0022-202X/79/7203-0131$02.00/0
THE JOURNAL OF INVESTIGATIVE DERMATOLOGY, 72:131-132, 1979

Vol. 72, No. 3
Printed in U.S.A.

HLA-Antigens and Contact Hypersensitivity

GÖSTA ROUPE M.D., LENNART RYDBERG M.D., AND GUNNAR SWANBECK M.D.

From the Department of Dermatology (GR and GS) and the Blood Centre (LR), University of Gothenburg, Sahlgren's Hospital, S-413 45 Gothenburg, Sweden

The HLA-A, -B, -C typing of 100 bricklayers was performed. 50 bricklayers had developed contact allergy to chromium while 50 were healthy bricklayers. The distribution of HLA antigens were equal in the 2 groups.

Many associations between HLA (human leukocyte antigen) type and disease have been established during the last years [1]. In several species the immune response has been shown to be genetically controlled. Thus, in guinea pigs and mice autosomal dominant genes were found to govern the antibody response to synthetic polypeptide antigens [2]. A genetic control of contact sensitivity in mice was also found by contact sensitization with picryl chloride [3], and in guinea pigs an association between such genes and delayed hypersensitivity skin reactivity has also been described [4]. In man the locus for production of a reaginic antibody has been found to lie outside the HLA-complex proper [5], while in guinea pigs and mice genes controlling antibody response and delayed hypersensitivity reactions seem to be linked to those controlling the major histocompatibility antigens [2,3].

In humans we have very little knowledge about association of liability to develop contact allergy with different genetic markers. Especially with regard to patients developing allergic contact dermatitis, it is essential to have a relevant control group as a coupled association otherwise may give rise to false positive results. We have therefore studied chromate allergy in bricklayers as it has been possible to find a control group matched with regard to age, sex and exposure to chromate.

HLA antigen frequency of 50 contact allergic bricklayers compared with 50 nonallergic bricklayers and with 500 healthy blood donors.

HLA	Allergic (n = 50) No.	%	Nonallergic (n = 50) No.	%	Blood donors (n = 500) No.	%	Relative risk compared to nonallergic
A 1	14	28	21	42	134	27	0.54
2	29	58	29	58	293	59	1.00
3	14	28	15	30	146	29	0.91
9(w23)	1	2	0	0	6	1	—
9(w24)	9	18	5	10	83	17	1.98
10(25)	2	4	5	10	25	5	0.38
10(26)	5	10	2	4	33	7	2.67
11	7	14	4	8	44	9	1.87
w19(29)	4	8	0	0	19	4	—
w30	1	2	2	4	17	3	0.49
w31	0	0	2	4	28	6	—
w32	2	4	4	8	18	4	0.48
w33	1	2	0	0	0	0	—
w19 UNS[a]	1	2	2	4	5	1	0.49
28	1	2	3	6	43	9	0.32
B 5	4	8	6	12	46	9	0.64
7	13	26	14	28	140	28	0.90
8	12	24	16	32	125	25	0.67
12	14	28	8	16	125	25	2.04
13	1	2	2	4	11	2	0.49
14	1	2	2	4	23	5	0.49
15	11	22	14	28	117	23	0.73
w16(w38)	0	0	0	0	3	1	—
w16(w39)	2	4	2	4	16	3	1.00
17	1	2	3	6	24	5	0.32
18	4	8	2	4	39	8	2.09
w21	2	4	2	4	11	2	1.00
w22	2	4	1	2	15	3	2.04
27	2	4	4	8	53	11	0.48
w35	4	8	4	8	63	13	1.00
37	4	8	3	6	17	3	1.36
40	9	18	10	20	95	19	0.88
w41	2	4	0	0	5	1	—
W47	0	0	0	0	1	0	—
TT*	0	0	0	0	2	0	—
Cw1	4	8	4	8	41	8	1.00
w2	2	4	3	6	47	9	0.65
w3	19	38	18	36	201	40	1.09
w4	6	12	5	10	77	15	1.23
w6	0	0	0	0	8	2	—

[a] Cells giving positive reactions with sera defining the w19-complex but with weak or uncertain reactions with sera defining the splits.

