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Chronic Streptococcus pyogenes tonsillitis, with rheumatic arthritis and myocarditis
(An immunological study using the SWT)

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Introduction

The precise cause of rheumatic fever is unknown. However, there is much evidence that it is related to infection with group A haemolytic streptococci, possibly on the basis of an antigen common to the heart and streptococcus. The disease is often preceded by tonsillitis or pharyngitis, one to three weeks earlier (Macleod, 1982). The actual manner in which streptococci provoke acute rheumatic fever is not clear, but certain clinical and laboratory features provide strong support for an immunologic rather than a toxic mechanism (Kenneth, 1965). When the human host is infected with group A streptococci,the foreign antigen is immunologically recognisable, resulting in antibody formation; but, because of an antigenic similarity of the streptococcal antigen to components of human tissue,the host antibody attacks its own myocardial cells, resulting in the presence of antibody to heart tissues in the serum of patients with rheumatic fever, and subsequent myocardial damage (Kaplan, 1978).

The Skin Window Test (SWT) was first described by Roebuck and Crowley (1955) as a method of studying local inflammatory reactions in normal subjects and diseased patients. The test has been used to study the cellular inflammatory response in a variety of haematological conditions (Roebuck *et al.*, 1958; Trepel and Begemann, 1966; Ghosh *et al.*, 1973), and to study the state of immunity in rhinoscleroma patients and contacts (Toppozada *et al.*, 1981,1984).

The purpose of this work was to study the macrophages, skin cellular kinetics and lymphoblastic transformation in patients with streptococcus pyogenes tonsillitis, with rheumatic arthritis and myocarditis, and to assess its possible use in evaluating their immunologic state.

Material and method

The group under study included 35 patients, classified in the following groups:

A–Ten cases of chronic Streptococcus pyogenes tonsillitis.

B–Ten cases of chronic Streptococcus pyogenes tonsillitis with rheumatic arthritis.

C–Ten cases of chronic Streptococcus pyogenes tonsillitis with rheumatic myocarditis.

D–Five controls having no Streptococcus pyogenes in their nose and throat.

Complete history taking, clinical and laboratory examination was done to select the above controls and patients according to Jones' criteria. Tonsillar swabs were cultured on blood agar plates, incubated for 24 hours at 37°C., and examined for the isolation of haemolytic colonies group A streptococci, identified by their sensitivity to Bacitracin.

The Skin Window Test was performed on all patients and controls. The preparation of the bacterial antigen and the technique of the test used was that used by Toppozada *et al.* (1981), using saline control, the patient's own organism and foreign Streptococcus pyogenes organism as antigen.

Results

There was an immediate neutrophilic response, followed by a monocytic one; then neutrophils started to diminish while the monocytes increased with time. The lymphoblastic transformation of the cellular population during the period of examination varied:

A–*Saline control*:
No lymphoblastic transformation occurred at any period of examination. (Table I)

B–*Patient's own Streptococcus pyogenes as antigen*:
The lymphoblastic transformation was : (Table II, Fig. 1)

Chronic tonsillitis	7 –9 per cent
Rheumatic arthritis	5.5–7 per cent
Rheumatic myocarditis	4 –4.6 per cent

C–*Foreign Streptococcus pyogenes as antigen*:
The lymphoblastic transformation was : (Table III, Fig. 2)

Chronic tonsillitis	14–20 per cent
Rheumatic arthritis	11–12.5 per cent
Rheumatic myocarditis	8–9.5 per cent

D–*Control subjects*:
The lymphoblastic transformation in subjects having no Streptococcus pyogenes in their nose and throat was 27 - 32 per cent (Table IV, Fig. 2)

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TABLE I

MEAN PERCENTAGES AND ONE STANDARD DEVIATION OF THE CELLULAR RESPONSES IN THE SWT TO SALINE, IN PATIENTS OF CHRONIC STREPTOCOCCUS PYOGENES TONSILLITIS, WITH RHEUMATIC ARTHRITIS, MYOCARDITIS AND CONTROLS

Types of cells	After 24 hours	After 48 hours	After 72 hours
	Mean % ± S.D.	Mean % ± S.D.	Mean % ± S.D.
Lymphoblasts	—	—	—
Neutrophils	52.55 ± 11.28	51.55 ± 9.96	46.13 ± 9.62
Lymphocytes	7.97 ± 1.64	7.00 ± 1.96	7.1 ± 2.0
Monocytes	38.17 ± 6.24	42.1 ± 4.71	47.3 ± 5.18

TABLE II

MEAN PERCENTAGES AND ONE STANDARD DEVIATION OF THE CELLULAR RESPONSES IN THE SWT IN CHRONIC STREPTOCOCCUS PYOGENES TONSILLITIS, WITH RHEUMATIC ARTHRITIS AND MYOCARDITIS, USING PATIENT'S OWN ORGANISM AS ANTIGEN

