THE INHERITANCE AND DISTRIBUTION OF THE *DUFFY* BLOOD GROUPS

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THE discovery of a new human blood group system, called *Duffy*, was briefly reported by Cutbush, Mollison and Parkin (1950) ; a fuller account was given by Cutbush and Mollison in the last number of this journal.

The antibody which enabled the new blood group antigen to be recognised was found in the serum of a man suffering from hæmophilia who had had several blood transfusions during the previous 20 years. Cutbush and Mollison found the antigen to be present in 64·9 per cent. of 205 blood samples from unrelated English adults. It was demonstrated that the antigen was not any of those previously recognised, and enough blood samples were further tested for the *ABO* and *Rh* groups to show that the distribution of the new antigen was independent of these groups.

Tests on 27 families with 36 children showed that the antigen was inherited by means of a gene expressing itself in single and double dose.

The form of notation designed for the *Lutheran* and *Lewis* groups (Andresen *et al.*, 1949) was adopted for the new system.

System	*Duffy*
Genes	Fy^a and Fy^b
Genotypes	Fy^aFy^a, Fy^aFy^b and Fy^bFy^b
Phenotypes	$Fy(a+)$ and $Fy(a-)$
Antibody	anti-Fy^a

The system is called *Duffy* by permission of the patient of that name in whose serum the antibody was found. The gene giving rise to the recognisable antigen is called Fy^a and its allelomorph, which is at present only recognisable in a negative way, is called Fy^b.

The identification of other examples of anti-Fy^a followed quickly on the finding of the Duffy serum. Ikin, Mourant and Plaut (1950) found the antibody in the serum of a man (J. S.) suffering from a peptic ulcer who had had a reaction to his third transfusion. Van Loghem and Hart (1950) found the antibody in the serum of a man (Pluym) suffering from hæmophilia who had received more than 30 blood transfusions. Rosenfield, Vogel and Race (1950) found the antibody in the serum of a man (Rom.) suffering from a benign prostatic tumour and who had had a hæmolytic reaction to his first

transfusion. Allen (pers. com.) found the antibody in the serum of a woman (And.) who had suffered two transfusion reactions because of it.

In all these cases the antibody is in the incomplete form. The interaction of antibody and antigen is made apparent only by the indirect anti-globulin test and not by the albumin nor by the trypsin methods ; in this the antibody differs from incomplete anti-*Rh*.

ORIGINAL WORK

The work to be described was done for the following reasons :—

(1) To provide further figures which could be added to those of Cutbush and Mollison for the calculation of gene frequencies :

(2) To establish that no serological relationships existed between the *Duffy* antigens and any of the other blood group antigens, relationships such as that known to exist between the *MN* and *S* antigens :

(3) To provide further material to test the genetic theory of Cutbush and Mollison, and to see whether genetic linkage could be detected between the *Duffy* genes and any of the other blood group genes, or between the *Duffy* genes and sex or between the *Duffy* genes and the ability to taste phenyl thio-carbamide.

The work was made possible by a generous supply of the *Duffy* serum, the gift of the discoverers. Tests were carried out by the indirect anti-globulin method.

Phenotype, gene and genotype frequencies

Samples of blood from 255 unrelated Londoners were tested with anti-*Fy^a*. The results, together with those of Cutbush and Mollison, are given in table 1.

TABLE 1

The frequency of the Duffy *phenotypes in England*

	Number tested	$Fy(a+)$		$Fy(a-)$	
Cutbush and Mollison . .	205	133	*64·88* per cent.	72	*35·12* per cent.
Present series . . .	255	167	*65·49* ,,	88	*34·51* ,,
Total . . .	460	300	*65·22* ,,	160	*34·78* ,,

Assuming that the theory that the phenotype $Fy(a-)$ represents the genotype $Fy^b Fy^b$ is correct, then the gene frequencies may be derived in the usual way :—

$$\text{frequency of the gene } Fy^b = \sqrt{0·3478} = 0·5898$$
$$\text{and the frequency of the gene } Fy^a = 1 - 0·5898 = 0·4102$$

The genotype frequencies are therefore :—

$$Fy^aFy^a \quad 0 \cdot 4102^2 \qquad\qquad\qquad = 0 \cdot 1683$$
$$Fy^aFy^b \quad 0 \cdot 4102 \times 0 \cdot 5898 \times 2 = 0 \cdot 4839$$
$$Fy^bFy^b \quad 0 \cdot 5898^2 \qquad\qquad\qquad = 0 \cdot 3478$$

Using the Pluym serum van Loghem and Hart tested 212 Dutch blood samples of which 127 or 59·9 per cent. were $Fy(a+)$. We have had the opportunity of testing 28 French samples of which 19 or 67·9 per cent. were $Fy(a+)$. There is no significant difference between these and the English frequencies.

