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ANTISTREPTOLYSIN AND ANTISTAPHYLOLYSIN TITRES IN ALLERGIC SKIN CONDITIONS

*Observations on 6104 Patients Suffering from
Various Eczemas and Urticaria*

By

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Clinical experience has convinced many authors of the considerable significance of focal infection in certain dermatoses and allergic conditions. Asthma, for example, may in certain cases show a connection with sinusitis. Accidental infections of the respiratory organs may aggravate the skin condition in atopic subjects. Cases of chronic urticaria may sometimes be dramatically cured after removal of dental foci (1, 2, 3, 12, 16, 20, 29). In these conditions the clinical consequences of the infection are as a rule not due to a spread of the infection, but to an allergic response of a sensitized individual to bacterial products released from the focus. According to *Epstein* (3) therefore the term "focal allergy" appears more appropriate than "focal infection". In skin diseases the focal or bacterial allergy plays its greatest role in infectious eczemas. But it is evident that allergic pruritus in cases of atopic eczema through the patient's scratching is followed by bacterial invasion into the damaged skin with all its consequences of sensitization. The purpose of this paper is to study to what extent the determination of antistreptolysin titre (AST) and antistaphylolysin titre (ASTA) in serum may be helpful in judging the role of streptococci and staphylococci in eczematous and urticarial skin diseases.

The antistreptolysin titre (AST) introduced in 1932 by *Todd* (25) as a serological method for detection of streptococcal infections has been widely studied in rheumatic diseases, purpura, erythema nodosum, psoriasis, and other conditions where focal infections were thought to play a role.

AST below 200 units per ml serum was originally considered normal, whereas AST 200 or above 200 was considered pathologic. Control series in 1932-58 showed raised titres in about 12 per cent. The highest AST range in a control group of blood donors, 36.7 per cent, was seen by *Ingestad & Winblad* (7). AST 250 or 300 as the upper limit for normal values has been proposed by *Lagercrantz* (11), *Huriez et al.* (6), *Köhler* (9), and *Ingestad & Winblad* (7).

ASTA below 2.0 is considered normal. *Serly et al.* (19) found ASTA ≥ 2.0 in control series in 5 per cent, *Lack & Towers* (10) only in 2 per cent. *Steen & Schøne* (23) obtained raised titres in 22 per cent of their control cases and are inclined to move the upper limit of normal values for ASTA to 3.5 units. According to *Widholm* (26) the upper limit of normal ASTA is 1.0 in young children, 2.0 units in the age group 5-60 years and 1.2 units per ml in control persons more than 60 years of age. However, in a control group of blood donors *Ingestad & Winblad* (7) observed ASTA ≥ 3.0 in 28 per cent of the cases, and *Mustakallio* (14) calculated the titre of 6.4 units per ml to be a safe lower limit of seropositivity.

In 1946 *Norrilind* (16) reported raised AST ≥ 200 in four atopic patients and pointed out the importance of avoiding infections which could aggravate the atopic eczema. *Heløe, Oker-Blom & Pätälä* (5) studied the AST in 44 children with eczema infantum or atopicum, 5 of which showed raised titres above 200. In 9 out of 24 adults with prurigo the AST was > 200 , too. ASTA was determined in only 11 cases of children's eczema and found within normal limits.

The first observations of AST and ASTA in a somewhat larger series of eczematous patients were reported in 1954 by *Sonck & Widholm* (21, 22). Their series comprised 340 patients with various eczemas, including 91 cases of atopic eczema. Raised titres (AST ≥ 200 , and ASTA ≥ 2.0) were seen most frequently in atopic eczema (in 48, and 52 per cent) and in chronic and microbial eczema (in 41, and 43 per cent respectively). In a control group of healthy students raised AST values were found in 14 per cent of cases. Out of 50 cases of urticaria *Sonck & Widholm* (21, 22) noted raised AST in 19 cases (38 per cent), but raised ASTA only in 3 cases (6 per cent). *Farris & Zocchi* (4) found AST values ≥ 200 in 23 of a series of 45 eczema cases (incl. 21 dyshidrosiform hand eczemas). All their patients with raised AST showed infectious foci, either dental or tonsillar. The number of patients studied is similarly small in many other reports: 25 cases of microbial and 36 of atopic eczema (*Nicolau et al.* (15)), 37 cases (*Huriez et al.* (16)), 31 cases (*Témime et al.* (24)). In a series of 61 cases of neurodermatitis *v. Zenzschwitz* (28) found raised titres in about 50 per cent of the cases. *Zaun & Heite* (27) observed AST values > 200 in 55

