Miscellaneous correspondence, notes, meeting programmes etc.

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PENROSE, L.S. (Colchester, England). Maternal age, order of birth and developmental abnormalities.

A positive association is demonstrable between maternal age and the incidence of Mongolian imbecility, gross malformation of the nervous system and central placenta praevia. The independent effect of birth order is not easy to demonstrate conclusively. Primogeniture, however, is likely to be a significant factor in determining the incidence of gross malformation of the nervous system and of congenital pyloric stenosis. The study of maternal age and birth order usefully precedes the investigation of the genetical backgrounds of these conditions. Mongolism and some other malformations may have their origins in chromosome anomalies. The underlying cause of congenital pyloric stenosis seems to be a recessive diathesis.

MUNRO, T.A. (Colchester), PENROSE, L.S. (Colchester), & TAYLOR, G.L. (London).

A Study of the Linkage Relationship between the Genes for Phenylketonuria and the ABR Allelomorphs in Man.

The paper describes the analysis of 25 sibships in search of genetic linkage between the gene for phenylketonuria and the ABR allelomorph series. The sib pair method gives results which suggest that the loci of the two sets of genes are situated on the same chromosome. The application of u-function technique presents some difficulties because not all the parental genotypes could be identified. If the value of the u-function for each sibship is weighted in accordance with the probability that the sibship gives information about linkage, a significantly positive result is obtained.

RACE, R.R., TAYLOR, G.L., and VAUGHAN, J.M. (London, England). A genetic investigation of Acholuric Jaundice.

An account will be given of a joint investigation, undertaken by workers in haemotological and genetical laboratories, of families in which occur cases of the blood disease Acholuric Jaundice. The essential underlying abnormality of this condition is a diminished resistance to haemolysis, or increased fragility of the red blood cells.

Though the disease is generally believed to behave as a dominant Mendelian character, in many of the families hitherto published there has been a preponderance of normal children from matings where one parent was a sufferer. In these families it would be expected that the affected children would equal the normal. It was thought that the explanation probably lay in the fact that many of the published pedigrees are based on clinical examination only. This is misleading owing to the presence of a fairly common latent form of the disease in which there are no symptons nor signs of the abnormality which can only be shown to be present by an elaborate investigation of the blood. Even when this has been done mistakes have arisen owing to the use of an insufficiently delicate technique. A more accurate quantitative technique has now been elaborated which has been used throughout our investigations.

Of special interest has been the question of the existence of so called "acquired cases" in which both parents of a sufferer were free from the abnormality. If such cases did occur, too frequently to be explained by mutation, could any genetic light be thrown on their nature by a wider examination of their relatives?

In the hope of detecting linkage relations, if they exist, between the gene for acholuric jaundice and any of the recognizable common human genes we have examined all the members of our series for the following characters:-

Blood groups ABO and M & N
Ability to shed the ABO factors in the saliva.
Ability to taste Phenyl-thio-carbonide
Iris colour.
Attachment or not of the ear lobes.
Colour of the hair

An account will be given of the families examined up to the time of the Congress.

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1941

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PICKARD, J. N.: Institute of Animal Genetics, King's Buildings, West Mains Road, Edinburgh 9
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SLIZYNSKI, B. M.: Institute of Animal Genetics, King's Buildings, West Mains Road, Edinburgh 9
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WILLIAMS, R. D.: University College, Aberystwyth, Wales
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WATERMAN, Miss N. M.: 303 Woolwich Road, London, S.E. 2

Members are requested to notify any change of address to Dr K. Mather, John Innes Horticultural Institution, Mostyn Road, London, S.W. 19.

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On the inheritance & linkage relations of Acholuric jaundice.

R.R.Race

Annals of Eugenics Vol.11 Part 4 pp 365-384 1942

The report of a search for linkage between the gene for Acholuric jaundice and the common "physiological" genes, carried out at the Galton Laboratory University College, London and the British Postgraduate Medical School, Hammersmith.

Nearly 200 members of 26 families were examined haematologically for the signs of Acholuric jaundice by Dr. Janet Vaughan and Miss Olive Booth. They were also tested for the A_1A_2 BO and MN blood groups and for the ability to secrete the ABO antigens in the saliva, and to taste phenyl-thiocarbamide. Eye colour and freeness or attachment of the ear lobes were also scored although the manner of inheritance of these characters is not on the sure basis of those mentioned before.

The war brought the investigation to an end but not before evidence had been collected against partial sex linkage and against close autosomal linkage with any of the genes responsible for the A_1A_2BO blood groups, the MN blood groups, secretion of the ABO antigens in the saliva, eye colour and attachment of ear lobes. The figures for taste testing were inconclusive.

A year or so after the close of the investigation the Rh groups were discovered, so that the work is already incomplete. This indicates what a laborious business the great work of mapping the human chromosomes will be.

Title An "incomplete" antibody in human serum.
Author R.R.Race
Journal Nature 153 771-2 June 24 1944

The discovery of an "incomplete" antibody in certain anti-Rh sera indicates that there is still much to be learnt about this versatile system of antigens and antibodies. By an incomplete antibody is here meant one which will combine with its specific antigen on the red cell, but which is not a suitable partner for the agglutination stage.

Human anti-Rh serum of the type called by Wiener "Standard" agglutinates red cells of the gene Rh_1 and also those of Rh_2. Anti-Rh_1 serum agglutinates the former but not the latter. If, however, cells of the genotype Rh_2Rh_2 or Rh_2rh are suspended in anti-Rh_1 serum, which causes no agglutination, and after a few minutes are separated from this serum, washed and resuspended in saline, then these treated cells can no longer be agglutinated by standard anti-Rh serum. These treated cells are agglutinated as well as ever by anti-Rh_2 serum and by St serum. In other words it is only one of the three Rh antigens which must be present on Rh_2 cells which is being blocked, the other two are left free and ready for agglutination. This interpretation was supported by absorption experiments. The inhibited antigen is that one which would normally react with the standard anti-Rh antibody and the author considers the inhibiting agent an incomplete form of this antibody.

Five out of six anti-Rh_1 sera contained the incomplete antibody in good strength, the sixth in weak but definite amount. One standard anti-Rh serum contained the incomplete as well as the

complete form of the antibody. In such a natural mixture, or in one artificially made, the incomplete antibody wins the race for antigen when red cells are added, and the expected agglutination does not occur.

A brief account is given of R.A.Fisher's formulation of the relationships found in the rhesus factor. This is referred to elsewhere in this issue.

Work done between Oct 1st 1944, October 1st 1945

800 Families investigated.

(American panels, & miscellaneous groupings excluded)

Oct 1st 1943 – Oct 1st 1944.

663 families investigated.

For Professor Fisher

22.1.45

Moore Summary.

Moore serum probably contains γ' as well as γ (γ' = the incomplete form of γ, not previously found). Two other immune antibodies are present, M_1 and M_2 these can only conveniently and unequivocally be used on O R_1R_1 people. This group O R_1R_1 previously thought to be homogeneous is shown by Miss Moore's serum to be divisible into four kinds.

It is becoming very doubtful whether the M_1 and M_2 antigens are really confined to certain cells of the genotype R_1R_1.

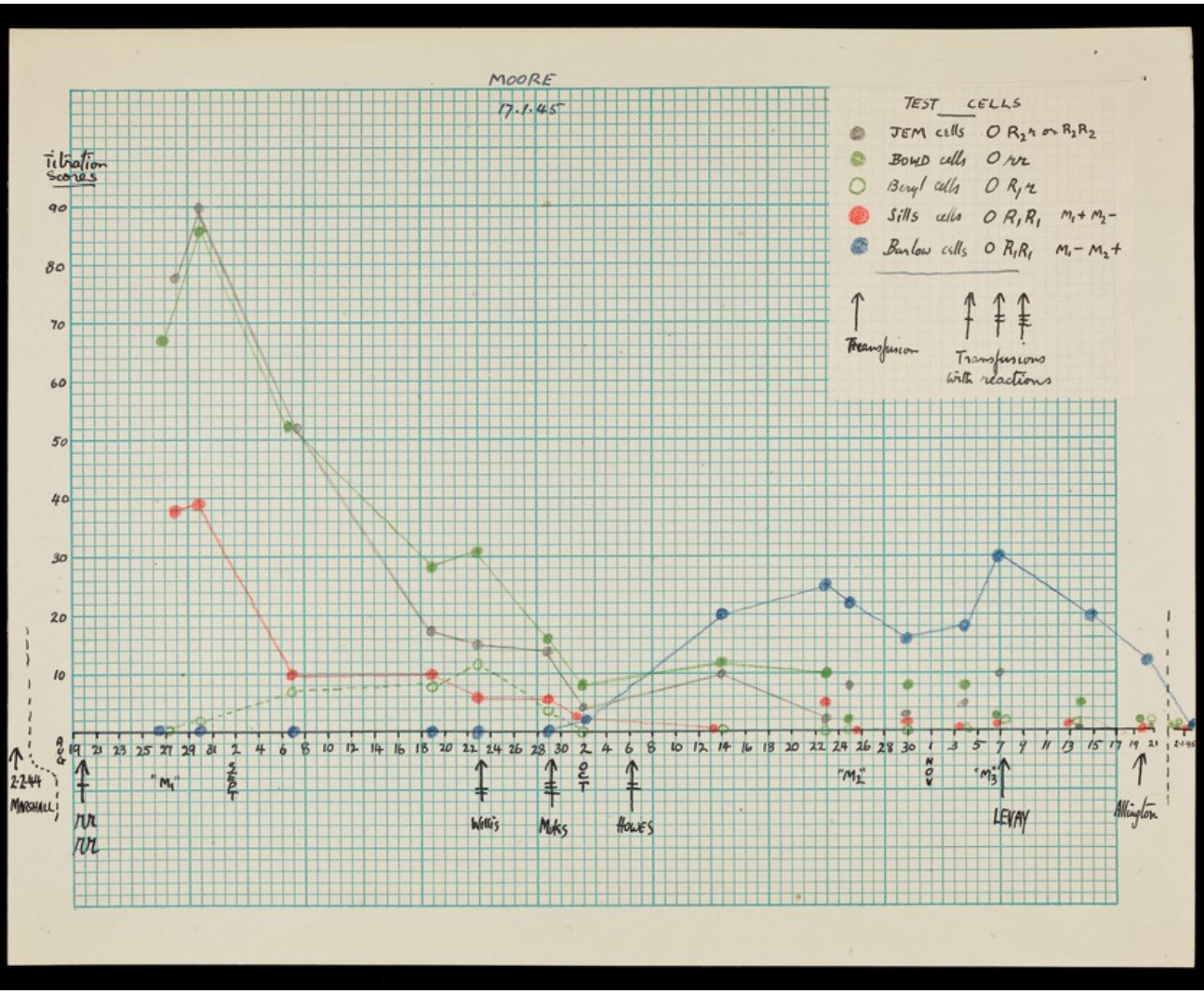
Miss Moore has made one rare and three hitherto unknwon antibodies almost certainly all in response to blood transfusions.

Dr. Callender's magnificent collection of specimens of serum from Miss Moore.

The graph shows the titrations of 5 cells with all the sera. The ordinates are not titres but scores, (#^{v} = 10 # = 8 etc., this is not ideal). The abscissae show the passed time. Some observations on the graph:-

(a) The extraordinary weakness of the reaction of the R_1r cells used, compared with the strength of reaction with cells of a double dose of c antigen. (The difference being out of proportion to that shown by Steadman serum).

(b) The perhaps significant rise then sudden fall around 31.8.44 of both γ and M_1 special antibody (red) suggest to me that both were of recent and the same origin. That both were produced by the transfusion of two pints of


MOORE
17.1.45
Titration scores
TEST CELLS
JEM cells O R_2r or R_2R_2
BOWD cells O rr
Beryl cells O R_1r
Sills cells O R_1R_1 $M_1+ M_2-$
Barlow cells O R_1R_1 $M_1- M_2+$
Transfusion
Transfusions with reactions
"M_1"
SEPT
OCT
"M_2"
NOV
"M_3"
LEVAY
WATTS
MILKS
HOWES
Allington
2·244 MARSHALL

rr (Lutheran and ?) on 19.8.44 - twelve days before the peak of γ and M_1. If γ had been caused by transfusion Marshall (R_1r) 2.2.44 then there should have been an immediate reaction to the two pints of rr, should't there? There was not such a reaction but six days later jaundice appeared. If the rr had stimulated the γ, in six days it might have been just strong enough to attack the remaining rr cells. On this thesis one of the rr bloods must have the special M_1 antigen as well, and M_1 antibody may have helped to cause the jaundice.

(c) The idea that M_1 was naturally occurring has gone overboard for there is neither M_1 nor M_2 antibody left on 2.1.45. Overboard also is the idea of a sudden conversion of M_1 antibody into M_2, such a conversion might have been expected to look like this:-

not as it does like this:-

It looks as if M_1 like γ just faded out. It looks likely and seems reasonable that M_2 was made in response to transfusion Willis (O R_1R_1 M_1- M_2+), on 23.9.44, the antibody being recognisable nine days later. Why Willis caused a reaction is very far from clear for it is γ negative and also M_1 negative. Mules R_1r (29.9.44) would be in time to catch the effect of γ, but although the reaction was severe it curiously has not sent up the γ titre. Howes 6.10.44 O R_1R_1 M_1- M_2+ would catch the M_2 antibody now waxing, and might assist in the waxing. Levay and Allington which did not cause reactions are also theoretically compatible which is a good thing, both being O R_1R_1 M_1- M_2+ (like 80%

of R_1R_1; Willis and Howes both being M_1- M_2+ was very lucky for us, $\frac{1}{25}$ lucky).

(d) By good fortune the sera used in many tests and called M_1 (28.8.44) M_2 or M_3 (25.10.44 and 7.11.44) were taken at the top of the curve of the two extra antibodies - "M_1" and "M_2".

The Alpha trouble.

Miss Moore is group O. Half a volume of AB saliva will neutralize the α in M_1 but not in M_2. That it was α or α_1 that was left in the latter and not M_2 antibody was proved by visible agglutination occurring when the mixture was added to A_1 cells on a slide. This M_3 plus saliva does not react on a slide nor in a tube with A_2 cells. Why can α (or α_1) be neutralized easily in M_1 and not in M_3? It isn't that there is more α (or α_1) in M_3. The reactions of M_1 M_2 & M_3 with A_1 & A_2 R_1R_1 cells are identical and mediocre.

Heterophile antibody.

No excessive agglutinin for sheep cells found. M_1 M_2 & M_3 all agglutinated sheep cells at $^1/_4$ to $^1/_8$.

Frequencies.

Amongst O R_1R_1 people of the special antigens recognised by M_1 and M_2.

M_1	M_2		
-	-	46	·807
-	+	7	·123
+	+	1	·018
+	-	3	·053
		57	1·001

The unreasonable (idea c) that the two antigens are caused by genes not at the same locus nor at the Rh locus (though both hypostatic to c) still fits the distribution very closely. Calling the two antigens I & II

I is present in ·071 of the R_1R_1 population and is absent from ·929

II is present in ·141 of the R_1R_1 population and is absent from ·859

Expected - - = ·929 x ·859 = ·80 obs = ·81

\- + = ·929 x ·141 = ·13 obs = ·12

\+ + = ·071 x ·141 = ·01 obs = ·02

\+ - = ·071 x ·859 = ·06 obs = ·05

I am feeling shaky about the hypostasis, and wondering whether it isn't after all possible for St + people to be M_1 or M_2 +. Of which see later. If this was true, idea c would become much more reasonable.

Serum 30.8.44.

This specimen has been examined in some detail.

Extract from protocol 17.1.45.

Serum Moore 30.8.44. 1/32 thousand

Bowd	rr	cells	++	+	+	+	(+)	+	+	+	?	?	?	w	+	w	?	(+)	-
Vera	R_1R_2	cells	w	-	?	-	-	w	(+)	+	+	-	?	-	-	-	-	-	-
Robarts	R_2r	cells	+	+	?	+	+	+	(+)	?	(+)	+	w	w	?	+	-	?	-

This moth-eaten appearance in titration is exactly what I observed in a serum (James) that contained a mixture of Δ & Δ' (the complete Δ and the incomplete). In the case of James a first absorption by an equal volume of packed cells, of the moth-eaten type, removed all the moth-

eaten appearance for these same cells. This is because Δ' beats Δ in competition for D antigen sites.

Protocol 15.4.44.

J.E.M. (R_2R_2 or R_2r) cells

Mrs. James unabsorbed	(+)	w	?	–	–	?	w	?	?	?
Mrs. James absorbed JEM cells	#v	#	#	#	#	+	(+)	+	(+)	?
Mrs. James absorbed JEM twice	#v	#	+	?	–	–	–	–	–	–

The only established cause of zoning in anti-Rh sera is incomplete antibody so I feel certain that Moore 30.8.44 must have γ and γ'. Unequivocal demonstration of this is proving rather troublesome, but this looks like it, although not knock down like James.

Sera	Cells:- Beryl				
M. 30.8.44	–	–	–	–	–
M. 30.8.44 absorbed x Beryl eq. vol.	–	?	–	–	–
M. 30.8.44 absorbed x Beryl x Beryl	(+)	+	w	(+)	–

Curiously enough the two absorptions seem to have improved the special M_1 antibody as these titrations ō Sills cells (O R_1R_1 M_1+ M_2-) suggest.

M. 30.8.44	#	+x	+x	#x	w	–	–	–	–
M. 30.8.44 x Beryl	#	#v	#v	#	w	?	?	–	–
M. 30.8.44 x Beryl x Beryl	#	#x	#x	(+)x	#x	#x	#x	w	–

This will need investigating. Beryl certainly hasn't recognisable M_1 antigen, the stimulating effect her cells have on the M_1 antibody may belong to the order of phenomena found in the original St serum, and which I attributed to the change of pH resulting from contact of serum and cells. (Briefly, stored St was failing to react with the single

dose c and with some double dosers. Absorption with St negative or sheep cells restored the activity, so did bubbling CO_2 through the serum). The stars indicate a peculiar appearance noticed not invariably but time after time although I do not think I have mentioned it before in these reports. The agglutinates given by O $R_1 R_1$ M_1 positives with M_1 serum are good ones but there are very many unagglutinated cells. This is sometimes very striking indeed and when very struck I indicate it with a star. The M_2 antibody does not give this appearance with O $R_1 R_1$ M_2 positives.

The direct demonstration of has had some success using Cheadle (St) serum.

Wiener's technique		My technique	
(Suspected serum + test cells, wait, add test serum)	Cheadle serum added done three times	Test cells + suspected serum, remove cells, and add to them test serum.	
2% Beryl + eq. vol. M 30.8.44	ω ω ?	2% Beryl coated M 30.8.44	ω
2% Beryl + eq. vol. inert serum	# # #v	2% Beryl uncoated "	#

Do the M_1 & M_2 antigens occur on cells other than $R_1 R_1$?

M_1 antigen

I thought it did not, or at least could not be demonstrated but was shaken by this:-

Moore 30.8.44.

O R_1 r	Beryl	—	—	—	—	—	—	—	—	#rs	—	—
	Elliott	#x	#x	#x	#	(#)	(#)	?	ω	?	—	

Elliott showed the special type of agglutination just described as being peculiar to the M_1 antibody-antigen reaction. So Miss Elliott differed qualitatively from Beryl, she also

differed quantitatively. (Serologically speaking).

And later (on 25.1.45)

	M. 30.8.44.	1/32	
Blair	## ## ## + ##x +		Blair is doubtful R_1r or R'r ? Wiener's intermediate
6 O R_1r	– – – – – –		
O R_1r Beryl again	– – – – – –		
O R_1r Miss Elliott again	##v ##v ## ## ##(#) etc		

Is it significant that HPH who I suspected for other reasons to be R_1R' and Blair who may be R'r are both M_1+? A person R'R' (- - - +) was negative with M_1 however. More titrations and fewer words are obviously needed. Reviewing as a result the tests with M_1 on people not R_1R_1, I now see that there is no adequate evidence that they cannot be M_1 positive and I am sorry I have misled over this. The supposed similarity in nature between M_1 and M_2 antibody thus goes overboard too, for this was their common and peculiar feature.

<u>M_2 antigen</u>

The evidence that people not R_1R_1 could not be M_2+ had a much better foundation for I could fairly easily remove γ from M_2 (there isn't much γ, v. graph). M_2 absorbed by Bowd (rr) is practically γ free has been negative with these O's:-

43 R_1r

19 R_1R_2

17 R_2r or R_2R_2

11 rr etc.,

and on each separate occasion it has reacted well with an

R_1R_1 M_2+ control. M_2 unabsorbed is positive with about 14% of R_1R_1 persons. This is obviously highly significant, yet the following contradicts this. The following protocol seems to mean that cells other than R_1R_1 <u>can</u> be M_2+.

	M_2 unabsorbed	M_2 x Bowd (rr) x Bowd
O R_1R_1 Barlow	++ ++ ω 1/3 −	++ ++ (+) (+) ? −
O R_1R_2 Mother Sills	+ ? − −	− − − − − −
O R_1R_2 Brother Sills	++ ++ ++ ω	++ ++ ++ (+) − −

I will have to do more people with M_2 x Bowd (rr) x Bowd.

<u>Conclusion.</u>

More people of all genotypes must be titrated $\bar{c}$ M_1 and M_2 unabsorbed. I may have been going astray thinking the familiar y was present.

13.4.45.

Moore I	Unrelated, unselected people		
	+	−	Total
Unabsorbed with 0 $R_1 R_1$	8	91	99
Absorbed with A&B $R_1 R_1$	0	6	6
	8	97	105
	·0762	·9238	
Unabsorbed with 0 $R_1 r$	5	43	48
Absorbed with A&B $R_1 r$	1	3	4
	6	46	52
	·1154	·8846	
Unabsorbed with 0 $R_1 R_2$	4	19	23
Absorbed with A&B $R_1 R_2$	0	2	2
	4	21	25
	·1600	·8400	
$R_1 r$ }	10	67	77
$R_1 R_2$ }	·1299	·8701	

$R_1 R_1$ v { $R_1 r$ / $R_1 R_2$ }		+	−	
$R_1 R_1$		8	97	105
$R_1 r$ }		10	67	77
$R_1 R_2$ }				
		18	164	182

$$\chi^2 = \frac{34280792}{23866920} = 1{\cdot}4$$

Moore 2	Unrelated, unselected people		
	+	-	Total
Unabsorbed with O $R_1 R_1$	9	92	101
Absorbed R_3 only with AB $R_1 R_1$	0	6	6
Absorbed R_3+ SC with AB $R_1 R_1$	0	3	3
	9	101	110
	·0818	·9182	
Unabsorbed with O $R_1 r$	1	48	49
Absorbed R_3 only with A&B $R_1 r$	0	4	4
Absorbed R_3+ SC with A&B $R_1 r$	0	15	15
	1	67	68
	·0147	·9853	
Unabsorbed with O $R_1 R_2$	1	18	19
Absorbed R_3 only with A&B $R_1 R_2$	0	3	3
Absorbed R_3+ SC with A&B $R_1 R_2$	0	3	3
	1	24	25
	·0400	·9600	
$R_1 r$ } $R_1 R_2$ }	2	91	93
	·0215	·9785	

$R_1 R_1$ v ($R_1 R_2$ / $R_1 r$)		+	-	
	$R_1 R_1$	9	101	110
	$R_1 R_2$ } $R_1 r$ }	2	91	93
		11	192	203

$$\chi^2 = \frac{77279867}{21605760} = 3{\cdot}6$$

11. 5. 1945.

When a woman has anti-Rh and has had a still birth what happens to the ensuing pregnancies?

Such mothers	S.B.	Misc.	I.G.N.	Normal	
46	58	14	36	4	2 of these rr 2 not tested

I.G.N. 36 → died 29, recov. 7

Born dead 72

Born Alive 40

Dead in a week or so 101

Surviving 11

Some or many of these women may have had their serum sent for examination because they had a long list of disasters.

Of the 7 I.G.N. who recovered 6 were transfused.
Of the 29 who died one may possibly have been transfused.
(This was Tong and I think Stanbury said the physician prevented the transfusion until the child was moribund).

Of the 29 who died & were not transfused a lot were born in 1943 & three in either 44 or 45.

July 1945

Not published:
evolved into Nature letter. = RAF. aug 20th 1945
appeared Jan 12. 1946.

& the gene freq part into the French paper.

Rh gene frequencies in England

R. R. RACE

(Working on behalf of the Medical Research Council)

From the Galton Laboratory Serum Unit at the Department of Pathology, Cambridge.

Suspensions of red cells from 927 blood transfusion donors have been tested for agglutination by sera containing the first four types of Rh antibodies shown in Table I, that is Γ Δ H and γ. The sample was selected only in that it contained an excess of group O blood. This total does not include the first 154 bloods tested with the four sera, (Race, Taylor, Cappell and McFarlane 1944), nor does it include any members of the first 100 families so tested. (Race, Taylor, Ikin and Prior 1944, 1945).

The isolation of the genes shown within the enclosure in Table I and the determination of their reactions with the various types of antisera, was arrived at independently by Wiener (1943) and by ~~English~~ British Workers. (Race and Taylor 1943; Race, Taylor, Boorman and Dodd 1943; Race, Taylor, Cappell and McFarlane 1944; ~~McCall, Race and Taylor~~). The ~~latter~~ British workers, in the fortunate possession of St. serum (γ), were able to detect the presence or absence of a further Rh antigen. St serum ~~is~~ also isolated a seventh gene now called Rh_z.

