologic contributing factors.

Micronutrient	Etiology
Thiamine	- Decreased intake - Decreased absorption - Reduction of the hepatic reserves - Alcohol intake prevents the metabolization in its active substrate
Vitamin B12	- Decreased intake - Decreased absorption - Reduction of the hepatic reserves
Folic Acid	- Decreased intake - Decreased absorption - Reduction of the hepatic reserves
Retinol	- Decreased absorption - Impaired hepatic mobilization
Vitamin K	- Decreased absorption - Reduction of the hepatic reserves
Vitamin D	- Decreased intake - Decreased absorption - Reduction of the exposure to UV light - Impaired liver hydroxylation in its active metabolite
Zinc	- Decreased intake - Diets with restriction of animal origin protein - Decreased absorption - Treatment with diuretics
Selenium	- Decreased intake - Decreased absorption
Magnesium	- Decreased intake - Treatment with diuretics disease

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Treatment

The diet of patients with CLD is based on a standard diet with supplements addition as necessary. In fact, in most cases it is possible to give a practically normal diet. Restrictions may be harmful and should be individualized. The treatment goals are to improve the level of PCM, to ensure an adequate amount of nutrients, to achieve a positive nitrogen balance and to avoid hepatotoxic agents

The use of BCAA-enriched formulae can improve the prognosis of patients with advanced cirrhosis. These supplements may reduce the progression of liver failure, improve quality of life, reduce the severity and frequency of HE and increase survival. In patients with compensated cirrhosis without malnutrition, the ingestion of 1.2-1.5 g/kg (weight) daily protein is recommended. In malnourished patients, 1.0-1.8 g/kg (weight) is recommended, depending on the severity of malnutrition and liver disease. Protein needs are higher in malnourished patients and in stress situations (such as bleeding, infection or surgery), provided that there is no renal dysfunction (in which may be necessary a protein restriction).

Additionally, treatment should maintain adequate caloric and protein intake together with fundamental micronutrients. The consumption of frequent small meals including late night snack are recommended to be more efficient. For the patients who cannot meet their daily requirements with normal diet should be supported by enteral and parenteral nutrition. The consultation of the crucial part of the clinical management.

Malnutrition is a potentially preventable and reversible that can be identified and treated appropriately, can lead to enhanced results in patients with chronic liver disease.

Chapter 19: Nutritional Aspects in Oncology

Delivery of adequate nutriments to the gut does not always result in rapid nutritional restoration of the starving patient because malnutrition may have led to malabsorption, and a vicious cycle thereby ensues. In the severely malnourished patient, the columnar gastrointestinal mucosal cells become cuboidal, and the brush border is reduced in height. Decreased mucosal cell production and migration from the crypts occur, and gastrointestinal motility diminishes, allowing overgrowth of facultative and anaerobic bacteria. Absorption of glucose, protein and fat may be greatly impaired. All of these morphologic, absorptive and environmental abnormalities are reversible following protein-calorie replenishment, but the process is slow because adequate enteral nutriments are initially partially malabsorbed, and the uncomfortable symptoms of nausea, diarrhea, crampy abdominal pain and bloating limit the patient's desire to eat or to obtain nutriments via feeding tubes. Thus, malnutrition itself can result in a spectrum of malabsorptive defects, ranging in degree from minimal to great. Enteral nutrition can repair all but the most severe abnormalities. Weight loss occurs when energy expended by an organism is not balanced by equal energy or calorie sources gained.

Adequate nutritional replenishment of the malnourished adult patient requires the provision of substrates necessary for energy production and for synthesis of tissue containing protoplasm and extracellular fluid. Energy requirements can be met by supplying glucose and probably fat; requirements for lean tissue anabolism can be met by supplying amino acids or protein hydrolysates, minerals and vitamins.

Metabolism in cancer patients

Disturbances of protein, carbohydrate, and lipid metabolism, energetic imbalance, specific deficiency syndromes, as well as secondary metabolic disorders, are all described in cancer patients.

However, it should be emphasized that the deregulation of protein metabolism plays the crucial role in the development of cancer-related cachexia, encompassing the abnormal exacerbation of protein degradation,

mainly involving the myofibrillar proteins of skeletal muscles, with concomitant inhibition of anabolic processes.

Clinical consequences of metabolic deregulation

Cancer has long been perceived as a disease leading to a progressive decrease of body weight, up to extreme prostration of the organism. However, it should be stressed that cancer-related cachexia is not a synonym of simple malnutrition, and loss of body weight alone is not sufficient to establish the diagnosis.

According to the international consensus, cancer-related cachexia is defined as a compound syndrome of metabolic disorders leading to loss of lean body mass, mainly skeletal muscles, which is irreversible or not fully reversible by conventional nutritional support and leads to progressive functional impairment. It is most commonly associated with appetite loss, while both conditions together form the cancer anorexia-cachexia syndrome.

Nutritional support in oncology

Appetite deficiency is one of the most important components leading to the negative protein and energy balance that is a hallmark of cancer-related cachexia. The anorexigenic influence of multiple biologically active agents, as well as gastrointestinal adverse effects of oncological treatment, results in reduction of food intake. Moreover, altered anatomical conditions due to extensive surgery and enzymatic deficiencies frequently observed in cancer patients hinder effective digestion of food and proper absorption of nutritional elements.

Nutrition of oncological patients by means of natural products may prove insufficient due to abnormalities of appetite, digestion and absorption. Consequently, they often require additional administration of nutritional support.

According to the European Society for Clinical Nutrition and Metabolism (ESPEN), the main methods of nutritional support include enteral nutrition, that is nutrition via the gastrointestinal tract by means of so-called industrial diets administered orally, directly to the stomach or enterally, as well as parenteral nutrition.

Standard Enteral nutritional management

When cancer is diagnosed in today's health environment, the patient is usually adequately nourished, and tumor volume is small. However, in some malignant diseases, such as leukemia and lymphoma, tumor bulk may be large when initial diagnosis is made, and weight loss may be a presenting symptom.

Emphasizing the importance of adequate oral intake during therapy is often all that is required to stimulate the patient to eat. Most chemotherapy results in anorexia for only 3 - 4 days; nutritional depletion will not occur in this short time if nutrition was adequate initially and if resumption of sufficient oral intake occurred as early as possible following chemotherapy.

Nutritional supplementation via the gastrointestinal tract can be time-consuming, and the operative insertion of feeding tubes can impose on the patient an acute surgical stress that further delays nutritional restoration. Nasogastric feeding tubes can play an important role in the nutritional maintenance of otherwise healthy patients who are receiving radiation treatment for cancer of the head and neck or in the postoperative management of head and neck cancer patients until normal swallowing function returns; aspiration is not a significant hazard for either group.

Conclusion

Neoplastic disease, as a generalized multi-organ disease, requires complex multimodal treatment, including special consideration of metabolic and nutritional aspects. It is essential in malignancies irrespective of clinical stage and treatment phase – from diagnosis to palliative care. The knowledge about the influence of cancer on metabolism and nutrition, as well as about the impact of proper nutrition augmented by targeted pharmacological treatment on the quality of life and prognosis, should urge earlier commencement of proper management.

Chapter 20: Nutrition in Renal Failure

Nutritional management of patients with renal disease tailors dietary intake to diminished renal function while continuing to meet all nutrient requirements. Normally, the kidney has primary responsibility for maintaining the volume and composition of body fluids, and, with approximately two million nephrons, it possesses great functional reserve. During the gradual progression to renal failure, through a process known as glomerulotubular balance, water, electrolyte, and acid-base balance are maintained until 70 to 80% of renal function is lost. Diet, the source of metabolic substrates including water, electrolytes and potential acid and base, must be modified during this time of advancing renal insufficiency to limit the kidney's excretory load. Another goal of diet therapy is to prevent or to correct the nutritional deficiencies that frequently accompany the progression to uremia.

The aims of nutritional support in patients with renal failure are dependent on the degree and character of kidney impairment, degree of malnutrition and associated disease. Patients with chronic renal insufficiency but without concurrent disease are at a high risk of malnutrition due to uremia associated factors, metabolic acidosis, impaired appetite and oral food intake and the gastrointestinal side effect of uraemia.

The main purpose of nutritional management is to prevent malnutrition, to reduce or control the accumulation of waste products, and to prevent bone and cardiovascular disease. Chronic renal replacement therapy leads to the loss of some nutritional substrates, such as amino acids and water soluble vitamins, but also to activation of protein catabolism. An adequate supply of energy, protein and vitamins amount must therefore be given to these patients. In patients with renal insufficiency complicated by an acute catabolic disease and/or in patients with acute renal failure the stimulation of immunocompetence, wound healing and other reparative functions is the principal goal of nutritional therapy.

Renal Failure:

Renal failure is a pan-metabolic and pan-endocrine abnormality affecting more or less every metabolic pathway of the body. Despite differences in metabolic presentation (and nutritional needs) in various forms of renal

failure and during the course of disease in the individual patient, there are some common features in their metabolic changes. Energy metabolism is not grossly affected by renal dysfunction (which rather decreases than increases oxygen consumption) and is more determined by associated complications.

Renal replacements therapies are associated with multiple metabolic side effects. Among those are the loss of nutritional substrates, such as amino acids and water soluble vitamins, but also systemic effects, such as activation of protein catabolism and increase in lipid peroxidation as a consequence of bioincompatibility. In patients with acute renal failure (ARF) continuous renal replacement therapies (CRRT) have become the standard treatment modalities, the metabolic side effects of which are clinically relevant because of the continuous mode of therapy and the high fluid turnover. These effects have to be considered in designing a nutritional program for a patient with ARF.

Nutritional treatment can be considered under 3 main headings:

– The patient with stable chronic renal failure

– The patient on renal replacement therapy

– The patient with acute renal failure

Nutritional state

The patients however, are at a high risk of malnutrition, because of uremia associated factors, metabolic acidosis and concurrent disease, impaired appetite and oral food intake, gastrointestinal side effect of uremia, and potentially ill directed dietary regimens.

Aims of nutritional management

The purpose of nutritional management is to prevent malnutrition at an early stage of renal disease and/or to maintain an optimal nutritional status, to reduce or control accumulation of waste products, to prevent cardiovascular disease by treating hyperlipidemia, bone disease by treating vitamin D deficiencies and hyperparathyreoidismus and to retard progression of renal dysfunction.

Patients on Acute renal replacement therapy

In ARF the aim of nutritional treatment is not the alleviation of uremic toxicity and retardation of progression of renal disease (as in CRF), but – as in other acute disease – the stimulation of immunocompetence, of wound healing and other reparative functions. In most clinical situations, requirements will exceed the minimal intake recommended for stable CRF patients or the recommended daily allowances (RDA) for normal subjects.

Patients on Chronic renal replacement therapy

Patients on chronic renal replacement therapy (haemodialysis – HD, chronic ambulatory peritoneal dialysis – CAPD) are frequently malnourished or at extreme risk of developing malnutrition. This is because HD per se is a catabolic event with 10–13 g of amino acids lost per day in the dialysate. CAPD 8–9 g of protein are lost daily in the dialysate, although up to 125 g of glucose may be gained. The problem in these patients is not that they eat too much but too little.

Solution used for nutritional support

1. Enteral nutrition

Enteral nutrition has become the main type of nutritional support used in patients with renal failure despite the fact that little is known of the impact of renal disease on gastrointestinal function. Three types of enteral diets have been used:

- (Semi) – elemental powder diets developed for CRF patients (should no longer be used)
- Standard polymeric ready-to-use liquid diets developed for non-uremic patients can also be used for subjects with ARF(Cave: development of hyperkalaemia)
- Polymeric «nephro&raquo diets (ready-to-use liquid preparations)

2. Parenteral nutrition

- **Amino acid solutions**
  Solutions of exclusively essential amino acids should no longer be used in ARF. Use solutions including all essential and nonessential amino acids in standard proportions or in a special composition to

counteract metabolic changes in renal failure («nephro»-solutions). Some of the latter contain tyrosine (which is conditionally essential in renal failure) as a dipeptide (because tyrosine has a low-water solubility).

- **Parenteral nutrition administration**
  Solutions including amino acids, glucose, lipids plus vitamins, trace elements and electrolytes contained in a single bag (All-in- One Solutions) have become the standard. Insulin can be added to the solution or be administered separately.

Complications and monitoring of nutritional support

Complications of nutritional support are similar in non-uremic and renal failure subjects but because of impairment of gastrointestinal function, reduced tolerance to volume load and electrolytes and alterations in utilization of various nutrients, the frequency of metabolic complications is high. Thus, nutritional therapy in patients with renal failure requires a tight schedule of monitoring.

BCAA in Renal Failure

During renal failure, abnormalities of BCAA and branched-chain keto acid (BCKA) metabolism are due to both the lack of renal contribution to amino acid metabolism and the impact of renal failure and acidosis on whole-body nitrogen metabolism. Abnormal BCAA and BCKA metabolism result in BCAA depletion as reflected by low plasma BCAAs and cellular valine. BCAA metabolic disturbances can alter tissue activities, particularly brain function, and nutritional status.

In dialysis patients, BCAA oral supplementation can induce an improvement of appetite and nutritional status. During chronic renal failure, the aims of nutritional interventions are to minimize uremic toxicity, avoid malnutrition and delay progression of kidney disease.

BCAA and BCKA supplements have been proposed to decrease further protein intake while maintaining satisfactory nutritional status. In this setting, BCAAs or BCKAs have not been administrated solely but in association with other essential AA or keto analogs. Therefore, the proper effects of BCAAs and/or BCKAs have not been studied separately. Protein restriction together with keto acids and/or essential AAs has been reported to improve insulin sensitivity and hyperparathyroidism and to be

compatible with a preservation of nutritional status. Nonetheless, a careful monitoring of protein-calorie intake and nutritional status is needed.

A recent meta-analysis concluded that reducing protein intake in patients with chronic renal failure reduces the occurrence of renal death by approximately 40% as compared with larger or unrestricted protein intake. The additional effect of essential amino acids and keto acids on retardation of progression of renal failure has not been demonstrated.

Chapter 21: Nutrition in Burn Patients

Nutritional support is a critical aspect of the treatment of burn patients. The metabolic rate of these patients can be greater than twice the normal rate, and this response can last for more than a year after the injury. Severe catabolism accompanies the hyper metabolic state and leads to a tremendous loss of lean body mass as well as a decline of host immune function. Significant nutritional support to meet increased energy expenditure is vital for burn patients' survival.

The Hypermetabolic state

Severe burns cause a profound pathophysiological stress response and a radically increased metabolic rate that can persist for years after injury. Trauma and sepsis also result in hypermetabolism, although to a much lesser degree and for a significantly shorter duration.

Hypermetabolism after burn is very complicated and not yet fully understood. The underlying mechanisms of this vast metabolic, hormonal, and inflammatory dysregulation are still being actively investigated. At a cellular level, increased whole-body oxygen consumption supports greater adenosine triphosphate (ATP) turnover and thermogenesis. ATP-consuming reactions represent an estimated 57% of the hypermetabolic response to burns, including ATP turnover for protein synthesis, ATP production for hepatic gluconeogenesis, and the cycling of glucose and fatty acids. Because ATP turnover does not completely account for burn-induced hypermetabolism, it implies that mitochondrial oxygen consumption exceeds ATP production after severe burn.

Adequate and prompt nutrition is extremely important for preventing numerous complications, although nutrition has a complex relationship with the hyper metabolic state. In animal models, early nutrition, usually defined as within 24 h of injury, has been shown to actually mitigate burn-induced hypercatabolism and hypermetabolism, although data in humans have not borne this out.

Caloric requirements

The primary goal of nutritional support in burn patients is to fulfill the increased caloric requirements caused by the hypermetabolic state while

avoiding overfeeding. Numerous formulas to estimate the caloric needs of burn victims have been developed and used throughout the years.

The earliest formulas for burn patients consisted of milk and eggs, and although these simple mixtures were relatively successful at providing adequate nutrition, they were very high in fat. Numerous commercially prepared enteral formulas have been developed since that time, all with differing amounts of carbohydrates, protein, fats, and micronutrients. Glucose is the preferred energy source for burn patients and they should therefore be administered a high-carbohydrate diet. Parenteral formulas usually consist of 25% dextrose, 5% crystalline amino acids, and maintenance electrolytes. This is often supplemented with infusions of 250 mL of 20% lipid emulsions three times a week to meet essential fatty acid needs.

Immune-enhancing diets, or immunonutrition, are nutritional formulas that have been enriched with micronutrients in an effort to improve immune function and wound healing.

Monitoring of nutritional support

It is challenging to objectively assess the success of nutritional support of a burn patient, as the true endpoint of therapy is global and cannot be measured by one variable. The overall goal of therapy is to reestablish normal body composition and metabolic equilibrium, and commonly measured variables include body weight, nitrogen balance, imaging of lean body mass, and measurement of serum proteins. Functional measures such as exercise tolerance have also been proposed as a possible metric.

