TISSUE IRON AND THE RETICULO-ENDOTHELIAL SYSTEM IN RHEUMATOID ARTHRITIS

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The cause of the normocytic hypochromic anaemia characteristic of rheumatoid arthritis remains unknown. Iron is absorbed normally from the gut (Roy, Alexander, and Duthie, 1955), but in an investigation of the iron content of the bone marrow (Richmond, Gardner, Roy, and Duthie, 1956) it was shown that stainable marrow iron was absent in nineteen of 61 cases and that there was no correlation between the presence or absence of iron in the marrow and the degree of anaemia.

It appeared likely that an unknown factor was interfering with the utilization of iron for the synthesis of haemoglobin. An increased tissue avidity for iron comparable to that postulated by Cartwright and Wintrobe (1952) as a cause of the anaemia of infection seemed a possible explanation. Earlier studies (Roy and others, 1955) had shown that saccharated oxide of iron injected intravenously was rapidly removed from the plasma of patients with rheumatoid arthritis. This observation supported the suggestion of the existence of a state of overactivity or of hyperplasia of the reticulo-endothelial system (Freireich, Ross, Bayles, Emerson, and Finch, 1957). Some evidence for such a hyperplasia was available from morphological studies (Sinclair and Cruickshank, 1956). Overactivity of the reticulo-endothelial system appeared to be a possible explanation for the paradox that iron found histologically in the bone marrow was not utilized in the synthesis of haemoglobin (Richmond and others, 1956).

On the basis of this hypothesis, it was postulated that in rheumatoid arthritis the organs comprising the reticulo-endothelial system might contain more iron than those of comparable subjects not suffering from this disease. The present investigation was planned to examine the validity of this hypothesis.

The analysis was conducted in parallel by histological and biochemical methods. The bone marrow although part of the reticulo-endothelial system was not examined since it had been studied previously (Richmond and others, 1956).

Material

Samples of tissue from liver, spleen, lymph node, suprarenal, and lung were obtained from 34 patients with rheumatoid arthritis who died in hospital and from 43 patients not suffering from this disease.

Cases of Rheumatoid Arthritis (Tables I and II, opposite site).—In fifteen cases there was evidence that the patient had not been given medicinal iron in any form. The organs of the reticulo-endothelial system of each were examined histologically, but in only seven were chemical analyses made. In the remaining eight cases, the available tissues were embedded in paraffin and extraction was found to interfere with the subsequent chemical estimation of iron.

Material was available from nineteen further patients to whom iron had been given by mouth, by intravenous or by intramuscular injection, or in the form of whole blood by transfusion. The tissues of eighteen were examined histologically and of seventeen chemically.

Cases without Rheumatoid Arthritis (Tables I and II).—Material was obtained from 43 patients. Chemical analyses were made on organs from each case, but in only 25 cases were all the organs examined histologically. This control material was divided into groups for comparison with the cases of rheumatoid arthritis.

Methods

Histological.—Tissue collected at necropsy was placed in clean glass containers with precautions to exclude contamination by environmental iron. Paraffin sections from this material were cut at 5–7 μ . and stained for iron by a modification of the Prussian blue reaction (Richmond and others, 1956; Gardner, 1958). The

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TABLE I
TESTS CARRIED OUT IN CASES OF RHEUMATOID ARTHRITIS AND CONTROLS

Source of Material										Analysis	
										Histological	Chemical
34 Cases of Rheumatoid Arthritis	Total No. of Cases									33	24
	Males			Total						10	9
				Treated with Iron						5	6
				NOT treated with Iron						5	3
	Females			Total						23	15
				Treated with Iron						13	11
NOT treated with Iron						10	4				
Mean Age (yrs)									58	60	
									Range (yrs)		
43 Control Cases	Total No. of Cases									25	43
	Group 1 (10) Sudden Death in Young Persons						Male Female		4	7	
									3	3	
	Group 2 (16) Rapid Death in Older Persons						Male Female		4	8	
									5	8	
	Group 3 (9) Comparable to Rheumatoid Arthritis Patients						Male Female		1	6	
									1	3	
	Group 4 (8) Excess Storage Iron						Male Female		3	3	
4									5		