The part of Table I, ~~above and to the left of the darker line,~~ within the enclosure, shows the interaction of genes and antibodies known at the time when Professor Fisher proposed his theory. (Race 1944). The theory was based mainly on the antithetical reactions of the 70% and the 80% sera with the various genes. Up to that time it had been generally supposed that there were seven alleles at one locus. Fisher, however, postulated three closely linked loci, each with two alleles. The alleles, six in all, each having their particular antibody.

Antibody	Genes, or antigens, on chromosome	Antibody
Γ	C or c	γ
Δ	D or d	∫
H	E or e	η

As such a chromosome could be built up in eight different ways an eighth gene, Rh_y, had to be postulated. Also two more antibodies were required, ∫ and η, bearing the same relation to Δ and H as that born by γ to Γ. The theory was

immediately of practical use as a rationalisation and aid to memory of the rather bewildering and apparently arbitrary reactions of the various sera. Several of the predictions have been realized, so that there is now strong supporting evidence for the scheme. The theory demanded that Rh_z should be $\Gamma+$ and it was later shown to be so (Murray, Race and Taylor 1944), by a fortunate segregation in the family of the second Rh_z person I had found. The reaction with Γ & Δ of the Rh_z in this persons blood had previously been obscured by the presence of Rh_1 in the genotype. That Rh_z was found to be $\Delta+$ did not give any supporting evidence, for had it been $\Delta-$ it would have fitted Rh_y. Mourant (1945) has found a serum which is undoubtedly η; it gives approximately the expected frequency of positives in a random sample of bloods and it reacts with Rh_1, Rh_2, rh, Rh" and Rh' in the way predicted for η. There is good reason to think that Levine's anti-Hr serum (Waller and Levine 1944) is the missing ζ (Race, Cappell and McFarlane 1945). Rh_y remains to be found. The predicted reactions are shown outside the enclosure in Table I, those in brackets have yet to be verified.

The reactions given by 927 bloods.

The results of testing this number of bloods with sera of the four types are given in Table II. Although neither serum was used in the investigation, the Table includes the reactions of both ζ and η, and the distinctions they make; some confirmed and some still theoretical. The genotypes involving the hypothetical Rh_y gene are also included although their existence has not yet been demonstrated.

The gene frequencies.

From the distribution observed in the four reacting groups an estimate can be made of the frequencies of each gene in the English population.

The gene frequency of rh has been taken as the square root of the frequency of - - - + bloods, this is 0·3844.

The group + - - + consists only of Rh'rh, so the frequency of Rh' can be taken as $\frac{0\cdot0065}{2x0\cdot3844}$ or 0·0085.

The group - - + + consists almost entirely of Rh"rh so the frequency of Rh" can be taken as $\frac{0\cdot0129}{2x0\cdot3844}$ or 0·0168.

The group -+ - + consists almost entirely of Rh_0rh so the frequency of Rh_0 can be taken as $\frac{0\cdot0248}{2x0\cdot3844}$ or 0·0323.

The group + + - - consists of Rh_1Rh_1 and Rh_1Rh' so $(Rh_1)^2 + 2\ Rh_1Rh' = 0\cdot1974$ and $Rh_1 = 0\cdot4359$.

The group + + + - consists almost entirely of Rh_1Rh_2 Rh_3 so the frequency of Rh_2 can be taken as $\frac{0\cdot0011}{2x0\cdot4359}$ or 0·0013.

By difference $Rh_2 = 0\cdot1208$. These frequencies are summarised in Table III.

From these gene frequencies have been calculated the expected frequencies of the 28 genotypes which must exist, (provided none of them are lethal). These are given on the right of Table II. For example, the expected frequency of the genotype Rh_2Rh_2 equals the square of the frequency of the gene Rh_2. The expected frequency of the genotype Rh_1Rh_2 equals twice the gene frequency of Rh_1 multiplied by the gene frequency of Rh_2.

In some compartments the expected frequencies give a good check on those observed. For example the gene frequency of rh is calculated from the - - - + group, and that of Rh_1 from the + + - - group. The expected frequency of the genotype Rh_1rh is 2 x 0·3844 x 0·4359 or 0·3351. To this is added the expected frequency of the two rarer members of this group, Rh_0Rh' and Rh_1Rh_0, and the total is 0·3638. That is 36% of all bloods are expected to belong to this group and 35% were found to do so.

Technique.

The tests were made in tubes 7 mm in diameter and 5 cms long. A volume of about 1/120 c.c. of the red cells suspension was added to an equal volume of serum. The

volumes were measured with a small Pasteur pipette. Economy of serum was the only reason for using such very small volumes, which with a lot of practice can be managed easily. Some of the sera were used undiluted, some were used half strength, having been diluted with an equal volume of saline. The cell suspensions were about 1% packed cells in saline. The mixtures of sera and cells were allowed to settle for an hour or more in an incubator at 37°C. The greater part of the deposit of cells was then carefully transferred to a slide, with a small Pasteur pipette. If agglutination on the slide was not obvious to the naked eye it was examined microscopically. Some further observations on the tests will be made under the heading of the appropriate serum, for which Fisher's notation is used followed by that of Wiener (~~recent~~ 1944).

⌐ sera. (Anti-Rh').

Two sera of this type, from Rh negative mothers of haemolytic babies, were used in nearly all the tests. A third and fourth were also used ~~as well~~ if there was any doubt about the result.

The ten sera of this type that I have so far examined have all had the "incomplete" or non-agglutinating form of Δ (Race 1944), which may conveniently be called Δ'. These sera are really therefore ⌐Δ'. Certain of them may occasionally agglutinate Rh_2 cells weakly; as these cells lack C it is probable that such sera also contain a subliminal amount of Δ; ~~as well;~~ are perhaps in fact ⌐Δ'Δ. The technique used ~~by me~~ seldom shews this Δ reaction, but I have found that if Rh_2 cells are suspended in the acid glucose citrate mixture, of p.H. about 5·6, which is used for storing transfusion blood. (Loutit, Mollison and Young, 1943), then this reaction sometimes becomes definite and the cells might be thought to be ⌐ positive.

Very infrequently, apparent Rh_1 rh cells $\left(\frac{CDe}{cde}\right)$ are agglutinated strongly by one or two ⌐ sera but not by others. One blood behaving in this way was noticed in the present series.

Δ was excluded as the cause of the strong reaction which was given by only two out of four Δ' sera. Further I was unable, with Δ', to block the D in these curious cells which remain a puzzle.

Δ sera. (Anti-Rh_0).

Most of the specimens were tested with two sera of this type. The donors of the sera were rh rh mothers of haemolytic babies. There was only one difficult blood in the 927, it was scored as Rh_1 rh but it may have been Rh'rh, or perhaps more probably Wiener's "intermediate" called $Rh^{\prime}_{(0)}$, the brackets indicating the weak reaction. (Wiener 194). This blood gave weak reactions with five Δ sera and a negative reaction with one. The remaining 926 were clearly negative or positive. A second specimen of this unusual blood gave similar results. The blood of available relatives of the donor threw no light on the problem. "Intermediates" are said to be relatively common amongst American negroes (Wiener, (Unger and Sonn 1945) but they are clearly very rare in the English population.

I have tested in all about two thousand bloods with the four sera. Two, neither in the series now reported, have given the reactions of Rh'Rh', that is + - - -. As Rh'Rh' is only to be expected once in about 10,000 bloods, this finding is a little disturbing. One of the Rh'Rh' persons has been tested on four separate occasions, on the last of which a weak reaction was given with a very powerful Δ serum. The donor's family was not accesible, but it seems possible that the true gentoype may have been $Rh'Rh^{\prime}_{(0)}$.

H sera. (Anti-Rh").

Two sera of this type were used. One of them, the original serum J, (Race et al 1943), was from an Rh_1 rh mother of a haemolytic baby. This was a pure H serum. It was used only in the first 400 tests. The other very powerful H serum was used in all the tests,

it was from an Rh negative mother of a haemolytic baby. The latter serum was originally $\Delta\Delta^1 H$ and contained α and β as well. Δ, Δ^1, α and β were all removed by three absorptions with A_1 B Rh_1Rh_1 cells $\left(\frac{CDe}{CDe}\right)$. The resulting absorbed serum, containing only H, is very powerful and has been used diluted 1/2 in saline, although probably a dilution of 1/4 or 1/8 would have been satisfactory. No difficulties were encountered in the tests with these two sera.

The H - E reaction is sensitive to differences in pH. If cells containing E are suspended in acid citrate glucose (pH about 5·6) they may react not at all, or perhaps only with undiluted H. As the pH of the citrate used for the cell suspension and the serum dilution is increased, the titre rises to a maximum, at about pH 7. At this pH the E cells are agglutinated by a dilution of $\frac{1}{256}$ of the H serum (the stronger of the two mentioned above). At a higher pH the titre begins to fall.

γ sera (called originally St).

Three sera of this kind have been employed, all from Rh_1Rh_1 $\left(\frac{CDe}{CDe}\right)$ mothers of haemolytic babies. Nearly all of the 927 samples were tested against two of these three sera.

In 1943 I found that the original St serum (Race and Taylor 1943) was apparently "going off", although it was stored at about - 20°C. The serum became negative with many bloods representing a single dose of c (e.g. Rh_1rh $\frac{CDe}{cde}$). This could be remedied and the pristine reaction restored by absorbing the serum with cells lacking c, (e.g. Rh_1Rh_1 $\frac{CDe}{CDe}$) or, even more surprisingly, with sheep cells. Later I noticed that the serum which had "gone off" when tested with, say, Rh_1rh cells suspended in saline, reacted perfectly well with the same cells if they were suspended in the acid citrate mixture already mentioned. It seemed possible that the serum on storage had become gradually more alkaline and that the absorption

with cells was effective because the serum was thereby made more acid. If CO_2 was bubbled through the serum it was restored to its full activity.

Dosage effect of the genes.

The interaction of St serum and its antigen, that is the γ- c reaction, has for some time been known to show a distinct dosage effect (Race, Taylor, Boorman and Dodd 1943). When, for example, γ serum is titrated against cells of the type $Rh_1 rh \left(\frac{CDe}{cde}\right)$ the titre is constantly lower than that found on titrating cells with a double dose of c such as $Rh_2 rh \left(\frac{cDE}{cde}\right)$.

With Γ, Δ and Η sera a dosage effect is far less obvious. It does exist nevertheless, although perhaps not apparent in a single titration. If, however, three $Rh_1 rh$ and three $Rh_1 Rh_1$ bloods are titrated with three different Γ sera, and scores are given for the strength of reaction in each tube, on adding up the totals it will generally be found that the $Rh_1 Rh_1$ cells come out top. Δ and Η sera behave in the same way. Although this difference undoubtedly exists, the method described for detecting it is too laborious and not sufficiently reliable to be of much practical use. Mourant (1945) found a distinct dosage effect with the η serum.

Other tests with the four sera.

Table 4 shows the results of the present tests and also those of four other series. In the series of Mexican Indians it is likely that apparent $Rh_1 rh$ bloods are really $Rh_1 Rh_0$ since the gene rh is so rare in this population. For the same reason the apparent $Rh_0 rh$ is probably $Rh_0 Rh_0$, and the nine "Rh_2" are probably $Rh_2 Rh_2$.

Summary.

The results are given of testing samples of blood from 927 donors against four different types of anti-Rh sera (Γ, Δ, Η and γ). From these an estimate has been made of the frequencies in England of the seven known forms of the Rh gene.

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Table 1

The interaction of antibodies and antigens.

ANTIBODIES					GENES							
					Wiener, Race et al.	Rh_1	Rh_2	rh	Rh_0	Rh''	Rh'	Rh_3	Rh_y
					Wiener more recent	Rh'_0	Rh''_0	rh	Rh_0	Rh''	Rh'		
					Fisher	CDe	cDE	cde	cDe	cdE	Cde	CDE	CdE
Approximate % positive (Wiener)	Wiener, Race et al.	Wiener more recent	Fisher	Coppell after Fisher									
70	anti-Rh_1	anti-Rh'	Γ	anti-C		+	−	−	−	−	+	+	(+)
85	anti-Rh_0	anti-Rh_0	Δ	anti-D		+	+	−	+	−	−	+	(−)
30	anti-Rh_2	anti-Rh''	H	anti-E		−	+	−	−	+	−	+	(+)
80	St.		γ	anti-c		−	+	+	+	+	−	−	(−)
65			δ	anti-d		−	−	+	(−)	(+)	(+)	(−)	(+)
96			η	anti-e		+	−	+	(+)	−	+	(−)	(−)
87	~~anti-Rh'~~	anti-Rh_1	ΓΔ	anti-CD	give no further information								
87	anti-Rh''	anti-Rh_2	ΔH	anti-DE									

Fisher based his theory on the reactions within the enclosure, particularly on the antithetical reactions of the 70% serum and the 80% serum. All the reactions without the enclosure were predicted by the theory, those ~~of them~~ in brackets are yet to be confirmed serologically.

Table 2

Results of ~~927~~ testing 927 bloods.

Observed total and frequency.	Sera used in the tests. Γ Anti-Rh′	Δ Anti Rh_0	H Anti Rh″	γ st	Sera not used δ	η	Expected frequency of the genotypes, calculated from the gene frequencies.		
113 0·1219	−	+	+	+	−	−	R_2R_2	0·0146	0·1205
					+	−	R_2R''	0·0041	
					+	+	R_2r	0·0929	
							R_0R''	0·0011	
					−	+	R_2R_0	0·0078	
126 0·1359	+	+	+	+	−	−	R_2R_3	0·0003	0·1234
					+	−	R_2R_y		
							$R''R_3$	0·0000	
					+	+	R_2R'	0·0021	
							R_1R''	0·0146	
							R_0R_y		
							R_3r	0·0010	
					−	+	R_1R_2	0·1053	
							R_0R_3	0·0001	
326 0·3517	+	+	−	+	+	+	R_1r	0·3351	0·3638
							R_0R'	0·0005	
					−	+	R_1R_0	0·0282	
137 0·1478	−	−	−	+	+	+	rr	0·1478	0·1478

(Table 2 continued)

183 0·1974	+ + − −	+ +	R_1R'	0·0070	0·1970
		− +	R_1R_1	0·1900	
12 0·0129	− − + +	+ −	$R''R''$	0·0003	0·0132
		+ +	$R''r$	0·0129	
23 0·0248	− + − +	+ +	R_0r	0·0248	0·0258
		− +	R_0R_0	0·0010	
6 0·0065	+ − − +	+ +	$R'r$	0·0065	0·0065
1 0·0011	+ + + −	− −	R_3R_3	0·0000	0·0011
		+ −	R_3R_y		
		+ +	R_1R_y		
			R_3R'	0·0000	
		− +	R_1R_3	0·0011	
0 0·0000	+ − + +	+ −	$R''R_y$		0·0003
		+ +	$R'R''$	0·0003	
			R_yr		
0 0·0000	+ − − −	+ +	$R'R'$	0·0001	0·0001
0 0·0000	+ − + −	+ −	R_yR_y		0·0000
		+ +	R_yR'		

Table 3

Gene frequencies: estimates based on testing 927 people.

Rh_1	0·4359
rh	0·3844
Rh_2	0·1208
Rh_0	0·0323
Rh''	0·0168
Rh'	0·0085
Rh_z	0·0013

Table 4

Tests with the four anti-Rh sera

	English[1] 154		English[2] 927		Australian Whites[3] 225		Mexican Indians[4] 95		American Whites[5] 124	
	Total	percent	Total	percent	Total	percent	Total	percent	Total	percent
R_1R_1	27	17.5	183	19.7	53	23.6	39	41.1	33	26.6
R_1r	56	36.4	326	35.2	71	31.6	7*	7.4	42	33.9
R_1R_2	20	13.0	126	13.6	37	16.4	36	37.9	14	11.3
R_2r or R_2R_2	28	18.2	113	12.2	28	12.4	9**	9.5	11	8.9
R_0r	1	0.6	23	2.5	0		1***	1.1	2	1.6
rr	19	12.3	137	14.8	33	14.7	0		18	14.5
R^1r	2	1.3	12	1.3	1	0.4	0		1	0.8
$R'r$	1	0.6	6	0.7	1	0.4	0		3	2.4
$R'R'$	0		0		1	0.4	0		0	
$R'R''$	0		0		0		0		0	
R_1R_2	0		1	0.1	0		3	3.2	0	

* Perhaps all R_1R_0

** Perhaps all R_2R_2

*** Probably R_0R_0

1 Race Taylor Cappell and McFarlane 1944.

2 Present series

3 Simmons (1945)

4 Wiener, Zepeda, Sonn and Polivka 1945.

5 Wiener, Davidsohn and Potter 1945

5.7.45

Rh gene frequencies in England

R. R. RACE

(Working on behalf of the Medical Research Council)

From the Galton Laboratory Serum Unit at the Department of Pathology, Cambridge.

Suspensions of red cells from 927 blood transfusion donors have been tested for agglutination by sera containing the first four types of Rh antibodies shown in Table I, that ia Γ Δ H and γ. The sample was selected only in that it contained an excess of group O blood. This total does not include the first 154 bloods tested with the four sera, (Race, Taylor, Cappell and McFarlane 1944), nor does it include any members of the first 100 families so tested. (Race, Taylor, Ikin and Prior 1944, 1945).

The isolation of the genes shown within the enclosure in Table I and the determination of their reactions with the various types of antisera, was arrived at independently by Wiener (1943) and by ~~English~~ British Workers. (Race and Taylor 1943; Race, Taylor, Boorman and Dodd 1943; Race, Taylor, Cappell and McFarlane 1944; ~~McCall, Race and Taylor~~ British workers). The ~~latter~~, in the fortunate possession of St. serum (γ), were able to detect the presence or absence of a further Rh antigen. St serum ~~xx~~ also isolated a seventh gene now called Rh_z.

The part of Table I, ~~above and to the left of the darker line,~~ within the enclosure shows the interaction of genes and antibodies known at the time when Professor Fisher proposed his theory (Race 1944). The theory was based mainly on the antithetical reactions of the 70% and the 80% sera with the various genes. Up to that time it had been generally supposed that there were seven alleles at one locus. Fisher, however, postulated three closely linked loci, each with two alleles. The alleles, six in all, each having their particular antibody.

Antibody	Genes, or antigens, or chromosome	Antibody
Γ	C or c	γ
Δ	D or d	δ
H	E or e	η

As such a chromosome could be built up in eight different ways an eighth gene, Rh_y, had to be postulated. Also two more antibodies were required, δ and η, bearing the same relation to Δ and H as that born by γ to Γ. The theory was

immediately of practical use as a rationalisation and aid to memory of the rather bewildering and apparently arbitrary reactions of the various sera. Several of the predictions have been realized, so that there is now strong supporting evidence for the scheme. The theory demanded that Rh_z should be Γ+ and it was later shown to be so (Murray, Race and Taylor 1944), by a fortunate segregation in the family of the second Rh_z person I had found. The reaction with Γ & Δ of the Rh_z in this persons blood had previously been obscured by the presence of Rh_1 in the genotype. That Rh_z was found to be Δ + did not give any supporting evidence, for had it been Δ - it would have fitted Rh_y. Mourant (1945) has found a serum which is undoubtedly η; it gives approximately the expected frequency of positives in a random sample of bloods and it reacts with Rh_1, Rh_2, rh, Rh" and Rh' in the way predicted for η. There is good reason to think that Levine's anti-Hr serum (Waller and Levine 1944) is the missing ζ (Race, Cappell and McFarlane 1945). Rh_y remains to be found. The predicted reactions are shown outside the enclosure in Table I, those in brackets have yet to be verified.

The reactions given by 927 bloods.

The results of testing this number of bloods with sera of the four types are given in Table II. Although neither serum was used in the investigation, the Table includes the reactions of both ζ and η, and the distinctions they make; some confirmed and some still theoretical. The genotypes involving the hypothetical Rh_y gene are also included although their existence has not yet been demonstrated.

The gene frequencies.

From the distribution observed in the four reacting groups an estimate can be made of the frequencies of each gene in the English population.

The gene frequency of rh has been taken as the square root of the frequency of - - - + bloods, this is 0·3844.

The group + - - + consists only of Rh'rh, so the frequency of Rh' can be taken as $\frac{0\cdot0065}{2x0\cdot3844}$ or 0·0085.

The group - - + + cinsists almost entirely of Rh"rh so the frequency of Rh" can be taken as $\frac{0\cdot0129}{2x0\cdot3844}$ or 0·0168.

The group -+ - + consists almost entirely of Rh_0rh so the frequency of Rh_0 can be taken as $\frac{0\cdot0248}{2x0\cdot3844}$ or 0·0323.

The group + + - - consists of Rh_1Rh_1 and Rh_1Rh' so $(Rh_1)^2 + 2\ Rh_1Rh' = 0\cdot1974$ and $Rh_1 = 0\cdot4359$.

The group + + + - consists almost entirely of Rh_1Rhz so the frequency of Rh_2 can be taken as $\frac{0\cdot0011}{2x0\cdot4359}$ or 0·0013.

By difference $Rh_2 = 0\cdot1208$. These frequencies are summarised in Table III.

From these gene frequencies have been calculated the expected frequencies of the 28 genotypes which must exist, (provided none of them are lethal). These are given on the right of Table II. For example, the expected frequency of the genotype Rh_2Rh_2 equals the square of the frequency of the gene Rh_2. The expected frequency of the genotype Rh_1Rh_2 equals twice the gene frequency of Rh_1 multiplied by the gene frequency of Rh_2.

In some compartments the expected frequencies give a good check on those observed. For example the gene frequency of rh is calculated from the - - - + group, and that of Rh_1 from the + + - - group. The expected frequency of the genotype Rh_1rh is 2 x 0·3844 x 0·4359 or 0·3351. To this is added the expected frequency of the two rarer members of this group, Rh_0Rh' and Rh_1Rh_0, and the total is 0·3638. That is 36% of all bloods are expected to belong to this group and 35% were found to do so.

Technique.

The tests were made in tubes 7 mm in diameter and 5 cms long. A volume of about 1/120 c.c. of the red cells suspension was added to an equal volume of serum. The

volumes were measured with a small Pasteur pipette. Economy of serum was the only reason for using such very small volumes, which with a lot of practice can be managed easily. Some of the sera were used undiluted, some were used half strength, having been diluted with an equal volume of saline. The cell suspensions were about 1% packed cells in saline. The mixtures of sera and cells were allowed to settle for an hour or more in an incubator at 37°C. The greater part of the deposit of cells was then carefully transferred to a slide, with a small Pasteur pipette. If agglutination on the slide was not obvious to the naked eye it was examined microscopically. Some further observations on the tests will be made under the heading of the appropriate serum, for which Fisher's notation is used followed by that of Wiener (~~recent~~ 1944).

Γ sera. (Anti-Rh').

Two sera of this type, from Rh negative mothers of haemolytic babies, were used in nearly all the tests. A third and fourth were also used ~~as well~~ if there was any doubt about the result.

The ten sera of this type that I have so far examined have all had the "incomplete" or non-agglutinating form of Δ (Race 1944), which may conveniently be called Δ'. These sera are really therefore ΓΔ'. Certain of them may occasionally agglutinate Rh_2 cells weakly; as these cells lack C it is probable that such sera also contain a subliminal amount of Δ; ~~as well;~~ are perhaps in fact ΓΔ'Δ. The technique used ~~by me~~ seldom shews this Δ reaction, but I have found that if Rh_2 cells are suspended in the acid glucose citrate mixture, of p~~H~~H. about 5·6, which is used for storing transfusion blood (Loutit, Mollison and Young, 1943), then this reaction sometimes becomes definite and the cells might be thought to be Γ positive.

Very infrequently, apparent Rh_1 rh cells $\left(\frac{CDe}{cde}\right)$ are agglutinated strongly by one or two Γ sera but not by others. One blood behaving in this way was noticed in the present series.

Δ was excluded as the cause of the strong reaction which was given by only two out of four Δ' sera. Further I was unable, with Δ', to block the D in these curious cells which remain a puzzle.

Δ sera. (Anti-Rh_0).

Most of the specimens were tested with two sera of this type. The donors of the sera were rh rh mothers of haemolytic babies. There was only one difficult blood in the 927, it was scored as Rh_1 rh but it may have been Rh'rh, or perhaps more probably Wiener's "intermediate" called $Rh^{1'}_{(0)}$, the brackets indicating the weak reaction. (Wiener 194). This blood gave weak reactions with five Δ sera and a negative reaction with one. The remaining 926 were clearly negative or positive. A second specimen of this unusual blood gave similar results. The blood of available relatives of the donor threw no light on the problem. "Intermediates" are said to be relatively common amongst American negroes (Wiener, 194 ; Unger and Sonn 1945) but they are clearly very rare in the English population.

I have tested in all about two thousand bloods with the four sera. Two, neither in the series now reported, have given the reactions of Rh'Rh', that is + - - -. As Rh'Rh' is only to be expected once in about 10,000 bloods, this finding is a little disturbing. One of the Rh'Rh' persons has been tested on four separate occasions, on the last of which a weak reaction was given with a very powerful Δ serum. The donor's family was not accesible, but it seems possible that the true gentoype may have been $Rh'Rh^{1'}_{(0)}$.

