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Anaemia in adolescent girls: effects on cognitive function and activity

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L'anémie chez les adolescentes: effets sur la fonction cognitive et l'activité physique

RÉSUMÉ

Chez les filles, l'adolescence est un temps où la masse musculaire et le volume sanguin augmentent rapidement. L'apparition de la menstruation est une charge supplémentaire sur les nutriments. On estime que, pour répondre à cette demande, les besoins en fer augmentent de 70 pour cent après l'âge de 10 ans.

Il semble qu'une proportion importante des adolescentes britanniques ne disposent pas de cette augmentation de l'apport en fer. De plus, seule une petite proportion du fer de l'alimentation est d'origine animale. Ceci a des implications sur l'absorption du fer. Un apport insuffisant en fer entraîne des réserves de fer pauvres, et la déficience en fer et l'anémie par déficience en fer sont courantes, mais légères, chez les adolescentes britanniques.

Les causes des niveaux faibles de ferritine et d'hémoglobine sont liées à la fois au niveau de la captation du fer et à des facteurs qui influencent la disponibilité, l'absorption et l'utilisation du fer. Ces facteurs incluent la source du fer: le fer héminique qui est mieux absorbé, et le fer non-héminique qui est moins bien absorbé. Ils comprennent également l'état nutritionnel de l'individu, par exemple ses réserves en fer, en vitamine A et en riboflavine. L'absorption est aussi influencée par d'autres substances présentes dans les aliments qui augmentent ou inhibent l'absorption.

On sait que l'anémie grave, comme on en voit dans certain pays, affecte la fonction cognitive, mais il n'existe pas d'indication que les déficiences légrères en fer telles qu'on les voit en Grande-Bretagne affectent la fonction cognitive telle qu'on la mesure par toute une variété de tests.

L'activité et les performances physiques sont aussi fortement affectées par l'anémie grave, et on a la preuve que l'anémie a des effets à court terme sur la capacité de performance et la récupération après l'activité physique même chez les sujets britanniques. Bien que les effets de l'anémie légère sur la capacité d'apprendre ne soient pas démontrés, leurs conséquences potentielles imposent qu'elles soient étudiées de façon approfondies. Il est possible que les effets à plus long terme soient des conséquences secondaires résultant des effets de la déficience en fer sur l'activité physique dans l'adolescence.

Adolescence in girls is a time of rapid increase in both muscle mass and blood volume. The onset of menstruation adds a further nutrient burden. To meet this demand,

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Table 1. *Iron intakes in British adolescents*

Reference	Age (years)		Intake (mg/d) Male	Female
Hackett *et al.* (1984)	11·5–13·5		10·6	
Bull (1985)	15–18		11·0	8·5
Department of Health (1989)	10–11		10·0	8·6
	14–15		12·3	9·3
Crombie *et al.* (1990)	11–13		10·0	10·0
Nelson *et al.* (1990)	11–12		11·2	10·0
Nelson *et al.* (1993)	12–14		12·3	9·6
Adamson (1992)	11–12		11·7	11·2
Doyle *et al.* (1994)	12–13		10·9	9·7
Southon *et al.* (1994)	13–14	Calculated	14·9	9·7
		Analysed	13·2	9·8

requirements for Fe increase by an estimated 70% after the age of 10 years (Department of Health, 1991).

A substantial proportion of British adolescent girls apparently fail to achieve the necessary increase in Fe intake. Mean intakes range from 8·5 to 11·2 mg/d (Table 1). Moreover, only a small proportion of dietary Fe is derived from animal sources. This has important implications for Fe absorption. Moynihan *et al.* (1994) reported that 18% of the Fe intake in girls came from meat and other animal sources, the remainder (82%) coming from breakfast cereals (13), bread (12), potatoes (11), drinks (8), other bakery products (8), vegetables (6, of which one-third is from baked beans), chocolate (4) and other sources (20).

The consequence of low Fe intake is low Fe stores, and Fe deficiency (ID) and Fe-deficiency anaemia (IDA) are common in British adolescents, especially in girls (Table 2). Estimates in girls range from 0 to 22% prevalence, based on low haemoglobin levels (<120 g/l), and from 4 to 43%, based on low ferritin levels (<10 μg/l or <12 μg/l). The variation observed may be partly related to differences in region, ethnic origin and socio-economic group (as well as real differences in diet), and partly to differences in blood sampling methods (capillary *v*. venous) and in haemoglobin or ferritin analysis.