Nutrition after discharge

It is important that patients continue to receive adequate nutrition after discharge from the hospital, but data on the optimal diet after the acute post burn phase are virtually nonexistent. Because the hypermetabolic state can persist for over a year after burn injury, increased caloric intake with a high protein component is usually recommended for about a year after discharge. Resistance exercise is also recommended to combat continued loss of muscle mass.

Section IV: Nutritional Assessment and Support

Chapter 22: Nutritional Evaluation and Screening

Interest in nutrition screening has increased rapidly due to regulatory requirements as well as the known adverse impact of nutrition deficits on outcomes of hospitalization. Screening programs now in use in acute care are often complex and difficult to administer. Current interest in evaluation of all aspects of healthcare using evidence-based methods requires that nutrition screening programs be thoroughly evaluated. Clinicians attempting to evaluate evidence in support of different methods to identify patients who might have nutrition problems are often confronted with research that blurs the distinction between screening and assessment. Therefore, before identifying methods to conduct nutrition screening, it is necessary to have a thorough understanding of the difference between screening and assessment.

What Is Screening?

The World Health Organization defines screening as "the use of simple tests across a healthy population in order to identify the individuals who have disease, but do not yet have symptoms." The U.S. Preventive Services Task Force states that screening is "Those preventive services in which a test or standardized examination procedure is used to identify patients requiring special intervention." Appropriate use of screening tests requires much thought beyond identifying the disease screened for and selecting a test to implement.

Key Concepts in Evaluation of Nutrition Screening Tests

Any discussion of a screening process in healthcare necessitates consideration of methods to analyze the ability of the screen to accurately identify those patients in need of further evaluation. Evaluation of a screening test requires knowledge of how sensitivity, specificity, positive predictive value, and negative predictive value describe test accuracy. In general, sensitivity and specificity refer to the test itself whereas the positive and negative predictive value refers to interpretation of test results for a given patient.

a) Sensitivity and Specificity

Sensitivity and specificity are important concepts that assist in quantifying the ability of a test to correctly identify nutrition risk in those who have a nutrition problem as well as ensuring that those who do not have nutrition problems will have a negative screen. A test that is highly sensitive can be assumed to correctly rule out nutrition problems if patients have negative screening results. Both sensitivity and specificity evaluate the accuracy of a test in patients who are known to have or not have nutrition problems.

b) Positive and negative predictive value

When the initial nutrition screen is conducted, the status of the patient is unknown. The clinician needs to know the predictive value of the screening test, that is, the proportion of people with a given test result (positive or negative) who do or do not have a nutrition problem. Determination of the predictive value of a nutrition screen requires knowledge of the prevalence of the nutrition problem in the population being screened.

c) Validity and Reliability

A valid nutrition screening test is one that accurately identifies the nutrition problem of interest. Test reliability refers to the ability of a test to produce the same results. A test that is reliable will yield very similar results every time it is used under given testing conditions.

Screening Tools

There are 2 screening tools available for use in inpatient settings that meet our criteria. The **Malnutrition Screening Tool (MST**) was developed for use in identifying patients who might have nutrition problems in acute care. Parameters found to have the highest sensitivity and specificity was unintentional weight loss and decreased intake.

The **Malnutrition Universal Screening Tool (MUST)** has been recommended for use in inpatient care settings. The MUST also include evaluation of weight loss and adequacy of intake with the addition of calculation and evaluation of BMI and estimation of the severity of the medical condition.

	Nutrition Screen	Nutrition Assessment
Intake	Recent changes in intake	Changes in specific nutrient intake Changes in energy intake Impact of changes
Anthropometrics	Weight Change in weight	Body mass index Body composition
Medical tests, laboratory tests, and procedures	Not usually included	Medical diagnosis Impact of medical diagnosis on ability to meet needs
Nutrition-focused physical exam	General appearance	Review of systems Physical examination
Client history	Not usually included	Medical and surgical history Planned therapies Medication history Social history

Chapter 23: Assessment of Nutritional Requirements

What is Nutrition Assessment?

Nutrition assessment is a more detailed evaluation and interpretation of multiple parameters and seeks to define the risk of developing nutrition-related medical complications. It can also be used to monitor the course of nutritional therapy. Thus, nutrition screening is a brief evaluation to identify a subset of people at high risk, whereas nutrition assessment is a more complex process applied to this subset to delineate further their nutrition status.

The types of data collected in the nutrition assessment are often similar to data collected in the screening process but are in more depth. It gathers more in-depth information regarding body composition (anthropometric data), client history, medical tests, laboratory tests or procedures, and nutrition-focused physical examination.

NUTRITION ASSESSMENT TOOLS

Ambulatory Population:

The Mini Nutritional Assessment (MNA) targeted the frail elderly and organized in four main areas: diet intake, anthropometrics, general assessment, and self (patient) assessment. Based on this information, the MNA places patients into one of three categories:

1) Well-nourished (>24 points)
2) At risk for malnutrition (17 to 23 points)
3) Malnourished (<16 points)

Hospitalized Population:

Subjective Global Assessment is used primarily by clinicians to assess nutritional status in hospitalized patients. It uses physical findings and four areas of the medical history: change in weight over the past 2 weeks and 6 months, change in dietary intake, gastrointestinal symptoms, and functional capacity. This information is used to classify patients into one of three categories of nutritional status: well nourished, moderately malnourished,

or severely malnourished. This technique has good sensitivity and specificity.

Another nutritional assessment approach based on physiologic function as well as the history and physical examination has been developed for use in hospitalized patients, primarily those who are undergoing surgery. This method uses weight change along with a brief history and functional evaluation of various systems (respiratory, muscle, skin integrity) to determine nutritional status. This method was validated in preoperative patients and predicted postoperative complications primarily in those with evidence of physiologic impairment.

DETAILED NUTRITION ASSESSMENT

As in other areas of medicine, nutrition assessment can be approached in an organized fashion through evaluation of the patient's history, physical examination, and laboratory assessment. Integration of these components then leads to rational clinical interpretation of nutritional status.

1. History

The two main areas of interest in the history are the patient's medical history and nutritional history. Elderly patients may have memory problems that make it difficult to obtain an accurate history. Family members or previous medical records, if available, can be helpful in this situation to provide historical information. The following items related to weight should be obtained: usual weight (in the recent past before any weight loss or illness), current weight, amount and duration of weight loss. Alterations in fluid status, particularly among critically ill patients, such as dehydration, edema, and ascites, should be taken into consideration when interpreting weight changes.

A history of weight loss can be one of the most important pieces of information in the nutrition screening and assessment process. Involuntary weight loss is an ominous sign and should be investigated. Weight loss of more than 5% in 1 month or 10% in 6 months can be considered clinically significant. Medications that are used, both prescription and nonprescription, should be reviewed because they can influence nutritional status in a number of ways, including drug-nutrient interactions, weight gain, anorexia, and altered gastrointestinal motility. Alcohol and tobacco

use, past and present, should be determined and quantified. Social factors can influence nutritional status.

2. Physical Examination

General observations of the patient can be useful as a preview to objective measurements discussed subsequently. This observation can include brief comments on obesity, body fat distribution, and wasting in terms of fat and lean tissue reserves. Muscle wasting can often be observed in the extremities, temples, or interosseous areas.

Body temperature should be measured. Fever can be one manifestation of the metabolic response to injury or illness. Fever raises energy expenditure up to 13% for each 1°C elevation, which may affect nutritional support goals.

3. Anthropometrics

Anthropometrics measures aspects of body composition. Changes in these parameters take place over a relatively long period of time and therefore are indicators of long-term nutritional status. Body weight is a simple and easily obtainable measurement and preferably should be measured rather than reported. Fluid status should be taken into consideration when interpreting weight. Height should also be measured, and comparison of actual with ideal body weight from height-weight tables can be done. If height cannot be obtained because of inability to stand or amputations, other measures can be used, such as knee height or arm span.

This includes BMI calculation. Body fat distribution can be estimated by measuring the waist circumference. Measurement of the waist circumference should be obtained at the level of the iliac crests. Triceps and other skinfold thicknesses measure subcutaneous fat and are an indication of body fat stores.

4. Laboratory Tests

Albumin is commonly thought of as a good marker of nutritional status and visceral protein stores. Albumin levels, however, are primarily affected by illness. There is increased Catabolism; decreased synthesis, and particularly redistribution into the extravascular space of albumin as part of the metabolic response to injury or illness. This response can occur acutely within 24 to 48 hours. Other serum proteins that have been used in nutrition assessment are transferrin, prealbumin, and retinol binding

protein. These proteins are also affected by illness and injury, similar to albumin, and so offer little advantage over albumin in nutrition assessment.

A 24-hour urinary total or urea nitrogen can be interpreted as corresponding to the degree of protein catabolism and therefore protein requirements. Many factors can affect this measurement, including adequacy of collection, diuretics, renal function, and protein intake, and so this test needs to be interpreted carefully.

Creatinine is produced from muscle metabolism, and urinary values reflect muscle mass. Dietary intake and renal function also influence urinary creatinine. In clinical practice, use is limited because of the need to obtain a 24-hour urine collection and the lack of influence on nutritional support recommendations.

Markers of immune function have been used in nutrition assessment. Delayed cutaneous hypersensitivity and total lymphocyte count have been used, and impairment correlates with poorer outcome.

5. Functional Assessment

Functional testing, such as grip strength and respiratory muscle strength, can be a useful component of nutrition assessment. Changes in metabolism and function can occur long before alterations in body composition detected by anthropometrics. Electrical stimulation of muscle has the advantage that it does not depend on voluntary effort.

Synthesis of Information

It is necessary to take into consideration all of the available information from the nutrition assessment before making nutrition recommendations. Integrating information from the nutritional and medical history, physical examination, and appropriate laboratory studies requires clinical judgment and experience.

Chapter 24: Types of Nutrition Support

The provision of enteral or parenteral nutrients is to treat or prevent malnutrition. Nutrition Support Therapy is part of Nutrition Therapy which is a component of medical treatment that can include oral, enteral, and parenteral nutrition to maintain or restore optimal nutrition status and health. The nutritional needs of patients are met through a variety of delivery routes and with an array of nutritional formulation components and administration equipment.

1. Enteral nutrition (EN)

Enteral nutrition is another way people can receive the nutrition they need. Also called "tube feeding," enteral nutrition is a mixture of all the needed nutrients. It is thicker than parenteral nutrition and sometimes it looks like a milk shake. It is given through a tube into the stomach or small intestine.

Long-term nutrition: If nutritional support is likely to be needed for more than a few weeks, a tube is passed through the skin and muscle of your abdomen straight into your stomach or small bowel made of polyurethane and has a wire to aid passing the tube. The wire is removed once the tube has been passed but should be kept in a safe place in case the tube has to be re-passed.

- Gastrostomy: Gastrostomy tubes (g-tubes) require that the stomach should be working properly. There is a clear disc or "bumper" at the place on the skin where the tube enters the body; this prevents the tube from slipping inside, keeping it appropriately placed on the outside of the body.

- Jejunostomy: (j-tubes) are used for a number of reasons: aspiration problems, GERDS, poor gastric emptying, etc. There is a valve between the stomach and the intestines which in theory prevents the back flow from intestine to stomach. The theory is to feed below that valve - directly into the small intestine. The intestine, however, has no pouch and cannot store food, so these feedings must be done very slowly and in small amounts. In 99%

of the cases j-tube feedings use a pump which can insure slow feedings.

Short-term nutrition: If you only need nutritional support for a short time, the tube may be passed through the nose down into the stomach. They are made of polyvinylchloride (PVC) and can remain in place for between 3-10 days. “Single use” is usually recommended.

- Nasogastric feeding: These are the most commonly used delivery routes but depend on adequate gastric emptying. They allow the use of hypertonic feeds, high feeding rates and bolus feeding into the stomach reservoir. Tubes are simple to insert but are easily displaced.

- Nasoduodenal feeding: Nasoduodenal (ND) feeding tube placement is a procedure in which an x-ray monitor is used to guide the placement of a soft feeding tube through the nose into the small bowel (duodenum). ND feeding tubes may be used for long-term enteral nutrition.

- Nasojejunal feeding: These reduce the incidence of gastro-oesophageal reflux and are useful in the presence of delayed gastric emptying. Post-pyloric placement can be difficult but may be aided by intravenous prokinetics or fibre-optic observation.

Feed preparations

Various nutritionally complete pre-packaged feeds are available:

Standard enteral feeds:
These contain all the carbohydrate, protein, fat, water, electrolytes, micronutrients (vitamins and trace elements) and fiber required by a stable patient.

'Pre-digested' feed/Oligomeric formula:
These contain nitrogen as di, tri-peptides or free amino acids and aim to improve nutrient absorption in the presence of pancreatic insufficiency or inflammatory bowel disease.

The fiber content of feeds is variable and some are supplemented with vitamin K, which may interact with other medications.

Nutrients such as glutamine, arginine and essential omega-3 fatty acids are able to modulate immune function. Enteral immunonutrition may decrease major infectious complications and length of hospital stay in surgical and some critically ill patients.

2. Parenteral nutrition (PN)

Parenteral nutrition (PN) refers to the administration of nutrients by the intravenous route. It is usually administered via a dedicated central or peripheral placed line and is generally used where there is:

a. Failure of gut function (e.g. with obstruction, ileus, dysmotility, fistulae, surgical resection or severe malabsorption) to a degree that definitely prevents adequate gastrointestinal absorption of nutrients

b. The consequent intestinal failure has either persisted for several days (e.g. >5 days) or is likely to persist for many days (e.g. 5 days or longer) before significant improvement.

Parenteral nutrition is one of the ways people receive nutrition when they cannot eat or use their gut via tube feeding. It is a special liquid mixture given into the blood through an intravenous tube into a vein. The mixture contains all the protein, sugars, fats, vitamins, minerals, and other nutrients needed. It was once called "total parenteral nutrition," "TPN," or "hyperalimentation."

- Total Parenteral Nutrition (TPN): Total parenteral nutrition is formulated to meet the patient's individual nutritional requirements and is most commonly provided as a two-in-one mixture of dextrose and amino acids, with fat emulsions infused as a separate solution. It is administered into the largest vein in your body, the Superior Vena Cava, and it provides the majority of your nutritional needs. Minerals, vitamins, and other additives are incorporated into total parenteral nutrition formulations to meet daily nutritional needs.

- Peripheral Parenteral Nutrition (PPN): If the nutritional solution is given into veins outside the Superior Vena Cava, it is called Peripheral Parenteral Nutrition, or PPN. It is administered via the peripheral venous route. Typical indications for PPN include short-term use, modest needs, and contraindications to central access (subclavian or jugular catheters) placement, such as radical neck dissection.

Enteral vs Parenteral:

The gastrointestinal tract is always the preferred route of support, i.e., "If the gut works, use it". Most would agree that EN is safer, more cost effective, and more physiologic that PN. Improvements over the past few years have greatly expanded choices in enteral formulas, equipment, and techniques.

Potential benefits of enteral nutrition over PN include:

Physiologic

- Nutrients are metabolized and utilized more effectively via the enteral than the parenteral route.
- The gut and liver process enteral nutrients before their release into systemic circulation.
- The gut and liver help maintain the homeostasis of the amino acid pool as well as the skeletal muscle tissue.

Immunologic

- Gut integrity is maintained by enteral nutrients through the prevention of bacterial translocation from the gut, sytemic sepsis, and potential increased risk of multiple organ failure.
- Lack of GI stimulation may promote bacterial translocation from the gut without concurrent enteral nutrition.
- Provision of early enteral nutrition may minimize risk of gut related sepsis.

Safety (avoid complications related to intravenous access)

- Catheter sepsis
- Pneumothorax
- Catheter embolism
- Arterial laceration

Cost

- Cost of EN formula is less than PN.
- Cost of equipment and personnel for preparation and administration is less.

Combination feeding can be used as a bridge between parenteral and enteral (or oral) nutrition in patients whose clinical status does not warrant full enteral nutrition, but whose nutritional status is best managed with some form of enteral nutrition. Thus, patients following a combination feeding regimen receive parenteral and enteral nutrition simultaneously. Even a small amount of enteral nutrition will preserve the entero-hepatic circulation and barrier function of the GI tract.

Section V: Total Parenteral Nutrition - TPN

Chapter 25: A Review to Parenteral Nutrition

Indications for Parenteral Nutrition

Parenteral Nutrition (PN) can sustain life when patients are unable to take sufficient nourishment via the gastrointestinal tract for prolonged periods. However, PN is associated with significant risks and complications. Alternative methods of nourishing patients should be considered in every case. A nutrition support algorithm is presented.

Where possible, oral or enteral nutrition are preferred options.

PN is necessary when the patient cannot be sustained with either increased intake of oral supplements or enteral nutrition alone. The use of PN should be considered when normal oral intake or enteral nutrition cannot be started after a period of five days.

Short-term PN is appropriate in malnourished and/or severely catabolic patients unable to be adequately nourished enterally. In this patient group, the risks of complications of nutrition depletion are greater and PN should be started earlier.

