Cutaneous manifestations of nutritional deficiency

Michelle L. Heath[a] and Robert Sidbury[b]

Purpose of review

Nutritional deficiency, a global problem, remains uncommon in developed nations. Associated morbidity and mortality make it imperative that clinicians remain familiar with the clinical signs and symptoms of nutritional deficiencies to facilitate diagnosis. This article will review the cutaneous findings and recent literature regarding B12, niacin, zinc, vitamin A, kwashiorkor, biotin and selenium deficiencies, along with the clinical entities of noma and phrynoderma.

Recent findings

Much of our understanding of the clinical manifestations of nutritional deficiencies comes from old literature; however, recent case reports and series have highlighted several patient populations that may be at risk from acquired deficiencies, including patients with anorexia nervosa, cystic fibrosis, patients receiving long-term tube-feeding and those with perceived or real food allergy. There can be significant clinical overlap between various micronutrient, protein and vitamin deficiencies. Additionally, providers should consider the possibility of multiple deficiencies coexisting in individual patients.

Summary

Reports of nutritional deficiency continue to surface in developed nations and pediatricians need to have a basic understanding of their clinical manifestations. The skin is commonly affected and can be the presenting sign of illness. A higher clinical suspicion needs to be maintained in certain populations.

Keywords

acrodermatitis enteropathica, B12, biotin, kwashiorkor, niacin, pellagra, phrynoderma, selenium

Curr Opin Pediatr 18:417–422. © 2006 Lippincott Williams & Wilkins.

[a]Department of Medicine and [b]Department of Pediatrics, Division of Dermatology, Children's Hospital and Regional Medical Center, University of Washington School of Medicine, Seattle, Washington, USA

Correspondence to Robert Sidbury, Department of Pediatrics, Division of Dermatology, M2-7, Children's Hospital and Regional Medical Center, University of Washington School of Medicine, Seattle, WA 98105, USA
Tel: +1 206 987 5134; fax: +1 206 987 2217;
e-mail: Robert.sidbury@seattlechildrens.org

Current Opinion in Pediatrics 2006, 18:417–422

Abbreviations

AE	acrodermatitis enteropathica
CF	cystic fibrosis
PEM	protein energy malnutrition

1040-8703

Introduction

Dietary B12 is obtained from foods of animal origin. Deficiency can arise from numerous etiologies including pernicious anemia, atrophic gastritis, achlorohydria, disorders of small bowel malabsorption and a strict vegan diet, as well as several rare autosomal recessive genetic conditions including Imerslund–Grasbeck syndrome or congenital transcobalamin deficiencies. Imerslund–Grasbeck syndrome results from defective ileal uptake of B12 secondary to defective specific receptors, and patients present with B12 deficiency and proteinuria. While common in the adult population, B12 deficiency is rare in the pediatric population. Exclusively breastfed infants of mothers who are deficient are at higher risk [1].

Extracutaneous manifestations of cobalamin deficiency include megaloblastic anemia and an array of neurologic changes, from personality alteration and poor school performance to hypotonia, ataxia or seizures [2]. Simsek *et al.* highlight these changes seen in a 16-month-old, exclusively breastfed infant whose mother was B12-deficient. In addition to the hematologic and neurologic abnormalities, this child presented with extensive hyperpigmentation [3]. Cutaneous signs that have been associated with B12 deficiency include hyperpigmentation and mucosal changes. The pigmentary changes have been described as deep brown or brownish-black predominantly affecting the hands and feet. The dorsal fingers and toes display the most pronounced pigmentation, often with accentuation over the interphalangeal joints and over the terminal phalanges [4]. Nails are uncommonly affected. In the largest published series, Baker *et al.* reviewed 15 adults and six children with only two patients having affected nails – one with uniform pigmentation and the other with longitudinal bands [4]. Five of the six children also had pigmentary changes of the medial thighs, arms and axilla. While the acral pigmentation is more common, several reports have described a diffuse pattern that can resemble patients with Addison's disease [4–6]. The vast majority of reports of cutaneous hyperpigmentation secondary to B12 deficiency have been in darker pigmented races from India and Africa, with limited reports of affected Caucasians [7,8]. Rapid response to supplementation is the norm, with the majority resolving within 2–12 weeks. Baker *et al.* found that on average infants respond more quickly than adults.

