Nutritional factors and hair loss

D. H. Rushton

School of Pharmacy and Biomedical Sciences, University of Portsmouth, Portsmouth, UK

Summary

The literature reveals what little is known about nutritional factors and hair loss. What we do know emanates from studies in protein-energy malnutrition, starvation, and eating disorders. In otherwise healthy individuals, nutritional factors appear to play a role in subjects with persistent increased hair shedding. Hård, 40 years ago, demonstrated the importance of iron supplements in nonanaemic, iron-deficient women with hair loss. Serum ferritin concentrations provide a good assessment of an individual's iron status. Rushton *et al*. first published data showing that serum ferritin concentrations were a factor in female hair loss and, 10 years later, Kantor *et al*. confirmed this association. What level of serum ferritin to employ in subjects with increased hair shedding is yet to be definitively established but 70 μg/L, with a normal erythrocyte sedimentation rate (< 10 mm/h), is recommended. The role of the essential amino acid, L-lysine in hair loss also appears to be important. Double-blind data confirmed the findings of an open study in women with increased hair shedding, where a significant proportion responded to L-lysine and iron therapy. There is no evidence to support the popular view that low serum zinc concentrations cause hair loss. Excessive intakes of nutritional supplements may actually cause hair loss and are not recommended in the absence of a proven deficiency. While nutritional factors affect the hair directly, one should not forget that they also affect the skin. In the management of subjects with hair loss, eliminating scaling problems is important as is good hair care advice and the need to explain fully the hair cycle. Many individuals reduced their shampooing frequency due to fear of losing more hair but this increases the amount seen in subsequent shampoos fuelling their fear of going bald and adversely affecting their quality of life.

Introduction

The literature reveals what little is known about nutritional factors in hair loss in otherwise healthy individuals. It was therefore no surprise to learn that most medical students have little or no knowledge of the role of nutrition in skin diseases, even where there is a proven nutritional basis; acrodermatitis enteropathica.[1] Except in severe malnutrition[2] starvation and the eating disorders anorexia and bulimia nervosa[3] even less is known about the effect of nutrition in hair loss. Fortunately the vast majority of patients seeing their general practitioner or dermatologist will in all probability have no recognized illness and a nutritional basis for their hair loss should be considered.

Animal coats are not only functionally important but also fundamental for signalling (i.e. aggression) and a loss of fur could have serious consequences for survival. In humans, the loss of scalp or body hair is non life-threatening; neither is it of any significance for survival. It can however, adversely affect an individual's quality of life.[4] The integrity of normal skin and hair function relies largely on an adequate and balanced nutritional intake. Dietary imbalance, whether in the form of an

Correspondence: Dr D. H. Rushton, School of Pharmacy and Biomedical Sciences, University of Portsmouth, Portsmouth, Hants, PO1 2DT, UK. Tel/Fax: +44 20 7637 4853. E-mail: rushton@btinternet.com

overall deficiency, specific shortage, excess of one component over another, can disturb this equilibrium.

In animals nutritional factors and hair loss have been reported over the past 70 years. Cunningham in 1932 noted hair loss in iron deficient rats[5] while in 1941 Sullivan and Nicholls[6] found hair loss in rats deficient in riboflavin. Hair loss in both rats[7] and mice[8] has been reported due to zinc deficiency. It has long been recognized that diet influences the coat of animals and while the affect of poor grazing and low fleece weight have been known for many years[9] just how poor nutrition effects fur, hair and wool growth is not fully understood. In 1954 Van Koetsveld[10] reviewed the influence of feeding on the animal coat, while Flesch[11] briefly reviewed the effect of diet on hair growth. Yet despite unlimited grazing or a variety of special feeds, which have been shown to increase the hard keratin composition of wool in sheep, the amount and composition of wool that can ultimately grow is genetically controlled.[12] The influence of proteins, carbohydrates, fats, minerals, and vitamins in various animals is reviewed by Ryder[9] and worth reading for those wanting a historical perspective.

In humans, the association of nutrition with skin and hair changes emanates primarily from studies on protein-energy malnutrition.[2,13] Hair root response to protein malnutrition has been studied widely in children with kwashiokor, marasmus, and marasmic-kwashiokor conditions and reviewed comprehensively by Bradfield and Bailey;[14] the hair is easily epilated, finer in diameter; less curly, depigmented, breaks off, falls out, and has a lower daily rate of growth.[15] There are also notable changes in skin keratinization, hyper- and hypopigmentation, and delayed wound healing. Hughes[16] reported not only hair loss and hypopigmentation but loss of hair curl in African children following pantothenic acid and riboflavin deficiency.

