

## Typing of HLA antigens in a child population with nephrosis syndrome

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Using the microlymphocytotoxicity test of Terasaki, HLA—A, B, Cw antigen typing was done for 37 antigens in 28 children with steroid-sensitive nephrosis and five children with steroid-resistant nephrosis. Evaluation was made by the  $\chi^2$  test as corrected by the method of Yeates.

In steroid-sensitive nephrosis the frequency of HLA—B 8 antigen was 33.3% and in the resistant cases 40% as against 18.5% in the controls. The difference, however, was not significant, the B 12 and B 13 antigens were more frequent in both steroid-sensitive and resistant nephrosis, though not significantly.

Infantile idiopathic nephrosis syndrome (NS) is an immune-pathological process. Thomson et al. [11] found the HLA—A 1/B 8 antigen combination (haplotype) and the HLA—B 12 antigen to be more frequent in atypical and non-atypical steroid-sensitive NS while other authors [6] found no connection between NS and HLA antigens. Noss et al. [7] demonstrated in minimal change NS (MCNS) a significant correlation with the HLA—B 8, 13 antigens and interpreted the greater frequency of B8 antigen as a confirmation of the immune origin of MCNS. These contradictory literary data have motivated a study of HLA antigens in child patients with nephrosis syndrome.

### MATERIALS AND METHODS

The patient population consisted of 23 children with NS; of these 18 had steroid-sensitive NS (SS—NS), and five steroid-

resistant NS (SR—NS). Kidney biopsy was performed in 15 patients; the diagnosis established on the basis of histology and immune fluorescence is given in Table I. In eight cases no kidney biopsy was performed, but the existence of idiopathic NS was based on the clinical picture and the laboratory findings. The SR—NS cases received chlorambucil and/or indometacin treatment after initial steroid therapy.

The diagnostic criteria of NS were a proteinuria of more than 2 g per day pronounced hypalbuminaemia, and oedema.

HLA—A, B, Cw antigen typing was carried out for 37 antigens by the microlymphocytotoxicity test of Terasaki [10]; 222 healthy blood donors serves as controls. The difference in the frequency of the various HLA antigens in NS as compared with the control group was calculated using Yeates's  $X^2$  correction test and giving the P value.

### RESULTS

Table I shows the HLA phenotypes of the SS—NS and SR—NS cases.

TABLE I  
HLA-phenotypes in nephrotic syndrome

Patient No.	SS-NS		Cw	Diagnosis
	HLA-A	B		
1.	3	7, 14		—
2.	w24, w31	w15, 53	3, 4	MCNS
3.	3, w23	12	4	MSGN
4.	— 3, w24	5, 12	2	—
5.	1, 28	8, 15	3	—
6.	2, 11	12, 27		
7.	1, 26	8, 35	4	MCNS
8.	1, w23	8, 13	2	MSGN
9.	1, 2	8, 13		MCNS
10.	1, 2	8, 18		
11.	1, 2	8, w50		MSGN
12.	2, 28	5, w50		
13.	2, w24	13, 18		
14.	11, 26	18, 22		MCNS + FSGS
15.	3, 9	12, 41		
16.	2, 11	35, 38		
17.	2, 11	12, 27		—
18.	3, 24	5, 12	2	

  

HLA-phenotypes in steroid-resistant nephrotic syndrome				
1.	2, 32	12, 15	3, 4	MPGN
2.	1	7, 8		MSGN
3.	2	27		MSGN
4.	1, 25	17, 35		MSGN
5.	2, w24	8, 18		MPGN