H sera. (Anti-Rh").

Two sera of this type were used. One of them, the original serum J, (Race, ~~Taylor, Boorman and Dodd),~~ et al 1943) was from an Rh_1 rh mother of a haemolytic baby. This was a pure H serum. It was used only in the first 400 tests. The other very powerful H serum was used in all the tests,

it was from an Rh negative mother of a haemolytic baby. The latter serum was originally $\Delta\Delta'H$ and contained α and β as well. Δ, Δ', α and β were all removed by three absorptions with $A_1B\ Rh_1Rh_1$ cells $\left(\frac{CDe}{CDe}\right)$. The resulting absorbed serum, containing only H, is very powerful and has been used diluted 1/2 in saline, although probably a dilution of 1/4 or 1/8 would have been satisfactory. No difficulties were encountered in the tests with these two sera.

The H - E reaction is sensitive to differences in pH. If cells containing E are suspended in acid citrate glucose (pH about 5·6) they may react not at all, or perhaps only with undiluted H. As the pH of the citrate used for the cell suspension and the serum dilution is increased, the titre rises to a maximum, at about pH 7. At this pH the E cells are agglutinated by a dilution of $\frac{1}{256}$ of the H serum (the stronger of the two mentioned above). At a higher pH the titre begins to fall.

sera (called originally St).

Three sera of this kind have been employed, all from Rh_1Rh_1 $\left(\frac{CDe}{CDe}\right)$ mothers of haemolytic babies. Nearly all of the 927 samples were tested against two of these three sera.

In 1943 I found that the original St serum (Race and Taylor 1943) was apparently "going off", although it was stored at about - 20°C. The serum became negative with many bloods representing a single dose of c (e.g. Rh_1rh $\frac{CDe}{cde}$). This could be remedied and the pristine reaction restored by absorbing the serum with cells lacking c, (e.g. Rh_1Rh_1 $\frac{CDe}{CDe}$) or, even more surprisingly, with sheep cells. Later I noticed that the serum which had "gone off" when tested with, say, Rh_1rh cells suspended in saline, reacted perfectly well with the same cells if they were suspended in the acid citrate mixture already mentioned. It seemed possible that the serum on storage had become gradually more alkaline and that the absorptio-

with cells was effective because the serum was thereby made more acid. If CO_2 was bubbled through the serum it was restored to its full activity.

Dosage effect of the genes.

The interaction of St serum and its antigen, that is the γ- c reaction, has for some time been known to show a distinct dosage effect (Race, Taylor, Boorman and Dodd 1943). When, for example, γ serum is titrated against cells of the type $Rh_1 rh$ $\left(\frac{CDe}{cde}\right)$ the titre is constantly lower than that found on titrating cells with a double dose of c such as $Rh_2 rh$ $\left(\frac{cDE}{cde}\right)$.

With Γ, Δ and H sera a dosage effect is far less obvious. It does exist nevertheless, although perhaps not apparent in a single titration. If, however, three $Rh_1 rh$ and three $Rh_1 Rh_1$ bloods are titrated with three different Γ sera, and scores are given for the strength of reaction in each tube, on adding up the totals it will generally be found that the $Rh_1 Rh_1$ cells come out top. Δ and H sera behave in the same way. Although this difference undoubtedly exists, the method described for detecting it is too laborious and not sufficiently reliable to be of much practical use. Mourant (1945) found a distinct dosage effect with the γ serum.

Other tests with the four sera.

Table 4 shows the results of the present tests and also those of four other series. In the series of Mexican Indians it is likely that apparent $Rh_1 rh$ bloods are really $Rh_1 Rh_0$ since the gene rh is so rare in this population. For the same reason the apparent $Rh_0 rh$ is probably $Rh_0 Rh_0$, and the nine "Rh_2" are probably $Rh_2 Rh_2$.

Summary.

The results are given of testing samples of blood from 927 donors against four different types of anti-Rh sera (Γ, Δ, H and γ). From these an estimate has been made of the frequencies in England of the seven known forms of the Rh gene.

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Table 1

ANTIBODIES

GENES

Approximate % positive White People	Wiener & Race et al	Wiener ~~& Levine~~ more recent	Fisher's names	Cappell after Fisher	Wiener & Race et al: Rh_1	Rh_2	rh	Rh_o	Rh"	Rh'	Rh_z	Rh_y
					Wiener ~~& Levine~~ more recent: Rh'_o	Rh''_o	rh	Rh_o	Rh"	Rh'		
					Fisher & ~~Race~~ et al: CDe	cDE	cde	cDe	cdE	Cde	CDE	CdE
80	Anti Rh_1	Anti-Rh'	Γ	Anti-C	+	−	−	−	−	+	+	(+)
85	Anti-Rh_o	Anti-Rh_o	Δ	Anti-D	+	+	−	+	−	−	+	(−)
30	Anti Rh_2	Anti-Rh"	H	Anti-E	−	+	−	−	+	−	+	(+)
80	~~Affected~~ Strum	Anti-hr	γ	Anti-c	−	+	+	+	+	−	−	(−)
65 ~~66~~	~~probably~~ Levine	anti-hr	δ	Anti-d	−	−	+	(−)	(+)	(+)	(−)	(+)
9%	~~found by~~ Mourant & Brown		η	Anti-e	+	−	+	(+)	−	+.	(−)	(−)

87	Anti-Rh'	Anti-Rh_1	ΓΔ	Anti CD
87	Anti-Rh"	Anti-Rh_2	ΔH	Anti-DE

} give no further information.

particularly on the antithetical reactions of the 70% serum & the 80% serum.

Fisher based his theory on the reactions within the enclosure. All the reactions without this enclosure were predicted by ~~his~~ the theory, those ~~of them~~ in brackets are yet to be confirmed.

antithetical

Table 2

Observed Total & frequency	SERA USED IN TESTS Γ Anti-Rh′	Δ Anti-Rho	H Anti-Rh″	Y Anti-Sf	NOT USED δ	η	Expected frequency of the genotypes Expectation calculated from the gene frequencies	
113 ·1219	−	+	+	+	−	−	R_2R_2 ·0146	·1205
					+	−	R_2R'' ·0041	
					+	+	R_2r ·0929	
							R_0R'' ·0011	
					−	+	R_2R_0 ·0078	
126 ·1359	+	+	+	+	−	−	R_2R_z ·0003	·1234
					+	−	R_2R_y	
							$R''R_z$ ·0000	
					+	+	R_2R' ·0021	
							R_1R'' ·0146	
							R_0R_y	
							R_zr ·0010	
					−	+	R_1R_2 ·1053	
							R_0R_z ·0001	
326 ·3517	+	+	−	+	+	+	R_1r ·3351	·3638
							R_0R' ·0005	
					−	+	R_1R_0 ·0282	
137 ·1478	−	−	−	+	+	+	rr ·1478	·1478

183	+	+	−	−	++	R_1R'	.0070	.1970
.1974					−+	R_1R_1	.1900	
12	−	−	+	+	+−	$R''R''$	.0003	.0132
.0129					++	$R''r$	.0129	
23	−	+	−	+	++	R_0r	.0248	.0258
.0248					−+	R_0R_0	.0010	
6	+	−	−	+	++	$R'r$	.0065	.0065
.0065								
1	+	+	+	−	−−	R_3R_3	.0000	.0011
.0011					+−	R_3R_y		
					++	R_1R_y, R_3R'	.0000	
					−+	R_1R_3	.0011	
0	+	−	+	+	+−	$R''R_y$		.0003
.0000					++	$R'R''$, R_yr	.0003	
0	+	−	−	−	++	$R'R'$	.0001	.0001
.0000								
0	+	−	+	−	+−	R_yR_y		.0000
.0000					++	R_yR'		

Table 3

Gene frequencies: estimates based on testing 927 people:

Rh_1	0.4359
rh	0.3844
Rh_2	0.1208
Rh_0	0.0323
Rh''	0.0168
Rh'	0.0085
Rh_z	0.0013

Table 4

Tests with the four anti-Rh sera

	English[1] 154		English[2] 927		Australian Whites[3] 225		Mexican Indians[4] 95		American Whites[5] 124	
	Total	Percent	Total	Percent	Total	Percent	Total	Percent	Total	Percent
R_1R_1	27	17.5	183	19.7	53	23.6	39	41.1	33	26.6
R_1r	56	36.4	326	35.2	71	31.6	7*	7.4	42	33.9
R_1R_2	20	13.0	126	13.6	37	16.4	36	37.9	14	11.3
R_2r or R_2R_2	28	18.2	113	12.2	28	12.4	9**	9.5	11	8.9
R_0r	1	0.6	23	2.5	0		1***	1.1	2	1.6
rr	19	12.3	137	14.8	33	14.7	0		18	14.5
$R''r$	2	1.3	12	1.3	1	0.4	0		1	0.8
$R'r$	1	0.6	6	0.7	1	0.4	0		3	2.4
$R'R'$	0		0		1	0.4	0		0	
$R'R''$	0		0		0		0		0	
R_1R_z	0		1	0.1	0		3	3.2	0	

* Perhaps all R_1R_0

** perhaps all R_2R_2

*** probably R_0R_0

1. Race Taylor Coppell and McFarlane 1944.
2. Present Series.
3. Simmons 1945.
4. Wiener, Zapeda, Sonn and Polivka 1945. 5. Wiener, Davidsohn and Potter 1945.

Medical Research Council
Emergency Blood Transfusion Service
at Department of Pathology. Univ of Cambridge
8/8/45

Dear

As there is no knowing when the following will appear in print I am sending my results in this form, in the hope that they may be of some interest.

The total of 927 includes practically all the genotype tests I have done on unrelated normal English donors. This total does not include the first 154 people to be examined with the four sera (Race. Taylor Cappell & McFarlane. Nature June 1944 (153, 52)

ΓΔHy	Total	Frequency	Blood Factor genotype & gene group
− + + +	113	·1219	$R_0 r$
+ + + +	126	·1359	$R_1 R_2$
+ + − +	326	·3517	$R_1 r$
− − − +	137	·1478	$1 r$
+ + − −	183	·1974	$R_1 R_1$
− − + +	12	·0129	$R' r$
− + − +	23	·0248	$R_0 r$
+ − − +	6	·0065	$R' r$
+ + + −	1	·0011	$R_1 R_2$
+ − + +	0		$R' R''$
+ − − −	0		$R' R'$
+ − + −	0		$(R_0) R'$

ESTIMATE OF GENE FREQUENCIES

R_1	·4359
r	·3844
R_2	·1208
R_0	·0323
R''	·0168
R'	·0085
R_2	·0013

Γ = 70% Δ = 95% H = 30% & y = 90%

Yours sincerely
R Race

TO WIRE OR NEWS DESK --- SCIENCE SERVICE SCHEDULE 8/27/45

SPOT:
New uses for hemp required if war-born American industry is to continue - 340
Fungus-proof cotton fabric fails to rot during six months' burial - 235
American occupation of southern Korea satisfactory to country's people - 465
New under-water cutting of steel plates combines arc and hydrogen gas - 190
Rh blood incompatibility may cause idiocy; research program urged - 235

For special service, wire or write Science Service 1719 N St., N.W., Washington 6, D.C.

**********TEAR OFF HERE**********

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**********TEAR OFF HERE**********

Science Service Aug. 27, 1945

GREAT PROGRAM OF COOPERATIVE RESEARCH URGED TO STUDY PROBLEM OF RH BLOOD INCOMPATIBILITY WHICH MAY BE IMPORTANT CAUSE OF FEEBLEMINDEDNESS AS WELL AS INFANT DEATH

By Science Service

LONDON -- The dramatic achievements of medical skill in saving the lives of babies threatened with death because the Rh factor in their blood is incompatible with the blood of their mothers may be followed by the tragedy of having a living idiot instead of a dead baby. Calling attention to this, the British Medical Journal editorially urges an extensive program of cooperative research in this field.

Drs. R. R. Race and A. E. Mourant, of the Galton Laboratory Serum Unit of Cambridge, England, have already offered their services and facilities for such a program, it was announced.

The disease caused by Rh incompatibility, erythroblastosis fetalis, is responsible for more deaths than is any other inherited condition -- perhaps for more than all of them put together, the editorial states. But studies recently made in the United States show that a much larger percentage of feebleminded children are Rh positive with Rh negative mothers than would be expected on the basis of statistics for the whole population. This indicates that damage to the baby's brain may occur before birth.

"Rh incompatibility," the editorial declares, "raises a problem in negative eugenics second to no other ... it seems futile to suggest that the 15% of women who are Rh negative should have 85% of the male population barred to them; yet the dangers are relatively great. It is clear that more research is urgently called for along a number of different lines."

Mothers.

4.9.45

All Rh negatives

Δ found			Noaaf	
	A_1	A_2	A_1	A_2
	46	27	44	24
		37.0%		35%

All Rh positives

A_1	A_2	Total
124	32	156
	20.5%	

(Galton Lab 22.0%)

It can't be that anti-Rh is easier to spot in A_2 people. If this were so it would certainly have explained the excess of A_2 in the anti-Rh found groups but it would lead to an excess of A_1 and shortage of A_2 in the no a.a.f groups.

It looks as if an A_2 mother must make anti-Rh more easily than an A_1 and both of them more easily than an O.

Rh −

A_1	A_2
90	51

	A_1	A_2	
Rh Neg	90	51	141
Rh Pos	124	32	156
	214	83	297

3449

$$\chi^2 = \frac{\left[(90 \times 32) - (124 \times 51)\right]^2 297}{141 \times 156 \times 83 \times 214} = \frac{352757392}{390692952}$$

2880 6324

21996

$$= 9.0$$

$$p = .001$$

1/1000

4.9.45

Galton Lab
A_2 = 22% of A_1

Anti-Rh & $A_1 : A_2$

	Rh neg mothers & Anti-Rh		Rh- but not aaf		Rh+	
	A_1	A_2	A_1	A_2	A_1	A_2
Aug 44 to Oct 42	30	12	29	14	82	17
		29%		33%		17%

20 about should be in this group → where Rh is not involved

← Leaving about 20 where Rh was involved but could not be found

But they all seem to show the Rh effect on $A_1 : A_2$

A_1	A_2	Total
59	26	85
	31%	

Rh negative MOTHERS

Δ no. aaf

	A1	A2	A1	A2
AUG. 1944				
17.			BEVAN	
16.				SHREEVE
4			MELIA	
JULY 1944				
29	MARSDEN			
24.			HAWKINS	
20		HAYWARD		COGDEN
3				HENSON
JUNE 1944				
30				
27		CATER		
2	GOWLAND			
MAY. 1944				
15.	DAVIES		HUDSON	
11			RADFORD	
9.		LUNT		
1.			TEALE	
APR. 1944				
28.	CLARK			
22.			EYRE	
19.		COOPER		
14.				KENNELL
6.			McCAINE	
3.		BURTON		
MARCH 1944				
30.		TURNER		
20			CHARLISH	
14	HERBERT	RICHARDSON	JENKINS	
13.			COLEMAN	
11	SMITH			
FEB. 1944				
29.	RIDGEON			
26.				BUTT
21	FORD			
18.		STEPHENS		
	8	8	11	5

Rh+ MOTHERS

	A1	A2
31·8·44	BONSHILL	
29·8·44	LEE	
28·8·44		ASHTON
25·8·44	MARGREN	
	WADE	
18·8·44		BRAND
14·8·44	NEWLOMBE	
10·8·44	CASSELL	
9·8·44	LAMBERT	
4·8·44	WOODHEAD	
24·7·44	COOKE	WORTHINGTON
21·7·44	HERRING	
11·7·44	SAVAGE	
6·7·44		LEIGHTON
30·6·44	MILLAR	
23·6·44	CORKHILL	
22·6·44	WARD	
16·6·44	BURNETT	
9·6·44	SOUTHGATE	
1·6·44	WILLMOTT	
31·5·44	CUNNINGHAM	
27·5·44	CARPENTER	
26·5·44	McEVOY	
24·5·44	SHENSON	
	KING	
23·5·44		MORGAN
19·5·44	HUDSON	
10·5·44	RIDGEON	
9·5·44	NICHOLL	
6·5·44	TUFFNELL	
6·5·44	FROST	
2·5·44	WORTHINGTON	
25·4·44	STEARN	
13·4·44	CHARVET	
6·4·44	HARRISON	
30·3·44	SLOAN	
29·3·44	ELLISTON	
28·3·44	DANDY	
23·3·44		WARWICK
20·3·44	WILSON	
17·3·44	GAYMORN	
16·3·44	BOWEN	
"	LAMB	
15·3·44	HARRIS	
10·3·44	LAYER	
9·3·44	ROE	WILSON
29·2·44	TAYLER	MORLEY
28·2·44	DYSON	
23·2·44	MUIR	
16·2·44	GOULD	
	45	8

Rh negative MOTHERS

Rh+ MOTHERS

Δ no aaf

	A1	A2	A1	A2		A	A2
FEB. 1944.					18·2·44	FEWSTER	
18	HALL-SMITH				14·2·44	WHITE	
					12·2·44		MASON
17	KNIBBS						
16				BURTON			
15			PARKER				
2.	FAIRBROTHER		HILLS				
JAN. 44.					24·1·44	HICKS	
24		STEPHENS		PUGH	22·1·44	ROBARTS	
					20·1·44	RENNIE	
18	JAMES				18·1·44	GRANT	
					15·1·44	ORPWOOD	
6				HODGHTON	14·1·44	RUSSELL	
					7·1·44		STOBART
					5·1·44		McDUFF
					3·1·44		BIDMEAD
DEC. 1943					24·12·43	BYERS	
17			COWEN		20·12·43		SLATTER
					16·12·43	HALL	
11.		PEARSON			11·12·43	GRAHAM	
					2·12·43	SIBLEY	
3	EMMERSON				1·12·43	PRYDDERCH	
2.			ASH				
NOV. 1943.					26·11·43	ELLETT	
30.	SLINGER						
30.	STRATTON						
29.	AUSTIN						
23.			HULLOCK				
19	TAYLOR						
OCT. 1943					28·10·43	GISSING	
29.	PRIOR				26·10·43	NEWSON	
					28·10·43		MALLOCK
26			JAMES				
16	NORGROVE		SIMPSON				
SEPT. 1943					30·9·43	WALTON	
24	ORD				28·9·43	DAY	
22			POTTS				
3.	ATKINSON						
AUG 1943					30·8·43	NORDLEY	
19				MORGAN	12·8·43	EVANS	
					9·8·43	HUNTER	
9			ARCHER		7·8·43	BOVILL	
3.	HINDE						
JULY 1943					30·7·43	MCGINNETY	BRADLEY
30			ROBINSON		29·7·43	EDWARDS	
					19·7·43	KENNEDY	
26			NOWELL		12·7·43	SMEDLEY	
21.	FLEMINGS						
7	SCOTT						
1.			FREEMAN				
	16.	2	12	4		26	7

(3)

Rh negative MOTHERS

Δ no anf

Rh + MOTHERS

	A_1	A_2	A_1	A_2		A_1	A_2
JUNE 1943							
28	SCHOFIELD			CROUCH	10·6·43	HARRIS	
10			DEACON				
MAY 1943							
27	SHANKS				31·5·43	BAILEY	
11			GRAHAM				
7	SMITH						
APR. 1943							
22			PILLING		13·4·43	BROHAM	
					4·4·43		HOLLANDER
2				MOIR			
MAR. 1943							
29				ROSE	30·3·43	HUNT	
					24·3·43	FLOOD	
25			FAWCETT				
13	WARD						
FEB 1943							
22				SELBIE	12·2·43	CHARLSLEY	
12	KELLY						
JAN. 1943					1·2·43		GREY
27	LUCAS				9·1·43	DOMONE	
DEC. 1942							
					21·12·42	LOCK	
16			ALDERSTEIN		16·12·42	NEWELL	
10		LYMAN					
NOV. 1942							
27				BETTS	19·11·42	FITZACKERLEY	
OCT. 1942							
23					13·10·42	TOSTIN	
		GRABBE					
14			L'LYNN				
	6	2	6	5		11	2

Rh −

A		A'		naaf	
A_1	A_2	A_1	A_2	A_1	A_2
9	6	7	9	15	10

16 : 15

31 : 25

45%

Rh +

A_1	A_2	
42	15	57
·74	·26	

A_1	A_2	
31	25	56
42	15	~~4~~57
~~7~~3	40	113

$$\chi^2 = \frac{\left[(42\times 25) - (31\times 15)\right]^2 113}{56\cdot 57\cdot 40\cdot 73} = \frac{3867\ \cancel{+1425}}{\cancel{9320640}}$$

$$= \approx 4\cdot 14$$

1/20

A Rh negative MOTHERS.

Rh + MOTHERS

Δ Δ' no aaf

	A_1	A_2	A_1	A_2	A_1	A_2		A_1	A_2
AUG 1945					Mrs GRIFFIN		24·8·45	Mrs JONES	
28							23·8·45	Mrs NEALE	
				Mrs OVERTON			20·8·45	Mrs NYE	
23							18·8·45	Mrs CHRISTIE	
							18·8·45	Mrs ANDERSON	
21			Mrs THORPE				17·8·45	Mrs HIGHAM	
					Mrs ARBIN		13·8·45	Mrs BRANDER	
20							10·8·45	Mrs HILLS	
	Mrs NICHOL					Mrs GALLONE	2·8·45	Mrs BARNES	3·8·45 Mrs ASHTON
3					Mrs WILSON				
3					Mrs TAYLOR				
2									
JULY 1945				Mrs EMMERSON		Mrs IMPEY	24·7·45		Mrs NENDICK
25							23·7·45		Mrs JOHNS
						Mrs BEESLEY	21·7·45	Mrs NUNNS	
25							19·7·45	PEARSON	
			Mrs RYDER				18·7·45	CHRISTY	
21							11·7·45	BEESON	
					Mrs FISHER		9·7·45	SPOONER	
19							6·7·45	COOMBS	
					Mrs COMINS		2·7·45	EDWARDS	
18									
					Mrs METCALF				
11									
				Mrs DUCKWORTH					
10									
						Mrs COLLINS			
9									
			Mrs COLLEY		Mrs POLLOCK				
5									
					Mrs M°INTOSH				
4									
		Mrs BAILEY							
2									
JUNE 1945				Mrs (Tues) ENGLAND			22·6·45		REE
28							22·6·45		JARVIS
				Mrs (C·T) WHEATLEY			19·6·45	SNELLING	
21							15·6·45		KELLY
	Mrs TALBOT			Mrs GATLEY			12·6·45	OWEN	
18	Mrs CRAIK						11·6·45	BEASLEY	
						Mrs OLBOURNE			
14									
			Mrs BLAKEY						
8									
				Mrs BENNETT					
7									
	Mrs JARVIS								
4									
MAY 1945			Mrs KNIGHT				28·5·45		WATSON
25							24·5·45	POTTER	
			Mrs ?A' WALKER				19·5·45	NOOK	
19							18·5·45	PURLEY	
				Mrs BROOKS			11·5·45		BRADY
15							10·5·45	HOBSON	
		Mrs SPACKMAN					3·5·45	BOREHAM	
12							2·5·45	MEAD	
					Mrs MARSHALL		1·5·45	NICHOLSON	
4									
	Mrs FORD								
2									

Rh negative MOTHERS

	△		△'		no aaf.	
APRIL/45	A_1	A_2	A_1	A_2	A_1	A_2
10.					Mrs GRIFFIN	
9	Mrs LOXTON					
6.						Mrs SAUNDERS
6.						Mrs ASHTON
3.		Mrs BAILEY		Mrs MOUND		Mrs O'BRIEN
MARCH/45						
22	Mrs COLLINS					
21			Mrs HAMMOND			
15						Mrs LYDON *
9					Mrs DAY	
2.		Mrs TELLIS				
FEB. 45						
20	Mrs RODD					
17.	Mrs WHITTLE					
16					Mrs LEVEINE	
14					Mrs WOODMERE	
13.					Miss E. KING.	
9.		Mrs IVORY				
9.		Mrs WHITING				
1.						Mrs COLE

Rh+ MOTHERS

	A	A_2
24.4.45	CLARK	
20.4.45		LINS
17.4.45		CLARK
13.4.45	MILLWARD	
9.4.45		FRIEND
6.4.45	PONDER	
6.4.45	GRIFFITHS	
5.4.45	MORT	
27.3.45		FOX
19.3.45		3rd Pr. (Mother)
14.3.45	PENN.	
5.3.45	JOHNSON	
5.3.45	HUGHES	
2.3.45	LEWIS	
2.3.45	ALLEN	
21.2.45		RUDD
15.2.45	ERICKSON	GREY
11.2.45	WALTON	
10.2.45	MEISZNER	
8.2.45	LOWRIE	
6.2.45	GOOCH.	
1.2.45	ALLEN	CAVANAGH