Four anti-Fy^a sera (Duffy, Pluym., Rom., and And.) gave identical results when tested in parallel against 50 English blood samples (Rosenfield, Vogel and Race, 1950). There is therefore as yet no hint of subgroups of this system.

The independence of the Duffy groups

All of the 255 blood samples were tested for the A_1A_2BO groups and for the Rh groups as defined by anti-C-c-C^w-D-E and anti-e. All but one of the samples were tested for the MN and S groups ; and all but a few were tested for the P, *Lutheran*, *Kell* and *Lewis* groups. The distribution of the *Duffy* phenotypes within these other divisions is given in table 2. The probabilities given by χ^2 tests on the 2 ×2, 2 ×3 and 2 ×5 tables of table 2 are given in table 3.

TABLE 2

The distribution of the Duffy *phenotypes relative to other blood groups, to sex and to phenyl thio-carbamide tasting*

	♂	♀	EE	Ee	ee	DD	Dd	dd	CC	Cc	cc	O	A_1	A_2	B	A_1B and A_2B
$Fy(a+)$	69	89	2	35	130	25	95	47	13	82	72	95	48	8	11	5
$Fy(a-)$	40	44	2	17	69	24	48	16	14	50	24	48	21	5	9	5

	M	MN	N	$S+$	$S-$	$P+$	$P-$	$K+$	$K-$	$Lu(a+)$	$Lu(a-)$	$Le(a+)$	$Le(a-)$	Sec.	Non-sec.	Taster	Non-taster
$Fy(a+)$	50	77	40	77	90	134	32	9	146	6	150	19	120	12	6	46	16
$Fy(a-)$	30	40	17	51	36	61	23	8	72	2	73	11	52	5	2	22	15

It will be seen that in the two associated comparisons involving C and D the probability is below 1 in 20. We are convinced that this lack of proportion is due to chance for it is not shown by the data of

Cutbush and Mollison and it is only to be found in the first half of our own material. Had the disturbance been other than a chance one it should have shown in both halves. The lack of proportion

TABLE 3

The probability of obtaining by chance the results given in table 2

	Probability
Male : female .	0·56
$EE : Ee : ee$	0·80
$DD : Dd : dd$.	0·03
$CC : Cc : cc$	0·02
$O : A_1 : A_2 : B : A_1B$ and A_2B .	0·62
$M : MN : N$.	0·64
$S+ : S-$	0·05
$P+ : P-$	0·66
$K+ : K-$	0·93
$Lu(a+) : Lu(a-)$	0·65
$Le(a+) : Le(a-)$	0·48
Secretor : non-secretor	0·82
Taster : non-taster .	0·13
$CC : Cc : cc$, 1st 114 .	$p < 0·01$
$CC : Cc : cc$, 2nd 141	p 0·20

cannot be explained by the presence of unsuspected anti-*c* or anti-*d* in the *Duffy* serum for the donor of the serum was *cde/cde* and had produced anti-*D* (which antibody has to be removed by absorption before the serum is used).

The distribution of the groups other than *Duffy*, shown in table 2, is not typical of the general population. The samples, though un-selected for *Duffy*, were often selected in respect of other groups for reasons outside the present investigation.

The Duffy groups of 58 families

Table 4 shows the expected incidence of the various matings and of the relative frequency of $Fy(a+)$ and $Fy(a-)$ amongst the children of these matings. The calculations are based on the theory of Cutbush and Mollison that the *Duffy* groups are controlled by two allelomorphs, one of which in single or double dose determines the presence of the recognisable antigen.

In table 5 the observed results of testing 58 English families and 148 children are compared with the results expected according to the theory. It will be seen that the agreement is close and the theory strongly supported.

Ascertainment.—The ascertainment of the families was at random with respect to all blood groups.