TABLE II
CAUSES OF DEATH IN CASES OF RHEUMATOID ARTHRITIS AND CONTROLS

Group	Causes of Death	Total Cases
Rheumatoid Arthritis	Not Given Iron or Blood Transfusion Carcinoma of colon, 3; chronic bronchitis, 2; primary carcinoma of liver, carcinoma of bronchus, leukaemia, meningitis, pneumonia, congestive cardiac failure, epilepsy, cervical dislocation, vena caval thrombosis, and anaesthesia, one each	15
	Given Iron or Blood Transfusion Bronchopneumonia or purulent bronchitis, 3; amyloidosis, 3; carcinoma bronchus, carcinoma oesophagus, cor pulmonale, septicaemia, pyelonephritis, systemic candidiasis, hypertension, cardiac failure, cerebral infarction, aplastic anaemia, megaloblastic anaemia, gastric haemorrhage and steatorrhoea, and perforated stomal ulcer, one each	19
Controls	Group 1 Trauma, 6; anaesthesia, CO ₂ poisoning, methanol poisoning, and subarachnoid haemorrhage, one each	10
	Group 2 Myocardial infarction, 5; cerebrovascular accident, 4; pulmonary embolism, 3; cor pulmonale, 2; malignant hypertension, and fractured femur, one each	16
	Group 3 Bronchopneumonia, 3; cerebral haemorrhage, intestinal obstruction, chronic cholecystitis, chronic duodenal ulcer, perforated peptic ulcer, and myocardial ischaemia, one each	9
	Group 4 Haemosiderosis, 5; polycythaemia, 2; injected intravenously with 1 g. iron immediately before death from cerebral vascular disease, 1	8

amount of iron in representative microscopic fields was assessed visually and graded by a simple notation ranging from nil (no iron seen) to 5 (large amount of iron seen).

Sections were also stained with haematoxylin and eosin, and in a number of instances frozen sections were examined by the Weil-Davenport silver impregnation technique described by Marshall (1956). With this material the morphological state of the reticulo-endothelial system was assessed. In the liver, the distribution

of iron between hepatic and Kupffer cells was noted. Prominence of Kupffer cells and excessive numbers of mononuclear cells in the portal tracts were recorded. In the spleen and lymph nodes, lymphoid follicular hyperplasia, reticulum cell hyperplasia, erythrophagocytosis, and excess of plasma cells were tabulated. In the lung, lymphoid hyperplasia and excessive numbers of mononuclear cells were noted, and in the suprarenal the state of the phagocytic sinus cells was studied.

Chemical.—Material was collected at necropsy in clean jars and stored at -10° C. The method used for the chemical estimation of iron was essentially that of Ramsay and Campbell (1954). In a few instances fresh frozen tissue was not available and tissue which had been preserved in formalin for periods of up to 2 months was used (Kerr, 1957). Interference from haemoglobin was of significance only in tissues in which the concentration was very low. The method was shown to give a reasonable estimate of the non-haem iron concentration in all tissues with the exception of lung which was difficult to homogenize. Further difficulty was encountered where the lungs were those of city dwellers, on account of the presence of extraneous material of atmospheric origin.

Results

Morphological

I. IRON CONTENT (Table III)

Rheumatoid Arthritis.—In patients not given iron therapeutically, the livers contained more iron than in control groups 1, 2, and 3, but less than in group 4. The spleens also had a slightly higher mean iron content, but the amount of iron seen in lymph nodes, lungs, or suprarenals was so slight that differences between the groups were not defined.

Iron was distributed in the reticulo-endothelial system of cases of untreated rheumatoid arthritis in the same manner as in the comparable control groups 2 and 3. Thus, in the spleen, iron was present as haemosiderin granules within the splenic pulp or sinusoids, or within macrophages lining the sinusoids. In twelve cases more was present within

hepatic cells than within Kupffer cells.