out of 268 cases of eczema (20.5 per cent of cases). These comprised 40 out of 153 cases of microbial eczema, 5 out of 33 cases of contact dermatitis, and 8 out of 52 cases of atopic eczema. Other groups were too small to be evaluated. Among 20 cases of urticaria only one showed values > 200 . *Rajka* (17) observed $AST > 200$ in 34 out of 100 atopic patients and in 19 out of 100 control cases. *ASTA* values varied between 1.0 and 3.0 in his patients with atopic eczema. In a selected series studied by *Kompman & Salfeld* (8) all cases with known focal infections or previous (within 6 months) tonsillitis were excluded. AST values > 200 were found in 8 out of 25 cases of microbial eczema (32 per cent), in 11 out of 25 cases of leg eczema (44 per cent), in 5 out of 26 cases of contact dermatitis (19 per cent), and in 5 out of 26 cases of urticaria (19 per cent). *Mikhailov & Naumova* (13) observed in chronic urticaria AST values > 200 in 6 out of 14 cases. *Rufli-Hutter* (18) found AST values > 200 in 19 out of 318 cases of eczema (in 6 per cent), in 4 out of 64 urticaria cases (6 per cent), and in 4 out of 22 cases of erythrodermia (in 18 per cent). *Mustakallio* (14) investigated the *ASTA* level in a large series of atopic eczema and found raised titres ≥ 6.4 in 168 out of 1093 patients, i.e. in 15 per cent of the cases. In his series 135 out of 593 atopic subjects showed $AST \geq 250$ (23 per cent).

According to him, the severity of Besnier's prurigo seems to be rather closely related to the blood level of *ASTA*. *Mustakallio* (14) also studied the *ASTA* in other eczema groups, reporting values ≥ 6.4 units in 94 out of 1287 cases of infectious and chronic eczema (7.3 per cent), in 11 out of 224 cases of nummular eczema (4.9 per cent), in 57 out of 1293 cases of allergic contact dermatitis (4.4 per cent), in 7 out of 496 cases of seborrheic eczema (1.4 per cent), in 10 out of 349 cases of stasis dermatitis and eczema varicosum (2.9 per cent), and in 4 out of 67 cases of circumscribed neurodermatitis (6 per cent). The highest range was seen in cases of erythrodermia: $ASTA \geq 6.4$ was here found in 84 cases out of 170, i.e. in 49.4 per cent of the cases. *Mustakallio* pays special attention to penetrating skin damage induced by scratching or by xerotic breaking. Only one of 189 urticaria patients showed an $ASTA \geq 6.4$ units.

MATERIAL AND METHODS

The AST and *ASTA* were routinely examined in all patients admitted to the Department of Dermatology, University of Turku, during the period 1955-1970. In many cases several samples were taken, but only the highest values will be presented in this study. The material comprises examination of 6104 patients. The eczema cases were classified as presented in Table 1. It must be admitted that it was not always easy to make a clear distinction between the various eczema groups. We had to classify some long-standing cases as "non-determined chronic eczema". As controls we used the AST and *ASTA* values of 200 blood donors (100 males and 100 females) from the Red Cross Station in Turku, Nov.-Dec., 1971. These showed AST values ≥ 200 in 28 per cent and *ASTA*

TABLE 1
Summary of Cases Included in Study

Diagnoses	Total number	AST ≤ 200		AST ≤ 400		ASTA ≤ 2.0		ASTA ≥ 4.0	
		Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
Contact dermatitis (Eczema allergicum)	1592	611	38	227	14	462	29	126	8
Atopic eczema (Prurigo Besnier)	888	439	49	224	25	433	49	148	17
Non determ. chronic eczema	200	88	44	34	17	109	55	52	26
Dyshidrotic eczema	133	66	50	33	25	39	29	18	14
Infectious eczema (Eczema infectiosum)	666	309	46	160	24	221	33	73	11
Nummular eczema (Eczema nummular)	171	65	38	25	15	46	27	11	6
Seborrhoic eczema and intertrigo	562	205	36	67	12	119	21	29	5
Photodermatitis (Eczema solare)	83	38	46	13	16	24	29	5	6
Stasis dermatitis, varicotic leg eczema	1038	446	43	216	21	402	39	145	14
Exfoliative erythrodermia	115	63	55	49	42	78	59	47	41
Circumscrip neurodermatitis	101	39	39	14	14	30	30	6	6
Pustular bacterid	51	24	47	9	18	22	43	11	22
Urticaria	504	185	37	61	12	63	13	8	2
Total	6104	2578	42	1132	19	2048	34	680	11

values ≥ 2.0 in 11.5 per cent of the cases. AST ≥ 400 was found in 7 per cent and ASTA ≥ 4.0 in only 0.5 per cent of the control cases.