Types of patients	Types of cells	After 24 hours		After 48 hours		After 72 hours	
		Total response Mean % ± S.D.	Specific response	Total response Mean % ± S.D.	Specific response	Total response Mean % ± S.D.	Specific response
Chronic tonsillitis	Lymphoblasts	7.14 ± 1.4	7.14%	8.2 ± 1.54	8.2 %	8.9 ± 1.63	8.9 %
	Neutrophils	64.2 ± 12.6	11.6 %	59.2 ± 13.6	7.65%	58.3 ± 12.6	12.17%
	Lymphocytes	12.3 ± 2.3	4.3 %	14.6 ± 2.1	7.6 %	12.4 ± 2.3	5.3 %
	Monocytes	13.4 ± 4.8	−24.8 %	16.8 ± 4.9	−26.3 %	17.1 ± 5.3	−41.4 %
Rheumatic arthritis	Lymphoblasts	5.6 ± 1.63	5.6 %	6.6 ± 1.45	6.6 %	5.9 ± 1.48	5.9 %
	Neutrophils	50.1 ± 13.4	−2.45%	48.3 ± 12.8	−3.25%	47.2 ± 10.6	1.07%
	Lymphocytes	9.8 ± 6.4	1.83%	10.3 ± 7.1	3.3 %	8.95 ± 5.6	1.85%
	Monocytes	36.0 ± 4.8	−2.17%	37.0 ± 5.1	−5.1 %	37.0 ± 6.1	−11.3 %
Rheumatic myocarditis	Lymphoblasts	4.3 ± 1.32	4.3 %	4.6 ± 1.32	4.6 %	4.1 ± 1.21	4.1 %
	Neutrophils	56.1 ± 11.4	3.55%	54.0 ± 13.49	2.45%	48.2 ± 11.45	2.07%
	Lymphocytes	10.1 ± 2.4	2.13%	9.6 ± 7.8	2.6 %	9.4 ± 6.1	2.3 %
	Monocytes	30.3 ± 6.1	−7.87%	31.8 ± 3.8	−10.3 %	32.0 ± 3.8	−15.3 %

N.B. The specific response to antigen is the difference between the response to saline (Table IV) and the total responses to saline and antigen.

TABLE III

MEAN PERCENTAGES AND ONE STANDARD DEVIATION OF THE CELLULAR RESPONSES IN THE SWT IN CHRONIC STREPTOCOCCUS PYOGENES TONSILLITIS, WITH RHEUMATIC ARTHRITIS AND MYOCARDITIS, USING FOREIGN ORGANISM AS ANTIGEN

Types of patients	Types of cells	After 24 hours		After 48 hours		After 72 hours	
		Total response Mean % ± S.D.	Specific response	Total response Mean % ± S.D.	Specific response	Total response Mean % ± S.D.	Specific response
Chronic tonsillitis	Lymphoblasts	18.4 ± 3.6	18.4 %	14.3 ± 3.45	14.3 %	19.8 ± 3.55	19.8 %
	Nuetrophils	46.6 ± 10.8	−5.95%	44.6 ± 12.48	−6.95%	48.6 ± 10.69	2.47%
	Lymphocytes	5.3 ± 0.8	−2.67%	4.7 ± 0.8	−2.3 %	5.2 ± 1.78	−1.9 %
	Monocytes	31.0 ± 2.9	−7.17%	32.8 ± 6.85	−9.3 %	33.6 ± 7.21	−13.7 %
Rheumatic arthritis	Lymphoblasts	11.6 ± 3.12	11.6 %	12.3 ± 3.1	12.3 %	10.9 ± 2.8	10.9 %
	Neutrophils	64.0 ± 10.2	11.45%	59.3 ± 11.3	7.75%	60.3 ± 12.4	14.17%
	Lymphocytes	7.9 ± 3.2	−0.07%	8.1 ± 4.63	1.1 %	8.6 ± 5.65	1.5 %
	Monocytes	18.6 ± 4.2	−19.57%	21.3 ± 5.21	−20.8 %	22.4 ± 4.99	−24.9 %
Rheumatic myocarditis	Lymphoblasts	8.3 ± 1.85	8.3 %	9.4 ± 1.65	9.4 %	7.9 ± 1.45	7.9 %
	Neutrophils	60.6 ± 14.6	8.05%	54.0 ± 16.35	2.45%	54.0 ± 12.48	7.87%
	Lymphocytes	8.5 ± 2.95	0.53%	9.1 ± 2.83	2.1 %	10.2 ± 3.5	3.1 %
	Monocytes	24.4 ± 5.3	−13.77%	28.6 ± 6.1	−13.5 %	29.6 ± 5.82	−17.7 %

N.B. The specific response to antigen is the difference between the response to saline (Table IV) and the total responses to saline and antigen.

