Pediatric perioperative nutritional assessment and support

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ABSTRACT

Perioperative nutritional support reduces the healthcare burden of pediatric malnutrition and its risk. Strategic preventive, diagnostic and therapeutic nutritional management guidelines are now available for their optimization. The global needs for pediatric surgery are vast, amounting to millions of children and adolescents, with a corresponding workforce requirement, especially in less socioeconomically developed regions, and where malnutrition is endemic. Acute and elective surgery from neonate to adolescent, for congenital to infective, neoplastic and traumatic conditions, are involved. To identify, highlight and critique current perioperative pediatric nutrition guidelines with regard to availability, utility, affordability and accuracy. Advantages and limitations of nutritional methodologies are taken into account in an algorithmic approach to perioperative decision-making to optimise outcomes. Routine documentation, monitoring and surveillance of pediatric nutritional status as a contributor to surgical risk management should increase its benefits, and reduce costs.

Key Words: guidelines, nutritional assessment, perioperative nutrition, NSQIP-P analysis, SDGs

INTRODUCTION

Although the global deficit in surgical care, especially in low to middle income countries (LMIC), has been signalled by WHO and other agencies, as reported in the Lancet Commission on Global Surgery,[1] the surgical needs of many children are less well recognised than those of their older counterparts.[2] These needs may before acute or elective surgery from neonate to adolescent, for congenital to infective, neoplastic and traumatic conditions. Moreover, children from LMIC, are often at added risk and in greater need of perioperative prevention, diagnosis and treatment of endemically impaired nutritional status if outcome is to be optimised.[3] Hippocrates allegedly said more than 2000 years ago, "*Let food be thy medicine and medicine be thy food*".[3] Present medical and nutritional science focuses more on nutrients and pharmacotherapeutics than ***comprehensive food and nutritional management***, albeit this is changing for the better.[1,4] Indeed, the International Union of Nutritional Science (IUNS) has recommended that its science should be considered in 4 domains, biomedical, environmental, societal, and economic.[5] In this vein, it has become clear that population nutritional quality as judged by dietary biodiversity reduces health expenditure.[6]

National and global nutritional programs seek to reduce the burden of malnutrition and dietary disorders.[7] In clinical settings, especially where complexity obtains, as is often the

case with surgical nutrition, support teams are increasingly recognized as a vital part of patient management services. A ***nutritional support team (NST)*** will generally comprise a doctor, nurse, dietitian, and pharmacist, and draw on a variety of other hospital services provided by catering officers, supply managers, finance managers, and sterile services. Other medical disciplines or specialties, nursing staff, therapists, and pathology personnel are involved.[8] The ***perioperative period*** can be complicated by a wide range of energy (catabolic), homeostatic, gastrointestinal, cardiorespiratory, renal, immunoinflammatory, microbiomic and locomotor dynamics in which nutritional expertise is invaluable.[9] These are relevant to immediate, recovery, rehabilitative and longer-term outcomes. Yet surgeons may be hesitant to engage with a NST or incorporate systematic nutritional screening and support. ***Dietary support has been shown to reduce surgical problems*** by 80% and hospital stay by 59% in a 176 multi-surgical department study.[9] Only some 20% of surgeons used routine nutrition screening. Reasons for non-compliance often pecuniary (49%). (33 %).[10] These and other studies are the basis of nutritional guidelines for surgery as in Europe through ESPEN,[11] and 'to cover both nutritional aspects of the ***Enhanced Recovery After Surgery (ERAS)*** concept and the special nutritional needs of patients undergoing major surgery'.[11]

An international problem

In April 2021, WHO, UNICEF, and the World Bank released a joint report on worldwide trends in child malnutrition. It emphasized the need to accelerate progress towards the World Health Assembly's (WHA's) 2025 targets and the SDGs' 2030 targets. In 2020, there were 149.2 million stunted children, 45.4 million wasting children, and 38.9 million overweight children.[12]

In the 2020 Global Malnutrition Report, 20.5 million infants (14.6%) were underweight. Only 42.6% of babies were exclusively breastfed for six months.[13] Children's lack of adequate nutrition is exacerbated by inadequate surgical access, especially in lower-middle-income countries (LMICs). Surgical conditions in children represent a high burden of disease in the world's poorest regions.[14] Out of the 313 million surgical procedures done worldwide annually, only 6% occur in the poorest countries, where over 33% of the world population lives.[15] A WHO research bulletin in 2019 states that around 1.7 billion (67%) children and adolescents worldwide lacked access to surgical care in 2017.[16] Recent epidemiological studies of pediatric surgery in the United States in 2020 concluded that 3.9 million operations are annually performed on children 0 to 17 years of age. This rate remained stable between 2005 and 2018.[17] Data for malnutrition prevalence of malnutrition and its spectrum in

pediatric surgery come mostly from developed countries. Roberson et al, in their study of 2,056 pediatric operations, assessed the impact of malnutrition on pediatric surgery outcome;[18] 19% met at least one definition of malnutrition. Pawelek et al found 24.1% with malnutrition among 475 children aged 7.9 +/- 5 years.[19] Ross et al, over ten years of pediatric cardiac surgery practice found that 31% of children were underweight, 32% stunted, and 15% wasted.[20] Informative long-term large cohort studies on large paediatric surgical cohorts are rare. This probably reflects the findings of a 2019 systematic review by Jennifer Crawley et al. in Lancet Planet Health that "nutrition teaching is lacking in medical schools across the board. Ensuring good nutrition is a challenge for young doctors".[21] Malnutrition contributes to a child's recovery after surgery, necessitating prolonged hospitalization, intensive care, and parenteral nutrition. Yet oral or enteral nutrition are often usable. How they contribute in critical illness, with mechanical ventilation, prolonged fasting for surgery and post-surgery, and unanticipated eventualities is a matter for the NST.[22]

The present review places emphasis on evidence-based dietary approaches to pediatric peri-operative management which encourage pediatric surgeons and other stakeholders to engage in nutritional risk management and therapy. The humanistic benefits can be expected to be accompanied by economic advantage to the healthcare system.[23]

PEDIATRIC NUTRITION SCREENING TOOLS

Several screening scores or tests have been developed to identify patients at risk of malnutrition during hospitalization, thus enabling early detection and nutritional intervention. After screening, those identified as at-risk are intended to undergo further nutritional assessment be provided with appropriate intervention. Thus, nutritional screening tools help select those that might benefit most from a full nutritional assessment.[24]

Screening tool suitability:[25]

General pediatric practice

Screening Tool for the Assessment of Malnutrition in Pediatrics ***(STAMP)***

Pediatric Yorkhill Malnutrition Score ***(PYMS)***

Screening tool for Risk on Nutritional Status and Growth ***($STRONG_{kids}$)***

Pediatric Nutritional Screening Tools ***(PNST)***

Surgical practice:

Global Subjective Assessment (SGA) and Subjective Global Nutritional Assessment ***(SGNA)***

Oncology: Nutritional Screening tool for childhood Cancer (SCAN)- it was developed especially for children with cancer.[26]

Pulmonology: Nutritional screening tool for pediatric patients with cystic fibrosis (CF).