All the AST and ASTA determinations of the present study were performed at the Department of Serology and Bacteriology, University of Turku. Cultures were taken from the skin lesions in a great number of cases for bacteriological examination. Special attention was paid to the presence of focal infections in tonsils, nasal cavities, ears, teeth etc. However, the hospital records did not always give enough information in this respect.

RESULTS

Contact dermatitis (Eczema allergicum et toxicum) (Table 2)

733 males, 859 females, 1592 cases in all. 1148 were regarded as allergic, 444 as toxic contact eczemas. Mean age 46 years.

AST ≥ 200 in 611 (38 per cent), ≥ 400 in 227 cases (14 per cent). ASTA ≥ 2.0 in 462 (29 per cent), ≥ 4.0 in 126 cases (8 per cent). ESR > 12 mm in 727 cases.

In cultures from the skin *Staph. aureus* was quite predominating and present in 678 cases. *Staph. albus* was found in 207 cases, β -hemolytic streptococci in only 45 cases (38 of these strains belonged to group A).

Focal infections were mentioned in the records in 236 cases (15 per cent of cases). Dental foci were found in 92 cases, tonsillitis in 47, sinusitis in 28, and otitis in 18 cases. Other infections were mentioned in 51 cases. There was no significant difference in the range of titres or foci between the allergic and toxic group of contact eczemas.

Atopic eczema (Prurigo Besnier) (Table 3)

366 males, 522 females, 888 cases in all. Mean age 20 years.

AST ≥ 200 in 439 (in 49 per cent), ≥ 400 in 224 (in 25 per cent), and ≥ 800 in 57 cases (in 6 per cent). ASTA ≥ 2.0 in 433 (in 49 per cent), ≥ 4.0 in 148 (in 17 per cent), and ≥ 8.0 in 32 cases (in 4 per cent). ESR > 12 mm in 251 cases.

Cultures from the skin surface revealed β -hemolytic streptococci (group A) in 42 cases, other strains of streptococci in

TABLE 2
Contact Dermatitis.

		Male	Female	Total	Per cent	
AST	<200	428	553	981	62	
	200—399	182	202	384	38	14
	400—799	99	79	178		
	800>	24	25	49		
	Total		733	859	1592	
ASTA	>2.0	383	747	1130	71	
	2.0—3.9	157	179	336	29	8
	4.0—7.9	41	58	99		
	8.0>	20	7	27		
	Total		733	859	1592	
ESR > 12 mm		213	514	727		
Bact. cultures	Strept. nonhaem.	11	28	39		
	Strept. α -haem.	14	30	44		
	Strept. β -haem. (non A)	4	3	7		
	Strept. β -haem. A	14	24	38		
	Staph. aureus	241	437	678		
	Staph. albus	68	139	207		
Total		352	661	1013	64	
Focal infections	Tonsillitis	20	27	47		
	Otitis	8	10	18		
	Sinuitis	14	14	28		
	Dental foci	41	51	92		
	Other foci	9	42	51		
	Total		92	144	236	15

24, and *Staph. albus* in 62 cases. *Staph. aureus*, however, was the predominant invader, found in 368 cases. Focal infections were present in 170 cases (in 19 per cent): Acute or chronic tonsillitis in 55, sinuitis in 32, otitis in 19, and dental foci in 49 cases. Other infections such as furunculosis, bronchitis, and pneumonia were diagnosed in 15 cases.

The high range of ASTA values is quite well understood,

TABLE 3
Atopic Eczema (Prurigo Besnier).

		Male	Female	Total	Per cent
AST	< 200	155	294	449	51
	200—399	92	123	215	49
	400—799	92	75	167	
	800 >	27	30	57	
	Total	366	522	888	25
ASTA	> 2.0	186	269	455	51
	2.0—3.9	110	175	285	49
	4.0—7.9	55	61	116	
	8.0 >	15	17	32	
	Total	366	522	888	17
ESR > 12 mm		91	160	251	
Bact. cultures	Strept. nonhaem.	7	3	10	
	Strept. α -haem.	4	8	12	
	Strept. β -haem. (non A)	2	—	2	
	Strept. β -haem. A	22	20	42	
	Staph. aureus	154	214	368	
	Staph. albus	26	36	62	
Total		215	281	496	56
Focal infections	Tonsillitis	19	36	55	
	Otitis	7	12	19	
	Sinuitis	16	16	32	
	Dental foci	20	29	49	
	Other foci	5	10	15	
Total		67	103	170	19

considering the frequent invasion of *Staph. aureus* into the scratched skin. The high range of AST, however, is somewhat surprising. It is probably due to the numerous nasopharyngeal or respiratory infections. It may well be presumed that these infections had aggravated the patients' prurigo and thereby initiated a need for treatment about the time when the antistreptococcal titres had reached their climax.