The amount of iron found in the cases of rheumatoid arthritis treated with iron was greater than in those not so treated, in each of the organs examined. In five cases the Kupffer cells contained more iron than the hepatic cells. In patients who had been given iron by injection, iron was found in the phagocytic sinus cells and histiocytes of the lymph nodes. The iron content of the lung and suprarenal also conformed to this pattern, iron being present only in the phagocytic cells.

Control Groups.—The amount of iron found histologically varied considerably between the four groups. Iron was absent from the livers of cases in group 1, but was present in many of the livers of cases in groups 2 and 3, being seen as small granules scattered diffusely in the hepatic cells. Iron was present in the spleen in every case but tended to be present in greater amounts in the spleens of cases in groups 2 and 3 than in those of cases in group 1. It was most exceptional to find stainable iron in the lymph nodes, lungs, or suprarenals unless, as in group 4, there was some incidental clinical explanation for the local accumulation of iron-containing pigment.

II. HISTOLOGY (Table IV, opposite)

The state of the cells in the five principal organs of the reticular system (Marshall, 1956) is recorded in Table IV. There was evidence of frequent portal round cell infiltration, of splenic and lymph-nodular follicular hyperplasia, and of an excessive number

TABLE III
TISSUE IRON CONTENT ASSESSED HISTOLOGICALLY AND CHEMICALLY
Histological Results: Arithmetic mean of arbitrary units
Chemical Results: mg. Fe/100 g. wet weight of tissue

Group			No. of Cases	Tissue				
				Liver	Spleen	Lymph Node	Lung	Suprarenal
Control	1	Total	10					
		Histological	7	0	0.55	0	0	0
		Chemical	10	11.1	11.5	1.5	2.5	3.3
	2	Total	16					
		Histological	10	0.25	0.56	0.4	0.2	0
		Chemical	16	16.9	22.2	2.9	5.5	3.5
	3	Total	9					
		Histological	2	0.1	0.8	0	0.1	0
Rheumatoid Arthritis		Chemical	9	17.2	32.1	3.3	5.4	3.5
	4	Total	8					
		Histological	6	2.3	3.0	2.0	0.5	0.5
		Chemical	8	238.1	97.6	67.4	6.2	4.2
	No Iron	Histological	15	0.5	1.0	0.4	0.2	0.2
		Chemical	7	20.0	21.8	4.7	3.6	3.3
	Iron	Histological	18	1.6	2.6	1.1	1.0	0.6
		Chemical	17	70.0	127.8	21.3	8.3	11.7

TABLE IV
HISTOLOGICAL EXAMINATION OF ORGANS OF RETICULO-ENDOTHELIAL SYSTEM
IN CASES OF RHEUMATOID ARTHRITIS

Organ	No. Examined	Characteristic Recorded	Number in Which Found
Liver	34	Unusual prominence of Kupffer cells Excessive round cell foci Excess reticulum cells Abnormal number of round cells in portal tracts	1 6 4 18
Lymph Node	20	Follicular hyperplasia Sinus cell hyperplasia Excess reticulum cells Excess plasma cells	7 9 5 10
Spleen	34	Lymphoid follicular hyperplasia Erythrophagocytosis Excess reticulum cells Excess sinus cells Excess plasma cells	5 0 3 7
Lungs	34	Lymphoid hyperplasia Excess reticulum cells	7 1
Suprarenal	25	Sinus cell hyperplasia	0

of splenic and lymph-nodular plasma cells. However, it was difficult to define quantitatively any histological feature which indicated hyperplasia or hyperactivity of reticulo-endothelial cells. It was equally clear that the obvious possibility that there had been a hyperplasia of reticulo-endothelial cells without an alteration in their concentration could not be excluded.

Chemical (Tables V, VI)

Rheumatoid Arthritis.—The mean iron concentration in the tissues from seven patients with rheumatoid arthritis to whom iron had not been given therapeutically did not differ significantly from those for the entire control series. The number of tissue analyses was too small to allow of any attempt at correlation between iron concen-

tration and age and sex, but a tendency for values to increase with age, and to a higher level in males, was apparent.