Neonatal intensive care unit (NICU): Neonatal Nutritional Screening Tool ***(NNST)*** for infants in NICU.[27]

Community

The Clinical Assessment of Nutritional Status ***(CANS)*** score differentiates malnourished and appropriately nourished children.[28]

A relatively new computer-based malnutrition risk calculating tool called Pediatric Digital Scaled Malnutrition Risk screening tool ***(PeDiSMART)*** is a more comprehensive and complicated screening tool for children's ages. It incorporates four elements: WFH z scores on admission, nutritional intake levels, symptoms affecting intake (such as abdominal pain, nausea, diarrhea, or vomiting), and overall disease impact.[24]

Mental health

Nutrition Risk Score (NRS), Simple Pediatric Nutrition Risk Score (SPNRS), and St. Andrews Nutritional Screening Instrument (SANSI) for psychiatry.[25]

Screening tool performance

In a systematic review, Teixeira et al. found that ***the most used screening tools*** were STAMP, STRONGkids, PYMS, PNST, and SGNA.[29] Their sensitivity ranged from 59% to 100 %, with STAMP and STRONGkids having the highest. Specificity ranged from 53% to 93% with STAMP and STRONGkids having lowest at 7.7% and 11.54% respectively.[29] PYMS had high specificity at 92%. STRONGkids performed best according to inter-observer agreement ($k>0.60$-0.79).[30]

The ***STRONGkids tool*** was developed according to the European Society for Clinical Nutrition and Metabolism (ESPEN) recommendations. A questionnaire divides children into three risk groups utilizing a combination of weight change, clinical examination findings and questionnaire about nutritional status. A total score of 0 points constitutes the low-risk category; 1 to 3, the moderate risk; and 4-5 the high-risk category.[31]

STRONGkids has excellent sensitivity, is easy to use, and has a median completion time of 3 minutes. Koen Huysentruyt et al., in their validation study of STRONGkids found that children at low risk had a 5% probability of being acutely malnourished and a 1% probability of nutritional intervention during hospitalization.96 Other findings were substantial intra-rater (κ=0.66) and inter-rater (κ=0.61) reliabilities between observations, sensitivity and negative predictive values (NPV) of 71.9% and 94.8% respectively; favorable correlations between the STRONGkids score and length of stay (ṗ 0.25; OR 1.96; 95% CI, 1.25–3.07; both p<0.01); and likelihood of nutritional intervention during hospitalization (OR, 18.93; 95% CI, 4.48–80.00; p<0.01).

NUTRITIONAL ASSESSMENT

Medical history

Nutritional assessment in children with acute or chronic disorders has a rightful place in the overall medical evaluation. Dietary history (especially its adequacy and quality by way of biodiversity), physical examination, anthropometry for body composition and growth indices, together with selected investigations constitute a nutritional assessment for most children. Nutritional disorder may manifest as a dysnutritional spectrum, loosely referred to as 'malnutrition'. It may range from excessive to deficient energy or essential food component intake over need with body compositional disorders, such as overfatness in general and /or abdominal obesity, underweight, sarcopenia, osteopenia); or from accelerated to restricted growth velocity (tallness or shortness); or from bioactive food component or nutrient deficiency to toxicity (essential and phyto-nutrient statuses, contaminant intake). The associated nutritional morbidities, disabilities, and mortalities may be complex.

Documentation of ***current and past illness and disease*** is relevant to understanding a child's nutrition and development, each episode being a potential impediment. For instance, food intake may be compromised and nutrient loss accentuated by illness which affects any of appetite and hunger, chewing ability, swallowing, causes indigestion, vomiting, diarrhea or constipation. Tracking and being alert to these episodes, along with the associated states of hydration, body composition and indices of nutrient function, are clinical nutrition practice requisites.

Dietary history/ assessment of dietary intake

Eating habits differ based on socio-cultural norms, dietary choices, and resource availability. An eating history is basic to nutritional assessment. ***An index of food biodiversity and***

knowledge of the food system and preparation on which it provides guidance about nutritional quality.[32] Food preferences may distort nutritional quality. For example, young vegetarians may not obtain enough vitamin B12 or sufficiently bioavailable iron, or vitamin D if sunlight exposure is also limited. Regular physical activity with a commensurate energy throughput helps ensure that the required overall food intake quality is achieved. A ***rapid food intake enquiry*** (or recording) can be undertaken about the frequency across a week (week and weekend days) of food type usually eaten over a 24-hour period (at meals and as snacks eg 'ruminant meat 3/7' as the notation for an item three out of seven days). Made by the patient or guardian, in relation to other activities or behaviours, it will form a dependable basis for counselling and monitoring change. Here the extent of dietary biodiversity would be struck over a week where a sum in excess of 20 could be reassuring about the achieved dietary quality.[33] This approach meets the general objectives of the classical Burke food intake methodology.[34] Additional enquiry will depend on the clinical presentation or anticipated nutritionally related disorder. Among the many pursued might be food intolerances or eating disorders.[35,36]

Physical examination

During routine physical examinations, keep in mind the risk of nutritional insufficiency or excess. Obesity has changed the perspective of a normal-looking youngster. An NFPE is a comprehensive head-to-toe examination that assesses fat reserves, muscles, anthropometric measurements, and scans for nutrition deficiency signs.[37] A well-fed infant should have substantial fat reserves palpable or pinchable between fingers. Newborns and toddlers get their buttocks inspected, while older children do not. Bony prominences will show up after fat stores are gone. Examine the muscles above the scapula, quadriceps, and calves.[38]

Baker et al. designed a tool to assess surgical patients' nutritional status in 1982.[39] Clinical history and physical examination allowed categorisation as 'well-nourished', 'moderately malnourished', or 'severely malnourished'. The two malnourished groups had high sensitivity (0.82) and specificity (0.72) for predicting HAI. Detsky et al named this method ***Subjective Global Assessment*** in 1987. (SGA). The final SGA had four medical history parts and three physical exam elements.[40]

Anthropometry for growth & body composition

Anthropometry is intrinsic to nutritional assessment where more direct methods for body compositional ascertainment are unavailable, unaffordable or inconvenient. Anthropometric

measurements are quantitative assessments of muscle, bone, and fat tissue.41 In children, it includes length, weight, head circumference, MUAC, triceps skin thickness, and the derivation of Body Mass Index (BMI). Principally these measurements in childhood reflect how diet affects human growth and development, although various sociodemographic and behavioural factors are contributory. reliable body size and weight measures are required. Their utility in acute medical settings, of which surgery is an example, is dependent on the accuracy and precision with which they are obtained.

Length or height

Length is a linear growth indicator. Recumbent length is measured in newborns and toddlers where standing unaided is not possible. Calibration is to the nearest 0.1cm.

The head should be perpendicular to the scale when measuring length or height. A line connecting the region to the orbit's lower border is the Frankfurt plane (the notch above the tragus, the cartilaginous projection just anterior to the external opening of the ear).[42]

To find the infantometer's recumbent length, unfold the headboard and parallel the footboard. The device contains a scale with zero at the headboard's edge and measures the child's length at the footboard's edge. The child must be held supine by two adults. With the Frankfurt plane perpendicular to the backboard and the shoulders and hips at a right angle, one person supports the head securely on the headboard. The second person slides the footboard against the child's legs to measure the child's feet. The length is rounded to 0.1 cm.[43] Stature or standing height is measured for subjects older than 2 or 3 years who can stand erect by themselves. There are various ways to measure height, but the most popular practice is using a stadiometer. The child stands barefoot, with heels together, arms by his side, shoulder relaxed, and head in Frankfurt plane looking ahead. The heel, buttocks, scapulae, and back of the head should ideally be in contact with the vertical surface of the stadiometer. Before taking the measurement, the child should breathe deeply and hold his breath, maintaining an erect posture. At the same time, the headboard is lowered to the highest point of the head, and the reading is taken to 0.1cm.[43]

Serial measurements of length or height over time are plotted on a growth chart.

Knee height

Children with disabilities, such as cerebral palsy, are frequently measured at knee height. Knee height is a suitable alternative to recumbent length for children with mobility issues and a reliable predictor of height in children. The caliper is knee-high with a fixed lower arm and

a movable top arm. The caliper's lower arm is put beneath the heel, and the movable arm is taken till the condyles of the femur are proximal to the patella and measured. Different formulas can be used to get the total height using knee height: [37]

a. Patient <12 years, Stevenson method: Height = (2.69 x knee height) + 24.2

b. Patient >12 years, Chumlea method.

c. Male: Height = 64.19 – (0.04 x age) + (2.02 x knee height)

Females: Height = 84.88 – (0.24 x age) + (1.83 x knee height)

Tibial length

Tibial length is another alternative used to measurethe height of cerebral palsy children. A flexible, non-stretchable tape is needed to measure the length, starting from the medial joint line to the inferior edge of the medial malleolus. The following equation is used to calculate height using tibial length (TL):[44]

Height = (3.26 x TL) + 30.8

Weight

Paediatricians often check a child's weight. Low weight is often a sign of poor nutrition. They must be calibrated and error-free at least once a year to be used for weighing. Pan scales are used to weigh babies and toddlers. Weights are recorded to the gram. The weights of babies and toddlers are rounded up to 0.1 kg. For kids who can't stand up, bed scales or wheelchair scales can help them. Details like taking baseline measurements and getting rid of useless equipment are needed. A growth chart shows how your weight changes over time.

