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Educational Case: Understanding Kwashiorkor and Marasmus: Disease Mechanisms and Pathologic Consequences

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The following fictional case is intended as a learning tool within the Pathology Competencies for Medical Education (PCME), a set of national standards for teaching pathology. These are divided into three basic competencies: Disease Mechanisms and Processes, Organ System Pathology, and Diagnostic Medicine and Therapeutic Pathology. For additional information, and a full list of learning objectives for all three competencies, see http://journals.sagepub.com/doi/10.1177/2374289517715040.[1]

Keywords
pathology competencies, disease mechanisms, metabolic and nutritional mechanisms, nutrient deprivation, malnutrition, protein-energy malnutrition, kwashiorkor, marasmus

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Primary Objective

Objective MN 1.4: Malnutrition. Discuss the pathologic consequences of nutritional deficiencies other than vitamin deficiencies, with emphasis on severe protein-energy malnutrition, and discuss the pathologic states that have a significant impact on nutritional requirements.

Competency 1: Disease Mechanisms and Processes; Topic MN: Metabolic and Nutritional Mechanisms; Learning Goal 1: Nutrient Deprivation or Toxicity.

Patient Presentation

A 19-year-old woman presents to the walk-in clinic with concerns about her 3-year-old son. For the past 2 months, the child has not been feeding properly and has become listless, apathetic, and irritable. The mother notes that he has had repeated bouts of diarrhea for the past year and has developed swelling in the legs. Both mother and son arrived in the United States from Yemen 2 weeks ago as war refugees. In Yemen, the mother was displaced due to civil war and lived in a refugee camp for 4 years, where the child was born. He was breastfed for 9 months, at which point he was switched to a local maize and potato diet. Since arriving in the United States, they have been living in a camp with 32 other individuals and are being helped by a local church group until they can find accommodation and work.

Diagnostic Findings, Part 1

On physical examination, the child appears pale and withdrawn, and small for his age. He has dry skin that is peeling (scaling) and has patchy areas of "flaky paint" depigmentation (Figure 1). His hair is dry, brittle, and reddish. He is in the 25th percentile for weight-by-age, with a measured weight of 29 pounds, and in the 10th percentile for height by age with a height of 35.5 inches. There is symmetrical pitting edema 2+ bilaterally on the tibiae and feet. The abdomen is mildly

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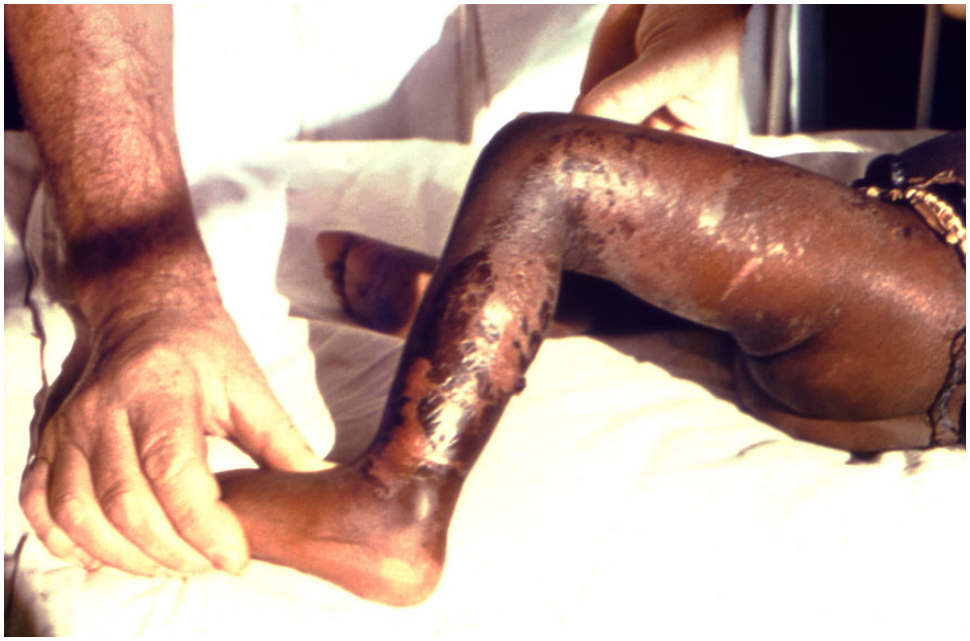

Figure 1. Left lateral view of the child's left leg. Note the characteristic pathologic changes involving the skin of the left lower extremity, including the sloughing and cracking of the skin, revealing a pink-colored, underlying cutaneous layer, irregular pigmentation, and underlying erythema. Also, note the pedal edema on the foot. (Image courtesy: image # 21259, public health image library, CDC. https://phil.cdc.gov/default.aspx permission as an open-access source.)

distended, and the liver is moderately enlarged, nontender, and palpable below the costal margin.

Questions/Discussion Points, Part 1

What Is the Differential Diagnosis for This Child?