The causes of low ferritin and low haemoglobin levels relate both to the level and type of Fe intake, and to factors which influence Fe availability, absorption and utilization. These factors fall into two classes relating to the form of Fe in the diet: haem or non-haem. Haem-Fe is generally better absorbed than non-haem-Fe. Up to 30% of haem-Fe may be absorbed, although its absorption can be inhibited by Ca present in the same meal (which may affect the active transport system in gut mucosal cells) and by high cooking temperatures (Hallberg *et al.* 1992). Absorption of non-haem-Fe, by contrast, is rarely above 10%, and may be as low as 2% (British Nutrition Foundation, 1995). Absorption is influenced by Fe status itself, vitamin A and riboflavin status (Powers *et al.* 1983). Bioavailability of non-haem-Fe is also altered by enhancing factors (e.g. vitamin C consumed with the meal; meat, fish and seafood; organic acids such as citric acid), and by inhibiting factors (e.g. Ca, phytate, phenols, dietary fibre and soyabean protein).

Little has been done in the UK to elucidate the roles of these factors. Studies in the UK suggest that low Fe intakes alone fail to explain the prevalence of ID and IDA

Table 2. *Prevalence (%) of iron deficiency (ID) in British adolescents*

Reference	Age (years)	Group or gender	ID* or IDA (%)
Goel (1978)	12–14	Caucasian	16 Hb <120
		Non-caucasian	20 Hb <120
Armstrong (1989)	14–18	Male	13 Hb <130
		Female	7 Hb <120
		Male	35 Ferr <10
		Female	43 Ferr <10
Nelson *et al.* (1993)	12–14	Male	4 Hb <130
		Female	11 Hb <120
		Male	1 Ferr <12
		Female	4 Ferr <12
Multiple criteria: Any two of: <3rd percentile Hb, <300 g/l MCHC; <20 μg/l Ferr		Male	2
		Female	11
Nelson *et al.* (1994)	11–14	Female	20 Hb <120
		White:	11 Hb <120
		Indian:	22 Hb <120
Southon *et al.* (1994)	13–14	Male	5 Hb <120
		Female	0 Hb <120
		Male	11 Ferr <10
		Female	21 Ferr <10
Doyle *et al.* (1994)		Male	8 Ferr <10
		Male	33 Ferr <20
		Female	28 Ferr <10
		Female	64 Ferr <20

Hb, haemoglobin (g/l); Ferr, ferritin (μg/l); IDA, Fe-deficiency anaemia, based on low Hb levels; MCHC, mean corpuscular Hb concentration.

* Based on low Ferr.

(Southon *et al.* 1994). Mean reported intakes of Fe in girls with haemoglobin <120 g/l were not significantly different from those of girls with haemoglobin above this level (9·2 *v.* 9·7 mg/d; Nelson *et al.* 1993). Intakes of vitamin C below the median (<67 mg/d) coupled with reported low Fe intakes (estimated from a food-frequency and amount questionnaire) were associated with higher prevalence of low haemoglobin levels (Table 3). Some aspects of lifestyle, such as slimming or the untutored adoption of vegetarian diets, were also associated with increased risks of low haemoglobin levels (Table 4).

The clinical signs of anaemia associated with very low haemoglobin levels (fatigue, headaches, inability to make sustained physical effort) are well recognized. Other consequences, such as reduced immune response (Brock & Mainou-Fowler, 1986; Dallman, 1987) and poorer outcomes of pregnancy (Godfrey *et al.* 1991) have also been described. The relationships between poor Fe status and poor behaviour or impaired cognitive function and reduced levels of physical activity are less-well documented and understood.

Table 3. *Percentage of children with low haemoglobin* amongst 399 British adolescents aged 12–14 years, according to iron and vitamin C intake* (From Nelson *et al.* 1993)

Vitamin C intake (mg/d)	Fe intake		
	<LRNI†	LRNI-RNI	>RNI
<67	14·5	9·3	2·8
>67	7·7	5·8	2·3

LRNI, lower reference nutrient intake; RNI, reference nutrient intake.
* Boys <120–126 g/l dependent on age, girls <120 g/l.
† Values for 11–18 year olds: males: LRNI 6·1, estimated average requirement (EAR) 8·7, RNI 11·3; females: LRNI 8·0, EAR 11·4, RNI 14·8 (Department of Health, 1991).