Rh negative mothers

Rh + mothers

	Δ A1	Δ A2	Δ' A1	Δ' A2	no aaf A1	no aaf A2		A	A2	
JAN. 1945							31.1.45	TALBOT		
31				THOMPSON			26.1.45	HORN WARD		
22.						MARTIN	"	SMALL		
							"	BAKER		
19.					BUTLER		25.1.45	MALTBY		
							22.1.45	LOCKHART		
16	TWISK						18.1.45	HARDY		
							14.1.45	PREW		
15					RUSHTON		13.1.45	MINNIKIN		
							8.1.45	CROMBIE		
10	JAGO									
2.	REES JONES									
DEC. 1944							18.12.44		ROBINSON	
27			SAMMS				11.12.44	BARBER		
26			BURGESS		WALKER					
22.				RENDELL						
21	"C"									
20			JEFFRIES							
16.				PARRY						
8.				LAWTON						
7.			PAMES							
NOV. 1944.							29.11.44	DAWSON		
28						WEBSTER	22.11.44	PARR		
							21.11.44	PASSEY		
24.	ROLLETT						20.11.44	GATLEY	PARKIN	
							15.11.44	MIKKELSON		
22.					GOUGH		14.11.44		UHL	
							13.11.44	BULLEN		
20.			TUBB.				8.11.44	MARSH		
							3.11.44	HEATH		
6.					MACKEW			ANGOOT		
							2.11.44	HAZLEWOOD		
2			HAMMOND				1.11.44	HUTCHINS		
OCT. 1944.							24.10.44	HUGHES		
30.		MIDDLEMASS					18.10.44	HALEY		
								ANDREWS		
21.						RICHARDSON	11.10.44		BOULDSTRY	6E
							4.10.44	BUSKY		
14.					NERSON					
12.			STEAD							
10.	TAYLOR.									
9		COLLIN								
SEPT. 44							27.9.44	BLOWMAN	EMMETT	
30.		MCELROY					22.9.44	MILLER.		
							21.9.44	ROSE	MCGUIRE	
27						RICHARDSON	20.9.44		BOYES ?	
							18.9.44	AUSTIN		
26.		HEFFER.					12.9.44		CARTER	
							12.9.44		SPOKES	
20		RAMSEY			WALKER		8.9.44	TURTON		
							7.9.44		BRETT	
9.		FLACK.								
	6	6	7	3	7	4		32	10	

19.9.45

Sera not sent as "anti-Rh found"

Pure Δ	Δ or Δ' weak or for other reasons not proved freefrom Γ or H	Δ+Γ	Δ+H	Γ	γ	H	Total
26	204	14	2	6	1	1	254
		6%	·8%	3%	·4%	·4%	

19.9.45

Sera not sent as "anti-Rh found"

Δ' only / Δ'' only

~~Angel~~
Bennett
Biddulph
Borthwick
Bradbury
Brooks
Buxton
Cooper
Eyre
Heffer
Helliwell
Herbert
Ingles
Johnson
Knotts
Ledbetter 16
Moore
Pringle
Rees
Richardson
Ridgeon
Rollett
Scott
Teale
Turner
Weedon 26

Δ or Δ+Γ or Δ+H } distinction not noted on card or too weak to make

abbott
anthony
armitage
ash
Atkinson
austin
Barber
Barnes
Barton
Beasley
Bell
Bibby
Blakey
Blennys
Brett Young
Brown
Burgess
Burland
Burton
Buxton
Butt
Callender
Carolan
Catts
Charlish
Checkell
Clark
Cochrane
Collin
Collins
Conway
Cope
Corner
Cornwall
Counsel
Cottle
Craik
Crouch
Davies
Davies
Dawson
Donovan
42

Duckworth
Duffey
Eaton
Eddleston
Emmerson
Emmerson
Fairhead
Fawcett
Fay
Fish
Flack
Floyd
Fogg
Ford
Ford
Frosdick
Fuller
~~Gandy~~
Gally
Gibson
Gluster
Glover
Goodacre
~~Gowland~~
Graham
Gray
Greaves
Hale
Hammond
Hammond
Harvey
Hassall
Hawkins
Hayward
Hazlewood
Heubner
Higgins
Flo Hill
Hinde
Hodgson
40

Holmes
Hudson
Higgins
Hollock
Ivory
Jackson
Jackson
Jackson
Jago
Jeffries
Jenkins
Johnson
Johnstone
Keay
Kelly
Kelman
Kydd
Lawrence
Lewis
Loewenstein
Lonnon
Lovett
Loxton
Lucas
Lyman 24
Male
Manley
Mann
Mason
Mayes
Meldrum
Metcalf
McKenna
Mingay
Morris
Moss
Moss
Mould
Myers
McNeil
McLean
McCauley
McDonald
McDougal
McElroy
McKeown
McKillen
46

Neil
Musgrove
O'Brien
Oxlade
Palmer
Parker
Parkin
Pash
Patterson
Patton
Payne
Pearson
Pease
Peebles
Pilling
Pugh
Purvis
Redburn
Ramsey
Read
Reeves
Ratcliffe
Riley
Roberts
Ross
Ryder
Rymer
Sanns
Saunders
Schilling
Schofield
Scott
Scott
Searle
Seaton
Sewell
Shanks
Shepherd
Shipley
Slinger
Smith
Smith
Smith
Snelgrove
Spackman
Stabler
Stead
47

Strain
Shatter
Stanton
Sutton
Talbot
Taylor
Taylor
Tellis
Thomas
Thorstensen
Tindale
Toms
Tuffnell
Tweedle
Ward
Walshaw
Watson
Weatherly
Webb
Webster
Wheatley
Whipps
Whiting
Wilkinson
Wood
Wrighton
Wylie
Young
Raymond 29

Δ+Γ

Bells
Collis
Davies
Gow
Hall-Smith
Lawton
Lunt 7
Pip
Smith
Stephens
Titchen
Winter
Wilkins
Yeoward 14

Δ+H

Walton
Teagle
2

pure H, " Γ & Y

Γ
Andrews
Brown
Jarvis
McLennan
Prior
Tingey
6

H
Martinot

Y
Gould
1

Children of $R_1 R_2$ fathers of EF 19.9.45

Father	Sound R_1 r	Sound R_2 r	affected R_1 r	affected R_2 r
Hale	Hale	Hale	Hale	
	Hale	Hale	Hale.	
McConkey	McConkey			McConkey.
	McConkey			
Parker	~~Parkin~~	Parkin		Parkin
Payne				Payne
Pringle			Pringle	
Ransay			Ransay	
Rees			Rees	
Ridgeon	Ridgeon	Ridgeon	Ridgeon	
Scott			Scott	
Thorsteinson		Thorsteinson		
Titchener	Titchener		Titchener	
	Titchener			
Tindall	Tindall			
Whipps				Whipps
Brown	Brown			
	Brown			Brown
Buxton	Buxton			Buxton
Corner	Corner			
Emmerson		Emmerson		Emmerson
Henbrey				Henbrey
Hullock			Hullock	
	12	6	9	8

21 14

35 — R_1 r, R_2 r — exp, obs

	obs	exp	o-e	o-e²	χ^2
R_1 r	21	17.5	3.5	12.25	.7
R_2 r	14	17.5			.7
					1.4

19.9.45

118 Fathers of EF

	R_1R_1	R_1R_2	R_1r	R_or	R_1R_2	R_2R_2 or R_2r	R_2r	R_2R_2	Tot
	37	1	18	1	38	20	2	1	118
						23			
observed percent	31.4	0.8	15.3	0.8	32.2	19.5			100.0
Expected appears % of Normal Rh+ men	24	0	42	3	16	15			100 ±
CHANGE	+7.4%	...	-26.7%	....	+16.2%	+4.5%		1.4	

19.9.45

R_1R_1

- Barton
- Beesley
- Biddulph
- Borthwick
- Charlish
- Cochrane
- Cope
- Davies
- Hallsmith
- Hazeldean
- Jackson
- Jenkins
- Lee
- Moss
- Onion
- A_2 Peebles
- A_1 Pipe
- O Roberts
- B Slinger
- A Smith
- O Stephens
- O Stratton
- A Sutton
- A Talbot
- A Taylor
- O Teale
- A R_1R_1
- O Waites
- O Wilkin 29

- Γ.... O Andrews
- AB Bryson
- O Beckwith
- O Wilson
- O Thompson
- A Colley
- A Metcalfe
- A Kestell
- Ballison

[37]

R_1R_2

- O Raymond 1

[1]

R_1r

- Callender
- Clark
- Cooper
- Davies
- Embleton
- Eyre
- Ford
- Gooderham
- Hayward
- Herbert
- Huggins
- Johnson
- Lowson
- Myers
- O Pearson
- O Shanks
- · Watson 17
- O Kraft

[18]

R_0r

- Gow 1

[1]

R_1R_2

- Austin
- Brown
- Buxton
- Davis
- Duckworth
- Emmerson
- Floyd
- Glister
- Heffer
- Heubner
- Howell
- Hullock
- Lunt
- Mole
- McNeil
- McConkey
- McDougall
- Parkin
- A_1 Patton
- A Payne
- O Pringle
- A_1 Ramsey
- O Rees
- O Ridgeon
- A Scott
- A Thomas
- A Thorpe
- O Thorbecke
- O Titchener
- O Trendell
- O Yeowart 31

- Γ... A Brown
- O Clazey
- AB Knight
- A Bailey
- O Sinnott
- O Marks
- A R_1R_2

[38]

R_2r or R_2R_2

- Burgess
- Collins
- Dunn
- Eaton
- Gallimore
- OBH
- Hassall
- Hudson
- Jones
- McElroy
- Mrs C. .
- O Pugh
- O Strain
- A Tupell
- O Wearden
- A Whipps 16
- ~~O [illegible]~~
- ~~A Teagle~~
- O James
- Taylor
- O Turner
- Pask

~~Last one forfeited. Afford to make 100~~

[20]

[19]

R_2r

- Richardson
- Teagle 2

[2]

R_2R_2

- Emmerson 1

[1]

Total 117

Count affected children of R_1R_2 parents

count normal children of ditto.

MEDICAL RESEARCH COUNCIL

Telephone : MUSEUM 3041.
MUSEUM 0943 (ACCOUNTS).
Telegrams : MEDRESCO, WESTCENT, LONDON.

PRIVY COUNCIL

Temporary Address:
c/o LONDON SCHOOL OF HYGIENE,
KEPPEL STREET, LONDON, W.C. 1.

28th September 1945

P.F.148/20

Dear Race,

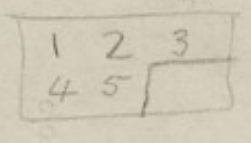
Our Finance Officer assures me that the view of your superannuation provision which you expressed to me the other day was unnecessarily gloomy. The total capital sum for which you are insured under your endowment policies is £3274 plus profits. On survival to 60 that should be worth about £4500, with which you could buy an annuity yielding nearly 8 per cent. If service were continued till 65, you would have in addition five years compound interest on the capital and five more premiums - and the annuity yield per cent would be higher. These calculations leave out of account any new policies in respect of future increments in salary Some of your present policies, by the way, are held by University College and some by the M.R.C.

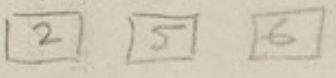
Of course you might not wish to buy an annuity; but that is the fair basis on which to reckon the pension value of the provision, and if you want a permanent investment at a lower rate of interest - i.e. to make the money do more than provide a personal pension - that is your affair.

I am, Yours sincerely,

A. Landsborough Thomson

R.R. Race, Esq.,M.R.C.S.,
Galton Laboratory Serum Unit,
Department of Pathology,
Cambridge.


1 2 3
4 5


2
5
6

29.10.45

European Geneticists.
Serks, Brachet, Mohr, Hagedoorn. Winge
Bonnier

The bloodgroups depend on antigens

Antibodies – some found in other members of the species
\ some only result of immunisation

1940 Rh system of groups
antibodies only under certain circumstances
② ~~immunisation~~ by transfusion
① immunisation by foetus

① diagram of foetus.

RR × rr pedigree
Rr × rr pedigree

1943 7 alleles at 1 locus

1944 R.A.F

Confirmation < R3 / ry – Ro
Genepeg
C–O

② Transfusion
hypersensitive recipient
Moore charts
Y
Lutheran
Willis – probably 12 genes ~~alleles~~ or combination
Levay
anti-N

Odd diagrams EF families
~~Map of England~~.
Map of ~~OxA ratio~~ in Europe

O. 38

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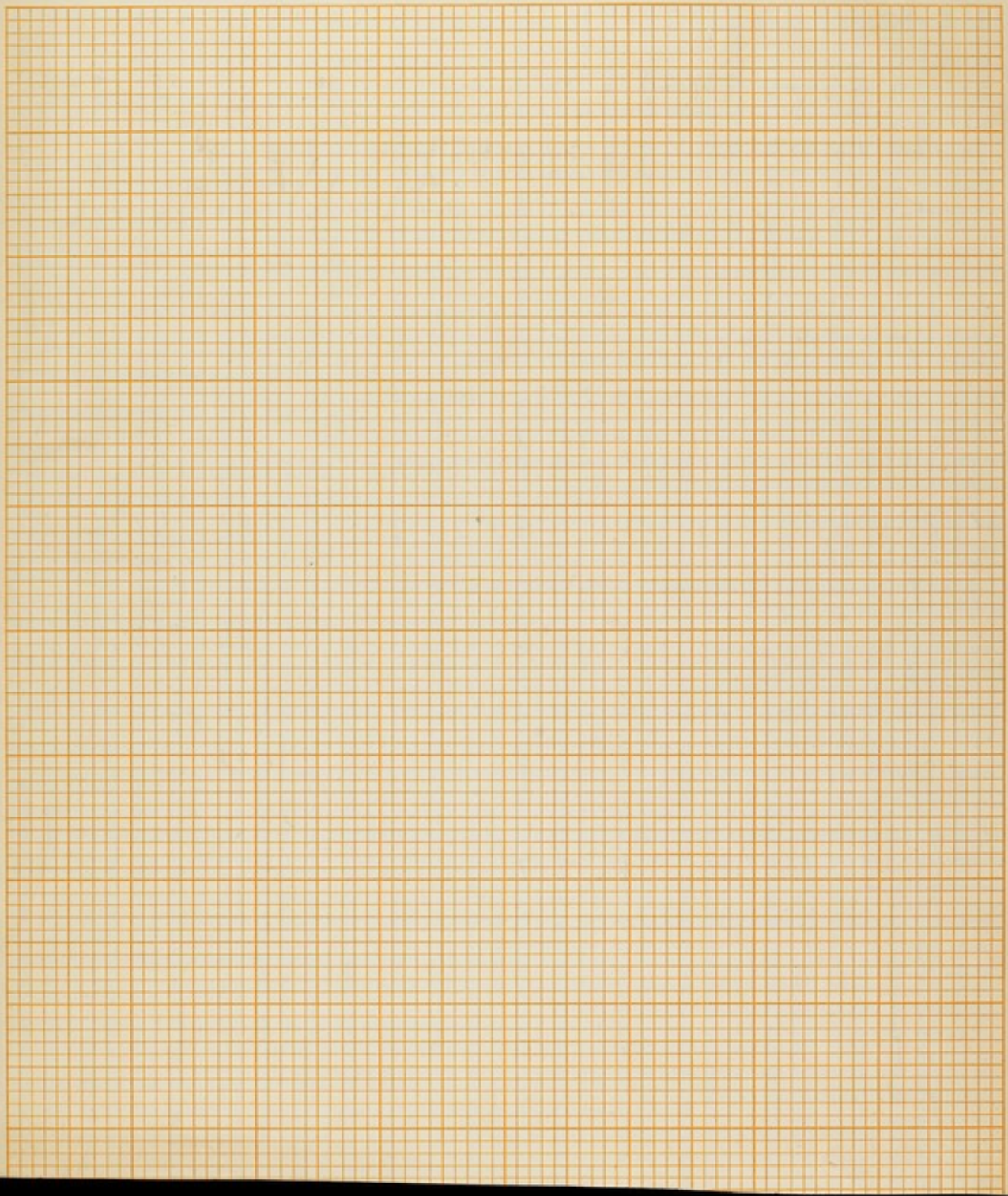
Telephone:

9.12.45

Rh

		without δ	with δ
For 12 "genes"	$\frac{1}{2}n(n+1)$ = 78 genotypes	& ~~38~~ 36	~~55~~ 54 phenotypes
For 8 "genes" (without C")	= 36 genotypes	18	27
For the 9 known "genes"	= 45 genotypes	& ~~26~~ ~~25~~ 24	~~38~~ 37? phenotypes

	A_1A_2BO	MN	P	Rh	Lutheran	Lewis	Combinations
Recognisable now without δ (9 Rh genes)	6	3	2	~~26~~ ~~25~~ 24	2	2	3,744 3456 ~~3,660~~
Probably recognisable now if only they would turn up (12 Rh genes) without δ.	6	3	2	~~38~~ 36	2	2	~~5,472~~ 5184
Phenot prob recog if they turned up (12 Rh genes) & 4 δ found	6	3	2	~~54~~ ~~55~~	2	2	~~7,920~~ 7776
Genotypes now known to be possible	10	3	3	45	3	3	36,450
Genotypes that probably exist	10	3	3	78	3	3	63,180



RAF's class, Loyrac term 1945

O M R_1R_1P

Pickles, T
Stovin, P

O M R_1R_2P

King, M
Wintersgill, P

O M R_1R_2p

Elliott, P
Watson-Williams, E

O M R_2r p

Brindley, G
Cooper, E
Heaton, J

O M rr P

Keeley, R

O M rr p

Strong, J
Williams, Peter (St. Jns)

O M R_1r P

Holden, G
Morrison, W

O M R_1r p

House, M
Lester, J
Richardson, A
Watkinson, R

A_1M R_1R_1 P

Vans Agnew, W

A_1 M R_2r P

Binns, W
Booth, C

A_1 M rr P

Brown, P

A_1 M R_1r P

Anderson, T
Dickinson, G
Eddington, J
Last, K

A_1 M R_1r p

Hockey, B
(Leeson, R
Leeson, S)
Williams-Rhys, T

A_2 M R_2r P

Hilary-Jones, P

A_2 M rr p

Williams, J (Clare)

B M R_1r P

Currie, J
Neame, J

B M R_1r p

Newman, M

A_1B M R_1R_2P

Barclay, A

O MN R_1R_1 P

Bond, G
Oram, G
Roffey, P
Tomson, P

O MN R_1R_2 P

Court, G
Eastwood, D
King, R
Lemmon, D
Shackleton, J
Wallace, A
Wynne, J

O MN R_1R_2 p

Kirk, E

O MN R_2r P

Sebag-Montefiore, S

O MN R_2R_2P

Williams, P (St. Cath)

O MN rr P

Crews, J
Jarvie, E
Kerr, J
Milligan, J
Shepard, R

O MN rr p

Hort, J
Perkins, K

O MN R'r p

Adrian, R

O MN R_1r P

Baxter, R
Corfield, N
Fairgrieve, J
Gray, B
Hill, J
Martin, P
McMullan, J
Perry, S
Steel, P
Williams, C
Williams, J.P (Emm)

O MN R_1r p

Fox, M
Hirons, R

A_1 MN R_1R_1 P

Barrett, E
Goodson, M
Mallick, P
Wagstaffe, P

A_1 MN R_1R_1 P

Sewart, J

A_1 MN R_1R_2P

Brian-Brown, P
Butcher, A
Draper, J
Nixseaman, D

A_1 MN R_2r P

Bates, A
Higgins, R
Thompson, P (St. Jms)
Wills, V

A_1 MN R_2R_2 P

Stewart, J

A_1 MN rr P

Bennett, J
Blakeway, I
Lister, K
Muir, B
Southill, J
Vint, G

A_1 MN rr p

Young, S

A_1 MN R_1r P

Garrod, D
McGregor, A

A_1 MN R_1r p

Rinsler, M

A_2 MN R_2r P

Lewin, D
Sykes, M

A_2 MN R_2R_2 P

Coats, E

A_2 MN R_1r p

Rowson, K

B MN R_2r P

Ives, M

B MN R_2r p

Simmonds, I

B MN rr p

Chambers, J

A_1B MN R_1R_1 P

Marshall, M

A_1B MN rr P

Owens, R

A_1B MN R_1r p

Gibbs, M

A_2B MN R_1R_1 P

Mackinder, F

O N R_1R_1 P

Whalley, L

O N R_1R_2 P

Hargreaves, G
Thomson, P

O N R_2r P

Cohen, C

O N rr P

Boyle, J

O N rr p

Kissack, P

O N R_1r P

Gordan, R
McCormick, J
McWhinney, I
Newton, J
Townsend, A
Young, N

A_1 N R_1R_1 P

Williams, I (Tr. H)

A_1 N rr P

Eckstein, H

A_1 N R_1r P

Huddy, P
Veldhuyzen, D

A_1 N R_1r p

Robinson, I
Russell, H

A_2 N rr P

White, R

A_2 N R_1r P

Durkin, M
Gough, J
Whitby, J

A_2N R_1r p

Craig, E

B N R_1R_1 P

Fowler, E

B N R_1r P

Freeman, P

A_2B N R_1r P

Edeleaner, J

A_2 MN R_2r P
Brown, I

-	R_1R_1	R_1R_2	R_2r	R_2R_2	rr	$R'r$	R_1r'	TOTALS P. p	
OMM	2.0	2.2	0.3		1.2		2.4	7.11	
A_1MM	1.0		2.0		1.0		4.4(+)	8. 4(+)	
A_2MM			1.0		0.1			1. 1	
BMM							2.1	2. 1	
A_1BMM		0.1						0. 1	
A_2BMM								0. 0	
MM	3.0	2.3	3.3		2.3		8.9	18.18	36
OMN	4.0	7.1	1.0	1.0	5.2	0.1	11.2	29. 6	
A_1MN	4.1	4.0	4.0	1.0	6.1		2.1	21. 3	
A_2MN			2.1	1.0			0.1	3. 2	
BMN			1.1		0.1			1. 2	
A_1BMN	1.0				1.0		0.1	2. 1	
A_2BMN	1.0							1.0	
MN	10.1	11.1	8.2	3.0	12.4	0.1	13.5	57.14	71
ONN	1.0	2.0	1.0		1.1		6.0	11. 1	
A_1NN	1.0				1.0		2.2	4. 2	
A_2NN					1.0		3.1	4. 1	
BNN	1.0						1.0	2. 0	
A_1BNN								0. 0	
A_2BNN							1.0	1. 0	
NN	3.0	2.0	1.0		3.1		13.3(+)	22. 4(+)	26
All	16.1	15.4	12.5	3.0	17.8	0.1	34.17(+)	97.36(+)	133

Adrian, R	O	MN	p	R'r	Elliott, P	O	M	p	R_1R_2
Anderson, T	A_1	M	P	R_1r	Fairgrieve, J	O	MN	P	R_1r
Barclay, A	A_1B	M	p	R_1R_2	Fowler, E	B	N	P	R_1R_1
Barrett, E	A_1	MN	P	R_1R_1	Fox, M	O	MN	p	R_1r
Bates, A	A_1	MN	P	R_2r	Freeman, P	B	N	P	R_1r
Baxter, R	O	MN	P	R_1r	Garrod, D	A_1	MN	P	R_1r
Bennett, J	A_1	MN	P	rr	Gibbs, M	A_1B	MN	p	R_1r
Binns, W	A_1	M	P	~~R_1R_2~~ R_2r	Goodson, M	A_1	MN	P	R_1R_1
Blakeway, I	A_1	MN	P	rr	Gordan, R	O	N	P	R_1r
Bond, G	O	MN	P	R_1R_1	Gough, J	A_2	N	P	R_1r
Booth, C	A_1	M	P	R_2r	Gray, B	O	MN	P	R_1r
Boyle, J	O	N	P	rr	Hargreaves, G	O	N	P	R_1R_2
Brian-Brown, P	A_1	MN	P	R_1R_2	Heaton, J	O	M	p	R_2r
Brindley, G	O	M	p	R_2r	Higgins, R	A_1	MN	P	R_2r
Brown, I	A_2	MN	p	R_2r	Hilary-Jones, P	A_2	M	P	R_2r
Brown, P	A_1	M	P	rr	Hill, J	O	MN	P	R_1r
Butcher, A	A_1	MN	P	R_1R_2	Hirons, R	O	MN	p	R_1r
Chambers, J	B	MN	p	rr	Hockey, B	A_1	M	p	R_1r
Coats, E	A_2	MN	P	R_2R_2	Holden, G	O	M	P	R_1r
Cohen, C	O	N	P	R_2r	Hort, J	O	MN	p	rr
Cooper, E	O	M	p	R_2r	House, M	O	M	p	R_1r
Corfield, M	O	MN	P	R_1r	Huddy, P	A_1	N	P	R_1r
Court, G	O	MN	P	R_1R_2	Ives, M	B	MN	P	R_2r
Craig, E	A_2	N	p	R_1r	Jarvie, E	O	MN	P	rr
Crews, J	O	MN	P	rr	Keeley, R	O	M	P	rr
Currie, J	B	M	P	R_1r	Kerr, J	O	MN	P	rr
Dickinson, G	A_1	M	P	R_1r	King, M	O	M	P	R_1R_2
Draper, J	A_1	MN	P	R_1R_2	King, R	O	MN	P	R_1R_2
Durkin, M	A_2	N	P	R_1r	Kirk, E	O	MN	p	R_1R_2
Eastwood, D	O	MN	P	R_1R_2	Kissack, P	O	N	p	rr
Eckstein, H	A_1	N	P	rr	Last, K	A_1	M	P	R_1r
Eddington, J	A_1	M	P	R_1r	Leeson, R	A_1	M	p	R_1r
Edeleaner, J	A_2B	N	P	R_1r	Leeson, S	A_1	M	p	R_1r

Lemmon, D	O	MN	P	R_1R_2	Simmonds, I	B	MN	p	R_2r
Lester, J	O	M	p	R_1r	Shepard, R	O	MN	P	rr
Lewin, D	A_2	MN	P	R_2r	Southill, J	A_1	MN	P	rr
Lister, K	A_1	MN	P	rr	Steel, P	O	MN	P	R_1r
Mackinder, F	A_2B	MN	P	R_1R_1	Stewart, J	A_1	MN	P	R_2R_2
Mallick, P	A_1	MN	P	R_1R_1	Stovin, P	O	M	P	R_1R_1
Marshall, M	A_1B	MN	P	R_1R_1	Strong, J	O	M	p	rr
Martin, P	O	MN	P	R_1r	Sykes, M	A_2	MN	P	R_2r
McCormick, J	O	N	P	R_1r	Thompson, P(St, J.)	A_1	MN	P	R_2r
					Thomson, P	O	N	P	R_1R_2
McGregor, A	A_1	MN	P	R_1r	Tomson, P	O	MN	P	R_1R_1
McMullan, J	O	MN	P	R_1r	Townsend, A	O	N	P	R_1r
McWhinney, I	O	N	P	R_1r	Vans Agnew, W	A_1	M	P	R_1R_1
Milligan, J	O	MN	P	rr	Veldhuyzen, E	A_1	N	P	R_1r
Morrison, W	O	M	P	R_1r	Vint, G	A_1	MN	P	rr
Muir, B	A_1	MN	P	rr	Wagstaffe, P	A_1	MN	P	R_1R_1
Neame, J	B	M	P	R_1r	Wallace, A	O	MN	P	R_1R_2
Newman, M	B	M	p	R_1r	Watkinson, R	O	M	P	R_1r
Newton, J	O	N	P	R_1r	Watson-Williams, E	O	M	p	R_1R_2
Nixseaman, D	A_1	MN	P	R_1R_2	Whalley, L	O	N	P	R_1R_1
Oram, G	O	MN	P	R_1R_1	Whitby, J	A_2	N	P	R_1r
Owen, R	A_1B	MN	P	rr	White, R	A_2	N	P	rr
Perkins, K	O	MN	p	rr	Williams, C	O	MN	P	R_1r
Perry, S	O	MN	P	R_1r	Williams, I(Tr.H.)	A_1	N	P	R_1R_1
Pickles, T	O	M	P	R_1R_1	Williams, J(Clare)	A_2	M	p	rr
Richardson, A	O	M	p	R_1r	Williams, J.P. (Emm)	O	MN	P	R_1r
Rinsler, M	A_1	MN	p	R_1r	Williams, Peter(StJ)	O	M	p	rr
Robinson, I	A_1	N	p	R_1r	Williams, P(St.C.)	O	MN	P	R_2R_2
Roffey, P	O	MN	P	R_1R_1	Williams-Rhys, T	A_1	M	p	R_1r
Rowson, K	A_2	MN	p	R_1r	Wills, V	A_1	MN	P	R_2r
Russell, H	A_1	N	p	R_1r	Wintersgill, P	O	M	P	R_1R_2
Sebag-Montefiore, S	O	MN	P	R_2r	Wynne, J	O	MN	P	R_1R_2
Sewart, J	A_1	MN	p	R_1R_1	Young, N	O	N	P	R_1r
Shackleton, J	O	MN	P	R_1R_2	Young, S	A_1	MN	p	rr

Towards an account of the genotype story JAN 46.