The child appears to have failure to thrive (FTT) due to malnutrition. Failure to thrive is not a diagnosis in itself but denotes a situation where there is inadequate growth or inability to maintain growth in early childhood. It is a sign of undernutrition that may have been precipitated by processes that can lead to malnutrition. The reasons for FTT malnourished state could be either one or a combination of 3 potential causes; inadequate intake of nutrition, nonabsorption of nutrients, or poor utilization of nutrients.[2] Inadequate intake or malnutrition would be one of the main differential diagnoses in this child. It is supported by the socioeconomic and dietary history and physical findings. However, a few other pathologic possibilities such as bacterial, viral, and fungal causes may be considered as well. Chronic infections such as tuberculosis and HIV need to be ruled out. One of the child's main presenting symptoms is chronic diarrhea, which can be seen in several diseases and disorders, especially in children.[2] Common causes include infections (viral, bacterial, or parasitic), functional gastrointestinal (GI) disorders, food allergies and intolerances, and inflammatory bowel disease, and so on, all of which may lead to malnutrition and malabsorption, and FTT.[2] Also, worth considering is that he has lived in a refugee camp in a war zone, which tend to be overcrowded with unhygienic living conditions, such as lack of lavatories and clean water supply. These could predispose to viral infections such as Rotavirus enteritis and bacterial and parasitic GI infections. The bacterial infections could include *Escherichia coli* and *Yersinia*. Chronic enteric parasitic infections could be due to *Giardia lamblia, Entamoeba histolytica, Cryptosporidium,* and worm infestations such as *Ascaris lumbricoides, Enterobius vermicularis, Ancylostoma duodenale,* and *Necator americanus* among the common ones.[3] All of these, especially the parasitic infections, form part of the differential diagnosis in this patient.

Among the GI functional disorders, there are 2 main causes of chronic diarrhea in children: toddler's diarrhea and irritable bowel syndrome (IBS). Toddler's diarrhea or chronic nonspecific diarrhea of childhood may be seen in toddlers and preschool-age children. It is precipitated due to a sugar excess in the diet relative to fat and fiber. However, children with toddler's diarrhea typically do not have FTT or growth restriction, as is seen in this patient.[4] IBS, the other functional disorder is associated with significant GI symptoms. Irritable bowel syndrome is uncommon in children and often does not cause excessive weight loss or significant stunting.

Food allergies, celiac disease, lactose intolerance, and dietary fructose intolerance are common causes of chronic diarrhea. Food allergies usually appear in the first year of life and may include weight loss or poor weight gain.[2] Celiac disease may affect children of any age and may cause malabsorption of nutrients critical to a child's normal growth and

development. This deficit may result in FTT in infants, slowed growth and short stature, irritability and apathy, anemia, and low levels of important nutrients such as iron and calcium.[2] However, in this scenario celiac disease can be excluded, as the child has maintained a consistent gluten-free diet after being weaned from his mother's breast milk. Lactose intolerance or lactase deficiency can be ruled out in this child as symptoms normally are not seen in childhood and become apparent in late adolescence or adulthood.[2] Hereditary fructose intolerance, an extremely rare inherited genetic disorder, can also be ruled out in this child due to his dietary intake of maize and potato only. Children with this disorder lack an enzyme needed to breakdown fructose; and the symptoms often include abdominal pain, vomiting, and diarrhea with liver and kidney failure.

Diagnostic Findings, Part 2

Initial laboratory investigations include a complete blood count and comprehensive metabolic panel, with results shown in Table 1. A representative image from the patient's peripheral blood smear (PBS) is shown in Figure 2.

Table 1. Laboratory Investigations for the Child.

Component	Child's results	Standard range
Complete blood count (CBC)		
White blood cells (WBC, $\times 10^6/\mu L$)	7.6	5.0-14.5
Red blood cells (RBC, $\times 10^6/\mu L$)	2.8	3.9-5.3
Hemoglobin (g/dL)	7.5	11.5-14.5
Hematocrit (%)	20	34.0-40.0
Mean corpuscular volume (MCV) (fL)	64.3	76.0-90.0
Mean corpuscular hemoglobin (MCH) (pg)	18.9	25.0-31.0
Mean corpuscular hemoglobin concentration (MCHC) (g/dL)	23.1	32.0-36.0
Red blood cell distribution width (RDW-CV) (%)	6.2	11.5-14.0
Platelet count (μL)	138 000	150 000-450 000
Complete metabolic profile (CMP)		
Glucose, serum (mg/dL)	78	70-110
Blood urea nitrogen (BUN), serum (mg/dL)	3.7	5-25
Creatinine, serum (mg/dL)	0.54	0.12-1.06
eGlomerular filtration rate (mL/min/1.73 m^2)	65	>59
BUN/creatinine ratio	6.85	8-27
Sodium, serum (mmol/L)	146	135-145
Potassium, serum (mmol/L)	3.3	3.5-5.2
Chloride, serum (mmol/L)	104	95-105
Calcium, serum (mg/dL)	8.1	8.7-9.8
Protein, total, serum (g/dL)	3.1	6-8
Albumin (A), serum (g/dL)	1.8	3.7-5.5
Globulin (G), total (g/dL)	1.3	1.5-4.5
A/G ratio	1.4	1.1-2.5
Bilirubin, total (mg/dL)	1.1	0.2-1.0
Alkaline phosphatase, serum (IU/L)	368	145-320
Aspartate transaminase (AST) (IU/L)	117	0-40
Alanine transaminase (ALT) (IU/L)	131	6-45

Questions/Discussion Points, Part 2

How Do the Laboratory Results Help Narrow the Differential Diagnosis?