Measures relative to weight

Weight/length alone does not provide a complete nutritional picture. It helps identify kids whose weight is appropriate for their age but not their height. Also, relative weight is a valuable size measure for abnormally short or tall children. It can distinguish between stunting and wasting in babies of any age. Stunting is caused by malnutrition, disease, or endocrine abnormalities. A stunted child is underweighting for their age. In addition to malnutrition, medical disorders including diarrhea and malabsorption contribute to wasting. Percentile based on WHO growth charts (0 to 2 years of age).[45] Weight for length is suggested for full-term infants up to two years old. After two years, BMI is advised. However, WHO BMI charts assess excess or undernutrition in children over six months. The BMI is calculated as weight in kilograms divided by height in meters squared (kg/m^2). A child's BMI is plotted

on the WHO BMI growth curve for children under two and the CDC BMI growth curve for children over two. A child's BMI is considered underweight if it is below the fifth percentile, overweight if it is between the 85th and 95th percentiles, and obese if it is above the 95th percentile.[45]

Head circumference

Head growth is rapid from birth to 3 years of age, and it slows beyond that. Head circumference is a proxy for brain growth and value for screening hydrocephalus. It is measured using a flexible tape, placed around the head across the frontal bones, just above the eyebrows and ears, and over the occipital protuberance at the back of the head until two parts of the tape touch each other. Reading is taken to the nearest 0.1cm.

Decreased head circumference is a sequel of chronic malnutrition and predicts delays in acquiring cognitive skills and psychomotor development.

Mid Upper Arm Circumference

Unlike weight, MUAC is unaffected by fluid movements or hydration state. MUAC is simple, accurate, and predicts malnutrition-related mortality with high sensitivity and specificity. MUAC 110mm predicts death from malnutrition within six months, according to Asian research.[46] The upper arm midway is between the acromion (shoulder) and olecranon (elbow), with the elbow at 90 degrees. The right arm is measured at this mid-point, with the arm relaxed by the side. The tape should be placed such that it contacts but does not squeeze the skin or alter the arm's form.

Skinfold measurement

Skinfold measurement is commonly used to estimate body fat percentage in older children and teens. Skinfold measurements are appealing because the equipment employed is inexpensive, readily available, and provides a reasonable estimate of body fat content, equivalent to results from more complex methods. It is assumed that the double thickness of skin and fatty tissue has constant compressibility, the thickness of the skin is negligible, or a constant fraction of skinfold thickness, and the fat content of adipose tissue is constant.[27] The most common site is the triceps skinfold thickness. Other potential sites to measure skinfold thickness are over biceps, anterior chest wall, mid axillary line in the thorax, subscapular region, abdominal, thighs, and medial calf.

Triceps skinfold measurement

The mid-point of the right arm is determined by the previously described method. The measurer stands behind the subject and skin over triceps in pinched between thumb and index finger of the left hand and uses the caliper with the right hand to measure the skinfold thickness perpendicular to the long axis of the arm.

Non-anthropometric indices of body composition

Fat, lean tissue, and bone composition require sophisticated technological approaches. Body fat is a sign of malnutrition. The body's protein stores are represented as lean mass. Children need to grow up strong and have healthy bones for lifelong skeletal health. Nutritional assessments should include these technical parameters for children at risk of malnutrition or chronically sick. Body composition measures are widely used in clinical practice after being developed as research tools.

Air displacement plethysmography

The evolution of densitometric methods in assessing body composition culminated in the advent of air displacement plethysmograph (ADP). The basic principle of ADP is that volume of subject = volume of the empty chamber – the volume of the chamber with the subject. Based on Boyle's law, the volume of gas is inversely proportional to the pressure in a constant temperature. So if a subject is placed inside a sealed chamber of known volume, any change in pressure and volume would be directly attributable to the volume of the subject.[48]

In 1995, Life Measurements Instruments (Concord,CA) designed an air displacement plethysmograph called Bod Pod. This device comprises a sealed measuring chamber with a reference chamber linked by a flexible diaphragm that creates small pressure changes between the chambers when perturbed. This machine then measures the inverse pressure-volume relationship between the two chambers to calculate the volume of the subject within the pod. This body volume, corrected for thoracic gas, is divided into body mass to determine the body density.[49] This technique of Bod Pod eliminates the need for the subject to be submerged in water instead of measuring air displaced in the chamber by the body; this is more comfortable and non-invasive. Once the density is calculated, it can be converted to percentage body fat using population-specific equations.

Later, the pediatric version of Bod Pod was called Pea Pod, and modification of Bod Pod with pediatric option came up. The Pea Pod or infant plethysmograph can accommodate children up to 8 kg. In infants, it offers distinct advantages over a DEXA scan, which is

highly accurate in body composition assessment, like it obviates the need for the infant to lie still, and its validity in fat percent calculation is similar as in methods like the deuterium method and 4 –compartment models.[48] The validity and accuracy of Pea Pod are subject to ongoing scrutiny. A literature review on more than 80 articles on the use of Pea Pods in infants concluded that though it is a convenient way to measure body composition in infants and maybe helpful in monitoring groups of infants, it appears to have modest accuracy for individual subjects. Various determinants that affect its accuracy are body moisture and temperature, objects attached to infants, extremes of body size, thoracic gas prediction equations, free fat mass (FFM) density, and fluctuation in FFM hydration factor. Investigations to further validate it against the gold standard four-compartment model are needed, especially in pre-term babies.[50]

Dual Energy X-ray Absorptiometry (DEXA)

DEXA scan is currently the clinical gold standard and the most widely used densitometric study for children throughout the world as it gives accurate measurements of whole-body fat mass, lean mass, and bone density.[51]

DEXA uses very low-energy X-rays; it measures the attenuation of x-rays as it passes through tissues of varying densities. For any given x-ray level, body tissues like fat, muscle, and bones have unique attenuation properties. The use of two energy beams of different intensities allows for the determination of two tissue compartments. The respective lean and fat tissue masses are determined as the x-ray beam passes over soft tissue regions. As the beam passes over a region of bone, the algorithm solves for bone versus soft tissue, assuming that the composition of soft tissue surrounding the bone is similar to the adjacent soft tissue of muscle and fat. This is a significant drawback of using DEXA to estimate body fat percentage. DEXA analysis also assumes constant hydration of lean soft tissue, but hydration varies with age, gender, medical conditions, which is another possible limitation.[52,53]

Bioelectrical Impedance Analysis

Bioelectrical impedance (BIA) is a portable, inexpensive method of body composition analysis that is very safe (avoided in patients with pacemakers). It requires minimal patient participation, thus making it a method of choice for large-scale studies. It’s based on the principle that electric currents are conducted through the water and electrolytes in the body, and the impedance to current is directly proportional to the lean tissue mass present. Impedance is a category of electric resistance and consists of two elements: resistance

(passive electrical resistance) and reactance (capacitive, active electrical resistance). Resistance refers to specific resistance characteristics of individual tissues and is inversely proportional to the water content. Reactance is associated with the electrical capacity of the cell membranes, which act as capacitors; it generally accounts for 10% of the impedance.54 Thus, lean tissue with water content is relatively a good conductor of electricity than fat that does not have water.

Generally, a low electrical current (800 μA) is used, which is hardly perceptible and does not interfere with nerve-muscle physiology. BIA device can be a single frequency that operates at 50 kHz or multiple frequencies when a wide range of frequencies are used. Single-frequency BIA (SF-BIA) is used for assessing total body water (TBW) and free fat mass but is limited in its ability to distinguish TBW into intracellular and extracellular compartments. Bioimpedance spectroscopy (BIS) or multifrequency BIA allows for the differentiation between total body water into intracellular and extracellular compartments, which is helpful to describe fluid shifts and fluid balance and explore fluctuations in water content.[55] This differentiation is also helpful in estimating body cell mass.