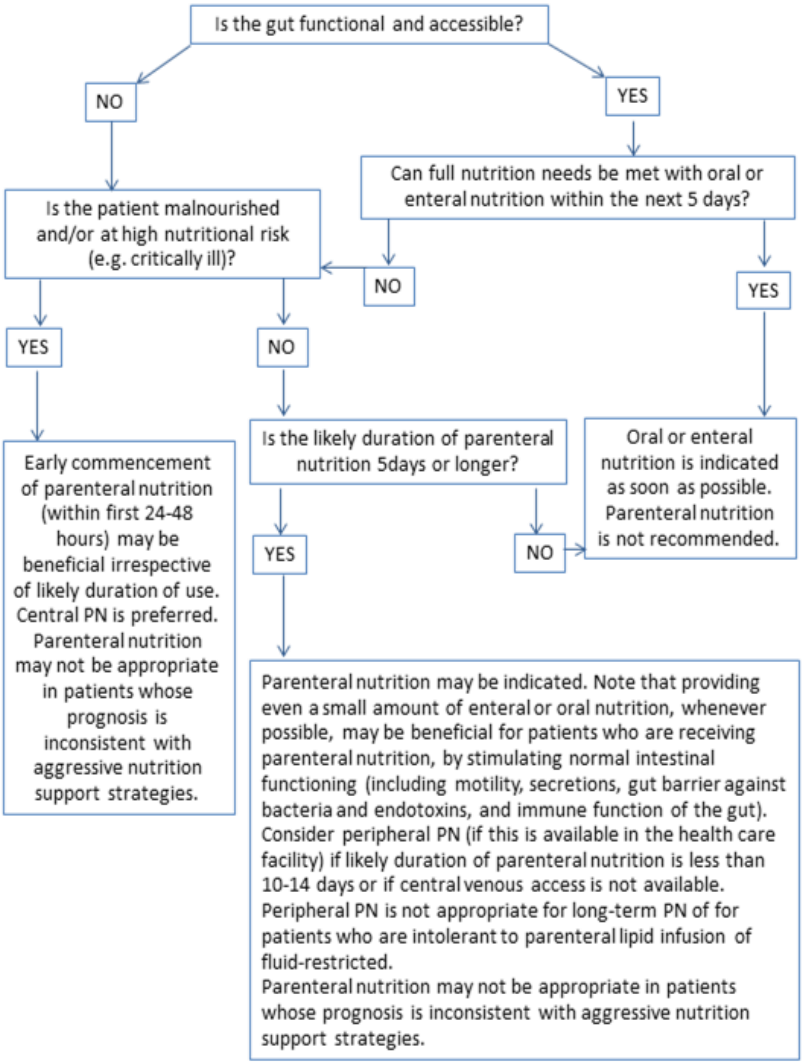
As PN is an invasive therapy, it must be used in a manner which limits the risk of sepsis, catheter insertion complications and metabolic complications.

PN is also a relatively expensive treatment which can only be justified for patients with clearly defined indications.

The basic indication for using PN is a requirement for nutrition when the gastrointestinal tract is either:

- not functional or leaking (e.g. obstruction, ileus, fistulae, dysmotility)
- cannot be accessed (e.g. intractable vomiting with inability to establish jejunal access)
- the patient cannot be adequately nourished by oral or enteral means (e.g. in malabsorption states such as short bowel syndrome, radiation enteritis or inability to establish full enteral feeding)

Nutrition support Algorithm



When is it not appropriate to use Parenteral Nutrition?

PN may not be appropriate in well nourished, non-catabolic patients where enteral nutrition is likely to be established within five days.

PN may not be appropriate where the prognosis is inconsistent with aggressive nutritional support.

Ethical and legal principles must be considered in decisions involving the withholding or withdrawing of nutrition support. PN should not be used to prolong life when there is little prospect of good quality in the eyes of the patient, the patient's family and the medical team.

Nutrition Assessment of the Adult PN Patient

The purpose of performing a nutrition assessment on the patient commencing PN is to determine nutritional status, identify nutrient and metabolic risks and establish a nutrition care plan regarding methods of nutrition support.

Nutrition assessment is a comprehensive approach to gathering pertinent data in order to define nutritional status and identify nutrition-related problems. The assessment often includes patient history, medical diagnosis and treatment plan, nutrition and medication histories, nutrition-related physical examination including anthropometry, nutritional biochemistry, psychological, social, and environmental aspects.

The following information should be collected as part of a comprehensive assessment:

PARAMETER EXAMPLES	TYPICAL INDICATORS
Clinical Medical and surgical history Severity of illness and duration	Conditions such as trauma, major abdominal surgery, chronic illness with acute complications, sepsis, losses (e.g. fistula, wounds, diarrhoea) altered mental state and large wounds increase risk of malnutrition and increase patient requirements.
Gastrointestinal factors	See Indications for parenteral nutrition. Note presence of anorexia, nausea, vomiting, abdominal distension, diarrhoea, gastrointestinal or hepatopancreaticobiliary obstruction or a fistula.
Medical history	Has the patient been on medication which has the potential to affect nutritional status, either through gastrointestinal side effects (e.g. nausea) or neurological side effects (e.g. confusion), or through direct drug-nutrient interactions.
Fluid balance	Dehydration, large losses, oedema, ascites, significant discrepancies in intake/output on fluid balance chart.
Physical examination	Visual appearance of muscle wasting, loss of subcutaneous fat, frailty, pallor, pressure ulcers, oedema, etc. Manifestations of likely vitamin deficiency e.g. angular stomatitis, glossitis, bleeding gums
Anthropometry Body weight, height, BMI	WHO BMI classifications Underweight: BMI<18.5 kg/m^2 Healthy weight: 18.5 - 24.9 kg/m^2 Overweight: 25-29.9 kg/m^2 Obese: > 30 kg/m^2 Note that BMI is an acceptable approximation of total body fat at the population level, but not always an accurate predictor in individuals e.g. liver disease3. In addition Asian, Indian and Indigenous Australian populations may need to have a lower cut-off for healthy weight, Pacific Islanders probably require a higher BMI cut-off of 26, and for adults over 65 years a higher BMI range of 22-26 is associated with better health status

Unintentional recent weight loss	Significant weight loss: • 5% weight loss in one month • 10% weight loss in six months Severe weight loss: • >5% body weight in one month, • 10% in three months
Current weight trend	If the patient is regaining some of the weight lost (fat or muscle rather than fluid gain), degree/risk of malnutrition is decreased.
Body composition	• Use of skin fold thickness measurement • Mid-arm muscle circumference • Calf circumference (There is a broad range of sophisticated methods for the measurement of body compartments. They are most useful in monitoring home PN requirements.)
Nutrition History Food intake	History/duration of poor oral intake or prolonged fasting periods Current intake compared with usual intake Other factors affecting intake e.g. dysphagia, taste changes, poor dentition, abdominal pain and/or depression Consideration of micro and macro nutrient intake is necessary here
Risk of re-feeding syndrome	Assessment of a patient's risk of refeeding syndrome is important in determining how aggressively parenteral nutrition can be advanced
Biochemical data	See "Monitoring of Parenteral Nutrition in Ward Patients"
Functional level Muscle strength, fatigue	Ability to perform own Activities of Daily Living Quality-of-life indicators Respiratory function - peak flow and FEV_1 Hand dynamometry if available
Immune function	Full blood count (consider effect of infection or haematological disorder)
Social and environmental	Psychosocial factors (e.g., social support; eating disorders; language barriers; family dynamics; personal, ethnic, cultural, or religious dietary prescriptions;

	substance abuse; psychiatric disorders) Socioeconomic factors (e.g., personal financial situation and reimbursement sources) Patient preferences and directives with regard to intensity and invasiveness of care; emotional response to current illness The patient's home environment Educational level or learning ability Activity pattern and lifestyle.

Chapter 26: PN via Venous Access

Venous Access for PN in the Adult Patient

Successful delivery of PN requires a dedicated lumen and appropriate vascular access.

The type of catheter and choice of vein depends on several factors including:

- Risks associated with the placement method
- Potential complications (thrombotic, infectious and mechanical)
- Ease of site care
- Number of infusions
- Anticipated duration of therapy.

There are a number of considerations that need to be made when choosing the route of venous access. These include:

- History of patient (history of thrombosis, multiple previous intravenous lines resulting in damaged veins and limiting the choice of either peripheral or central venous access, lymphoedema)
- Individual circumstances e.g. Haematological stability, allergies
- Resources available e.g. Access to skilled professionals, nutrition support teams, vascular access teams
- Osmolarity and pH of the solution
- Risk of infection
- Duration of PN
- Type of line access available
- Other IV therapies required by the patient, as a multilumen catheter may be needed.

If time and circumstances allow, discuss the options for different types of venous access devices (VAD) with the patient.

Central Venous Access

Most PN solutions have a high osmolarity and are therefore only suitable for delivery via a central venous line.

The main veins used for access to the central venous system are:

- Subclavian Veins
- Internal and External Jugular Vein
- Cephalic and Basilic Veins
- Femoral Veins (Least Preferred).

Tip Placement

The tip should end between the lower third superior vena cava and the atrial caval junction. When access to the superior vena cava is contraindicated, the inferior vena cava may be used.

A chest X-ray is necessary to confirm the position of the tip when:

a) the position of the tip has not been checked during procedure (x-ray or ultrasound)
b) the device is placed using the blind subclavian approach or other techniques carrying risk of pneumothorax
c) there is documented prior use of a catheter.

It is important to monitor the site for signs of thrombosis, thrombophlebitis, phlebitis, infection and/or displacement.

Types of Central Venous Access Devices

Non-tunnelled, non-cuffed catheters (central line)

- intended for short-term use
- may be inserted via subclavian, internal jugular or femoral vein
- may be antimicrobial impregnated
- account for the majority of catheter-related bloodstream infections.

Peripherally Inserted Central Catheters (PICC)

- typically used in the hospital, for mid-term therapy or when central venous access is indicated
- the exit site is on the arm. As with other central catheters, the tip is placed in the distal superior vena cava. A PICC should not be confused with other catheters placed in the arm (e.g. peripheral or midline)
- are not tunnelled and are only secured by external adhesive securement
- typically placed via basilic, cephalic or brachial vein.

Tunnelled

- follow a tract under the skin before entering a central vein and have a cuff
- most common type of long-term HPN access
- often called by a brand name (e.g. Broviac®, ,Hickman®)
- lower rate of infection than non-tunnelled catheters
- typically placed by a surgeon or interventional radiologist.

Implanted port catheters

- also called a "Port" or "Port-a-Cath"
- commonly used for intermittent access and not recommended for PN unless already *in situ*
- the port of an implanted catheter is completely under the skin
- typically placed into subclavian or internal jugular vein by a general surgeon or interventional radiologist.

Peripheral Venous Access

Peripheral access may be considered using either small gauge or midline, for short periods of time. Do not use veins in lower limbs. It is important to monitor the site for signs of phlebitis, infection and/or displacement. Hospitals should ensure that they have the appropriate protocols in place to administer and monitor peripheral PN safely.

There are two types of peripherally placed catheters:

- teflon/plastic cannulae
- midlines into the basilic or cephalic veins.

PN can be delivered into peripheral veins using normal cannulae, but these must be rotated regularly to prevent thrombophlebitis. Peripherally placed cannulae are best managed with regular rotation of catheters from side to side and using low osmolarity PN solutions (700 mOsm/L), which reduce damage to the vein endothelium (phlebitis) and risk of thrombosis. This limits the amount of nutrition that can be provided. It may be useful at the introduction of PN when short term nutritional support is required.

PN can be provided via a midline with similar success to central PN, provided the line is fine bore, and a "3 in 1" solution which has an osmolarity of ≤ 900 mOsm/L is used. To achieve this, the amount of lipid needs to be about 66% of non-protein calories (or 50% total calories) using a higher concentration of amino acids. With such a peripheral solution providing 110-120 kcal:1gN, postoperative patients can preserve their muscle mass. While this is a greater amount of lipid than generally

recommended, it has been used in a number of studies without increased morbidity.

An improved thrombophlebitis rate can be achieved with a mid-line placed about 15 cm into the basilic vein. There are a number of advantages to midlines because they can be placed without radiological guidance and can be monitored clinically for any tenderness over the vein. These lines should be 2-3F in size and can only be used for continuous infusion for rates up to 120 ml/h.

They cannot be used for resuscitation. Studies have demonstrated a reduced risk of sepsis with the use of midlines and they can be safely inserted and managed by nursing staff without the need for referral to the radiology department.

Care and Management of Vascular Access

Considerations for vascular access and ongoing care of line and site are important. Aseptic techniques and compliance with recommendations for equipment and dressing changes are essential if microbial contamination is to be prevented. Whenever the insertion site is exposed or the intravenous system is broken, aseptic technique should be practiced. One must also consider and follow institution's policy for central VAD management.

- If using single lumen catheter for PN, the line must be dedicated for PN only during administration
- PN must not be stopped for diagnostic tests and interventions
- If necessary, arteriovenous (AV) fistular access for PN may be considered
- Be aware of other potential complications that may impact on the device, such as catheter occlusion, precipitate, thrombosis

Refer to institution guidelines for care and management of VADs.

Minimizing Risk of Catheter Infection

Sepsis is the most common and serious complication of a central venous catheter. To reduce the risks of infection consider:

- single lumen when appropriate
- using PICC
- appropriate site selection
- ultrasound-guided vein puncture
- maximal barrier precautions during insertion

- education and training of all staff in central venous access device (CVAD) management
- adequacy of hand washing
- use of 2% chlorhexidine
- appropriate dressing of exit site
- adequacy of securement of CVAD
- cleaning of hubs/needle-free injectors
- changing of administration sets
- in high risk patients, consider using antibiotic-impregnated CVAD.

Dressing of VAD exit site

It is important to have appropriate dressing and monitoring of the exit site to prevent infection. Securing the catheter to prevent to and fro movement is recommended. Please refer to your institution guidelines.

Chapter 27: PN Requirements

PN Requirements for the Adult Patient

PN requirements should always be calculated based on the individual needs of the patient. Variations in nutritional requirements are dependent on the patient's body weight, age, sex, activity and metabolic requirements. Assessment should be performed by staff trained in nutrition assessment, such as a dietitian.

Patients at Risk of Refeeding Syndrome

When initiating PN it is important to consider if the patient is at risk of refeeding syndrome as this will require a slow introduction of nutrition support with close assessment and monitoring of nutrition requirements.

Refeeding syndrome is the state of very low blood levels of phosphate, potassium and magnesium which occurs when a patient is fed rapidly after a period of prolonged fast. The intracellular space suddenly expands with the uptake of glucose and other nutrients, causing a rise in intracellular electrolytes and a corresponding fall in extracellular electrolytes.

Serum electrolytes can fall to such a low level that the function of many important systems are impaired and may result in cardiac arrhythmia and death. At lesser degrees the low phosphate and magnesium levels may result in impaired oxygen transport and impaired white cell function, increasing the risk of sepsis.

A patient is defined as being a high refeeding risk if he/she has one or more of the following:

- BMI less than 16 kg/m2
- unintentional weight loss greater than 15% within the last 3–6 months
- little or no nutritional intake for more than 10 days
- low levels of potassium, phosphate or magnesium prior to feeding.

Or if the patient has two or more of the following:

- BMI less than 18.5 kg/m2
- unintentional weight loss greater than 10% within the last 3–6 months
- little or no nutritional intake for more than 5 days
- a history of alcohol abuse or drugs including insulin, chemotherapy, antacids or diuretics.

If a patient is considered at high risk of developing refeeding problems:

Provide intravenous supplements of potassium (likely requirement 2–4 mmol/kg/day), phosphate (likely requirement 0.3–0.6 mmol/kg/day) and magnesium (likely requirement 0.2 mmol/kg/day intravenous, 0.4 mmol/kg/day oral) unless pre-feeding plasma levels are high.

Blood should be taken a few hours after PN infusion commences. Daily monitoring is required and supplementation may be necessary until electrolyte levels are stabilised. Sometimes more frequent monitoring will be required in acute cases. Blood results should be checked before an increase in PN infusion rate is considered.

Provide thiamin 200–300 mg daily immediately before and during the first 10 days of PN, or full dose daily intravenous vitamin B preparation (if necessary) and a balanced multivitamin/trace element supplement once daily.

Start nutrition support at a maximum of 10 kcal/kg/day for the first 24 hours, increasing caloric input slowly with the aim of reaching the goal requirements by days 4-7. Biochemistry should be monitored twice daily. The time taken to reach goal rate will depend on the patient's biochemistry and the cardiovascular effects of the malnourished state e.g. fluid overload, heart failure.

Patients Not at Risk of Refeeding

PN may be commenced at the goal rate, however refer to monitoring.

Types of PN Solutions Available for Adult Ward Patients

Traditionally PN has been provided as modular components (i.e. amino acids, glucose and lipid emulsions) infused separately. There are now "2 in 1" (glucose and amino acids) and "3 in 1" (amino acids, glucose and lipid)

solutions commercially available. “3 in 1” PN solutions are now commonly used as standard base formulae for adult ward patients.