According to Stewart and Gutherie[17] in 1497 Vasco de Gamma recorded the deaths of 100 of his 160 sailors after scurvy had broken out during his voyage around the Cape of Good Hope. It took almost 300 years before James Lind confirmed the empirical link between scurvy and vitamin C. Of note was the fact that before death, skin haemorrhage and hair loss was observed.[17] Daniel Whistler in 1645 is credited with the first British clinical description of vitamin D deficiency in his DM Thesis on rickets but it was not until 1922 that McCullum *et al.* demonstrated the link with vitamin D.[18] More recently the beneficial role of vitamin D analogues in psoriasis has been established.[19] Other examples of dietary affects on skin are nicotinic acid and thiamine to name two, but whether there is a link with hair loss is unknown.

It took many years after the initial clinical observations for a link with a nutritional deficiency to be confirmed. The discovery and identification of vitamins played a critical role in the evolution of nutritional medicine. In 1912 vitamin A was the first vitamin to be described and over the next 36 years the remaining vitamins were isolated and identified, vitamins D, E, C, B_1, B_2, pantothenic acid, biotin, vitamins K, B_6, niacin, folic acid and finally, in 1948 vitamin B_{12}.[20]

As in animals, nutritional influences in humans can affect the skin and cause scaling maladies resulting in excessive hair shedding. It is important therefore to separate those nutritional factors that act directly on the skin, from those acting only on the hair follicle.

Scaling problems and hair loss: is there a nutritional basis?

It has long been recognized that some chronic scaling conditions of the scalp lead to increased hair shedding (telogen effluvium) and a temporary reduction in hair density (hairs per cm^2) due to pruritus and excoriations.[21] Less recognized is the possible involvement of nutritional factors in mild to moderate scaling conditions, i.e. scaling only slightly more severe than simple dandruff, which some clinicians would term mild seborrhoeic eczema (seborrhoeic dermatitis). Usually the lesions are restricted to the scalp, nasal fold, and eyebrows. In men the beard and chest are affected if more than a scattering of hair is present. The adverse affects of dairy produce in skin diseases are not new.[22] Food allergy and food intolerances are due to hypersensitivity type I mediated reactions. There is, however, considerable debate as to whether such reactions can affect the hair cycle. Even where there is strong evidence for an immunological involvement in the skin (IgE, mast cell, etc.), much scepticism surrounds any hair follicle involvement.[23]

Biotin deficiency is reported to cause dermatitis and hair loss in experimentally induced states[24,25] but establishing the presence of a deficiency in humans with a balanced diet has yet to be demonstrated. However, 1–2 mg of biotin daily for 2 months has anecdotal clinical support in unresponsive scaling problems and may be worth consideration.

As with biotin there is good animal data to support the role of an essential fatty acid (EFA) deficiency in dermatitis and hair loss, with some limited evidence established in humans.[26,27] Where it occurs naturally in humans, EFA deficiency is purely of dietary origin. Essential fatty acids are also known as polyunsaturated fatty acids and two groups are currently considered

important: the omega-6 EFAs derived from linoleic acid and present in vegetables and red meat; and the omega-3 EFAs derived from α-linolenic acid and present in oily fish and marine animals. The ideal ratio should be 5 : 1 (linoleic : α-linolenic acid) but currently in the UK it is reported to be 12 : 1.[28] both are involved in a multitude of physiologically important pathways. Links with atopic eczema and psoriasis have been suggested but there is little firm evidence that the manipulation of dietary EFAs in other skin conditions is of any benefit. In unresponsive scaling problems it might be worth considering trying an EFA supplement if the subject's diet is low in fish oil or red meat; unfortunately, there is no routine investigation available to assess this. In psoriasis a daily supplement of fish oil (providing 18 g of EFA) led to a clinical but not statistical improvement.[29] The rational for this stems from the low frequency of psoriasis in the Eskimo but recent investigations suggest this is due to a genetic factor[30] which affects how EFAs are metabolized rather than the level of EFA consumed.

The role of zinc in the rare congenital skin disease acrodermatitis enteropathica is well known to dermatologists[1,31] though few will have ever seen an actual case in clinical practice. The clinical manifestations associated with zinc deficiency arise primarily from the cutaneous changes similar to those found in acrodermatitis enteropathica.[32]

Nutrition and hair loss without scaling problems

Possibly one of the most contentious areas in dermatology is the role of nutritional factors in scalp hair loss in subjects without any observable scaling malady. The lack of objective data is obvious and stems primarily from difficulties in being able to quantitatively evaluate scalp hair loss. Matters are further complicated in females by the historical positioning of reference ranges now shown to have been derived from populations containing a large number of iron deficient women.[33]