The possible sources of error in BIA are variations in limb length, physical activity, nutrition level, hydration content, blood chemistry, ovulation, and placement of electrodes.52 The estimates of free fat mass from BIS were underestimated in individuals with average weight and overestimated in obese subjects when compared to DEXA.[55]

Hydrodensitometry

Hydrodensitometry, or underwater weighing, was once considered a gold standard for measuring body fat. It is based on the Archimedes Principle, which states that the volume of liquid displaced by a submerged solid is equal to its volume. Bodyweight is measured in air and water and calculated body density (Db). Fat mass and free fat mass (FFM) are then calculated using equations given by anthropometry pioneers Siri and Brozek et al.[56]

Siri: Percent fat = 4.95/ Db – 4.5

Brozek et al: Percent fat = 4.570/ Db – 4.142

An individual with a high free fat percentage (FFM) will weigh more in water as he'll have a low-fat percentage and vice versa. For an accurate body density calculation, body volume should be corrected for the amount of air present inside the lungs and gastrointestinal tract at the investigation time.

Hydrodensitometry demands extensive equipment, and the procedure is not well tolerated by many because it requires complete submersion in water. This is especially not suited for children who can't hold their breath voluntarily or have a pulmonary illness.[57]

Total body potassium

The four-cellular method divides fat, body cell mass (BCM), extracellular fluid (ECF), and cellular solids. The BCM is metabolically active and stores more than 98% of the body's potassium (as an intracellular cation). 0.012% of all potassium is the naturally occurring isotope ^{40}K, emitting a small but detectable amount of gamma rays.[27] Detection of these rays is the core principle of total body potassium (TBK) estimation.

A specially constructed whole body potassium counter is fitted with multiple gamma-ray detectors, and these are interfaced with a computer for data collection and interpretation

These detectors are susceptible to detecting a meagre amount of gamma radiation emitted from the subject, and it is shielded appropriately against background external radiation. The subject lies inside the chamber for 30 minutes. The TBK is calculated using the constant proportion of 40K to its major stable isotopes. This value also gives total body nitrogen, assuming a TBK to nitrogen ratio of 2.15 mmol K/gN. Subsequently, total body protein = 6.25 x total body nitrogen and BCM (in kg) = 0.0092 x TBK (mmol).[52]

Total body water/ hydrometry/ isotope dilution method

The non-fat content of the body is primarily composed of water, so measuring the total body water content can help us calculate total body fat and fat-free mass. Hydrometry is based on the dilution principle that the amount of solvent (TBW) can be calculated if the tracer's concentration (isotope) is known. The stable isotopes most commonly used are D_2O (deuterium oxide) and ^{18}O.

Body fluid samples (saliva, urine, or blood) are initially collected to determine the natural levels before administration of the isotope. Samples are again collected 3-4 hours after isotope administration, and isotope enrichment is measured by either isotope ratio mass spectroscopy or infra-red spectrophotometry. Hydration is assumed to be 73%, and fat-free mass is estimated from TBW using this assumption.[52] Since the percent of water in fat-free mass ranges from 71 to 76%, it would be wise to use population-specific references for calculation. This method is safe, non-invasive, highly accurate, involves minimum participant burden, and can be used in various settings. However, analysis of specimens to find isotope concentration is mainly performed in research laboratories, thereby limiting its wide-scale use.

Neutron activation

The human body is made up of more than 60 elements, but just four elements constitute 95% of the body: oxygen (65%), carbon (18%), hydrogen (10%), and nitrogen (3%). Other elements whose proportion is more than 0.05% are sodium, potassium, phosphorus, calcium, magnesium, chlorine, and sulfur.

Neutron activation analysis is a method to measure specific elements in the body. The subject lies within a chamber and is irradiated with low-dose neutron radiation. These neutrons interact with body tissues to excite the targeted element, creating unstable isotopes that release gamma rays.[58] A whole-body gamma radiation counter detects the energy emitted and the decay rate to determine the total quantity of the element present in the body.

This method is reserved for research purposes only; is highly impractical for use in children because of the risks involved and the minimal availability of neutron activation chambers worldwide.

Imaging technologies

Ultrasound: Bedside ultrasound has emerged as a standard tool to quantify muscle mass, commonly by measuring quadriceps (combined thickness of rectus femoris and vastus intermedius), muscle layer thickness (QMLT), or rectus femoris cross-sectional area; and subsequently lean body mass.[59] It has shown promise to emerge as a method to evaluate critically ill patients' lean muscle mass status.[60] In VALIDUM study by Paris et al., a multicentric trial to assess the validity of ultrasound technique, found that it had good Intra and inter-rater reliability and is helpful to assess longitudinal changes in muscles in hospitalized patients.[61]

Currently, the ultrasound technique cannot diagnose sarcopenia because of a lack of consensus on cut-off values or a theoretical protocol. The presence of edema also limits ultrasonography use. However, it is a cheap, portable, non-invasive method, able to identify short term changes and can be readily used for serial monitoring.[62]

Computerized Tomography (CT): CT has excellent accuracy in analyzing body compartments and sarcopenia in hospitalized patients as it allows assessment of visceral, intramuscular, subcutaneous, and skeletal muscle tissues in addition to fat infiltration into lean tissues.[63]

The method used to measure cross-sectional body composition is similar in CT and MRI. L3 vertebra is chosen as the axial landmark, as it includes the psoas, paraspinal muscles, and

abdominal wall muscles, thus making it optimal for skeletal muscle quantification for the whole body. Nevertheless, the amount of fat at this level will be variable according to age, sex, body type; hence for assessing visceral fat, measurements should be taken from several anatomic sections.[63]

The use of CT solely for body composition analysis has not yet gained acceptance. It is beneficial in patients who undergo CT scans due to their primary illness, like cancer patients. Apart from the high cost and radiation exposure, there is a possibility of evaluation bias related to inadequate selection and interpretation. Unlike ultrasound, CT has validated cut off points, has high image resolution, precision, and more qualitative and quantitative accuracy.[59]

Magnetic Resonance Imaging (MRI): MRI and MR spectroscopy scans are among the most accurate body composition analysis techniques; unlike CT, they don't use radiation and have better soft tissue definition, especially adipose tissue. MRI does not provide information on tissue density; segmentation of different tissue planes has to be done either by manual delineation, which is time-consuming, or automatic analysis algorithms, which may introduce errors in the accuracy of fat measurement. Most often, a semi-automated approach is taken.[57]

MRI has often been used to measure the volume of intra-abdominal fat, intermuscular adipose tissue, the volume of skeletal muscles and internal organs. MR spectroscopy is a further advancement that can help in the excellent assessment of intramyocellular and intrahepatic lipid fractions.[45] Quantitative magnetic resonance (QMR) has been developed in recent years; it uses the difference in the nuclear magnetic resonance properties of hydrogen nuclei in organic and inorganic environments to fractionate signals originating from fat, lean tissue and free water. QMR has advantages in being observer independent, fast scan time (<3 minutes), capacity to accommodate a person up to 250kg, and excellent precision.[57]

Cost considerations and sedation requirements in infants and children make these studies undesirable for research applications.

Investigatory nutritional indices

Nutrigenomics and epigenetics

Knowledge not only of one's intergenerational family medical history and, potentially, genomics may allow for more personalised dietary patterning to optimise health or manage disorders which are demonstrably nutritionally related.[64-66] Perhaps even more consequential might be how ancestral environmental or dietary exposures may have affected paternal or maternal gene expression, spermatogenesis,[67] or oogenesis.[68] Cross parental genomic

exchange may continue via the placenta antenatally,[69] and through breast milk exosomes during lactation.[70] Such phenomena may provide a deeper understanding of child growth and development, and long-term health, while perhaps of less immediate clinical relevance. The availability and application of such knowledge will be subject to socioeconomic and ethical constraints.

Haematology

Nutritional anaemia is among the most common and recalcitrant maternal and child health problems globally.[71] It is commonly not an intake problem, but a blood loss problem attributable to menstrual blood loss, intestinal helminthiasis (e.g. hookworm, ascariasis), medication, or other blood loss (most devastatingly postpartum). It is commonly regarded as an anemia of iron deficiency without direct evidence when it may be attributable to other nutrient deficiencies such as folic acid and vitamin B-12, reflect chronic disease or ill health, or infectious disease like malaria, or be genetic as in thalassaemia or G6PD deficiency.[71]

Assessment and diagnostic assumptions are often made, understandably, based on affordable and accessible finger prick blood obtained in the field for haematocrit or haemoglobin alone; and sometimes for ferritin and CRP to consider effects of chronic disease on iron status and storage. The prospects of more definitive causal diagnoses and appropriate interventions with technological advances are encouraging.

