THYMOL REACTION IN RHEUMATOID ARTHRITIS*

BY

K. KALBAK

From the Noerre Hospital, Copenhagen

New methods of examination in the study of rheumatoid arthritis, including the streptococcus agglutination test, the differential agglutination reaction with sensitized sheep corpuscles, determination of the antihyaluronidase inhibitor in serum, electrophoretic analysis of the serum proteins, and determination of 17-ketosteroids and glucocorticoids in the urine, yield characteristic findings and fit naturally into the symptomatic mosaic of this clinical entity.

The thymol reaction was first elaborated for practical use in 1944 by Maclagan, and it has since been employed in the diagnostic and prognostic estimation of various diseases of the liver, especially epidemic hepatitis. The prevailing view is that the reaction is due to certain changes in the gamma globulin, though some authors assert that it should rather be attributed to changes in the serum lipoproteins.

A positive thymol reaction in rheumatoid arthritis has been reported previously by Carter and Maclagan (1946), Stillerman (1948), and Poulsen (1949). Stillerman found the reaction positive in 82 per cent. of cases, but Carter and Maclagan did so in only 38 per cent., whereas the colloidal gold test gave a positive reaction in 76 per cent. of their material.

One purpose of the present investigation was to ascertain whether any definite relationship existed between the thymol reaction and the streptococcus agglutination reaction, chiefly because this sero-reaction, which is positive in about 70 to 80 per cent. of cases of rheumatoid arthritis, is also explained by most investigators as attributable to changes in the serum globulins.

Material

The present studies comprised 21 patients with typical rather severe rheumatoid arthritis, more than half having been troubled with rheumatic disease for more than 10 years. The control material consisted of patients from the same department, suffering from various medical diseases, mainly chronic in character but not including liver lesions. The average age of the patients in the two groups was about the same (60 years).

Method

The thymol is added to a serum under particular conditions, and a precipitate, consisting of thymol-serum-lipoid, appears. The degree of precipitation is read directly

* Aided by a grant from the National Danish Association Against Rheumatic Diseases.

in a photometer, and recorded in decimals. Values under 0.15 are considered normal, but values over 0.15 are considered decidedly pathological.*

Results

(1) **Control Material.**—In 31 patients with various medical lesions the thymol test gave the following results:

Normal values (0.0–0.15) in 29 patients (93 per cent.).

Increased values (≥ 0.15) in 2 patients (7 per cent.).

(2) **Patients with Rheumatoid Arthritis.**—The results of the thymol test in 21 patients were distributed as follows:

Normal values (0.0–0.15) in 5 patients (24 per cent.).

Increased values (≥ 0.15) in 16 patients (76 per cent.).

Thus a pathological increase in the value for the thymol reaction occurred about ten times more frequently among the patients with rheumatoid arthritis than in the control material.

The results of the streptococcus agglutination tests were distributed in the 21 rheumatoid-arthritic patients as follows:

Negative streptococcus agglutination in 6 patients (29 per cent.).

Positive streptococcus agglutination in 15 patients (71 per cent.).

This is quite in keeping with the findings reported previously by Goldie (1938), 75 per cent.; Cecil and deGara (1946), 60 per cent.; Edström and Winblad (1947), 76 per cent.; and Kalbak (1948), 77 per cent.

These results are all set out in Table I:

TABLE I
THYMOL TEST AND STREPTOCOCCUS AGGLUTINATION TEST
IN 21 CASES OF RHEUMATOID ARTHRITIS

Case No.	Sex	Age	Thymol Test		Streptococcus Agglutination Test		Duration of Illness (years)	Activity of Disease
			Reading	+ / 0	Titre	+ / 0		
1	F	32	0.18	+	1 : 40	+	9	+
2	F	40	0.11	0	1 : 80	+	3	++
3	F	54	0.22	+	1 : 40	+	1	+++
4	M	59	0.33	+	1 : 80	+	10	+++
5	M	63	0.26	+	1 : 320	+	6	+++
6	M	52	0.22	+	1 : 160	+	8	+++
7	F	71	0.67	+	1 : 80	+	7	+++
8	F	40	0.18	+	0	0	17	++
9	F	54	0.24	+	1 : 160	+	23	+++
10	M	52	0.25	+	1 : 160	+	11	+++
11	F	58	0.26	+	1 : 80	+	19	+++
12	F	54	0.10	0	0	0	30	++
13	F	53	0.11	0	0	0	15	++
14	M	56	0.25	+	1 : 160	+	14	+++
15	F	49	0.25	+	1 : 80	+	13	+++
16	F	69	0.06	0	0	0	4	++
17	F	15	0.08	0	1 : 160	+	1	+++
18	F	73	0.23	+	1 : 320	+	14	++++
19	F	57	0.16	+	0	0	1	++
20	F	20	0.16	+	0	0	6	++
21	M	59	0.41	+	1 : 160	+	19	++

* The thymol reactions were performed by the Medicinsk Laboratorium, Copenhagen.