TABLE 4

Non-Determined Chronic Eczema (Eczema chronicum non determ.).

		Male	Female	Total	Per cent	
AST	<200	63	49	112	56	17
	200—399	38	16	54	44	
	400—799	15	11	26		
	800>	5	3	8		
	Total		121	79		
ASTA	>2.0	44	47	91	45	26
	2.0—3.9	37	20	57	55	
	4.0—7.9	21	8	29		
	8.0>	19	4	23		
	Total		121	79		
ESR > 12 mm		60	39	99		
Bact. cultures	Strept. nonhaem.	1	1	2		
	Strept. α -haem.	3	2	5		
	Strept. β -haem. (non A)	2	—	2		
	Strept. β -haem. A	10	2	12		
	Staph. aureus	49	27	76		
	Staph. albus	8	8	16		
Total		73	40	113	57	
Focal infections	Tonsillitis	—	2	2		
	Otitis	—	—	—		
	Sinuitis	1	—	1		
	Dental foci	5	3	8		
	Other foci	8	4	12		
	Total		14	9	23	12

Non determined chronic eczema (Eczema chronicum non determ.) (Table 4)

121 males, 79 females, 200 cases in all. Mean age 52 years.

This is a heterogenous group of very chronic eczemas, partly contact allergic, partly probably infectious eczemas. Some of the eczemas were localized only to circumscribed

areas (hands and feet), in other cases large areas were involved.

AST ≥ 200 in 88 (44 per cent), ≥ 400 in 34 (17 per cent), and ≥ 800 in 8 cases (4 per cent). ASTA ≥ 2.0 in 109 (55 per cent), ≥ 4.0 in 52 (26 per cent), and ≥ 8.0 in 23 cases (12 per cent). ESR > 12 mm in 99 cases.

Cultures from the skin showed *Staph. aureus* in 76 cases, *Staph. albus* in 16, and β -hemolytic streptococci in 14 cases (strain A in 12).

Focal infections were mentioned in 23 cases (12 per cent). Two patients suffered from tonsillitis, 8 of dental foci.

As can be seen from Table 4, raised AST and ASTA values are frequently found in the very chronic eczemas. The range of raised ASTA is in this series equally high in disseminated and circumscribed cases.

Dyshidrotic eczema (Eczema dyshidrosiforme)

80 males, 53 females, 133 cases in all. Mean age 39 years.

AST ≥ 200 in 66 (50 per cent), ≥ 400 in 33 (25 per cent), and ≥ 800 in 6 cases. ASTA ≥ 2.0 in 39 (29 per cent), ≥ 4.0 in 18 (14 per cent), and ≥ 8.0 in 2 cases. ESR > 12 mm in 37 cases.

Cultures from the skin revealed *Staph. aureus* in 53 cases, *Staph. albus* in 6. Streptococci were comparatively often found, i.e. in 26 cases (*Strept. β -haemolyticus A* in 13 cases). Even from the high range of raised antistreptolysin titres (50 per cent of cases) it seems justified to ascribe to the streptococci a more prominent role than in other eczema groups.

Focal infections were found in 26 cases (20 per cent): Tonsillitis in 2, sinusitis in 4, otitis in 1, dental foci in 15, and other foci in 4.

Microbial eczema (Eczema infectiosum) (Table 5)

437 males, 229 females, 666 cases in all. Mean age 45 years.

TABLE 5
Microbial Eczema (Eczema infectiosum).

		Male	Female	Total	Per cent	
AST	<200	237	120	357	54	
	200—399	95	54	149	46	24
	400—799	66	37	103		
	800>	39	18	57		
	Total		437	229	666	
ASTA	>2.0	287	158	445	67	
	2.0—3.9	97	51	148	33	11
	4.0—7.9	44	14	58		
	8.0>	9	6	15		
	Total		437	229	666	
ESR	> 12 mm	229	167	396		
Bact. cultures	Strept. nonhaem.	16	7	23		
	Strept. α -haem.	10	14	24		
	Strept. β -haem. (non A)	6	7	13		
	Strept. β -haem. A	48	10	58		
	Staph. aureus	226	150	376		
	Staph. albus	45	24	69		
Total		351	212	563	85	
Focal infections	Tonsillitis	17	10	27		
	Otitis	13	10	23		
	Sinuitis	25	7	32		
	Dental foci	47	19	66		
	Other foci	31	20	51		
	Total		133	66	199	30

AST $\geq$ 200 in 309 (46 per cent), and $\geq$ 400 in 160 (24 per cent). AST $\geq$ 800 was found in 57 cases (9 per cent). ASTA $\geq$ 2.0 in 221 (33 per cent), and $\geq$ 4.0 in 73 (11 per cent). ESR > 12 mm in 396 cases.