Table 4. *Percentage of 11–14-year-old British girls with haemoglobin <120 g/l, according to vegetarian status and attempts to lose weight in the previous year*

Vegetarian	Attempted to lose weight	
	Yes	No
Yes	43	11
No	15	8

COGNITIVE FUNCTION

In developing countries, where anaemia is generally more severe than in the UK, associations of ID and IDA with poor cognitive function are evident (Table 5). Pollitt (1990) and others (Soemantri *et al.* 1985; see also Table 5) have described several studies in Indonesia and Thailand in which Fe supplementation of adolescents with poor Fe status has resulted in significant improvements in tests related to specific components of cognition, for example familiar figures test or general tests of academic ability. In slightly-younger children (9–11 years) non-anaemic children (Hb >100 g/l) were seen to perform better on language tests and Raven's matrices. In India, Seshadri & Gopaldas (1989) showed beneficial effects of 8 weeks of Fe supplementation (greater than those with a placebo) in a group of anaemic 8–15-year-old children. In North America, Webb & Oski (1973, 1974) reported better results on general performance ('Iowa') tests amongst non-anaemic children, and deficits in attention and perception amongst anaemic children.

In Britain, ID and IDA amongst UK adolescents, although common, is generally mild. The consequences of these mild levels of deficiency have not been fully investigated. There is only weak evidence of relationships between dietary status and cognitive function, and none which relates directly to Fe, in spite of the fact that ID is the most common nutrient deficiency in the UK (Nelson, 1992). In a study of 143 11–12-year-old schoolchildren from North London, Nelson *et al.* (1990) failed to show significant associations between baseline Fe intakes and cognitive function based on the Heims AH4 test (Heims *et al.* 1976) or two components, digit span and coding, of the Weschler Intelligence Scale for Children, Anglicised Revised Edition (WISC-R UK; Weschler, 1971). There were also no differences observed in the change in cognitive function

Table 5. *Relationships between iron status and cognitive function in adolescents*

Reference	Age (years)	Main findings
Webb & Oski (1973, 1974)	12–14	Non-anaemic better on (1973–4) Iowa Tests Anaemic had deficits in attention and perceptual tasks
Pollitt *et al.* (1985)	6–12	Fe intervention: 'familiar figures' test better than in placebo group
Soemantri *et al.* (1985)	9–11	Fe intervention: better achievement test scores
Pollitt *et al.* (1989)	9–11	Non-anaemic better on language tests and Raven's matrices
Seshadri & Golpaldas (1989)	8–15	Fe intervention: better mazes and clerical tasks
Southon *et al.* (1994)	13–14	No relationship between Fe status and cognitive function, or evidence of effects of supplementation
Ash (unpublished results)	11–15	Fe intervention: no significant effect on BAS short IQ tests

BAS, British Ability Scales; IQ, intelligence quotient.

between a group supplemented with a multi-vitamin and mineral preparation for 28 d and an age-, gender- and height-matched group given a placebo. In another study of 51 13–14-year-old children living in Norwich, Southon *et al.* (1994) reported no relationships between initial Fe status (based on dietary or biochemical assessments) and results from the WISC-R UK tests, nor any affect of a multi-vitamin and mineral supplement given daily for 16 weeks. In neither of these studies, however, was any attempt made to identify children who were initially anaemic in order to assess specifically the effect of Fe status or Fe supplementation on cognitive function.

Ash (unpublished results) has recently investigated the effect of Fe supplementation on cognitive function in a placebo-controlled trial amongst twenty-four anaemic adolescent girls in North London. An Fe–amino acid chelate containing 24 mg Fe^{2+} (or placebo) was administered to two age-matched groups three times weekly for 10 weeks. Cognitive function, based on the British Ability Scales Short IQ test, was determined before and after the supplementation period. There were no significant effects of supplementation on cognitive function. Further analyses and an increase in study size are planned.

PHYSICAL ACTIVITY

Physical activity has been shown to be markedly affected by Fe status, and improved by Fe supplementation in developing countries where anaemia is common and severe. Bhatia & Seshadri (1987) described poorer work capacity in a group of 8–12-year-old anaemic Indian boys compared with non-anaemic controls. Satyanarayan *et al.* (1990), also working in India, described poorer performance in a 1600 m run by anaemic boys. In the UK, there is evidence of short-term effects of anaemia on performance capacity and recovery from physical activity, assessed by heart rate (Nelson *et al.* 1994). Girls aged 12–14 years with haemoglobin levels <120 g/l had significantly elevated heart rates immediately after and 1 min after a 2 min step test compared with non-anaemic girls.