1

~~for~~ Originally intended for the Brit journal, but plans changed after writing

This paper is a review of ~~the work done by us and by~~ our own investigations, and those of our collaborators into the nature of the Rh blood groups. No attempt is made to describe ~~cover~~ the brilliant discovery of Rh and its clinical implications, by L. W & Levine. nor to do justice to the work of Wiener ~~on~~ the subgroups of Rh, much of which has ~~run~~ parallel with our own.

Although The names of the Rh antigens and antibodies used in this review will be the contemporary ones, ~~when we~~ and not those used at the time the work was done, ~~but~~ Fishers notation will not be given until the appropriate stage is reached in the story.

In 1942 when we first started to work on ~~the~~ Rh ~~groups~~, there we could distinguish 2 groups, Rh positive (by means of the serum anti-Rh of a mother etc) 85% and Rh negative 15% and two genes were presumed to exist Rh and rh. The frequency of the rh gene could be calculated ($\sqrt{15\%}$ = 39%. Therefore the frequency of Rh = 100% − 39% = 64%. and

Table I Oxford

The frequency of the genotypes

rh rh =	15%	Anti-Rh₀ Rh negative
Rh rh = 39% × 64% × 2 =		} Rh positive
Rh Rh = $39\%^2$		

The distinction between homozygous & het was a mathematical one which could not then be verified serologically.

In 1943 a serum from the mother of an erythroblastotic baby was sent to us by Dr A. J. McCall of Stoke-on-Trent. Dr McCall had found anti Rh in the serum although the mother was Rh positive

We called this serum St from the first two letters of the mothers name. It made the following distinction

	St + (80%)	St − (20%)
anti Rh$_0$ −	rh rh	
anti Rh$_0$ +	Rh rh	
	Rh Rh (some)	Rh Rh (some)

That is to say all Rh negatives tested were St +, so were all heterozygotes Rh rh (recognised as being the Rh positive children or parents of Rh negative persons). ~~St positive~~ Of the 36% homozygotes about half were St + and about half St −. There must therefore be two kinds of homozygotes and consequently two kinds of Rh genes, Rh$_1$ and Rh$_2$. The St negatives we supposed were homozygous ~~Rh$_1$ Rh$_1$~~ and called them Rh$_1$ Rh$_1$

From this it appeared that ~~This made it clear that St sera~~ St serum was agglutinating any blood containing rh, and that rh in the heterozygote Rh rh was not recessive in respect of the St serum. This strongly suggested that all Rh antibodies would react with single genes & not with "Subgroups" or phenotypes.

Of the ~~36~~ calculated 36 % of bloods homozygous, Rh Rh, St agglutinated about half. So there must be two kinds of Rh genes, Rh$_1$ and Rh$_2$. The St negative form we called Rh$_1$ and ~~were~~ supposed that the 20%

~~St negative~~ bloods which were St negative were homozygous $Rh_1 Rh_1$. The Rh+ homozygous bloods which were St + we supposed to be $Rh_1 Rh_2$ and $Rh_2 Rh_2$, St reacting with their Rh_2 gene. This stage can be tabulated thus

	St +	St −
anti-Rh_0 −	rh rh	
	Rh_1 rh	
	Rh_2 rh	
anti-Rh_0 +	$Rh_1 Rh_2$	
	$Rh_2 Rh_2$	
		$Rh_1 Rh_1$

	anti Rho	St
rhrh	−	+
Rh_1 rh	+	+
Rh_2 rh	+	+
$Rh_1 Rh_2$	+	+
$Rh_2 Rh_2$	+	+
$Rh_1 Rh_1$	+	−

This allowed the frequency of the ~~four~~ three genes to be calculated.

The frequency of the gene Rh_1 = $\sqrt{20\%}$ = ·44

" rh = $\sqrt{15\%}$ = ·36

and by difference the frequency of Rh_2 = 1 − ·44 − ·36 = ·2

At this stage Wiener had split Rh positive bloods into Rh_1 and Rh_2 types according to whether they were agglutinated by

(now called anti-Rh')

an abnormal anti Rh serum he had discovered ~~also~~. This serum agglutinated 64 % of Rh+ bloods, which were called subtype Rh_1. Using the gene frequencies just given ~~then~~ bloods containing what we called Rh_1 (Rh_1Rh_1, Rh_1Rh_2 and Rh_1rh) could be calculated to amount to just about 64 % of all Rh+ bloods. This was ample confirmation that we were both calling the same thing Rh_1.

The next step was taken when Miss Boorman and Miss Dodd, of the S.E. London Blood Transfusion Service, found an abnormal anti-Rh serum (from an Rh+ mother of erythroblastotic babies) ~~This~~ which was negative with the Rh negatives ~~and~~ but positive with only 30 % instead of 84 % of the population. ~~sent some of~~ some of this serum was sent to us and we found that it was also negative with the St negatives, (Rh_1Rh_1). The ~~first and~~ easiest guess, but which at first seemed too good to be true was that this serum was reacting with the gene Rh_2 [INSERT A] A fortnight later ~~we~~ an identical serum was sent to us by Dr C.V. Harrison of Liverpool. The guess proved to be correct and ~~No~~ such sera are now called anti-Rh". [expand]

The ~~main advance~~ distinctions made by this anti Rh" serum can be ~~are~~ tabulated thus.

	anti Rh" +	anti Rh" −
rh rh	about 14 in 15 here	about 1 in 15
Rh_1rh, Rh_2rh, Rh_1Rh_2, Rh_2Rh_2	some	some
Rh_1Rh_1	an occasional one	nearly all

Moreover
Of ~~Rh~~ Rh, rh bloods, "anti Rh" was constantly negative with bloods known to be Rh, rh. These were recognised by being children of matings Rh, Rh, × rh rh. ~~Rh2 The gene Rh2 calculated above~~ Using for the figure · 2 calculated above for the frequency of the gene Rh_2 it can be ~~calculated~~ shown that Rh_2 will be present in 30 per cent of bloods. which was just the frequency with which this serum, now called "anti-Rh" was positive

[A INSERT]

Somewhere for Rh_1 = R/r first right

It was soon found that anti-Rh" was not negative with all Rh negatives but that about 1 in 15 were positive and it was supposed that another gene Rh" was present and that these bloods were not R, rh rh but Rh" rh. as the gene couldn't be a frequent one it seemed improbable that these positives were Rh"Rh". That the gene Rh" was St + was made clear ∴ gene dosage

After a time a blood which was St negative was found which was positive with the anti-Rh" serum. so another gene Rh_z had to be postulated (Rh_z was at first time called Rh_3) Again it was supposed that this blood must be $Rh_1 Rh_z$ as Rh_z was too infrequent for the example to be expected to be $Rh_z Rh_z$. — but about Rh_z

Genes

	anti − Rho	− St	− Rh"
rh	−	+	−
Rh"	−	+	+
Rh_1	+	−	−
Rh_z	? ~~+~~	~~−~~	+
Rh_2	+	+	+

In the case of genotypes
The position ~~was thus:~~ was now:-

	anti -Rh_0	-St	-Rh"
rh rh	−	+	−
Rh" rh	−	+	+
Rh" Rh"	−	+	
Rh_1 rh	+	+	−
$Rh_1 Rh_1$	+	−	−
$Rh_1 Rh_2$	+	−	+
$Rh_1 Rh_2$	+	+	+
$Rh_2 Rh_2$	+	+	+
Rh_2 rh	+	+	+
Rh_1 Rh"	+	+	+
Rh_2 Rh"	+	+	+
$Rh_2 Rh_2$	+	+	+
$Rh_2 Rh_2$	?	−	+
Rh" Rh_2	?	+	+
Rh_2 rh	?	+	+

5 genes $\frac{1}{2}n(n+1)$

$2.5(6)$
$= 15$

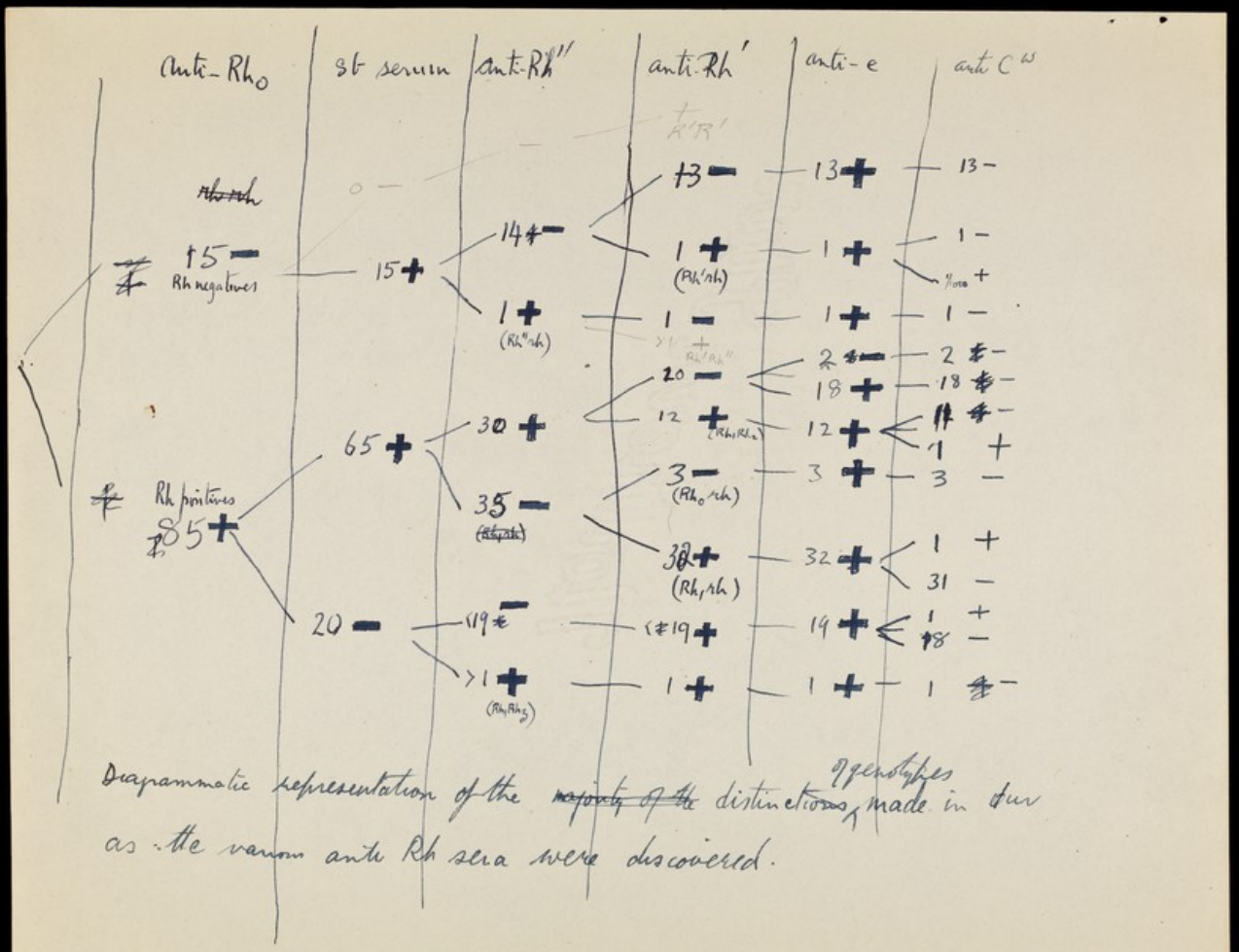
The next antiserum ~~to be~~ was found by Professor Caffell and Dr McFarlane then working in Dundee, ~~they found~~ a then serum was positive with 70% of the bloods tested. & they supposed it to be of the type Wiener had described – now called anti-Rh'. We were sent a large supply of this and were able to ~~tested~~ use it in parallel with the other three sera.

It was negative with all but about 1 in 14 ~~Rh negatives~~ supposed rh rh so that ~~there must~~ another gene was disclosed, now called Rh', as Rh' was obviously rather rare we supposed that the blood found was Rh'rh and not Rh'Rh'. Rh'rh cells gave with the St serum the single dose effect, due to the rh, i.e the gene Rh' was St negative. with Rh_1Rh_1 blood this anti-Rh' was constantly positive so the gene Rh_1 must be anti-Rh'+. With Rh"rh cells it was negative so Rh" must be anti-Rh'–. With Rh_1Rh_2 cells it was positive

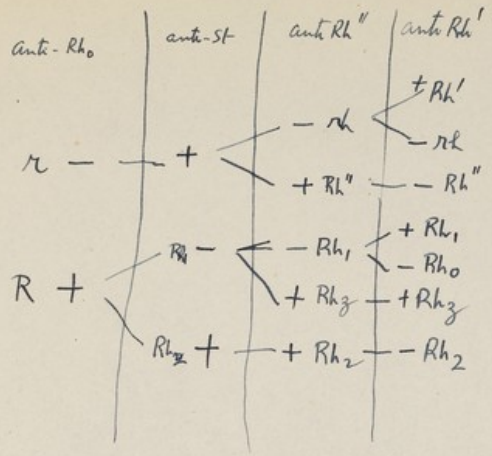
	Rh$_0$	St	Rh"	Rh'	
rh	–	+	–	–	✓
Rh"	–	+	+	–	✓
Rh'	–	+	–	+	✓
Rh_1	+	–	–	+	✓
Rh_2	?	–	+	?	
Rh_0	+	+	+	–	
	+	✓	✓	–	

but once again we could not tell what the reaction of Rh_2 alone would have been for the positive reaction would be caused by the Rh_1 anyway.

With blood of the ++– or Rh/rh undifferentiated group it was usually positive, but here again a further gene was disclosed for about 1 in 15 ++– bloods were negative with the anti-Rh'. This gene is now called ~~Rh~~ Rho. Again the blood was presumably Rho/rh since Rho Rho would be too rare to occur in the small sample examined. This blood gave the double dose effect with St serum so was ~~pseudo~~ St+ on its own account, ~~It was~~ a Rho rh was negative with anti Rh" serum So the gene Rho must be negative.



Diagrammatic representation of the ~~majority of the~~ distinctions, made in our genotypes as the various anti Rh sera were discovered.



Distinctions

Pathological Society of Great Britain and Ireland

The Seventieth Meeting of the Society will be held in the Medical School of the Westminster Hospital; 17, Horseferry Road, London, S.W.1, at 10 a.m. on FRIDAY, January 4th, and SATURDAY, January 5th, 1946. Demonstrations will be taken at 2 p.m. on FRIDAY; Private Business at 4.30p.m.

AGENDA

PRIVATE BUSINESS

1. Minutes of last meeting.
2. Election of new members (ballot paper enclosed).
3. Any other business.

PUBLIC BUSINESS

A. C. Lendrum.	"Pulmonary ferrosiderosis of hæmic origin."
R. A. Willis.	"Intra-pericardial teratoma in a child."
L. Dmochowski and R. J. Ludford.	"Experiments in the treatment of transplantable tumours with Stilbœstrol."
A. M. Barrett and L. B. Cole.	"Malignant pulmonary hypertension."
I. Doniach.	"Combined anterior pituitary necrosis and bilateral symmetrical cortical necrosis of the kidneys, following concealed accidental hæmorrhage."
A. Elkeles and L. E. Glynn.	"Mitral stenosis associated with parenchymatous ossification in the lungs."
D. M. Pryce.	"Dating of lower accessory lung."
R. D. Passey.	"Addison's Anæmia and gastric carcinoma."
A. D. Telford Govan.	"Observations on acidosis due to ammonium chloride."
R. A. M. Case.	"Toxic effects of 2, 2-bis (p-chlorphenyl) 1, 1, 1-trichlorethane (D.D.T.) in man."
A. W. Gledhill.	"Some properties of a thermo-labile antigen of Erysipelothrix rhusiopathiæ."
E. P. Abraham and E. S. Duthie.	"Effect of the hydrogen-ion concentration of the medium on the activity of penicillin, streptomycin and other chemotherapeutic substances."
D. F. Cappell and G. Harvey-Smith.	"Histological sections from sternal puncture biopsy."

PUBLIC BUSINESS—(continued).

A. W. Badenoch and E. M. Darmady.	"Partial occlusion of the renal artery in rabbits and its relation to traumatic uræmia."

DEMONSTRATIONS

A. J. Rhodes, S. W. G. Hargrove and J. H. Fodden.	"A case of malignant granuloma of the nose."
A. J. McCall.	"A case of cystic pneumatosis of the intestine."
Sheila Callender and R. R. Race.	"Transfusion made difficult."
A. E. Mourant and R. R. Race.	"Charts illustrative of Rh genes, antigens and antibodies."
J. C. White.	"An improved method of sectioning sternal puncture material."
Lucy D. Meyrick.	"Bilateral primary carcinoma of the fallopian tubes."

GENERAL

The meeting will be held at the Westminster Hospital Medical School, which is in Horseferry Road, north of the river, just opposite Lambeth Bridge. The nearest Underground Stations are St. James's Park and Westminster (District Railway), 10 minutes. Suitable buses are No. 88 (Oxford Circus to corner of Marsham Street and Horseferry Road), and No. 77 and 77a (from King's Cross to Lambeth Bridge).

It has not been possible to arrange lunch for the Society, but there are a number of restaurants in the vicinity where lunch can be obtained. Information about some of these will be given at the meeting.

The dinner of the Society will be held at Schmidt's Restaurant, 41, Charlotte Street, London, W.1 (the nearest Tube Station is Goodge Street, on the Northern Line). The price of the dinner will be 5/-, exclusive of drinks. Evening dress is not desirable. The postcard notifying members' wish to dine was circulated with the preliminary notice.

Tea will be in the Refectory at 4 p.m. on Friday.

Abstracts and short articles may be published in the Proceedings if received by the Editor before the close of the meeting on January 5th. Abstracts of papers shortly to be published in full in the *Journal* or elsewhere will not be published in the Proceedings. No abstract may exceed 1,000 words (about 1½ pages). It is undesirable that such abstracts should contain tabular matter and illustrations are not possible.

SECRETARIES' NOTICE

NOMINATION OF CANDIDATES FOR ELECTION.

The attention of members is drawn to rules 10 to 15, in which the method of election of members is laid down. The qualifications of candidates are considered in the first place by the committee, and candidates approved by the committee are balloted for by the Society, usually six months later. Names of candidates, together with a list of their contributions to pathological literature and other qualifications, should be in the hands of the secretaries *not later than July 5th*.

CHANGE OF ADDRESS.

A new edition of the Society's list is in preparation. Members are requested to assist the secretaries by sending notice of any change of permanent address without delay to J. H. Dible, British Post-Graduate Medical School, DuCane Road, London, W.12.

5761.12.45

R K Lacz

Seventh International Genetical Congress

1939

Programme

LONDON	- -	*August 15 – 17*
CAMBRIDGE	- -	*August 18 – 20*
EDINBURGH	- -	*August 22 – 30*

President—

Sections and Sectional Officers.

	Recorder.	Secretary.
A. Gene and Chromosome Theory.	H. J. Muller.	D. G. Catcheside.
B. Cytology.	C. D. Darlington.	P. C. Koller.
C. Physiological Genetics.	B. Ephrussi.	C. H. Waddington.
D. Animal Breeding in the light of Genetics.	A. D. Buchanan Smith.	Imperial Bureau of Animal Genetics.
E. Plant Breeding in the light of Genetics.	K. Mather.	S. Ellerton.
F. Human Genetics.	G. Dahlberg.	L. S. Penrose.
G. Genetics in relation to Evolution and Systematics.	J. S. Huxley.	W. B. Turrill.
H. Statistical Genetics.	R. A. Fisher.	F. Yates.
I. Genetical Aspects of Growth, Normal and Abnormal.	C. C. Little.	A. Haddow.

Organising Committee.

The above, together with C. Diver, R. R. Gates, J. B. S. Haldane, W. J. C. Lawrence, R. C. Punnett, E. R. Saunders and A. E. Watkins.

General Secretary—F. A. E. Crew.

During the Congress a daily news-sheet, showing all alterations in this programme, will be issued.

PRE-CONGRESS ACTIVITIES.

LONDON.

14th-15th August.

International Conference on Nomenclature and Terminology of Cytology and Genetics, organised by the International Union of Biological Sciences and the Institut International de Co-operation Intellectuelle.

The London Reception Room of the Congress will be in University College, Gower Street. (Tel. No. Euston 4400).

The London Reception Committee, Convener, R. A. Fisher; Secretary, Miss B. Schafer, has arranged the London Functions and Excursions.

Tuesday, 15th August.

10.00 a.m. The (London) Reception Room will be opened for registration, and for the issue of tickets for the London functions and excursions, and for the London-Cambridge-Edinburgh Pre-Congress tour.

8.30 p.m. Reception by the Royal Horticultural Society in the New Hall of the Society, Greycoat Street, S.W.1. Flower Show. Light refreshments. Dinner jacket. No special arrangements for transport for this function will be made.

Wednesday, 16th August.

9.00 a.m. Reception Room opens for registration and issue of tickets.

Excursions and Visits.

A. All day. To Whipsnade Zoological Park. Admission free by courtesy of the Zoological Society. Coach fare, 5/6; Lunch, 3/6. (Limited to 100.) The party will leave the Reception Room at 9.45 a.m.

B. All day. To East Malling Research Station, Kent. Members will be entertained to lunch and tea by the staff. Coach fare, 4/6. (Limited to 30.) The party will leave the Reception Room at 9.45 a.m.

C. Afternoon. To Rothamsted Experimental Station, Harpenden, Herts. Members will be entertained to tea by the staff. Coach fare, 4/6. (Limited to 100.) The party will leave the Reception Room at 2.15 p.m.

Wednesday—*continued*

D. Afternoon. To the Royal Horticultural Society's Gardens, Wisley. Members will be entertained to tea by the staff. Coach fare, 4/-. (Limited to 100.) The party will leave the Reception Room at 2.15 p.m.