Linkage.—The u statistics of Fisher, as elaborated by Finney (1940) have been applied to the results. In the case of A_1A_2BO, *MNS*, *Rh*, *Lutheran*, *Kell* and sex, use has been made only of the " certain " families in which the parental genotypes have been disclosed. In the case of the *P* groups, of the *Lewis* groups and of P.T.C., use has also been made of " doubtful " families, where for the parents the

phenotype alone was known, the score being weighted according to the probability of their heterozygosity. There were no " incomplete " families.

TABLE 4

The expected distribution of the Duffy *groups in parents and offspring on the assumption that the gene* Fy^a *is expressed in single and double dose*

GENOTYPES				
Matings		Children		
Type	Frequency	Fy^aFy^a	Fy^aFy^b	Fy^bFy^b
$Fy^aFy^a \times Fy^aFy^a$	0·0283	0·0283	...	...
$Fy^aFy^a \times Fy^aFy^b$	0·1629	0·0814	0·0814	...
$Fy^aFy^b \times Fy^aFy^b$	0·2341	0·0585	0·1171	0·0585
$Fy^aFy^a \times Fy^bFy^b$	0·1171	...	0·1171	...
$Fy^aFy^b \times Fy^bFy^b$	0·3366	...	0·1683	0·1683
$Fy^bFy^b \times Fy^bFy^b$	0·1210	...	...	0·1210
	1·0000			

PHENOTYPES			
Matings		Children	
Type	Frequency	$Fy(a+)$	$Fy(a-)$
$Fy(a+) \times Fy(a+)$	0·4253	0·8624	0·1376
$Fy(a+) \times Fy(a-)$	0·4537	0·6290	0·3710
$Fy(a-) \times Fy(a-)$	0·1210	...	1·0000
	1·0000		

TABLE 5

The Duffy *groups of 58 English families with 148 children*

Matings				Children			
Type	Number		Total number	$Fy(a+)$		$Fy(a-)$	
	obs.	exp.		obs.	exp.	obs.	exp.
$Fy(a+) \times Fy(a+)$	20	24·7	50	43	43·1	7	6·9
$Fy(a+) \times Fy(a-)$	29	26·3	74	40	46·5	34	27·5
$Fy(a-) \times Fy(a-)$	9	7·0	24	0	0·0	24	24·0
Total	58	58·0	148				

The results of the calculations are given in table 6. There is no evidence for linkage between the *Duffy* genes and any of the other genes studied, for $S(\lambda)$ is in each case less than $1 \cdot 64\sqrt{S(\kappa)}$.

TABLE 6

Linkage relations of the Duffy *genes*

	$S(\lambda)$	$S(\kappa)$	$1 \cdot 64\sqrt{S(\kappa)}$	5 per cent. fiducial lower limit to cross-over frequency
A_1A_2BO . . .	$+1 \cdot 0$	$31 \cdot 0$	$9 \cdot 1$	*21·4* per cent.
MNS	$+4 \cdot 0$	$22 \cdot 0$	$7 \cdot 7$	*13·5* ,,
P	$-4 \cdot 5$	$9 \cdot 8$	$5 \cdot 1$	*37·1* ,,
Rh	$-5 \cdot 0$	$35 \cdot 0$	$9 \cdot 7$	*31·6* ,,
Lutheran . . .	$-2 \cdot 0$	$12 \cdot 0$	$5 \cdot 7$	*22·3* ,,
Kell	$-3 \cdot 0$	$7 \cdot 0$	$4 \cdot 3$	*28·0* ,,
Lewis	$+0 \cdot 3$	$10 \cdot 2$	$5 \cdot 2$	*11·6* ,,
Partial sex . . .	$+6 \cdot 0$	$26 \cdot 0$	$8 \cdot 4$	*12·9* ,,
P.T.C.	$+0 \cdot 04$	$6 \cdot 3$	$4 \cdot 1$	*9·3* ,,

The last column of table 6 shows the 5 per cent. fiducial lower limit to cross-over frequency. This expression, for which the formula is

$$\chi = \tfrac{1}{2} - \tfrac{1}{2}\sqrt{\left\{\frac{S(\lambda)}{S(\kappa)} + 1 \cdot 645\left(\frac{1}{S(\kappa)}\right)^{\frac{1}{2}}\right\}}$$

was suggested by Finney as giving perhaps a better measure of the weight of evidence against linkage than does $S(\kappa)$.