Comparison with control groups 2 and 3 revealed an increase of iron concentration in the lymph nodes in rheumatoid arthritis. The iron content of the spleen was also significantly greater than that of the spleen in control group 1, but was not different from that of either group 2 or 3. The values for liver, lungs, and suprarenals from the rheumatoid cases did not differ from any control group.

Material was also available from seventeen patients with rheumatoid arthritis to whom iron had been given therapeutically. The results of the analyses of these tissues are compared with those of the untreated cases in Table VI (overleaf). Increased deposits of iron were found in all tissues examined, the increase being greatest in liver, spleen, and

TABLE V
MEAN TISSUE IRON CONTENT IN MATERIAL FROM PATIENTS WITH RHEUMATOID ARTHRITIS
AND FROM CONTROLS

Tissue	Mean Values for Tissue Iron in Seven Patients with Rheumatoid Arthritis NOT Treated with Iron		Mean Concentration of Tissue Iron in Control Groups 1 to 3	
	mg. Fe/100 g. Wet Weight Tissue $\pm$ S.D.	No. of Observations	mg. Fe/100 g. Wet Weight Tissue $\pm$ S.D.	No. of Observations
Liver	20.0 $\pm$ 11.2	7	15.2 $\pm$ 6.0	35
Spleen	21.8 $\pm$ 10.3	7	21.7 $\pm$ 7.9	35
Kidney	3.3 $\pm$ 1.5	7	4.1 $\pm$ 0.9	33
Suprarenal	3.3 $\pm$ 0.6	7	3.6 $\pm$ 0.8	29
Lymph Node	4.7 $\pm$ 3.1	7	2.6 $\pm$ 0.8	19
Cardiac Muscle	1.8 $\pm$ 1.5	4	2.9 $\pm$ 2.5	16
Skeletal Muscle	1.0 $\pm$ 0.4	3	2.1 $\pm$ 1.2	14
Brain	3.4 $\pm$ 1.8	5	1.7 $\pm$ 0.7	6
Pancreas	1.5 $\pm$ 0.7	5	1.5 $\pm$ 0.7	15
Thyroid	0.9 $\pm$ 0.3	5	1.0 $\pm$ 0.2	10
Lung	3.6 $\pm$ 1.2	4	4.8 $\pm$ 2.7	19
Pituitary	2.1	1	1.7	1
Ovary	0.6	1	1.1	1
Testes	5.0	2	—	—
Salivary Gland	1.2 $\pm$ 0.4	3	—	—

TABLE VI

MEAN VALUES FOR TISSUE IRON
Expressed as mg. Fe/100 g. wet weight of tissue: $\pm$ S.D.; N = Number of Observations