There are several advantages to using commercially pre-prepared “3 in 1” solutions. They are readily available, stable, easy to use and time saving. There are also potential savings in the cost of nutrient delivery. These “3 in 1” solutions contain carbohydrates, amino acids, lipids and electrolytes, in quantities designed to meet basic requirements of ward patients.

Whilst additions to the commercial “3 in 1” bags are possible under controlled, aseptic conditions, a disadvantage is the inability to remove substances from the pre-prepared bags. Patients with specific nutritional requirements that cannot to be met with a standard “3 in 1” solution may require the use of modular solutions.

It is important that the individual’s nutritional requirements are assessed on an ongoing basis to ensure standard “3 in 1” solutions are appropriate, or if a more specifically designed solution is required.

Constituents of Typical “3 in 1” PN Solutions

There is a wide variety of “3 in 1” PN solutions available with varying nutritional compositions. The following values represent typical ranges of nutrients contained in commercially available solutions.

Constituents of Typical “3 in 1” PN Solutions

CONSTITUENT	PER 1L OF PN SOLUTION*
Energy	900 – 1200kcal
Glucose	100 – 175g
Protein	35 – 50g
Lipid	25 – 50g
K+	25 – 35 mmol
Na+	30 – 40 mmol
Mg	2.5 – 5 mmol
PO4-	7.5 – 20 mmol
Fluid	1L

* The volume of a typical standard PN solution bag is 2 – 2.5 L.

PN Macronutrient Requirements for the Adult Ward Patient

The majority of patients are on PN for less than two weeks, when the aim of the PN is to limit losses while the patient's gut recovers. In this circumstance, being conservative with the amount of nutritional replacement is the safest option because overfeeding can have significant complications. However, underfeeding can also be detrimental because there is inadequate substrate to reverse the catabolic process, to improve the immune deficit and to improve muscle strength, thus defeating the purpose of providing PN. In the malnourished or in the case of longer term patients being treated for two or more months, this issue becomes very important for recovery.

Over a two-week period, changes in fat and muscle mass can be measured with anthropometric techniques or more accurate body composition measures to determine the net result of input and output.

When calculating nutrition requirements, care should always be taken not to overestimate the patient's requirements. Significant risks are associated with overfeeding, including liver dysfunction, hyperglycaemia, respiratory failure, hyperlipidaemia, acidosis and other longer term complications. It should be remembered that there is no urgency to give the full nutrition. If there is suspicion of complications from overfeeding, the PN should be reduced for 1-2 days to let the abnormal findings settle and then recommenced once the patient has recovered.

Energy

Energy requirements are usually determined using a range of standard predictive equations. These consider the patient's age, sex, height and weight and may make adjustment for the patient's degree of stress. For the majority of patients the stress can be resolved over a few days. Calorie requirements are expressed in terms of kcal/kg and refer to total calories. Patient's requirements should be reviewed on a regular basis, taking into account their clinical condition.

A safe starting point is 25kcal/kg/d (total calories) as an initial goal rate. Once reached this should be reviewed to assess the patient's tolerance, progress and nutritional needs.

In the case of severe stress or significant protein energy malnutrition, requirements may be higher. Ongoing monitoring is particularly important in these patients to prevent over- or underfeeding and to assess the patient's tolerance, progress and nutritional needs. An upper limit of

35kcal/kg/d should not be exceeded. Such patients can be referred to an expert centre (teaching hospital).

Determining Weight Value in Estimating Requirements

Actual weight should be used if the patient is underweight or normal weight.

If the patient is severely underweight, actual weight should be used initially. Once the patient is stable and if the nutritional status is not improving, the energy requirements should be gradually increased. An upper limit of 35kcal/kg/day should not be exceeded.

In overweight/obese patients, adjusted body weight should be used as a guide to estimating nutritional requirements, as 25kcal/kg may significantly overestimate requirements.

Adjusting for overweight/obesity

A common method is to use an adjusted weight where:

$$\text{Adjusted weight} = \left(\frac{\text{Actual weight} - \text{Ideal weight}}{2} \right) + \text{Ideal weight}$$

Ideal weight can be calculated using the Hamwi equation:

Males: 48.1kg for the first 152.4cm of height, + 2.72kg for each additional 2.54cm

Females: 45.4kg for the first 152.4cm of height, + 2.27kg for each additional 2.54cm.

Energy Recommendation

Basic (short term, unstressed) requirements: 25kcal/kg/day

Stressed/increased requirements: Up to 35kcal/kg/day

Obese patients: Use adjusted weight

Refeeding: For patients at risk of refeeding

Protein

Consensus statements from ASPEN, ESPEN, NICE and BAPEN provide broad protein ranges but do not provide clear guidance for clinicians.

Specific recommendations are difficult to make due to:

- the small number of studies examining this question
- differences in energy: nitrogen input provided and in nutritional status of patients

In order to ensure the patient is receiving adequate levels of protein:

- patients need to be assessed on an individual basis taking into consideration prior nutritional status, disease status/severity of illness, projected length of time on PN
- patients need to be monitored regularly for tolerance (intolerance is indicated by a rising blood urea concentration) and adequacy, and protein input adjusted accordingly.

ASPEN: 2002

For the unstressed adult patient with adequate organ function requiring specialised nutrition support, 0.8g/kg/day may be adequate, but requirements may rise with metabolic demands to levels about 2g/kg/day (or, rarely, even higher) (p23A).

BAPEN: 1996

Nitrogen balance can be obtained in most patients with 0.2 g N/kg body weight. Whereas some patients may utilize more nitrogen, exceeding 0.3g/kg does not confer benefit and may be dangerous.

NICE: 2006

In situations of metabolic stress, requirements may be higher although the Guideline Development Group (GDG) would not recommend the provision of levels greater than 1.5g/kg/ day or 0.24g nitrogen/kg) (p109)

ESPEN: 2009

In illness/stressed conditions a daily nitrogen delivery equivalent to a protein intake of 1.5g/kg ideal body weight (or approximately 20% of total energy requirements) is generally effective to limit nitrogen losses (ESPEN Guidelines on Parenteral Nutrition: Surgery 2009).

When PN is indicated, a balanced amino acid mixture should be infused at approximately 1.3-1.5g/kg ideal body weight per day in conjunction with an adequate (ESPEN Guidelines on Parenteral Nutrition: Intensive Care 2009)

Recommendation

Initial starting rate: 0.16-0.24g of Nitrogen/kg/d (1.0-1.5g/protein/kg/d)

Upper limit: 0.32g Nitrogen/kg/d (2g/protein/kg/d)

Considerations

- The patient's PN requirements need to be monitored regularly and adjusted accordingly to prevent under- or overfeeding.
- Some patients may need more protein (up to 2g protein/day or 0.32g N/kg/ day) e.g. burns, sarcopenia. Amounts above this are not recommended. The patient must be monitored for tolerance, progress and nutritional needs, and signs of under- or overfeeding.
- Care should be taken when using pre-mixed solutions. Achieving protein requirements may result in excess calories being provided.
- Health professionals not experienced with PN should consult tertiary referral hospitals.

Carbohydrate

Glucose is the preferred carbohydrate energy source. The maximal capacity to oxidize glucose is 5 mg/kg/min (35 kcal/kg/d from glucose). Infusion of carbohydrates above this rate may induce complications such as hyperglycemia and fatty liver.

Lipid

Lipids provide an additional source of energy and essential fatty acids. In PN solutions, lipids are an emulsion of phospholipids and triglycerides.

Lipids can be administered separately or as part of a "3 in 1" delivery system. Lipid is best delivered through a "3 in 1" delivery system. Using 20-30% rather than 10% lipid emulsions in the PN mix reduces the proportion of phospholipids, which reduces the adverse influence on the immune system. Rapid infusion of separately hung bottles results in lipaemia and clearance of the lipid through the reticulo-endothelial system.

This results in liver dysfunction and reduced clearance of endotoxins by the liver and lung.

It is generally recommended that PN be started slowly at 1g lipid /kg/d, and blood monitored for lipaemia. After the first day the infusion rate can be increased depending on the patient's requirements. The lipid infusion rate should not exceed a maximum of 2g/kg/day. Patients with severe liver and renal dysfunction should not exceed 1g/kg/day. Lipid should ideally be given as a continuous infusion over 24 hours which is better tolerated, metabolized more effectively and allows for the clearance of the lipid as a

chylomicron. Higher infusion rates are associated with complications such as fat overload syndrome and lipaemia which may damage the liver.

For patients on cyclic PN, if lipaemia develops an hour after cessation of the PN, reduce the amount of lipid being infused. Refer to the manufacturer's information on appropriate rates of lipid infusion.

For central PN, the average is 30% of total calories from lipid. However, this can be up to 50% in some cases. The greater amount of lipid reduces glucose intolerance. Lipid tolerance is reduced in some conditions such as pancreatitis, unstable diabetes, hyper-triglyceridaemia and severe liver disease.

For peripheral PN, solutions may contain lipid up to 40-60% total (66% non-protein) calories to reduce the osmolarity of their PN solution and minimise the risk of thrombosis or damage to the vein epithelium.

Traditionally lipid emulsions are based on soy which contains triglycerides high in omega 6 polyunsaturated fatty acids (PUFA). These have been shown to be pro-inflammatory by increasing prostaglandin synthesis. New lipid emulsions can be found in a number of different forms, including olive oil and SMOF (a mixture of soybean oil, medium chain triglycerides, olive oil and fish oil). The olive oil provides monounsaturated fatty acids which are immunologically neutral.

The medium chain fatty acids are considered to be more easily converted into energy. Fish oil provides ω-3 fatty acids which reduce the inflammatory response. These more complex lipids may improve the nutritional value of PN, but long term studies are not yet published and there is no conclusive evidence of the benefits of these lipid emulsions at this time.

Recommendation

Initial: 1g lipid/kg/d

Maximum: 2g lipid/kg/d (Patients with liver dysfunction: 1g lipid/kg/day max)

Or

Central: average 30% of total calories as lipid (up to 50%)

Peripheral: solutions may contain lipid at 40-60% of total energy

Fluid

Fluid requirements will depend on the following considerations:

- clinical condition
- fluid status/balance (dehydration or fluid overload)
- other sources of fluid input e.g. IV, oral, enteral
- fluid losses e.g. drains, urine, vomiting, diarrhoea, fistula.

PN Micronutrient Requirements for the Adult Ward Patient

Micronutrients need to be provided daily to the PN patient. Some commercially available bags already contain micronutrients in the solution, whereas others require that they be added.

Ideally, additions to PN should be undertaken by a qualified pharmacist in a clean-room environment using an aseptic technique under a laminar flow hood. However if this is not available, it may be necessary to run the micronutrients as a separate intravenous infusion. If this is the case, they should be infused over at least eight hours to minimise renal losses and side effects. Additions should be done as per manufacturer instructions.

There are a number of different trace element solutions available (both single ingredient and multi-ingredient preparations). The manufacturer of the product should be contacted for advice regarding compatibility with PN solutions, information regarding the volume of compatible intravenous solutions, recommended concentration and recommended infusion rates.

Consideration needs to be given to patients with clinical conditions which may result in increased or decreased requirements. Monitoring of trace micronutrient status is essential.

Recommendation Vitamins and trace elements should be included daily, in specified amounts from the onset of PN. Commercial products are available which provide a balanced trace element additive. Similarly intravenous vitamin products with recommended daily requirements of water- soluble and fat-soluble vitamins are commercially available. Vitamin K needs to be given as a further additive.

Current Recommended Adult Daily Oral and Parenteral Micronutrient Requirements *(ASPEN position paper 2012)*		
	Oral[a]	**Parenteral**
Fat-Soluble Vitamins		
Vitamin A	M, 900 mcg or 3000 IU; F, 700 mcg or 2333 IU[b] 770 mcg (preg); 1300 mcg (lact)	990 mcg or 3300 IU[b]
Vitamin D	Age 19–70 y: 15 mcg or 600 IU[c], Age >70 y: 20 mcg or 800 IU	5 mcg or 200 IU[c]
Vitamin E	15 mg; 19 mg (lact)	10 mg or 10 IU[d]
Vitamin K	M, 120 mcg; F, 90 mcg (AI)	150 mcg Water-Soluble Vitamins
Water-Soluble Vitamins		
Vitamin B1 (thiamine)	M, 1.2 mg; F, 1.1 mg 1.4 mg (preg/lact)	6 mg
Vitamin B2 (riboflavin)	M, 1.3 mg; F, 1.1 mg 1.4 mg (preg); 1.6 mg (lact)	3.6 mg
Vitamin B3 (niacin)	M, 16 mg; F, 14 mg 18 mg (preg); 17 mg (lact)	40 mg
Vitamin B5 (pantothenic acid)	5 mg; 6 mg (preg); 7 mg (lact) (AI)	15 mg
Vitamin B6 (pyridoxine)	Age 19–50 y: 1.3 mg Age >51 y: M, 1.7 mg; F, 1.5 mg 1.9 mg (preg); 2.0 mg (lact)	6 mg
Vitamin B12 (cyanocobalamin)	2.4 mcg; 2.6 mcg (preg); 2.8 mcg (lact)	5 mcg
Vitamin C (ascorbic acid)	M, 90 mg; F, 75 mg 85 mg (preg); 120 mg (lact)	200 mg
Folate	400 mcg; 600 mcg (preg); 500 mcg (lact)	600 mcg

Biotin	30 mcg; 35 mcg (lact) (AI)	60 mcg
Other Nutrients		
Choline	M, 550 mg; F, 425 mg 450 mg (preg); 550 mg (lact) (AI)	Not available for PN use
Trace Elements		
Copper	900 mcg 1000 mcg (preg); 1300 mcg (lact)	0.3–0.5 mg
Chromium	Age 19–50 y: M, 35 mcg; F, 25 mcg Age >51 y: M, 30 mcg; F, 20 mcg 30 mcg (preg); 45 mcg (lact) (AI)	10 – 15 mcg
Fluoride	M, 4 mg; F, 3 mg (AI)	Not routinely added in U.S.[e]
Iodine	150 mcg; 220 mcg (preg); 290 mcg (lact)	Not routinely added in U.S.[e]
Iron	Age 19–50 y: M, 8 mg; F, 18 mg Age >50 y: 8 mg 27 mg (preg); 9 mg (lact)	Not routinely added in U.S.[e] (given 25–50 mg/monthly as separate IV infusion when indicated)
Manganese	M, 2.3 mg; F, 1.8 mg 2.0 mg (preg); 2.6 mg (lact) (AI)	0.06–0.1 mg
Molybdenum	45 mcg; 50 mcg (preg/lact)	Not routinely added in U.S.[e]
Selenium	55 mcg; 60 mcg (preg); 70 mcg (lact)	20–60 mcg
Zinc	M, 11 mg; F, 8 mg 11 mg (preg); 12 mg (lact)	2.5–5 mg

Ranges include female (lower amounts) and male (higher amounts). This table does not include nutrient needs for pregnancy or lactation for ages <19 years. AI, Adequate Intake; F, female; IU, International Unit; IV, intravenous; lact, lactation; M, male; PN, parenteral nutrition; preg, pregnancy.

a: Enteral recommendations are the Recommended Dietary Allowance (RDA) unless one is not established, in which case the AI is listed and so noted in the table.

b: 1 mcg RAE (retinol activity equivalent) = 1 mcg retinol = 12 mcg β-carotene = 24 mcg α-carotene or β-cryptoxanthin.

c: 1 IU of retinol = 0.3 mcg retinol or 0.3 mcg RAE.

d: To convert IU α-tocopherol to mg: IU × 0.67 mg RRR-α-tocopherol, natural form ("d-α-tocopherol") or IU × 0.45 mg all-rac-α-tocopherol, synthetic form ("dl-α-tocopherol"). dl-α-tocopheryl acetate (1 IU = 1 mg = 1 USP unit) is used in IV multivitamin preparation.

e: Fluoride (0.57–1.45 mg), iodine (10–130 mcg), iron (1–1.95 mg), molybdenum (10–25 mcg), and cobalt (0–1.47 mg) are routinely added to PN products in Europe.

