IRON ABSORPTION IN RHEUMATOID ARTHRITIS

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Patients with rheumatoid arthritis frequently present with a low haemoglobin and a hypochromic peripheral blood picture which suggests a concomitant disturbance of iron metabolism. However, the cause of the anaemia is still uncertain (Pitcher, 1966). Some cases demonstrate true iron deficiency while other anaemic subjects have normal iron stores and the serum total iron-binding capacity is not raised. It has been suggested that iron absorption is defective (Roberts, Hagedorn, Slocumb, and Owen, 1963) and this possibility has been investigated.

Material and Methods

Fifteen patients with definite or classical rheumatoid arthritis (Ropes, Bennett, Cobb, Jacox, and Jessar, 1959) were studied, of whom two were males, ten were post-menopausal females, and three were menstruating females. In six subjects the arthritis had been present for less than 5 years and in nine for from 8 to 45 years. Clinical and haematological data are summarized in Table I.

Control subjects were normal, non-anaemic, symptomless, adult males and females in whom respectively 32 and 10 measurements of iron absorption were made.

Iron absorption was measured in a group of patients with iron deficiency anaemia who did not suffer from arthritis. Six patients whose haematological data most closely matched those of the six rheumatoid subjects who were frankly anaemic were selected from this group. Haematological details of these patients are given in Table II (overleaf).

The mean haemoglobin concentration was 10.1 g./100 ml., which is very similar to the mean of 9.9 mg./100 ml. for the anaemic rheumatoid subjects.

After fasting overnight, each subject was given an oral dose of 1.5 μ Ci ^{59}Fe , in 5 mg. carrier iron in the ferric state made up with water to a total volume of 150 ml. The subject fasted for a further hour after taking the dose.

Whole-body absorption was measured in the prototype or mobile shadow-shield whole-body monitors, utilizing a sodium iodide detector, 11.5 in. diameter by 4 in. and scanning-bed geometry (Boddy, 1967a, b). Each subject was measured in the supine and prone positions. A background measurement was made on each subject before iron administration to permit correction of subsequent counting-rates for the contribution of natural body potassium and caesium-137. Measurements were made after administration of the test dose, the counting-rate representing 100 per cent. retention, and about 20 days later giving the percentage iron absorption (Will and Boddy, 1967).

TABLE I
CLINICAL, HAEMATOLOGICAL, AND ABSORPTION DATA OF PATIENTS WITH RHEUMATOID ARTHRITIS

Case No.	Sex	Age (yrs)	Treatment	Duration of Disease (yrs)	Hb (g./100 ml.)	Packed Cell Volume (per cent.)	Mean Corpuscular Haemoglobin Concentration (per cent.)	Serum Fe (μ g./100 ml.)	Total Iron-binding Capacity (μ g./100 ml.)	Saturation (per cent.)	Film	Per cent. Fe Absorption
1	M	45	A	1	12.0	37	32	55	240	23	N	11.0
2*	F	21	A	1½	12.9	41	32	56	441	13	N	14.2
3	F	55	A	1	12.5	39	32	85	300	28	N	13.0
4	F	49	A	3	14.4	42	34	90	270	33	N	16.2
5*	F	20	A	3	7.4	26	28	40	460	10	HM	25.6
6	F	51	A	4	12.0	36	33	65	270	23	N	3.6
7	F	54	A	8	11.2	37	30	25	285	9	HM	16.5
8	F	53	A	8	10.2	34	30	20	255	8	HM	24.6
9	F	52	B	10	10.3	33	31	33	315	11	HM	12.8
10*	F	37	C	18	12.4	41	30	15	264	6	N	10.6
11	F	65	A	21	10.0	35	29	20	360	3.3	HM	41.8
12	M	67	C	25	10.4	35	30	5	195	3	HM	1.6
13	F	63	A	28	14.4	41	35	77	205	37	N	13.2
14	F	67	A	35	12.5	40	31	78	285	27	N	1.7
15	F	63	C	45	13.6	42	32	40	360	11	N	6.7

*Pre-menopausal.