Group			Sex	Age (yrs)	Tissue Iron									
					Liver		Spleen		Lymph Node		Lung		Suprarenal	
					mg./100 g.	N	mg./100 g.	N	mg./100 g.	N	mg./100 g.	N	mg./100 g.	N
Rheumatoid Arthritis	Not Given Fe	Total	60	20.0±11.2	7	21.8±10.3	7	4.7±3.1	7	3.6±1.2	4	3.3±0.6	7	
		Female	63	15.5	4	17.1	4	3.9	4	2.7	2	3.3	4	
	Male	54	26.0	3	28.1	3	5.8	3	4.5	3	3.3	3		
	Given Fe or Transfusion	Total	60	70.0 —	17	127.8 —	16	21.3 —	16	8.3 —	7	11.7 —	13	
		Female	61	84.7	11	126.9	10	26.5	10	8.4	5	11.8	8	
	Male	60	73.1	6	130.9	6	12.7	6	8.3	2	11.6	5		
Controls grouped according to Diagnosis	1	Total	34	11.1± 6.0	10	11.5± 6.8	10	1.7±0.8	6	2.3±0.8	4	3.8±1.7	10	
		Female	43	8.6	3	9.1	3	1.9	3	1.9	1	4.9	3	
	Male	30	12.1	7	12.3	7	1.5	3	2.5	3	3.3	7		
	2	Total	66	16.9± 6.7	16	22.2±11.8	16	2.9±1.2	10	5.5±2.3	8	3.5±1.1	12	
		Female	66	15.5	8	20.8	8	2.7	5	6.1	4	3.2	6	
	Male	66	18.3	8	23.7	8	3.1	5	5.2	4	3.9	6		
	3	Total	66	17.2± 6.5	9	32.1± 8.5	9	3.3±0.4	3	5.4±2.6	7	3.5±0.9	7	
		Female	70	14.9	2	29.7	2	2.9	1	4.3	1	3.9	2	
	Male	64	17.9	7	32.7	7	3.6	2	5.6	5	3.4	5		
	4	Total	53	238.1 —	8	97.6 —	8	67.4 —	6	6.2 —	3	4.2 —	4	
	1-3	Total	51	15.2± 6.0	35	21.7± 7.9	35	2.6±0.8	19	4.8±2.7	19	3.6±0.8	29	

lymph nodes. Division of this group into those receiving iron orally, intravenously, or intramuscularly, and those receiving blood by transfusion revealed a difference in distribution of the additional iron. Whereas in both groups the hepatic iron content was increased by a factor of 3.5, the splenic iron content was increased by a factor of 5 in the former group and of 10 in the latter. In lymphatic tissues the opposite was found, the greatest increase being in the tissues from the patients to whom iron had been given orally, intravenously, or intramuscularly.

The mean weights of the liver and spleen from thirty fatal cases of rheumatoid arthritis were contrasted with those from thirty control cases of comparable age and sex (Table VII).

TABLE VII
COMPARISON BETWEEN MEAN WEIGHTS OF LIVER AND SPLEEN IN THIRTY CASES OF RHEUMATOID ARTHRITIS AND IN THIRTY CONTROL PATIENTS OF COMPARABLE AGE AND SEX DYING FROM SIMILAR CAUSES

Series	Weight (g.)	
	Spleen	Liver
Rheumatoid Arthritis Patients	224	1,490
Control Cases	120	1,435
Difference between Means	104	55
Standard Error of Difference	26.1	86

The results showed that the mean weights of the liver in the two groups did not differ significantly but that the mean weight of the spleen in the cases of rheumatoid arthritis was significantly greater than that in the control group.

On the basis of this analysis, and in view of the results of the chemical estimations, it is suggested tentatively that the spleen in rheumatoid arthritis may contain appreciably more iron than is normal in healthy individuals of the same age.

Control Groups.—Iron was found in high concentration in the liver and spleen, only small amounts being present in other tissues. Analyses of the results suggested that the concentration of iron in the tissues increased with advancing age, the correlations reaching greater significance in the case of the spleen than in that of the liver (spleen: $p = 0.001$, liver: $p = 0.02$). There was also a tendency for more iron to be stored by males than by females. The mean iron content of liver and spleen in the male group were 16.4 and 22.9 mg./100 g., and in the female group 13.7 and 19.2 mg./100 g. respectively. This difference was emphasized by the fact that the male group was younger (mean age 52 years) than the female group (mean age 62 years).

The cases in groups 2 and 3 were originally chosen for comparison with the cases of rheumatoid

arthritis. Analyses of the results in the individual groups revealed that the mean tissue iron concentrations increased from group 1, to group 2, to group 3. These differences reached the level of significance for liver of $p = 0.02$, and for spleen of $p = 0.001$ when groups 1 and 3 were compared. If, however, the mean ages of these two groups (34 and 66 years respectively) were taken into account, the apparently increased storage of iron with increasingly severe disease could be explained simply on the basis of advancing age.

As might be anticipated from previous reports of the iron content of tissues in iron storage diseases, the mean values obtained in group 4 were greatly increased by contrast with the other groups, irrespective of age.

