Terminology

NOMENCLATURE FOR FACTORS OF THE HL-A SYSTEM*

At the Third Conference on Histocompatibility Testing, held at Saint-Vincent, Italy, in July 1967, the participants agreed to appoint, by postal vote, a Nomenclature Committee drawn from among specialists in tissue typing, immunology and human genetics; that Committee was asked to propose a nomenclature for leucocyte antigens, which, it was hoped, might prove internationally acceptable. The Secretariat of the World Health Organization was asked to facilitate and assist in the work of the Committee. The following is the text of the memorandum drawn up by the Committee.[1]

After description of the first human leucocyte iso-antigen, Mac, in 1958, several other leucocyte and platelet specificities were defined by agglutination, complement-fixation and cytotoxicity techniques. These factors were found on a variety of tissue cells and the possibility that they were histocompatibility antigens was proposed. Definition of antigenic specificities and of genetic relationships among them was greatly facilitated by the introduction of computer analysis. Many leucocyte and platelet factors have now been detected. The intricate relationships among them, evident from population and linkage studies, led to the concept that most of these specificities belonged to a single complex system. This was confirmed by family studies combining serology, skin grafting, and lymphocyte-culture techniques. An international nomenclature committee proposed that the major locus be designated HL-A.[2] The present report concerns the nomenclature of well-recognized specificities within the HL-A system. It does not relate to other antigenic systems.

Until now, most of the specificities defined by anti-leucocyte antibodies have been given different names by various laboratories. In devising a new nomenclature, the Nomenclature Committee attempted to use numbers which coincided, whenever possible, with those already in most common use, without regard to priorities or supposed genetic relationships.

Unanimous agreement was reached on naming certain specificities for which evidence had been obtained during histocompatibility-testing workshops and by exchange of sera (see the table).

Description of nomenclature

The use of subscripts, italics, lower-case letters, and similar devices was avoided for ease in composition, communication and computation.

The Committee recommended that a distinct specificity should be designated by number. Closely related but slightly different specificities should be distinguished by the addition of a figure after a full point. Specificities designated by a given number will have a high positive correlation coefficient, generally greater than 0.90. To establish that two closely related specificities are different, the discordant reactions must be shown to be reproducible. Identification of the donor of the antibody and the date of bleeding are considered to be an essential part of the description and designation of a serum in all reports.

A series of serological factors, such as the HL-A specificities, are grouped into a system if the recombination fractions between their corresponding genetic determinants are small. The effective limit on these recombination fractions is set by the resolution

* A French version will be published in a later issue.

[1] The members of the Committee were: Dr F. H. ALLE'N New York Blood Center, New York, N.Y., USA; Professor D. B. AMOS, Duke Medical Center, Durham, N.C., USA (*Chairman*); Dr J. R. BATCHELOR, Queen Victoria Hospital, East Grinstead, Sussex, England; Dr W. F. BODMER, Stanford University School of Medicine, Palo Alto, Calif., USA; Professor R. CEPPELLINI, Institute of Medical Genetics, University of Turin, Turin, Italy; Professor J. DAUSSET, Institut de Recherches sur les Maladies du Sang, Hôpital St-Louis, Paris, France; Dr R. D. OWEN, California Institute of Technology, Pasadena, Calif., USA (*Vice-Chairman*); Dr ROSE PAYNE, Stanford University School of Medicine, Palo Alto, Calif., USA; Dr J. J. VAN ROOD, University of Leiden, Leiden, Netherlands; Dr N. R. SHULMAN, National Institute of Arthritis and Metabolic Diseases, Bethesda, Md., USA; Dr P. I. TERASAKI, University of California School of Medicine, Los Angeles, Calif., USA; Dr Z. TRNKA, Immunology, World Health Organization, Geneva, Switzerland (*Acting Secretary*); Dr R. L. WALFORD, University of California School of Medicine, Los Angeles, Calif., USA.

[2] Amos, D. B. (1968) *Science*, **160**, 659-660.

NEW HL-A NOMENCLATURE AND PREVIOUS DESIGNATIONS [a]

New HL-A nomenclature [b]	Amos	Batchelor	Ceppellini	Dausset	Kissmeyer-Nielsen	Payne/Bodmer	van Rood	Shulman	Terasaki	Walford
HL-A1	19	1	To-8	11	LA1	LA1	LA1	—	1	Lc-1
HL-A2, or HL-AMac	1	5	To-9	1 or Mac	LA2	LA2	8a	PlGrLy^{B1}	2	Lc-2
HL-A3	4	—	To-10	12	LA3	LA3	LA3	Hill	8	Lc-3
HL-A4										
HL-A5	45	25	To-5	5	—	—	Da5	—	6	—
HL-A6										
HL-A7	2	—	To-20	10	—	4d	7c	—	5	Lc-8
HL-A8	41	2	To-7	8	—	7d	7d	—	11	Lc-7

[a] A dash (—) indicates that no symbol has been allocated within the nomenclature concerned.
[b] HL-A4 will be reserved for one of the higher frequency 4[a] factors, and HL-A6 for 4[b]. Before assigning these specificities, an exchange of serum among collaborating laboratories will be necessary.

of human pedigree studies and so is unlikely to be much less than 1%. A frequent, but not necessary, consequence of such close linkage is association among the factors at the population level. This association may vary from one population to another. The recognition of a new factor belonging to a system, such as HL-A, depends, therefore, not only on a population correlation analysis with established HL-A factors but also on family studies. The families studied must be directly informative with respect to recombination involving the postulated new factor. The Committee recommends that, in order to be assigned to the HL-A system, a new factor should show no recombination among a total of at least 20 genetically informative children from at least 3 families. This makes independence between the new factor and the HL-A system unlikely, though it does not exclude comparatively loose linkage—for example, with a recombination fraction of about 10% at a probability level of 0.1. Further family studies showing recombination between HL-A factors at a level below 1%, or chemical evidence leading to an understanding of gene–antigen relationships may, in the future, justify subdivision of the HL-A system into smaller genetic units. The assignment to such a subdivision would then be indicated by a common symbol immediately preceding the numbers defining the subunit factors.

