Review article

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Erythroderma (exfoliative dermatitis). Part 2: energy homeostasis and dietetic management strategies

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Summary

Erythroderma (exfoliative dermatitis) is associated with important metabolic changes that include an enhancement in energy expenditure. The key components to total energy expenditure (TEE) include basal metabolic rate (~68% of TEE), physical activity (~22% of TEE) and thermic effect of food (~10% of TEE). In the erythrodermic state, there are likely multiple contributors to the increase in basal metabolic rate, such as 'caloric drain' resulting from increased evaporation of water from enhanced transepidermal water loss, increased activity of the cardiovascular system (including high-output cardiac failure), increased nonshivering thermogenesis and hormonal changes such as hypercortisolaemia. A change in the patient's level of physical activity and appetite as a result of ill health status may further impact on their TEE and energy consumption. In Part 2 of this two-part concise review, we explore the key constituents of energy homeostasis and the potential mechanisms influencing energy homeostasis in erythroderma, and suggest much-needed dietetic management strategies for this important condition.

Introduction

Erythroderma (exfoliative dermatitis) is associated with important metabolic changes that include an enhancement in energy expenditure. There is a heightened inflammatory response within the skin and the increase in dermal blood flow leads to enhanced heat loss that in turn results in increased energy expenditure to mitigate the development of hypothermia. These concurrent processes of generalized inflammation, combined with increased dermal heat loss, conspire to create an inherently catabolic state. In this paper, we explore the key constituents of energy homeostasis and the potential mechanisms affecting energy homeostasis in erythroderma, and suggest much-needed dietetic management strategies for this important condition.

Energy homeostasis

Energy homeostasis refers to the balance between energy input via food consumption and total energy expenditure (TEE). The three key constituents of TEE are basal metabolic rate (BMR; constitutes ~60%–80% of TEE), thermic effect of food (TEF; ~8%–12% of TEE) and physical activity-related expenditure (~15%–30%

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of TEE).[1] TEF refers to the energy spent to digest, process and store macronutrients (e.g. carbohydrates, proteins and fat). Factors such as larger meal sizes, intake of carbohydrate and protein as opposed to fat, and a low-fat plant-based diet can increase energy expenditure from TEF.[2] Situational factors such as thermoregulation, growth and immune costs may further influence final TEE.[3]

Potential mechanisms impacting on energy homeostasis in erythroderma

There is a paucity of studies investigating energy homeostasis in skin diseases. The literature relevant to energy homeostasis in erythroderma is discussed below with supportive evidence drawn from the general medical literature presented in Table 1.

Increase in cardiac output

Research into the metabolic features of erythroderma originated in 1965, with reports of increased BMR in 9 of 11 sedated patients with erythroderma or generalized psoriasis.[4] The authors did not report the use of inotropes during sedation and did not describe the method used for measuring BMR. Although biochemical euthyroidism was confirmed in all the participants, levels of urinary vanillylmandelic acid (a metabolite of epinephrine and norepinephrine, and reflective of sympathetic and adrenal–medullary activity) were above or at the upper limit of normal in five of the eight participants studied.[4] The authors hypothesized that an increased cardiac output may have contributed towards an increase in BMR in at least some of the participants, and suggested that impairments in heat conservation and elimination may have resulted from impaired vasoconstriction and enhanced energy expenditure, respectively. Taheri *et al.*[5] described the mechanisms underlying the increase in cardiac output in erythroderma and how to manage fluid balance safely in these patients.

Increase in transepidermal water loss

Studies have identified a 'caloric drain' as a source of energy loss in erythroderma. A 'caloric drain' describes the excessive loss of energy through the loss of heat from the skin from evaporation of excessive water. This process results from increased transepidermal water loss (TEWL), secondary to increased porosity of inflamed skin. Noor and Hussein[6] reported increased TEWL in acute and chronic erythroderma, with an equivalent severity of TEWL in cases of erythroderma of varying causes.[6] Moskowitz *et al.*[7] published a study of 10 hospitalized children with ichthyosis, reporting that the estimated elevations in total daily TEWL resulted in a caloric drain of 433 ± 272 kcal/day (21 ± 9.8 kcal/kg/day) through heat of evaporation.