A large number of women complain of persistent increased hair shedding (chronic telogen effluvium, CTE). Many will have sought professional help but without much success. Too often, they are dismissed because the hair loss is not obvious.[34] Men complaining with CTE are even more difficult to evaluate as during the active phase of male balding increased hair shedding is a notable clinical feature.[35] Compounding matters is the frequency of balding in men, which increases with age[36] thus potentially masking any nutritional problem that might have developed due to a dietary imbalance. Although no published data could be found for the frequency of men presenting with CTE, it should be higher in females if low iron stores turn out to be a primary cause of CTE. The percentage of balding men with a serum ferritin below 40 μg/L in 1990 was less than 4% (D. H. Rushton, unpublished data), while in women with reduced hair density it was 72%.[37]

The frequency of hair loss in the general female population is unknown. In an attempt to determine how many women might be affected, females from Japan, the USA and UK were questioned about their hair status compared to 5 years earlier. The results for those aware of increased hair shedding are given in Table 1. We were surprised to find 34% of premenopausal women reporting increased hair shedding. In an attempt to see if there was a possible link between CTE and nutritional factors, 200 women presenting with unexplained persistent hair shedding but having a normal scalp hair density, as assessed with the unit area trichogram[38] were investigated. Table 2 presents the data obtained and shows the frequency of blood variables believed to be affected by nutrition (haemoglobin, ferritin, vitamin B_{12}, folic acid, and zinc), which extends the initial work of Rushton published in 1993.[39]

There is widespread popular belief that zinc deficiency can cause hair loss. However, the published data shows no link at all in alopecia areata[40] or telogen effluvium.[41] In Table 2 serum Zn concentrations were below the lower limit of normal in 7%, however, when these women were treated with the essential amino acid L-lysine, only one of the 14 originally 'deficient' women required Zn supplementation (Table 3). This suggests that the true frequency of Zn deficiency in women with CTE in the UK is around 0.5% and much lower than previously thought. Correcting the Zn deficiency in this subject did not resolve her CTE.

Table 1 Frequency of women in the general population reporting increased hair shedding compared to the level they were aware of 5 years earlier.

Country	Frequency (%)
UK ($n = 964$)	35.4
Japan ($n = 490$)	35.1
USA ($n = 396$)	30.8
Total sampled (1820)	Mean 33.8%

Data colected in the UK (Cardiff, London, Portsmouth), USA (New York, Los Angeles) and Japan (Tokyo) from women attending churches, banks and shopping malls.

Table 2 Biochemical results obtained in 200 apparently healthy women complaining of increased hair shedding for longer than 6 months (CTE).

Variable	Hb (g/L)	TIBC (μmol/L)	S-Ferritin (μg/L)	Vitamin B_{12} (ng/L)	S-Folate (nmol/L)	S-Zinc (μmol/L)
Reference range	> 120	45–70	40–400*	200–1100	5–35	10.6–22.6
Mean ± SD	131 ± 9.7	61.3 ± 9.3	36.8 ± 24.4	538 ± 275	25.1 ± 12.1	13.8 ± 2.3
Median	132	61.2	32.0	480	22.0	13.1
Below range	11.0%	1.5%	65.0% or 96.0%†	2.0%	0.5%	7.0%
Above range 0.0%	0.0%	17.5%	0.0%	2.5%	28.5%	0.0%

*Reference range from Rushton *et al.*[37] †For a serum ferritin of 70 μg/L. S, Serum; TIBC, total iron binding capacity.

Table 3 Change in mean serum zinc concentration after supplementation with the essential amino acid. L-lysine (1.5–2 g/day) for 16 weeks in the 14 individuals in Table 2 with a serum concentration below the lower limit of normal.

Reference range (10.6–22.6 μmol/L)	Zinc (t = 0)	Zinc (t = 16 weeks)
Mean	9.7	14.6*
SD	0.74	3.26
(range)	(7.8–10.6)	(9.9–20.0)

Morning samples following a 12-h overnight fast. *Statistical analysis was by paired Student's *t*-test ($P < 0.00003$).

Essential amino acids

The role of essential amino acids in anaemia is well known but their possible impact on hair growth has never been investigated. This is probably due to the abundance of body stores and as with the essential fatty acids, amino acid deficiency in well-nourished individuals is unlikely. However, the rate limiting essential amino acid L-lysine is a noteworthy exception. The bioavailability of L-lysine is restricted primarily to meat, fish, and eggs; consequently reducing the consumption of these foods could result in a shortfall between uptake and utilization resulting in a negative balance. While the body could make up any shortfall from the muscle reserves, it could arguably prioritize their availability for the essential tissues leaving nonessential tissue such as scalp hair compromised.