The need to recognize co-existent disease like malaria as a contributor and complication of management strategy in nutritional anaemia mitigation programs is critical. Iron supplementation in malarious areas can increase the risk of overwhelming and fatal malaria. Thus, preference for iron biofortified food and concomitant malarial eradication are advised. Perioperative nutrition would need to take this into account.[72]

Immuno-inflammatory

The child requiring surgery for other than elective purposes is likely to be affected by inflammation or be immuno-stimulated, with responses dependent on nutritional status. The current state of clinical practice would that this be recognised and taken into account without recourse to biomarkers, other than perhaps simple and readily accessible measures like a blood film, white cell counts ESR or CRP (C reactive protein). This may change as immunoinflammatory indices become more diagnostic and prognostic.

The ***link between malnutrition and infectious disease*** as the 2 most prevalent and interconnected global health problems is a major challenge. It has been strikingly evident with

the 2019 Covid-19 pandemic, especially with socioeconomic disadvantage, societal distrust and poor governance.[73-75]

Cytokine response with surgery: Both pro-and anti-inflammatory cytokines are released to surgical stress. Few prominent ones one:

IL-1β: This is the earliest cytokine released in the intra-operative period, but it's short-lived and precedes the increase in IL-6 levels. IL-1β levels increase in adults undergoing significant surgeries; however, there has been no detectable IL-1β response in children undergoing cardiac bypass.[76]

IL-1 receptor antagonist: IL-1ra is a competitive inhibitor of IL-1 and is one of the earliest detected cytokines in the postoperative period in both adults and children.

Tumour necrosis factor α (TNF-α): It's a potent mediator of immune response to stress and infection. Circulating TNF-α is rarely detected in uncomplicated pediatric surgeries; its increased level is associated with severe operations and death.[77] TNF-α is produced locally at the injury site even in the absence of circulating levels and has the potential to start a cytokine cascade.

IL-6: This is the most consistently elevated cytokine in the postoperative period in both adults and children. Its levels correlate with the severity and length of surgery, and it may not be detected after minor procedures. The increased level is seen as early as the 4th postoperative hour and peaks between 6 and 24 hours postoperatively. Following the development of any postoperative complication, its levels may remain elevated.[78]

IL-10 plays a dominant role in the down-regulation of immune response and, thus, is a powerful immune-suppressant. IL-10 is significantly elevated in pediatric cardiac patients, where increased levels are observed just after the initiation of bypass. Levels usually return to preoperative values in 2-3 days.[77]

Microbiomics

Pathways that link and modulate diet and health outcomes involve our microbiomes, notably in the gut, but also cutaneous, reproductive (genitalia and breast), urinary, oral, nasopharynx and respiratory.[79] The ***healthfulness of a microbiome*** is largely conferred by its biodiversity which dietary diversity can foster.[80,81] This probably applies to the several gut microbial kingdoms, bacterial, fungal, viral and archaeal. It is becoming clear that the evaluation and management of human nutritional status is a cross-kingdom consideration.[82]

Of practical ***perioperative relevance*** are the preservation of maternal to neonatal microbiomic transfer with vaginal delivery rather than Caesarean;[83] preoperative microbiomic

integrity for ERAS (Enhanced Recovery after Surgery);[84] judicious use of antibiotics insofar as they compromise microbiomics, and contribute to multiple antibiotic resistance.[85] It should be possible with diet to mitigate ARG (antibiotic resistance gene) development in the gut by dietary means.

Biochemistry & metabolomics

Biochemical tests for assessing nutritional status can be divided into two groups: static and dynamic or functional. Advances in analytical technology, especially highly sensitive chromatography linked to mass spectroscopy have also made it possible to look simultaneously at whole metabolic pathways, referred to as 'Metabolomics'. As access and affordability improve, tiny biological specimens of blood, saliva or excreta (urine, feces or sweat) will be amenable to metabolomics.

Pediatric nutritional metabolomics are now applied to the evaluation of various aspects of nutritional biology in conjunction with nutrigenomics and microbiomics. Examples have to do with energy regulation and body composition86, cognitive function, and mental health,[88] and biorhythms like sleep.[89]

Static biochemistry typically assesses the current concentration of a nutrient or biomarker in a biological sample, like blood, urine, or body tissue. Examples include serum measurement of albumin or calcium and hemoglobin in the blood. While these tests are readily available, they fail to reflect the overall nutrient status of an individual. For instance, a single static serum calcium value is not a complete indicator of total body calcium reserves. The other group of tests called functional tests measures the physiologic response, and homeostatic robustness of the body that relates to a nutrient of interest.[90] Examples include the oral glucose tolerance test (function of insulin in maintaining blood glucose) and measurement of dark adaptation (for Vit. A deficiency). The limitation of functional tests is that they do not necessarily have the specificity required to identify a nutrient deficiency.

Nutritional diagnosis is a more comprehensive health assessment than conveyed by any particular laboratory investigation. Perioperatively, there is a complex interplay between underlying disease or precipitant injury, inflammatory and reparative processes and surgical stress. Each phenomenon has nutritional consequence which may amount to malnutrition. Adverse nutritional outcomes are more likely when the perioperative period is associated with anorexia, a catabolic state, and increased resting energy requirements as with infection, inflammation or some investigatory activities. These may blunt nutritional intervention and

make therapy less efficacious.[91] Biochemical, metabolomic and other investigatory manoeuvres are adjunctive to overall 'bedside' assessment, diagnosis and care.

Protein nutrition and its deficiency are inevitably linked to is corresponding energy and nutrient statuses.; hence it has attracted the short-hand descriptor of 'protein-energy malnutrition (PEM)'. Any laboratory assessment of body protein must be contextualised by information from clinical, diet history, physical examination, and anthropometry inter alia. Anatomically and functionally, protein has two compartments- somatic, represented by skeletal muscle, and visceral, comprising stores in internal organs, predominantly the liver. The somatic compartment is first affected during reduced energy intake or starvation, as happens in the marasmus. Continued starvation results in visceral protein store depletion, as in kwashiorkor, a more ominous condition.[92] During acute stress or an inflammatory state, the liver prioritizes protein synthesis, decreases visceral protein synthesis, along with acute phase proteins, with correspondence to disease severity.

Albumin

Albumin is the most abundant available serum protein with a large pool (4-5 gm/kg body weight) and a relatively long half-life of 14-20 days. It is a negative acute phase reactant- it decreases in acute conditions, stress, and inflammation. Several factors determine serum albumin:[93]

Rate of synthesis: Biosynthesis can be decreased by lack of dietary proteins, physiologic stress, liver disorders, hypothyroidism, and increased cortisol levels.

Distribution: 30-40% albumin is found in blood and lymph, with the rest in lean tissue in the extravascular space, especially skin. Postoperatively, with systemic inflammation, and with burns, albumin shifts from the intravascular to the extravascular space and itself falls. In semi-starvation, albumin shifts from the extra to the intravascular space.

Rate of catabolism

Catabolism is increased in physiologic stress, and disease like the Cushing syndrome, some malignant tumors; and it is decreased in semistarvation.

Insofar as hypoalbuminemia in critically ill children is concerned, Leite et al found that an increase of 1 gm/dl of serum albumin from the time of admission resulted in a 73% reduction in the risk of death (60-day mortality), a 33% increased probability of ICU discharge, and 1.86 more ventilator-free days.[94] Serum albumin is an independent predictor of outcome in critically ill children. Treating hypoalbuminemia with albumin offers little benefit in clinical

outcome, and its serial measurement is an unreliable guide nutrition management.[95] This also undermines the utility of serial measurements, as serum albumin and pre-albumin levels do not correlate with nutrient delivery in surgically ill patients.