CONSEQUENCES OF ANAEMIA

In the short term, the consequences of poor Fe status amongst British adolescent girls may relate to learning ability and physical performance capacity. Even at the mild levels of ID generally found in the UK, it is not yet clear that cognitive function is unaffected. If cognitive function proved to be adversely affected by mild ID, this would have important implications regarding the need for screening of adolescent girls in order to identify those whose learning ability was potentially impaired. Similarly, physical performance capacity may have an influence on adolescents' attentiveness and learning ability, and the ability to sustain levels of activity commensurate with healthy physical development. Work in progress by Ash will help to elucidate these matters.

The long-term consequences of anaemia in adolescent girls may manifest themselves in later adult life, principally in terms of bone health and heart health. Risks of osteopaenia (bone loss) and osteoporotic fracture are inversely proportional to levels of exercise throughout life (Halioua & Anderson, 1989; Prince *et al.* 1991). Activity is an important protective risk factor in relation to heart disease. Activity levels in adolescence are likely to be reflected in activity levels at middle age (Fox, 1994). Thus, establishment in adolescence of a regular pattern of physical activity will provide a firm physiological foundation for healthy tissues and lay the foundation for good life-long habits. If anaemia in adolescence militates against the establishment of healthy physical activity patterns, it will only be possible to demonstrate the association with poor adult health prospectively. Studies of osteoporosis or heart disease in adulthood cannot establish Fe status in adolescence retrospectively.

If anaemia present in adolescence persists into the reproductive years, there are likely to be poorer outcomes of pregnancy (Godfrey *et al.* 1991), including increased risks of premature and still birth, low birth weight, and neonatal infection. There may also be higher risks of hypertension and heart disease in offspring born to anaemic mothers (Barker *et al.* 1990). There have been no studies of the risk of anaemia in pregnancy in relation to Fe status in adolescence. Again, such studies would need to be prospective in nature.

FUTURE RESEARCH

A number of public health issues concerning Fe status in UK adolescents remain to be resolved.

Which groups of British adolescents are most at risk of iron deficiency and Fe-deficiency anaemia?

Existing studies suggest that new vegetarians, girls who attempt to lose weight, and Asian and African girls are more likely to have poorer Fe status. There may also be social class or income group differences, particularly in very-low-income households.

What are the academic and behavioural consequences of iron deficiency and Fe-deficiency anaemia in British adolescents?

It is not yet clear whether mild anaemia has an adverse effect on cognitive function and learning ability in British adolescents. If even minor deficits in learning are evident amongst those with poorer Fe status, this has important implications regarding screening and supplementation. Robust, well-designed studies will need careful implementation and analysis.

Is anaemia in adolescence a transient phenomenon?

The increased demand for Fe which occurs at the onset of the adolescent growth spurt is not a wholly transient phenomenon. Whilst the demand for additional Fe related to increased tissue mass and blood volume will persist only during the period of growth, the final attained body size will require more Fe than at the start of the growth spurt. In addition, in girls, the onset of menstruation means that Fe needs to be supplied at a rate higher than that needed for the increased body size alone. There is no longitudinal evidence currently available to clarify whether the anaemia is transient, disappearing once the growth spurt is completed and intake and loss can once more be brought into balance, or if the imbalance in Fe persists after the growth spurt. Moreover, the changes in dietary pattern which take place around adolescence (e.g. adoption of a vegetarian diet, increased tea drinking, etc.) may affect Fe availability. The totality of the influences on Fe status at this crucial transition need clarifying, and the relative importance of a number of factors on Fe status need to be elucidated.

Does anaemia in adolescent girls predict anaemia in pregnancy?

Follow-up at first pregnancy of adolescent populations screened for Fe status will help to clarify whether risk to mother and offspring are in part determined in adolescence. If such a relationship were demonstrated, it could be appropriate to address the problem at its inception in adolescence, rather than to wait until the first antenatal clinic appointment.

The title of this Symposium is *Adolescent nutrition: are we doing enough?* Given the importance of the potential consequences of poor Fe status in British adolescent girls, the answer has to be 'No'. Obtaining the answers to the research questions outlined here will require a coherent programme of assessment of diet and nutritional status in a large cross-sectional study of adolescence which includes cognitive function and physical activity testing, and the ability to follow-up subjects for at least 5–10 years. Longer-term follow-up could help to clarify broader questions regarding the role of adolescent nutrition in adult health.

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