LABORATORY FINDINGS IN FIBROSITIS

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IN this review of the biochemical characteristics found in fibrositic conditions the scope will include fibrositis due to trauma and occupation, "gouty fibrositis", the periarticular type in which the manifestations are in the periarticular tissues without involvement of the joints themselves, and some cases of sciatica in which the nerve symptoms are secondary to fibrositis.

Most of the data are obtained from routine examinations made in the hospital laboratories during the last five years, but the numbers of the various types bear no relation to the incidence of the types admitted for treatment; further, as the hospital serves a large industrial community, the cases of occupational or industrial fibrositis naturally preponderate.

In general the laboratory findings in the type of disease under consideration show no deviations from the normal, but these negative findings are by no means without value, since they serve to exclude those diseases which give abnormal results.

One of the most useful laboratory tests in all rheumatic diseases is the determination of the suspension stability of the erythrocytes (sedimentation rate), and especially so if it is combined with the determination of the cell volume as suggested by Collins *et al.*¹ This method not only gives the suspension stability (S.S.), but also detects an excess or deficiency of red cell volume, which is correlated with the amount of hæmoglobin present, and any marked deviations from the normal in the number of leucocytes present. The colour of the plasma also yields useful information, an excess being often due to an excess of bilirubin, while a deficiency is usually associated with a lack of carotinoid bodies, one of which is provitamin A.

During the past five years the S.S. has been determined on some 620 cases of fibrositis of all types, and the results are shown in Figs. 1 and 2, which relate to the males and females respectively. This division was made because the normal values for the two sexes are different owing to the lower average red cell counts in

females, which is reflected in a lower cell volume and reduces the S.S. by approximately 5 per cent.

In Fig. 1 it will be seen that, although a very large proportion

FIG. 1.

show but little or no deviation from the normal, there is an appreciable number in which the stabilities are so lowered as to resemble those found in rheumatoid arthritis. In Fig. 2 the cases with a

FIG. 2.

low stability are greater in number and seem to form a definite group, although it must not be overlooked that the separation into two groups is somewhat accentuated by the relatively smaller incidence of the industrial type found in females.

In both sexes the spread of the normal groups is undoubtedly extended by the cell volume factor, and if the readings had been corrected to a standard cell volume these variations from the normal would have been very materially reduced and the sex effect would probably disappear.

An analysis of these cases demonstrated that whilst several factors were apparently involved in the production of the low stability, its association with the periarticular type of fibrositis was well defined, and the following table shows that it was low—in an appreciable number very low—in over 80 per cent. of the cases. Many of these results are appreciably more abnormal than any reported by Slocumb,² but the tendency towards lower stabilities with increase of the duration of the symptoms is also quite definite in this series.

<i>Suspension Stability.</i>	<i>Periarticular Fibrositis.</i>			<i>Gouty Fibrositis.</i>		
	<i>Males.</i>	<i>Females.</i>	<i>Total.</i>	<i>Males.</i>	<i>Females.</i>	<i>Total.</i>
41-50 ..	2	1	3	1	1	2
51-60 ..	6	7	13	2	3	5
61-70 ..	5	5	10	3	1	4
71-80 ..	4	4	8	4	2	6
81-90 ..	3	4	7	5	1	6
91-100 ..	0	1	1	5	1	6
	20	22	42	20	9	29

In “gouty fibrositis”, for which the results are shown in the same table, a few low stabilities are found but, as in the articular type, the results are very variable. A further contrasting feature between these two types lies in their response to treatment, the periarticular one being much less responsive than the gouty.

In seventeen patients diagnosed as sciatica secondary to fibrositis the S.S. was normal, or practically so, in all cases. In none was there any muscle wasting which was noted previously³ and is often associated with a marked reduction of the S.S.

The results with the fibrositis group as a whole are very similar to those reported in 1929,³ but it is now recognised that the lower results generally found in females as compared with males are due largely to the lower red cell volumes natural to the female sex. This physiological difference between the sexes is generally accepted, and according to the data of Williamson,⁴ who examined 919 samples by spectrophotometric methods, the variation commences before the first decade of life, reaches a maximum in early adult life, and continues to the end of the seventh decade.

It has been suggested that this physiological difference between the sexes is not confined to the red cells, and that similar variations are to be found in the plasma constituents.⁵

URIC ACID.—The existence of "gouty fibrositis" as a distinct syndrome is still controversial among those interested in rheumatic and allied diseases, and whilst it is commonly recognised in this country, an attitude of extreme scepticism prevails in North America, where one prominent rheumatologist has expressed the view that he is unable to accept the "gouty" qualification until one single case can be produced showing a uratic tophus. A tophus is essentially a uratic deposit in the superficial tissues, and consequently a visible one, but there is no obvious reason they should not occur in the deeper tissues. The use of unfornolised sections from nodules in cases of "gouty fibrositis" may possibly lead to a solution of the problem. It is a matter for discussion whether the gross evidence of tophi is a more reliable index of gout than a high level of uric acid in the blood associated with clinical characteristics of the disease.

The uric acid content of whole blood from cases of "gouty fibrositis" and from a number of non-gouty fibrositic ones is given in the following table:

	<i>Males.</i>		<i>Females.</i>	
	<i>No.</i>	<i>Average Uric Acid (Mg. per Cent.).</i>	<i>No.</i>	<i>Average Uric Acid (Mg. per Cent.).</i>
Gouty fibrositis ..	43	4.79	16	4.35
Non-gouty fibrositis ..	35	3.54	24	3.27

In a review of the laboratory findings in this hospital for the period 1923-1927⁵ a much higher average was reported for both male and female cases of fibrositis, but the difference is largely due to changes in the method employed for the estimation of uric acid. The earliest quantitative method included the "combined uric acid" of French workers, a substance later proved to be thioneine and found almost exclusively in the red cells. In 1930⁶ Folin developed a uric acid reagent of much greater specificity, and the results given in this contribution were obtained with this reagent. Many workers on the Continent and in North America have eliminated the error due to thioneine by employing blood plasma, but it should be remembered that the red cells contain comparatively little uric acid, so that the plasma figures are much greater than those for whole blood.