At the present time little is known about the specific role that essential amino acids might have in hair growth and even less about their influence in trace element uptake and utilization. L-lysine appears to play a role in iron and Zn uptake. In iron deficiency without anaemia, the typical (classic) biochemical response of the haematological variables are: low haemoglobin, serum iron, percentage of iron saturation and ferritin, and a raised total iron binding capacity (Table 4). Such individuals respond to iron supplementation, i.e. elemental Fe 50 mg twice daily; however, in some women only a modest increase in serum ferritin concentration is achieved. In these individuals there is a lower than expected total iron binding capacity, high percentage of iron saturation with a low Hb and ferritin (Table 4). Adding the essential amino acid L-lysine (1.5–2 g/day) to their existing iron supplementation resulted in a significant ($P < 0.001$) increase in the mean serum ferritin concentration (Table 5). How L-lysine affects iron uptake is unknown but is the subject of ongoing research.

What is the evidence for iron deficiency and excessive hair shedding?

The need to transport oxygen and remove carbon dioxide from animal tissue is a fundamental requirement of life, which is independent of age or sex.[42] The role of iron in humans and many other mammals is central to this process.[43,44] In the absence of

Table 4 Relationship between serum variables in response to iron deficiency in women with chronic telogen effluvium, without anaemia compared to the respective reference range: (A) classical response (B) with insufficient first class protein intake.

Variable	Hb	S-Iron	Iron saturation (%)	TIBC	Ferritin
(A) Classical response	Low or normal	Reduced	Reduced	Raised	Reduced
(B) Suboptimal first class protein intake	Low or normal	Raised or normal	Raised or normal	Reduced or normal	Reduced
Reference range	120–160 g/L	10–30 μmol/L	20–55	45–70 μmol/L	40–400 μmol/L*

*Reference range from Rushton *et al.*[37] S, Serum; TIBC, total iron binding capacity; Hb, haemoglobin.

	Ferritin (t = 0) (μg/L)	Fe 100 mg/day Ferritin (t = 6 months) (μg/L)	Fe 100 mg/day + L-lysine 1.5 g/day Ferritin (t = 12 months) (μg/L)
Mean	27.4	27.7	58.6*
SD	20.86	14.3	21.54
Median	27	26	59
(range)	(7–68)	(12–47)	(28–85)

Table 5 Changes in serum ferritin concentration in seven women with CTE who failed to respond to iron supplementation alone but subsequently responded when the essential amino acid L-lysine was co-administered.

*Statistical analysis: Paired Student's *t*-test, $P < 0.001$.

inflammatory disease, it is well established that serum ferritin is a good indicator of body iron stores.[45]

Cunningham in 1932 noted hair loss in iron deficient rats[5] and in 1963 Hård[46] first demonstrated the role of iron as an aetiological factor in diffuse hair loss in nonanaemic, iron deficient women. However, the role of iron in hair loss is still the subject of much debate with those against citing the fact that some women with iron deficiency or iron deficiency anaemia do not complain of telogen effluvium. While this may be true these individuals do not present to the dermatologist complaining of hair loss! Perhaps we need to consider individuals with hair loss a subpopulation and, thus, blood parameters employed for those without hair loss are inappropriate.

The evidence for this can be found in Table 2, which shows the most frequent abnormal nutrient in women presenting with CTE is a low serum ferritin. Sixty-five per cent had a concentration below 40 μg/L the lowest control value obtained in women without hair loss[37] a level just above the lower limit of normal for males quoted in some laboratories.[34] However 96% had a serum ferritin below 70 μg/L, the upper 99% confidence limit for iron staining in the bone marrow.[45] Low serum ferritin concentrations in women with hair loss have recently been reported by Kantor *et al.*[47] supporting the initial observation of Rushton in 1993.[39]

In 22 women with CTE, Rushton *et al.*[48] demonstrated a significant ($P < 0.0001$) decrease in the percentage of hair in the telogen phase after 6 months' treatment with a daily iron (Fe 72 mg) and L-lysine (1.5 g) supplement. Compared to baseline, this represented a mean percentage decrease in hair shedding of 39%. In addition, a significant ($P < 0.0001$) increase in the mean serum ferritin level also occurred (Table 6). To confirm these findings a double-blind, placebo controlled study was undertaken using the same iron and lysine regimen and the results obtained are presented (Table 7). A significant ($P < 0.05$) increase in the mean serum ferritin concentration was found in the treated but not in the placebo group. Compared to baseline, a decrease in the percentage of hair in the telogen phase, representing a 31% reduction in the amount of hair shed was observed in treated subjects compared with a 9% increase in those receiving placebo (Fig. 1).

Table 6 Within-group comparison (mean ± SE) for the percentage of telogen hair and serum ferritin concentration obtained from 22 women taking an oral, daily nutritional supplement providing 72 mg of elemental iron and 1.5 g of the essential amino acid L-lysine for 6 months.