The child's investigation results reveal many expected and characteristic findings that would be seen in a patient with malnutrition and especially severe acute malnutrition (SAM). The low red blood cell (RBC) count and hemoglobin levels suggest nutritional deficiency anemia. Peripheral blood smear examination shows marked anisocytosis, anisochromasia, and a predominant microcytic hypochromic picture. Thus, PBS findings along with the mean corpuscular volume (MCV) of 64.3 fL indicate an iron deficiency anemia. The total protein level of 3.1 g/dL is very low, indicating an overall protein deficiency.[5] Additionally, the child has electrolyte disturbances, such as mild hypernatremia, hypokalemia, and hypocalcemia. Given this patient's hepatomegaly, the elevated liver enzymes, aspartate transaminase, and alanine transaminase are consistent with a pathologic process involving the liver.

The diagnostic bilateral pitting edema is explained by the noted hypoalbuminemia, which causes abnormal water distribution throughout the body.[6,7] Hypoalbuminemia is characteristic of this type of SAM. The microcytic hypochromic picture seen on PBS suggests iron deficiency anemia. Anemia is observed in SAM and is more pronounced in edematous rather than nonedematous SAM children. Anemia in SAM is thought to be due to ineffective erythropoiesis in the presence of nutritional deficiencies[5] and in kwashiorkor is likely from vitamin B9 (folate/folic acid) and iron deficiency.[8,9] The hypernatremia could be due to reduced renal filtration and dehydration.[6] Hypokalemia and hypocalcemia often accompany malnutrition and can be explained by a lack of nutritional input or lack of supplementation.

Had a Liver Biopsy Been Performed in View of the Enlarged Liver and Elevated Transaminases, It Would Have Shown the Appearance of the Images in Figure 3. What Is Your Histologic Diagnosis?

The liver histopathology shows a diffuse fatty change. The liver biopsy reveals predominantly diffuse macrovesicular steatosis and over 50% of the hepatocytes have marked and diffuse fatty change due to deposition of both coarse and fine fatty droplets. The lobular structure is preserved, and normal portal triads and a central vein are also seen. Additionally, there are areas of diffuse macrovesicular fatty change where hepatocytes are filled with microvesicles. Special stain for fat with Oil Red O confirms the presence of both micro and macrovesicular structures containing fat droplets (presumably triglycerides) within the hepatocytes. There is no fibrosis or cirrhotic change, for example, pseudolobular formation. Ballooning of

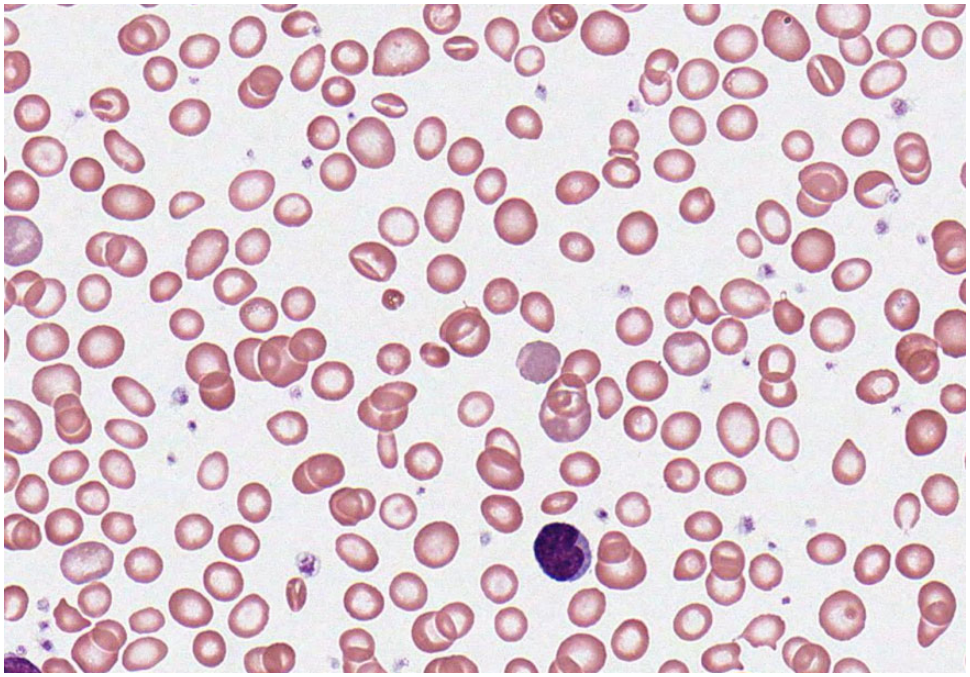

Figure 2. The peripheral blood smear shows anisocytosis and hypochromia with a predominant microcytic hypochromic picture. Microcytosis can be confirmed by comparing the RBC size to the lymphocyte seen in the image. (Image courtesy: Dr. Stephen M Wiesner, University of Minnesota, USA.). ×400.

hepatocytes and Mallory bodies are also not seen. Patients with kwashiorkor are described to have the described characteristic evidence of fatty liver.[9]

What Is the Final Unifying Diagnosis?

A diagnosis of SAM and kwashiorkor is made based on history, clinical findings, and diagnostic studies.

Diagnostic Findings, Part 3

The 19-year-old mother appears emaciated, thin, pale, and frail. The thinness of her body is accentuated by a lack of musculature and marked bony prominences. The wasting effect is especially manifest in very thin arms and legs lacking thigh musculature. On inquiry, she admits to loss of appetite. She notes she has not had her period for 2 years now and often feels faint. She says, "War and refugee camps will do that to you! At least now we are in a good place." The mother appears considerably older than her stated age, with noticeable skin wrinkles and thinning brittle hair. She has her arms wrapped around her body and a slight shiver is noted as if she is chilled. Her lips and mucous membranes appear dry and there is some scaling on the lips. She is 5′4″ tall, and her weight is 75 pounds; body mass index (BMI): 12.9 kg/m^2.