Atrophic glossitis is the classic mucosal alteration resulting from B12 deficiency; however, this may be a late

finding [9]. Glossodynia, angular cheilitis, erythematous mucositis, stomatodynia and recurrent aphthae have been associated, and may represent earlier findings [10].

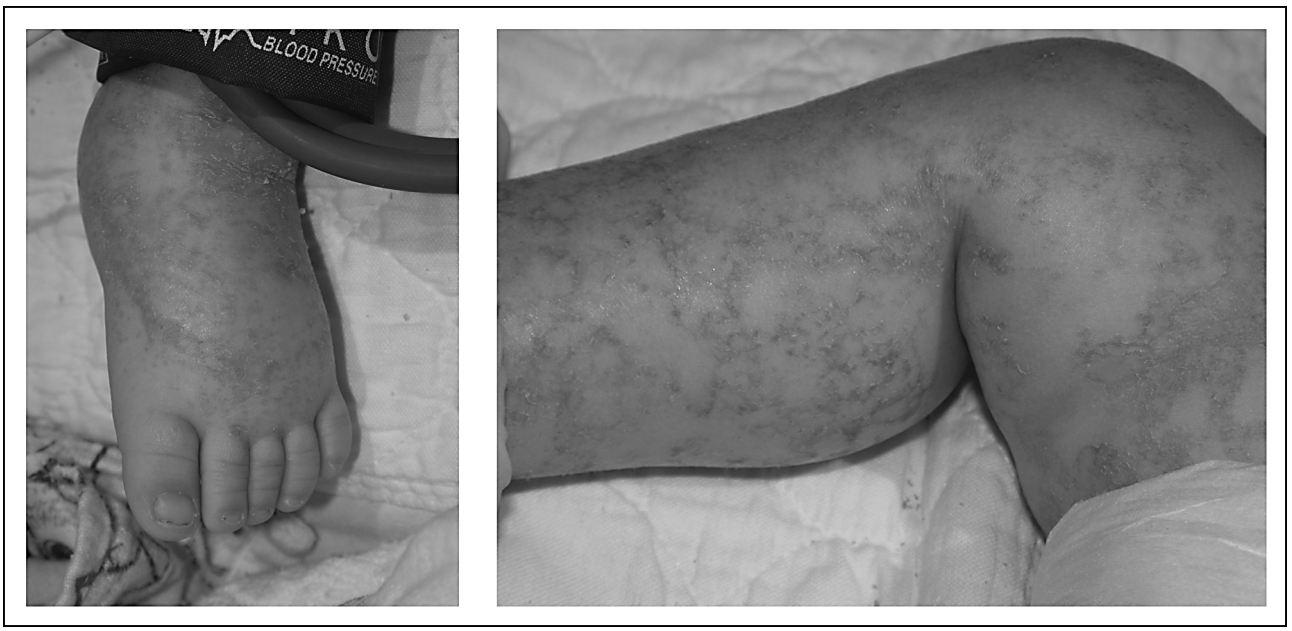
Kwashiorkor

Kwashiorkor, a form of protein-energy malnutrition, remains a devastating problem globally and is predominantly seen in developing countries. It is defined as a total body weight of 60–80% that expected for age and height with either edema and/or hypoalbuminemia. Affected children may have associated anorexia, diarrhea, nausea and increased susceptibility to infections. It has profound effects on a child's development and growth. In more developed nations, where states of food excess remain more problematic, there continues to be a disturbing series of reports of kwashiorkor [11–15]. A recent publication by Katz *et al.* [16••] highlights two infants subsisting solely on a rice-based supplement due to perceived food allergy, who presented with cutaneous changes, edema and hypoalbuminemia. Of note, such publications have led the majority of manufacturers to modify their labeling to help families avoid utilizing rice beverages as a primary source of nutrition in children under 5 years of age. In a larger series, Liu *et al.* reviewed 12 cases, ages ranging from 1 to 22 months, of kwashiorkor unrelated to chronic illness seen within the US [17]. Half of these cases were attributable to either nutritional ignorance, food faddism, presumed food allergy and/or specific food avoidance. In two of the 12 cases poverty and, perhaps more significantly, social chaos were significant factors affecting the children's nutritional intake. The most common presenting finding in this series was a rash, although this may reflect a referral bias to dermatologists.