In cultures from the skin surface β -hemolytic streptococci were grown in 71 (58 belonged to group A), *Staph. aureus* in 376, and *Staph. albus* in 69 cases.

Focal infections were present in 199 cases (in 30 per cent). Dental foci were found in 66, naso-pharyngeal infections in 59, and otitis in 23 cases. Other infections, 51 in all, comprised furunculosis, paronychia, bronchitis chronica, cholecystitis, osteomyelitis etc.

Nummular eczema (Eczema nummulara) (Table 6)

97 males, 74 females, 171 cases in all. Mean age 42 years.

AST ≥ 200 in 65 (38 per cent), ≥ 400 in 25 (15 per cent), and ≥ 800 in 6 cases. ASTA ≥ 2.0 in 46 (27 per cent) and ≥ 4.0 in 11 cases (only in males!). ESR > 12 mm in 65 cases.

β -hemolytic streptococci were grown from the skin in 4 cases, *Staph. aureus* was found in 39 cases.

Focal infections were very frequently found in this group, i.e. in 53 cases (in 31 per cent of the cases). Dental foci in 25, naso-pharyngeal infections in 18, otitis media in 3, and various other infections in 5 cases.

Seborrhoic eczema and intertrigo (Eczema seborrhoicum et intertriginosum) (Table 7)

251 males, 311 females, 562 cases in all. (293 were regarded as seborrhoic, 269 as intertrigo.) Mean age 50 years.

AST ≥ 200 in 205 (36 per cent), ≥ 400 in 67 (12 per cent), and ≥ 800 in 19 cases. ASTA ≥ 2.0 in 119 (21 per cent), and ≥ 4.0 in 29 cases (5 per cent).

Streptococci were cultivated from the skin in 74 cases (only in 11 cases *Strep. β -haemolyticus A*), *Staph. aureus* in 198 cases, and *Staph. albus* in 71. Diabetes was found in 30 out of the 269 intertrigo cases, and *Candida albicans* was grown from the lesions in 65 cases.

Focal infections were present in 82 cases (15 per cent). Dental foci were found in 33, tonsillitis in 11, sinuitis in 7, and chronic otitis media in 16 cases. (External otitis, common in seborrhoic patients, was not regarded as a focus.)

TABLE 6
Nummular Eczema (Eczema nummulare).

	Male	Female	Total	Per cent
AST				
<200	61	45	106	62
200—399	22	18	40	38
400—799	11	8	19	
800>	3	3	6	
Total	97	74	171	15
ASTA				
>2.0	63	62	125	73
2.0—3.9	23	12	35	27
4.0—7.9	8	—	8	
8.0>	3	—	3	
Total	97	74	171	6
ESR > 12 mm	40	25	65	
Bact. cultures				
Strept. nonhaem.	—	—	—	
Strept. α -haem.	1	1	2	
Strept. β -haem. (non A)	1	—	1	
Strept. β -haem. A	2	1	3	
Staph. aureus	20	19	39	
Staph. albus	8	2	10	
Total	32	23	55	32
Focal infections				
Tonsillitis	4	4	8	
Otitis	2	1	3	
Sinuitis	7	3	10	
Dental foci	15	10	25	
Other foci	6	1	7	
Total	34	19	55	31

Photodermatitis (Eczema solare)

44 males, 39 females, 83 cases in all. Mean age 44 years. All cases of photodermatitis are included in this group.

AST ≥ 200 in 38 (46 per cent), ≥ 400 in 13 (16 per cent), ≥ 800 in 5 cases. ASTA ≥ 2.0 in 24 (29 per cent), ≥ 4.0 in 5 (6 per cent), and ≥ 8.0 in 3 cases. ESR > 12 mm in 36 cases.

TABLE 7

Seborrhoic Eczema and Intertrigo (Eczema seborrhoicum et intertriginosum).

		Male	Female	Total	Per cent	
AST	<200	151	206	357	64	12
	200—399	64	74	138	36	
	400—799	26	22	48		
	800>	10	9	19		
	Total	251	311	562		
ASTA	>2.0	190	253	443	79	5
	2.0—3.9	43	47	90	21	
	4.0—7.9	16	10	26		
	8.0>	2	1	3		
	Total	251	311	562		
ESR	> 12 mm	96	181	277		
Bact. cultures	Strept. nonhaem.	6	30	36		
	Strept. α -haem.	7	18	25		
	Strept. β -haem. (non A)	1	1	2		
	Strept. β -haem. A	5	6	11		
	Staph. aureus	71	127	198		
	Staph. albus	30	41	71		
	Total	120	223	343	61	
Focal infections	Tonsillitis	4	7	11		
	Otitis	5	11	16		
	Sinuitis	3	4	7		
	Dental foci	16	17	33		
	Other foci	7	8	15		
	Total	35	47	82	15	

Cultures from the lesions showed *Staph. aureus* in 19, and *Staph. albus* in 11 cases. No β -hemolytic streptococci were found.