	Time (months)	
	0	6
Hair in the telogen phase (%)	19.5 ± 1.1	11.3 ± 1.0
(range)	(8.5–28.9)	(4.4–21.9)
P	< 0.0001*	
Serum ferritin (μg/L)	33 ± 4	89 ± 11
(range)	(5–84)	(27–211)
P	< 0.0001†	

*Wilcoxon Signed Rank test (paired samples). †Student's *t*-test (paired samples). Reproduced from Rushton *et al.*[48] with permission.

Excessive supplementation

A link between excessive vitamin A intake and hair loss is well established[49] and other fat-soluble vitamins may also pose a potential problem. There is some evidence for an adverse effect on hair growth following excessive vitamin E intake, where a significant decrease in serum thyroid hormone levels was found in volunteers taking 600 IU of vitamin E per day for 28 days. While this dosage was around 30 times the daily recommend intake,[49] even higher levels appear to be well tolerated. Currently, mega-doses of vitamin E are consumed in the belief that it reduces the level of free radicals in the body. Current opinion considers vitamin E to be one of the least toxic fat-soluble vitamins. For other fat-soluble vitamins and trace elements, an association with hair

Table 7 Within-group comparison (mean ± SE) for serum ferritin concentration obtained in a double-blind placebo controlled study of women taking an oral nutritional supplement providing 72 mg of elemental iron and 1.5 g of the essential amino acid L-lysine for 6 months.

	Treated group ($n = 5$)		Treated group ($n = 7$)	
Time (months)	0	6	0	6
Serum ferritin (μg/L)	26.0 ± 3.5	28.4 ± 5.8	41.3 ± 6.9	68.9 ± 11.3
(range)	(20–39)	(7–42)	(18–70)	(26–112)
P	NS*		< 0.05*	

*Students *t*-test (paired samples).

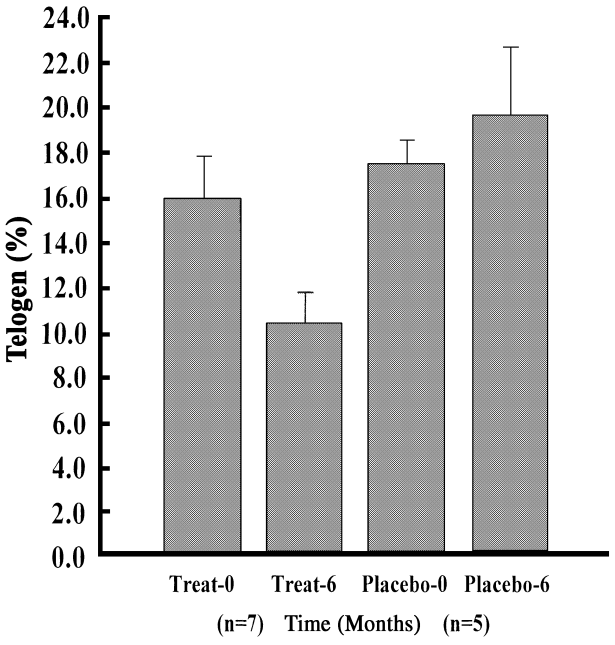

Figure 1 Change (mean ± SE) in the per cent of hair in the telogen phase after taking a daily supplement providing 72 mg of elemental iron and 1.5 g L-lysine (treated group) or nothing (placebo group) for 6 months in women with CTE.

loss is not established. Even less well understood is the effect of taking excessive amounts of water-soluble vitamins, which traditionally were thought to be excreted and not stored, thus posing no toxic threat. However, while gross toxicity may not be an issue the position may need re-evaluation with regard to hair loss. Table 2 shows that a significant proportion of women with CTE had a raised serum folic acid concentration and on questioning the majority revealed that they were taking multivitamin supplements because of their hair loss. Over-the-counter preparations often contain concentrations of folic acid at the recommended daily allowance (400 μg) but clearly there appears to be no allowance for the fact that most diets contain considerable amounts of folic acid.

Many multivitamin formulations fail to allow for problems arising from interactions between other elements. If the level of zinc is equal to that of iron then iron uptake is significantly decreased: a ratio of 3 : 1 (Fe : Zn) is desirable to prevent competitive interference. Whether excessive intake of relatively high doses of multivitamins or trace elements are a factor in CTE is unknown but they could pose potential problems. One should therefore be alert to patients taking excessive amounts of nutritional supplements. In such individuals elevated red cell folic acid concentrations are found where folic acid is present in their supplementation regimen. In the absence of quantitative data supporting any beneficial or detrimental affect of multivitamin or trace element supplementation, avoidance is recommended.