MCNS = minimal change NS

MSGN = mesangio-proliferative glomerulonephritis

MPGN = membranoproliferative glomerulonephritis

FSGS = focal segmental glomerular sclerosis

TABLE II  
Distribution of HLA-antigens in steroid-sensitive

HLA-A	SS-NS		SR-NS		SS-NS+SR-NS		Controls	
	n	per cent	n	per cent	n	per cent	n	per cent
1	6/18	33.3	2/5	40	8/23	34.8	49/222	22.1
2	9/18	50.0	3/5	60	12/23	52.2	110/222	49.5
3	4/18	22.2	0/5	0	4/23	17.4	43/222	19.4
9	1/18	5.6	0/5	0	1/23	4.3	55/222	24.77
11	4/18	22.2	0/5	0	4/23	17.4	33/222	14.9
23	2/18	11.1	0/5	0	2/23	8.7	23/222	10.36
w24	4/18	22.2	1/5	20	5/23	21.7	32/222	14.4
25	0/18	0	1/5	20	1/23	4.3	19/222	8.5
26	2/18	11.1	0/5	0	2/13	8.7	24/222	10.8
28	2/18	11.1	0/5	0	2/23	8.7	22/222	9.9
w31	1/18	5.6	0/5	0	1/23	4.3	6/222	2.1
32	0/18	0	1/5	20	1/23	4.3	13/222	5.8

Table II shows the occurrence of HLA antigens in SS-NS and SR-NS patients separately and in both groups together, with absolute numbers and percentage, the results of the  $\chi^2$  test and P values as compared to the values of the control group. The frequency of the various HLA-A (Table II) and HLA-B antigens (Table III) was also compared between the SS-NS and the SR-NS groups.

The frequency of HLA-B 8 was 33.3% in SS-NS and 40% in SR-NS; it was 34.8% in both groups together as against 18.5% in the controls, but the difference was not significant in any of the groups. Neither was there a significant difference in the occurrence of HLA antigens in SS-NS and SR-NS.

The frequency of B 12 antigen was 33.3% in SS-NS, 20.4% in SR-NS, and 30.4% in the whole material. The difference from the 19.8% of the control group was not significant.

The frequency of B 13 antigen was higher in the SS-NS group (16.7%) than in the control group (8.1%), but it was 0% in the SR-NS group, and 13% in the whole material. The differences between the groups were not significant.

## DISCUSSION

Le Petit et al. [4] found a connection with the HLA-DR 3 antigen in idiopathic membranous nephritis (IMN), but Alfiler et al. [1] were the first to report on a significantly higher frequency of HLA-DR w 7 antigen in 5 R-NS, namely 71% vs 29.8% in the [controls. Nunez-Roldan et al. [8] confirmed this higher frequency of HLA-DR 7 in SS-NS and the low frequency of antigen DR 2. Noss et al. [7] underlined the significantly higher frequency of Aw 30/31 in MCNS (20% as against 5.4% in the controls). Still, on the basis of the findings of Bertrams and

and steroid-resistant nephrotic syndrome

SS-NS-SR-NS		SS-NS-Controls		SR-NS-Controls		SS-NS+SR-NS-Controls	
X <sup>2</sup>	P	X <sup>2</sup>	P	X <sup>2</sup>	P	X <sup>2</sup>	P
0.06	0.99	0.64	0.41	0.17	0.63	1.24	0.27
0.01	0.99	0.04	0.99	0.00009	0.99	0.0004	0.99
0.24	0.99	0.0002	0.99	0.26	0.69	0.002	0.99
0.49	0.99	2.44	0.096	0.56	0.49	3.84	0.03
0.24	0.99	0.24	0.99	0.08	0.99	0.0003	0.99
0.01	0.99	0.09	0.99	0.00009	0.99	0.01	0.99
0.26	0.99	0.3	0.99	0.08	0.99	0.39	0.5
0.49	0.99	0.7	0.42	0.009	0.99	0.09	0.9
0.01	0.99	0.12	0.99	0.001	0.99	0.001	0.99
0.01	0.99	0.06	0.99	0.0005	0.99	0.03	0.99
0.49	0.99	0.001	0.99	1.07	0.21	0.04	0.99
0.49	0.99	0.26	0.7	0.13	0.84	0.03	0.99

