LOSSES OF IRON FROM THE BODY AS THE BASIS FOR THE DETERMINATION OF DIETARY IRON REQUIREMENTS

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The amount of a nutrient needed in the diet is determined by the proportion of it which is absorbed, the amounts needed to fulfill normal increments and to replace losses from the body. The present paper considers the last topic in the case of iron.

The amount of iron loss indicates the amount which should be absorbed from the diet if a state of metabolic equilibrium is to be maintained. Hence, losses of iron measured at a particular time in a sample of a population should indicate normal dietary requirements. But, this would only be true if losses were not themselves directly influenced by the level of dietary intake and were reasonably constant from time to time in an individual and between different individuals. Furthermore, estimates of iron losses to be of value must be accurate.

CHANNELS OF IRON LOSS

Milk

The administration of iron to the mother fails to raise the level in milk (Underwood, 1962). There is, however, a marked variation in the amounts of iron which have been estimated in milk. Feuillen and Plumier (1952) found from 27 to 121 µg./100 ml. in pooled samples, with a mean of 58 µg./100 ml.; and Karmarkar and Ramakrishnan (1960) 172 to 210 µg./100 ml. in different samples. Vestermark and Anderson (1966) found a mean for 12 samples of 22.7 µg./100 ml. and 19.7 µg./100 ml. according to the method of analysis used. There was a range of 18.2 to 26.8 µg./100 ml.

The amount of iron in milk may be determined by the amount of milk protein to which it is bound (Blanc, 1964).

These values suggest that during lactation there may be a marked variation in the loss of iron by different women. Variability will be accentuated by variation in the amounts of milk removed. A commonly used figure is 800 ml. a day and at this level iron losses could range from 0.2 to 1.7 mg. a day. Loss of iron through milk might not affect the majority of women in a country because of the widespread use of bottle-feeding, and those who breast-feed their infants often do so for only about three months.

Urine

The amount of iron lost in the urine varies with the individual, and with the level of iron in the diet. On usual diets repeated estimations of the mean amounts of iron in the urine formed over 24 hours by a number of adult subjects has shown a variation from about 63 to 270 µg. (Man and Wadsworth in preparation).

Skin

The loss of iron from the skin is that contained in eccrine and apocrine sweat and desquamated dermal cells. An appreciable number of studies have been made of losses of iron from the body surface with quite variable results. There is general agreement that most of the iron is contained in desquamated cells. A summary of the results of different investigations is given in Table I.

In the most recent study (Coltman and Rowe, 1966) some of the samples of cell-free sweat obtained by iontophoretic stimulation contained amounts of iron which were too small to be accurately determined by the method employed and may, therefore, have been zero. Adams *et al* (1950) also found many samples of cell-free sweat to contain no iron. Because of the small amounts of iron involved there is a possibility that "pure" eccrine sweat does not contain any iron, and that which has been detected may have come from contamination of the skin surface, or may have been released from desquamated cells during the collection and processing of the sweat. In any case the total amount of iron in whole sweat contributed by the cell-free fluid is only about 5 per cent (Adams *et al*, 1950). Therefore the marked differences which can occur under different circumstances in the amount of insensible perspiration is not of much importance in relation to iron loss. The major loss of iron from the body surface will be largely determined by the concentration of iron in epidermal cells, and the rate at which these cells are shed.

Epidermis stripped from 1 g. of whole skin contains from 0.6 to 2.9 µg., with a mean of 1.44 µg. (Moore, 1964). The life-span of skin cells ranges according to the technique employed, the age of the subject and the area of the body. Katzberg (1952) estimated that the life-span of basal epithelial cells varies with age (Table II).

Renewal time for the whole skin thickness varied from 17 days for the arm to 30 days for the thigh. Assuming a middle value of 25 days, one twenty-fifth of the skin would be lost each day. Skin represents about 7 per cent of the body weight (Moore, 1964). Thus the weight of skin on a 50 kg. body would be about 3.5 kg. The amount of skin lost each day would be about 140 g. and this would contain 0.2 mg. of iron in the corresponding epithelial cells. Cameron and Short (1948) state that skin represents 16 per cent of the body weight in which case the estimated iron loss would be about 0.4 mg. However, the rate of epidermal proliferation can be extremely variable and mechanical removal of superficial epidermis can increase mitotic activity over fourfold (Pinkus, 1952). Thus rate of proliferation and life-span probably vary appreciably because of friction by clothing and frequency and vigour of washing the body (Rothman, 1954).

Apocrine gland cells contain iron (Bunting, Wislocki and Dempsey, 1948), but the amount of the element in apocrine sweat is small, although occasionally it is sufficient to produce staining of the underarm part of garments (Hurley and Shelly, 1960). Owing to the restricted distribution of apocrine glands and their intermittent activity they contribute only a minor portion of the total skin loss of iron. Individuals vary in the amount of material which they secrete from these glands. Johnston, McMillan and Evans (1950) found that the iron content of sweat was not influenced by the recent intake of iron salts by mouth.