Focal infections were found in 15 cases (18 per cent), tonsillitis in 2, sinuitis in 1, dental foci in 7, and other infections in 5 cases.

TABLE 8

Stasis Dermatitis, Varicotic Leg Eczema and Ulcers (Eczema varicosum et ulcus cruris).

	Male	Female	Total	Per cent	
AST	<200	179	413	592	57
	200—399	69	161	230	43
	400—799	37	98	135	
	800>	27	54	81	
	Total	312	726	1038	21
ASTA	>2.0	171	465	636	61
	2.0—3.9	82	175	257	39
	4.0—7.9	42	64	106	
	8.0>	17	22	39	
	Total	312	726	1038	14
ESR > 12 mm	167	488	655		
Bact. cultures	Strept. nonhaem.	27	42	69	
	Strept. α-haem.	13	32	45	
	Strept. β-haem. (non A)	2	5	7	
	Strept. β-haem. A	20	30	50	
	Staph. aureus	145	395	540	
	Staph. albus	37	99	136	
	(Pseudomonas)	10	25	35	
	Total	244 (254)	603 (628)	847 (882)	82
Focal infections	Tonsillitis	4	14	18	
	Otitis	—	2	2	
	Sinuitis	4	3	7	
	Dental foci	14	29	43	
	Other foci	19	37	56	
	Total	41	85	126	12

Stasis dermatitis, varicotic leg eczema and ulcers (Eczema varicosum et ulcus cruris) (Table 8)

312 males, 726 females, 1038 cases in all. Mean age 52 years. This group consists of various leg eczemas (with or

TABLE 9

Exfoliative Erythrodermia. (Erythrodermia exfoliativa universalis).

		Male	Female	Total	Per cent	
AST	<200	35	17	52	45	} 42
	200—399	12	2	14	} 55	
	400—799	21	3	24		
	800>	24	1	25		
	Total		92	23	115	
ASTA	>2.0	30	17	47	41	} 41
	2.0—3.9	16	5	21	} 59	
	4.0—7.9	22	1	23		
	8.0>	24	—	24		
	Total		92	23	115	
ESR	> 12 mm	70	7	77		
Bact. cultures	Strept. nonhaem.	3	—	3		
	Strept. α -haem.	1	—	1		
	Strept. β -haem. (non A)	1	—	1		
	Strept. β -haem. A	4	—	4		
	Staph. aureus	39	11	50		
	Staph. albus	4	1	5		
Total		52	12	64		
Focal infections	Tonsillitis	1	—	1		
	Otitis	—	—	—		
	Sinuitis	—	—	—		
	Dental foci	8	3	11		
	Other foci	7	—	7		
	Total		16	3	19	18

without ulcers) due to postthrombotic, varicotic or cardiac stasis, as well as vascular failure on arteriosclerotic, diabetic or other basis. (55 patients suffered from diabetes, 22 males and 53 females had deep thrombosis.)

AST ≥ 200 in 446 (43 per cent), ≥ 400 in 216 (21 per cent), and ≥ 800 in 81 cases (8 per cent). ASTA ≥ 2.0 in

402 (39 per cent), ≥ 4.0 in 145 (14 per cent), and ≥ 8.0 in 39 cases. ESR > 12 mm in 655 cases.

Cultures from the lesions revealed *Staph. aureus* in 540 cases, β -hemolytic streptococci only in 57 cases (50 of these strains belonged to group A). *Pseudomonas aeruginosa* was grown in 35 cases. Focal infections were found in 126 cases (12 per cent): Dental foci in 43, naso-pharyngeal infections in 35.

The raised ASTA values are probably due to the chronic invasion of *Staph. aureus* into the lesions.

Exfoliative erythrodermia (Erythrodermia exfoliativa universalis) (Table 9)

92 males, 23 females, 115 cases in all. Mean age 58 years.

This is a clinically rather conform, but etiologically heterogeneous disease group with contact-allergic, atopic, seborrheic or "idiopathic" background. Malignancies were present in 10 cases.

AST ≥ 200 in 63 (55 per cent), ≥ 400 in 49 (42 per cent), and ≥ 800 in 25 cases (22 per cent). ASTA ≥ 2.0 in 78 (59 per cent), ≥ 4.0 in 47 (41 per cent), and ≥ 8.0 in 24 cases (21 per cent). ESR > 12 mm in 77 cases.

Staph. aureus was grown from the skin in 50 cases, *Staph. albus* in 5, and β -haemolytic streptococci in 5 cases.