A comparison of the outcome of the thymol reaction with that of the streptococcus agglutination test may be tabulated as follows:

TABLE II

Thymol Reaction	Positive (16)	Negative (5)
Streptococcus Agglutination Test .. { Negative (6) Positive (15)	3 13	3 2

Thus it will be noticed that a positive thymol reaction occurs more frequently in the group having a positive streptococcus agglutination reaction—which was to be expected if both reactions are expressions of changes in the serum globulin concentration.

A comparison of the outcome of the thymol reaction with the degree of activity of the joint disease* may be tabulated as follows:

TABLE III

Thymol Reaction	Activity of Joint Disease				Total Cases
	+	++	+++	++++	
0·0·15	—	4	1	0	5
≥0·15	—	5	10	1	16
Total	—	9	11	1	21

It thus appears highly probable that a positive thymol test is more likely to occur in patients whose joint disease is at a more active stage.

In keeping with previous investigations, a positive thymol reaction has been demonstrated in about 75 per cent. of the patients with rheumatoid arthritis. Furthermore, this reaction is found to be positive more often when the disease is at a more active stage. The incidence of positive thymol reactions and positive streptococcus agglutination reactions runs fairly parallel, which favours the hypothesis that the two reactions are both attributed to the changes in the serum proteins. Sufficiently detailed studies have not yet been carried out on the behaviour of the thymol reaction in rheumatoid arthritis for any appraisal of its diagnostic and prognostic value in this disease, but it can already be established that a positive thymol reaction fits very well into the mosaic of biochemical reactions characterizing the picture of advanced rheumatoid arthritis.

Summary

The thymol reaction in 21 patients suffering from rheumatoid arthritis was found to be positive in about 75 per cent. The incidence of positive thymol reactions is similar to the incidence of positive streptococcus agglutination reactions.

* According to the standards set up by the American Rheumatism Association (1949).

REFERENCES

- Carter, A. B., and MacLagan, N. F. (1946). *Brit. med. J.*, **2**, 80.
 Cecil, R. L., and deGara, P. F. (1946). *Amer. J. med. Sci.*, **211**, 472.
 Edström, G., and Winblad, S. (1947). *Nord. Med.*, **33**, 506.
 Goldie, W. (1938). *Lancet*, **2**, 246.
 Kalbak, K. (1948). *Acta med. scand.*, **130**, 358.
 Poulsen, E. (1949). *Ibid.*, Suppl. 234, p. 268.
 Stillerman, H. B. (1948). *J. Lab. clin. Med.*, **33**, 565.

Réaction du Thymol dans l'Arthrite Rhumatismale

RÉSUMÉ

Sur 21 malades atteints d'arthrite rhumatismale la réaction du thymol fut positive dans environ 75% des cas. La fréquence des réactions du thymol positives est similaire à celle des réactions positives d'agglutination du streptocoque.

Reacción de la Turbidez del Timol en la Artritis Reumatoide

RESUMEN

De 21 enfermos con artritis reumatoide la reacción de la turbidez del timol fué positiva en cerca de 75% de los casos. La frecuencia de las reacciones de la turbidez del timol positivas es similar a la de las reacciones positivas de aglutinación del estreptococo.

VARIATIONS IN THE THYMOL REACTION IN RHEUMATOID ARTHRITIS PATIENTS UNDER TREATMENT WITH CORTISONE AND ACTH*

BY

K. KALBAK

From the Noerre Hospital, Copenhagen

As demonstrated by various investigators (Carter and MacLagan, 1946; Stillerman, 1948; Poulsen, 1949; Kalbak, 1951), the thymol reaction is positive in rheumatoid arthritis patients at a somewhat advanced and active stage of the disease. This positive reaction is assumed to be due to changes in the serum proteins.

Patients with rheumatoid arthritis generally show marked changes in the serum proteins in the form of increased total protein, hypo-albuminaemia, and increase in α globulin and, especially, γ globulin. These shifts in the serum proteins follow rather closely the curve of the erythrocyte sedimentation rate, and also to some extent, the variations in the clinical state of the patient.

When rheumatoid arthritis is being treated with cortisone or ACTH decisive changes take place in the serum proteins. The hypoproteinaemia subsides, and the albumin/globulin ratio becomes normal.

In keeping with the theory that the positive thymol test is due to pathological

* Aided by grant from the National Danish Association Against Rheumatic Diseases.