Diffuse fine reddish-brown scale resembling 'flaky paint' is the classic cutaneous finding, but erosions in areas of friction and vesicles or bullae may be seen (Fig. 1). Areas of hyper- and hypopigmentation are common. Lightening of the hair has been described, and the 'flag sign', comprising of alternating lighter and darker areas of hair pigmentation, can reflect inconsistent states of nutritional intake.

Confounding this clinical picture is accompanying edema that can mask the underlying muscle and subcutaneous tissue atrophy, heightening the importance of detecting cutaneous clues to diagnosis [17] (Fig. 1). The findings are not all specific and the differential diagnosis may be broad. Initial clinical impressions of the 12 patients reviewed by Liu *et al.* included atopic dermatitis, viral exanthem, staphylococcal scalded skin syndrome, zinc deficiency, scabies, tinea corporis, Langerhans cell histiocytosis, epidermolysis bullosa and hypothyroidism, highlighting the difficulty in proper diagnosis of this condition. Cystic fibrosis (CF) must also be considered in the diagnosis of protein energy malnutrition (PEM) and the clinician must remain mindful that sweat chloride testing may be falsely elevated in the setting of severe PEM. Values will normalize once the nutritional status has improved [18].

Figure 1 Erythematous and scaly eruption with a 'flaky paint' appearance with edema associated with kwashiorkor



Photographs courtesy of Dr Albert Yan.

Biotin deficiency

Biotin (vitamin H) serves as an essential cofactor in multiple metabolic pathways, including gluconeogenesis, amino acid catabolism and fatty acid synthesis. Historically, biotin deficiency first presented in patients who consumed large amounts of raw egg whites which contain biotin-binding avidin. It is now rare to encounter biotin deficiency due to nutritional intake, but both acquired and congenital forms can occur. Biotinidase and holocarboxylase deficiency, collectively referred to as multiple carboxylase deficiency, as well as a more recently described defect in biotin transport [19] are autosomal recessive diseases that can result in biotin deficient states. Holocarboxylase deficiency classically presents in the first few weeks of life with vomiting, hypotonia, metabolic acidosis and organic aciduria, whereas the signs and symptoms of biotinidase deficiency typically have a later onset in infancy or early childhood with seizures, ataxia, alopecia and cutaneous findings [20]. Screening for biotinidase deficiency has become standard practice. Several recent papers highlight some of the potential pitfalls of the standard fluorimetric and colorimetric tests performed on dried blood samples. Hyperchylomicronemia secondary to lipoproteinlipase deficiency [21] and neonatal jaundice can result in false-positive results [22]. False-negatives have been linked to blood transfusions and sulfonamides [20]. The importance of follow-up of abnormal or inconclusive tests was highlighted by Hoffman *et al.* in a case report of a 15-month-old boy with profound biotinidase deficiency whose initial screening test was inconclusive [23•]. He presented later with laryngeal stridor, ataxia and lactic acidosis. While symptoms largely resolved with biotin supplementation, residual deafness and mental retardation persisted. Adequate early treatment with biotin supplementation was shown to significantly decrease the potential for permanent impairments in a retrospective comparative review of 34 children with biotinidase deficiency [24].

There is a wide range of severity and timing of clinical presentation. Symptoms and findings can remain very mild as highlighted in a review of asymptomatic family members of affected patients [25••] and by a recent report of a 7-year-old otherwise healthy boy presenting with only facial erythema and onychoschizia (distal splitting of the nail) [26].

Two recent reports highlight the potential for acquired biotin deficiency in children. Fujimoto *et al.* describe a 5-month-old infant who had been fed an amino acid formula since 4 weeks of age due to 'dyspepsia' [27]. The presenting symptoms included a periorificial erythematous, scaly eruption involving the diaper area and scalp with associated alopecia. Kimura *et al.* describe a 5-year-old boy with 'intractable eczema' since age 3 [28]. Due to congenital central nervous system abnormalities the patient required tube feeding from birth with a single formula used from 2 years of age. The child subsequently developed alopecia and an eczematous eruption in a periorbital and inguinal distribution that was unresponsive to topical steroids, zinc and copper supplementation. Ultimately biotin levels, multiple carboxylase and biotinidase activity were found to be low. The cutaneous findings and biochemical abnormalities rapidly responded to supplementation. Biotin has been shown to regulate gene expression in various enzymes in its metabolic pathways [29] providing a possible explanation for reversible abnormal enzymatic activities that were observed in this child.