The uric acid results given in the table show a significant

difference between the "gouty fibrositis" and non-gouty groups, and whilst an abnormal uric acid content is certainly not a specific indication of gout, it does suggest that the fibrositis may have a gouty basis.

VITAMINS.—In the predecessor of this journal⁷ the writer reviewed the relationship of vitamins to rheumatic diseases and included a number of data as to the amounts of vitamins A and C found in the blood of fibrositic patients. Since then laboratory methods have advanced to such a degree that it has been possible to extend the investigation to the determination of vitamin B₁.

The process used was essentially that of Wang and Harris,⁸ in which the amount of the vitamin excreted in the urine is estimated after the removal of the preformed thiochrome by extraction with *iso*-butanol. A small amount of the extracted sample is oxidised with potassium ferricyanide in alkaline solution and the thiochrome extracted with *iso*-butanol, which is then washed with water and compared visually against a standard solution of pure vitamin B₁ under an ultraviolet lamp. The process enables very small amounts of the vitamin to be estimated with a reasonable degree of accuracy.

A twenty-four-hour sample of urine is collected, and bacterial development must be prevented by the addition of a suitable preservative such as toluene, for many types of micro-organisms are able to produce appreciable amounts of the vitamin. According to Professor L. J. Harris (verbal communication) it is also essential that the patient should not be treated with aspirin or similar preparations. The writer has found that cases of rheumatoid arthritis under treatment with myocrysin occasionally excrete comparatively large quantities—over 1,000 international units (I.U.) per litre—of some substance that reacts in the test exactly like vitamin B₁.

The results expressed as I.U. per diem are shown below together with some normals for comparison:

Normals: 90, 75, 80, 68, 87, 45, 60, 108. After injections of benerva 175.

Fibrositis: 19, 28, 30, 26, 29, 19, 32, 38, 34, 28, 36, 25, 28, 37, 23. After taking betaxin 190.

Wang and Harris,⁸ using eleven normal subjects consisting of laboratory assistants and research workers, found a minimum excretion of 30 I.U. per diem and a maximum of 150 I.U., the

majority being between 50 and 80 I.U. In some nerve diseases they obtained much lower results: subacute combined degeneration, 15, 16; disseminated sclerosis, 16; peripheral neuritis, 26, 0, 0; anorexia nervosa, 19, 20; and in simple anorexia, 29, 16, the results being obtained at various dates on the same patient. They remark: "The subnormal values found . . . may presumably be attributed to 'conditioned' deficiency (or partial deficiency) arising from faulty absorption or utilisation or restricted diet."

The writer has found that other types of rheumatic patients excrete vitamin B₁ in amounts somewhat similar to those found in the urine of fibrositic ones, and the deficiency must therefore be mainly attributed to some common factor, which in the patients admitted to this hospital is probably a dietary deficiency due to the economic conditions obtaining in the class from which they are chiefly drawn.

In previous work⁷ the vitamin C content of the blood was found to vary with the economic strata of the patients, and in view of the deficiencies of vitamins A and C found in the patients admitted to this hospital a similar deficiency of B₁ was considered probable.

A number of the vitamin B₁ values found in the cases of fibrositis were no greater than some of those found by Wang and Harris in definite neurological diseases, but they were not accompanied by any symptoms attributable to vitamin B₁ avitaminosis. Many of the patients were males, apparently healthy apart from localised fibrositis, who had been capable of doing a full day's work in heavy occupations. The vitamin deficiencies in such cases suggest that there is a very considerable margin between pathological and optimal levels of vitamin content. Immediately above the pathological level is evidently a suboptimal zone of considerable depth and of great importance from the point of view of national nutrition. It seems very desirable that vitamin studies should be made on a cross-section of the population of the country to determine the depth of this suboptimal zone, for it is not impossible that the present optima are extravagantly high and that what is now regarded as a "conditioned" deficiency really represents merely a low margin of safety. Whilst the importance of vitamins should be fully appreciated, there is a possibility that zeal has outstripped discretion, and that some of the present optimal levels represent

an abundance rather than sufficiency. Perhaps the war will provide a large-scale experiment in this direction.

INDOLE AND INDICAN.—In 1935 Forbes and Neal,⁹ using improved methods for the estimation of indole and indican, examined urine samples from a number of rheumatic cases and reported considerable variations from the normal. Various types—infective arthritis (specific), rheumatoid arthritis, and osteo-arthritis—showed a markedly increased excretion of indole, whilst as regards indican the arthrides as a whole tended towards subnormal excretions, which was accentuated in the osteo type. A few high results were obtained in the rheumatoid type.

A series of cases in the Devonshire Royal Hospital has been studied by the methods used by Forbes and Neal, but the investigation has not yet reached the stage that warrants publication of the whole data. As regards fibrositis it will suffice to state that, although many cases show an increased urinary excretion of indole, the findings do not necessarily implicate the rheumatic condition. Little or no variation from the normal excretion of indican has been found, but the results definitely confirm the contention of Sharlet¹⁰ that the usual figures (4 to 20 mg. per diem) found in text-books are much too low. His results for twenty-four-hour specimens varied from 40 to 150 mg., whilst Forbes and Neal⁹ found an average of 73 mg. with a range from 30 to 165 mg.; the writer's results agree with these values.

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