Notational system

In the presentation of the data the factors typed for and the typing reagents should be specified. Serological factors are indicated by the number following the symbol for the system, e.g., HL-A1, HL-A2, etc. Other factors having a high positive correlation with a primary factor are indicated by a second number following a full point, e.g., HL-A2 for the original factor and HL-A2.1 for the associated factor.

An individual's complex phenotype may be presented in a table reporting the serological reactions. In the text the phenotype should be represented by the system symbol followed by the numbers corresponding to the factors which were found to be positive, these being separated by commas. For example, a donor who is positive with factors 1, 2, 7, and 8 and negative with 3 would be designated HL-A1,2,7,8. To make this meaningful, the antisera used must be listed, so that *negative* reactions may be known even though they are not indicated directly in the statement of the phenotype.

The genotype must be derived from family segregation analysis that identifies the two sets of factors controlled by the two homologous chromosomes. These sets, or haplotypes, are indicated within parentheses by the factors that are inherited in coupling; thus, for the example given above, the haplotypes could be HL-A(1,8) and HL-A(2,7). The genotype is indicated by the two haplotypes separated by an oblique stroke (solidus), for example, HL-A(1,8/2,7).

Allocation of numbers

The following procedures are recommended for obtaining international designations for HL-A factors. Until certification is obtained, a local designation [1] is appropriate; numbers preceded by the symbols HL-A should not be used.

Preliminary testing in laboratory of origin. The investigator should screen sera suspected of defining new specificities on his own cell panel, comparing them with antisera defining known HL-A specificities. The following steps are recommended:

1. The investigator should attempt to obtain more than one serum defining the supposed new specificity.

2. The reagents should be available in quantities of at least 200 ml. (Smaller quantities of high-titred serum could be considered equivalent.)

3. The reagents should give a reproducibility of at least 95% by a recognized technique designated by the investigator.

4. They should be mono- or oligospecific on the basis of absorptions with at least 10 positive cells when retested on the immunizing donor or on at least 10 highly reactive cells.

Certification.

1. The sera should be tested on members of 3 or more genetically informative families containing at least 20 children and should show no recombination with HL-A factors.

2. When these criteria have been fulfilled, the evidence should be submitted to a WHO collaborating laboratory. The laboratory may make available to the investigator cells, fresh or frozen, from its own panel of characterized donors. Details of the procedure will be agreed upon by the investigator and the laboratory involved.

3. Ultimately, the reagent must be shown to be operationally monospecific by absorption with, in general, cells from not fewer than 30 positive subjects if the frequency of reaction is greater than 15%, or from 15 positive donors if the frequency is less than 15%.

4. If the specificity is confirmed as apparently new, verification should be obtained from a second collaborating laboratory.

5. All relevant data will be submitted to the Acting Secretary of this Nomenclature Committee, who will circularize collaborating laboratories for a postal vote.

6. The Acting Secretary will then allocate a designation, if the specificity does not correspond to any previously designated factor.

Two sera can be considered to define the same specificity only if they give identical results when tested on a panel containing approximately 100 cells, of which at least 10 should be positively reacting and 10 negative. Any discrepancies that exist on first testing should disappear on repeated testing or following absorption.

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Laboratories that have consented to act on a voluntary basis as WHO collaborating laboratories for leucocyte antigens are those of:

Dr D. B. Amos and C. Zmijewski, Department of Microbiology and Immunology, Duke Medical Center, Durham, N.C., USA.

Dr J. R. Batchelor, McIndoe Memorial Research Unit, Blond Laboratories, Queen Victoria Hospital, East Grinstead, Sussex, England

Professor R. Ceppellini, Institute of Medical Genetics, University of Turin, Turin, Italy

Professor J. Dausset, Institut de Recherches sur les Maladies du Sang, Hôpital St-Louis, 2 Place du Docteur-Fournier, Paris X^{e}, France

Dr P. Ivanyi, Institute of Experimental Biology and Genetics, Czechoslovak Academy of Sciences, Budejovicka 1083, Prague 4, Czechoslovakia

Dr F. Kissmeyer-Nielsen, Blood Bank and Blood Grouping Laboratory, Aarhus Community Hospital, Aarhus, Denmark

Dr P. J. Morris, Department of Surgery, University of Melbourne, Parkville N.2., Melbourne, Australia

[1] See: Curtoni, E. S., Mattiuz, P. L. & Tosi, R. M., ed. (1967) *Histocompatibility testing 1967; Report of a Conference and Workshop, Torino and Saint-Vincent, Italy, 14–24 June 1967*, Copenhagen, Munksgaard.

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