Discussion

The storage of iron in body tissues in some human diseases has been sporadically investigated (Sheldon, 1935; Cappell, Hutchison, and Jowett, 1957). In health, the liver and the spleen are known to be the principal sites of iron storage and it is believed that 95 to 97 per cent. of such iron is available for haemoglobin synthesis (Finch, Hegsted, Kinney, Thomas, Rath, Haskins, Finch, and Fluharty, 1950). It seems reasonable to suppose that the liver and spleen in rheumatoid arthritis may contain a greater amount of iron than normal, since it is known that in this disease the red cells are hypochromic while the capacity to absorb iron from the small intestine is not impaired (Roy and others, 1955).

In the present investigation a comparison was made between the concentration of iron in the organs of the reticulo-endothelial system from cases of rheumatoid arthritis and that in those from cases selected to provide suitable control material. The spectrum of control cases was chosen to include young, healthy individuals, older persons dying unexpectedly, and persons of the same mean age as the group with rheumatoid arthritis dying from similar causes. As a result of this division it became clear that allowance must be made for the influence of age and sex on tissue iron concentration. It was shown that the concentration of iron in the liver and spleen of persons with rheumatoid arthritis was not significantly higher than that in controls of similar mean age dying from analogous causes. The iron concentration in lymph nodes, suprarenals, and lungs from cases of rheumatoid arthritis was also not significantly raised.

There is therefore no evidence to support the suggestion that the main iron storage organs in rheumatoid arthritis contain a greater concentration of iron than is usually the case. At the same time,

histological examination of those tissues containing elements of the reticulo-endothelial system has provided no easily measurable evidence of reticulo-endothelial hyperplasia or of reticulo-endothelial overactivity. However, there is an impression of hyperplasia of germinal follicles of the lymph nodes in many parts of the body and of the spleen. It is impossible to estimate the volume of lymphoid tissue in lymph nodes and throughout the viscera. Whether it is present in excess in rheumatoid arthritis is therefore not known, but measurement of weight has indicated that the spleen in rheumatoid arthritis is significantly larger than in control persons of the same age and sex. This suggests that the large spleen may contain a greater absolute amount of iron than usual and that the spleen may act as a reservoir for the iron absorbed, but not used in haemoglobin synthesis.

This interpretation must be viewed with some reserve. With the exception of the spleen, there is no suggestion of excessive storage of iron in rheumatoid arthritis. Low serum iron and the absence of stainable iron from the bone marrow may be explained by faulty absorption from the gut or excessive excretion of iron by the kidneys. The evidence at present available lends no support to these theories (Roy and others, 1955). It appears possible that further studies with labelled iron compounds may throw additional light on this problem. The present results may be regarded as providing an impetus to the extension of such observations.

Summary

Samples of liver, spleen, lymph node, lung, and suprarenal were collected at necropsy from 34 patients with rheumatoid arthritis who died in hospital. Similar samples were obtained from 43 control cases who died from other causes. The control cases were chosen in such a way that the influence of age and of sex on the tissue iron concentration could be assessed. The organs were examined histologically for iron by the Prussian blue reaction. Comparable tissue samples were analysed chemically for non-haem iron.

The concentration of iron in the liver, spleen, lungs, lymph nodes, and suprarenals in cases of rheumatoid arthritis not known to have received treatment with iron therapeutically or blood by transfusion was compared with that in the same organs of control cases. No difference in tissue iron concentration was found which could not be explained by invoking the demonstrated increase of storage iron with age, particularly in the male.

Histological examination of the organs of the reticulo-endothelial system revealed no satisfactory

evidence for the nature of the hyperplasia or over-activity of this system which has been suggested as a likely explanation for the abnormal rapidity with which injected saccharated oxide of iron is removed from the plasma in patients with rheumatoid arthritis. Evidence of lymphoid hyperplasia was provided by the demonstration of significant splenic enlargement.