Appendages

Hair contains about 2.5 mg. of iron per 100 g. (Green and Duffield, 1956), but a wide variation has been found by different investigators (Table III). The amount of hair lost will depend on how much is removed by cutting, the rate of growth, life-span of individual hairs, and the number and kinds of hairs on different parts of the body. All of these can vary considerably between individuals.

With a loss of 20 g. of hair a year (Myers and Hamilton, 1951) and a mean content of 2.5 mg./100 g. the total loss of iron by this route in one year would amount to 0.5 mg. or 0.00014 mg. a day.

Johnston (1958) studied the loss of hair by 12 women and estimated this to be 70.7 g. a year, with a range from 41.4 to 106.0 g. The mean iron content was 1.8 mg. (range 1.28 to 3.28 mg.) per 100 g. The amount of iron in hair removed by cutting can be different from that in hair removed in the process of combing; the respective values in one subject being 2.43 and 1.90 mg./100 g. The mean annual loss of iron in hair was estimated to be 1.22 mg. with a range from 0.73 to 1.78 mg., that is about 0.005 mg. a day.

Jacobs and Jenkins (1960) found that in people over 10 years of age the amount of iron in finger nails was about 200 µg./g. dry weight; very much higher concentrations were present at a younger age the highest being in the newborn. There are variations in the rate of nail growth according to the particular digit, the length of the digit and the season (Le Gros Clark and Buxton, 1938). The weight of nail loss does not seem to have been determined so that an estimate of iron loss from this source is not possible, but must be very small.

Menstruation

There is a discrepancy in the observations of different investigators about the variability in the amount of menstrual loss from time to time in the same individual. Millis (1951) found considerable variation but Hallberg *et al* (1966) and others found remarkable constancy. All agreed, however, that there is marked variation in the loss by different individuals.

Hallberg *et al* (1966) determined that at each menstruation the mean loss of blood was 34 ± 2.4 ml. In 95 per cent of 117 women the amount was less than 86.8 ml. and the median value was 26.2 ml. At a blood haemoglobin level of 13.6 g./100 ml., a menstrual loss of 40 ml. and a menstrual interval of 29 days there would be an average loss of iron equivalent to 0.6 mg. a day. But at least 50 per cent of women lose less than this.

Pregnancy

At delivery there is a loss of iron in the foetus and placenta and from haemorrhage.

McCoy *et al* (1961) found a mean iron content in 50 placentas of 75 mg. with a range from 34 to 175 mg. Widdowson and Spray (1951) found that newborn babies contained

TABLE I

AMOUNT OF IRON IN SWEAT
(Derived from Coltman and Rowe, 1966)

Author	Iron Concentration µg./100 ml.		Source
	Cell-rich Sweat	Cell-free Sweat	
Johnston & Hagan, 1949	—	2 to 6	Whole body
Mitchell & Hamilton, 1949	100 to 200	—	Whole body
Johnston *et al*, 1950	—	27	Whole body
Adams *et al*, 1950	705	29.6	Upper extremity
Foy & Kondi, 1957	30 to 600	10 to 20	—
Hussain *et al*, 1960	161	44	Upper extremity
Moore, 1961	40 to 150	34.6	Forearm
Hussain & Patwardhan, 1959	115	34	Upper extremity
Apte & Vankatachalam, 1962	33 to 62.2	19 to 25	Upper extremity
Prasad *et al*, 1963	120±36	46±11	Upper extremity
Coltman & Rowe, 1966	—	17.2±7.8	Forearm

TABLE II

LIFE-SPAN OF BASAL EPITHELIUM ACCORDING TO AGE
(From Katzberg, 1952)

Age (Years)	Life-span (Days)
0—20	91.2
21—40	43.1
41—60	28.5
61—80	27.5

TABLE III

IRON CONTENT OF HAIR
(From Johnston, 1958)

Authors	Iron mg./100g.	Type of Hair
Bagchi & Ganguly, 1941	14.1	Black
Dutcher & Rothman, 1951	2.71	Black
	2.43	Blonde
	9.78	Red
Goldblum, Derby & Lerner, 1953	0.08 to 1.10	—
Kikkawa, Ogita & Fujito, 1955	2.90	Black
	0.68	Mid-brown
	0.11	Blonde
Johnston, 1958	1.28 to 3.28	—

75 mg. of iron per 1 kg. body weight so that a child of 3.5 kg. would contain about 260 mg.

Recently Mathie and Snodgrass (1967) determined the amount of blood lost at delivery by 524 women. The average amount was 186 ml. with a range of 5 to 1600 ml. Taking these values and a haemoglobin concentration of 12 g./100 ml. the iron loss would vary from about 2 mg. to 640 mg. with a mean value of 75 mg.