Focal infections were mentioned only in 19 cases (18 per cent): Dental foci in 11, tonsillitis in one, and other infections in 7. Thus, the highly raised titres are probably due to the chronic invasion of bacteria into the damaged skin.

One patient, a 57-year-old man, showed quite exceptionally high titres. On Febr. 15th, AST was 89,600 units, ASTA 20.0 units, ESR 102 mm. On Febr. 28th, the AST was 25,600 units, and ESR 53 mm. On March 9th, the AST was 12,800, and ASTA 5.0 units. On March 30th, the AST was 3,200 units, ASTA 1.4 units, and ESR 35 mm. Cultures from the skin revealed *Strep. β -haemolyticus* A, *Staph. aureus*, *Proteus mirabilis* and *Pseudomonas*.

Circumscript neurodermatitis (Neurodermatitis circumscripta, Lichen chronicus Vidal)

59 males, 42 females, 101 cases in all. Mean age 50 years.

AST ≥ 200 in 39 (39 per cent), ≥ 400 in 14 (14 per cent). Only one patient had AST 800. ASTA ≥ 2.0 in 30 (30 per cent), ≥ 4.0 in 6 cases. ESR > 12 mm in 46 cases.

Cultures from the lesions revealed *Staph. aureus* in 30 cases, *Staph. albus* in 9, and streptococci in 5 cases (β -haemol. A in 2).

Focal infections were reported in 23 cases (Tonsillitis in 7, sinusitis in 2, dental foci in 5, other infections in 9).

Pustular bacterid (Andrews) (Pustulosis palmo-plantaris)

27 males, 24 females, 51 cases in all. Mean age 45 years.

AST ≥ 200 in 24 (47 per cent), ≥ 400 in 9 (18 per cent), and ≥ 800 in 3 cases. ASTA ≥ 2.0 in 22 (43 per cent), ≥ 4.0 in 11 (22 per cent), and ≥ 8.0 in 2 cases. ESR > 12 mm in 28 cases.

Cultures from the lesions revealed *Staph. aureus* in 18 cases, *Staph. albus* in 5, and *Strept. β -haemolyticus* in only 3 cases.

Focal infections were found in 16 cases (31 per cent): Sinusitis in 3, otitis media in 2, and dental foci in 10 cases. In one case the pustular lesions occurred in connection with a periappendicular abscess. Six of the 10 patients with dental foci showed raised ASTA values. The role of focal infections in connection with pustular bacterid has been pointed out a.o. by Epstein (3). It can, however, be seen in our series, that cases classified as dyshidrosiform eczema showed a higher range of raised AST but a lower range of ASTA than those which were clinically held as pustular bacterid.

Urticaria (acute and chronic) (Table 10)

218 males, 286 females, 504 cases in all. Mean age 37½ years.

AST ≥ 200 in 185 (37 per cent), and ≥ 400 in 61 (12

TABLE 10
Urticaria.

	Male	Female	Total	Per cent	
AST	<200	129	190	319	63
	200—399	57	67	124	37
	400—799	27	23	50	
	800>	5	6	11	
	Total	218	286	504	12
ASTA	>2.0	185	256	441	87
	2.0—3.9	27	28	55	13
	4.0—7.9	6	2	8	
	8.0>	—	—	—	
	Total	218	286	504	2
ESR > 12 mm	75	86	161		
Focal infections	Tonsillitis	12	14	26	
	Otitis	2	3	5	
	Sinuitis	12	9	21	
	Dental foci	21	24	45	
	Other foci	31	22	53	
	Total	78	72	150	30

per cent). AST ≥ 400 and ASTA ≥ 4.0 in 63 (13 per cent), and ≥ 4.0 in 8. ESR > 12 mm in 161 cases.

Focal infections in 150, i.e. in 30 per cent of cases. Dental foci were found in 45, tonsillitis in 26, sinuitis in 21 and otitis in 5 of the cases. Other infections, 53 in all, comprised acne, furunculosis, pyoderma, infectio acuta, pneumonia, cholecystitis, febris rheumatica etc.

As to the AST and ASTA range there was no significant difference between acute and chronic urticaria.

DISCUSSION AND CONCLUSIONS

If we consider AST ≥ 400 and ASTA ≥ 4.0 units as pathological values elevated AST values are found in only about 7 per cent and elevated ASTA values in only 0.5 per cent of

the control cases. The frequency of pathologically raised AST and ASTA titres is significantly higher than in controls in all the eczematous conditions. Erythrodermas showed the highest frequency, 42 per cent, of seropositive AST titres (≥ 400 units) of all eczematous dermatoses, followed by atopic and dyshidrosiform eczemas (25 per cent each), microbial eczemas (24 per cent), varicous leg eczemas (21 per cent), and pustular bacterids 18 per cent. In contact dermatitis raised AST (≥ 400) were seen in 14 per cent, and in the group of seborrhoic and intertriginous eczemas in 12.