Daily Oral or Enteral Recommended Daily Allowances (RDA) for Pediatric Age Groups (ASPEN position paper GL 2012)								
	Age Groups							
	0–6 mo	**7–12 mo**	**1–3 y**	**4–8 y**	**9–13 y**	**14–18 y**	**<18 y Pregnant**	**<18 y Lactating**
Fat-Soluble Vitamins								
Vitamin A, mcg[a]	400[b]	500[b]	300	400	600	M, 900; F, 700	750	1200
Vitamin D, mcg/IU	10/400[b]	10/400[b]	15/600	15/600	15/600	15/600	15/600	15/600
Vitamin E, mg	4[b]	5[b]	6	7	11	15	15	19
Vitamin K, mcg	2[b]	2.5[b]	30[b]	55[b]	60[b]	75[b]	75[b]	75[b]
Water-Soluble Vitamins								
Vitamin B_1 (thiamine), mg	0.2[b]	0.3[b]	0.5	0.6	0.9	M, 1.2; F, 1.0	1.4	1.4
Vitamin B_2 (riboflavin), mg	0.3[b]	0.4[b]	0.5	0.6	0.9	M, 1.3; F, 1.0	1.4	1.6
Vitamin B_3 (niacin), mg	2[b]	4[b]	6	8	12	M, 16; F, 14	18	17

Vitamin B_5 (pantothenic acid), mg	1.7[b]	1.8[b]	2[b]	3[b]	4[b]	5[b]	6[b]	7[b]
Vitamin B_6 (pyridoxine), mg	0.1[b]	0.3[b]	0.5	0.6	1	M, 1.3; F, 1.2	1.9	2.0
Vitamin B_{12} (cyanocobalamin),mcg	0.4[b]	0.5[b]	0.9	1.2	1.8	2.4	2.6	2.8
Vitamin C (ascorbic acid), mg	40[b]	50[b]	15	25	45	M, 753; F, 65	80	115
Folate, mcg	65[b]	80[b]	150	200	300	400	600	500
Biotin, mcg	5[b]	6[b]	8[b]	12[b]	20[b]	25[b]	30[b]	35[b]
Choline, mg	125[b]	150[b]	200[b]	250[b]	375[b]	M, 550; F, 400[b]	450[b]	550[b]
Trace Elements								
Copper, mcg	200[b]	220[b]	340	440	700	890	1000	1300
Chromium, mcg	0.2[b]	5.5[b]	11[b]	15[b]	M, 25; F, 21[b]	M, 35; F, 24[b]	29[b]	44[b]
Fluoride, mg	0.01[b]	0.5[b]	0.7[b]	1[b]	2[b]	3[b]	3[b]	3[b]
Iodine, mcg	110[b]	130[b]	90	90	120	150	220	290
Iron, mg	0.27[b]	11	7	10	8	M, 11; F, 15	27	10
Manganese, mg	0.003[b]	0.6[b]	1.2[b]	1.5[b]	M, 1.9; F, 1.6[b]	M, 2.2; F, 1.6[b]	2[b]	2.6[b]
Molybdenum, mcg	2[b]	3[b]	17	22	34	43	50	50
Selenium, mcg	15[b]	20[b]	20	30	40	55	60	70
Zinc, mg	2b	3	3	5	8	M, 11; F, 9	12	13

F, female; IU, International Unit; M, male.

b: No Recommended Daily Allowance (RDA) available; Adequate Intake (AI) is listed.

a: 1 mcg RAE (retinol activity equivalent) = 1 mcg retinol = 12 mcg β-carotene = 24 mcg α-carotene or β-cryptoxanthin; 1 IU of retinol = 0.3 mcg retinol or 0.3 mcg RAE.

Current Daily Parenteral Recommendations for Infants and Children (ASPEN position paper GL 2012)		
	Infants	**Children**
Fat-Soluble Vitamins		
Vitamin A[a]	150–300 mcg/kg/d	150 mcg/d
Vitamin D	0.8 mcg/32 IU per kg/d	10 mcg/400 IU per d
Vitamin E	2.8–3.5 mg/kg/d	7 mg/d
Vitamin K	10 mcg/kg/d	200 mcg/d
Water-Soluble Vitamins		
Vitamin B_1 (thiamine)	0.35–0.5 mg/kg/d	1.2 mg/d
Vitamin B_2 (riboflavin)	0.15–0.2 mg/kg/d	1.4 mg/d
Vitamin B_3 (niacin)	4.0–6.8 mg/kg/d	17 mg/d
Vitamin B_5 (pantothenic acid)	1–2 mg/kg/d	5 mg/d
Vitamin B_6 (pyridoxine)	0.15–0.2 mg/kg/d	1 mg/d
Vitamin B_{12} (cyanocobalamin)	0.3 mcg/kg/d	1 mcg/d
Vitamin C (ascorbic acid)	15–25 mg/kg/d	80 mg/d
Folate	56 mcg/kg/d	140 mcg/d
Biotin	5–8 mcg/kg/d	20 mcg/d

Trace Elements		
Copper	20 mcg/kg/d (no max stated)[b]	20 mcg/kg/d (500 mcg/d max[c,d]) [b]
Chromium	0.2 mcg/kg/d (max 5 mcg/d)[e]	0.2 mcg/kg/d (max 5 mcg/d[c])[e]
Fluoride	No recommendations	No recommendations
Iodine	1 mcg/d[f]	1 mcg/d[f]
Iron	Premature: 200 mcg/kg/d[f] Infant: 50–100 mcg/kg/d[f]	50–100 mcg/kg/d[f]
Manganese	1 mcg/kg/d (max 50 mcg/d[c])	1 mcg/kg/d (max 50 mcg/d[c])
Molybdenum	Premature: 1 mcg/kg/d Infant: 0.25 mcg/kg/d (max 5 mcg/d[c])	0.25 mcg/kg/d (max 5 mcg/d[c])
Selenium	Premature: 2–3 mcg/kg/d Infant: 1–3 mcg/kg/d (no max stated)	1–3 mcg/kg/d (100 mcg/d max[c,d])
Zinc	Premature: 450–500 mcg/kg/d Infants <3 mo: 250 mcg/kg/d Infants >3 mo: 50 mcg/kg/d (max 5000 mcg/d)	50 mcg/kg/d (max 5000 mcg/d[c])

IU, International Unit; max, maximum; PN, parenteral nutrition.

a: 1 mcg/kg RAE (retinol activity equivalent) = 1 mcg/kg retinol.

b: Authors recommend monitoring plasma copper and ceruloplasmin concentrations in long-term PN patients and patients with burns or cholestasis with appropriate adjustment of doses as needed.

c: Refers to maximum dose for routine supplementation; however, higher doses may be indicated in patients with established deficiency or increased requirements.

d: Maximum dose was not specified in above reference but is included in this table as the maximum dose based on the recommended adult dose.

e: Authors state that chromium contaminates in PN products satisfies requirements; therefore, additional supplementation is unnecessary.

f: Not currently added to PN in U.S.

Current Parenteral and Enteral Vitamin and Trace Element Recommendations for Preterm and Term Neonates *(ASPEN position paper GL 2012)*				
	Preterm Neonates		**Term Neonates**	
Route of Administration	**Parenteral**	**Enteral**	**Parenteral**	**Enteral**
Fat-Soluble Vitamins				
Vitamin A[a]	700–1500 IU/kg/d	700–1500 IU/kg/d	2300 IU/d	1333 IU/d 400 mcg/d
Vitamin D	40–160 IU/kg/d	150–400 IU/kg/d goal 400 IU/d	400 IU/d	400 IU/d
Vitamin E	2.8–3.5 IU/kg/d	6–12 IU/kg/d	7 IU/d	6 IU/d
Vitamin K	10 mcg/kg/d in PN +500 mcg IM at birth	8–10 mcg/kg/d	200 mcg/d +500 mcg IM at birth	2 mcg/d
Water-Soluble Vitamins				
Vitamin B1 (thiamine)	200–350 mcg/kg/d	180–240 mcg/kg/d	1.2 mg/d	0.2 mg/d
Vitamin B2 (riboflavin)	150–200 mcg/kg/d	250–360 mcg/kg/d	1.4 mg/d	0.3 mg/d
Vitamin B3 (niacin)	4–6.8 mg/kg/d	3.6–4.8 mg/kg/d	17 mg/d	2 mg/d
Vitamin B5 (pantothenic acid)	1–2 mg/kg/d	1.2–1.7 mg/kg/d	5 mg/d	1.7 mg/d

Vitamin B6 (pyridoxine)	150–200 mcg/kg/d	150–210 mcg/kg/d	1000 mcg/d	14 mcg/kg/d
Vitamin B12 (cyanocobalamin)	0.3 mcg/kg/d	9.3 mcg/kg/d	1 mcg/d	0.4 mcg/d
Vitamin C (ascorbic acid)	15–25 mg/kg/d	18–24 mg/kg/d	80 mg/d	40 mg
Folate	56 mcg/kg/d	25–50 mcg/kg/d	140 mcg/d	65 mcg/d
Biotin	5–8 mcg/kg/d	3.6–6 mcg/kg/d	20 mcg/d	5 mcg/d
Trace Elements				
Copper[a]	29 mcg/kg/d	120–150 mcg/kg/d	20 mcg/kg/d	200 mcg/d
Chromium	0.05–0.3 mcg/kg/d	0.1–2.25 mcg/kg/d	0.2 mcg/kg/d	0.2 mcg/d
Iodine[b]	1 mcg/kg/d	10–60 mcg/kg/d	1 mcg/kg/d	110–130 mcg/d
Iron	100–200 mcg/kg/d if PN only >2 mo	2000–4000 mcg/kg/d	250–670 mcg/kg/d if PN only >2 mo	2000–4000 mcg/kg/d
Manganese	1 mcg/kg/d	0.7–7.5 mcg/kg/d	1 mcg/kg/d	0.3 mcg/d

Molybdenum	0.25 mcg/kg/d	0.3 mcg/kg/d	0.25 mcg/kg/d	2 mcg/d
Selenium	1.5–4.5 mcg/kg/d	1.3–4.5 mcg/kg/d	2 mcg/kg/d	15 mcg/d
Zinc	400 mcg/kg/d	1000–3000 mcg/kg/d	250 mcg/kg/d	2000 mcg/d

IM, intramuscular; IU, International Unit; PN, parenteral nutrition.
a: Copper dose may need to be removed or reduced in infants with obstructive jaundice. Check serum copper and ceruloplasmin concentration to determine need for dose change.
b: Insufficient data at this time to support routine parenteral iodine supplementation in preterm infants.

Trace Element Allowances in PN Therapy

Trace elements are essential nutrients that act as coenzymes and cofactors involved in metabolism. It is difficult to measure the exact amount in PN solutions and in the blood because of the low levels. It is better to measure enzyme activity particularly for zinc, selenium and copper.

The most common trace element deficiencies seen in PN occur with zinc, selenium and copper. These trace elements are most likely to be low in patients with diarrhoea (particularly patients with short bowel syndrome) and patients in intensive care. Such patients may require increased amounts in their PN solution. Patients with severe malnutrition are also at risk of developing deficiencies when renourished.

Trace element needs for the individual patient on PN are dictated by pre-existent nutritional status, losses in stool and urine and nutrient bioavailability

When considering the dosing of trace elements, adjustments may need to be made in certain settings, as an individual's requirements may vary based on factors such as organ function, disease state, metabolic condition, and administration route and medication usage.

Giving excess trace elements to individuals who do not need them may be harmful. Therefore it is important to monitor these stressed individuals even over the first two weeks of PN support.

Contamination

Many of the components of the PN formulation have been shown to be contaminated with trace elements such as zinc, copper, manganese, chromium, selenium and aluminium10.

As the contamination level of various compounds of PN can significantly contribute to total intake, serum concentration should be monitored with long term use10.

As a result of contamination, patients receiving long term PN therapy are at risk of trace element toxicity, which is why serum monitoring is necessary

Trace Element Allowances in PN Therapy

TRACE ELEMENT	PN DOSE	TOXICITY DOSE	SPECIAL CONSIDERATIONS	DEFICIENCY SIGNS
Chromium	10-20µg	–	Increased dose: Stress including physical trauma, and burns, Infection Decreased dose: Renal failure/ impairment	• Glucose intolerance, insulin resistance, hyperglycemia, glycosuria, weight loss, metabolic encephalopathy with confusion, ataxia, paresthesias and peripheral neuropathy, increased respiratory. • Deficiency should be suspected in patients on PN with progressive impairment of glucose tolerance.

Copper	0.3-1.5mg	–	Increase dose: 0.4-1.3mg in excessive gastrointestinal losses Decreased dose: for patients with liver dysfunction	• Hypochromic microcytic anaemia and neutropenia diffuse osteoporosis, delayed bone age, widened cupped metaphyses with breaks, subperiosteal hematomas, ossifications in the shafts of long bones, diaphyseal fractures, oedema of the limbs with pseudoparalysis, neurologic abnormalities, and hyperlipidemia • Depigmentation, kinked hair, vascular degeneration and osteopenia with skeletal abnormalities
Iodine	0-1 µmol/day	–	–	• Hypothyroidism, goiter (earliest clinical feature), cretinism, impaired reproductive outcomes, increased childhood mortality, impaired mental and physical
Iron	Only if true Fe deficiency present	Single doses of iron sucrose >500mg are not recommended	• Menstruating women, and patients with blood loss may be more prone to developing Fe deficiency	• Iron deficiency has three stages where the majority of physical indicators and symptoms are not seen until the final stage (iron deficiency anaemia). It is important to interpret iron studies in the context of the patient's clinical condition. • The first sign of iron deficiency is "low serum iron" which is indicated by low serum ferritin and a decrease in iron-binding capacity. • In the acute phase

				response, ferritin high and transferrin low • Iron deficiency is indicated by low serum transferrin saturation, increased erythrocyte protoporphyrin concentrations, and increased serum transferrin receptors • Iron-deficiency anemia (final stage) symptoms include: • Decrease work capacity • Delayed psychomotor development in infants • Impaired cognitive function • Impaired immunity • Adverse pregnancy outcomes
Manganese	Maximum 60-100µg/d	500µg/d excessive	• Manganese should not be supplemented if the patient has liver disease with an elevated bilirubin or decreased bile excretion + hepatobiliary disease	• Impaired glucose tolerance, impaired growth, impaired reproduction function, alterations in carbohydrate and lipid metabolism, hypocholesterolemia, scaly dermatitis, hair depigmentation, reduced vitamin K dependent clotting proteins, decreased bone mineral density

Molybdenum	Only in the rare instance of suspected deficiency at ~20-200µg/day	–		• Molybdenum deficiency is rare or nonexistent in adult PN patients, • tachycardia, tachypnea, headache, central scotomas, nausea, vomiting, vision problems/night blindness, disorientation and coma
Selenium	20-80 µg/day	>1500mg considered toxic	• Increased dose: 300-1000µg/ day may benefit mortality in the first month with general ICU patients	• Increases in plasma T4 and decreases in T3, Keshan disease (results in cardiac myopathy, heart failure, arrhythmias, premature death), Kashin-Beck disease (cartilage condition), low blood and hair levels, impaired immune function • Skeletal muscle myopathy • Selenium and iodine deficiency combined increases risk of cretinism
Zinc	2.5 - 6.4mg	Toxicity range: 23 - 300mg	• Increased dose: Acute catabolic stress/burns, Diarrhea syndromes/ Chronic diarrhea or high output fistulae • Patients with low pancreatic output due to disease or surgical resection might be at increased risk of toxicity	• Clinical manifestations similar to those of acrodermatitis enteropathica; seborrheic or psoriatic skin lesions of the nasolabial folds and scrotum, followed by non-scarring alopecia, glossitis and stomatitis • Diarrhea and depression and/or confusion may present 3-6 weeks after the appearance of the skin lesions. Hyperammonemia may occur with even marginal deficiency, which could potentially exacerbate

				acid-base disorders and hepatic encephalopathy • Impaired wound healing, loss of taste (hypogeusia), behavior disturbances, night blindness and immune deficiency. • Glucose intolerance • Immunological defects of lymphopenia and depressed T-cell responses

PN for the Critically Ill Adult Patient

There is increasing awareness that early nutrition support in critically ill patients is desirable. Despite this, many aspects remain unclear. Early enteral nutrition is the preferred route, but if not successful PN should be considered. Practice varies as to when to commence PN, but emerging evidence suggests a significant mortality benefit for commencing early PN, compared to EN that is delayed for longer than 24hours.

Due to poor outcomes with high caloric PN, a reasonable approach early in the course of critical illness is to use moderate calorie levels of 25kcal/ kg/day with careful attention to glucose control. Increase the calories cautiously as the critically ill patient recovers.

There has been considerable research interest in the potential of nutritional components to modify the disease process in critical illness. Many of the studies have been small and have used varying combinations and ratios of macro and micro nutrients, making interpretation difficult. No clear recommendations for glutamine, micronutrients, antioxidants and modified lipids can be made at this time.

Key Recommendations

- Early enteral nutrition is the first option in patients with an intact GI tract
- PN should be considered in critically ill patients when EN will be delayed, but there are insufficient data to recommend supplementation of EN with PN when EN is adequate.

- Basic energy requirements in critical illness are 25kcal/kg/day
- Prevention of hyperglycaemia by avoiding overfeeding and initiation of insulin where appropriate
- Micronutrients including vitamins and trace elements should be added in usual daily requirements unless specific deficiencies are known.

Monitoring Adult Patients on PN

Monitoring during PN is particularly important because the patient is at greater risk of toxicity, deficiency and other complications.

Key aspects of monitoring include:

- risk of refeeding syndrome
- indicators of overfeeding
- hyperglycemia and hypoglycemia
- micronutrient deficiency and toxicity
- complications of line access including line infection
- other long term complications

A stable patient indicates a patient who is at target rate of PN and the clinical indicator in question is stable within a clinically acceptable range.