A total loss of 335 mg. (260 + 75 mg.) spread over a year would amount to just less than 1 mg. a day. In the United Kingdom the mean number of children for each woman of fertile age is about two. Hence, the extra loss of iron due to pregnancy would on the average affect women for less than 2 years in their total life span. Put in another way each year less than 10 per cent of women of fertile age are pregnant. Therefore if extra iron is needed because of pregnancy the amount to be added to the communal supply would be relatively small.

Gastrointestinal Tract

Iron may leave the body by the intestinal canal in desquamated mucosal cells, bile and other secretions and blood. However, much of the iron from each of these sources is probably available for reabsorption. In any case insufficient information is available about the actual amounts of iron in bile and other secretions to estimate how much leaves the body initially in them. Moreover, the quantities of these secretions vary considerably with eating habits and the individual. The adult probably secretes 800 to 1000 ml. of bile a day, but because very little bile salts are found in the faeces much of this seems to be reabsorbed.

50 to 80 g. of intestinal mucosal cells are lost each day (Leblond and Walker, 1956). In so far as these remain undigested any iron in them would be lost from the body; an estimate based on radioactive studies is about 0.4 mg. a day (Dubach and Moore, 1955).

Small losses of blood into the intestinal canal may often occur (Hughes-Jones, 1958). The amounts are up to about 1 ml. a day so that the quantity of iron lost would be 0.5 mg. These losses of iron, of course, may have been included in the estimates made by Dubach and Moore (1955) quoted above.

OVERALL LOSS OF IRON

Estimates of the total loss of iron from the body have been made by measuring the rate of disappearance of radioactivity after the introduction into the body of radioactive iron. This would be an ideal method if at least two assumptions were true, namely, that the radioactive iron was distributed adequately throughout all the different locations of iron, and that the rate of loss of radioactive iron was consistently parallel with the rate of loss of ordinary iron.

There is evidence that when radioactive iron is introduced parenterally it does not immediately mix with all the iron compartments. Some of it may immediately enter tissue cells including those of the epidermis, (Weintraub *et al*, 1965) kidney, and intestinal mucosa (Saito, 1960). This cellular radioactive iron would then soon be lost by desquamation. Saito *et al* (1960) found that there were elevated levels of radioactivity measured by a whole body counter at cycles of 120 days corresponding to release of radioactive iron from the effete labelled generation of erythrocytes. Changes in the radioactive counts can only be accounted for by changes of location in the radioactive iron thus changing the geometry of the counting system. In studies extending over four years Finch (1959) found evidence that full mixing of Fe^{55} with all non-radioactive iron in the body was not achieved until one year. Assumptions can be made about the size of the "miscibe" pool of iron from which losses from the body occur (Saito *et al*, 1960; Price, 1962) but the true size of this cannot actually be known. Therefore for this and other reasons the reliability of estimating the amount of ordinary iron being lost from the body by extrapolation of the results of radioactive loss remains uncertain.

An average estimate of a loss of 0.6 mg. of iron a day, with an increase in pregnancy to 2 mg. has been made on the results of radioactive studies. However, the rate of loss of radioactivity has varied in different investigations and between different individuals (Table IV).

CONCLUSIONS

The criteria necessary for determining dietary requirements from the amounts of iron lost from the body are not fulfilled. Whilst overall loss of iron is the quantity relevant to the question, nevertheless a knowledge about the separate components of loss is desirable because each may vary independently of the other, and to various degrees in different individuals.

Because only a small proportion of dietary iron is absorbed small variations in iron loss may be appreciable when interpreted in terms

TABLE IV

WHOLE-BODY COUNTER STUDIES OF IRON EXCRETION IN NORMAL CONTROLS

(From Reizenstein and Hoglund, 1966)

Author and Year	Ref.	Number of Subjects Studied	Time Period (Days)	Average Percent Lost Daily
Bonnet *et al*, 1960	(20)	1	1—500	0.14
Reizenstein *et al*, 1961	(166)	2	20—100	0.136±0.0348
Reizenstein & Brann, 1965	(168)	6	10—194	0.193[a]
Price *et al*, 1962	(162)	3	20—100	0.110—0.182
Saito *et al*, 1964	(179)	7	0—300	0.162
Heyssel *et al*, 1964	(84)	?	?	0.05

[a] Normal males, and females in the menopause.

of amounts of iron needed in the diet. Assuming that the total loss of iron from the body is 1 mg. a day and that 10 per cent of dietary iron is absorbed, then the dietary requirement would be 10 mg. A loss of 2 mg. a day would need a dietary level of iron of 20 mg. Differences of dietary iron of this magnitude are of great practical importance. So far there is not enough evidence that corresponding amounts of iron loss from the body from which dietary requirement could be estimated can be determined with sufficient accuracy.

Furthermore, there is evidence that losses at least through some routes can vary in amount according to dietary levels of iron. Therefore, the loss of body iron which itself varies with the dietary level cannot be used as a criterion for determining what that level should be.

Iron in the adult body has been acquired to a considerable extent during growth, and therefore a knowledge of losses of iron during childhood is important. However, there do not seem to have been any studies of total loss of iron except in adults.

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