Initial laboratory investigations include a complete blood count, comprehensive metabolic panel, and thyroid function tests with results shown in Table 2. The PBS reveals microcytic hypochromic RBCs suggesting an iron deficiency anemia similar to the child. A chest X-ray is also done that is normal with no evidence of any other chronic illness.

Questions/Discussion Points, Part 3

Interpret the Significance of the Mother's Investigation Results?

The mother's low MCV, low hemoglobin, and low RBC count, indicating microcytic anemia, are significant and likely result from nutrient deficiency and additional ineffective erythropoiesis.[9] Her total protein level at 5.8 g/dL is the low end of normal. Although she also has some hypoalbuminemia, it is not as pronounced as the child's and explains the absence of edema.[7] She presents with mild hypernatremia, hypochloremia, and hypocalcemia with her potassium levels within normal range. The mother's hypernatremia is indicative of dehydration which may be causing blunted renal function and a reduced glomerular filtration rate (GFR), while the other deficits in electrolytes may be a result of decreased nutritional input.[10] Thus, her estimated GFR, at the lower end of normal may be due to mild dehydration rather than poor renal filtration. Her BUN to creatinine ratio is low, which could be due to a low-protein diet leading to reduced muscle mass, and in her case, chronic malnutrition. She has high liver enzymes indicating parenchymal liver injury. Lastly, her TSH and T4 values are in accord with the decline in BMI and account for hypothermia,

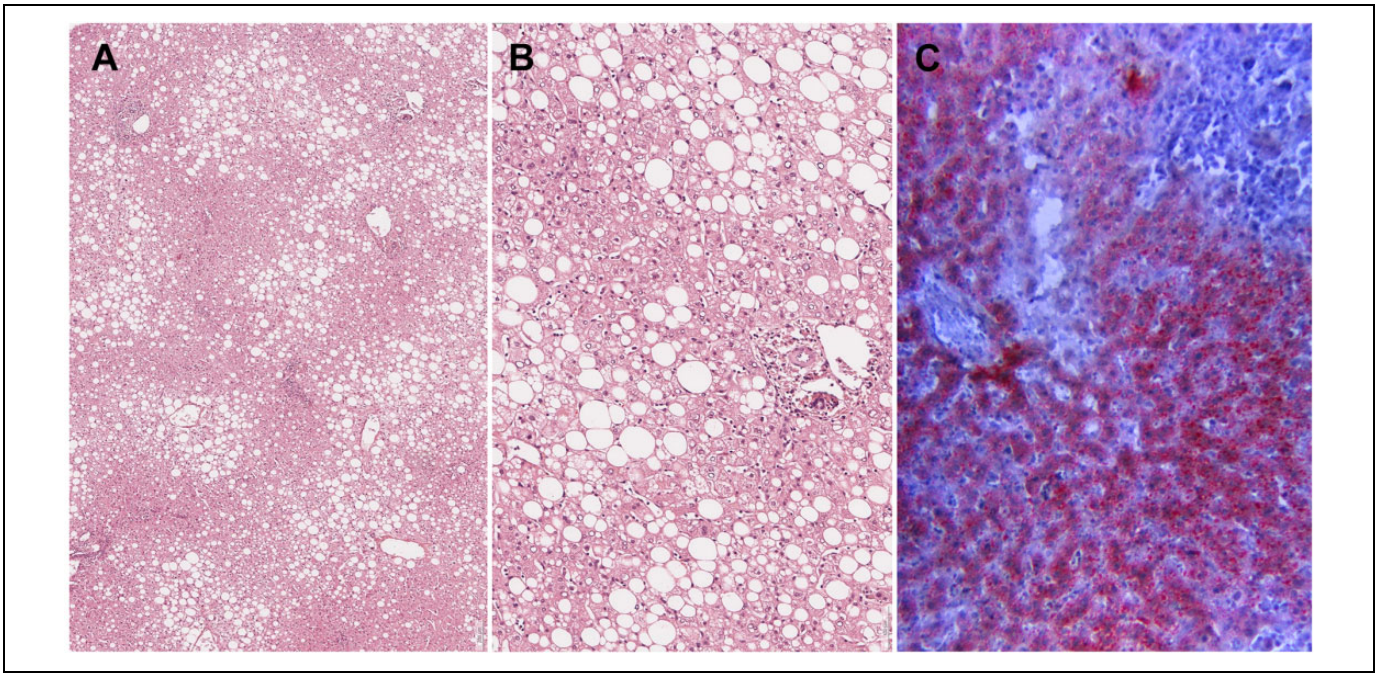

Figure 3. A, Histopathology photomicrograph of the liver biopsy. Low-power view to show the liver architecture. Hematoxylin-eosin staining (Bar: 200 μm). (Image courtesy: Prof. Dr. P. Schirmacher, medical director, pathological institute of the university, Heidelberg, Germany). B, Histopathology photomicrograph of the liver biopsy. High-power view to show the liver architecture. Hematoxylin-eosin staining (bar: 100 μm). (Image courtesy: Prof. Dr. P. Schirmacher, medical director, pathological institute of the university, Heidelberg, Germany). C, Fat-stained liver tissue specimen. Oil red-O staining ×100 (Image courtesy: image #22824, public health image library, CDC/Dr. Ron Johnson. https://phil.cdc.gov/default.aspx). Permission as an open-access source.

often seen with malnourished patients, and could explain her constant feelings of being cold.[11]

How Do the Mother's Laboratory Result and Overall Diagnosis Differ From Her Child's?