Table 1 Potential mechanisms impacting on energy homeostasis in erythroderma.

Potential mechanism	Examples of supporting literature or discussion on potential mechanism or useful references
Hypercortisolaemia due to acute physical and psychosocial stress	Any acute physical illness or psychosocial stress can associate with hypercortisolaemia, which in turn increases protein breakdown and enhance basal metabolic rate.[18] Aalto-Korte and Turpeinen[21] gave infused hydrocortisone to nine healthy adults on three occasions at 0, 80 and 200 μg/kg/h, respectively. Acute hypercortisolaemia increased protein breakdown by 5%–20%, while higher cortisol infusion rate increased resting energy expenditure by 9%–15%
Energy expenditure on skin barrier repair	Skin blistering in erythroderma (e.g. toxic epidermal necrolysis, epidermolytic ichthyosis and immunobullous diseases) is associated with weight loss[22] through direct loss of skin (contains proteins and lipids) and a corresponding increase in dietary energy requirements. European guidelines recommended elevated protein ingestion (1.5–2 g/kg in adults, 3 g/kg in children) during the first weeks following major burns injury[18]
Increased energy expenditure in cancer	This mechanism is relevant to paraneoplastic erythroderma. Indirect calorimetry at baseline demonstrated that basal metabolic rate, fat oxidation and protein oxidation were significantly greater in patients with cancer than in healthy controls[23]
Shivering due to thermodysregulation	See Mistry *et al.*[24] and Rothe *et al.*[25] for more details
Change in physical activity due to acute illness	Studies reported a reduction of physical activities during acute illness, especially during hospital admission. See Valkenet *et al.*[26] for further details
Change in appetite	Cancer cachexia is associated with negative protein and energy balance, muscle loss with or without loss of adipose tissue. See Aoyagi *et al.* for discussion of mechanism of cancer cachexia and its impact[27]
Poor nutrition/malabsorption	Erythroderma (due to zinc deficiency) may associate with severe forms of poor nutrition and malabsorption (e.g. due to cystic fibrosis)[28]

It seems likely that 'caloric drain', with its associated excessive heat loss from evaporation and TEWL, represents a major contributor to enhanced energy expenditure in erythroderma. Such a scenario can prove life-threatening through risk of dehydration, hypotension and clinical shock and hypothermia. In response, energy expenditure (including nonshivering thermogenesis) increases, as a means of enhancing heat production to mitigate against the risk of hypothermia.[8] There may be exacerbation of overall energy expenditure from the additional cardiovascular work that ensues from dehydration through a 'high-output' state, which stems from generalized peripheral vasodilation within the dermal vasculature, in response to the inflammatory processes that characterize erythroderma. These multiple mechanisms conspire to result in sustained enhancement of BMR.

Loss of protein through exfoliation

In erythroderma, there is an increase in keratinocyte transit time through the epidermis leading to exfoliation,[9] and the exfoliated scales retain amino acids, proteins and nucleic acids.[10] The literature reports that the desquamation process may increase protein loss by 25%–30% in erythroderma caused by psoriasis, and by 10%–15% in other causes.[10] Hypoalbuminaemia (not clinically significant to impact on health) was observed in 35.6% of 309 patients with erythroderma in Brazil.[11]

Hormone dysfunction

There are limited studies investigating hormone dysfunction in erythroderma. It is well recognized that transient or subclinical biochemical or hormone dysfunctions may be detected using *in vitro* tests during acute illness, such as sick euthyroid syndrome. Zheng *et al.*[12] reported that the highest likelihood of thyroid dysfunction (hypothyroidism) occurred in erythrodermic psoriasis compared with other forms of psoriasis, such as psoriasis vulgaris, psoriatic arthritis and generalized pustular psoriasis but it is unclear if these findings are transient. Co-occurrence of hyperthyroidism and erythroderma was reported in one case, although no autoimmune cause for the changes in thyroid function was identified, and the erythroderma resolved with normal thyroid function after a few weeks.[13] Primary hypothyroidism requiring thyroxine replacement was reported in one patient with prostate adenocarcinoma, in whom erythroderma may have developed due to a paraneoplastic syndrome.[14]