Monitoring Patients on Parenteral Nutrition

Nutrient intake from oral, enteral or parenteral nutrition	To ensure that the patient is receiving adequate / appropriate nutrients to meet requirements and to consider if PN is still appropriate.	Daily	2 x week
Fluid Balance Charts	To monitor fluid status and ensure the patient is not becoming over/under hydrated	Daily	Daily
Weight	To monitor fluid status, and to determine whether nutritional goals are being achieved	Daily	2 x Week

Observations: Temperature, blood pressure, pulse, respiratory rate	Monitor for infection and fluid balance	4 hourly	4 hourly
Glucose	To assess glucose tolerance and identify need for insulin requirements.	6 hourly	Daily. Monitor for risk of hypoglycemia when ceasing PN particularly in patients receiving insulin.
Sodium, potassium, urea, creatinine	Assessment of renal function and fluid status and risk of refeeding syndrome	Daily	2 x week
Magnesium, Phosphate	Refeeding risk, depletion and toxicity	Daily	2 x week
Liver Enzymes and Bilirubin (LFTs)	Overfeeding or hepatobiliary dysfunction	Daily	2 x week
CRP	To assess the presence of an acute phase reaction (APR) as protein, trace element and vitamin results may be altered	2-3/week until stable	Weekly
Full blood count and MCV	Indicator of infection or sepsis anaemia, blood loss, iron & folate.	2 x week	Weekly
Cholesterol / Triglyceride	Overfeeding, calories, lipids and or glucose	Baseline (prior to starting	Weekly

		PN)	
Zinc	Risk for trace element deficiency/toxicity Acute phase response causes Zn ↓ and Cu ↑	On starting PN	Every 2 weeks
Copper	Risk of toxicity in biliary dysfunction.	On starting PN	Every 2 weeks (if available)
Selenium	Deficiency likely in severe illness and sepsis, or long-term nutrition support	On starting PN	Every 2 Weeks (if available)
Iron studies	Assess iron status. Deficiency common in long term parenteral nutrition	on starting PN	Monthly
Folate, B12	Assess if serum folate/B12 sufficient	On starting PN	Monthly
Manganese	Excess provision to be avoided red blood cell or whole blood better measure of excess than plasma	On starting PN	Monthly (if available)
25-OH Vit D	Low in high-risk groups	On starting PN	Monthly
Bone densitometry	To diagnose metabolic bone disease. To be used together with lab tests for metabolic bone disease	Not routinely done in short term PN patients.	On starting home PN Then every 12 months

Chapter 28: PN Complications

Liver Dysfunction

It is acceptable for markers of liver function to rise slightly after the commencement of PN, but these biochemical markers should return to normal once PN ceases. If biochemical markers continue to rise, the following need to be considered:

(Note: Underlying sepsis may cause liver dysfunction. This may be from the abdomen or low grade organisms culturing the central line.)

Hepatic Steatosis

This is the most common liver dysfunction in adults receiving PN, defined as an accumulation of fat in the hepatocytes and characterized by a non-specific rise in liver function tests. The main reason for hepatic steatosis is excessive calories and specifically an excess of carbohydrate calories (a fat-free bag). Although more rare, it can occur when fat is included.

Gall Bladder and Biliary Complications (Cholestasis and Cholethiasis)

These are more common in pediatric PN patients, but are also likely in adults who have a complete lack of enteral/oral nutrition, short bowel, on long-term PN nutrition or are overfed total calories. The impaired release of, or a complete obstruction of, bile is characterized by a rise in bilirubin, ALP and GGT (although these can be elevated due to other reasons).

Management of Liver Dysfunction

1. Ensure a balance of carbohydrate, lipid and amino acid in the parenteral formula.
2. Do not exceed overall calories. For patients with liver dysfunction, the maximum amount of fat is 1g/kg/day and the maximum of carbohydrate is 4g/kg/day.
3. Initiate oral or enteral nutrition, even if it is very small amounts, as this stimulates gall bladder emptying.
4. Cyclic PN (i.e. running it over a smaller period of time each day, usually 8-14 hours) provides fasting time to reduce insulin levels and help reduce liver dysfunction. Note that care must be taken as this means a higher infusion rate when the PN is running and this

can also result in hyperinsulinemia and fatty acid deposition. Intermittent/ cyclic PN should only be trialled for long term patients and those displaying clear signs of gall bladder dysfunction.

5. Some research into the role of the amino acid carnitine indicates it may prevent hepatic steatosis but there is no clear evidence on adults at this point.
6. Choline deficiency has also been reported as a cause of hepatic steatosis in PN patients. It does appear that choline supplementation may be beneficial but more research is needed before changes in practice are made.
7. Initiate blood cultures.

Transitional Feeding

The decision to recommence oral or enteral nutrition requires an assessment of GI tract anatomy, function and absorption and requires multidisciplinary input. If the patient is re-introduced to oral or enteral feeding and is absorbing and tolerating this, the PN rate can be titrated down in proportion to their oral/enteral energy and protein intake.

Ceasing PN

PN may be ceased for a number of reasons:

- recommencing or established oral/enteral feeding
- line sepsis
- withdrawal of therapy
- unresolving acute liver failure.

When ceasing PN, it is important to monitor for hypoglycemia.

In adults, if the patient is not on insulin therapy, a reasonable and fairly conservative approach is to decrease the PN rate by 50% and continue to infuse for 1-2 hours before ceasing.

This step-down process avoids the need for strict glucose monitoring after PN is discontinued. It is no longer considered essential to cease PN by tapering the rate down over many hours or even days. This practice used to be recommended in the era when excessive amounts of glucose in PN were used, occasionally leading to rebound hypoglycemia after PN was ceased abruptly. With the advent of “3 in 1” solutions and change in practice to avoid high glucose loads, several small studies have demonstrated that

abrupt discontinuation of PN does not cause hypoglycemia in the majority of patients.

For patients on an insulin infusion or subcutaneous insulin, more care needs to be taken when ceasing PN. Insulin dosing will need to be adjusted accordingly. If PN must be ceased suddenly, then a glucose infusion should be established for 12 hours after the last insulin dose. If the patient has Type 1 diabetes, insulin should continue to be given along with carbohydrate either in the form of intravenous glucose infusion or oral/enteral carbohydrate. A consultation with the endocrinology team should be sought.

Otsuka Pakistan Ltd.

EN Products

Aminoleban Oral

Aminoleban Oral is a specially formulated nutritional formula for patients with chronic liver impairment. It is a nutritional supplement that contains high concentration of Branched-chain amino acids.

DESCRIPTION AND COMPOSITION

Aminoleban is an orange flavored powder each 50 grams of which provides the following:

Energy	210 kcal
Proteins	13.5 grams
Carbohydrates	32.35 grams
Fats	3.5 grams

Each 50 grams of Aminoleban Oral contains:

Alanine	0.655 g	Vitamin B6	0.2015 mg
Arginine	0.695 g	Vitamin B12	0.5 mcg
Aspartic Acid	0.43 g	Vitamin C	7.24 mg
Carnitine	25 mg	Vitamin E	9.86 mg
Glutamic Acid	0.855 g	Vitamin K	5.5 mcg
Glycine	1.68 g	Folic Acid	0.05 mg
Histidine	0.235 g	Pantothenic Acid	1.09 mg
Isoleucine	1.76 g	Nicotinic Acid	1.4 mg
Leucine	2.03 g	Biotin	25 mcg

Lysine	0.42 g	Choline	5.05 mg
Methionine	0.06 g	Sodium	47 45 mg
Phenylalanine	0.16 g	Potassium	162 mg
Proline	0.98 g	Calcium	69 mg
Serine	0.215 g	Magnesium	20.2 mg
Threonine	0.29 g	Chloride	218.9 mg
Tyrosine	0.04 g	Phosphorus	83.75 mg
Tryptophan	0.08 g	Iron	*1.315 mg*
Valine	1.635 g	Zinc	5 mg
Vitamin A	139.8 mcg	Copper	141 mcg
Vitamin D	1.165 mcg	Iodine	9.55 mcg
Vitamin B1	0.086 mg	Manganese	0.175 mg
Vitamin B2	0.155 mg		

The concentration of BCAA is almost 45% in Aminoleban Oral.

INDICATIONS

Indicated for the improvement of nutritional state in chronic liver impairment including those with hepatic encephalopathy

CONTRAINDICATIONS
Aminoleban Oral is contraindicated in patients with a history of allergy to milk.

DOSAGE AND ADMINISTRATION
In adults the usual dosage is 50 grams (1 sachet) daily.
50 grams of powder (about 5 level scoops) should be mixed with 180 mL of warm water (50 C). Stir thoroughly. The dissolved solution is about 200 mL and provides energy about 1 kcal/mL. Boiling water should not be used as it may cause denaturation of proteins.

The dosage may be reduced in the elderly to 50 grams twice daily.

The osmolarity of the solution is 600 mOsm/L. Prepared solution should be kept in a refrigerator and used within 24 hours.

PREGNANCY AND LACTATION
The amount of vitamin A should not exceed 10000 I.U. daily during pregnancy. Aminoleban Oral contains 466 I.U. (139.8 mcg). Thus it can be administered to pregnant women who have liver impairment.

PEDIATRIC USE
The safe use of this product has not been established in children (insufficient clinical experience).

PHARMACEUTICAL PRECAUTIONS
The lid should be tightly closed and kept in a cool, dry place. Once the can is opened, it should be consumed in 1 month.

Proten Gold

Special Dietary food for

Mal Nutrition

Composition

- Soy Milk (61.5%)
- Sucrose
- Maltodextrin
- Vanilla powder
- Sodium Chloride
- Milk flavor
- Vitamin Premix
- Zinc Sulphate
- Ferrous Sulphate
- Macro & Micro Nutrients
- Selenium
- Chromium

Total Energy: 230 kcal

Proteins: 10 grams

Fats: 6 grams

Carbohydrates: 32 grams

Linoleic acid: 3.3 grams

Insoluble fiber: 6 grams

Osmolarity: 500 mOsm/L (Approx)

NUTRITION FACTS (APPROX)

Serving Size: 1 Sachet (52g)

	Unit	Per 100 g	Per 100 kcal	Per 52 g
Total Energy	kcal	430	100	230
Energy from Fat	kcal	110	25.6	60
Total Fat	g	12.0	2.8	6.0
Saturated	g	2.1	0.5	1.1
Linoleic Acid	g	6.3	1.5	3.3
Cholesterol	mg	0.0	0.0	0.0
Protein	g	20.0	4.7	10.0
Carbohydrate	g	61.0	14.2	32.0
Total Sugar	g	36.8	8.6	20.0
Lactose	g	8.0	1.9	4.0
Soluble Fiber	g	0.2	0.0	0.1
Insoluble Fiber	g	12.0	2.8	6.0

Vitamins	Unit	Per 100 g	Per 100 kcal	Per 52 g
Vitamin A	µg	63.0	14.7	32.7
Vitamin B1	µg	169	39.3	87.9
Vitamin B2	µg	77.5	18.0	40.3
Vitamin B3	µg	1380	320.9	717.6

Vitamin B5 (Calcium D-Pantothenate)	Mg	4.35	1.0	2.3
Vitamin B6	µg	123.0	28.6	64.0
Vitamin C	mg	26.1	6.1	13.6
Vitamin E	µg	303.0	70.5	157.6
Biotin	µg	130.2	30.3	68.0

Minerals	**Unit**	**Per 100 g**	**Per 100 kcal**	**Per 52 g**
Sodium	mg	340	79.1	180.0
Potassium	mg	1176.9	273.7	612.0
Calcium	mg	56.6	13.2	29.4
Copper	µg	586.0	136.3	304.7
Iodine	µg	55.6	12.9	28.9
Manganese	mg	1.2	0.3	0.7
Phosphorus	mg	348.9	81.1	181.4
Selenium	µg	10.4	2.4	5.4
Zinc	mg	5.2	13.8	2.7
Chromium	µg	38.7	9.0	20.1

Dosage and Serving:

Adults:

One sachet is mixed with 200ml water, given 2 to 6 times a day together with food to fulfill daily protein requirements.

Children:

Day 1: Half sachet mixed with 200ml water, given twice a day

Day 2 and after: 1 sachet mixed with 200ml water, given 1 to 4 times a day together with food to fulfill the daily protein requirements.

Dosage and serving is adjusted to tolerance and individual needs.

Otsuka Pakistan Ltd.

PN Products

AMINOLEBAN®

(Special Formula 8% Amino Acids)

Amino acids Injection for hepatic encephalopathy

Etiologically the onset of hepatic encephalopathy has been related to excess ammonia, short-chain fatty acids and mercaptans. Recent studies have emphasized the importance of other contributory factors involved in severe hepatic impairment: disturbance of the free amino acid pattern in plasma characterized by an increase of phenylalanine, tryptophan, tyrosine and methionine, and a decrease of branched-chain amino acids such as leucine, isoleucine and valine.

The disturbance of the free plasma amino acids pattern causes disturbances in the transport of amino acids across the blood-brain barrier, increasing synthesis of false neurotransmitters in the brain, resulting in the disturbance of the overall cerebral amine metabolism. This disturbance of cerebral amine metabolism is suspected to be the major cause of hepatic encephalopathy.

With these findings as background information, Fischer et al developed a special formula of amino acids, containing high concentrations of branched-chain amino acids and low concentrations of phenylalanine, tryptophan and methionine, without tyrosine, to correct the disturbance of the plasma free amino acids pattern. They have conducted experimental and clinical studies of the special formula for the treatment of hepatic encephalopathy and demonstrated that the normalization of the plasma free amino acids pattern is effective in improving hepatic encephalopathy.

AMINOLEBAN injection is prepared with an amino acids composition identical to that of Fischer's formula. Clinical studies have shown that the injection is effective in correcting plasma amino acids concentration and the clinical symptoms of hepatic encephalopathy.

DESCRIPTION

AMINOLEBAN is a clear and colorless solution for injection.

pH: 5.5 - 6.5

Specific gravity (20°C): 1.025

Osmotic pressure ratio (to physiological saline): Approx. 3

COMPOSITION

Each 1000 mL of AMINOLEBAN contains:

Aminoacetic acid J R,	9.0 g
L-alanine U.S.P.	7.5 g
L-arginine HCl J.P.	7.3 g
(L-arginine equivalent)	(6.0 g)
L-cysteine HCl monohydrate U.S.P.	0.4 g
(L-cysteine equivalent)	(0.3 g)
L-histidine HCl monohydrate J.P.	3.2 g
(L-histidine equivalent)	(2.4 g)
L-isoleucine J.P.	9.0 g
L-leucine J.P.	11.0 g
L-lysine HCl J.P.	7.6 g
(L-lysine equivalent)	(6.1 g)
L-methionine J.P.	1.0 g
L-phenylalanine J.P.	1.0 g
L-proline U.S.P.	8.0 g
L-serine U.S.P.	5.0 g
L-threonine J.P.	4.5 g
L-tryptophan J.P.	0.7 g
L-valine J.P.	8.4 g
Water for injection U.S.P.	q.s.

Amino acids	7.99% (w/v)
Branched-chain amino acids	35.5% (w/w) of total amino acids
Fischer's Ratio*	37.05
E/N ratio	1.09
Total Nitrogen	12.2 g/L
Na (Approx)	14 mEq/L
Cl (Approx)	94 mEq/L
* Molar ratio of (valine + leucine + isoleucine) / (tyrosine + phenylalanine) This product contains Sodium bisulfite 0.3 g/L as a stabilizer.	

INDICATIONS

AMINOLEBAN is indicated for the treatment of hepatic encephalopathy, in patients with chronic liver disease.

CONTRAINDICATIONS

AMINOLEBAN is contraindicated in the following patients: Patients with severe renal disorder (The amount of water tends to be excessive and the patient's clinical condition may be worsened. Urea and other metabolites may be retained, which may worsen the patient's clinical condition.)

Patients with abnormal amino acids metabolism (Since the infused amino acids are not adequately metabolized, the patient's clinical condition may be worsened)

DOSAGE AND ADMINISTRATION

The usual adult dose of AMINOLEBAN is 500-1000 mL per dose, infused via a vein. The usual peripheral infusion rate is 500 mL over 180-300 minutes (about 2540 drops/minute) in adults. For total parenteral nutrition, 500-1000 mL of AMINOLEBAN should be combined with dextrose or other solutions and administered over 24 hours via a central vein. The dosage may be adjusted according to the patient's age, symptoms, and body weight.

PRECAUTIONS

1. **Careful administration** (**AMINOLEBAN** should be administered with care in the following patients.)
    a. Patients with severe acidosis (The patient's clinical condition may be worsened.)
    b. Patients with congestive cardiac failure (An increase in the circulating blood volume may worsen the patient's clinical condition.)
2. **AMINOLEBAN** contains about 14 mEq/L sodium and 94 mEq/L chloride. Concomitant use with an electrolyte solution or administration of a large dose requires careful monitoring of electrolyte balance.
3. **Use in The Elderly:** Since elderly patients often have reduced physiological function, it is advisable to take such measures as reducing the dose by decreasing the infusion rate.
4. **Pediatric Use:** The safety in children has not been established (no clinical experience).

ADVERSE REACTIONS

Reported incidence rates are based on data from 3,324 patients with chronic liver disease, and a total of 35 patients (1.1%) experienced 52 adverse reactions.

