Serum complement levels in recurrent aphthous ulceration

An intraindividual pilot study of sequential C3, C4 & C1 esterase inhibitor estimations

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No alterations on different occasions in serum complement levels could be detected in patients suffering from recurrent aphthous stomatitis. General laboratory tests were also normal and these findings are further evaluated in the discussion. It was also found that it is possible to store serum at very low temperature for months and still carry out rather sofisticated laboratory analysis.

Key-words: Stomatitis; aphthous; complement; immunology

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Both humoral and cellmediated autoimmune-activity against the oral mucosa in RAU*) have in recent years been discussed in several papers (*Lehner*, 1969 a, b, 1972; *Dolby*, 1969, 1970). Information on serum complement still has been lacking. The following paper is a report of sequential serum complement (C1 est. inhib., C3 and C4) levels in patients suffering from RAU.

Serum complement

Human serum complement, C, is a number of factors, at present twelve serum proteins, which when activated take part in several immune reactions. Mostly these reactions are designed to destroy foreign agents, usually infectious, to benefit the organism. In several instances, however, activation of complement, after binding to antigen-antibody-complexes, results in tissue damage, cellysis. The whole mechanism is not yet fully understood, but it is well known that alterations in serum complement levels are seen and taken as criterion for humoral antibody-activity in autoimmune disorders (*Ruddy et al.*, 1972). It would therefore be of interest to make estimations of serum complement levels in patients with RAU.

*) Recurrent aphthous stomatitis.

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MATERIAL AND METHODS

For this study, designed as a pilot study, three otherwise healthy patients, with severe RAU (minor type), from the ordinary referred body of clients were chosen. To ensure the diagnosis of RAU, the patients were questioned and routinely examined and followed every three days during at least one episode of RAU. Perifer blood from the arm vein was taken at three occasions, see below, immediately centrifugated, and pipetted into two test-tubes, ten ml each; one of the tubes coated with EDTA. The tubes were frozen in carbonic acid snow and stored in a special freezer at —90°C awaiting transport for

Table I. *Results of sequential serumcomplement estimations*

	L. P. ♀ 49 yrs			A. S. ♀ 24 yrs			H. G. ♂ 54 yrs		
C 3	94	86	86	116	128	—	106	108	108
C 4	27	26	23	37	35	—	37	39	35
C 1 est. inhib.	21	23	24	22	24	—	25	25	27
Sample number*)	1	2	3	1	2	3	1	2	3
Normal limits C 3	70—170 mg/100 ml								
C 4	9— 44 mg/100 ml								
C 1 est. inhib.	19— 29 μg/ml								

*) See text for explanation.

analysis. The reason for the freezing arrangement was that C is very sensitive to temperature, and analysis can not be done if serum is exposed to room temperature for any longer period. The analysis was performed by professor Laurell, Lund, Sweden. »Rocket-technique», a kind of cross-electroforesis in a special diffundable agar gel was used.

The time from the first sample occasion until final analysis, was more than three months and consequently it is quite possible, with the described method, to store serum this long and still perform rather complicated and sensitive analysis, a fact well worth notice.

Timing of sequential estimations. The first blood sample, *1*, was taken when a new ulcer was not older than six hours, the second sample, *2*, when the ulcer was in definite healing phase. Finally, the third sample, *3*, was taken at a symptomfree interval, when no ulcers were present. One female patient, A.S., had so many and frequent ulcers, she never had symptomfree periods. Therefore, her third bloodsample was excluded. Routine laboratory tests were done on each sample occasion.

RESULTS

Normal laboratory values were found according to the number of white blood cells and differential counting. This ensured that the three patients in this study did not suffer from any serious disease that could inflect upon the interpretation of the C level estimations. The results of the sequential complement estimations, levels of C1 est. inhib., C3 and C4 are listed in Table I.

DISCUSSION

Estimations of serum C levels are used both for pathogenic information, diagnostic criterion, and prediction of prognosis in a record of autoimmune and immune-complex diseases (*Laurell*, 1973). Both decrease, consumption of C, and increase, overproduction, are seen in different conditions of many serious diseases. As a rule, C1 est. inhib. levels are normal, but the levels of C3 and C4 are low in a progress of an autoimmune disorder. On the other hand high levels are generally seen in exacerbations of rheumatic arthritis and in several infectious diseases (*Laurell*, 1973).

The C levels found in this pilot study are within normal limits and show very small differences from one sample occasion to another. Because of this, one can conclude, that it is possible to develop minor RAU without any greater alterations in the serum C level. It is quite possible that the relatively small, and for the organism as a whole, rather harmless lesions, are not capable of reflecting changes in the serum C level. It is possible that the results would have been different if patients with major RAU (Sutton's disease or Periadenitis mucosae necroticans recurrens) or Behçet's syndrome had been included in the study. In favor of this, it is interesting to notice that the largest difference between two sample occasions, C3 116—128 mg/100 ml, 12 units, was found in the female patient, A.S., who had the greatest trouble with her RAU.

Since all the C factors react in a determined and sequential way, with dependency on each other (*Laurell*, 1973; *Ruddy et al.*, 1972), analysis of the other ones would hardly at present give further information on the nature of RAU and especially its connection with humoral immunity. In recent years more interest has been drawn to cellmediated immunereactions in RAU (*Dolby*, 1969, 1970; *Lehner*, 1972) and despite these often are accompanied by humoral immuneactivity, further estimations of serum levels in patients with RAU, minor type, would hardly be desirable.

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