stronger association with All, BW35 and B40. Especially the combinations of All+BW35 and BW35+B40 were significantly raised in high anti DNA antibody group as shown in Fig. 1.

In other connective tissue diseases,

significant associations of B7, DW1 and DW2 with MCTD and DW3 with Sjogren's syndrome were observed although none of HLA-types were significantly associated with patients with PSS and PM.

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—Heart Valvular Disease and Aortitis Syndrome—

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The frequency of HLA-A and B locus antigens in 130 patients with heart valvular disease and 53 patients with aortitis syndrome was compared with that of 225 normal persons. The conclusion was as follows. 1) Mitral stenosis was associated with HLA-B7 (RR=3.3, X^2 ; 9.1, $P<0.003$). This association was stronger in male than female patients (male RR; 5.2, female RR; 2.4). 2) Aortitis syndrome was associated with HLA-Bw52 (RR; 4.5, X^2 ; 8.62, $P<0.004$). This association was confined to female patients (female RR; 3.5, male RR; 1.1).

The association of HLA with subgroup of rheumatic valvular disease (RHD) and aortitis syndrome has been reported by us. We continue to try to increase the number of patients HLA-typed and to find the definite and more significant association. In this report the reanalysed data and some new findings will be presented.

MATERIALS AND METHODS

One hundred and thirty patients with heart valvular disease were classified clinically and sexually into 8 subgroups; total rheumatic valvular disease (RHD) total mitral stenosis (MS), female MS, male MS, total aortic valvular disease (AVD), rheumatic AVD, total mitral regurgitation (MR), and rheumatic MR. All patients were diagnosed at the Second Department of Internal Medicine and the Department of Cardiac Surgery of Fukuoka

University Hospital, using patient's history physical examination, chest X-ray film, ECG. PCG, UCG, cardiac catheterization, cardiovascularography and records at cardiac surgery.

Forty three female and 10 male (total=53) patients with aortitis syndrome from the Second Department of Internal Medicine of Fukuoka University Hospital and the Cardiovascular Clinic and the Second Department of Surgery of Kyushu University Hospital were reviewed by medical records.

All the patients and 225 normal controls were HLA typed for HLA-A and B locus antigens. Five A locus specificities, A2, A9, A10 All and Aw19, and 8 B locus specificities, B5, B7, B12, B15, Bw16 broad Bw22, Bw35 and B40 complex were determined in the present study, because they were common among Japanese. Twenty two patients with aortitis syndrome and 102

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normal persons were determined for the splits of HLA-B5; Bw52 and 51, in order to know which split of B5 has association with aortitis.

Frequency of each specific HLA antigen was calculated on each patient and control group. In order to compare the frequency of HLA antigen between patient group (and subgroup) and normal controls, relative risk and X^2 of specific HLA antigen in each particular group was determined.

RESULTS

In case of HLA-A locus antigens, lower occurrence of HLA-A9 in MR group was only weakly significant among heart valvular disease subgroup, as shown in Table 1. The higher occurrence of HLA-A10 in AVD group reported previously was disappeared in the present series, although the tendency of frequent A2 in MR and A9 in MS was still recognized. Table 1 also shows the higher frequency of A9 in aortitis group especially among female patients.

The rule that HLA-B locus antigens are more closely related to most of diseases than A locus antigens is compatible with the present study as clearly shown in Table 2. Among heart valvular groups, HLA-B7 in total RHD total and male MS

Table 1. Comparizon (Relative Risk: RR and X^2) of frequency of HLA-A locus antigens between patients and controls

	N	A2		A9		A10		A11		Aw19	
		RR	X^2	RR	X^2	RR	X^2	RR	X^2	RR	X^2
total RHD	109	1.3	0.6	0.9	0.1	0.8	0.6	1.0	0.0	1.3	0.5
total MS	60	1.4	0.9	1.7	2.1	0.5	2.5	1.0	0.1	0.9	0.2
female MS	40	1.6	1.3	1.9	1.9	0.5	2.7	1.0	0.0	1.0	0.1
male MS	20	1.1	0.0	1.4	0.1	0.7	0.6	0.8	0.3	0.8	0.5
total AVD	35	0.6	1.7	0.8	0.5	0.9	0.3	1.7	0.9	1.1	0.0
rheumatic AVD	26	0.7	1.0	0.8	0.7	0.8	0.6	1.1	0.0	1.2	0.0
total MR	27	2.0	2.2	0.5	4.9*	1.2	0.0	0.6	1.1	2.4	2.3
rheumatic MR	15	2.4	1.8	0.3	6.0*	1.0	0.0	1.2	0.1	1.7	0.1
total aortitis	53	0.8	0.6	2.1	3.1	0.4	3.7	1.0	0.0	0.9	0.2
female aortitis	43	0.9	0.4	3.0	5.0*	0.4	3.3	0.6	1.3	0.7	0.8
male aortitis	10	1.1	0.0	0.7	0.7	0.5	1.3	3.2	1.9	1.7	0.0
control	N=225	+	+	+	+	+	+	+	+	+	+
		87	138	152	73	44	181	39	186	29	196

*P < 0.05 (uncorrected) RHD: rheumatic valvular disease
MS: mitral stenosis AVD: aortic valvular disease
MR: mitral regurgitation

occured more frequently with statistical significance. The most close relation with B7 was obtained in group of male patient with MS. The significantly lower occurrence of B40 complex in MR group was also noticed as in the previous series. The lesser frequency of Bw35 in female patients with MS was obtained with weak statistical significance.