1. Clinically significant adverse reactions

1) Hypoglycemia (frequency unknown)
Hypoglycemia may occur. If the patient develops hypoglycemia, glucose should be administered promptly by intravenous infusion. In addition, appropriate nutrition management is recommended in such patients.

2) Hyperammonemia (frequency unknown)
Hyperammonemia has been reported. If the patient develops persistent hyperammonemia during the administration of AMINOLEBAN, discontinue administration of nitrogen sources including AMINOLEBAN and institute appropriate measures.

2. Other adverse reactions

If adverse reactions are observed, discontinue the administration, and institute appropriate treatment.

Reactions	Frequency		
	Unknown	0.1% - <5%	<0.1%
Hypersensitivity	[Rash, etc.]		
Gastrointestinal		Nausea, Vomiting, etc.	
Cardiovascular	[Chest discomfort, palpitation, etc.]		
Metabolic	Transient increase in blood ammonia		
Large dose and Rapid administration	[Acidosis]		
Others	[Chills, fever]		Vascular pain, headaches

[ ]: common adverse reactions in amino acids injections

OVERDOSAGE

Hyperammonemia has been reported when an amino acids solution, including this solution was administered in combination with oral intake of nitrogen (total nitrogen: 160 g).

PHARMACOKINETICS

C-Labeled amino acids formulated in **AMINOLEBAN** were readily distributed to almost the entire body after intravenous Infusion in rats. In 6 hours 50 to 70 % of the administered amino acids were taken up into protein fractions. The ratio of branched-chain amino acids to the total amino acids in the protein fractions was highest in the brain. Up to 72 hours 41.7 % of the administered dose was excreted in the expired air, 5.9 % in the urine and 2.6 % in the feces.

PHARMACOLOGY

1. **AMINOLEBAN** normalized the Fischer's ratio in the plasma and brain improved monoamine metabolism in the brain, and

corrected a sleep-wakefulness pattern in portacaval-shunted rats (chronic hepatic insufficiency model).

2. When infused to portacaval-shunted rats loaded with ammonia, **AMINOLEBAN** normalized the Fischer's ratio in the plasma and brain decreased blood ammonia levels and Improved EEG and monoamine metabolism in the brain.

Storage and Precautions

- Use the solution after warming to near body temperature during cold environmental conditions
- Administer slowly via a vein
- When vascular pain occurs use an alternate site or discontinues the administration
- Do not remove the outer wrap until use.
- Do not use the product if the outer wrap covering the product has been damaged, the solution is discolored, or a precipitate that cannot be dissolved by shaking has formed.
- Do not mix with other drugs and additives.
- For intravenous administration by infusion only
- Store at room temperature, do not refrigerate or freeze.
- Keep away from direct sunlight
- Keep all medicines out of the reach of children
- Use as instructed by the Physician
- Use the solution within 24 hours after removing from Aluminum Bag.
- Do not use the bottle if Oxygen Absorber sachet is not present inside the Aluminum Bag or the color of solution has changed.
  Do not use if bottle is leaking, solution is cloudy or contains any foreign matter
  Discard unused portion of solution.

Packaging

500 mL solution in plastic graduated bottles sealed in aluminum bag with Oxygen Absorber and packed in unit boxes.

AMINOVEL® 600

Amino Acids, Carbohydrates, Electrolytes, Vitamins

AMINOVEL 600 is a well-balanced mixture of L-Amino acids optimally proportioned for maximum protein synthesis.
Sorbitol, vitamins, and electrolytes supplement or nutritional needs for the body.

COMPOSITION (Each 1000 mL contains):

Amino acids (L-form)	50.0 g
D-Sorbitol	100.0 g
Ascorbic acid	400.0 mg
Inositol	500.0 mg
Nicotinamide	60.0 mg
Pyridoxine HCl	40.0 mg
Riboflavin Sodium Phosphate	2.5 mg
Water for Injection	q.s.
Electrolytes	
Sodium	35 mEq/L
Potassium	25 mEq/L
Magnesium	5 mEq/L
Acetate	35 mEq/L
Malate	22 mEq/L
Chloride	38 mEq/L
CONTENTS OF 50.0 g AMINO ACIDS:	
L-Isoleucine	3.20 g
L-Leucine	2.40 g
L-Lysine (calculated as base)	2.00 g
L-Methionine	3.00 g
L-Phenylalanine	4.00 g

L-Threonine	2.00 g
L-Tryptophan	1.00 g
L-Valine	3.20 g
L-Arginine (calculated as base)	6.20 g
L-Histidine (calculated as base)	1.00 g
L-Alanine	6.00 g
Glycine	14.00 g
L-Proline	2.00 g

AMINOVEL 600 is a sterile aqueous solution supplying approx. 600 calories per liter. Each lot is examined by exothermic substance test, sterility test and toxicity test, and is manufactured under the severe standard.

INDICATIONS

AMINOVEL 600 is recommended for parenteral nutrition supply in the following conditions:

1. As supplement nutrition in the case of the impairment of the gastrointestinal tract as in clinical situation of short bowel syndrome, anorexia, and severe gastrointestinal disorder.
2. Prolonged gastrointestinal rest is necessary as in case of enterocutaneous fistulae and involving the gastrointestinal tract.
3. In increased metabolic need as in the cases of severe burns, trauma, and after surgery.
4. In other critical cases, which require exogenous nutrition such as tumor, severe infections, severe stress, and protein deficiency.

DOSAGE AND ADMINISTRATION

1. For internal disorder or pre surgical protein deficiency: The usual adult dosage is 500 mL of AMINOVEL® 600 by intravenous drip infusion over 4-6 hours (20-30 drops per minute) simultaneously or followed by a 10% sugar solution 500 mL over 2 hours (60-80 drops per minute).
   These infusions are repeated at 12 hours intervals for 5-7 days.
   The intervals may be prolonged to 24 hours according to patient's condition and response.

2. For postsurgical impairment of protein synthesis: The usual adult dosage is 500 mL of AMINOVEL 600 by intravenous drip infusion over 4-6 hours (20-30 drops per minute) following drip infusion of Darrow's solution 1000 mL over 4 hours (60-100 drops per minute) and followed by drip infusion of a 10% sugar solution 500 mL over 2 hours (60-100 drops per minute). These infusions are started on the third postsurgical day and repeated at 24 hours intervals for 5-7 days. Careful checking should be done for urine volume not to be less than 60-70 mL per hour and reexamination of dosage schedule is necessary when the volume falls below the level.

ACTIONS AND CHARACTERISTICS

AMINOVEL 600 supplies the following essential components for parenteral nutrition:

1. L-forms of amino acids which can be only utilized in the body for the synthesis of its various constituents;
   It is known that the body does not normally preserve nitrogen balance with D-isomers of amino acids.
   - The eight essential amino acids: L-Isoleucine, L-Leucine, L-Lysine, L-Methionine, L-Phenylalanine, L-Threonine, L-Tryptophan, and L-Valine are indispensable for protein synthesis.
   - The semiessential amino acids:
     - L-Histidine utilizes optimally amino acid mixtures and is essential for infants and in uraemia;
     - L-Arginine utilizes optimally amino acid mixtures and is essential for detoxication.
     - L-Alanine and L-Proline are necessary for optimal utilization of amino acid mixtures.
   - Glycine is a source for nonspecific nitrogen.
2. Sorbitol to supply sufficient nonnitrogen calories to meet metabolic energy requirements.
3. Vitamins to prevent deficiencies and to promote the biosynthesis of protein.
4. Minerals to maintain electrolyte balance and to promote synthesis of protein.
5. Water to meet the body's requirements.

AMINOVEL 600 provides all these substances in the optimal and exactly balanced proportions ensure maximum protein synthesis without depletion of the body's own reserves.

CAUTION

1. Careful checking should be done for urine volume not to be less than 60-70 mL per hour and reexamination of dosage schedule is necessary when the volume falls below the level.
2. Use immediately after breaking the seal and do not use the remaining solution.
3. Take special care of handling the instruments for injection as these preparation are liable to propagate germs.
4. Maximum infusion rate is 3 cc per minute.

STORAGE AND PRECAUTIONS

- Do not remove the outer wrap until use.
- Do not use the product if the outer wrap covering the product has been damaged, the solution is discolored, or a precipitate that cannot be dissolved by shaking has formed.
- Do not mix with other drugs and additives.
- For intravenous administration by infusion only
- Store at room temperature, do not refrigerate or freeze.
- Keep away from direct sunlight
- Keep all medicines out of the reach of children
- Use as instructed by the Physician
- Use the solution within 24 hours after removing from Aluminum Bag.
- Do not use the bottle if Oxygen Absorber sachet is not present inside the Aluminum Bag or the color of solution has changed.
  Do not use if bottle is leaking, solution is cloudy or contains any foreign matter
  Discard unused portion of solution.

Packaging

500 mL solution in plastic graduated bottles sealed in aluminum bag with Oxygen Absorber and packed in unit boxes.

Pan Amin G

Composition:

Each 1000 mL contains:

D-Sorbitol	**50.0 g**
L-Arginine HCl	**2.7 g**
L-Histidine HCl H2O	**1.3 g**
L-Isoleucine	**1.8 g**
L-Leucine	**4.1 g**
L-Lysine HCl	**6.2 g**
L-Methionine	**2.4 g**
L-Phenylalanine	**2.9 g**
L-Threonine	**1.8 g**
L-Tryptophan	**0.6 g**
L-Valine	**2.0 g**
Glycine (Aminoacetic acid)	**3.4 g**
Water for Injection	**q.s.**
Free AA	**2.7% (w/v)**
E/N	**3.1**
Total Nitrogen:	**~ 4.3 g/L**
Osmolarity	**~ 507 mOsm/L**

Indications: Recommended for provision of amino acids and energy in patients who require intravenous nutrition. Such conditions include hypoproteinemia, malnutrition, and disorders of the gastrointestinal tract, infections, inadequate intake or refusal to eat.

Dosage and Administration: The usual adult dosage of Pan-Amin G is 500 mL via intravenous infusion over 50-100 minutes (130-80 drops/min). The dosage should be increased or decreased according to the age and body weight of the patient and the severity of the condition. The infusion rate should be slowed in elderly and severely ill patients. The maximal daily dose of sorbitol should not exceed 100 g.

Contraindications: Hypersensitivity to any ingredient of the preparation. Hereditary fructose intolerance, hepatic coma, azotemia, congestive cardiac failure, severe acidosis and disturbances of amino acid metabolism.

Precautions: Pan-Amin G should be administered with care in patients with severe hepatic and renal disorders, diabetes mellitus and in elderly.

Adverse Events: Hypersensitivity, chest discomfort and palpitations may occur. Occasionally nausea, vomiting, chills, fever, and electrolyte imbalance may occur.

Packaging**: 500 mL plastic graduated bottles sealed in aluminium foil and packed in unit boxes**

KIDMIN®

7.2 % Amino Acid Injection
(Special Formula for Renal Failure Patients)

KIDMIN is a 7.2% amino acid injection containing large amounts of branched-chain amino acids, leucine, isoleucine and valine which inhibit the breakdown of muscle protein and promote muscle protein synthesis. KIDMIN also contains some non-essential amino acids, except for glycine, the demand for which is increased in renal insufficiency. The ratio of essential to non-essential amino acids of this solution is 2.6 and each 100 mL contains 1 g of nitrogen with no chloride and a small amount of sodium and it is thus easy to calculate the nitrogen content of a given dose and to adjust the amount of electrolytes for electrolyte balance.

COMPOSITION Each 1000 mL contains :			
L-Leucine	14.0 g	L-Cysteine	1.0 g
L-Isoleucine	9.0 g	L-Tyrosine	0.5 g
L-Valine	10.0 g	L-Arginine	4.5 g
L-Lysine acetate	7.1 g	L-Histidine	3.5 g
(L-Lysine equivalent)	(5.05)g	L-Alanine	2.5 g
L-Threonine	3.5 g	L-Proline	3.0 g
L-Tryptophan	2.5 g	L-Serine	3.0 g
L-Methionine	3.0 g	L-Aspartic Acid	1.0g
L-Phenylalanine	5.0 g	L-Glutamic Acid	1.0 g
		Water for Injection	q.s.

Total free amino acids	72.05g	Total Nitrogen	10.00 g
Essential amino acids (E)	52.05g	Na^+	Approx. 2 mEq
Non-essential amino acids (N)	20.00g	Cl^-	None
E/N ratio	2.6	Acetate	Approx. 46mEq
Branched-chain amino acids	45.8 % (w/w)		

PRODUCT DESCRIPTION

KIDMIN is a clear and colorless solution for injection. pH: approx. 7.0 (mean obtained immediately after manufacture) and 6.5 -7.5 (specification)

Specific gravity (20^oC): 1.022

Osmotic pressure ratio (to physiological saline): Approx. 2

PHARMACOLOGY

1. KIDMIN, administered by TPN exerted the following nutritional effects in animals such as chronic renal failure (7/8 nephrectomy rats and 7/8 renal artery-ligated dogs) and acute renal failure animals (mercuric chloride-induced renal failure rats and total nephrectomy rats):
    - Favorable body weight gain and nitrogen balance
    - Normalized aminograms in blood and BCAA levels in muscle
    - Increased uptake of ''N-leucine into blood protein fraction
    - Smaller increase in blood urea nitrogen
2. The amino acid providing effect of KIDMIN was studied in 7/8 nephrectomized rats on a low-protein diet and the following nutritional effects were observed:

- Improvement in nutritional status as evidenced by body weight gain, nitrogen balances and normalized blood aminogram
- No increase in blood urea nitrogen

PHARMACOKINETICS

When C-labeled KIDMIN was infused to normal 12-week-old rats and to 7/8 nephrectomized rats by **TPN,** the radioactivity was rapidly distributed throughout the body, with 50 - 90% incorporation to the protein fractions of the plasma, muscle and major organs such as liver, kidney and spleen from 3 to 72 hrs. after infusion. The expiratory excretion relative to the administered radioactivity was 32% in normal rats and 34% in nephrectomized rats up to 72 hrs. after infusion and the urinary excretion relative to the administered radioactivity was 4.6% and 4.9% respectively.

CLINICAL STUDIES

Clinical trials were conducted in 218 patients with acute or chronic renal failure, mainly those who needed blood purification treatment and the following results were obtained:

1) In the total parenteral nutrition (central vein infusion) in patients in whom oral nutrition was not tolerated, KIDMIN showed favorable effects on serum total protein, albumin and rapid-turnover protein with smaller changes in serum aminograms and alleviated an increase in blood urea nitrogen.
2) In the peripheral use of KIDMIN as a supplement to the oral intake of protein, the nutritional parameters such as serum total protein, transferrin and Val/Gly ratio were favorably maintained.

INDICATIONS

KIDMIN is indicated for the provision of amino acids in the following instances in patients with acute or chronic renal failure: Hypoproteinemia, malnutrition and before and after surgery.

DOSAGE AND ADMINISTRATION

Chronic Renal Failure

1) **Peripheral vein infusion**: The usual adult dosage is 200 mL per day, infused via a peripheral vein. The usual infusion rate in adults is 100 mL over 60 min (approximately 25 drops per min) and it should be slowly infused in children, the elderly and seriously ill patients. The dosage may be adjusted according to the patient's condition, body weight and age. When administered during hemodialysis, it should be infused via the vein side injection port of dialysis circuit starting 90-60 min before the end of hemodialysis therapy. Regarding calories, more than 1500 kcal per day is recommended to be provided for the efficiency of amino acid utilization.

2) **Central vein infusion:** The usual adult dosage is 400 mL per day, infused via a central vein by total parenteral nutrition. The dosage may be adjusted according to the patient's condition, body weight, and age. More than 300 kcal of non-protein calories should be administered per 1 g of nitrogen (100 mL of this product) for the efficiency of amino acid utilization.

Acute Renal Failure

The usual adult dosage is 600 mL per day, infused via a central vein by total parenteral nutrition. The dosage may be adjusted according to the patient's condition, body weight and age. More than 300 kcal of non-protein calories should be administered per 1 g of nitrogen (100 ml of this product) for the efficiency of amino acid utilization.

Precautions in dosage and administration:

1) Since it has been reported that hyperammonemia or consciousness disorder occurred when an amino acid injection for renal failure was administered as the sole amino acid source, discontinue use of this product immediately when abnormalities including slow reaction to being called or greetings or reduction in spontaneous motor activity or expressing opinions are observed.
2) Since azotemia or metabolic acidosis may be enhanced in case of inadequate administration of calories, the patients must be carefully observed during administration. If abnormalities are found, institute appropriate measures such as withdrawing administration.

PRECAUTIONS

1) Careful administration (KIDMIN should be administered with care in the following patients) :

- Patients with cardiovascular dysfunction [an increase in the circulating blood volume may worsen the patient's clinical condition].
- Patients with hepatic disorder or gastrointestinal bleeding [excess accumulation of amino acids or hyperammonemia may be induced].
- Patients with severe electrolyte imbalance or abnormal acid-base balance [the patient's clinical condition may be worsened].
- Patients with severe acidosis [the patient's clinical condition may be worsened].

