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Selection of the most compatible graft recipient by computer program, used in regional tissue typing laboratory of Hellas (R.T.T.L)

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Abstract The purpose of this study was to present the new computer program that we developed in the regional tissue typing laboratory (R.T.T.L.) and use for the selection of the most suitable recipient for cadaveric allografts in a more efficient way. This new program was written and compiled in TURBO PASCAL 6.0, sorts all possible recipients to the HLA type of a donor, checks for the existence of splits and utilises them, and when requested, gives out results to more specific inquiries, i.e. all compatible recipients from 2DR2B2A to 1DR0B0A matching. It can also forecast success percentages according to different factors, i.e. combination of donor's and recipient's ages, HLA matching etc. The material used for this study were the patients who are registered in the formal cadaveric tranplantation list of R.T.T.L. We have used this program since 2 January 1992 together with the old one. Since then we found that the new program is faster in sorting all the possible recipients of cadaveric renal allografts according to the criteria already mentioned. The total selection time, with all the criteria activated, averages a few seconds, whereas with the old program it took approximately 2 min just for the sorting of HLA matching, without any other criteria activated. In the printout of the final result of each inquiry are all the possible recipients in the sorted order together with relevant data (telephone number, address etc.). As a result, the laboratory personnel has been free from the tedious task of this sorting which was initially done by hand and the possibility of error has been eliminated. The program was developed exclusively by doctors and all the updates needed are done by the users. More important, however, is the fact that in many cases the time of cold ischaemia was reduced by more than 30 min with all the obvious advantages for the longevity of the graft's life.

Key words Recipient selection
Allocation program
Computers in transplantation

Introduction

The purpose of this study was to present the new computer program that we have developed and use in the regional tissue typing laboratory (R.T.T.L.) for the selection of the most suitable recipients of cadaveric renal allografts. The program called H.C.F.M.-II (Histocompatibility Factor Matching-II) became a necessity in the R.T.T.L. as good HLA matching proved to be a major factor for a better survival rate in renal allograft transplantation [1, 2]. The number of patients listed for cadaveric renal transplantation keeps growing every month and has reached about 1000 during October 1993, making selection by hand more difficult than ever before. However, the fact that we have such a large number of listed patients gives us a good chance of finding a 2 DR 2 B match [3]. Moreover, the advances in tissue typing that have been achieved with the use of new alloantisera and the new DNA techniques have made the number of HLA antigens that can be typed easily ever-growing. This made the selection a task that demanded millions of comparisons between the HLA types of the donor and the recipients.

In Greece there is yet another problem that has to be accounted for in the making of a program such as this, i.e. the lack of a national strategy concerning the criteria used for selection. This forced us to make a program that can be easily modified by the user to meet the current standards set at any given time. We also allowed the physician group in charge of the selection have the last word, as there are many cases that are yet not well defined and could not fit in a standard procedure.

Software

H.C.F.M.-II was developed in Turbo Pascal 6.0 and is now compiled in Borland Pascal. It runs in protected mode and can use the whole of the available memory in the computer. If, however, there is not enough memory in the computer for H.C.F.M.-II to complete the task, a special subroutine takes over and redirects everything to the much slower but bigger hard disk. Thus the amount of memory available is not a restricting factor for the number of patients to be searched. The program has an object-like structure and contains more than 200 subroutines. The allocation algorithm uses a special code to deal with splits.

If the donors HLA type contains a split and the program is asked to use splits in its query, then the split is recognised and H.C.F.M.-II searches for the exact match for the split as well as for the corresponding broad antigen and for all the splits this antigen possesses. For instance, if the donors HLA type contains an A antigen with the value of 29 (split), then the program searches between the recipients for the A 29, the A 19 (broad corresponding to A 29), as well as for the A 30, A 31, A 32 and A 33 (all splits of the A 19 antigen). Even if the donor's HLA type does not contain a split but its' broad antigens possess splits, then H.C.F.M.-II can search for these splits between the recipients [4].

When dealing with an *X antigen*, H.C.F.M.-II can be set to find recipients with X antigen as a special criterion or to regard X as an unknown antigen that cannot be matched between patients.

The ABO compatibility is also dealt with in a different than usual fashion as the current policy is to use the extended ABO compatibilities. So, H.C.F.M.-II finds the recipients using (1) the exact match for the ABO group, (2) the standard compatibility of the ABO group or (3) the "extended" compatibility of the ABO group [5]. The latter is done when the patients in the waiting list have an ABO group type distribution that is different to the normal population, with the B and A type well above the normal average. The program has a special function that makes it easy to see at any given moment in a graph what the current situation is and select which one of the three modes to enable. The patients selected with the HLA match and the ABO match as criteria are then sorted in descending order (from full house to zero HLA match [1].

After this stage is completed, a second sorting follows of the patients with the same compatibility score using the PRA (panel reaction antibodies) level as a criterion. This can be done in an ascending or descending order by command. This way patients with a good HLA match and a high PRA level can be treated favourably if they have a negative crossmatch. Furthermore, it gives out advisory comments concerning the fitness of the graft for each selected patient using the graft's mass to patient's body weight ratio.

The secondary functions of the program are to act as an interface for the database containing the recipients and to give out statistical results for the waiting patients. All the data about splits and ABO compatibility can easily be modified by the user, keeping up with the latest developments.