TABLE III  
HLA-antigens in steroid-sensitive and steroid resistant nephrotic

HLA—B	SS—NS		SR—NS		SS—NS+SE—NS		Controls	
	n	per cent	n	per cent	n	per cent	n	per cent
5	3/18	16.7	0/5	0	3/23	13.0	28/222	12.6
7	1/18	5.6	1/5	20	2/23	8.7	30/222	13.5
8	6/18	33.3	2/5	40	8/23	34.8	41/222	18.5
12	6/18	33.3	1/5	20	7/23	30.4	44/222	19.8
13	3/18	16.7	0/5	0	3/23	13.0	18/222	8.1
14	1/18	5.6	0/5	0	1/23	4.3	15/222	6.7
15	2/18	11.1	1/5	20	3/23	13.0	16/222	7.2
17	0/18	0	1/5	20	1/23	4.3	18/222	8.1
18	3/18	16.7	1/5	20	4/23	17.4	34/222	15.3
22	1/18	5.6	0/5	0	1/23	4.3	12/222	5.4
27	2/18	11.1	1/5	20	3/23	13.0	29/222	13.1
38	3/18	5.6	0/5	0	1/23	4.3	10/222	4.5
w35	2/18	11.1	1/5	20	3/23	13.0	50/222	22.5
41	1/18	5.6	0/5	0	1/23	4.3	5/222	2.25
53	1/18	5.6	0/5	0	1/23	4.3	—	—
50	2/18	11.1	0/5	0	2/23	8.7	5/222	2.25

Baur [2], they considered the higher frequency of HLA—A w 30/31 a secondary phenomenon in view of their frequent linkage to the B 13 antigen.

Unlike the mentioned authors, we detected HLA—Aw 31 antigens in a single case only and we found no Aw 30 antigens in any of our cases.

The frequent occurrence of the haplotype Al/B8 is well-known in several well-defined immune pathological processes [3, 5, 9].

Comparing the frequency of HLA—B antigen found by the above authors [1, 4, 7] with the values found by us, it is seen that in the SR—NS material of Alfiler et al. [1] the antigens HLA—B8, 12 and 13 showed no significant increase; in the MCNS material of Noss et al. [7] B8 antigen with a frequency of 42.2% against 20.5% in the controls, and B 13 antigen with 20% against 4.3% of

the controls, were significantly more frequent, in the IMN material of Le Petit et al. [4] B8 with 53.4% against 14.4% in the controls was also significantly more frequent. Although in our material the antigens B8, 12 and 13 also occurred in a higher than usual percentage, their frequency level was not significant. Further investigations are necessary to clarify the correlation between HLA antigen and the different types of NS.

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## syndrome-cases

SS-NS-SR-NS		SS-NS-Controls		SR-NS-Controls		SS-NS+SR-NS-Controls	
X <sup>2</sup>	P	X <sup>2</sup>	P	X <sup>2</sup>	P	X <sup>2</sup>	P
0.05	0.99	0.02	0.99	0.02	0.99	0.07	0.99
0.01	0.99	0.36	0.58	0.06	0.99	0.11	0.74
0.06	0.99	1.49	0.23	0.4	0.48	2.52	0.11
0.0006	0.99	1.12	0.29	0.31	0.59	0.85	0.64
0.05	0.99	0.64	0.4	0.03	0.99	0.01	0.91
0.49	0.99	0.08	0.99	0.09	0.99	0.000003	0.99
0.05	0.99	0.02	0.99	0.04	0.99	0.34	0.56
0.49	0.99	0.63	0.46	0.01	0.99	0.05	0.81
0.24	0.99	0.03	0.99	0.11	0.99	0.001	0.99
0.49	0.99	0.26	0.99	0.22	0.99	0.2	0.66
0.05	0.99	0.02	0.99	0.04	0.99	0.1	0.75
0.49	0.99	0.15	0.99	0.38	0.8	0.0009	0.99
0.05	0.99	0.69	0.41	0.16	0.99	0.62	0.56
0.49	0.99	0.11	0.99	0.5	0.7	0.27	0.61
0.49	0.99	—	—	—	—	—	—
0.01	0.99	2.02	0.18	1.44	0.24	1.23	0.27

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