Nutritional consequences of hair treatment: anti-androgen therapy

Over the past 20 years women with a diffuse hair loss (androgenetic alopecia) have been treated with a combination of the oral anti-androgen, cyproterone acetate (CPA) and ethinyl oestradiol (EE_2) or CPA and Dianette.[50,51] Ramsay and Rushton[52] first demonstrated an interaction between CPA and a reduction in serum vitamin B_{12} concentrations. While CPA caused a significant decrease in serum vitamin B_{12} concentration in all those treated, this did not adversely affect any haematological variable.[52] There was also no evidence that lower serum vitamin B_{12} concentrations were associated with increased hair shedding but this has yet to be confirmed. The typical lower reference ranges for serum vitamin B_{12} in the UK are between 180 and 200 ng/L. However, vitamin B_{12} levels below 300 ng/L have been found to cause anxiety and neurological changes in both men and

women.[53] Anxiety and depression is a frequently reported side-effect of CPA/EE_2 and oral contraceptive therapy. Barth *et al.*[54] reported around 20% of women taking Dianette, which contains 2 mg of CPA, or Dianette plus CPA developing depression while on treatment, unfortunately no vitamin B_{12} evaluations were undertaken. In women being treated with oral CPA and EE_2, concurrent oral vitamin B_{12} supplementation (100–200 μg per day) maintained serum B_{12} concentrations above 300 μg/L.[52] In the diet, vitamin B_{12} is only found in meat, chicken, fish and eggs. Assessing the vitamin B_{12} concentration before starting CPA therapy with subsequent follow-up at 4 months is advisable.

Conclusion

With the exception of iron and the essential amino acid L-lysine, in otherwise healthy individuals nutritional factors play only a minor role in patients presenting with unexplained increased hair shedding (CTE). However, in those who selectively avoid certain foods imbalances occur with adverse consequences for both skin and hair.

Hård[46] almost 40 years ago demonstrated the importance of iron supplements in nonanaemic, iron deficient women with hair loss. Rushton *et al*. in 1990 first published data showing that serum ferritin concentrations may be a factor in diffuse hair loss in women, fertility[55] and CTE.[39] Kantor *et al.*[47] ten years later confirmed the link between hair loss and low serum ferritin concentrations. The double-blind data presented confirmed the open study of Rushton *et al.*[48] suggesting that a significant number of women with CTE will respond positively to L-lysine and iron therapy. While independent confirmation is awaited it would seem appropriate to consider the nutritional status of women with CTE. Further, there appears to be a minimum ferritin concentration required to optimize treatments in diffuse hair loss.[51,56] What level of serum ferritin to use is still not fully resolved but 70 μg/L, with a normal erthrocyte sedimentation rate (< 10 mm/h) is a recommended level to achieve. The level of supplementation or dietary change needed to maintain serum ferritin concentrations above 70 μg/L is the subject of continuing research. Preliminary analysis of the data suggests that daily iron supplementation of between 24 and 48 mg is needed in menstruating women, with a lower level required in postmenopausal females. Contrary to popular belief there is no evidence to support the view that a low serum Zn is involved in CTE.

While nutritional factors affect the hair directly, one should not forget that they also affect the skin. In the management of subjects with hair loss, eliminating scaling problems is important as is good hair care advice and the need to explain fully the hair cycle. Many individuals reduced their shampooing frequency due to fear of losing more hair but this just increases the amount seen in subsequent shampoos fuelling their fear of going bald and adversely affecting their quality of life.