The highly significant occurrence of HLA-B5 in aortitis syndrome was presented in Table 2. However, it seems to be confined to female patients with aortitis. Male patients with aortitis might be related at least in part with Bw16 (or BwSN-2 according to the data not pre-

Table 2. Comparizon (Relative Risk: RR and X^2) of frequency of HLA-B locus antigens between patient and controls

	N	B5		E7		B12		B15		Bw16		Bw22		Bw35		B40 complex	
		RR	X^2	RR	X^2	RR	X^2	RR	X^2	RR	X^2	RR	X^2	RR	X^2	RR	X^2
total RHD	109	1.3	0.9	2.9	10.3**	1.3	0.3	1.3	0.3	0.6	1.5	0.8	0.9	0.6	2.8	0.6	5.3*
total MS	60	1.3	0.5	3.2	9.1**	1.2	0.0	0.5	2.2	0.6	0.9	1.1	0.0	0.4	3.7	0.8	0.7
female MS	40	1.4	0.6	2.4	2.9	1.2	0.0	0.6	1.3	0.3	2.2	0.9	0.2	0.3	3.8*	1.0	0.0
male MS	20	1.1	0.0	5.2	9.5*	1.2	0.0	0.4	1.8	1.4	0.0	1.5	0.2	0.6	0.9	0.6	1.9
total AVD	35	1.8	2.1	1.3	0.0	0.3	2.2	2.4	3.3	1.2	0.0	0.6	1.6	0.3	3.1	0.6	3.0
rheumatic AVD	26	2.0	2.1	1.3	0.0	0.4	1.5	2.6	3.0	1.0	0.1	0.3	3.9	0.5	1.7	0.5	3.7
total MR	27	1.2	0.0	1.7	0.3	2.5	1.7	2.5	2.6	0.5	1.2	0.4	2.5	2.4	2.6	0.2	9***
rheumatic MR	15	0.9	0.3	3.5	2.8	3.9	3.4	2.6	1.3	0	2.6	1.3	0.2	1.4	0.0	0.2	8.4*
total aortitis	53	2.8	10.3**	0.2	4.3*	2.5	3.9*	0.6	1.5	1.9	1.0	0.9	0.1	0.1	8.0	0.3	12.6***
female aortitis	43	3.5	12.6**	0	5.7	2.5	3.0	0.7	0.7	0.9	0.2	0.9	0.1	0	8.8	0.3	12.2***
male aortitis	10	1.1	0.0	1.1	1.0	2.7	1.3	0	2.8	8.2***	8.7***	0.9	0.3	0.6	0.8	0.5	2.5
control	N=225	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
		83	142	21	204	19	206	28	197	17	208	50	175	34	191	109	116

*P < 0.05 ***P < 0.005 ****P < 0.001 (all uncorrected) RHD: rheumatic valvular disease
MS: mitral stenosis AVD: aortic valvular disease MR: mitral regurgitation

sented). The significantly lesser frequency of B40 complex and Bw35 in aortitis group might express mirror image of the increase of HLA-B5. According to the typing data of the splits of HLA-B5 in 22 patients with aortitis and 102 normal controls, the HLA-Bw52 was found out as the antigen related with aortitis syndrome (patient; 52% control; 25%, relative risk; 4.45, X^2 ; 8.62, $P < 0.005$).

DISCUSSION

The results of the present series were considered to be essentially the same as previous ones, though there were minor differences. The new finding of present heart valvular disease series was definitely significant association of HLA-B7 with MS, especially with male patients with MS. Other findings need the increase of the number of patients diagnosed correctly.

Although the previous report already pointed out the close relation of HLA-Bw52 with aortitis syndrome especially with female patients, the present result verified

it clearly and supported the report by others. The positive and very high linkage disequilibrium of A9-Bw52 among Japanese population reasonably supports the present conclusion and might explain the more frequent occurrence of aortitis syndrome among Japanese than Westerners. The previous suggestion that male aortitis syndrome might not be correlated with HLA-Bw52 became more likely in the present report, because 10 male patients with aortitis were never frequent in B5 (relative risk; 1.14, X^2 ; 0.02) and frequent in Bw16 (relative risk; 8.16, X^2 ; 8.72). This was also supported by the fact that identical female sib's with aortitis syndrome had both same HLA Phenotype with Bw52 (A2, Aw31, Bw22, Bw52), but male sib's pair with aortitis syndrome were completely different each other in the view of haplotype (patient 1: A2, A9, B15, Bw35, Cw3, patient 2: A9, A11, Bw52, Bw54, Cw1, father: A9, Bw35, Bw52, Cw3, mother: A2, A11, B15, Bw54, Cw1).

Supplementary: Genetic Factor in Takayasu Disease

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Takayasu disease is characterized by a pulseless condition which most often occurs in young females from Asian or South American areas. The cause of this disease remains obscure. Recently we encountered monozygotic, Japanese identical twin sisters, both of whom were diagnosed as having Takayasu disease (Circulation 58: 173, 1978). A population study on HLA typing analyses in A and B loci of 65 patients with Takayasu disease revealed a

high frequency of HLA A10 and B5 as compared with 128 healthy Japanese (x^2 : 15.3, $p < 10^{-4}$, 17.0, $p < 10^{-4}$) and we postulated that was probably a genetically related factor in the pathogenesis of Takayasu disease (Amer Heart J 98: 153, 1979). Subgroups of B5, BW51 and BW52 and D locus antigens were successively studied in 75 patients. BW52 and DHO antigens were confirmed in 44% and 40% of patients, a statistically significant frequency with the