Members will be welcomed at the following institutions between the hours stated. For these visits no special transport has been arranged, but particulars of train and bus services will be found in the Reception Room.

11.00 a.m.-5.00 p.m.—University College, Gower Street: Galton Laboratory and Department of Biometry.

10.00 a.m.-6.00 p.m.—Bureau of Human Heredity, 115 Gower Street.

11.00 a.m.-6.00 p.m.—John Innes Horticultural Institution, Mostyn Road, Merton Park.

Thursday, 17th August.

9.00 a.m.-3.00 p.m. Congress Office opens.

Excursions and Visits.

A. All day. To the John Innes Horticultural Institution. Members will be entertained to lunch and tea by the staff. Coach fare, 3/6. (Limited to 50.) The party will leave the Reception Room at 10.15 a.m.

B. Afternoon. To the Courtauld Genetical Laboratory, Regent's Park. Members will be entertained to tea by the staff. The party will meet at the Courtauld Laboratory at 2.30 p.m. No special arrangements for transport will be made. Particulars of bus services will be found in the Reception Room.

C. Afternoon. To the Natural History Museum, South Kensington. Special Exhibition. Members will be entertained to tea by the Trustees. The party will meet at the Natural History Museum at 2.30 p.m. No special arrangements for transport will be made. Particulars of bus services will be found in the Reception Room.

D. Afternoon. To the Royal Botanic Gardens, Kew, Surrey. Coach fare, 3/-. The party will leave the Reception Room at 2.00 p.m.

E. All day. To the Zoological Society's Gardens, Regent's Park. Admission free by courtesy of the Zoological Society. (Limited to 100.) Tickets (from Reception Room) admit from 9.00 a.m. till 11.00 p.m. No special arrangements for transport will be made. Particulars of bus services will be found in the Reception Room.

Thursday—*continued*

Members will be welcomed at the following institutions between the hours stated. For these visits no special transport has been arranged, but particulars of train and bus services will be found in the Reception Room.

11.00 a.m.-5.00 p.m.—University College, Gower Street; Galton Laboratory and Department of Biometry.

10.00 a.m.-6.00 p.m.—Bureau of Human Heredity, 115 Gower Street.

2.00 p.m.-6.00 p.m. John Innes Horticultural Institution, Mostyn Road, Merton Park. Members will be entertained to tea by the staff.

5.00 p.m.—Members will be cordially welcomed at the biennial Galton Lecture, which is to be given by E. B. Ford, on "Genetic Research in Lepidoptera," in the Galton Laboratory, University College, Gower Street. Tea at 5.00 p.m.

CAMBRIDGE.

Friday, 18th August.

Members taking part in the Pre-Congress Tour, London-Cambridge-Chester-Windermere-Edinburgh by motor coach, will assemble at the Congress Reception Room at 9.00 a.m.

Cost of tour—£7 : 10 : 6; this includes coach fare, hotel accommodation, breakfast, lunch, dinner, all gratuities, and the services of a representative of the Travel Agents.

The party will proceed to Cambridge. The Cambridge Reception Committee (Convener, F. T. Brooks; Secretary, D. G. Catcheside) has made the following arrangements. The Congress Reception Room and Office will be at the Botany School, Downing Street, where there will be found an Information Bureau and a representative of the Travel Agents.

On arrival in Cambridge about noon, the members will proceed to their quarters. After lunch they will assemble at the Congress Reception Room.

Excursions and Visits.

A. Afternoon. To the Plant Breeding Institute, the Horticultural Research Station, and to the National Institute of Agricultural Botany, where the members will be entertained to tea. The party will leave the Reception Room at 2.30 p.m.

Friday—*continued*

B. Afternoon. To the Animal Research Station. Members will be entertained to tea. The party will leave the Reception Room at 2.30 p.m.

8.30 p.m.—Reception at one of the Colleges. Light refreshments.

Saturday, 19th August.

10.15 a.m.—To the Potato Virus Station and the Botany School Field Station. The party will assemble at the Reception Room.

2.00 p.m.—Tour of Colleges. The party will assemble at the Reception Room.

4.15 p.m.—Demonstrations in the Botany School. The party will be entertained to tea by Professor F. T. Brooks.

The Cambridge Reception Committee extends a cordial invitation to any member of the Congress who, though not wishing to take part in the whole of the Pre-Congress tour, desires to visit Cambridge. Will those members who intend to accept this invitation please notify the Congress office in London on the 14th to 16th of August.

Special arrangements will be made for those members who desire to visit places and institutions not included in the Cambridge formal programme.

Sunday, 20th August (200 miles).

The party will assemble at 9.00 a.m. at the Reception Room, and will then proceed via Huntingdon-Northampton-Leamington-Warwick (lunch)-Stratford-on-Avon-Droitwich-Kidderminster-Shrewsbury-Whitchurch-to Chester (7.30 p.m.).

Monday, 21st August (111 miles).

The party will assemble at 10.00 a.m., and will proceed via the Mersey Tunnel-Liverpool-Southport-Preston (lunch) Lancaster-Kendal-Lake District-Windermere (4.00 p.m.).

Tuesday, 22nd August (150 miles).

The party will assemble at 9.00 a.m., and will visit Wray Castle Fresh Water Biological Station, and thereafter proceed via Grasmere-Keswick-Bothel-Carlisle (lunch)-over the Border-along the Valley of the Annan-Moffat-The Devil's Beef Tub-Peebles-Edinburgh (6.00 p.m.).

EDINBURGH.

The journey will end at the Edinburgh Congress Reception Room (The Common Room, King's Buildings), and thereafter the party will be distributed among the different hotels and hostels. (Map. Ref.—Common Room—P 8, 9; Suffolk Road Hostels—P 8.)

10.00 a.m.—The Edinburgh Congress Office in the Geology Department opens for registration and the issue of tickets. The Reception Room opens. Congress Office, Tel. 43031.

9.00 p.m.—Informal Reception by the President and Committee of the King's Buildings Common Room in the Reception Room.

Wednesday, 23rd August.

9.00 a.m.—Congress Office opens.
Meeting of the Organising Sub-Committee in the Committee Room (Geology Department).

10.30 a.m.—PLENARY SESSION of the Congress in the McEwan Hall, Teviot Place. (Map Ref.—N 6)
Chairman—Otto L. Mohr, Chairman of the International Committee.

Address of welcome by Bailie Edward, representing the City of Edinburgh.

Address of welcome by Sir Thomas Hudson Beare, Dean of the Faculty of Science, representing the University of Edinburgh.

The Congress will elect its Vice-Presidents.

The Congress will elect a committee to nominate members of the permanent International Committee and to report to the Plenary Session of 29th August.

The Congress will give to this International Committee so appointed, authority to select the place and date of the next Congress.

The Congress will elect a committee to prepare resolutions to be presented at the Plenary Session of 29th August.

The Chairman will invite Official Representatives to present their credentials at the Congress Office before 27th August.

The Chairman will address the Congress.

The Session will adjourn until 5.30 p.m. on 29th August.

2.15 p.m. **THEME 1.** SECTIONS A AND B.

Gene and Chromosome Theory.

Zoology Lecture Theatre. *Chairman*—O. L. MOHR.

Stadler, L. J.	"Genetic Studies with Ultra-Violet Radiation."
Painter, T. S.	"Salivary Chromosomes and their relation to Genetics."
Darlington, C. D.	"The Prime Variables of Meiosis."
Timofeeff-Ressovsky, N. W.	"The Mechanism of Point Mutations."
Muller, H. J.	"The Mechanism of Structural Change in Chromosomes."

2.15 p.m. **THEME 2.** SECTION D.

Livestock Improvement.

Geology Lecture Theatre. *Chairman*—Sir ROBERT GREIG.

McPhee, H. C.	"Recent Attempts to Co-ordinate Genetic Research on Farm Animals in the U.S.A."
Bonnier, G.	"Theoretical and Practical Possibilities of Genetics in contributing to the Improvement of Livestock."
Plank, G. M. van der and Hirschfeld, W. K.	"Genetics and Animal Breeding."
Hagedoorn, A. L.	"Concentration of Effort in Selection by means of the Nucleus Plan of Breeding Farm Livestock."

2.15 p.m. **THEME 3.** SECTION F.

Abnormal Human Characters.

Engineering Lecture Theatre. *Chairman*—B. S. BURKS.

Lenz, F.	"Was bedeutet 'erblich' und 'nicht-erblich' beim Menschen?"
Penrose, L. S.	"Maternal Age, Order of Birth and Developmental Abnormalities."
Munro, T. A. and Penrose, L. S.	"Tests for Linkage in Phenylketonuria."

Lundholm, I.	"Inheritance of Hypochromic Anæmia."
Nachtsheim, H.	"Krampfbereitschaft und Genotypus."
Sanders, J.	"A Family with Pick's Disease."
Ferriman, D.	"The Genetics of True Oxycephaly and Acrocephalosyndactyly."

2.30 p.m. **Tours.**—Conducted sight-seeing tour round the City. Coach fare, 8/6, including admission fees. Place of departure—Reception Room. Tickets should be obtained from the Travel Agent's Counter in the Congress Office. Route—Princes Street, Castle, Scottish National War Memorial, St. Giles' Cathedral, John Knox's House, Palace of Holyroodhouse, etc. (Guide lecturer.)

Also, choice of several other shorter unconducted tours round the City. Coach fares, 1/6 to 2/6. Particulars of these tours are given in leaflets obtainable at the Travel Agent's Counter.

6.00 p.m. **Lecture**——MAX HARTMANN.
"Das Wesen und die Stofflichen Grundlagen der Sexualität."
Zoology Lecture Theatre. *Chairman*—F. BALTZER.

9.00 p.m.—Reception by the City in the Assembly Rooms, George Street. (Map Ref. M 5). Evening dress; orders and decorations. Dancing. Light refreshments. Tickets for this function should be obtained from the Congress Office before midday on the 23rd August. Buses will be available for the conveyance of members to and from the hostels.

Thursday, 24th August.

9.00 a.m. Congress Office opens.
Meeting of the Organising Sub-Committee in the Committee Room.

9.15 a.m. **THEME 1.** SECTION C.

Physiological Genetics.

Zoology Lecture Theatre. *Chairman*—MAX HARTMANN.

Wright, Sewall.	"A Quantitative Study of the Interactions of the Major Colour Factors of the Guinea Pig."
Beadle, G. W.	"Genetic Control of the Production and Utilisation of Hormones."

Baltzer, F. "Ueber die Rolle des Kerns in der Embryonalentwicklung : Typen der Letalität und Austauschbarkeit artverschiedener Kerne bei Bastarden.'

Wettstein, F. v. "Ueber cytoplasmatische Vererbung und das Zusammenwirkungen von Kern und Cytoplasma."

9.15 a.m. **THEME 2.** SECTION D.

Livestock Improvement in the Tropics.

Geology Lecture Theatre. *Chairman*—Sir ARTHUR OLVER.

Bisschop, J. H. R. "Bionomic Studies on Indigenous and Exogenous Cattle in the Semi-Arid Regions of the Union of South Africa."

Nichols, J. E. "Genotype and Environment. Some Aspects of Selection of Merino Stock for Wool Production under Pastoral Conditions."

Rhoad, A. O. "A Method of Assaying the Genetic Differences in the Adaptability of Cattle to Tropical and Sub-Tropical Climates."

Manresa, M., Reyes, N. C., Gomez, F., Zialcita, L. P. and Falcon, P. R. "The Influence of Atmospheric Temperature upon Hæmoglobin and other Constituents of the Blood of Cattle."

10.00 a.m.–6.00 p.m. Demonstrations and Exhibits in the Zoology and Engineering Departments.
The Garden : Genetics Department.

10.00 a.m.-12.00 a.m. Blood Grouping, Taste Testing, etc. G. L. TAYLOR and Colleagues. Zoology Department.

2.15 p.m. **THEME 1.** SECTION G.

Genetics in relation to Evolution and Systematics.

Zoology Lecture Theatre. *Chairman*—A. ERNST.

Dobzhansky, Th. "On the Genetic Structure of Natural Populations of Drosophila."

Tischler, G. "Die Bedeutung chromosomaler Rassendifferenzen für Systematik und Pflanzengeographie."

Huxley, J. S. "Systematics in Relation to Genetics."

Turrill, W. B. "Taxonomy and Cytogenetics in Plants."

Harland, S. C. "Genetical Studies in the genus Gossypium and their Relation to Evolutionary and Taxonomic Problems."

2.15 p.m. **THEME 2.** SECTION D.

Livestock Improvement in the Tropics—*continued.*

Geology Lecture Theatre. *Chairman*—Sir ARTHUR OLVER.

French, M. H. "Cattle Breeding in Tanganyika Territory and some Developmental Problems encountered."

Khishin, A. F. E. "The Present Conditions of Animal Breeding and Husbandry in Egypt."

Stewart, J. L. "Livestock Improvement in the Northern Territories of the Gold Coast."

Murari, Sri T. "Cross-Breeding Experiments with Cattle in the Madras Presidency."

Kelley, R. B. "Animal Industries in the Australian Tropics."

2.15 p.m. **THEME 3.** SECTION I.

Growth, Normal and Abnormal.

Zoology Lecture Theatre No. 2. *Chairman*—E. B. FORD.

Cramer, W., and Horning, E. S. "On the Association in Inbred Strains of Mice between Brown Degeneration of the Adrenals and the Incidence of Mammary Cancer."

Kreyberg, L. "The Relationship between Brown Degeneration of the Adrenals and Breast Cancer in Mice."

Howard, A., and Huskins, C. L. "Chromosome Studies in Mice."

Woolley, G. W. "The Effect of Male Secretions upon Tumor Incidence in Mice."

Gorer, P. A. "The Question of Dominance in Spontaneous Cancer."

Thursday—*continued*

2.30 p.m. **Tours.**—If desired, yesterday's conducted tour will be repeated. Particulars of other tours are given in leaflets obtainable at the Travel Agent's Counter.

Entertainment for ladies by the Ladies' Committee. Particulars will be found on the Notice Board in the Reception Room.

6.00 p.m. **Lecture**—Sir DANIEL HALL.
"How the Plant Breeder goes to Work."
Zoology Lecture Theatre.
Chairman—Sir WILLIAM WRIGHT SMITH.

9.00 p.m. **Group Meetings.**
Cytology Films. Zoology Lecture Theatre No. 1.
Mouse. Zoology Lecture Theatre No. 2.
Committee Meeting: the International Group for Human Heredity. Zoology Colloquium Room.
Meeting of Plant Geneticists: Convener—O. H. FRANKEL. Zoology Department.
Meetings of the Nominating and Resolutions Committees. Genetics Department.

Friday, 25th August.

9.00 a.m. Congress Office opens.
Meeting of the Organising Sub-Committee in the Committee Room.

9.15 a.m. **THEME 1.** SECTION E.

Plant Breeding in the Light of Genetics.

Zoology Lecture Theatre. *Chairman*—R. A. EMERSON.

Lindstrom, E. W.	"Analysis of Modern Maize Breeding Principles and Methods."
Mangelsdorf, P. C.	"The Origin of Maize."
Rasmusson, J.	"Quantitative Inheritance in Root Crops."

9.15 a.m. **THEME 2.** SECTION F.

Mental Inheritance in Man.

Engineering Lecture Theatre. *Chairman*—E. FISCHER.

Hogben, L. T.	"Normal Intelligence and Inheritance."

Friday—*continued*

Pohlisch, K.	"Die Erblichkeit der Geisteskrankheiten."
Roberts, J. A. F.	"Inheritance of Mental Deficiency."
Dahlberg, G.	"Rare Psychological Defects from the Point of View of the Population."

9.15 a.m. **THEME 3.** SECTION D.

Artificial Insemination.

Geology Lecture Theatre. *Chairman*—E. P. CATHCART.

Bonadonna, T.	"Ricerche sulla Fecondazione Artificiale in Italia."
Phillips, R. W., Schott, C. E. T., Terrill, C. E. and Gildow, E. M.	"Long-range Transportation of Ram Semen for Use in Artificial Insemination."
Teodoreanu, N.	"Investigations on Artificial Insemination in Sheep."
Olbrycht, T. M.	"The Lwow Methods of Artificial Insemination."
Anderson, J.	"Artificial Insemination in Sheep and Cattle in Kenya."
Edwards, J., and Walton, A.	"Problems of Semen Production related to Artificial Insemination."

10.00 a.m.–6.00 p.m. Demonstrations and Exhibits in the Zoology and Engineering Departments.
The Garden: Genetics Department.

2.15 p.m. **THEME 1.** SECTIONS A AND B.

Radiation Effects and the Mechanism of Structural Change in Chromosomes.

Zoology Lecture Theatre. *Chairman*—L. J. STADLER.

Catcheside, D. G.	"The Mechanism of Radiation-induced Chromosome Rearrangements."
Fabergé, A. C.	"An Experiment on Chromosome Fragmentation by X-rays in *Tradescantia*."

Marshak, A.	" Chromosome Structure in Meiosis and Mitosis with Reference to the Mechanism of Crossing-over."
Camara, A.	"The Effect of X-radiation on the Chromosomes of *Aloë arborescens*."
Sidky, A. R.	" Translocation between Sperm and Egg Chromosomes as Evidence that Breakage precedes Union."

2.15 p.m. Section D. Sectional Excursion to University Farms. Transport will be provided. Place of Departure; Reception Room. Will those members wishing to take part in this excursion please notify the Congress Office before 12 o'clock on the 25th August. Fare 2/-.

2.15 p.m. **THEME 2.** SECTIONS E. AND H.

Varietal Trials and Selective Improvement.

Geology Lecture Theatre. *Chairman*—E. W. LINDSTROM.

Yates, F.	" Modern Experimental Design and its Function in Plant Selection."
Rasmusson, J.	" Field Trials in Sugar Beet Breeding."
Goulden, C. H.	" Problems in Plant Selection."
Day, B. B., and Austin, L.	" The Use of the Three Dimensional Quasi-Factorial Design for Testing a Large Number of Ponderosa Pine Progenies."
Hoblyn, T. N.	" Testing New Varieties of Fruit Plants."
Hutchinson, J. B. and Panse, V. G.	" The Application of Genetics to Plant Breeding. II. The Inheritance of Quantitative Characters and Plant Breeding."
Mather, K.	" Selection of Polygenic Characters."
Brieger, F. G.	" Statistical Analysis of the Inheritance of Quantitative Characters."

2.15 p.m. **THEME 3.** SECTION F.

Feeblemindedness.

Engineering Lecture Theatre.
Chairman—H. THOMASSON.

Murphy, D. P.	" Reproductive Characteristics of Parents of Congenitally Malformed Children."

Brugger, —	" The Genetic Uniformity of Mental Deficiency without Marked Physical Signs."
Frets, G. P.	" Families with Feeblemindedness."
Berry, R. J. A.	" An Investigation into the Mental States of the Parents and Sibs of 1050 Mentally Defective Persons."

2.15 p.m. **THEME 4.** SECTION G.

Hybridization.

Chemistry Lecture Theatre No. 2.
Chairman—A. L. HAGEDOORN.

Bellamy, A. W.	" Interspecific Hybrids in Different Fishes."
Federley, H.	" Hybridization between different Species and Races of Lepidoptera with different Chromosome Number."
Carothers, E. E.	" Interspecific Grasshopper Hybrids."
Cousin, G.	" Analyse biométrique d'une Hybridation interspécifique chez les Gryllides."
Patterson, J. T., Stone, W., and Griffen, A. B.	" Crosses between Members of the *Drosophila virilis* Group."
Ghigi, A.	" Incroci Interspecifici nei Fagiani."
Cavazza, F.	" Alcune osservazioni sull' Ibridismo Interspecifico dei Mammiferi."

2.15 p.m. **THEME 5.** SECTION I.

Growth, Normal and Abnormal.

Zoology Lecture Theatre No. 2.
Chairman—N. DOBROVOLSKAIA-ZAVADSKAIA.

Macklin, M. T.	" An Analysis of Tumors in Monozygous and Dizygous Twins."
Lemser, H.	" Hypophysentumor und Zwillingsdiagnose."
Geyer, H.	" Die Erbpathologie der Geschwülste des Zentralnervensystems und seiner Hüllen."

Schweitzer, M. D. "The Inheritance of Leukemia in Mice."

Bagg, H. J. "The Selection of Genetic Material for the Study of the Inheritance of Mammary Tumours in Mice and Rats."

Gorer, P. A. "Transplantation and the Differentiation of the Malignant Cell."

2.45 p.m. **THEME 6.** SECTION C.

Cytoplasmic Heredity.

Chemistry Lecture Theatre No. 1.
Chairman—Fr. v. WETTSTEIN.

Michaelis, P. "Plasmavererbung und Entwicklungsphysiologie."

Sirks, M. J. "Genotypical Predetermination."

Oehlkers, F. "Die Bedeutung der Plastiden für dem Ablauf der Meiosis."

2.30 p.m. **Tour.** Afternoon Tour to Melrose, Dryburgh Abbey, Abbotsford House, Bemersyde, etc. Coach fare, 11/6, including admission fees and tea. Place of departure: Reception Room.

6.00 p.m. **Lecture.** C. W. METZ.
"Species Hybrids, Evolutionary Chromosome Changes, and the Mechanism of Chromosome Rearrangement in Sciara."

Zoology Lecture Theatre. *Chairman*—O. WINGE.

9.00 p.m. Reception by His Majesty's Government in the Rooms of the Royal Scottish Academy. Evening dress; orders and decorations. Light refreshments. Tickets for this function should be obtained from the Congress Office before midday on the 25th August. Buses will be available for the conveyance of members to and from the hostels.

Saturday, 26th August.

9.00 a.m. Congress Office opens.

Meeting of the Organising Sub-Committee in the Committee Room.

9.15 a.m. **THEME 1.** SECTIONS A AND B.

Radiation Effects and the Mechanism of Structural Change in Chromosomes—*continued.*

Zoology Lecture Theatre. *Chairman*—L. J. STADLER.

Jones, D. F. "Segmental Exchange in Somatic Cells of Maize."

Whiting, A. R. "Susceptibility to X-rays of Meiotic Stages in Eggs of Habrobracon."

Hertwig, P. "Erbänderungen bei Mäusen nach Röntgenbestrahlung von Männchen oder Weibchen."

Bauer, H. "Röntgeninduktion von Chromosomenmutationen bei Drosophila."

9.15 a.m. **THEME 2.** **Sex.** SECTION C.

Geology Lecture Theatre. *Chairman*—H. de WINIWARTER.

Whiting, P. W. "The Cytogenetics of Sex-Determination."

Shull, A. F. "The Nature of the Intermediacy of Adult Intermediate-winged Aphids and its Bearing on the Manner of their Production."

Vandel, A. "Génétique de la Sexualité chez les Isopodes terrestres."

Montalenti, G. "Richerche quantitative sull'azione dei geni della striature (barring) nelle penne maschili e femminili dei polli Barred Plymouth Rocks."

Dantchakoff, V. "On the Agencies of the Genetic Determination of Sex in the Higher Vertebrates."

9.15 a.m. **THEME 3.** SECTIONS D AND H.

Statistics and Animal Experimentation.

Genetics Lecture Theatre. *Chairman*—J. F. TOCHER.

Yates, F.	"Statistical Aspects of Animal Experimentation."
Berge, S.	"The Number of Offspring required in Genetical Experiments with Slow-breeding Animals."
Lush, J. L.	"Methods of Measuring the Heritability of Individual Differences among Farm Animals."

9.15 a.m. **THEME 4.** SECTION E.

Disease and Vigour.

Chemistry Lecture Theatre No. 1. *Chairman*—D. F. JONES.

Singleton, W. R.	"Hybrid Vigour in Maize and its Utilisation in Sweet Corn Breeding.'
Jenkins, M. T.	"The Segregation of Genes affecting Yield of Grain in Maize."
Salaman, R. N.	"Breeding for Immunity to Blight and other Diseases in the Potato."
Müller, K. O.	"Physiologisch-genetische Untersuchungen zur Analyse der Phytophthora-Resistenz der Kartoffel."
Walker, J. C.	"Disease Resistance in Crucifers."
Jagger, I. C., and Whitaker, T. W.	"The Inheritance of Immunity to Mildew (*Bremia lactucæ*)."
Crepin, C., Bustarret and Chevalier.	"Création pour la France de Variétés de Blé résistantes à la Carie."

9.15 a.m. **THEME 5.** SECTION F.

Blood Groups.

Engineering Lecture Theatre. *Chairman*—R. A. FISHER.

Friedenreich, V.	"Genetical Problems in Recent Research in Blood Groups."
Taylor, G. L., and Prior, A. M.	"The Distribution of the M. and N. Factors in Random Samples of Different Races."

Gates, R. R.	"Blood Groups and Race."
Hyman, H. S.	"On Blood Groups."
Turpin, R., Piton, J., and Caratzali, A.	"Recherche sur les corrélations Leucocytaires des Jumeaux."
Finney, D. J.	"Linkage between Blood Groups and Allergic Diseases."

9.15 a.m. **THEME 6.** SECTION G.

Comparative Genetics and Evolution.

Chemistry Lecture Theatre No. 2. *Chairman*—H. FEDERLEY.