Concerning the ASTA the high range of pathological titres is very impressive. Here again the highest percentage of pathological titres (ASTA ≥ 4.0) is seen in erythrodermas, i.e. in 41 per cent of the cases, in contrast to the 0.5 per cent found in control series. Rather high levels are seen also in the group of chronic eczemas (26 per cent), pustular bacterids (22 per cent), and in atopic eczemas (17 per cent of cases). Among other dermatoses treated at our Department of Dermatology only psoriasis guttata, erysipelas, scabies and papulonecrotic tuberculids have shown a higher range of raised AST than erythrodermas. In no other dermatoses have we seen ASTA titres as high as in erythrodermas or in chronic and atopic eczemas.

Cultures from the surface of the skin lesions revealed predominantly *Staph. aureus* in all eczema groups. β -hemolytic streptococci were obtained less frequently.

The ratio *Strept. β -haemolyticus* : *Staph. aureus* was :

in erythrodermia	1:10
atopic eczema	1:9
chronic eczema	1:5
infectious eczema	1:5
pustular bacterid	1:6
dyshidrosif. eczema	1:4
varicous leg eczema	1:9
contact dermatitis	1:15
nummular eczema	1:10

circumscript neurodermatitis	1:15
seborrhoic and intertrig. eczema	1:18

Focal infections were mentioned in the hospital records most frequently in pustular bacterid and nummular eczema (in 31 per cent each) and in infectious eczema (in 30 per cent), thereafter in neurodermatitis circumscripta (23 per cent), dyshidrosiform eczemas (20 per cent), atopic eczemas (19 per cent), and erythrodermas (18 per cent). They were somewhat less frequently noted in contact dermatitis and seborrhoic dermatitis (in 15 per cent each). In the group of undetermined chronic eczemas and in varicous leg eczemas focal infections were mentioned only in 12 per cent of the cases. They were, however, frequently found in urticaria (30 per cent of cases).

We are well aware of the fact that an analysis of prolonged series of titres—e.g. before and after treatment and cure of skin lesions or removal of foci—probably could give a better information than an analysis based on single or few titres. In a material of these dimensions it would, however, have been expensive and difficult to carry through.

On the basis of our experience we are inclined to attribute to both AST and ASTA a certain value on estimating the infect-allergic situation in eczematous and urticarial conditions.

When elevated titres are found, it is advisable to look for the cause, which may be either a hidden focus or the invasion of bacteria into the damaged skin, or both. An antibacterial therapy may be considered, too. It should be kept in mind, however, that the allergic state is a complicated one, depending on many factors. The focal infection or "focal allergy" should therefore be regarded merely as a link in a chain. In spite of that, the removal of infectious foci has in some cases—as shown by the clinical experience—been successful. Thus, antistreptolysin and antistaphylolysin determinations may serve as a valuable serological aid in the search for infectious components in the chain.

SUMMARY

Antistreptolysin (AST) and antistaphylolysin (ASTA) levels were determined 1955-1970 in 5600 cases of eczemas and 504 cases of urticaria in the hope to clarify the possible role of infect-allergic factors in these conditions. Attention was paid to the presence of focal infections and to the bacteriology of the eczematous skin lesions. An unselected group of 100 male and 100 female blood donors served as controls. Some of the "control persons" may well have had a tonsillitis in the past or a hidden focus. Thus the range of "normal" controls, $AST \geq 200$ in 28 per cent, $AST \geq 400$ in 7 per cent, as well as $ASTA \geq 2.0$ in 11 per cent, and $ASTA \geq 4.0$ in 0.5 per cent, may rather be regarded as somewhat too high. Considerably higher ranges of elevated titres were found in all the 12 eczematous groups studied, AST was frequently raised in urticaria, too. Cases of erythrodermia universalis, and chronic or atopic eczema showed raised antistreptolysin titres ≥ 200 units in 55, 44, and 49 per cent, and $AST \geq 400$ units in 42, 17, and 25 per cent, respectively. The range of raised antistaphylolysin titres ≥ 2.0 units was 59, 55, and 49 per cent, and for $ASTA \geq 4.0$ units 41, 26, and 17 per cent, respectively. In dyshidrosiform eczemas the AST was comparatively high, too, raised titres ≥ 200 in 50 per cent, and ≥ 400 units in 25 per cent of cases. Focal infections were most frequently mentioned in nummular and infectious eczemas, and in pustular bacterid (30-31 per cent). *Staph. aureus* was the predominating invader of the scratched and damaged skin.

The usefulness of AST and ASTA as a serological aid in the clinic is discussed.

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