The mother's laboratory investigations also suggest SAM, like her son. However, the results suggest an overall highly pronounced calorie deficit, as compared to the pronounced protein deficit seen in her son.

The patient is diagnosed as adult SAM and marasmus based on history, clinical features, and results of the investigations.

What Disorders Form the Clinical Spectrum of Malnutrition Syndrome?

Malnutrition is a complex disorder that develops as a consequence of macro and/or micronutrient deficiencies. It includes:

1. *Stunting:* A disorder that may develop due to a maternal chronic macronutrient and micronutrient deficiency in the prenatal period or during early childhood due to insufficient nutritional input. It manifests as low birthweight accompanied by irreversible cognitive (loss of IQ points) and physical stunting.[12,13]
2. *Severe acute malnutrition*, on the other hand, is a macronutrient deficiency that may be seen in both children and adults. It encompasses a spectrum of protein-energy deficiency states that have kwashiorkor at one end, marasmus (wasting) on the other end; and marasmic-kwashiorkor with overlapping symptoms in between. The SAM individual is in a net negative energy balance which manifests as weight loss and reduced metabolic rate; along with mild, moderate, or severe degrees of muscle wasting, fat stores depletion, decreased cardiorespiratory capacity, thinning of skin prone to injury, ulceration, and delayed wound healing, hypothermia, and immunodeficiency.[12,14,15]
3. An additional secondary malnutrition syndrome may be seen due to acute or chronic underlying diseases (medical or oncologic) and presents as *wasting* or cachexia-like features. These patients with severe or chronic underlying disease generally present as low BMI, that is, cachexia or with progressive weight loss due to depletion of subcutaneous fat and wasting of muscles especially in the arms, legs, and chest wall.[15-17]

What Are the Major Pathophysiologic Changes Seen in SAM?

Severe acute malnutrition leads to starvation of all organs and tissues of the body. The biochemical changes due to prolonged starvation include complex metabolic, hormonal, and glucoregulatory mechanisms. Metabolic changes progress from the early phase, where there is rapid gluconeogenesis by the use

Table 2. Laboratory Investigations for the Mother.

Component	Mother's results	Standard range
Complete blood count (CBC)		
White blood cells (WBC, $\times 10^6/\mu L$)	11.2	4.8-10.8
Red blood cells (RBC, $\times 10^6/\mu L$)	4.2	4.70-6.10
Hemoglobin (g/dL)	9.4	12.6-17.4
Hematocrit (%)	27	37.0-51.0
Mean corpuscular volume (MCV) (fL)	73.2	80.0-94.0
Mean corpuscular hemoglobin (MCH) (pg)	24.1	27.0-31.0
Mean corpuscular hemoglobin concentration (MCHC) (g/dL)	28.6	33.0-37.0
Red blood cell distribution width (RDW-CV) (%)	8.6	11.6-14.8
Platelet count (μL)	158 000	130 000-400 000
Complete metabolic profile (CMP)		
Glucose, serum (mg/dL)	68	70-110
Blood urea nitrogen (BUN) (mg/dL)	5	5-20
Creatinine, serum (mg/dL)	0.64	0.76-1.27
eGlomerular filtration rate (mL/min/1.73 m^2)	58	>59
BUN/creatinine ratio	7.8	8-27
Sodium, serum (mmol/L)	147	135-145
Potassium, serum (mmol/L)	4.7	3.5-5.2
Chloride, serum (mmol/L)	93	95-105
Calcium, serum (mg/dL)	8.2	8.7-10.2
Protein, total, serum (g/dL)	5.8	6-8.5
Albumin, serum (g/dL)	3.2	3.5-5.5
Globulin, total (g/dL)	2.4	1.5-4.5
A/G ratio	1.3	1.1-2.5
Bilirubin, total (mg/dL)	1.2	0.0-1.2
Alkaline phosphatase, serum (IU/L)	128	38-126
Aspartate transaminase (AST) (IU/L)	66	0-40
Alanine transaminase (ALT) (IU/L)	94	0-55
Thyroid-stimulating hormone (TSH) (mIU/L.)	0.5	0.5-5.0
Free thyroxine (T4) (ng/dL)	0.8	0.8-1.8

of amino acids, pyruvate, and lactate. Later in the disease metabolic usage shifts to a protein conservation phase, where body fat stores are utilized as a primary fuel source instead of the less available glucose, resulting in the development of ketosis. Fat mobilization occurs leading to lipolysis. Fatty acids and ketone bodies become the primary energy source used to fuel the body and brain.[12] Insulin and thyroid hormone levels decrease, and cortisol concentrations increase which further contributes to lipolysis. Once the patient's body fat has been depleted, the patient is in the longer term starvation mode. At this point, the body's main fuel source is the protein that is broken down to be used to source essential metabolic processes, with the main process being an increase in the ubiquitin-proteasome pathway.[12] There is catabolism of protein stores in the somatic and visceral protein compartments.[8,9] In marasmus with continued lack of nutrition, nearly all the body's fat stores are depleted, and lean muscle tissue may be cut in less than half.[12] Muscle wasting may also be attributable to autophagy, in which key muscle cells that are implicated in muscle metabolism and contraction are broken down and degraded, ultimately contributing to nonfunctional muscle cells and severe muscle loss.[12] In kwashiorkor, the major protein depletion happens in the visceral compartment. Hepatomegaly and fatty infiltration are especially noted, as it develops as a consequence of reduced availability of carrier lipoproteins due to reduced production.[6,8,9,12]