A Enteric-coated salicylate.

B Paracetamol.

C Salicylate + 0.5 mg. Betnelan daily.

N Normochromic normocytic.

HM Hypochromic microcytic.

TABLE II
HAEMATOLOGICAL AND ABSORPTION DATA OF SIX ANAEMIC SUBJECTS NOT SUFFERING FROM RHEUMATOID ARTHRITIS

Case No.	Hb (g./100 ml.)	Packed Cell Volume (per cent.)	Mean Corpuscular Haemoglobin Concentration (per cent.)	Serum Fe (μ g./100 ml.)	Total Iron-binding Capacity (μ g./100 ml.)	Saturation (per cent.)	Per cent. Fe Absorption
1	10.4	34	30	60	360	16	40.1
2	11.0	38	29	51	296	17	46.0
3	11.5	36	30	50	384	13	60.5
4	11.8	40	29	65	315	22	38.0
5	9.0	32	29	14	459	3	22.1
6	6.6	28	23	10	285	3.5	45.0

Results

The percentage absorption of iron by each patient with rheumatoid arthritis is given in Table I. Absorption ranged from 1.6 to 41.8 per cent. The mean absorption for all patients was 14.2 per cent. (S.E. 2.7). Males and non-menstruating females had a mean absorption of 13.6 per cent. (S.E. 3.3) and menstruating females a mean of 16.8 per cent. (S.E. 4.5). The six patients who presented with haemoglobin levels of less than 12 g./100 ml. and hypochromic microcytic peripheral blood films had a mean absorption of 20.5 per cent. (S.E. 5.6), while the nine remaining patients with haemoglobin of 12 g./100 ml. or higher and normochromic normocytic blood films had a mean of 10.0 per cent. (S.E. 1.7). The mean absorption by patients with arthritis of less than 5 years' duration was 13.9 per cent. (S.E. 3.0) and for those with disease of longer than 5 years' duration 14.4 per cent. (S.E. 4.2).

The anaemic subjects not suffering from rheumatoid arthritis paired haematologically with the anaemic rheumatoid patients, had a mean absorption of 42.0 per cent. (S.E. 5.1). Individual results are given in Table II.

Male control subjects had a mean iron absorption of 9.6 per cent. (S.E. 0.9), female controls a mean of 11.4 per cent. (S.E. 2.2), and all controls a mean absorption of 10.0 per cent. (S.E. 0.9). These findings are summarized in Table III.

TABLE III
ABSORPTION OF 5 mg. ORAL IRON BY NORMAL SUBJECTS

Sex	No. of Measurements	Absorption Range (per cent.)	Mean Absorption (per cent.)	Standard Error (per cent.)
Male	32	1.2-21.5	9.6	± 0.9
Female	10	0.8-23.7	11.4	± 2.2

Comparison of the mean absorption by all patients with rheumatoid arthritis v. all control subjects, males and post-menopausal females v. control males, menstruating females v. control females, and patients with arthritis of less than 5 years' duration v. patients with arthritis of longer than 5 years' duration, showed that the paired means were not significantly different ($P > 0.05$). Rheumatoid patients who were also iron deficient had a greater mean absorption than non-anaemic rheumatoid patients ($P < 0.05$), but a mean absorption less than half that of anaemic subjects not suffering from rheumatoid arthritis ($0.02 > P > 0.01$).

Discussion

Anaemia is commonly associated with rheumatoid arthritis, Nilsson (1948) reported the incidence of anaemia as 63 per cent. for women and 42 per cent. for men, and almost the same incidence was recorded by Alexander and Duthie (1962).

Morphologically, the anaemia has been classified by Jeffrey, Freundlich, Jackson, and Watson (1955) into two main types: a hypochromic and often microcytic anaemia which responds well to parenteral iron therapy and a normochromic anaemia similar to the anaemia of infection which is refractory to all therapy.

