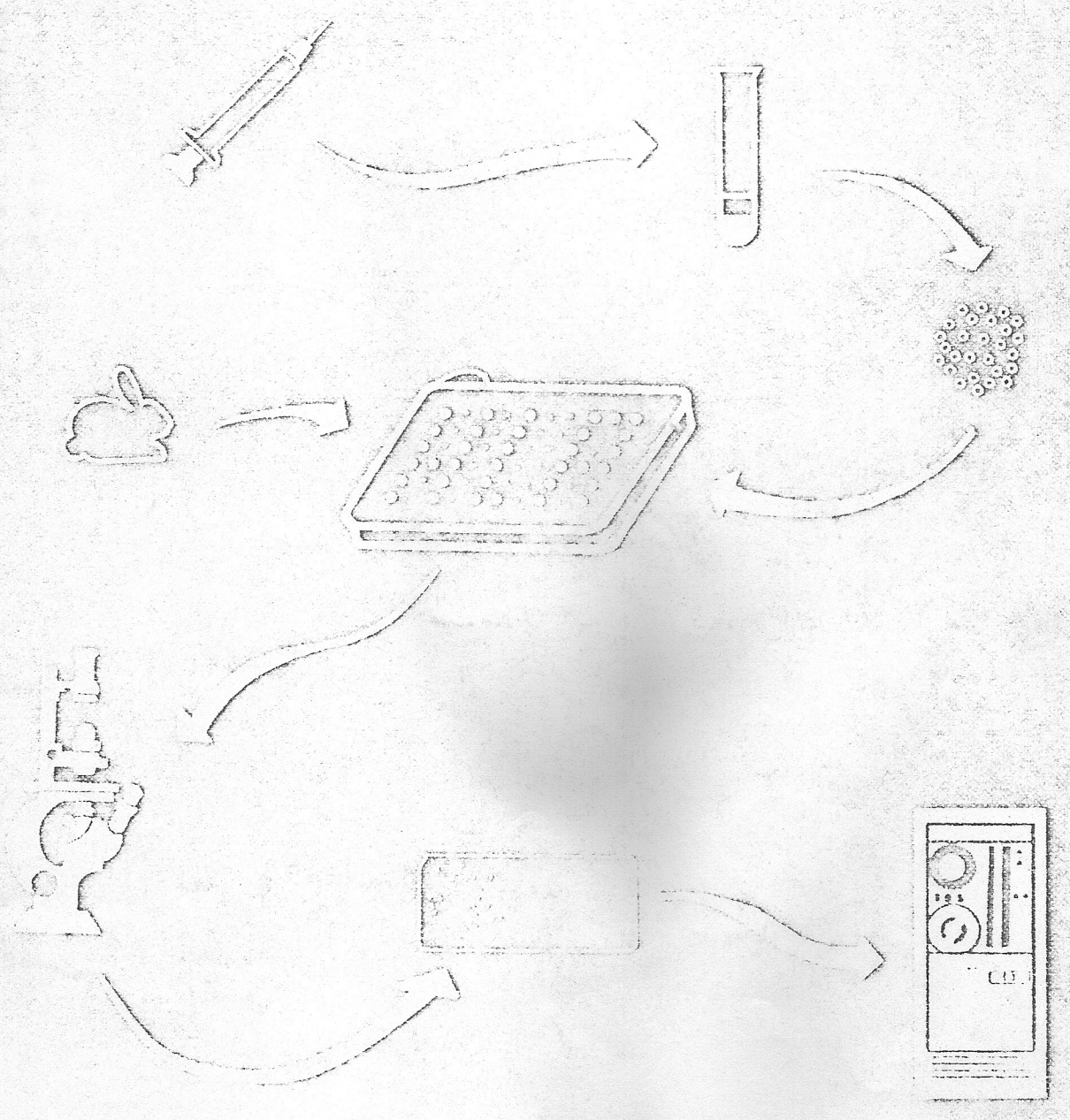
Histocompatibility Testing 1980



HLA COMPLEX IN WERNER'S DISEASE

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During the 8th International Workshop, we studied family 01, where five patients with Werner's disease were identified in the first generation. Werner's Syndrome is a rare entity (1,2), with a recessive pattern of inheritance (3), where consanguinity between parents is expected to be increased. In our family we found that individuals 300 and 301 were first cousins (Fig. 1). It is relevant at this point to report that this family comes from Quibor, a small town in Venezuela, where a group of German immigrants settled in the middle of the 19th century, creating a highly inbred population. Quibor still maintains some German characteristics in architecture, habits, and people with Caucasian features.

Due to the fact of an inherited recessive disease, we typed 30 individuals within this family for the HLA-A,B,C, and DR loci, looking for disease genes linked to the HLA complex (Fig. 1). Eleven different haplotypes were clearly defined in Table 1 and genotypes on patients, normal siblings, and parents are in Table 2. We could not identify transmission of the disease gene by given HLA haplotypes, since patients' genotypes are *ac, ad,* and *bd,* and normal siblings *ac* and *ad* (Table 2).

It is surprising to find 'missing antigens' for C and DR loci in haplotypes *a* and *c,* in individuals 401, 407, and 408 when these antigens are clearly defined in their children (Tables 3,4).