In the example in Table 1, H.C.F.M.-II was asked to find all the possible recipients for a donor of ABO group 0, with the HLA type A10A29B05B08DR05DR06. In this part of the result sheet, one can see (1) the ability of the program to spot the antigens with splits (i.e. A 29) and

Table 1 Results of a random selection

Donor:

Name	First name	ABO	HLA
Donor	Donor	0	A10 A29 B05 B08 DR05 DR06

Results from HCFM-II V 10.1
Criteria for the selection: Splits: Yes, Extended ABO compatibility: Yes, Show all until 1DR0B0A match
Sort with PRA level descending

	Name	First name	ABO	HLA	COMMON	Categ	PRA	%
1	Recip	Recipient	0+	A10 A24 B05 B13 DR05 DR06	2DR1B1A	(5 Br)	100593	0
2	Recip	Recipient	0+	A24 A30 B05 B35 DR11 DR13	2DR1B1A	(5 Sp)	080493	0
3	Recip	Recipient	0+	A01 A26 B05 B18 DR05 DR06	2DR1B1A	(5 Sp)	080493	0
4	Recip	Recipient	0+	A02 A00 B08 B27 DR05 DR06	2DR1B0A	(6 Br)	210193	0
5	Recip	Recipient	B+	A02 A00 B05 B44 DR06 DR11	2DR1B0A	(6 Sp)	080493	0
6	Recip	Recipient	0+	A01 A02 B60 B00 DR11 DR14	2DR0B0A	(9 Sp)	240393	90
7	Recip	Recipient	0+	A02 A03 B27 B35 DR05 DR06	2DR0B0A	(9 Br)	210193	25
8	Recip	Recipient	0−	A01 A09 B35 B00 DR11 DR06	2DR0B0A	(9 Sp)	100593	0
9	Recip	Recipient	B+	A01 A28 B05 B08 DR03 DR05	1DR2B0A	(12 Br)	170593	0
10	Recip	Recipient	0+	A32 A26 B05 B16 DR05 DR00	1DR1B2A	(13 Sp)	060593	37
11	Recip	Recipient	0+	A25 A26 B05 B38 DR04 DR05	1DR1B1A	(14 Sp)	180393	25
12	Recip	Recipient	0+	A09 A10 B05 B22 DR05 DR04	1DR1B1A	(14 Br)	080493	0
13	Recip	Recipient	0+	A26 A28 B05 B07 DR06 DR07	1DR1B1A	(14 Sp)	310393	0
14	Recip	Recipient	0+	A24 A26 B05 B13 DR03 DR05	1DR1B1A	(14 Sp)	040293	0
15	Recip	Recipient	0+	A11 A32 B18 B52 DR04 DR13	1DR1B1A	(14 Sp)	260593	0

search for all the splits that correspond to the broad antigen of A29, which is A19. The splits are A30, A31, A32 and A33. The matching antigens are underlined. (2) There are a few lines informing of the criteria used for this particular selection (3). The recipients have been chosen from the ABO group 0 with the use of "extended" compatibility for the ABO group and so there are a few recipients with ABO type B. (4) In the column marked as COMMON are the matches that the program located. (5) In the column marked "categ" is the category where the recipient belongs (26 categories: 1st is a full 2DR2B2A match recipient and 26th is a 0DR0B1A recipient). The letters beside the category are (a) "Sp" if the recipient has been selected with the use of splits and (b) "Br" if the recipient has only got broad antigens. (6) Within the same category, the recipients are sorted in descending order using the PRA level as a criterion, i.e. recipients 6–8 all belong to category 9 (2DR0B0A) and the first one has a PRA level of 90% while the last one has a PRA level of 0%.

Hardware

H.C.F.M.-II runs on any IBM compatible computer of the 80 × 86 family from 80286 upwards running MS-DOS. However, with small modifications, it can be recompiled and run under UNIX and other operating systems. The minimum amount on memory required is 1 MB and it works with any type of screen adapter (CGA, EGA, VGA, Hercules, SVGA etc.). The whole selection program can even run on a terminal with on hard disk.

Our system consists of a 80486DX2–66 CPU with 16 MB RAM, a 640 MB hard disk and an SVGA screen adapter. The above mentioned hardware allows us to complete the selection within less than 1 s in most cases.

Conclusions

The use of H.C.F.M.-II has enabled us to make the selection of the most matched recipient an easy task, relieving the laboratory personnel from tedious hours of selection. It used to take more than 2 h, in most cases late at night, to sort the patients by hand, while now it takes less than 1 min. Furthermore, we are able to fully utilise all the new techniques of HLA typing and their results without worrying about the extra effort that the selection would then demand. Above all, H.C.F.M.-II keeps a record of all the recipients in the list, the chosen and sorted recipients who match the criteria that have been set and the criteria set for every selection. Thus, a complete

record of the whole project is kept every time, which enables the users to look back at any given transplantation.

H.C.F.M.-II was written and supervised by doctors only and has the advantage of the medical know-how. During the 2 years of trial there has been no case of malfunction and all the updates in the criteria were done by the users. Additionally, the fact that the selection time is less than 1 min, results in a gain of at least 0.5–1 h of cold ischaemia in most cases. H.C.F.M.-II is considered by us to be a stable platform that is able to cope with increasing clinical criteria and results in a more complete selection in the Greek allocation program.

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