Role of inflammation

Serum proteins, mainly albumin and retinol-binding protein(RBP have been regarded as useful indicators of protein depletion in critically ill children.[96,97] However, the current interpretation of their kinetics, advanced by Tekgüç et al in 2018, is that the moderate correlations between daily energy intake and serum pre-albumin (r=0.432, p<0.001) or RBP and daily protein intake(r=0.330, p<0.001) are attributable to related changes in serum albumin, RBP, and C-reactive protein (CRP) during intensive care. Increases in pre-albumin and RBP are explicable by decreases in CRP (r=-0.546 and 0.646, p<0.001), rather than to improved nourishment.[98] This does not preclude possible effects of nutritional factors not studied or mediated by alternative pathways, however.

A case in point is the association between inflammation and serum protein. The ratio of the inflammatory marker CRP to albumin or prealbumin is used to predict morbidity and mortality during parental nutrition. Talaveron has showed that CRP, albumin, and the CRP/albumin ratio are more prognostic of mortality and morbidity than prealbumin or the CRP/prealbumin ratio; and that CRP/albumin is a determinant of death, infection, sepsis and liver failure during parenteral nutrition.[99]

Maldigestion/malabsorption/enteric protein loss:[96]

Fat malabsorption: fecal fat assessed by 72 hours collection with diet record is an accurate method to quantify fat malabsorption.

Pancreatic insufficiency: in addition to the above test, the determination of fecal elastase aids in diagnosing pancreatic insufficiency.

Carbohydrate malabsorption: Low fecal pH and reducing substances are indicators of unabsorbed carbohydrates. This simple test can be done bedside with a pH strip.

Hydrogen breath testing: Breath hydrogen of a child is measured at baseline and again after an oral load of carbohydrate of interest (eg-lactose). A rise in hydrogen above baseline is indicative of maldigestion.

Stool α-1 Antitrypsin: Unlike albumin, α-1 Antitrypsin passes into stool undegraded and reflects enteric protein loss but does not point towards etiology.

Metabolic response to surgery in infants and children- nutritional resilience

The physiology of infants and children in the peri-operative period differs from adults in terms of energy and fluid requirements, thermoregulation, and metabolic changes. These can vary even within different age groups of children. While a neonate is still adapting to the external environment with its limited energy reserves, the older infant is still growing and adapting their physiological and nutritional needs to balance growth and development—any form of stress challenges this homeostasis.

'Stress response' is defined as a constellation of events, which begins with a stimulus (stressor), which precipitates a reaction in the brain (stress perception), which subsequently results in the activation of specific physiologic systems in the body (stress response);[100, 78] it's also called as an acute metabolic response (AMS). Surgical trauma triggers a whole range of inflammatory pathways like that seen after injury, hypothalamic-pituitary axis (HPA), and sympathetic nervous system activation, along with a range of metabolic, endocrinologic, and immunological responses. There are three phases of stress response seen in children:[101]

The acute phase after the traumatic event requires increasing vital organ support and can last hours to days depending upon the initial insult.

Stable phase: Stabilisation or weaning of vital organ support, different aspects of the stress response are not yet completed. This may last for days to weeks.

Recovery phase: Clinical mobilization with normalization of neuro-endocrine, immunologic and metabolic alterations; it can last for weeks to months.

A short-term stress response is Mother nature's mechanism for enhancing protection and performance under stress;[102] short-term stress induces increased immunoprotection by enhancing innate and adaptive immune responses, enhancing wound healing, moderating favorable immune-pathological responses, and increasingthe efficacy of vaccination. As we know, stress, if chronic, is deleterious, causes a continued escalation of pro-inflammatory and type-2 cytokine-driven immune responses, and exacerbates inflammatory and autoimmune diseases.[103] Enhanced recovery after surgery (ERAS) pathways developed for adults and been used for more than two decades are now increasingly employed in pediatric surgical patients. The primary motive of ERAS is to promptly return the patient to baseline function by maintaining preoperative organ function and attenuating the neuro-endocrine stress response after surgery.[104] An excessive stress response to surgery can lead to systemic inflammatory response syndrome (SIRS) and prolonged catabolism of body stores. The goal of nutrition in

this setting is to augment the initial short-term beneficial response to injury while minimizing any long-term consequences.

Energy Requirements

Energy needs in children can be divided into four components:[105, 106]

- Basal metabolic rate- energy consumed in whole-body homeostasis.
- Diet-induced thermogenesis- energy involved in digestion and assimilation
- Physical activities
- Growth

Neonates having minimal energy reserves and cannot tolerate a prolonged period of starvation. They also have a significantly higher metabolic rate than older children, reflected in a higher resting energy requirement (REE). The ratio of minimal metabolic rate (in g/kg/day) to non-protein energy reserves (in g/kg), which represents the number of days of energy reserve, is only two days at 28 weeks of gestation and increases to 20 days for a healthy term infant and 100 days in adults. This underscores the need for prompt adequacy of energy intake for low birth weight neonates.[107]

Resting energy requirements (REE) have a wide variation among full-term infants (100-120 kcal/day) and premature babies (110-160 kcal/day), with corresponding variations in maintenance metabolism. REE may double during activities like crying, but most surgical children are at rest 80-90% of the time.[107]

Adults and children differ greatly in the quantity of stored protein. The protein reserve (per kg body weight) in an adult is nearly twice that of a neonate, leaving little neonatal buffer to cover illness or injury.[108]

Postoperative REE in children contrasts with that in adults. the increase in REE is much less in children. Mitchel and colleagues showed that, the REE of children, postoperative of cardiac surgery, fell less than that found in healthy children who had not undergone surgery. Thus, surgical stress is associated with less energy adjustment requirement in children than thought.[109] This is evident in a number of reported pediatric surgical settings.[105,110] Thus, infants and children may divert protein and energy from growth to wound healing without increasing energy expenditure. Koletzko et al. consider that increased energy provision for septic or surgical children is probably not warranted.[111]

Endocrine and metabolic responses

Stress activates the hypothalamic-pituitary axis (HPA) and sympathetic-adrenal-medullary axis releasing catecholamines, cortisol, and glucagon. There is a cascade of biochemical

reactions, with an increased breakdown of proteins (mainly by cortisol), fat, and carbohydrates. Lipolysis, mainly stimulated by catecholamines, releases glycerol and fatty acids; glycerol is a substrate for gluconeogenesis and fatty acids for ketogenesis. Structural protein production is aborted; acute phase proteins appear in the blood. An acute metabolic syndrome, or hypermetabolic, hypercatabolic state reduces endogenous tissue stores, increases energy expenditure, and increases protein breakdown.[112] It is the metabolic response to injury of any kind in adults and children. It can be monitored by measuring REE using indirect calorimetry, and hormonal concentrations.

Postoperatively, serum cortisol remains increased beyond 24 hours od in adults, but in children for a much shorter period and with greater magnitude. Cortisol response after pediatric surgery is high and returns to baseline mostly by 6 hours postoperatively.[78] The hormonal responses are proportional to the degree of surgical stress. Lisa et al. found that with anesthesia in healthy children subject to minimal and moderate invasive urologic procedures, the cortisol stress response peaked at 1 hour postoperatively.[113] Nakamura et al., in children of different age groups, plasma cortisol peaked just after surgery; and was lower in neonates than in older children. Plasma IL-6 levels peas hours after surgery, in neonates and infants higher than in older children. Plasma IL-10 peaks just after surgery with no difference by age group.[114]

Overfeeding and acute metabolic stress (AMS)

After uncomplicated elective surgery, pediatric energy expenditure increases marginally above baseline. The hypermetabolic response to surgical stress is attenuated and is of shorter duration than in adults. Overfeeding during acute metabolic stress can increase the metabolic impact of acute injury. The present inability of nutritional measures to reverse the metabolic stress associated with critical illness, is compounded by excessive energy delivery and increases morbidity and mortality in both pediatric (young children are more vulnerable) and adult patients.[112]

Avoidance of overfeeding during nutrition support and nutritional resuscitation can be pursued by energy repletion which takes account of measured resting energy expenditure (mREE). Overfeeding can be arbitrarily (given the lack of established clinical endpoints) defined as the ratio of energy intake/mREE; or by comparison of the measured respiratory quotient (RQ) to that predicted from macronutrient intake (RQmacr).[115]

Pathophysiology: Excess glucose is diverted to lipogenesis. Fatty acid oxidation is the predominant energy-generating pathway in the response to acute injury and it produces more

carbon dioxide than does glucose oxidation. Excess work of breathing to expel the extra CO_2 produced can result in compromised pulmonary function and prolonged ventilator requirement.[116] An increased risk of infection occurs secondary to hyperglycaemia and immunologic suppression with inactivation of the complement system and depressed natural killer cell activation.[117] An increase in liver dysfunction due to hepatic steatosis and cholestasis is also seen. These factors contribute to increased mortality associated with overfeeding.