Zinc deficiency

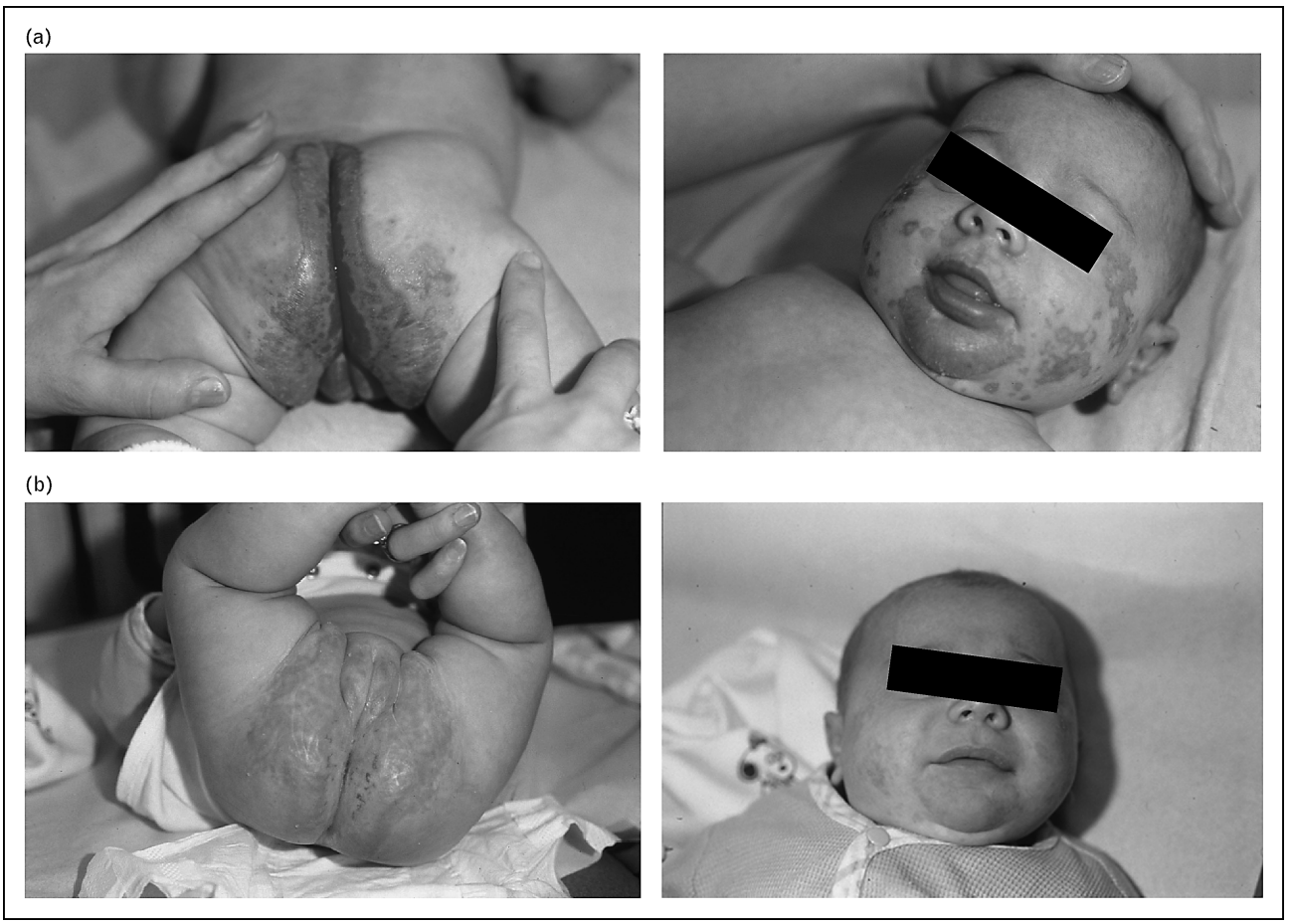
Zinc is a micronutrient found in most dietary items of animal origin, human breast milk and legumes. The classic disease associated with zinc deficiency is acrodermatitis enteropathica (AE), a rare autosomal recessive disorder, that commonly presents following weaning with the triad of diarrhea, alopecia, and a perorificial and acral rash. Onychodystrophy, paronychia, blepharitis and conjunctivitis may additionally be seen. Only 20% of patients will manifest all three of the signature findings at presentation. The cutaneous findings include erythema, scale, erosions and/or vesiculo-bullous eruptions often quite dramatically in the diaper area (Fig. 2A) that are exquisitely responsive to zinc supplementation (Fig. 2B).