2) Important Precautions

This product should be used in patients who need parenteral nutrition because oral or enteral nutrition is inadequate or not possible.

3) Use in the Elderly

Because elderly patients often have reduced physiological function and are likely to develop hepatic or cardiovascular dysfunction, it is advisable to consider reducing the dose by decreasing the infusion rate.

4) Use during Pregnancy, Delivery, or Lactation

The safety in pregnant women has not been established. Therefore, this product should be used in pregnant women and women who may possibly be pregnant only if the expected therapeutic benefits outweigh any possible risk.

5) Pediatric Use

The safety of KIDMIN Injection in children has not been established (insufficient clinical experience).

1) Physiological systems for the metabolism of various amino acids may not be fully developed in children. It is therefore advisable to take special precautions such as reducing the infusion rate when administering KIDMIN Injection to pediatric patients.

2) KIDMIN Injection may induce hyperkalemia in low birth weight infants. If hyperkalemia develops, discontinue administration and take appropriate measures to reduce serum potassium levels.

6) Precautions Concerning Use

(1) At the time of preparation

Physicochemical changes of the solution such as precipitation may occur when this product is combined with the following drugs. Changes should be observed.

a) Drugs which are designed to be stable in alkaline conditions.
b) Drugs which are not soluble in water.

(2) Before administration

a) To minimize the risk of infection, carry out all procedures under aseptic conditions.
b) In cold environmental conditions, the solution should be warmed to near body temperature before use.
c) Use the solution immediately after opening the container. After use, discard all unused solution.

(3) During administration

a) Because the solution contains approximately 46 mEq/L of acetate, a large dose or concomitant use with an electrolyte solution requires careful monitoring of electrolyte balance.
b) Administer the solution slowly via vein.
c) When vascular pain occurs, use an alternate site or discontinue the administration

7) Adverse Reactions

Of a total of 2964 patients evaluated for adverse reactions in clinical trials, there were 122 adverse reactions reported in 74 patients (2.5%) (Data at the time of reexamination, 2007, Japan). If adverse reactions are observed, institute appropriate measures such as withdrawing administration.

Reactions	Frequency unknown	<0.1%	0.1% ?<5%
Hypersensitivity	[Rash]		
Gastrointestinal			Nausea, Vomiting
Cardiovascular	[Chest discomfort, palpitation]		
Hepatic			Abnormal liver function test values (increases in AST (GOT), ALT (GPT), gamma-GTP, ALP, LDH, LAP, or total bilirubin), hyperammonemia
Renal			Increases in blood urea nitrogen or creatinine
Large dose and rapid administration	[Acidosis]		
Other	[Chills, fever, feeling of warmth, vascular pain]	Lower extremity edema, dry mouth, headache	Hyperpotassemia

[ ]: Common adverse reactions in amino acid injections (Drug Efficacy Reevaluation, Part 15, 1979, Japan)

CONTRAINDICATIONS (KIDMIN Injection is contraindicated in the following patients.)

1) Patients with hepatic coma or a risk of hepatic coma [Administration may enhance amino acid imbalance and hepatic coma may be worsened or induced.]

2) Patients with hyperammonemia [Because of excess load of nitrogen, hyperammonemia may be worsened.]
3) Patients with inherited abnormal amino acid metabolism [Because the infused amino acids are not adequately metabolized, the patient's clinical condition may be worsened.]
4) Patients with severe renal disorder or azotemia (the amount of water tends to be excessive and the patients clinical conditions may be worsened. Urea and other amino acids metabolites may be retained, which may worsen the patient's clinical condition.

Storage:
For intravenous administration by infusion only
Store at room temperature
Keep away from direct sunlight
Keep all medicines out of the reach of children
Use as instructed by the Physician
DO NOT USE IF BOTTLE IS LEAKING, SOLUTION IS CLOUDY OR CONTAINS FOREIGN MATTER, DISCARD UNUSED PORTION.

Packaging
100 mL solution in plastic graduated bottles sealed in aluminium foil and packed in unit boxes.

AMIPAREN

(10% Amino Acids)

Description

AMIPAREN is a clear and colorless solution for injection.

pH: Approx. 6.9 (mean value obtained immediately after manufacture), and 6.5 -7.5 (specification value) osmotic pressure ratio (relative to physiological saline): Approx. 3

Composition

Each 500 ml of AMIPAREN contains following ingredients;

L-Leucine	7.00 g	L-Arginine	5.25 g
L-Isolcueine	4.00 g	L-Histidine	2.50 g
L-Valine	4.00 g	L-Alanine	4.00 g
L-Lysine Acetate	7.40 g	L-Proline	2.50 g
(L-Lysine equivalent)	(5.25 g)	L- Serine	1.50 g
L-Threonine	2.85 g	Glycine	2.95 g
L-Tryptophan	1.00 g	L-Aspartic acid	0.50 g
L-Methionine	1.95 g	L-Glutamic acid	0.50 g
L-Phenylalanine	3.50 g		
L-Cysteine	0.50 g		
L-Tyrosine	0.25 g		

Total free amino acids	50.00 g	E/N ratio	1.44
Essential amino acids (E)	29.55 g	Branched chain amino acids	30.0 %w/w
Non-essential amino acids (N)	20.45 g	Na+ (Approx)	1 mEq/L
Total nitrogen	7.84 g	Cl^-	-
		$Acetate^-$	120 mEq/L

*Sodium bisulfite 0.2 g/L is used as an additive.
**Glacial acetic acid is used as a pH adjuster.

Pharmacology

The effect of AMIPAREN Injection as a source of amino acids in total parenteral nutrition was assessed using normal rats and surgically stressed rats.

1) AMIPAREN Injection readily corrected and favorably maintained nitrogen balance, demonstrating a favorable nitrogen sparing effect in these animal models.
2) AMIPAREN Injection increased synthesis of plasma total protein and albumin.
3) The urinary 3-methylhistidine/creatinine ratio as an indicator of protein catabolism in the muscle under stressed condition was low after AMIPAREN Injection infusion, indicating a potent inhibitory effect on muscular protein breakdown.
4) Plasma concentrations of free amino acids, including branched-chain amino acids, showed only minor fluctuation during AMIPAREN Injection infusion, and amino acid metabolism was thought to be stable during AMIPAREN Injection therapy.

Pharmacokinetics

(Reference data in rats):

Carbon-labeled amino acids formulated in AMIPAREN Injection were readily distributed to plasma protein fractions after intravenous infusion in normal

rats at 3, 7, and 57 weeks of age. The radioactivity was high in the protein fractions of the pancreas, liver, and kidneys and distributed rapidly in the muscles. The excretion of radioactivity into expired air over 72hours post dosing accounted for 37.1% to 44.2% of the infused dose. The recovery rates in the urine and feces accounted for3.9% – 5.2% and 1.2% – 3.1% of the infused dose, respectively. Urinary amino acid fractions contained only 1.1%–1.5% of the infused dose. The total retention of amino acids in the body amounted to more than 98.5% of the infused dose.

Indications

Provision of amino acids in the following instances: hypoprotenemia, malnutrition, and before and after surgery.

Dosage

Infusion via central vein

The usual adult dosage of AMIPAREN is 400 - 800 ml per day, infused via a central vein. The dosage may be adjusted according to the patient's age, symptoms, and body weight.

Infusion via peripheral vein

The usual adult dose of AMIPAREN is 200 - 400 ml per dose, Infused via a peripheral vein. The infusion rate may be adjusted to provide about 10 g of amino acids over 60 minutes in order is achieve optimal utilization of amino acids. The standard infusion rate in adults is 100 mL over 60 minutes. The rate should be slowed in children, the elderly and severely ill patients. Dosage may be adjusted according to patient's age, symptoms, and body weight. A combination of AMIPAREN with a carbohydrate solution is highly recommended for more efficient utilization of amino acids.

Contraindications

AMIPAREN is contraindicated to the following patients.)

1) Patients with hepatic coma or a risk of hepatic coma
   [Because of inadequate amino acid metabolism. the patient's clinical condition may be worsened.]
2) Patients with severe renal disorder or azotemia
   [The amount of water tends to be excessive and the patient's clinical condition may be worsened. Urea and other amino acid

metabolites may be retained, which may worsen the patient's clinical condition.]

3) Patients with abnormal amino acid metabolism
[Since the infused amino acids are not adequately metabolized, the patient's clinical condition may be worsened.]

Warnings and Precautions

Careful Administration (AMIPAREN should be administered with care in the following patients.)

1) Patients with severe acidosis
[The patient's clinical condition may be worsened]
2) Patients with congestive cardiac failure
[An increase in the circulating blond volume may increase the workload on the heart, which may worsen the patient's clinical condition.]
3) Patients with hypoprotenemia
[The patient's clinical condition may be worsened.]

Use in the Elderly

Since elderly patients often have reduced physiological function, it is advisable to take such measures as reducing the dose by decreasing the infusion rate.

Pediatric Use

The safety of AMIPAREN in preform neonates, term neonates, infants and children has not been established (insufficient clinical data).

Precautions Concerning Use

(1) Before administration

i. To minimize the risk of infection, carry out all procedures under aseptic conditions.
ii. In cold environmental conditions, the solution should be warmed to near body temperature before use.
iii. Use the solution immediately after opening the container. After use, discard all unused solution.

(2) During administration

i. The solution contains about 120 mEq/L of acetate. A large dose or concomitant use with an electrolyte solution requires careful monitoring of electrolyte balance.
ii. Administer the solution slowly via a vein.
iii. When vascular pain occurs, use an alternate site or discontinue the administration.

Adverse Effects

Reported incidences arc based on 3971 patients, and a teal of 35 (0.88%) patients experienced 39 adverse reactions including abnormal laboratory values (data at the time of reexamination, 1993 Japan).

If adverse reactions are observed, discontinue the administration and institute appropriate treatment.

Reactions	Frequency		
	Unknown	0.1% - < 5%	< 0.1%
Hypersensitivity	[Rash etc.]		
Gastrointestinal		Nausea, vomiting, etc.	
Cardiovascular	[Chest discomfort, palpitation, etc.]		
Hepatic		increases in AST (GOT) or ALT (GPT)	Increase in total bilirubin
Renal		Increase in blood urea nitrogen	
Large dose and rapid administration	[Acidosis]		
Others	[Chills, fever, feeling of warmth, headache]		Vascular pain

[ ]: common adverse reactions in amino acids injections (Drug Efficacy Reevaluation, Part 15, 1979, Japan)

Pharmaceutical Precautions

- Do not remove the outer wrap until use.
- A crystalline precipitate may form due to temperature changes during storage. Shake the solution at temperature of 15°C–25°C to dissolve the precipitate before use.
- Do not use the product if the outer wrap covering the product has been damaged, the solution is discolored, or a precipitate that cannot be dissolved by shaking has formed.
- Do not mix with other drugs and additives.
- For intravenous administration by infusion only
- Store at room temperature, do not refrigerate or freeze.
- Keep away from direct sunlight
- Keep all medicines out of the reach of children
- Use as instructed by the Physician
- DO NOT USE IF BOTTLE IS LEAKING, SOLUTION IS CLOUDY OR CONTAINS FOREIGN MATTER, DISCARD UNUSED PORTION IMMEDIATELY AFTER USE.

Packaging

500 mL solution in plastic graduated bottles sealed in aluminium foil and packed in unit boxes.

Appendix

Terminologies Related To Nutrition

Allergic reaction: Immunologically induced tissue response to a foreign substance (allergen).

Alpha-linolenic acid: 18 carbon fatty acid with three double bonds; the first double bond is on the third carbon atom from the methyl end and therefore it is called n-3 fatty acid. It is abbreviated as 18: 3 n-3.

Amino acid: The fundamental building block of proteins.

Anabolism: Process by which complex materials in tissues and organs are built up from simple substances.

Antioxidants: A group of substances that prevent the damage caused by the oxidation of fatty acids and proteins by oxygen free radicals.

Balanced Diet: A diet containing all essential (macro and micro) nutrients in optimum quantities and in appropriate proportions that meet the requirements.

Beta-Carotene: A yellow - orange plant pigment which yields vitamin A by oxidation in the body.

Bifidus factor: A substance in human milk which stimulates the growth of a micro-organism (Lactobacillus Bifidus) in the infants' intestine.

Body Mass Index: Body weight in relation to height. Body weight in kilograms divided by 2 height in meters.

Calorie: Unit used to indicate the energy value of foods. Quantitative requirements are expressed in terms of energy, i.e., kilocalories (Kcals). Newer unit for energy is Kjoules.

Catabolism: Process of breakdown of complex organic constituents in the body.

Cholesterol: A lipid constituent of blood and tissues derived from diet as well as from synthesis within the body.

Colostrum: The milk produced by mammals during the first few days after delivery.

CU: Consumption Unit. - One unit represents Recommended Dietary Allowance of energy for a sedentary man.

Empty calories: Term used for foods that provide only energy without any other nutrient, e.g. White sugar and alcohol.

Enzymes: Biological catalysts which enhance the rate of chemical reactions in the body.

Essential fatty acids (EFA) : Fatty acids like linoleic acid and alpha linolenic acid which are not made in the human body and must be supplied through the diet.

Essential nutrients: Nutrients that either cannot be made in the body or cannot be made in the quantities needed by the body; therefore, we must obtain them from food.

Fatty acids: Fundamental constituents of many lipids.

Fiber: Collective term for the structural parts of plant tissues which are resistant to the human digestive enzymes.

Flavonoids: Pigments widely distributed in nature in flowers, fruits and vegetables.

Food Exchange: Foods are classified into different groups for exchange. Each "exchange list" includes a number of measured foods of similar nutritive value that can be substituted inter-changeably in meal plans.

Free radicals: Highly reactive oxygen-derived species formed in the body during normal metabolic processes. They have the capacity to damage cellular components by oxidation.

High-density lipoproteins (HDL): These transport cholesterol from the extra-hepatic tissues to the liver. They are anti-atherogenic.

Hormones: Substances produced by a gland (endocrine) which are secreted directly into the blood stream to produce a specific effect on another organ.

Hyperlipidemia: An increase in the concentration of blood lipids (triglycerides and cholesterol).

Invisible fats: Fat present as an integral component of plant and animal foods such as in cereals, legumes and spices.

Lactoferrin: Minor protein of milk containing iron. Lactose intolerance: Disorder resulting from improper digestion of milk sugar called lactose, due to lack of an enzyme, lactase, in the intestinal mucosa.

Linoleic acid: Fatty acid containing 18 carbon atoms and two double bonds. The first double bond is on the sixth carbon atom from the methyl end. Therefore it is called n-6 fatty acid and is abbreviated as 18:2 n-6.

Lipids: A technical term for fats. They are important dietary constituents. The group includes triglycerides, steroids, cholesterol and other complex lipids.

Lipoproteins: Lipids are not soluble in blood; they are therefore transported as lipid and protein complexes.

Low-density lipoproteins (LDL): These transport cholesterol from the liver to tissues. High blood levels indicate that more cholesterol is being transported to tissues.

Macrocytic anemia: Anemia characterized by red blood cells which are larger than normal.

Macronutrients: Nutrients like carbohydrates, proteins and fats which are required in large quantities.

Metabolism: Includes catabolism and anabolism.

Microcytic anemia: Anemia characterized by red blood cells which are smaller than normal.

Micronutrients: Nutrients which are required in small quantities, such as vitamins and trace elements.

Monounsaturated fatty acids: Unsaturated fatty acids with one double bond. n-6 PUFA : Linoleic acid and its longer chain polyunsaturated fatty acids are collectively called n-6 PUFA. n-3 PUFA : Alpha-linolenic acid and its longer-chain polyunsaturated fatty acids are collectively called n-3 PUFA.

Phytochemicals: General name for chemicals present in plants.

Polyunsaturated fatty acids (PUFA): Unsaturated fatty acids with two or more double bonds.

Processed foods: Foods that are produced by converting raw food materials into a form suitable for eating.

Protein Energy Malnutrition (PEM): A marked dietary deficiency of both energy and protein resulting in under nutrition.

Recommended Dietary Allowances (RDA): The amounts of dietary energy and nutrients considered sufficient for maintaining good health by the people of a country.

Refined foods: Foods which have been processed to improve their appearance, color, taste, odor or keeping quality.

Saturated fatty acids: Fatty acids containing maximum number of hydrogen atoms that each carbon atom can carry. They do not have double bonds.

Satiety: Feeling of satisfaction after food intake.

Trans-fatty acids: Are mainly produced during hydrogenation of oils; a few also occur naturally in very small quantities.

Triglycerides (Neutral fat): The major type of dietary fat and the principal form in which energy is stored in the body. A complex of fatty acids and glycerol.

Unsaturated fatty acids: Fatty acids in which there is a shortage of hydrogen atoms. The carbon atoms then become linked by double bonds. Unsaturated fatty acids are less stable than saturated fatty acids.

Visible fats: Fats and oils that can be used directly or in cooking.

Weaning foods: Foods which are used during gradual transition of the infant from breastfeeding to a normal diet.

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