The decline in basal metabolic rate leads to hypothermia and easy fatigue. Fatigue is further accentuated due to anemia and hypokalemia that may lead to rapid muscle fatigue. Decreased respiratory muscle mass may affect pulmonary capacity and accentuate electrolyte disturbances. The resultant hypokalemia may also affect cardiac muscle and, along with other metabolic changes, may potentially lead to bradycardia and decreased stroke volume. The resulting hypotension may cause poor tissue perfusion and possible abrogation of renal function.[9,12,15] Although some abrogation of the renal function occurs due to hypovolemia, kidney function is relatively well preserved until late in the course, when impaired glomerular filtration and signs of tubular dysfunction are noted.[12] Thus, overall, the marked changes in glucose production and protein breakdown are associated with decreased urea production and attenuated renal function with reduced urinary fluid losses.[12] For kwashiorkor patients, the intravascular volume may be diminished at the same time as the oncotic pressure fails due to hypoalbuminemia and this may cause cellular and capillary leakage leading to first dependent edema and then progressing to anasarca,[7,12] although the evidence in literature is controversial.

Thinning of the skin with loss of subcutaneous fat leaves patients susceptible to cutaneous infections. Nutritional and micronutrient deficiencies cause depigmentation and hair atrophy, making the hair brittle and susceptible to breakage.

Ineffective erythropoiesis and resultant gelatinous transformation of the marrow can lead to pancytopenia. Additionally, protein deficiency causes a state of immunodeficiency with atrophy of the lymphoid tissues and suppression of cell-mediated immunity, as well as a demise of the integrity of skin, respiratory, and GI mucosal barriers.[12] This places the malnourished patient at high risk for opportunistic infections.[12] Moreover, it has been noted that children with severe malnutrition have elevated markers of pro-inflammatory cytokines such as tumor necrosis factor, interleukin (IL)-1, IL-6, and IL-12, all of which play a role in growth pathways that ultimately lead to more pronounced muscle wasting and poor growth.[12]

In recent years, 2 other factors have been described that contribute to the development of SAM. Environmental enteric dysfunction is seen in children and adults, with compromised nutrition, throughout the developing world. It is characterized by pathophysiology similar to celiac disease.[18] Prolonged SAM leads to atrophy and blunting of the intestinal villi further reducing nutrient absorption, diarrhea, and malabsorption. This may complicate the effectiveness of therapeutic feeding. Digestion of food is further affected due to impaired exocrine pancreatic function and decreased gastric and biliary secretions.[18] Environmental enteric dysfunction results in

malabsorption of nutrients and impaired mucosal immunity. A second, related risk factor for the development of acute malnutrition is a disturbed configuration of the intestinal microbiome in malnourished individuals.[18,19] This change in the microbiome is thought to be causal rather than a consequence of malnutrition.

The brain is preserved longer than other organs; however, cerebral atrophy is seen in children with irreversible and delayed cognitive development as a complication and lifelong consequence of SAM.[6,9,12,15,20] Malnutrition has been recognized to cause reductions in the numbers of neurons, synapses, dendritic arborizations, and myelinations, all of which result in decreased brain size.[21] These children present with slowed movements, irritability, and altered speech for reasons that remain unclear.[12] Long-term studies are still needed to fully understand the long-term implications of SAM on neurological and psychological function.

What Are Some of the Specific Distinguishing Features of Kwashiorkor and Marasmus?

The clinical features of SAM are due to the inadequate energy intake that leads to various physiologic adaptations, for example, growth restriction; loss of fat, degradation of muscle, and reduced visceral mass. Attendant reduced basal metabolic rate and reduced total energy expenditure are a direct result of this adaptation. It has been suggested that marasmus may represent an adaptive response to starvation while kwashiorkor is a maladaptive response.

The clinical features of SAM depend on the type of protein compartment affected, either visceral or somatic. The child described above is a classic presentation of kwashiorkor. Kwashiorkor patients have more severe depletion of the visceral protein compartment represented by protein stores mainly in the liver.[6,12,22] Consequently, patients with kwashiorkor have characteristic bilateral pitting edema, hypoalbuminemia, distended abdomen, and fatty livers.[8,9,22] Risk of kwashiorkor increase around the age of 18 months, a stage where protein requirement increases substantially in the post-weaning period. In the given case presentation, the child was surviving on a maize diet alone in this post-weaning period. He also has diarrhea with undigested food in the stool from lack of digestive enzymes and lack of gut microbiota that are needed for digesting food and harvesting energy.[19] Normally, the symptoms of kwashiorkor develop 4 to 12 months after the onset of nutrition deficient feeding. In rural Africa, roughly 50% of children experience growth restriction (both prenatal and postnatal) due to undernutrition.[15]

The mother has marasmus in which she is especially lacking adequate calorie/energy intake[20] that is borne out by her BMI of 12.9 kg/m^2 indicating that she is underweight. The scores of nutritional screening tools for nutritional status and the physical examination findings point toward marasmus. Signs of marasmus include wasting evidenced by loss of subcutaneous fat, moderate to a severe loss of muscle mass especially in the axilla and groin region progressing to thighs arms, and buttocks. The emaciation is a result of an adaptive catabolic response and depletion of the somatic protein compartment or musculature and subcutaneous fat.[15,20] As most of the protein catabolism and loss is restricted to the somatic compartment, plasma proteins and circulating albumin levels are not affected as much. This ensures that oncotic pressure is maintained in capillary beds and dependent edema does not develop.