References

1 Moynahan EJ. Acrodermatitis enteropathica: a lethal inherited human zinc deficiency disorder. *Lancet*, 1974; **ii**: 399–400.
2 Jelliffe DB. Protein-calorie malnutrition in tropical preschool children. *J Pediatr* 1959; **54**: 227–56.
3 Gilbert S. Eating disorders. In: Garrow JS, James WPT, eds. *Human Nutrition, Dietetics*, 9th edn. Edinburgh: Churchill Livingstone, 1993: 752–60.
4 Kingsley DH. The development and validation of a quality of life measure for the impact of androgen-dependent alopecia. PhD Thesis. University of Portsmouth, Portsmouth, Hants, UK.
5 Cunningham IJ 1932 The influence of dietary iron on hair and wool growth. *NZ J Agric* 1999; **44**: 335–7.
6 Sullivan M, Nicholls J. Nutritional dermatosis in the rat. IV. Riboflavin deficiency. *J Invest Dermatol* 1941; **4**: 181–91.
7 Day HG, McCollum EV. Effects of acute dietary zinc deficiency in the rats. *Proc Soc Exper Biol Med* 1940; **45**: 282–4.
8 Day HG. The effects of zinc deficiency in the mouse. *Am Inst Nutr; Federation Proc* 1942; **1**: 188–9.
9 Ryder ML. Nutritional factors influencing hair and wool growth. In: Montagna W, Eliss RA, eds. *The Biology of Hair Growth.* New York: Academic Press, 1958: 305–6.
10 Van Koetsveld E. Influence of feeding on the coat and its structure in animals. *Tijdscher Diergeneesk* 1954; **79**: 405–16.
11 Flesch P. Hair growth: nutritional factors. In: Rothman S, ed. *Physiology and Biochemistry of the Skin.* Chicago: University of Chicago Press, 1954: 601–61.
12 Reiss PJ, Schinkel PJ. Some effects of sulfur-containing amino acids on growth and composition of wool. *Aust J Biol Sci* 1963; **16**: 218–30.
13 Golden BE. Primary protein-energy malnutrition. In: Garrow JS, James WPT, eds. *Human Nutrition, Dietetics*, 9th edn. Edinburgh: Churchill Livingstone, 1993: 440–55.
14 Bradfield RB, Bailey MA. Hair root response to protein undernutrition. In: Montagna W, Dobson RL, eds. *Biology of Skin, Hair Growth*, **Vol. IX**; VII. Oxford: Pergamon Press, 1969: 109–19.
15 Sims RT. The measurement of hair growth as an index of protein synthesis in malnutrition. *Br J Nutr* 1968; **22**: 229–36.