Energy requirements and metabolic monitoring

The total energy expenditure (TEE) is defined as the amount of heat energy used by the human body for daily functioning and can be divided into three main components:

- Basal energy expenditure (EE) or resting EE (REE): energy used to sustain vital functions at rest,
- Diet-induced thermogenesis: energy used during substrate metabolism postprandial,
- Activity EE: Energy used in physical activity.

REE is the energy required to maintain the body's primary cellular metabolic activity and vital functions, such as respiration and body temperature, in the absence of recent food intake, physical activity, and psychological stress.[118,119]

Longitudinal measurement of REE in critically ill patients has confirmed the ebb and flow phase of metabolic response to injury. The ebb phase is marked decreased metabolism immediately following the onset of the injury. The flow phase follows after 24-48 hours with a hypermetabolic period whose magnitude corresponds to the severity of the injury, peaks during the second week and gradually declines thereafter. Underfeeding and overfeeding in these patients are risks (see above). Negative energy balance in the ill compromises nitrogen and protein balance,[120,121] increases infectious complications,[122] wound complications, prolonged mechanical ventilation,[123] prolonged hospitalization, and mortality.

The determination of energy requirements can inform energy management during peri-operative periods and critical illness. Energy expenditure may be assessed by various techniques including indirect calorimetry, tracer dilution studies, or the reverse Fick method. But technical difficulties and risk limit the use of the tracer dilution method and Fick's equation in children.

Indirect calorimetry - gas exchange

Indirect calorimetry (IC) is based on the fact that energy metabolism ultimately depends on oxygen ventilation (VO_2) and carbon dioxide production (VCO_2). Thus, expired air contains less oxygen and more carbon dioxide than inspired air. The body's energy expenditure can be calculated when the volume of expired air is known and the difference in oxygen and carbon dioxide concentrations. Energy estimation by indirect calorimetry is nearly identical to direct calorimetry. Indirect calorimetry has been established as the gold standard for estimating energy requirements in critically ill patients of all age groups.[124] Apart from REE, and other parameters can be derived from IC, such as substrate (carbohydrates, fat, and protein) utilization. Indeed, the ratio between VCO_2 and VO_2 (VCO_2/VO_2) defines the respiratory quotient (RQ) corresponding to substrate use. The complete oxidation of glucose generates an RQ value of 1.0, while an RQ of 0.7 is indicative of a mixed substrate oxidation.[118]

Several techniques can be used in indirect calorimetry. Closed-circuit calorimetry open circuit calorimetry, more commonly connected to computerized metabolic monitors and handheld devices measuring resting metabolic rate and oxygen consumptions, has been described. The handheld device is either a standalone device or an extension of a mechanical ventilator offers a point of care testing, and treatment decisions can be made within minutes at the bedside.[119]

Indications for indirect calorimetry:[125]

- Assessment of energy expenditure in patients who fail to respond to estimated nutritional needs adequately.
- Assessment of energy expenditure in patients with single or multiple organ dysfunction who need prolonged ICU care and artificial nutritional support
- Assessment of the effects induced by artificial nutrition on the cardiocirculatory and respiratory systems in mechanically ventilated patients with acute and chronic respiratory failure monitoring of VO_2 while weaning from mechanical ventilation

NUTRITION SUPPORT

Delivery of nutrient support – parenteral and enteral nutrition[126]

See Table 1

Parenteral

Indication

- When oral feeding is not possible.

- Clinical conditions: Gastrointestinal (short-bowel syndrome, malabsorption, intractable diarrhea, bowel obstruction, protracted vomiting, inflammatory bowel disease, enterocutaneous fistulas), congenital anomalies (gastroschisis, bowel atresia, volvulus, meconium ileus), radiation therapy to the gastrointestinal tract, chemotherapy resulting in gastrointestinal dysfunction, and severe respiratory distress syndrome in premature infants.
- Deficient birth weight infants typically require parenteral nutrition within the first 24 hours of birth.

Venous access:

Peripheral venous line use is limited by a high risk of extravasation, inflammation and skin necrosis. Peripherally inserted central catheters (PICC lines) with a relatively small diameter are inserted from a peripheral arm or leg vein and directed to the central venous system. They can be maintained for several weeks with a low incidence of infection. Central venous catheters can be used in infants or children who require more extended periods of parenteral nutrition. Generally, in children, external jugular or subclavian veins are used. In low-birth-weight infants, the internal jugular and femoral veins may be used because of the small calibre of other vessels.

Parenteral nutrition composition

Maintenance fluid requirements

The most common method of calculating water loss (and therefore water requirement) is the Holliday- Segar nomogram: this formula relates water loss to caloric expenditure. This nomogram approximates daily fluid loss and therefore requirements as:

-100 ml/kg for the first 10 kg of weight

-50 ml/kg for the next 10 kg weight.

-20 ml/kg for the remaining weight.

Total fluid requirements are calculated on a 24-hour basis, for practical purposes this is broken down to hourly rates leading to 4-2-1 formula:

-100 ml/kg/24-hours = 4 ml/kg/hr for the 1st 10 kg

-50 ml/kg/24-hours = 2 ml/kg/hr for the 2nd 10 kg

-20 ml/kg/24-hours = 1 ml/kg/hr for the remainder

<u>Dextrose</u>

Dextrose is the most common carbohydrate source used in parenteral nutrition. Other carbohydrates have no added advantage over dextrose and can produce severe complications in preterm children. Glucose infusion rate (GIR) is calculated as mg of glucose provided per kg of body weight per minute. Plasma glucose levels balance glucose utilization, exogenous glucose intake, and endogenous glucose production (glycogenolysis and gluconeogenesis). During critical illness, glucose metabolism is blunted with increased β cell dysfunction and increased insulin resistance, which increases the risk of hyperglycemia. With restricted glucose use in acute illness, lower doses are advised during this phase compared to the more stable and recovery phases.

Amino acids

Amino acid requirements are lower in parenteral nutrition than in enteral nutrition due to bypass of the the gastro-intestinal tract. The PEPaNIC trial concluded that early administration of amino acids in parenteral nutrition was negatively associated with PICU (Pediatric Intensive Care Unit) length of stay, newly acquired infections, and weaning from mechanical ventilation. Current recommendations suggest withholding amino acids in parenteral nutrition during the first week of illness.[127]

After the acute phase is over, undernourishment and immobilization further contribute to muscle wasting. ESPGHAN/ESPEN/ESPR/CPNN guidelines advise from day eight onwards to provide a minimum amino acid intake of 1.0 mg/kg/min in stable term infants and 0.7 mg/kg/min in children from 1 month to 18 years to avoid a negative nitrogen balance while the maximum amino acid intake should not exceed 2.1 mg/kg/min in neonates, 1.7 mg/kg/min in infants and children up to 3 years and 1.4 mg/kg/min in older children.[128]

Metabolic complications related to amino acids such as azotemia and acidosis have occurred in infants receiving more than 4 mg/kg/day. For older critically ill children, inadequate protein nutrition has been associated with respiratory failure, muscle weakness, and sepsis.

Lipids

The role of intravenous fat in parenteral nutrition is to provide nonprotein energy, provide essential fatty acids, a ‘balanced’ energy source, and energy more tolerable for patients with limited ability to excrete CO_2.

Few acceptable lipid emulsions are available:[129]

Intralipid is a soybean oil-based lipid emulsion. Long-term use has been implicated in the development of intestinal failure associated liver disease (IFALD). In the setting of intestinal failure or is long-term use, cycled PN emulsion use, reducing the lipid dose to 0.5 to 1 g/kg/day and monitoring for essential fatty acid deficiency can be undertaken.