Again, there are 'missing antigens' in child 408. We repeatedly failed to demonstrate them in at least two tissue types from different bleedings.

AW31 antigen is present in haplotype *c,* giving constant strong reactions with sera 526 and 351, which were reported by Bernoco to give positive reactions with both AW30 and AW31 antigens. The same pattern was observed with serum 234. Serum 294 was found to have antibodies for AW33, AW34, and some A26 in pretesting; these three antigens are absent in family 01 and consistently strong positive reactions were found in this family, probably due

Table 1.

HLA HAPLOTYPES IDENTIFIED IN FAMILY 01

a	A11; Bw35; Cw4; DRw1.
b	A9; B15; Cw3; DRw--.
c	Aw31; B12; Cw6; DRw6.
d	A2; B41; Cw--; DRw4.
e	Aw30; B7; Cw--; DRw2.
f	A29; B5; Cw--; DRw6.
g	A9(Aw24); Bw35; Cw1; DRw4.
h	Aw31; B--; Cw6; DRw--.
i	A--; B12; Cw--; DRw8.
j	A2; Bw47; Cw3; DRw4.
k	A9(Aw23); B5; Cw1; DRw7.
l	A2; Bw35; Cw1; DRw4.
n	A2; B5; Cw--; DRw3.
s	A9(Aw24); B5; Cw--; DRw5.
t	A2; B5; Cw3; DRw4.

Table 2.

Parent 1:	A11;Bw35;Cw4;DRw1 / A9;B15;Cw3;DR--	a / b	
Parent 2:	Aw31;B12;Cw6;DRw6 / A2; B41;C--;DRw4	c / d	
Sib. 401:	A11;Bw35;C--;DRw1 / Aw31;B12;Cw6;DRw6	a / c	Cw4 missing in a.
*Sib. 408:	A11;Bw35;Cw4;DRw1 / Aw31;B12;Cw6;DR--	a / c	DRw6 missing in c.
*Sib. 402:	A11;Bw35;Cw4;DRw1 / A2;B41;C--;DRw4	a / d	
*Sib. 404:	A11;Bw35;Cw4;DRw1 / A2; B41; C--;DRw4	a / d	
Sib. 407:	A11;Bw35;Cw4;DR-- / A2; B41;C--; DRw4	a / d	DRw1 missing in a.
*Sib. 403:	A9; B15;Cw3;DR-- / A2; B41; C--;DRw4	b / d	
*Sib. 406:	A9; B15;Cw3; DR-- / A2; B41;C--; DRw4	b / d	

*Werner's Disease.

Table 3.

407 (father):	A11;Bw35;Cw4;DR-- / A2; B41; C--;DRw4	a / d	DRw1 missing in a
307 (mother):	A2;Bw35;C--;DRw4 / A2; B5; C--;DRw3	l / n	Cw1 missing in l
Children:			
621 :	A11;Bw35;Cw4;DRw1 / A2; Bw35;Cw1;DRw4	a / l	
622 :	A11;Bw35;Cw4;DRw1 / A2; B5; C--;DRw3	a / n	
623 :	A2; B41; C--;DRw4 / A2;Bw35;Cw1;DRw4	d / l	
620 :	A2; B41; C--;DRw4 / A2;Bw35;Cw1; DRw4	d / l	

to AW31. Table 5 shows individual reactions for AW31 antigen, being identified mainly by sera 526, 294, 234, and 351.

AW41 antigen, present in haplotype *d* was clearly defined by sera 758 and 166, both prescreened as 41 weak, while serum 748 gave 25% false negative reactions (three out of 12 BW41 individuals). The question arises as to whether we have a short or restricted BW41 antigen in this family.

Serum 183 was submitted as A10 and prescreened as A25, A26, AW34, AW33, A11 weak, and A28 weak. This serum reacted positive with 10/12 individuals carrying haplotype *a* (A11-BW35), and 4/6 carrying haplotype *b* (A9-B15). Since the incidence of A11 is rather low in our population (6%) we do not have any A11 individuals within our controls for this Workshop, therefore, we also wonder if serum 183 is recognizing some other restricted specificity within this family.

Finally, we would like to call attention to the fact reported here, in relation to 'missing antigens' on HLA-C and DR loci in either parental or children's haplotypes, since it could be of particular interest when testing for paternity.

REFERENCES

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Table 4.

408 (mother):	A11;Bw35;Cw4;DRw1 / Aw31;B12;Cw6;DR--	a / c	DRw6 missing in c.
310 (father): (not typed)	A9; B5; C--; DRw5 / A2; B5; Cw3; DRw4	s / t	
Children:			
625 :	Aw31;B12;C--;DRw6 / A9; B5; C--; DRw5	c / s	Cw6 missing in c.
626 :	Aw31;B12;C--;DR-- / A2; B5; Cw3; DRw4	c / t	Cw6 and DRw1 missing in c.
627 :	A11;Bw35;Cw4;DRw1 / A2; B5; Cw3; DRw4	a / t	
628 :	A9; B5; C--;DRw5 / Aw31;B12;C--;DRw6	s / c	Cw6 missing in c.

Table 5.

ID#	SERUM # 526	351	234	294
401	8	8	8	8
408	8	8	6	8
625	1	8	1	8
628	8	8	8	8

Figure 1.