Acquired disease may be due to a number of etiologies; several recent case reports highlight some risk factors for deficiency [30,31]. Quirk *et al.* describe a patient with anorexia nervosa who presented with a 1-week vesiculobullous eruption on her hands, feet and vulva with associated brittle sparse hair that had lightened in color [30]. Laboratory data revealed hypozincemia and a low serum iron. The patient responded rapidly to zinc supplementation. This case highlights the need for clinicians to consider coexisting deficiencies, as this patient's hair changes may in part have been attributable to low iron stores.

Two recent reports describe the cutaneous findings of AE as the presenting signs of CF [32,33]. CF should be considered in the differential of infants presenting with this clinical picture and the associated PEM can lead to spurious sweat chloride tests. Additionally in the setting of CF, essential fatty acid deficiency and/or protein deficiency (kwashiorkor-like malnutrition) can cause AE-like skin findings even in the setting of normal zinc levels.

Diagnostic tests include a serum zinc level; however, in a 'Letter to the editor' Chen *et al.* [34] reminds us that hypozincemia may not be a consistent finding. Alkaline phosphatase, a zinc-dependent enzyme, may be used as

Figure 2 Periorificial erythematous and erosive eruption of acrodermatitis enteropathica in a 3-month-old



(a) At presentation and (b) 5 days post-zinc supplementation.

an additional surrogate marker. Mack *et al.* argue that in the setting of normal laboratory parameters a small bowel biopsy can aid in diagnosis [35].

Selenium deficiency

Selenium deficiency has been associated with cardiomyopathy; however, cutaneous alterations may occur. A recent report by Kanekura *et al.* [36•] described an 18-month-old boy receiving parenteral nutrition resulting in selenium deficiency that led to cardiomyopathy as well as xerosis, erythematous scaly papules and plaques on the cheeks, hips, thighs and popliteal areas as well as erosions in the diaper area. Cheilitis and sparse light-colored hair were also noted.

Noma

Noma is a noncommunicable infectious disease that occurs primarily in children less than 4 years of age [37]. The World Health Organization estimated the annual global incidence was 140 000 in 1998, although this is likely a significant underestimation as many affected individuals do not present to medical attention. Clinically noma presents as an ulceration that starts on an oral mucosal surface with rapid spread, ulceration and destruction of bony and soft tissues. Enwonwu *et al.* found a significant association with low body weight, wasting and increased interleukin-18, with chronic malnutrition and infection etiologically implicated [37].

Vitamin A deficiency and phrynoderma

Phrynoderma was originally described in 1933 in a population of African prisoners with associated night blindness and xerophthalmia which responded to cod liver oil (containing vitamin A), establishing a link between this deficiency and the cutaneous findings of phrynoderma [38]. A recent article by Maronn *et al.*, however, serves as a reminder that the characteristic findings of hyperkeratotic papules typically distributed on the extremities, shoulders and buttocks are not specific to vitamin A deficiency, but may represent a manifestation of severe malnutrition, alternative vitamin deficiencies or essential fatty acid malnutrition [39•]. Phrynoderma is rare in

western countries and this report is the first description in a child in the past 20 years. This article describes a gaunt 14-month-old boy with hyperkeratotic papules coalescing into annular hyperkeratotic plaques, associated failure to thrive, feeding difficulties and coarse, sparse hair. Multiple nutritional parameters and vitamin levels, including vitamin A, were within normal limits. Ultimately, improved nutritional status led to resolution of the skin findings, although no definitive etiology was identified. In a large review of 105 children, aged 5–17, with the cutaneous findings of phrynoderma and lacking ocular or vision changes, Nakjang *et al.* found only a small percentage of patients with low levels of vitamin A, further supporting the notion that alternative nutritional deficiencies likely play a role in this condition [40].