16 Hughes W. Achromotrichia in tropical malnutrition. *Br Med J* 1946; **II**: 85–8.
17 Stewart CP, Guthrie D. *Lind* "S Treatise on Scurvy. Edinburgh: Edinburgh University Press, 1953: 145–8.
18 McCollum EV, Simmonds N, Becker JE, Shipley PG. Studies on experimental rickets. XXI. An experimental demonstration of the existence of a vitamin which promotes calcium deposition. *J Biol Chem* 1922; **53**: 293–312.
19 Kragballe K, Gjertsen BT, de Hoop D *et al.* Double blind, right/left comparison of calcipotriol and bethamethasone valerate in treatment of psoriasis vulgaris. *Lancet* 1991; **337**: 193–6.
20 Scott T, Brewer M, eds. Vitamins. In: *Concise Encyclopedia of Biochemistry.* Berlin: Walter de Gruyter and Co, 1983: 499.
21 Dawber R. Diseases of the scalp and skin diseases involving the scalp. In: Rook A, Dawber R, eds. *Diseases of the Hair and Scalp*, 2nd edn. Oxford: Blackwell Scientific Publications, 1991: 493–539.
22 Lessof MH, Wraith DG, Merritt TG, Merritt J, Buisseret PD. Food allergy and intolerance in 100 patients-local and systemic effects. Q J Med 1980; **49** (259): 271.
23 Chapel H, Haeney M. Skin diseases. In: *Essentials of Clinical Immunology*, 3rd edn. Oxford: Blackwell Scientific Publications, 1993: 179–206.
24 Baugh CM, Malone JH, Butterworth DE. Human biotin deficiency induced by raw egg consumption in a cirrhotic patient. *Am J Clin Nutr* 1968; **21**: 173–82.
25 Nisenson A. Seborrheic dermatitis of infants: treatment with biotin injection for the nursing mother. *Pediatrics* 1969; **44**: 1014.
26 Riella MC, Broviac JW, Wells M, Scribner BH. Essential fatty acid deficiency in human adults during total parenteral nutrition. *Ann Intern Med* 1975; **83**: 786.
27 Skolnik P, Eaglstein WH, Zibouth VA. Essential fatty acid deficiency. *Arch Dermatol* 1977; **113**: 939.
28 Gurr M. Fats. In: Garrow JS, James WPT, eds. Human Nutrition and Dietetics, 9th edn. Edinburgh: Churchill Livingstone, 1993: 88–93.
29 Bittiner SB, Tucker WFG, Cartwright I, Bleehen SS. A double-blind, randomised, placebo-controlled trial of fish oil in psoriasis. *Lancet* 1988; **I**: 378–80.
30 Horrobin DF. Low prevalences of coronary heart disease (CHD), psoriasis, asthma and rheumatoid arthritis in Eskimos: are they caused by high dietary intake of eicosapentaenoic acid (EPA), a genetic variation of essential fatty acid (EFA) metabolism or a combination of both? *Med Hypoth* 1987; **22** (4): 421–8.
31 Gartside JM, Allen BR. Treatment of acrodermatitis with zinc sulphate. *Br Med J* 1975; **3**: 521–2.
32 Abou-Mourad NN, Farah FS, Steel D. Dermopathic changes in hypozincemia. *Arch Dermatol* 1979; **115** (8): 956–8.
33 Rushton DH, Dover R, Sainsbury AW, Norris MJ, Gilkes JJH, Ramsay ID. Why should women have lower reference limits for haemoglobin and ferritin concentration than men? *BMJ* 2001; **322**: 1355–7.
34 Van Neste DJJ, Rushton DH. Hair problems in women. In: Clinics in Dermatology. New York: Elsevier Science Inc, 1997; **15**: 113–125.
35 Rushton DH, Ramsay ID, Norris MJ, Gilkes JJH. Natural progression of male pattern baldness in young men. *Clin Exp Dermatol* 1991; **16**: 188–92.
36 Birch MP, Messenger AG. Genetic factors predispose to balding and non-balding in men. *Eur J Dermatol* 2001; **11**: 309–14.
37 Rushton DH, Ramsay ID, James KC, Norris MJ, Gilkes JJH. Biochemical and trichological characterisation of diffuse alopecia in women. *Br J Dermatol* 1990; **123**: 187–97.
38 Rushton DH, James KC, Mortimer CH. The unit area trichogram in the assessment of androgen-dependent alopecia. *Br J Dermatol* 1983; **109**: 429–37.
39 Rushton DH. Investigating and managing hair loss in apparently healthy women. *Can J Dermatol* 1993; **4**: 455–61.
40 Ead RD. Oral zinc sulphate in alopecia areata – a double blind study. *Br J Dermatol* 1981; **104** (4): 483.
41 Arnaud J, Beani JC, Favier AE, Amblard P. Zinc status in patients with telogen defluvium. *Acta Derm Venereol (Stockh)* 1995; **75** (3): 248–9.
42 Bothwell TH, Charlton RW, Cook JD, Finch CA. *Iron Metabolism in Man.* Oxford: Blackwell Scientific, 1979: 7–43.
43 Hallberg L. Iron absorption and iron deficiency. *Human Nutr, Clin Nutr* 1982; **36C**: 259–78.
44 Dallman PR. Biochemical basis for the manifestations of iron deficiency. *Annu Rev Nutr* 1986; **6**: 13–40.
45 Puolakka J. Serum ferritin in the evaluation of iron status in young health women. *Acta Obstet Gynecol Scand Suppl* 1980; **95**: 35–41.
46 Hård S. Non-anemic iron deficiency as an etiological factor in diffuse loss of hair of the scalp in women. *Acta Derm Venereol* 1963; **43**: 562–9.
47 Kantor J, Jay K, Brooks D, Cotsarelis G. Decreased serum ferritin is associated with alopecia in women: a case controlled study. *J Invest Dermatol* 2001; **117** (2): 435.
48 Rushton DH, Norris MJ, Dover R, Busuttil N. Causes of hair loss and the developments in hair rejuvenation. *Int J Cosmet Sci* 2002; **24**: 17–23.
49 McLaren DS, Loveridge N, Duthie G, Bolton-Smith C. Fat soluble vitamins. In: Garrow JS, James WPT, eds. *Human Nutrition, Dietetics*, 9th edn. Edinburgh: Churchill Livingstone, 1993: 208–38.
50 Mortimer CH, Rushton DH, James KC. Effective medical treatment for common baldness in women. *Clin Exp Dermatol* 1984; **8**: 342–50.
51 Rushton DH. Ramsay ID. The importance of adequate serum ferritin levels during oral cyproterone acetate and ethinyl oestradiol treatment of diffuse androgen-dependent alopecia in women. *Clin Endocrinol* 1992; **2** (36): 421–7.
52 Ramsay ID, Rushton DH. Reduced serum Vitamin B12 levels during oral cyproterone acetate and ethinyl oestradiol therapy in women with diffuse androgen-dependent alopecia. *Clin Exp Dermatol* 1990; **15**: 277–81.

53 Lindenbaum J, Healton EB, Savage DG, *et al.* Neuropsychiatric disorders caused by cobalamin deficiency in the absence in the absence of anaemia or macrocytosis. *New Engl J Med* 1988; **318**: 1720–8.
54 Barth JH, Cherry CA, Wojnarowska F, Dawber RP. Cyproterone acetate for severe hirsutism: results of a double-blind dose-ranging study. *Clin Endocrinol* 1991; **35** (1): 5–10.
55 Rushton DH, Ramsay ID, Gilkes JJH, Norris MJ. Ferritin and fertility [letter]. *Lancet*, June 22nd, 1991; **i**: 1554.
56 Rushton DH, Fenton D. A. Quantitative evaluation of topical 5% minoxidil in the treatment of diffuse androgen-dependent alopecia in females. *Br J Dermatol* 1992; **127**: 423.