Dietary management recommendations

The increased energy expenditure of erythroderma may contribute to the associated failure to thrive in infants. A prospective observation study of 50 infants and children with congenital ichthyoses reported that 16 of 50 patients (32%) had nutritional deficiencies, of whom 12 of the 16 (75%) had growth impairment.[15] Congenital erythroderma may further be associated with iron, vitamin D, selenium and zinc deficiencies.[15–17]

Clinical guidelines for dermatoses often comment on a need for adequate dietetic support; however, there is a lack of dietary support guidance for erythroderma. This seems remarkable, and is an important oversight given the sustained caloric loss that typifies erythroderma, and the clear need to address this caloric deficit through dietary means to avoid weight loss and potential malnutrition.

European guidelines recommended increasing protein intake, trace elements and vitamin substitution in the first weeks following major burns injury.[18] We cautiously recommend that individuals with chronic erythroderma could also benefit from a nutritionally replete diet, with a higher caloric intake than they would usually have, and consider vitamin and trace element supplementation. The National Institute for Health and Care Excellence recommendation for weekly to fortnightly monitoring of weight for specified patient groups[19,20] could also be relevant to patients with chronic erythroderma. Those who cannot maintain their weight should prompt consideration of a dietetic referral.

Future studies are required to explore energy expenditure in patients with erythroderma. This will provide objective evidence, through comparison with normal controls, of the extent and nature of enhanced energy expenditure in erythroderma, and its chronicity. Such data will help to inform focused dietary guidance that addresses the caloric loss of erythroderma (commensurate with enhanced energy expenditure), which complements the typical temporal progression of the erythroderma-associated hypermetabolic state. Using such an approach, it should be possible to match recommended caloric intake to excessive caloric loss from enhanced energy expenditure during the clinical course of erythroderma, thereby mitigating a potential risk of unhealthy weight loss and macronutrient malnutrition.

Conclusion

The mechanisms that mediate enhanced energy expenditure in patients with erythroderma should form a focus for future research.

Learning points

- Erythroderma is a catabolic state.
- There is a requirement for guidelines on dietary support, including how to address the macronutrient and caloric requirements of patients with erythroderma.

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CPD questions

Learning objective

To understand the important metabolic changes associated with erythroderma, in order to inform improved holistic care.

Question 1

Which of the following is responsible for the largest portion of total energy expenditure (TEE) of the body in people who are well?

(a) Basal metabolic rate.
(b) Immune costs.
(c) Physical activity.
(d) Thermic effect of food.
(e) Thermoregulation.

Question 2

Which of the following is associated with increased energy expenditure in cases of erythroderma?

(a) Decreased transepidermal water loss (TEWL).
(b) Lower cardiac output.
(c) Lowered inflammatory response.
(d) Lower levels of urinary vanillylmandelic acid.
(e) Nonshivering thermogenesis.

Question 3

Which of the following best describes erythroderma?

(a) Anabolic state.
(b) Catabolic state.
(c) Homeostatic state.
(d) Postabsorptive state.
(e) State of reduced inflammation.

Question 4

Which of the following is associated with erythroderma?

(a) Hypostimulation of the hypothalamus–pituitary–adrenal axis.
(b) Normal levels of vitamin D.
(c) Raised levels of selenium.
(d) Raised levels of zinc.
(e) Sick euthyroid syndrome.

Question 5

Based on the current evidence, what is the most relevant dietary advice for patients with erythroderma?

(a) Fluid restriction.
(b) Higher-calorie diet.
(c) Low-protein diet.
(d) Low-iron diet.
(e) Low-zinc diet.

Instructions for answering questions

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Users are encouraged to

- Read the article in print or online, paying particular attention to the learning points and any author conflict of interest disclosures.
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- Register or login online at http://www.wileyhealthlearning.com/ced and answer the CPD questions.
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