# HLA-DR antigens in alopecia areata

## Preliminary report[1]

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**A study of 13 American Caucasians with alopecia areata of the universalis or totalis pattern showed a trend of increased frequency of HLA-DR4 and HLA-DR5. The association of HLA-DR4 and HLA-DR5 with alopecia areata was independent of the pattern of alopecia, age of onset, or the patient's origin or sex.**

**Index terms:** Alopecia areata • HLA antigens

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Alopecia areata is a hair-loss disease clinically observed as partial or complete alopecia with an increased frequency of dystrophic nails and atypical or premature whitening of the hair. Currently, it is thought to be an autoimmune disorder with immunoregulatory defects. This hypothesis has been supported by an increased association of alopecia areata with other autoimmune diseases such as pernicious anemia,[1] vitiligo,[2] autoimmune adrenal insufficiency,[1] Hashimoto's thyroiditis,[3] and atopic dermatitis.[4] Autoantibodies to thyroglobulin,[3] parietal cell,[1] adrenal cell,[1] thyroid cell,[5] and smooth muscle[6] have also been found in alopecia areata patients. In addition, therapeutic responses to immunosuppression and immunostimulation with such drugs as corticosteroids[1] and dinitrochlorobenzene[7] also support the hypothesis of an immunoregulatory defect.

Several previous studies to confirm a genetic marker for alopecia areata with HLA studies have been contradictory and inconclusive. Recently, the HLA-DR antigen locus on the human chromosome has been hypothesized to be the site of the immune response and the immunosuppressive gene. To determine if an association was present between HLA-DR antigen type and alopecia areata, we analyzed the frequency of HLA-DR antigens in 13 patients with alopecia areata of the totalis or universalis pattern.

### Methods

Thirteen American Caucasians with alopecia areata of the universalis or totalis pattern were tested for type of seven HLA-DR antigens by microdroplet cytotoxicity tests with the use of B lymphocytes. The control group consisted of 979 normal American Caucasians tested during a 1980 histocompatibility workshop.[8] The antigen frequencies were compared with use of the Poisson distribution analysis.

### Results

The data are presented in *Table 1*. In this group of patients, there was an increased frequency of HLA-DR4 ($p = 0.49$) and HLA-DR5 ($p = 0.28$). Although not statistically significant

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**Table 1.** Alopecia areata

| HLA-DR Antigen | No. patients with this antigen | Frequency | Control frequency |
|---|---|---|---|
| 1 | 3 | 0.231 | 0.200 |
| 2 | 3 | 0.231 | 0.253 |
| 3 | 1 | 0.077 | 0.222 |
| 4 | 7 | 0.538 | 0.273 |
| 5 | 6 | 0.462 | 0.194 |
| 6 | 5 | 0.385 | 0.236 |
| 7 | 0 | 0 | 0.072 |

Statistical analysis of the data revealed a trend toward an increased frequency of HLA-DR4 ($p = 0.49$) and HLA-DR5 ($p = 0.28$).

**Table 2.** Patient data

| Patient no. | HLA | Age of onset (yr) | Sex | Rheumatoid factor | Antimicrosomal antibodies | Elevated IgE (< 260 U/ml) |
|---|---|---|---|---|---|---|
| 1 | 3,5 | 58 | M | – | – | – |
| 2 | 2,5 | 22 | M | – | – | – |
| 3 | 2,5 | 37 | F | – | 1:100 | 28 |
| 4 | 2,5 | 16 | M | – | – | 153 |
| 5 | 5,7 | 44 | M | – | – | – |
| 6 | 4,7 | 4 | F | – | – | 249 |
| 7 | 4,7 | 41 | M | – | – | 14.6 |
| 8 | 4,5 | 25 | F | + | – | 102 |
| 9 | 4 | 27 | M | – | – | 57 |
| 10 | 1,4 | 30 | F | – | – | 226 |
| 11 | 1,4 | 19 | M | – | – | 16.3 |
| 12 | 4,7 | 2 | M | – | – | 368 |
| 13 | 1,7 | 10 | M | – | – | – |

due to the small number of patients investigated, these results are of interest because of the association of HLA-DR4 and HLA-DR5 with certain other autoimmune diseases.

## Discussion

Reported associations of HLA antigens in alopecia areata have included HLA-B12 in a Finnish population,[9] HLA-B18 in a Jerusalem population,[10] HLA-B40 in an American family,[11] and HLA-A2 in another American family.[11] Kuntz et al[12] showed a trend (though not statistically significant) toward an increased frequency of HLA-A9 and HLA-B8 in a West German population. There have been reports of associations between systemic lupus erythematosus and HLA-DR2 and HLA-DR3;[13] between dermatitis herpetiformis,[14] juvenile rheumatoid arthritis, diabetes mellitus, Sjogren's syndrome, myasthenia gravis,[8] and HLA-DR3; between Hashimoto's thyroiditis and HLA-DR5;[15] and between vitiligo,[16] adult rheumatoid arthritis,[8] and HLA-DR4. None of our patients had these diseases or gave a family history of them at the time of the study.

The HLA-DR type in these alopecia areata patients appeared to have no relationship to the age of onset of alopecia, sex, or response to therapy. There was no correlation with the patient's HLA-DR type and the presence or absence of rheumatoid factor, antimicrosomal antibodies, or elevated IgE levels (*Table 2*).

In agreement with a recent report by Frentz and Thomsen,[17] this preliminary study suggests a trend of an increased frequency of HLA-DR4 and HLA-DR5 antigens in patients with alopecia areata of the universalis or totalis pattern. In the future, a larger group of patients will be evaluated to substantiate these findings statistically.

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