Smoflipid is a lipid emulsion containing soybean oil, medium-chain triglycerides, olive oil, and fish oil. Emerging data suggest that Smoflipid may be more hepatoprotective than standard soybean oil-based lipid emulsion. Smoflipid is currently only approved by the US Food and Drug Administration (FDA) for use in children 16 years or older.

Omegaven, is an entirely fish oil-based emulsion and has been shown to reverse some of the manifestations of IFALD. However, Omegaven is not FDA approved and can only be obtained in the United States through a compassionate use protocol. In pediatrics, 20% lipid emulsions are the most used and provide 10 kcal/g of lipid, 2 kcal/mL of lipid emulsion, and 5 mL fluid/g of lipid. The 20% intravenous fat has a lower phospholipid-to triglyceride ratio than the 10% intravenous emulsion. Because phospholipid inhibits lipoprotein lipase, the primary enzyme for intravenous fat clearance, the 20% emulsion is cleared more efficiently and probably preferable. The typical dosing for PN lipid emulsions is 2 to 3 g/kg/day unless lipid minimization is indicated. Infusion rates of lipid emulsions should not exceed 0.15 g/kg/hour. Tolerance of the lipid emulsion is monitored via serum triglycerides, which should ideally be maintained under 250 mg/dL.

Other additives to parenteral nutrition are electrolytes, vitamins, minerals, trace elements, carnitine, and heparin.

Complications of parenteral nutrition:

Infections are associated with venous catheters.

Mechanical complications:

- Complications following placement of central catheters include
- Air embolism
- Pneumothorax, hemothorax, hydrothorax
- Perforation of an organ
- Pericardial effusion
- Malposition: arrhythmias, cardiac tamponade, brachial plexus injury, diaphragmatic palsy
- Thrombotic events and thrombophlebitis
- Extravasation: Skin sloughing and subcutaneous injury

- Mechanical catheter-related events: crack or breakage of the catheter, catheter occlusion

Acute Metabolic Considerations

- Refeeding syndrome
- Dehydration/fluid overload
- Hyperglycemia/ hypoglycemia
- Hypernatremia/ hyponatremia
- Hyperkalemia/ Hypokalemia
- Hypermagnesemia/ Hypomagnesemia
- Hyperphosphatemia/ Hypophosphatemia
- Hypercalcemia/ hypocalcaemia
- Azotemia
- Hyperlipidemia/ essential fatty acid deficiency
- Deficiency and toxicities of trace elements

Long term metabolic considerations:

- Hepatobiliary dysfunction- cholestasis, steatosis, intestinal failure-associated liver disease
- Metabolic bone disease- osteopenia, rickets, fractures
- Renal disease- calculi, decreased renal function

Enteral Nutrition

Indications:

- Prematurity
- Cardiorespiratory illness
- Chronic lung disease
- Cystic fibrosis
- Congenital heart disease
- Gastrointestinal tract disease and dysfunction
- Inflammatory bowel disease
- Short bowel syndrome
- Biliary atresia
- Gastroesophageal reflux disease
- Protracted diarrhea of infancy
- Chronic nonspecific diarrhea
- Renal disease

- Hypermetabolic states
- Burn injury
- Severe trauma or closed head injury
- Cancer
- Neurologic disease or cerebral palsy
- Oral motor dysfunction
- Inadequate spontaneous oral intake

Conclusions

Clinical nutrition requires greater emphasis in health care professional training, notably of doctors and nurses. Its place in preventive, diagnostic and therapeutic medicine and healthcare in general is not only self-evident, but supported by substantial evidence that healthcare system burden and expenditure is in part contingent on it. Some, like Jean Carper, reckon that 'food is the breakthrough drug of the 21st century'. Acute and chronic malnutrition among children who are hospitalized children is problematic, especially for the socioeconomically vulnerable, already prone to nutritionally related comorbidity. They come to surgery for these and other reasons; and, when they do, perioperative nutritional diagnosis and care affect outcomes like infection, recovery rates, and length of stay. Recognition, documentation and monitoring of nutritional status with screening, bedside and reliable history and examination methods allow for and encourage targeted nutrition interventions. These include body compositional assessment with anthropometry or more sophisticated technology. Advances in rapid accessible and affordable measurements of nutritional genomics, metabolomics, immune function, microbiomics, and inflammasomics can be expected to expand and better inform future nutritional care. In the meantime, validated and relatively non-invasive assessment and monitoring tools are available for early and sensitive ongoing detection of impaired nutritional status. 'Strongkids' and STAMP are examples of instruments which can be part of the clinical nutrition decision-making architecture (Figure 1).

AUTHOR DISCLOSURE

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Table 1. Indications for peri-operative nutritional intervention[97]

Preoperative malnutrition	Increased infectious complications Delayed recovery	Preoperative nutrition
Long starving	Increased infectious complications Delayed recovery	Pre- and intraoperative nutrition: prefer enteral parenteral route nutritional attention to co-morbidity
Intraoperative surgical stress	Catabolism, immunosuppression, organ dysfunction	Early enteral nutrition Minimally invasive surgery
Catabolism/muscle loss	Increased overall morbidity Increased fatigue Delayed recovery	Active rehabilitation Early oral nutrition
Severe complications (ileus, high output fistula, intestinal bleeding haemorrhage)	Enteral nutrition contraindication	Parenteral nutrition

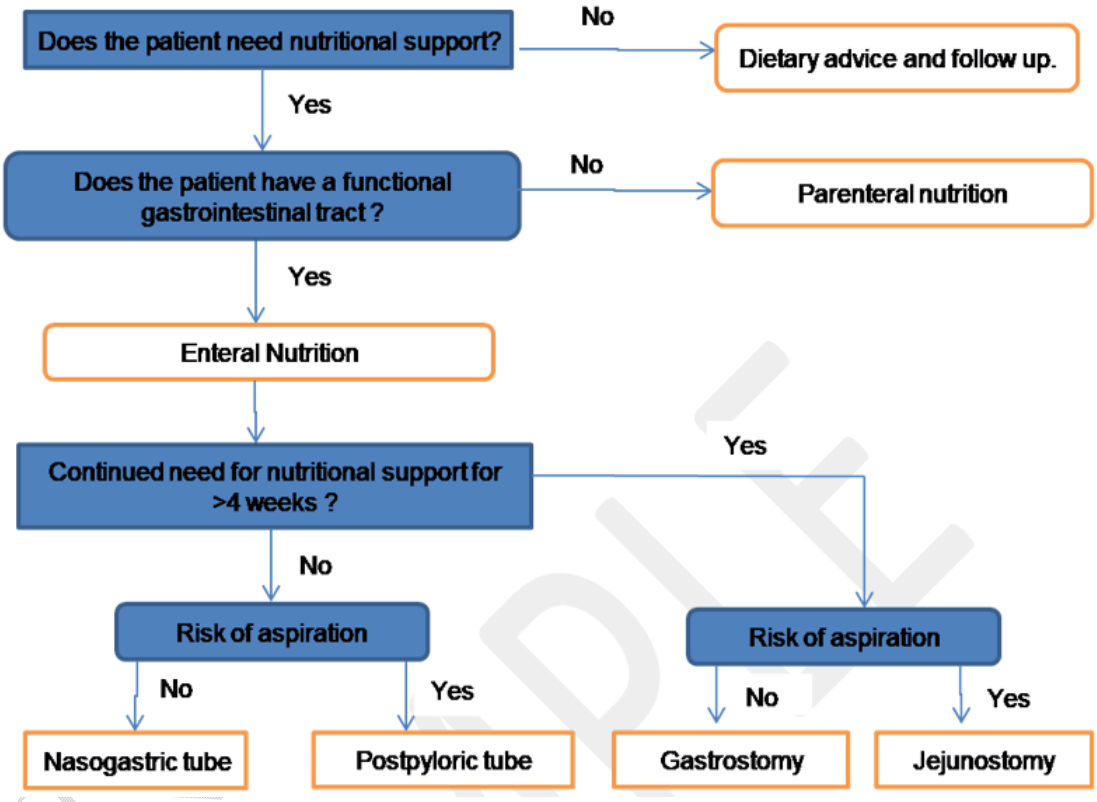

Figure 1. Pediatric perioperative nutritional care algorithm.