Niacin deficiency

Niacin (B3) is a water-soluble vitamin found in meats, dairy, eggs and legumes. It is additionally supplemented in breads and cereals. Humans are able to metabolize dietary tryptophan to niacin in the presence of B6 (pyridoxine) and thiamine, which are cofactors in the metabolic conversion. It is postulated that clinical disease requires not only niacin deficiency, but a lack of either tryptophan or one of the vitamin cofactors in addition. Pellagra, the clinical manifestation of niacin deficiency, is often described by the four 'Ds': dermatitis, dementia, diarrhea and, ultimately if not corrected, death.

The cutaneous findings of pellagra include a symmetrical dermatitic eruption in sun-exposed sites, or areas of friction or pressure. Early on there may be pain or a burning sensation. With time, the erythema will often darken to a brown hue, become brittle, rough, hyperkeratotic or scaly. Nearly all (77–97%) of patients will have involvement of the dorsal hands [41]. A characteristic finding is Casal's necklace – a broad symmetric hyperpigmented, scaly and erythematous collar around the neck.

Pellagra was once problematic worldwide, but improved diets and supplementation have made this uncommon in developed countries. Secondary causes of pellagra can include various malabsorptive gastrointestinal conditions, carcinoid tumors, human immunodeficiency virus, Hartnup's syndrome, excessive alcohol (in the setting of poor nutritional intake) and various medications [42]. A recent case report [43•] and a review of the literature [44] identify several cases seen in the setting of anorexia nervosa. Cutaneous findings were the initial presenting symptoms in the majority of these patients, with photosensitivity as well as photodistributed or bullous acral desquamating and depigmenting eruptions being described. In the case of the latter description with acral bullae the patient had concomitant zinc deficiency [43•]. Given the distribution and description we postulate that the zinc deficiency may have played a role in the physical findings in addition to niacin deficiency.

Conclusions

Malnutrition, as defined by an imbalance between a person's protein, energy (caloric) and micronutrient needs and their intake, is a worldwide problem. It is estimated that 800 million persons, 20% of all people within the developing world, are affected to various degrees. There is no population impacted more greatly than children. In 2001, the World Health Organization estimated that 54% of childhood deaths were either indirectly or directly attributable to malnutrition (http://www.wpro.who.int/health_topics/protein_energy). While the number of affected persons globally is staggering, in developed countries this problem is rare and the overall incidence remains unknown. The skin is commonly affected and can provide clues to providers. Much of what we know of these disorders comes from old literature; however, the recent articles highlighted provide insight into risk factors and population subtypes that may be at higher risk including patients with anorexia nervosa, cystic fibrosis, those receiving long-term tube-feeding and with perceived or real food allergy. The clinical manifestations can have overlap between various micronutrient, protein and vitamin deficiencies. Additionally, providers should consider the possibility of multiple deficiencies coexisting in individual patients. Though these remain uncommon in developed countries, the significant potential for high morbidity and mortality mandates that clinicians remain familiar with the various presenting signs and symptoms.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 477).

1 Weiss R, Fogelman Y, Bennett M. Severe vitamin B12 deficiency in an infant associated with a maternal deficiency and a strict vegetarian diet. J Pediatr Hematol Oncol 2004; 26:270–271.

2 Rasmussen SA, Fernhoff PM, Scanlon KS. Vitamin B12 deficiency in children and adolescents. J Pediatr 2001; 138:10–17.

3 Simsek OP, Gonc N, Gumruk F, Cetin M. A child with vitamin B12 deficiency presenting with pancytopenia and hyperpigmentation. J Pediatr Hematol Oncol 2004; 26:834–836.

4 Baker S, Ignatius M, Johnson S, Vaish S. Hyperpigmentation of skin. BMJ 1963; 1713–1715.

5 Lin SH, Sourial NA, Lu KC, Hsueh EJ. Imerslund–Grasbeck syndrome in a Chinese family with distinct skin lesions refractory to vitamin B12. J Clin Pathol 1994; 47:956–958.

6 Mori K, Ando I, Kukita A. Generalized hyperpigmentation of the skin due to vitamin B12 deficiency. J Dermatol 2001; 28:282–285.

