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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*

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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

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changes in the serum proteins, it seemed reasonable to expect this reaction to approach normal, when the patients were treated with these hormones.

Clinical Findings

Of four patients suffering from typical rheumatoid arthritis, one was treated with cortisone, while three were given ACTH. In three of the patients the thymol reaction, which was decidedly positive before the institution of treatment, was controlled by repeated determinations, the normal limit for the thymol test being set at 0.13-0.15.*

The results are shown diagrammatically in the Figure, which also shows dosage. ACTH was given intramuscularly in small quantities, 5 to 10 mg., several times daily.

Case 1. Male, aged 53, in an advanced stage of rheumatoid arthritis.

Thymol reaction repeatedly strongly positive (0.24).

Erythrocyte sedimentation rate about 80 mm. in 1 hour.

Cortisone acetate† was given for 10 days (altogether 750 mg.); this treatment had an excellent clinical effect, and the thymol reaction at once showed a tendency to fall, and minimum values (about 0.08) were obtained for about 2 weeks after discontinuing the treatment. After this, the thymol reaction increased again to an even higher level (about 0.32) than before. This was in keeping with the aggravation of the clinical state of the patient, as well as with a rise in the erythrocyte sedimentation rate to about 100 mm. in 1 hour. The thymol reaction and erythrocyte sedimentation rate ran parallel.

Case 2. Female, aged 56, confined to bed with severe rheumatoid arthritis.

Thymol reaction distinctly positive (0.25).

ACTH‡ therapy (40 mg. daily for 30 days) had only a moderate clinical effect, whereas the thymol reaction decreased to a normal level (about 0.12). Two weeks after discontinuing treatment the thymol reaction had risen to the initial level (about 0.25).

Case 3. Female, aged 40, with moderately severe rheumatoid arthritis.

Thymol reaction before treatment, normal (0.12).

During treatment with ACTH, which was given for about two months, the level of the thymol reaction decreased. At the beginning and towards the end of the course ACTH was given in fairly large doses (40 mg. daily), and in the intervening longer period the daily dose was only 10 mg. In spite of a relatively small dosage of ACTH a fairly good clinical effect was maintained, except in the final period, when the decrease in the clinical effect was accompanied by an increase in the level of the thymol test—apart from a brief fall after an increase in the dosage of the hormone. On the whole, the outcome of the thymol test and the E.S.R. ran parallel except in the final phase, when the E.S.R. fell steadily in spite of the decrease in clinical effect and increasing thymol reaction.

Case 4. Female, aged 31, with rather severe rheumatoid arthritis (Stage III).

Thymol reaction slightly increased (0.15).

Brief treatment (6 days) with moderate doses of ACTH brought about a considerable fall in the thymol values (down to 0.08). The minimum value was reached about two weeks after discontinuing the treatment and then rose at once to values above the initial level. A second course of ACTH produced a further fall in the thymol reaction, but when small doses of the hormone were given throughout a considerable period, the thymol values again increased, being accompanied by a fairly parallel rise in the erythrocyte sedimentation rate. The output of 17-ketosteroids, which was increasing under the hormone

* The thymol tests were performed by Medicinsk Laboratorium, Copenhagen.

† Cortisone was kindly furnished for experimental purposes by Merck & Co., U.S.A.

‡ ACTH (RMC) was kindly furnished by the Roskilde Medical Company, Denmark.

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therapy, fell during the final phase when only small amounts of ACTH were given daily—and thymol reaction and erythrocyte sedimentation rate increased.

Discussion

In the variegated multiplicity of clinical-biological, biochemical, and serological examinations, each of which contributes to our estimation of the effect of the hormonal therapy in rheumatoid arthritis, the thymol test appears to deserve consideration.

During the administration of cortisone or ACTH the thymol reaction as a rule falls sharply, but it increases again after discontinuing the treatment, most often to values higher than the initial level.

As in this disease the abnormal serum protein values become normal under hormone treatment, it seems reasonable to attribute changes in the thymol reaction to the decrease in the serum proteins, which supports the theory that an abnormally increased thymol reaction is due to changes in the serum protein.

In the cases cited above the variations of the thymol reaction matched those of the E.S.R. and of the clinical state of the patient (except in Case 3). The sedimentation test may still be regarded as the simplest and most reliable laboratory test in estimating the effect of cortisone and ACTH therapy in rheumatoid arthritis.

Summary

The thymol reaction which is normally pathologically increased in rheumatoid arthritis, becomes normal during treatment with cortisone or ACTH. This reaction may be included in the tests of the effect of these hormones.

The observations here reported support the view that a positive thymol reaction is due to changes in the serum proteins.

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Variations de la Réaction du Thymol chez les Malades atteints d'Arthrite Rhumatismale Traités par la Cortisone et par l'ACTH

RÉSUMÉ

La réaction du thymol, généralement augmentée pathologiquement dans l'arthrite rhumatismale, devient normale pendant le traitement par la cortisone et par l'ACTH. Cette réaction peut donc faire partie des tests sur l'effet de ces hormones.

Les observations rapportées ici renforcent le point de vue qu'une réaction du thymol positive est due aux modifications dans les protéines sériques.

Variaciones de la Reacción de la Turbidez del Timol en los Enfermos con Artritis Reumatoide Tratados por la Cortisona y por la ACTH

RESUMEN

La reacción de la turbidez del timol, que suele ser patológicamente aumentada en la artritis reumatoide, se vuelve normal durante el tratamiento con cortisona o ACTH. Esta reacción puede ser incluida en las pruebas sobre el efecto de estas hormonas.

Las observaciones aquí relatadas refuerzan el punto de vista de que una reacción de la turbidez del timol positiva se debe a alteraciones en las proteínas del suero.