On the basis of this splenic enlargement it is tentatively suggested that the spleen may contain approximately twice as much iron in this disease as is normally the case. Proof of this suggestion must await chemical analyses of total splenic iron in further cases of rheumatoid arthritis.

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Fer tissulaire et système réticulo-endothélial dans l'arthrite rhumatoïdale

RÉSUMÉ

On étudia les prélèvements de foie, rate, ganglions lymphatiques, poumon et surrénale, effectués à l'autopsie de 34 malades atteints d'arthrite rhumatoïdale décédés à l'hôpital. Des prélèvements similaires furent obtenus chez 43 témoins morts de diverses autres causes. Les témoins furent choisis de manière à permettre une étude comparée de l'influence de l'âge et du sexe sur le

taux ferrique tissulaire. Histologiquement, le fer fut recherché dans les organes à l'aide du bleu de Prusse. Des échantillons comparables furent examinés chimiquement pour déterminer le fer non-hématique.

Le taux de fer dans le foie, la rate, les poumons, les ganglions lymphatiques et dans les surrénales des cas d'arthrite rhumatoïdale, n'ayant pas reçu, autant qu'on sache, de thérapie martiale ou de transfusion sanguine, fut comparé à celui dans les mêmes organes des témoins. On ne trouva dans les taux de fer tissulaire que des différences attribuables à l'emmagasinement augmenté de ce métal avec l'âge, surtout chez les hommes.

Les examens histologiques des organes du système réticulo-endothélial ne révélèrent rien qui puisse expliquer d'une manière satisfaisante la nature de l'hyperplasie ou de l'activité exagérée de ce système, invoquées comme causes possibles de la vitesse anormale avec laquelle l'oxyde saccharé de fer, injecté aux malades atteints d'arthrite rhumatoïdale, est éliminé de leur plasma. L'hyperplasie lymphoïde fut prouvée par le fait que la rate était appréciablement augmentée de volume.

Cette augmentation du volume splénique nous fait penser que dans cette maladie la rate peu bien contenir deux fois plus de fer qu'une rate normale. Pour prouver cette hypothèse on devra attendre les résultats de l'analyse chimique du fer splénique total dans d'autres cas d'arthrite rhumatoïdale.

Hierro tisular y el sistema reticulo-endotelial en la artritis reumatoide

SUMARIO

Se recogieron muestras de hígado, bazo, ganglios linfáticos, pulmón y suprarrenales en necropsias de 34 enfermos con artritis reumatoide fallecidos en hospital. Muestras similares se obtuvieron en 43 testigos que fallecieron de otras diversas causas. Los testigos fueron elegidos de tal forma que la influencia de la edad y el sexo en la concentración de hierro tisular pudiera ser estudiada comparativamente. El hierro de los órganos se investigó histológicamente con la reacción del azul de Prusia. Muestras comparables se examinaron químicamente para determinar el hierro no hemático.

La concentración de hierro en hígado, bazo, pulmones, ganglios linfáticos y suprarrenales en casos de artritis reumatoide, en los que se conocía no haber recibido terapéutica férrica, directa o por transfusión sanguínea, se comparó con la hallada en los mismos órganos de los testigos. No se encontró ninguna diferencia en la concentración tisular de hierro que no fuese explicable por el demostrado incremento de almacenaje de hierro con la edad, especialmente en el varón.

Exámenes histológicos de órganos del sistema reticulo-endotelial no produjeron datos para explicar satisfactoriamente la naturaleza de la hiperplasia o hiperactividad de dicho sistema, aducida como causa posible de la abnormal rapidez con que es eliminado del plasma el óxido sacarado de hierro inyectado en enfermos con artritis reumatoide. Prueba de la existencia de hiperplasia linfocítica fue encontrada en el significativo aumento del volumen del bazo.

Dicho aumento del volumen esplénico induce a pensar que el bazo puede contener, en casos de esta enfermedad, doble de la cantidad de hierro presente normalmente. Prueba de tal hipótesis debe esperar el análisis químico de la cantidad total de hierro esplénico en otros casos de artritis reumatoide.