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Erythroderma (exfoliative dermatitis) part two: energy homeostasis and dietetic management strategies

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Abstract

Erythroderma (exfoliative dermatitis) associates 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 non-shivering thermogenesis and hormonal changes (such as hypercortisolaemia). A change to patient's level of physical activity and appetite as a result of ill health status may further impact on their total energy expenditure and energy consumption. In part two of this two part concise review, we explore the key constituents of energy homeostasis, the potential mechanisms impacting on energy homeostasis in erythroderma and suggest much needed dietetic management strategies for this important condition.

Introduction

Erythroderma (exfoliative dermatitis) associates 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 generalised inflammation, combined with increased dermal heat loss conspire to create an inherently catabolic state. We hereby explore the key constituents of energy homeostasis, the potential mechanisms impacting on 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 (~8-12% of TEE) and physical activity related expenditure (~15-30% of TEE).¹ Thermic effect of food (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 impact on final total energy expenditure.³

Potential mechanisms impacting on energy homeostasis in erythroderma

There is a paucity of studies investigating energy homeostasis in skin diseases. Literature relevant to energy homeostasis in erythroderma are 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 generalised psoriasis.⁴ The authors did not report the use of inotropes during sedation and did not describe the method for measuring BMR. Although biochemical euthyroidism was confirmed in all the participants, levels of urinary vanillylmandelic acid (a metabolite of adrenaline and noradrenaline and reflective of sympathetic and adrenal-medullary activity) were above normal, or at the upper limit of normal in 5 of 8 participants studied.⁴ The authors hypothesised 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 (2019) describes the mechanisms underlying the increase in cardiac output in erythroderma and how to manage fluid balance safely in these patients.⁵

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 (2013) reported an increased TEWL in acute and chronic erythroderma, with an equivalent severity of TEWL in cases of erythroderma with different causes.⁶ Moskowitz et al (2004) reported in 10 hospitalised children with ichthyosis, the estimated elevations in total daily TEWL resulted in a caloric drain of 433 ± 272 kcal/day (21 ± 9.8 kcal/kg per day) through heat of evaporation.⁷

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 non-shivering thermogenesis) increases,

as a means of enhanced heat production to mitigate against 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 generalised peripheral vasodilation within the dermal vasculature, in response to the inflammatory processes that characterise 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 nuclear acids.¹⁰ The literature reported 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 erythrodermic patients in Brazil.¹¹

Hormone dysfunction: There are limited studies investigating hormone dysfunction in erythroderma. It is well recognised that transient or subclinical biochemical or hormone dysfunctions may be detected from in vitro tests during acute illness, for example, sick euthyroid syndrome. Zheng et al (2020) reported patients with erythrodermic psoriasis had the highest likelihood of thyroid dysfunction (hypothyroidism) when compared to other forms of psoriasis, such as psoriasis vulgaris, psoriatic arthritis, and generalised pustular psoriasis¹² but it is unclear if these findings are transient. Co-occurrence of hyperthyroidism and erythroderma was reported in one case, although no auto-immune cause for the changes in thyroid function were 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 which 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 16/50 (32%) patients had nutritional deficiencies, of which, 12/16 (75%) had growth impairment.¹⁵ Congenital erythroderma may further associate with iron, vitamin D, selenium, and zinc deficiencies.^{15,16,17}

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 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 increase in 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 caloric intake higher than what they would usually have, and consider vitamin and trace element supplementation. National Institute for Health and Care Excellence's 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. Through such an approach, it should be possible to match recommended caloric intake with 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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<i>Potential mechanism</i>	<i>Examples of supporting literature or discussion on potential mechanism or useful references</i>
Hypercortisolemia due to acute physical and psychosocial stress	Any acute physical illness or psychosocial stress can associate with hypercortisolaemia that in turn increase protein breakdown and enhance basal metabolic rate. ¹⁸ Aalto-Korte and Turpeinen (1995) infused hydrocortisone to 9 healthy adults on three occasions at 0, 80 and 200mcg/kg/hr. Acute hypercortisolemia increased protein breakdown by 5-20%. Higher cortisol infusion rate increased resting energy expenditure by 9-15%. ²¹
Energy expenditure on skin barrier repair	Skin blistering in erythroderma (e.g. toxic epidermal necrolysis, epidermolytic ichthyosis and immunobullous diseases) associates with weight loss ²² through the direct loss of skin (contains proteins and lipids) and a corresponding increase in dietary energy requirements. European guidelines recommended elevated protein requirements (1.5-2g/kg in adults, 3g/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 cancer patients than in healthy controls. ²³
Shivering due to thermo-dysregulation	See Mistry et al (2015) ²⁴ and Rothe et al (2005) 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 (2019) for further details. ²⁶
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 (2015) 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
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Table 1. Potential mechanisms impacting on energy homeostasis in erythroderma.