TABLE IV

MEAN PERCENTAGES AND ONE STANDARD DEVIATION OF THE CELLULAR RESPONSES IN THE SWT USING STREPTOCOCCUS PYOGENES ORGANISM AS ANTIGEN IN SUBJECTS HAVING NO STREPTOCOCCUS PYOGENES IN THEIR NOSE AND THROAT (CONTROLS)

Types of cells	After 24 hours		After 48 hours		After 72 hours	
	Total response Mean % ± S.D.	Specific response	Total response Mean % ± S.D.	Specific response	Total response Mean % ± S.D.	Specific response
Lymphoblasts	31.4 ± 3.05	31.4 %	27.2 ± 3.83	27.2%	31.8 ± 2.95	31.8%
Neutrophils	42.2 ± 3.1	−10.35‰	41.0 ± 2.64	−10.55%	41.4 ± 1.52	−4.73%
Lymphocytes	7.2 ± 2.68	−0.77%	8.8 ± 1.92	0.2 %	7.8 ± 1.92	0.7 %
Monocytes	19.2 ± 3.63	−18.97%	22.0 ± 2.45	−20.1 %	21.0 ± 6.82	−26.3 %

N.B. The specific response to antigen is the difference between the response to saline (Table IV) and the total responses to saline and antigen.

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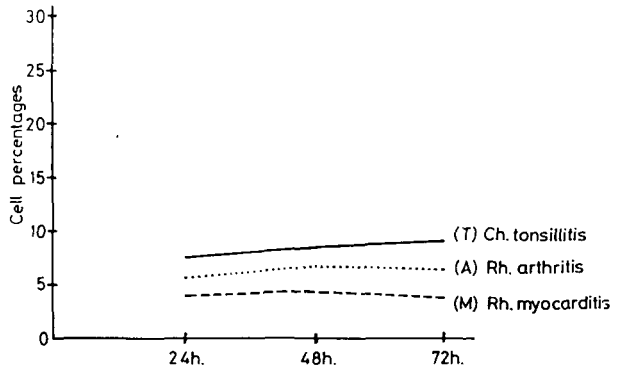


FIG. 1

Lymphoblastic transformation in chronic Streptococcus pyogenes tonsillitis, with rheumatic arthritis and myocarditis using patient's own organism as antigen.

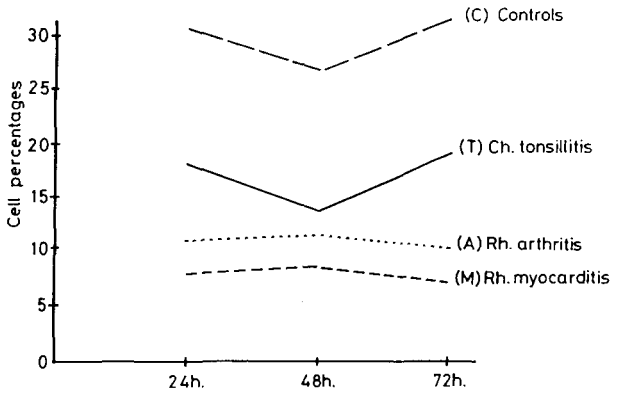


FIG. 2

Lymphoblastic transformation in chronic Streptococcus pyogenes tonsillitis, with rheumatic arthritis, myocarditis and controls, using foreign organism as antigen.

Discussion

The use of Streptococcus pyogenes antigen (foreign or patient's own) in the Skin Window Test gave the highest response of lymphoblastic transformation in patients with chronic tonsillitis; next with rheumatic arthritis, and the lowest with rheumatic myocarditis. This may be related to an impaired T-lymphocyte function. The more impaired the cell mediated immunity, the lower the level of lymphoblastic transformation. Thus, patients with chronic tonsillitis have the least depressed T-lymphocyte function, while rheumatic myocarditis patients have the most depressed one. Patients with rheumatic arthritis lie in between. Hence, deficiency of the cellular immune response can be considered as a contributory factor in the development of rheumatic arthritis and myocarditis from an ongoing streptococcal pyogenes tonsillitis, where there is progressive failure of immunological responsiveness. Such failure may be the result of structural and pathological changes accompanying this disease, or may be due to attenuated immunity resulting from the long-standing absorption of toxic bacterial products from the throat.

The use of Streptococcus pyogenes as antigen in the Skin Window Test gave a higher percentage response of lymphoblastic transformation when using foreign organism than when using the patient's own organism. This may be due to a state of tolerance to the already present streptococcal antigen in the throat. When the same organism was used in normal controls, a more potent lymphoblastic transformation was obtained.

The application of the Skin Window Test, using Streptococcus pyogenes as antigen, can be useful in the diagnosis of chronic Streptococcus pyogenes tonsillitis with oncoming rheumatic arthritis and myocarditis. The administration of prepared foreign Streptococcus vaccine can help to raise the individual's immune status. This will raise the cellular-mediated immunity and consequently diminish the susceptibility to such infection or its hazards.

Conclusion

The SWT was performed on 10 patients with chronic Streptococcus pyogenes tonsillitis, 10 with rheumatic arthritis, 10 with rheumatic myocarditis, and five controls with no streptococcus in their nose and throat. Foreign organisms and the patients' own organisms were used as antigen.

The lymphoblastic transformation occurred with decreasing prevalence in the above order. The failure of cellular immune response as a contributory factor in the development of rheumatic arthritis and myocarditis is discussed. The possible value of prepared vaccine in prevention is mentioned.

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