Manuscript received June 21, 1978; accepted for publication September 9, 1978

This work was supported by a grant from the Work Environment Fund.

Reprint requests to: Gösta Roupe, M.D., Department of Dermatology, University of Gothenburg, Sahlgren's Hospital, S-413 45 Gothenburg, Sweden.

Abbreviations:

HLA: human leukocyte antigen

MATERIALS AND METHODS

Patients

The study included 100 male bricklayers who had had their occupation for 5 yr or more. 50 of these had developed contact eczema to chromate while working as bricklayers, while the other 50 bricklayers had had no skin problems. The 2 groups were age-matched and the chromate allergy was determined by a positive chromium patch test (Trolle-Lassen, M. Pharm., Denmark).

Tissue Typing

Peripheral blood lymphocytes were separated from whole ACD-blood by the Ficoll-Isopaque density gradient centrifugation technique [6]. The separated lymphocytes were typed for 14 HLA-A, 20 B and 5 C-series antigens using the lymphocytotoxic microtechnique [7].

The HLA antigen frequencies obtained from 50 patch test positive bricklayers were compared with those of 50 bricklayers with negative patch test and with the HLA antigen frequencies of 500 healthy blood donors.

RESULTS

Phenotype antigen frequency of the patient group as compared with the controls is presented in the Table. A few HLA-antigens seem to carry an increased risk of developing contact allergy to chromium. No statistical difference was, however, obtained using X^2-analysis.

DISCUSSION

The present investigation shows no statistical difference with regard to HLA-ABC antigens in chromate allergic and nonallergic bricklayers. Even if the number of patients and controls studied had been doubled, with the same frequency of the HLA-ABC antigens, no statistical difference would have been obtained. We therefore do not regard determination of the studied HLA-ABC antigens as a useful predictive test for workers running a risk to develop contact sensitivity to chromate. Determination of relative risks on the basis of HLA frequencies seem to be of little value when no statistical difference is found.

We have not determined the frequencies of HLA-D and DR-antigens among the bricklayers. The genes for these antigens are probably more closely related to Ir genes than the genes for HLA-ABC antigens. We cannot by this study exclude an association between HLA-D or DR antigens and chromium allergy.

From a study in northern Sweden, Lidén et al [8,9] reported an overrepresentation of HLA-A3 and B7 and the combination of the 2 in a group of contact allergic patients. However, this study was not done with matched controls as in the present study.

REFERENCES

1. Svejgaard A, Platz P, Ryder LP, Staub-Nielsen L, Thomsen M: HL-A and disease associations—a survey. Transpl Rev 22:3–43, 1975
2. McDevitt HO, Benacerraf B: Genetic control of specific immune responses. Advan Immunol 11:31–74, 1969
3. Schultz LD, Bailey DW: Genetic control of contact sensitivity in mice: Effect of H-2 and non H-2 loci. Immunogenetics 1:570–583, 1975
4. Geczy AF, de Weck AL: Genetic control of sensitization to structurally unrelated antigens and its relationship to histocompatibility antigens in guinea-pigs. Immunology 28:331–342, 1975
5. Blumenthal MN, Amos DB, Noreen H, Mendell NR, Yunis EJ: Genetic mapping of Ir locus in man: Linkage to second locus of HL-A. Science 184:1301–1303, 1974
6. Thorsby E, Brattlie A: A rapid method for production of pure lymphocyte suspensions, Histocompatibility Testing. Munksgaard, Copenhagen, 1970, pp 655–656
7. Kissmeyer-Nielsen F, Kjerbye KE: Lymphocytotoxic microtechnique. Purification of lymphocytes by flotation, Histocompatibility Testing. Munksgaard, Copenhagen, 1967, pp 381–383
8. Liden S, Beckman L, Cedergren B, Göransson K, and Nyquist H: HLA antigens in allergic contact dermatitis. Acta Dermatovener (Stockh) Suppl 79, 53–56, 1978
9. Liden S, Beckman L, Cedergren B, Göransson K, and Nyquist H: HLA antigens in allergic contact dermatitis. J Invest Dermatol 70:231–232, 1978