Ernst, A.	"Heterostylie als Problem der Evolution."
Cross, J. C.	"On the Cytology of some Mammals."
Boyden, A. A.	"Genetics and Animal Relationship."
Eyster, W. H.	"Genetic Study in the genus Tagetes."

9.15 a.m. **THEME 7.** SECTION I.

Growth, Normal and Abnormal.

Zoology Lecture Theatre No. 2.
Chairman—J. P. LOCKHART-MUMMERY.

Strong, L. C.	"Cancer of the Mammary Gland in Mice. Is it a Genetic, Congenital, or Acquired Disease?"
Dobrovolskaia-Zavadskaia, N.	"Heredity and Environmental Factors in the Origin of different Cancers."
Curtis, M. R., and Dunning, W. F.	"Host Constitution and the Incidence of Chemically induced Tumors."
Bonser, G. M.	"The Effect of Genetic Constitution in determining the Response of the Animal to Carcinogenic Agents."
Andervont, H. B.	"The Use of Inbred Strains of Mice in Experimental Cancer."
Bittner, J. J.	"The Influence of Foster Mother on the Incidence of Breast Cancer in Mice."

10.00 a.m.–6.00 p.m. Demonstrations and Exhibits in the Zoology and Engineering Departments.
The Garden : Genetics Department.

2.15 p.m. **THEME 1.** SECTIONS A AND B.

Structural Changes and Position Effect in Free and Chromocentral Regions.

Zoology Lecture Theatre. *Chairman*—H. BAUER.

Demerec, M.	"The Nature of Changes in the Notch-White Region of the X-chromosome of *Drosophila melanogaster*."
Sutton, E.	"The Structure of Euchromatic and Heterochromatic Translocations in the Salivary Gland Chromosomes of *Drosophila melanogaster*."
Kaufmann, B. P.	"Distribution of induced Breaks along the X-chromosome of *Drosophila melanogaster*."

2.15 p.m. **THEME 2.** SECTION C.

Sex—*continued.*

Geology Lecture Theatre. *Chairman*—M. CAULLERY.

Quintanilha, A.	"Genetical Work on Basidiomycetes."
Peklo, J.	"Relative Sexuality in *Fomes pinicola*."
Singh, B. N.	"Certain Aspects of the Physiology of Sex in Higher Plants."
Gottschewski, G.	"Das Geschlechtverhältniss in Bastard Kreuzungen von *D. pseudo-obscura*."
Whiting, P, W.	"Sex Determination in Habrobracon."

2.15 p.m. **THEME 3.** SECTION D.

Inbreeding, Lethals and Defects.

Genetics Lecture Theatre. *Chairman*—J. HAMMOND.

Eaton, O. N.	"The Effect of Crossing Inbred Lines of Guinea Pigs upon the Characteristics of the Hybrids."
Herre, W.	"Alteration in the Species Formation of Domestic Animals and the Applicability of the Preventive Proteinase Reaction in the Study of Inheritance."
Prawochenski, R.	"New Lethal Genes in the Horse."
Johansson, I.	"Variations in the Manifestation of Lethal Characters in the Swedish Breeds of Cattle."
Addington, L. H., and Cunningham, O. C.	"An Inherited Double Teat in Milk Goats."

2.15 p.m. **THEME 4.** SECTION E.

Principles of Plant Breeding.

Chemistry Lecture Theatre No. 1.
Chairman—E. TSCHERMAK VON SEYSENEGG.

Akerman, A.	"Spring Wheat Breeding in Sweden."
Frankel, O. H.	"Some Reflections on Breeding Wheat for Baking Quality."
Philp, J.	"On Wheat Breeding and Genetics."
Love, R. M.	"The Role of Cytology in Hexaploid Wheat Improvement."
Briggs, F. N.	"The Use of the Back-cross in Plant Breeding."
Hutchinson, J. B., and Panse, V. G.	"Application of Genetics to Plant Breeding. I. The Genetic Interpretation of Plant Breeding Problems."
White, O. E.	"Genes, Species, Variability and Plant Breeding."

Saturday—*continued*

2.15 p.m. **THEME 5.** SECTIONS F. and H

Statistical Methods in Human Genetics.

Engineering Lecture Theatre. *Chairman*—SEWALL WRIGHT.

Fisher, R. A. "The Detection and Measurement of Linkage in Man."

Haldane, J. B. S. "New Data on Partial Sex-Linkage."

Gini, C. "L'Importanza Relativa dei Fattori Ereditari e non Ereditari nel determinare L'etereogenita di una Generazione."

Dahlberg, G. "Analysis of Dominance and Recessivity in Polymeric Inheritance."

Penrose, L. S. "Testing for Linkage in Human Sib Data."

Hogben, L. T. "Biological Models for Statistical Treatment of Human Genetics."

2.15 p.m. **THEME 6.** SECTION G.

Comparative Genetics and Evolution—*continued.*

Chemistry Lecture Theatre No. 2. *Chairman*—A. GHIGI.

Ibsen, H. L., and Bogart, R. "Pigmentation in Relation to Colour Inheritance in Mammals."

Blaringhem, L. "Hérédité et Evolution chez les Plantes."

Marchlewski, T. "Change of Dominance in Canine Colour Genetics."

Mensinkai, S. W. "Evolution in the genus Allium."

2.15 p.m. **THEME 7.** SECTION I.

Growth, Normal and Abnormal.

Zoology Lecture Theatre No. 2.
Chairman—L. KREYBERG.

Ford, E. B. "The Genetics of Growth and Differentiation."

Saturday—*continued*

Ernst, A. "Vererbung teratologischer Merkmale durch labile Gene."

Lockhart-Mummery, J. P. "Somatic Mutation as a Cause of Tumours."

Ludford, R. J. "Can Somatic Cell Mutations explain the Properties of Malignant Cells ?"

Cloudman, A. M. "Evidence for Genetic Determination of Site and Tumour Type Incidence in Mice."

2.15 p.m. **Tour.** Short afternoon tour to the Forth Bridge and Roslin. Place of departure: Reception Room. Coach fare, 2/6. Particulars of the tour may be obtained at the Travel Agent's Counter.

4.30 p.m. Entertainment for ladies by the Ladies' Committee. Visit to Scottish Zoological Park, Corstorphine (Map Ref. G 6). Place of departure: Reception Room.

6.00 p.m. **Lecture.** O. VOGT.
"Variation im Lichte Topistischer Krankheiten."
Zoology Lecture Theatre. *Chairman*—R. J. A. BERRY.

8.30 p.m. **Group Meetings.** CHEMISTRY DEPARTMENT.

Colchicine Group. Round-table discussion to be opened by—

Blakeslee, A. F. "The Induction of Polyploids and their Genetic Significance."

Open Meeting of the International Group for Research in Human Heredity. Chemistry Lecture Theatre No. 1,

Sunday, 27th August.

All day tour by rail to Stirling, Callander, Balquhidder, Lochearnhead, Comrie, Crieff, Gleneagles, Dunblane, Stirling, etc. Fare, 11/-, including lunch and tea. Time of departure, 10.30 a.m. Arrive back in Edinburgh about 6.00 p.m. Tickets for this tour should be obtained from the Travel Agent's Counter not later than Thursday mid-day.

9.00 p.m. Informal gathering in the Reception Room. Music. Light Refreshments.

Discussion on Teaching Methods: (*a*) the statistical requirements of students of Genetics (opened by C.D. Darlington); (*b*) the use of models in the teaching of Cytogenetics (opened by J. S. Huxley). Genetics Lecture Theatre.

Monday, 28th August.

9.00 a.m. Congress Office opens.

Meeting of the Organising Sub-Committee in the Committee Room.

9.15 a.m. **THEME 1.** SECTIONS A AND B.

Structural Changes and Position Effect in Free and Chromocentral Regions—*continued.*

Zoology Lecture Theatre. *Chairman*—H. BAUER.

Oliver, C. P. "The Relationship between Chromosomal Disarrangements and a Morphological Variant in *Drosophila melanogaster*."

Schultz, J. "The Function of Heterochromatin."

9.15 a.m. **THEME 2.** SECTION C.

Embryological Mechanisms.

Geology Lecture Theatre. *Chairman*—J. NEEDHAM.

Landauer, W. "Teratological Correlations and the Mechanism of Gene Expression."

Russell, W. L. "Physiological Genetics of Guinea Pig Coat Colour."

Bonnevie, K. "The Manifestation of Hydrocephalus in Mice."

Hadorn, E., and Ris, H. "Zur Entwicklungsphysiologie einer Letalmutante von *Drosophila melanogaster*."

Quisenberry, J. H. "Relationship of Genetic and Nutritional Factors in the Production of Developmental Anomalies."

Steinberg, A. G. "The Growth Curves of Bar and Wild Type Eye Discs of *Drosophila melanogaster*."

9.15 a.m. **THEME 3** SECTION D.

Inheritance of Milk Yield.

Genetics Lecture Theatre. *Chairman*—Lord ROWALLAN.

Krüger, L. "Die Bestimmung von Leistungswert, Erbwert, Erbanlagen und Erbquanten bei der Milchleistung."

Lörtscher, H. "Causes of Variations of Yearly Herd Averages in a Dairy Herd."

Csukás, Z. de "The Genetics of the Curve of Lactation."

Ward, A. H. and Campbell, J. T. "Evaluation of Dairy Sires in New Zealand."

Marchlewski, T. "Indications of Sex-Linkage in Milk Yield Inheritance in Cattle."

9.15 a.m. **THEME 4.** SECTION E.

Cereals.

Chemistry Lecture Theatre No. 1.
Chairman—N. H. NILSSON-EHLE.

Hunter, H. "Cereal Breeding."

Robertson, D. W. "Studies of Barley Genetics in Colorado."

Jones, E. T. "A Comparison of the Segregation of Wild *v.* Cultivated Base in the Grain of Diploid, Tetraploid and Hexaploid Species of Oats."

Ellison, W.	"The Cytology of certain Diploid and Tetraploid *Avena* Hybrids."
Tavcar, A.	"Vererbungsart von zwei, drei, vier und sechsgliedrigen Blattwirben bei *Zea Mays* L."
Nieves, R.	"Rye Breeding Problems in the Argentine."
Saulescu, W.	"The Genetics of Wheat."

9.15 a.m. **THEME 5.** SECTION F.

Selection in Human Populations.

Engineering Lecture Theatre. *Chairman*—C. GINI.

Haldane, J. B. S.	"Natural Selection in Man."
Charles, E.	"Differential Fertility."
Price, B.	"An Interpretation of Differential Birth Rate Statistics."
Gini, C.	"Considerazioni a cui Danno Luogo i Caratteri Concatenati a Seguito dell' Intercambio."
Verschuer, O. v.	"Bemerkungen zur Gen-Analyse beim Menschen."

9.15 a.m. **THEME 6.** SECTION G.

Micro-evolution.

Chemistry Lecture Theatre No. 2. *Chairman*—G. TISCHLER.

Plough, H. H.	"The Influence of Temperature in Evolution as shown by Studies of Lethal Mutation in Drosophila."
Ives, P. T.	"A High Frequency of Lethal Mutations in a Wild Population of Drosophila."
Lamprecht, H.	"The Limit between *Phaseolus vulgaris* and *multiflorus* from the genetical point of view."
Miczynski, K.	"The Inheritance of Some Characters in the Intervarietal Crosses of Aegilops."
Riley, H. P.	"Morphogenesis of Flower Parts in Two Species of Iris."

10.00 a.m.–6.00 p.m. Demonstrations and Exhibits in the Zoology and Engineering Departments.
The Garden: Genetics Department.

2.15 p.m. **THEME 1.** SECTION B.

Meiosis-segregation and Crossing-over.

Zoology Lecture Theatre.
Chairman—TH. DOBZHANSKY.

White, M. J. D.	"Chromosomal Evolution and the Mechanism of Meiosis in Praying Mantids."
Koller, P. C.	"Crossing-over in the Sex-chromosomes of Mammals."
Sansome, E. R.	"Abnormal Meiosis in *Pisum sativum*."
Pätau, K.	"The Pairing Coefficient."
Huskins, C. L., and Newcombe, H. B.	"Chromatid and Chiasma Interference in *Trillium erectum* L.

2.15 p.m. **THEME 2.** SECTION C.

Embryological Mechanisms—*continued.*

Geology Lecture Theatre. *Chairman*—K. BONNEVIE.

Waddington, C. H.	"The Mechanism of the Genetic Control of Development."
Poulson, D. F.	"The Developmental Effects of a Series of *Notch* Deficiencies in the X-chromosome of *Drosophila melanogaster*."
Reed, S. C.	"Interaction between the Autosomes of *D. melanogaster* as Measured by Viability and Rate of Development."
Reed, S. C., and Henderson, J. M.	"Determination of Hair Pigments."
Child, G. P., Blanc, R. and Plough, H. H.	"The Effects of High Temperatures on the Development of Heterozygous Recessives of *Drosophila melanogaster*."

2.15 p.m. **THEME 3.** SECTION D.

Cattle and Sheep.

Genetics Lecture Theatre. *Chairman*—R. G. WHITE.

Pontecorvo, G.	"Problems in connection with Selection of Beef and Draft Cattle."
Jones, I. C.	"Red, Roan and White Coat Colour in Shorthorn Cattle."
Dry, F. W.	"Kemp in the New Zealand Romney."

2.15 p.m. **THEME 3a. Poultry.** SECTION D.

Zoology Lecture Theatre No. 2. *Chairman*—C. BONNIER.

Lauprecht, E.	"Versuch zur Vererbung des Eigewichtes bei Hühnern."
Ghigi, A.	"Genetica dell' Ernia Cerebrale nei Polli."
Greenwood, A. W.	"A Study in Fecundity in the Domestic Fowl."
Hays, F. A.	"Inheritance of Comb Type and Ear Lobe Color in Rhode Island Reds."
Hutt, F. B.	"The Association of Physiological Traits with Breed Characteristics in the Fowl."
Jaap, R. G.	"Proportional Body Shape and Growth in the Domestic Fowl."
Landauer, W.	"The Role of Unspecific Growth Retardation in the Expression of Inherited Traits (Creeper Fowl, etc.)."

2.15 p.m. SECTION E. Visit to the Scottish Plant Breeding Station, Corstorphine (Tea) and to Seed Testing Station, East Craigs, Corstorphine. (Limited to 50.) Group discussions. Chemistry Lecture Theatres Nos. 3 and 4.

2.15 p.m. **THEME 4.** SECTION F.

Twinning.

Engineering Lecture Theatre.

Chairman—O. v. VERSCHUER.

Slater, E.	"Inheritance of Twinning."
Jenkins, R. L., and Gwin, J.	"Rigorous Analysis of the Interrelations of the Frequencies of Plural Births."
Malán, M.	"Zwillingsuntersuchungen über die Orientierungsfähigkeit."
Murphy, D. P.	"The Outcome of 625 Pregnancies in Women subjected to Pelvic Radium or Roentgen Irradiation."

2.15 p.m. **THEME 5** SECTION G.

Micro-evolution.

Chemistry Lecture Theatre No. 2. *Chairman*—M. CHRISTOFF.

Zarapkin, S. R.	"The Measurement of Divergence."
Larambergue, M. de	"Races aphalliques et euphalliques de *Bulinus contortus*, recherches sur le déterminisme génotypique de l'aphallie."
Cleland, R. E.	"Analysis of Wild American Races of Oenothera (Onagra)."
Gates, R. R.	"The Geographical Relationships and Evolution of the sub-genus Onagra."
Banta, A. M.	"Genetics and Evolution of Cladocera."

2.15-4.15 p.m. Demonstration on Blood Grouping, Taste Testing, etc. G. L. TAYLOR and Colleagues, Zoology Department.

2.30 p.m. **Tour.** Afternoon tour to the Pentland Hills, Carlops, Peebles, Innerleithen, Glentrees, Newbattle Abbey, etc., Coach fare, 7/6 (including tea). Place of departure: Reception Room.

4.30 p.m.-6.30 p.m. SECTIONS A. and B.

Session on Protein and Virus Studies in Relation to the Problem of the Gene.

Engineering Lecture Theatre.
Chairman—J. B. S. HALDANE.

Astbury, W. T.

Crowfoot, D. "Recent Work on the Structure of Crystalline Proteins and Viruses."

Wrinch, D. M. "The Structure of Biologically Active Proteins."

Gulick, A. "Analysis of Nuclear Material obtained by Differential Centrifugation of Finely Powdered Glandular Tissue."

Caspersson, T. "On the Role of the Nucleic Acids in the Cell."

8.30 p.m.-10.30 p.m.

Kausche, G. A. "Untersuchungen zum Problem der biologischen Charakterisierung von phytopathogenen Virusproteinen."

McKinney, H. H. "Virus Genes."

Gowen, J. W. "Behaviour of Viruses and Genes under Similar Stimuli."

L'Héritier, P., and Teissier, G. "Une Monstruosité physiologique héréditaire."

Tuesday, 29th August.

9.00 a.m. Congress Office opens.
Meeting of the Organising Sub-Committee in the Committee Room.

9.15 a.m. **THEME 1.** SECTION B.

Meiosis—*continued.*

Zoology Lecture Theatre. *Chairman*—M. M. RHOADES.

Lindegren, C. C. "Excessive Serial Two-strandCrossing-over in *Neurospora crassa*."

Piza, S. de T. "Two Normal Spindle Attachments in the Meiotic Chromosomes of the Brazilian Scorpion."

Ludwig, W. "Bemerkungen zur Chiasmabildung und zur Interferenz."

Körösy, K. de "Outlines of a Theory of Interference."

Weinstein, A. "The Interrelations of Genetic Functions."

9.15 a.m. **THEME 2.** SECTION C.

Physiological Characters.

Chemistry Lecture Theatre No. 1. *Chairman*—A. VANDEL.

Winge, O. "On Inconstancy in Single Cell Cultures of Micro-organisms owing to Segregation and on Hybridization in Yeast."

Csik, L. "Sauerstoffverbrauch der Drosophila-Puppen verschiedenen Genotypus."

Jucci, C. "Genetica del Baco da Seta."

Heilbronn, A. "Genetisch bedingte Störungen des Generationswechsels."

9.15 a.m. **THEME 3.** SECTION D.

Small Mammals.

Genetics Lecture Theatre. *Chairman*—J. RITCHIE.

Bamber, R. C. "A Time Factor in the Inheritance of White-Spotting in Cats."

Grüneberg, H. "Inherited Macrocytic Anæmias in the House Mouse."

Kobozieff, N. and N. A. Pomriaskinsky-Kobozieff. "Nouvelles recherches sur le mode de Transmission héréditaire des Anomalies des Oreilles chez la Souris : ' abaissement du pavillon ' et ' pavillon trongué.' "

Strandskov, H. H. "Inheritance of Internal Organ and Skeletal Variations in Guinea Pigs."

Vicari, E. M. "Genetics of Histological Structure of the Parathyroid Gland in Breed Crosses among Dogs."

Wilson, W. King "Alternative Modes of Inheritance of Steel Grey Coat Colour in Rabbits."

9.15 a.m. SECTION D. All day excursion to farms and institutions in the West of Scotland. Place of Departure: Reception Room. Fare 12/6, including Lunch. Lord Rowallan will entertain the party to Tea.

9.15 a.m. **THEME 4.** SECTION E.

Reproduction and Species Hybrids.

Chemistry Lecture Theatre No. 2. *Chairman*—Sir DANIEL HALL.

Crane, M. B., and Thomas, P. T. "Reproductive Versatility in *Rubus*."

Olah, L. "Interspecific Hybrids in the Genus Phleum."

Lewis, D. M. "The Relationship between Polyploidy and Fruiting Habit in the Cultivated Raspberry."

Lamm, R. "Varying Cytological Behaviour in Reciprocal *Solanum* crosses."

Gisquet, P., Dufrenoy, J., and Dusseau, A. "Karyology and Genetics of Interspecific Hybrids of Nicotiana."

Hurst, C. C. "Generic Hybrids in Orchids."

9.15 a.m. **THEME 5.** SECTION F.

Abnormal Human Characters.

Engineering Lecture Theatre. *Chairman*—G. P. FRETS.

Henderson, D. K. "Eugenics and Insanity."

Kallman, F. J. "The Scientific Goal in the Prevention of Hereditary Mental Disease and Racial Inferiority."

Thomasson, H. "Investigations on Heredity of Manic-depressive Psychosis in Iceland."

Luxenburger, H. "Neuere genetische Probleme in der Schizophrenieforschung."

Robb, R. C. "The Relative Frequency of Inheritable Disorders among 100,000 Hospitalized Patients."

Patzig, B. "Die Schizophrenie als Genetisches Problem."

9.15 a.m. **THEME 6.** SECTION G.

Experimental and Wild Populations.

Geology Lecture Theatre. *Chairman*—C. S. ELTON.

Ford, E. B. "A Quantitative Population Study in Butterflies."

Emerson, S. "The Distribution of Self-sterility Allelomorphs in a Natural Population."

Barigozzi, C. "Analisi Citogenetica di Due Popolazioni Naturali di *Artemia salina*."

Zimmermann, K. "Some Results of Genetical Analysis in Populations of Wild Rodents."

Spencer, W. P. "Ecological Factors and the Distribution of Genes in *Drosophila hydei* Populations."

10.00 a.m.–6.00 p.m. Demonstrations and Exhibits in the Zoology and Engineering Departments.

The Garden: Genetics Department.

2.15 p.m. **THEME 1.** SECTION B.

Chromosome Structure.

Zoology Lecture Theatre. *Chairman*—M. DEMEREC.

Heitz, E. "Entwicklung der Frage über die Beziehung zwischen Kernstruktur, Chromosomenstruktur und Genen."

Manton, I. "Evidence on Chromosome Structure in Osmunda."

Slizynska, H., and Slizynski, B. M.	"A Salivary Gland Chromosome Map of *Drosophila funebris* Fabr."
Barber, H. N.	"The Origin and Behaviour of Diplochromosomes."
Berger, C. A.	"On the Origin and Fate of Different Types of Polyploid Nuclei."
Geitler, L.	"Polyploide Somakerne und ihre Entstehung durch Endomitose bei Heteropteren."

2.15 p.m. **THEME 2.** SECTION C.

Physiological Characters—*continued.*

Chemistry Lecture Theatre No. 1. *Chairman*—C. JUCCI.

Szabó, Z.	"The Connection between Genotype and Constitution."
Gordon, C., and Sang, J. H.	"The Effect of Environment on the Exhibition of 'Antennaless' in *D. melanogaster*."
Neel, J.	"Developmental Temperature, Body Size and Character Expression in Drosophila."
Schoenheimer, S. Gluecksohn.	"On a New Short Tail Mutation in Mice."
Smith, T. L.	"The Genetics of the Wax Moth, *Galleria mellonella*."

2.15 p.m. **THEME 3.** SECTION D.

Small Mammals—*continued.*

Genetics Lecture Theatre. Round-table discussion.

Smith, G. Ennis.	"Fox-breeding: Fundamentals of Line Breeding."

2.15 p.m. **THEME 4.** SECTION E.

Reproduction and Species Hybrids—*continued.*

Chemistry Lecture Theatre No. 2. *Chairman*—M. J. SIRKS.

Tschermak von Seysenegg, E.	"Neue Fälle von Hybridogener Parthenogenesis."

Thompson, W. P.	"The Frequency of Fertilisation and the Nature of Embryo and Endosperm Development in Intergeneric Crosses in Cereals."
Armstrong, J. M., White, W. J., McLennan, H. A., and Johnson, L. P. V.	"Genetic Investigations in *Triticum-Agropyron* hybrids."
Peto, F. H.	"Cytology of *Triticum-Agropyron glaucum* Back-crosses."
Janaki, E. K.	"Triplopolyploidy and the Production of Fertile Intergeneric Hybrids of Saccharum,"
Vandendries, R. and Gavaudan, P.	"Remarques concernant l'action de la Colchicine et l'Acénaphtène sur Quelques Organismes Inférieurs."
Haig-Thomas, R.	"On a Species which proved to be a Wild Hybrid."

2.15 p.m. **THEME 5.** SECTION F.

Abnormal Human Characters—*continued.*

Engineering Lecture Theatre.

Chairman—P. J. WAARDENBURG.

Schade, H.	"Beitrag zur Feststellung der Häufigkeit von Erbkrankheiten."
Roberts, J. A. F.	"Resemblances in Intelligence between Sibs selected from a Complete Sample of an Urban Population."
Hanhart, E.	"Neue Ergebnisse über die Vererbung des Diabetes mellitus."
Madissoon, H.	"Sur le caractère héréditaire de l'absence des deux reins."
Parker, M. M.	"The Constitutional Basis of Neuroses (studies on the Albino rat).

2.15 p.m. **THEME 6.** SECTION G.

Experimental and Wild Populations—*continued.*

Geology Lecture Theatre.

Chairman—N. W. TIMOFEEFF-RESSOVSKY.

Jenkin, T. J.	"Evolution in Wild Populations."
Teissier, G.	"Etude expérimentale de la Sélection Naturelle."

Buzzati-Traverso, A.	"Genetica di Popolazioni nelli Drosophilae Italiane."
Spurway, H.	"Autosomal Genes collected from Wild Populations of *Drosophila subobscura*."
Philip, U.	"A Genetical Analysis of Three Small Populations of *Dermestes vulpinus* F."

2.15 p.m. **THEME 7.** SECTION I.

Growth, Normal and Abnormal.