What Are the Potential Risk Factors and Predisposing Factors for Malnutrition?

Malnutrition is typically defined as primary, that is, nonillness related (stunting or SAM) or secondary, that is, illness-related disorder. The latter can be a result of an acute illness (infection, trauma, burns) or a chronic illness with or without inflammation.[6,15,20,22,23] Illness-related malnutrition can be a result of a triad of reduced energy intake, GI dysfunction, and additional catabolic stressors leading to altered utilization of nutrients.[6,15,20,23] Virtually, any chronic and/or critical illness can precipitate protein-energy malnutrition but among the most common are cystic fibrosis, chronic lung disease, and cancer.[17] Other factors such as HIV infection, diarrhea, pneumonia, measles, and malaria lead to anorexia with decreased dietary intake, increased energy expenditure, and poor nutrient absorption thereby increase the risk of secondary malnutrition.[6,12,14,20,24,25] Despite medical advances, malnutrition is an issue in the older population, even in the developed countries, and significantly compromises the outcomes of other comorbidities.[14]

Primary malnutrition (SAM) is a significant and highly prevalent public health problem especially in the developing world and poor nations and is a result of chronic food insecurity. Several factors and pathologic states may have an impact on adequate nutritional status. These include socioeconomic deprivation or poverty, environmental catastrophe, war and famine, ignorance about proper nutrition, self-imposed dietary restrictions (eg, vegan diet or specialized vegetarianism), a pathological restriction on diet (eg, anorexia nervosa), and additional factors such as acute or chronic illnesses, alcoholism and drug addiction, and so on. Other cofactors such as GI disorders, for example, diarrhea, worm infestations, malabsorption, and certain drug therapies may interfere with proper nutrient absorption and may cause malnutrition.[9,15]

In children, both maternal and nutritional causes are important. The first "1000 days" between conception and 2 years of age are critical for growth and development and any maternal or child food insecurity may lead to stunting. In the prenatal period, maternal undernutrition contributes to low birth weight, and post-birth continues as physical and cognitive stunting.[13] The presence of other social, environmental, and cultural factors that promote food insecurity place the child at elevated risk for acute malnutrition.[6,12,20] The post-weaning period, either prematurely or at the recommended 6 months of age, if not supplemented by proper nutrition places the child at risk for SAM. Post-weaning, the toddler is exposed to environmental

pathogens while suffering from a relative loss of high-quality protein, lipids, and micronutrients of breast milk.

Many cases of pediatric malnutrition, whether it be marasmus or kwashiorkor, are due to the family or the mother's nutritional awareness/education, socioeconomic status, geographical location, and past medical history.[22] Most cases of stunting or infantile malnutrition are due to inadequate prenatal care and maternal malnutrition. Kwashiorkor results from inadequate breastfeeding, early weaning, and/or post-weaning replacement with a high carbohydrate diet.[19] For this reason, all aspects of the child's background and history must be obtained or looked out for. Mothers should also be prepped on proper feeding of their infants, as there is a great lack of education and understanding of pediatric nutrition.

Both patients (mother and child) have primary malnutrition or SAM. In the mother's case, her severe malnutrition is rooted in her socioeconomic status and the starvation that ensued because of her country's turmoil and refugee status leading to an inadequate amount of food and nutrition. As for the child, although the same factors also play a role; his starvation is rooted partially in feeding habits where post-weaning, he had a maize and potato diet that provided a high carbohydrate and calorie load but not enough protein for his age.[25]

What Screening Tools Are Used for Malnutrition Evaluation in Pediatric Versus Adult Populations? In What Setting Is Each Test Appropriate?

For adult malnutrition cases, there are a series of screening tools that are often used in different settings to evaluate a patient's risk or severity of malnutrition. It is very important to screen adults for malnutrition, as the prevalence of PEM steadily increases with age in developing nations. Of all elderly persons living at home, 5% to 30% of the population are affected, while 16% to 70% of those in institutional care are affected and 20% to 60% of elderly persons in hospitalized settings are affected.[14] The screening tools are listed below. Mini nutritional assessment (MNA): for those who are 65+ and either in or out of the hospital setting.

- Malnutrition screening tool (MST): for all ages, just 2 questions related to unintentional weight loss and eating poorly because of decreased appetite.
- Malnutrition universal screening tool: universal, for all care settings.
- Nutritional risk screening 2002 (NRS 2002): for adults in hospital settings, the score is related to clinically relevant outcomes.
- Subjective global assessment: optimal tool for further nutrition assessment and takes resident's medical history and physical examination into account.
- Simplified nutritional assessment questionnaire: adults in community-dwelling and long-term care residents.