The two families shown in fig. 1 have been chosen from the 58 to illustrate the independent segregation of the *Duffy* genes and some of the other blood group genes.

SUMMARY

Samples of blood from 255 unrelated English persons have been tested with the *Duffy* antiserum. The *Duffy* antigen was present in 167 or 65·49 per cent. of the samples; a figure very close to the 64·88 per cent. found by Cutbush and Mollison in testing 205 English persons. From the combined results of the two series the following gene frequencies are derived : Fy^a 0·410 and Fy^b 0·590.

Fifty-eight families with 148 children have been tested for the *Duffy* groups; the results agree well with the genetic theory of Cutbush and Mollison. The families were also tested for the A_1A_2BO, *MNS*, *P, Rh, Lutheran, Kell* and *Lewis* blood groups, and for their ability to taste phenyl thio-carbamide. No linkage between the *Duffy* genes and any of the genes responsible for these characters was established. The *Duffy* genes could not be shown to be partially sex-linked.
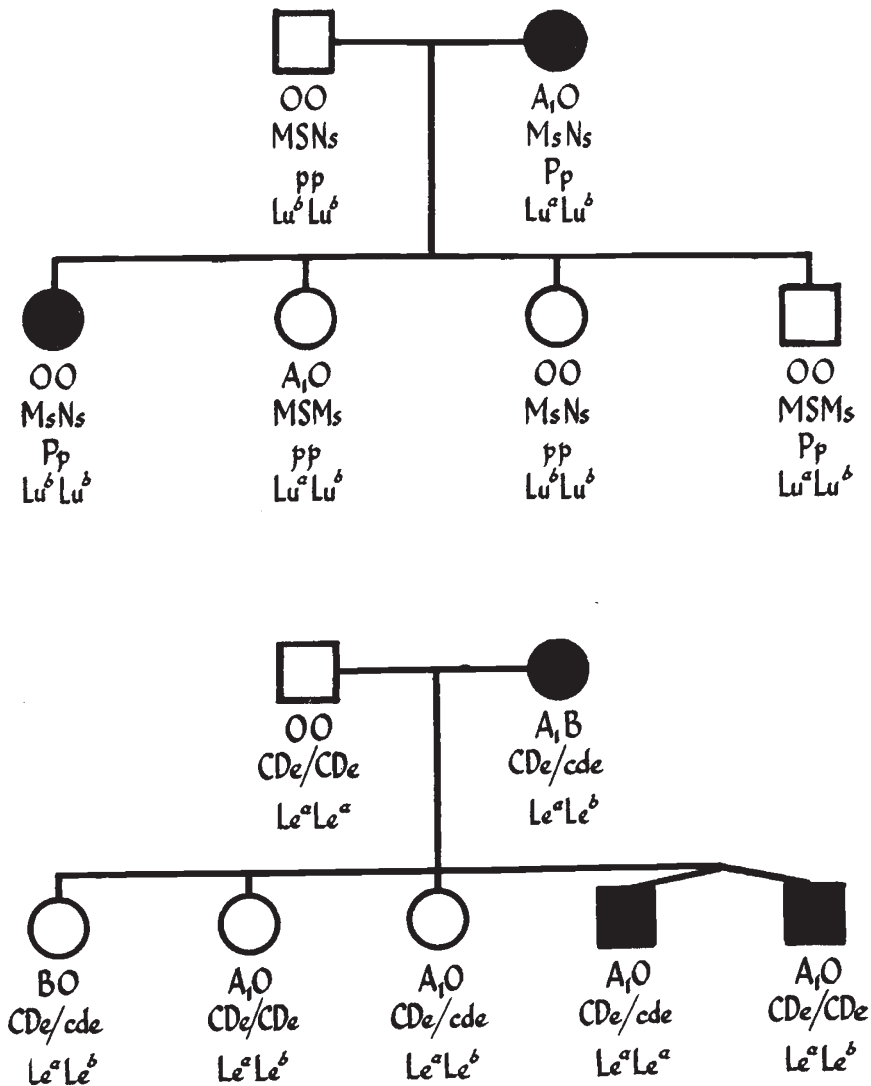
FIG. 1.—Two families illustrating independent segregation of the *Duffy* genes and certain other blood group genes.

Black = phenotype $Fy(a+)$, genotype Fy^aFy^b
White = phenotype $Fy(a-)$, genotype Fy^bFy^b

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