A possible cause of anaemia is chronic bleeding from the gastrointestinal tract as a result of prolonged ingestion of salicylates. Investigations by Scott, Porter, Lewis, and Dixon (1961) and Stubbé, Pietersen, and van Heulen (1962) demonstrated that moderate gastrointestinal haemorrhage induced by salicylates was found in from 60 to 70 per cent. of patients with rheumatoid arthritis. Only in isolated cases were these haemorrhages regarded as being conducive to anaemia, and these authors did not consider the use of salicylates to be a cause of hypoferraemia in patients with rheumatoid arthritis.

It has also been suggested that salicylate administration might depress absorption of iron by the chelating action of salicylic acid. Izak, Galewsky-Stein, Menczel, and Groen (1962), however, found no impairment of iron absorption during salicylate administration, and using a similar radioiron technique Davis and Deller (1967) demonstrated that chelation of iron by salicylic acid did not significantly affect absorption.

Several investigations have shown that the anaemia of rheumatoid arthritis often responds inadequately to oral iron therapy (Ross, 1950; Jeffrey, 1953; Sinclair and Duthie, 1949), and a defect in iron absorption has been suggested (Roberts and others, 1963; Raymond, Bowie, and Dugan, 1965; Engstedt and Strandberg, 1966). However, Roy, Alexander, and Duthie (1955), using an iron tolerance test, found no indication of impaired absorption in patients with rheumatoid arthritis, and Jeffrey and others (1955), using a radioiron technique, actually found that iron absorption was increased in arthritis patients compared with normal controls.

The present findings show that absorption of oral iron by patients with rheumatoid arthritis is not significantly different from that by normal controls. Rheumatoid patients presenting with a hypochromic peripheral blood picture had a mean absorption twice that of the rheumatoid patients

whose peripheral blood was normochromic. However, patients with iron deficiency anaemia who did not suffer from rheumatoid arthritis had a mean absorption significantly higher by a factor of 2 than rheumatoid patients with hypochromic anaemia of comparable severity. This suggests that the compensatory alimentary iron absorption mechanism still functions in anaemic rheumatoid patients but does so less efficiently than when iron deficiency anaemia is not associated with rheumatoid arthritis. So, in rheumatoid arthritis, if true iron deficiency is caused, say, by blood losses, compensatory iron absorption will be less effective.

It is interesting that the duration of the rheumatoid disease did not have a significant effect on the mean oral iron absorption.

Summary

Absorption of oral iron by patients with rheumatoid arthritis and by control subjects was measured by whole-body monitoring, and no significant difference was found. The mean absorption of hypochromic rheumatoid patients was twice that of normochromic patients. Non-rheumatoid patients with iron deficiency anaemia had a significantly higher mean absorption, by a factor of 2, than rheumatoid patients with hypochromic anaemia of comparable severity. The potential significance of these findings is discussed.

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L'absorption du fer dans la polyarthrite rhumatoïde

RÉSUMÉ

L'absorption du fer donné par voie buccale aux malades atteints de polyarthrite rhumatoïde et aux sujets témoins a été évaluée au moyen des traceurs radioactifs et aucune différence marquée n'a été trouvée.

La moyenne de l'absorption des malades rhumatoïdes hypochromiques était deux fois plus que celle des malades normochromiques. Les malades non-rhumatoïdes ayant une anémie causée par un manque de fer avaient une moyenne d'absorption beaucoup plus marquée, étant deux fois plus que celle des malades rhumatoïdes ayant une anémie hypochromique de sévérité comparable. La portée de ces observations est discutée.

Absorción de hierro en la poliartritis reumatoide

SUMARIO

La absorción de hierro administrado por vía oral, por pacientes con poliartritis reumatoide y por testigos fue medida por una técnica de observación minuciosa de isótopos radiactivos en todo el cuerpo, y no se encontró, ninguna diferencia significativa.

La absorción media por pacientes reumatoides hipocrómicos fue dos veces mayor que la de pacientes normocrómicos. Los pacientes no reumatoides con anemia de deficiencia de hierro revelaron una absorción media más elevada, por un factor de 2, que la de pacientes reumatoides con anemia hipocrómica de severidad comparable. Se discute el significado potencial de estos descubrimientos.