7 Gilliam J, Cox J. Epidermal changes in vitamin B12 deficiency. Arch Dermatol 1973; 107:231–236.

8 Sabatino D, Kosuri S, Remollino A, Shotter B. Cobalamin deficiency presenting with cutaneous hyperpigmentation: a report of two siblings. Pediatr Hematol Oncol 1998; 15:447–450.

9 Petavy-Catala C, Fontes V, Gironet N, *et al.* Clinical manifestations of the mouth revealing Vitamin B12 deficiency before the onset of anemia. Ann Dermatol Venereol 2003; 130:191–194.

10 Lu SY, Wu HC. Initial diagnosis of anemia from sore mouth and improved classification of anemias by MCV and RDW in 30 patients. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2004; 98:679–685.

11 Carvalho NF, Kenney RD, Carrington PH, Hall DE. Severe nutritional deficiencies in toddlers resulting from health food milk alternatives. Pediatrics 2001; 107:E46.

12 Tosh A, Fischer PR. A toddler with developmental regression. Clin Pediatr (Phila) 2004; 43:305–306.

13 Kuhl J, Davis MD, Kalaaji AN, *et al.* Skin signs as the presenting manifestation of severe nutritional deficiency: report of 2 cases. Arch Dermatol 2004; 140: 521–524.

14 Nguyen J, Cazassus F, Atallah A, *et al.* Kwashiorkor after an exclusion diet for eczema. Presse Med 2001; 30:1496–1497.

15 Eastlack JP, Grande KK, Levy ML, Nigro JF. Dermatosis in a child with kwashiorkor secondary to food aversion. Pediatr Dermatol 1999; 16:95–102.

16 •• Katz KA, Mahlberg MH, Honig PJ, Yan AC. Rice nightmare: Kwashiorkor in 2 Philadelphia-area infants fed Rice Dream beverage. J Am Acad Dermatol 2005; 52:S69–S72.

This report discusses the presentation of two children whose primary caloric intake was a rice-based beverage mistakenly believed to provide adequate nutritional support. Both children presented with classic findings of kwashiorkor. Both additionally had hypozincemia. The authors also review the literature of kwashiorkor reports in developed nations.

17 Liu T, Howard RM, Mancini AJ, *et al.* Kwashiorkor in the United States: fad diets, perceived and true milk allergy, and nutritional ignorance. Arch Dermatol 2001; 137:630–636.

18 Yigit H, Selimoglu MA, Altinkaynak S. Sweat test results in children with primary protein energy malnutrition. J Pediatr Gastroenterol Nutr 2003; 37:242–245.

19 Mardach R, Zempleni J, Wolf B, *et al.* Biotin dependency due to a defect in biotin transport. J Clin Invest 2002; 109:1617–1623.

20 Wolf B, Grier R, Allen R, *et al.* Biotinidase deficiency: the enzymatic defect in late-onset multiple carboxylase deficiency. Clin Chim Acta 1983; 131:273–281.

21 Santer R, Gokcay G, Demirkol M, *et al.* Hyperchylomicronaemia due to lipoprotein lipase deficiency as a cause of false-positive newborn screening for biotinidase deficiency. J Inherit Metab Dis 2005; 28:137–140.

22 Schulpis KH, Gavrili S, Tjamouranis J, *et al.* The effect of neonatal jaundice on biotinidase activity. Early Hum Dev 2003; 72:15–24.

23 • Hoffman TL, Simon EM, Ficicioglu C. Biotinidase deficiency: the importance of adequate follow-up for an inconclusive newborn screening result. Eur J Pediatr 2005; 164:298–301.

This is a case report of an adverse outcome after an inconclusive biotinidase newborn screening test without appropriate follow-up. It serves as a reminder of the importance of further laboratory confirmation and clinical follow-up in indeterminate initial screening tests.

24 Weber P, Scholl S, Baumgartner ER. Outcome in patients with profound biotinidase deficiency: relevance of newborn screening. Dev Med Child Neurol 2004; 46:481–484.

25 •• Baykal T, Gokcay G, Gokdemir Y, *et al.* Asymptomatic adults and older siblings with biotinidase deficiency ascertained by family studies of index cases. J Inherit Metab Dis 2005; 28:903–912.

Family studies of biotinidase-deficient individuals revealed 32 deficient family members of the 121 individuals who were screened in this study. The authors describe wide phenotypic variation in the previously undiagnosed family members, including individuals with profound deficiency who did not have clinical manifestations. This paper also suggests that we should be screening asymptomatic family members especially the siblings of the index cases.