A score of >2 for MST and a score of >3 are considered indicative of malnutrition where management is required. Although discussing the details of these tools is beyond the scope here. The reader is referred to 2 excellent reviews on the topic.[14,22] The mother's screening for malnutrition reveals an MST score of 3 and an NRS 2002 score of 4 suggesting severe malnutrition.

Screening for pediatric cases is different than for adult populations. At each doctor's appointment children should be measured for the following parameters[22]: (a) Weight gain velocity (for children younger than 2 years of age); (b) Weight loss (for children between 2 and 20 years of age); (c) Deceleration in weight-for-length/height z-score; (d) Evaluate for adequate nutrient intake; (e) Weight-for-height z-score; (f) BMI-for-age z-score; (g) Length/height-for-age (z-score); (h) Mid-upper arm circumference (MUAC; z-score). Details of the calculation of these scores and their importance in diagnosis are discussed in an excellent review and the reader is referred to it.[22] The measurements are interpreted according to the World Health Organization (WHO)'s growth standards for identification of SAM in infants and children.[24,26] The child in this case presentation had an MUAC of 87 mm, and a weight-for-height z-score is –3.2, indicative of malnutrition requiring management. According to the WHO, malnutrition can be categorized into mild, moderate, or severe malnutrition with a deceleration in weight-for-length/height z-score being a decline of 1 for mild, 2 for moderate, and 3 for severe.[26] Patients with mild malnutrition are at 75% of what is considered normal for expected weight gain and 5% weight loss of their usual body weight, moderate malnutrition patients are at 50% of the normal with a 7.5% weight reduction, and those with severe malnutrition are at 25% or less of the normally expected weight gain with a weight loss of 10% of their usual body weight.[26] In terms of z-scores for weight-for-length, BMI-for-age, and MUAC, patients with mild malnutrition range from −1 to −1.9, moderate from −2 to −2.9, and severe from −3 to −3.9.

What Are Treatment Options for Both Mother and Son?

It is reported that those with mild malnutrition are taking in 51% to 75% of the estimated needed energy/protein levels, 26% to 50% for those with moderate, and under 25% of the needed energy intake for those with severe malnutrition.[26] Although treatment for both mother and son is to increase protein and energy deficits, any underlying conditions or secondary conditions that have resulted from the malnutrition state must first be corrected.[6] It is important to be careful and take time and care when introducing fluids and nutrients back into the patients to prevent refeeding syndrome, which is a fatal shift in fluids and electrolytes from reintroducing food too quickly.[6] Providers should avoid parenteral feeding unless necessitated by an enteric condition. Normally, volume-based enteral feeding regimens should be used.[6] Parenteral nutrition should be cycled to allow for medication administration and oral and modular nutrition supplements should be introduced to increase energy and protein intake.[22] For the child in the case above, it will be important to change the eating environment to be more nutritionally aware and prevent any added stress or distractions. Incentive charts can be used to target nutrition

goals.[22] Additionally, the mother will need to be properly educated on infant/child nutritional needs and be given options on how to supplement his feeding to ensure that he gets adequate protein intake.[25]

Teaching Points

- The term malnutrition encompasses at least 3 distinct clinical syndromes. The 2 primary syndromes are (a) *stunting* that occurs due to chronic malnutrition prenatally or early childhood and involves both macro and micronutrient deficiency; (b) *severe acute malnutrition* (SAM) is a spectrum with *kwashiorkor* and *marasmus* at the 2 ends and involves mainly macronutrient deficiency. The third syndrome is a secondary syndrome, (c) *wasting* or cachexia that occurs secondary to acute or chronic underlying disorders.
- The clinical features of malnutrition include loss of lean body mass, muscle weakness, developmental delay, infections, and delayed wound healing.
- Malnutrition may cause multisystem organ dysfunction and altered pathophysiology that includes endocrine, gastrointestinal, cardiovascular, respiratory, hematological, and neurological dysfunction along with immune suppression.
- Complications of malnutrition in pediatric and adult populations risk the patient's long-term health and well-being. They include amenorrhea and infertility in adult females and irreversible delay in physical and neurological development leading to loss of cognitive development and physical stunting in children.
- Severe acute malnutrition or kwashiorkor and marasmus result from macronutrient dietary deficiency of calories and protein. However, the somatic protein compartment (eg, skeletal muscle) is affected more severely in the marasmus, as compared to kwashiorkor where the visceral protein compartment (eg, protein stores in the liver) is depleted more severely.
- The difference in protein depletion pattern accounts for the clinical signs and symptoms seen in the kwashiorkor and marasmus. Two major distinguishing features of kwashiorkor are pitting edema and fatty liver pathology, which are both absent in cases of marasmus.
- Risk factors for malnutrition correlate greatly with socioeconomic status, geography, and in children especially with maternal health and feeding practices. Other risk factors include acute or chronic illnesses and chronic alcoholism.
- Secondary malnutrition can be acute or chronic illness related, for example, self-imposed starvation or dietary restriction, gastrointestinal or liver disorders including malabsorption, infections, for example, HIV/AIDS or tuberculosis, hormonal or metabolic disorders, and the hypermetabolic state as possible mechanisms.
- The screening tools for malnutrition in adult versus pediatric populations differ. There are a series of screening tools that are used in adult populations to determine the nutritional status, for example, body weight and height and measures for fat stores, muscle mass, and protein stores; with each test targeting different populations and settings.
- Treatment for both pediatric and adult PEM is to treat the underlying disease, if any, and slowly reintroduce protein and calorie supplements into the diet.

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