26 Redondo-Mateo J, Urbon-Artero A. Facial erythema and onychoschizia. Arch Dermatol 2005; 141:1457–1462.

27 Fujimoto W, Inaoki M, Fukui T, *et al.* Biotin deficiency in an infant fed with amino acid formula. J Dermatol 2005; 32:256–261.

28 Kimura M, Fukui T, Tagami Y, *et al.* Normalization of low biotinidase activity in a child with biotin deficiency after biotin supplementation. J Inherit Metab Dis 2003; 26:715–719.

29 Leon-Del-Rio A. Biotin-dependent regulation of gene expression in human cells. J Nutr Biochem 2005; 16:432–434.

30 Quirk CM, Seykora J, Wingate BJ, Cotsarelis G. Acrodermatitis enteropathica associated with anorexia nervosa. JAMA 2002; 288:2655–2656.

31 Tran KT, Kress D, Lamb PM. Acquired acrodermatitis enteropathica caused by anorexia nervosa. J Am Acad Dermatol 2005; 53:361–362.

32 Muniz AE, Bartle S, Foster R. Edema, anemia, hypoproteinemia, and acrodermatitis enteropathica: an uncommon initial presentation of cystic fibrosis. Pediatr Emerg Care 2004; 20:112–114.

33 Martin DP, Tangsinmankong N, Sleasman JW, *et al.* Acrodermatitis enteropathica-like eruption and food allergy. Ann Allergy Asthma Immunol 2005; 94:398–401.

34 Chen MD, Song YM. An infant with acrodermatitis enteropathica-like symptoms but without hypozincemia. Pediatr Dermatol 2005; 22:280–281.

35 Mack D, Koletzko B, Cunnane S, *et al.* Acrodermatitis enteropathica with normal serum zinc levels: diagnostic value of small bowel biopsy and essential fatty acid determination. Gut 1989; 30:1426–1429.

36 • Kanekura T, Yotsumoto S, Maeno N, *et al.* Selenium deficiency: report of a case. Clin Exp Dermatol 2005; 30:346–348.

While this is a single case report, it deserves mention as this is the first description of significant cutaneous findings attributable to selenium deficiency. Response to selenium replacement supports that this deficiency was the etiologic factor of the cutaneous findings in this child.

37 Enwonwu CO, Phillips RS, Ferrell CD. Temporal relationship between the occurrence of fresh noma and the timing of linear growth retardation in Nigerian children. Trop Med Int Health 2005; 10:65–73.

38 Nicholls L. Phrynoderma: a condition due to vitamin deficiency. Indian Med Gazette 1933; 63:681–687.

39 • Maronn M, Allen DM, Esterly NB. Phrynoderma: a manifestation of vitamin A deficiency? The rest of the story. Pediatr Dermatol 2005; 22:60–63.

This is a case report with a good review of the literature. It highlights that phrynoderma is a clinical diagnosis without a specific underlying etiology. When discovered multiple nutritional deficiencies should be considered and investigated.

40 Nakjang Y, Yuttanavivat T. Phrynoderma: a review of 105 cases. J Dermatol 1988; 15:531–534.

41 Hegyi J, Schwartz RA, Hegyi V. Pellagra: dermatitis, dementia, and diarrhea. Int J Dermatol 2004; 43:1–5.

42 Shah GM, Shah RG, Veillette H, *et al.* Biochemical assessment of niacin deficiency among carcinoid cancer patients. Am J Gastroenterol 2005; 100:2307–2314.

43 • MacDonald A, Forsyth A. Nutritional deficiencies and the skin. Clin Exp Dermatol 2005; 30:388–390.

This is a case report of two individuals with dermatologic findings as their primary manifestation of nutritional deficiencies. One notably with anorexia resulting in pellagra, the other with atopic dermatitis and perceived and real food intolerances (presumed to flare the atopic dermatitis) resulting in significant self-imposed food restrictions. Multiple deficiencies were found in both patients, highlighting the overlap of deficiencies that can be seen and the need to screen for multiple concomitant deficiencies.

44 Prousky JE. Pellagra may be a rare secondary complication of anorexia nervosa: a systematic review of the literature. Altern Med Rev 2003; 8:180–185.