Zoology Lecture Theatre No. 2.
Chairman—H. B. ANDERVONT.

Auerbach, C.	"Tests of Carcinogenic Substances in respect of their Influence on Mutation in *Drosophila melanogaster*."
Lamy, R., and Muller, H. J.	"Evidence of the Non-Genetic Nature of the Lethal Effect of Radiation of Drosophila Embryos."
Cramer, W.	"Permanent Retardation of the Growth Rate of a Transplantable Mouse Carcinoma induced by Radiation."
Stark, M. B.	"The Origin of certain Hereditary Tumours in Drosophila."
Fekete, E.	"Genetic Differences in the Physiology of the Mammary Gland in Mice."

2.30 p.m. Entertainment for Ladies by the Ladies' Committee. Visit to the Royal Botanic Gardens (Map Ref. M 3). Place of departure: Reception Room.

5.30 p.m. PLENARY SESSION of the Congress to receive reports and consider resolutions.
Geology Lecture Theatre.

8.30 p.m. Reception by the President and Council of the Zoological Society of Scotland at the Zoological Park, Corstorphine (Map Ref. G 6). Lounge suit, light refreshments; buses will be available for the conveyance of members from and to the hostels. Tickets for this function should be obtained from the Congress Office before midday on Monday, 28th August.

NOTE.—An all-day excursion by rail or motor coach and steamer will be arranged if a sufficient number so desires, to Dunoon, Rothesay, Kyles of Bute, and the Clyde Lochs. Places should be booked at the Travel Agent's Counter before midday on Monday, 28th August.

Wednesday, 30th August.

9.00 a.m. Congress Office opens.
Meeting of the Organising Sub-Committee in the Committee Room.

9.00 a.m. All day excursions by rail or motor coach will be arranged if a sufficient number so desires, to Linlithgow, Stirling, Aberfoyle, Trossachs, Loch Katrine, Callander, Doune, Dunblane, Stirling, Forth Bridge, etc. Places should be booked at the Travel Agent's Counter before midday on Tuesday, 29th August.

9.15 a.m. **THEME 1.** SECTION A.

Gene Mutation.

Zoology Lecture Theatre No. 1. *Chairman*—P. W. WHITING.

Stubbe, H.	"Neue Forschungen zur experimentellen Erzeugung von Mutationen."
Hollaender, A.	"Wave Length Dependence of the Production of Mutations in Fungus Spores by Monochromatic Ultra-Violet Radiation (2180-3650A)."
Knapp, E., and Schreiber, H.	"Quantitative Analyse der mutationsauslösenden Wirkung monochromatischen U.-V.-Lichtes in Spermatozoiden von Sphaerocarpus."

Raychaudhuri, S. P.	"The Validity of the Bunsen-Roscoe Law in the Production of Mutations by Radiation of Extremely Low Intensity."

9.15 a.m. **THEME 3.** SECTION C.

Hormonal Relations.

Chemistry Lecture Theatre No. 1. *Chairman*—G. W. BEADLE.

Ephrussi, B., Vogt, M. and Goldstein, L.	"Hormonal Relations in Gene Manifestation, with Special Reference to the Quantitative Aspect of the Problem."
Tatum, E. L., Beadle, G. W., and Clancy, C. W.	"Effect of Diet on Growth and Eye-Colour Development in Drosophila."
Melchers, G.	"Neuere Untersuchungen über die Physiologie der Genwirkungen an Pflanzen."
Chevais, S.	"Contribution à l'étude du développement de l'Oeil du 'mutant' Bar de *Drosophila melanogaster*."
Caridoit, F.	"Phénomènes d'Heredité Liée du Sexe, d'Heredité Controlée par l'Hormone Testiculaire et de 'Crossing-over' dans les Sebright Doré et Sebright Argenté."
Anderson, R. L.	"Non-autonomous Development in Transplanted Eyes of Habrobracon."

9.15 a.m. **THEME 4.** SECTION D.

Nutrition and Genetics.

Genetics Lecture Theatre. *Chairman*—J. F. DUNCAN.

Winters, L. M.	"The Development of Record of Performance Standards for Meat Animals."
Murray, G. N.	"Growth Rate in Pigs and Cattle."
Dunlop, G., and Williams, S.	"Controlled Feeding Techniques for Measuring Genetical Differences."

9.15 a.m. **THEME 5.** SECTION E.

Plant Improvement.

Chemistry Lecture Theatre, No. 2. *Chairman*—A. MUNTZING.

Bangham, W. N.	"Breeding of *Hevea*."
Mann, C. E. T.	"Improvement of Yield in *Hevea brasiliensis*."
Stout, A. B.	"Hybridisation and Selective Breeding in the genus *Hemerocallis*."
Woodworth, C. M.	"Inhibiting Factors in Soybeans."
Schreiber, F.	"The Genetics of Partial Coloration in Beans."
Hansen, N. E.	

9.15 a.m. **THEME 6.** SECTION F.

Human Characters.

Engineering Lecture Theatre. *Chairman*—H. MADISSOON.

Kemp, T.	"The Human Chromosomes."
Burks, B. S.	"Autosomal Linkage in Man."
Waardenburg, P. J.	"Concerning Dominant X-chromosomal Inherited Mye-defects in Ean.'
Feldman, W. M.	"The Inheritance of Congenital Transposition of the Viscera."
Garth, L. T. R.	"A Review of Race Psychology."

9.15 a.m. **THEME 7.** SECTION G.

Polyploidy and Reproductive Mechanisms.

Geology Lecture Theatre. *Chairman*—A. F. BLAKESLEE.

Straub, D. I.	"Induced Polyploidy in *Vicia faba*."

Müntzing, A.	"Incompatibility and Fertility in Experimental and Natural Polyploids."
Christoff, M.	"Polyploidy and Apomictic Development in the Genus Potentilla."
Smith, S. G.	"Cytology and Parthenogenesis of *Diprion polytomum*, Hartig."
Sears, E. R., Smith, L., and O'Mara, J. G.	"Genetic and Cytological Investigations of Polyploid Series in *Triticum* and related Genera."
Stomps, T. J.	"On Artificially Produced Oenothera Lamarckiana Gigas."

10.30 a.m. **THEME 2.** SECTION B.

Cytological Analysis.

Zoology Lecture Theatre No. 2. *Chairman*—B. P. KAUFMANN.

Fankhauser, G.	"Polyploidy in Salamanders."
Saez, F. A.	"Efectos de la centrifugación sobre las Células sexuales de *Schistocerca paranensis*."
Matthey, R.	"Le Mythe des Hétérochromosomes chez les Sauropsides."

2.15 p.m. **THEME 1.** SECTION A.

Gene Mutation—*continued.*

Zoology Lecture Theatre No. 1.

Chairman—P. W. WHITING.

Rhoades, M. M.	"On the High Mutation Rate of the a_1 Allele in Maize induced by the Dt Gene."
Burgeff, H.	"Constructive Mutations in Marchanti."
Clemente, L. S.	"The Lethal Effect of the Combined Purple and Eyeless Genes in Drosophila."

Sung-Yün Ma,	"Die Ergebnisse der Experimentellen Untersuchungen über Hitzemodiakationen bei *Drosophila melanogaster*."
Plough, H. H., Child, G. P., and Ives, P. T.	"The Relative Importance of Temperature and Heredity for Mutation Frequency in Drosophila."

2.15 p.m. **THEME 2.** SECTION B.

Cytological Analysis—*continued.*

Zoology Lecture Theatre No. 2.

Chairman—O. ROSENBERG.

Bergner, A. D.	"Chromosome Association in Datura."
Levan, A.	"The Occurrence in Nature of Asynapsis in *Allium amplectens*."
Huskins, C. L., and Wilson, G. B.	"The Structure of Chromosomes during Meiosis in *Trillium erectum* L."
Bhadhuri, P. N.	"A Study of the Relation of Chromosomes to Nucleoli in Species of Scilla, Vicia, and Oenothera."
Pathak, G. N.	"Studies in the Cytology of Crocus and Cereals, with Special Reference to Satellites and Nucleoli."
Sikka, S. M.	"Cytological Investigations of Brassica Species and Hybrids."

2.15 p.m. **THEME 3.** SECTION C.

Biochemical.

Chemistry Lecture Theatre No. 1.

Chairman—M. R. VANDENDRIES.

Price, J. R.	"The Rate and Sequence of Gene Controlled Chemical Processes."
Lawrence, W. J. C.	"The Chemistry and Genetics of the Flower Colour Pigments in the Genus *Streptocarpus*."
Miege, E.	"L'Hérédité de la Composition Chimique chez les Hybrides Intergénériques."

Chouard, P., and Dufrenoy, J. — "Pigments of Hybrids of *Gentiana lutea* and *G. Bueseri*."

2.15 p.m. **THEME 4.** **Pig.** SECTION D.

Genetics Lecture Theatre. *Chairman*—G. SCOTT ROBERTSON.

McMeekan, C. P. and Hammond, J. — "The Relation of Environmental Conditions to Breeding and Selection for Commercial Types in Pigs."

Krizenecky, J. — "Elimination of External Factors in Progeny Testing in Pigs."

Donald, H. P. — "Genetic Aspects of the Growth Rate of Bacon Pigs."

Davidson, H. R. — "The Practical Aspects of Improving Pigs."

2.15 p.m. **THEME 5.** SECTION E.

Genetic Analysis.

Chemistry Lecture Theatre No. 2. *Chairman*—A. TAVCAR.

Boerger, A. — "Angewandte Genetik als entscheidender Faktor für das Vordringen des Weizenbaues im subtropischen Osten Südamerikas."

Ranganatha Rao, V. N. — "Hybridisation between Two Hybrids."

Hiorth, G. — "Versuche mit natürlichen Rassen der Amoena-Gruppe von Godetia."

Ramiah, K. — "Genic Symbolisation in Rice."

2.15 p.m. **THEME 6.** SECTION F.

Human Characters—*continued.*

Engineering Lecture Theatre. *Chairman*—T. KEMP.

Waadenburg, P. J. — "Concerning Recessive Sexlinked Eye-defects in Man."

Quelprud, T. — "Variability and Genetics of the Human External Ear."

Gemelli, A. — "La Trasmissione Ereditaria di Caratteri Intellettuali."

Hurst, C. C. — "Genetics of Intellect."

Race, R. R., Taylor, G. L., and Vaughan, J. M. — "A Genetic Investigation of Acholuric Jaundice."

2.15 p.m. **THEME 7.** SECTION G.

Polyploidy and Reproductive Mechanisms—*continued.*

Geology Lecture Theatre. *Chairman*—L. Blaringhem.

Skalinska, M. — "The Origin of Polyploidy in Aquilegia."

Kappert, H. — "Erbliche Polyembryonie bei Linum mit identischen und diplohaploiden Mehrlirgen."

Williams, R. D. — "Incompatibility Alleles in *Trifolium pratense L*: their Frequency and Linkage Relationships."

Jeffrey, E. C. — "Apomixis in the Genus Trillium."

Fleckinger, J. — "Caractères morphologiques et végétatifs, en relation avec la triploidie chez la Pommier et le Poirier."

Tinney, F. W. — "Cytology of Apomictic Seed Development in *Poa pratensis* L."

3.00 p.m. Entertainment for Ladies by the Ladies' Committee. Visit to University Departments. Place of Departure: Reception Room.

6.00 p.m. The Curtain will fall.

INDEX

To construct a programme of this kind is always difficult: in these days it is almost impossible. Those who recognise its faults, and they are many, will surely excuse them when they learn that after this programme had been printed, and only ten days before the actual opening of the Congress, no fewer than 50 names and titles had to be removed and the whole programme hurriedly recast.

Seventh International Genetical Congress 1939

SYNOPSIS OF Programme AND Excursions

answer to any questions? BMJ, sent 4.2.46

Question 2035

When Fisher's theory was proposed in 1944, it provided rhyme and reason for the rather bewildering Rh antigen-antibody reactions then known. It also made certain predictions which are gradually being verified. According to this theory three adjacent genes are responsible for the Rh blood group antigens, and not one gene as had been previously supposed. Each of these genes has at least two alternative forms, called C or c, D or d and E or e. Each chromosome must carry three genes, which may be CDe or cDE, etc ~~CD and E or CD and e or cD and E etc.~~

As an individual has two of each of the 24 different human chromosomes, he will have two of the Rh chromosomes, and ~~they~~ each may ~~each~~ carry any combination of the three alternative pairs. For example a person may have received CDe from one parent and cde from the other. This particular combination, CDe/cde, is common in Britain and U.S.A.. ~~amongst Europeans.~~ The six Rh genes produce six corresponding antigens on the red cell, each capable of inducing a corresponding antibody; (This must be qualified by saying that d at present represents only the absence of D. A year ago e denoted only the absence of E, but the discovery of an anti-e serum, predicted some time before by Fisher, makes it possible to recognize e as an antigen). Not counting d, there are 6 Rh antigens D, C, c, E, e and C^W (C^W is a third alternative to C or c, only recently discovered) which can be identified by positive tests. There is every reason to suppose that d will eventually

become recognisable as a positive character.

Rh_1 is the original name of the "gene" which, according to Fisher, actually consists of a short strip of chromosome involving three genes C D and e. Similarly Rh_2 = cDE, rh = cde, Rh_0 = cDe, Rh' = Cde, Rh" = cdE, Rh_z = CDE and Rh_y = CdE (Rh_y has not yet been isolated). These earlier names are often convenient, for example the genotype CDe/cDE is usually called $Rh_1 Rh_2$, or $r'R_1R_2$. The combinations involving C^W have not been given Rh names.

Successful detailed prediction such as that achieved by Fisher must be rare in biology.

A letter about the theory appeared in Nature for January 12th 1946 (157, 48).

THE GENETICAL SOCIETY

A MEETING of the Society will be held at 2 p.m. on THURSDAY, 25 APRIL 1946, at the ROYAL SOCIETY OF MEDICINE, 1 WIMPOLE STREET, LONDON, W. 1. (Stations *Oxford Circus* or *Bond Street*.) The meeting will take the form of a symposium on human genetics. Professor R. A. FISHER will be in the chair.

PROGRAMME

2 p.m.	J. A. FRASER ROBERTS	'Some further observations on the difference between the sexes in dispersion of intelligence.'
	W. J. B. RIDDELL	'Conditionally dominant sex-linked nystagmus.'
	L. S. PENROSE	'On the familial appearance of maternal-foetal incompatibility.'
	H. KALMUS	'Genetical antigenic incompatibility as a possible cause of the toxaemias occurring late in pregnancy.'
4 p.m.	TEA	
4.30 p.m.	J. B. S. HALDANE	'The linkage between colourblindness and haemophilia in man.'
5 p.m.	R. R. RACE and A. E. MOURANT	'*Rh* antigens and antibodies: Fisher's synthesis. Some "new" blood groups.'

Members are reminded that the names of candidates for election at the annual meeting, including those of temporary members wishing to be elected, should reach the Secretaries by 1 May. The names of three members who are willing to support the nomination must accompany each proposal.

Members are also reminded that their subscriptions are due on 1 June, and should be sent to the Acting Treasurer, Dr Catcheside, Botany School, Cambridge.

R. R. RACE, *Secretary*
Galton Laboratory Serum Unit, Department of Pathology, University of Cambridge

Some further observations on the difference between the sexes in dispersion of intelligence

J. A. Fraser Roberts

It is found as an empirical fact of observation that in performance on standard intelligence scales, boys are considerably more variable than girls. This is all the more strange as there is no difference in mean performance and no similar difference has been demonstrated in any other measurable characteristic. The difference in dispersion is a big one; the ratio of the variances is not less than 113 : 100, and is probably somewhat greater than this.

Evidence will be presented to show that over the range of chronological age for which information is available—9½–13 years—the ratio of the variances is constant. It is difficult to think of any plausible explanation. Environmental hypotheses are especially difficult, for even apart from the result just mentioned they would have to account for a substantial difference in variances combined with an identity in means. It seems more likely that the difference is to be referred to the genetic component in ability as measured by tests.

Conditionally dominant sex-linked nystagmus

W. J. B. Riddell

Rapid, involuntary oscillation of the eyeballs is a type of nystagmus which is frequently stated to be inherited in either a dominant or sex-linked recessive form. It may be associated with other inherited peculiarities such as head nodding, short sight and albinism.

This pedigree contains over one hundred and seventy individuals within five generations. Nine males and seven females were affected. The five affected males, known to have children, produced nine normal sons, ten normal daughters and five affected daughters. All the descendants of the unaffected males are normal. The condition was transmitted by two normal and three affected females to nine sons and one daughter. This girl (V. 63) had a normal mother, brother and sister, and an affected uncle and female cousin.

The nystagmus was of the rapid horizontal type, and in certain cases this was associated with myopia and head nodding. No albinos were found and there was no consanguinity. It is suggested that this is an example of sex-linked inheritance with incomplete penetrance in the heterozygote.

On the familial appearance of maternal-foetal incompatibility

L. S. Penrose

That erythroblastosis foetalis is primarily due to antigenic incompatibility could have been demonstrated by studying pedigrees. The theoretical appearances of such pedigrees are quite unusual. Pairs of sisters and pairs of brothers are more likely to have affected children than are brother-sister pairs. The consanguinity rate between the parents of affected offspring is low, but it can be high for the parents of the mother. The correlation between mother and child with respect to the condition is always negative. If the antigenic factor is either very rare or very common, pedigrees show characteristic peculiarities. Unknown factors, genetic or environmental, which influence the expression of the disease in the foetus can be allowed for, by making suitable assumptions. Examination of the pedigrees of familial cases of mongolism and some other types of developmental abnormality suggests that these conditions are antigenic in origin.

Genetical antigenic incompatibility as a possible cause of the toxaemias occurring late in pregnancy

H. Kalmus

The toxaemias of late pregnancy and among them eclampsia are probably due to some incompatibility of mother and foetus. More specifically, Schwartz and Levine have suggested that they may be caused by isoimmunization. Postulating a simple toxaemic configuration, the familial incidence of the toxaemias can be calculated for various relationships. Distributions related to those found in erythroblastosis or mongolism would be expected if the hypothesis was true. Even in the case of a greater complication by several alleles certain relatives of toxaemic pregnant women and their husbands would show a high incidence of toxaemia of pregnancy. Some actual data are quoted in support of the hypothesis.

The linkage between colourblindness and haemophilia in man

J. B. S. Haldane

Seventeen pedigrees have now been published from which information may be obtained as to the linkage between colourblindness and haemophilia. The mathematical methods used, and their relation to Fisher's method, are described. The frequency of recombination is about 12 per cent. In one pedigree it is possible, on the basis of linkage, to give a eugenical prognosis. The same method can be applied to pedigrees where two autosomal dominants appear to be linked. An example is described.

Rh antigens and antibodies: Fisher synthesis. Some 'new' blood groups

R. R. Race and A. E. Mourant

American and English work resulted in the isolation, in 1943, of seven forms of the *Rh* gene. These different forms were thought to be allelomorphs at one locus, but this theory was rather unsatisfactory for each gene resulted in the production of several antigens, each of which was also produced by some other allelomorphs. Fisher, examining the English work, pointed out that the supposition of three closely linked loci, each with at least two allelomorphs (*Cc*, *Dd* and *Ee*) was capable of absorbing all the facts known at that time. The theory made certain predictions, some of which have since been confirmed serologically. It has recently become necessary to postulate a third allele at the *C–c* locus, C^w. Although crossing-over has not been demonstrated in any family there is reason to think that it occasionally occurs. Fisher considers that the order of genes on the chromosome is *DCE*.

We are at present studying the following four 'new' blood groups:

Name of antigen	*Frequency of antigen (in England) approximate %*	*Antiserum found*
Lutheran	8	Twice
Levay	Very rare	Once
Gibson	26	Twice
Kell	7	Once

There are 24 serologically distinguishable *Rh* groups, 3 *MN*, 2 *P*, 6 A_1 A_2 *BO*, 2 Lutheran, 2 Levay, 2 Gibson and 2 Kell, making 13,824 different types of blood which could be recognized.

19.1.47 Distribution of 870 English blocks with 24 recognisable phr

19.1.47

(part 927)

	Δ	y	H	Γ^{v}_{s}	n	$\Gamma^{w}\Gamma$			
R_1R_1	+	−	−	+	+	−	+	145	·1667
R_1r	+	+	−	+	+	−	+	288	·3310
R_1R_2	+	+	+	+	+	−	+	105	·1207
R_2R_3	+	+	+	+	−	−	+	0	·0000
R_2R_2	+	+	+	−	−	−	−	23	·0264
R_2r	+	+	+	−	+	−	−	107	·1230
rr	−	+	−	−	+	−	−	147	·1690
R_0r	+	+	−	−	+	−	−	15	·0172
$R'r$	−	+	−	+	+	−	+	8	·0092
$R''r$	−	+	+	−	+	−	−	4	·0046
$R''R''$	−	+	+	−	−	−	−	0	·0000
$R'R'$	−	−	−	+	+	−	+	0	·0000
$R'R''$	−	+	+	+	+	−	+	0	·0000
R_3R_3	+	−	+	+	−	−	+	0	·0000
R_1R_3	+	−	+	+	+	−	+	4	·0046
$R_1^{w}R_1$	+	−	−	+	+	+	+	11	·0126
$R_1^{w}R_1^{v}$	+	−	−	+	+	+	−	0	·0000
$R_1^{w}r$	+	+	−	+	+	+	−	7	·0080
$R_1^{w}R_2$	+	+	+	+	+	+	−	6	·0069
$R'^{v}r$	−	+	−	+	+	+	−	0	·0000
$R''R''$	−	−	−	+	+	+	−	0	·0000
$R''R''$	−	+	+	+	+	+	−	0	·0000
$R_2^{w}R_3$	+	−	+	+	+	+	+	0	·0000
R_3R_3	+	−	+	+	+	+	+	0	·0000
$R'^{v}R'$	−	−	−	+	+	+	+	0	·0000

Total 870 ·9999

Tone frequencies

r cde ·4111

R' Cde ·0110

R'' cdE ·0056

$R^{w}H$	− + ...			
$R^{w}R^{w}$	− − − + + + −	0	·0000	870 ·9999
$R^{w}R''$	− + + + + + −	0	·0000	
$R^{w}R_{z}$	+ − + + + + +	0	·0000	
~~$R^{w}R_{z}$~~	~~+ − + + + + +~~	~~0~~	~~·0000~~	
$R^{w}R'$	− − − + + + +	0	·0000	

Gene frequencies

r	cde	·4111
R'	Cde	·0110
R''	cdE	·0056
R_0	cDe	·0204
R_1	CDe	·4084
R_z	CDE	·0055
	$C^{w}De$	·0138 (½ [illegible])
	$C^{w}de$	·0000 (known to exist)
R_2	cDE	·1242 ·1277

Δ y H Γ^{w} η Γ^{w} Γ

+ − − + + − +

		EXP.	OBS.
R_1R' ·0090		·1758	·1667
R_1R_1 ·1668			

+ + − + + − +

R_1r ·3358	·3529	·3310
$R'R_0$ ·0004		
R_1R_0 ·0167	(χ^2=1·8)	

+ + + + + − +

R_2R' ·0027	·1134	·1207
R_1R'' ·0046		
R_zr ·0045		
R_1R_2 ·1014	(χ^2= 0·46)	
R_0R_z ·0002		

Δ y H Γ Γ^{w} η Γ^{u} Γ

+ + + + − − +

	EXP.	OBS.
R_2R_z ·0014	·0015	·0000
$R''R_z$ ·0001		

+ + + − − − −

R_2R_2 ·0154	·0168	·0264
R_2R'' ·0014	(χ^2= ~~4·~~ 3·75)	

+ + + − + − −

R_2r ·1021	·1074	·1030
R_0R'' ·0002		
R_0R_2 ·0051	(χ^2= 2·2)	

− + − − + − −

rr	·1690	·1690

+ + − − + − −

R_0r ~~·0004~~ ·0168	·0172	·0172
R_0R_0 ·0004		

Δ y H Γ^{w} η Γ^{w} Γ

− + − + + − +

	EXP	OBS
$R'r$ ·0090	·0090	·0092

− − − + + − +

$R'R'$	·0001	·0000

Δ y H Γ Γ^{w} η Γ^{w} Γ

+ − − + + + −

	EXP.	OBS.
$C^{w}De/C^{w}de$ ·0000	·0002	·0000
$C^{w}De/C^{w}De$ ·0002		

+ − + + + + +

− + + + + − +

+++++++−+

R_2R'	·0027		
R_1R''	·0046		
R_2n	·0045	·1134	·1207
R_1R_2	·1014		
R_0R_2	·0002		

(χ^2 = 0.46)

R_2n	·1021		
R_1R''	·0002	·1074	·1230
R_0R_2	·0051		

(χ^2 = 42)

−+−−+−−

nn		·1606	·1650

++−−+−−

R_0n	~~·0004~~ ·0168	·0172	·0172
R_0R_0	·0004		

ΔγHΓʷηΓʷΓ

−+−++−+

	EXP	OBS
$R'n$	·0090	·0090 ·0092

−−−+++−+

$R'R'$	·0001	·0000

−++++−+

$R'R''$	·0001	·0000

−++−+−−

$R''n$	·0046	·0046

−++−−−−

$R''R''$	·0000	·0000

+−+++−+

R_1R_2	·0045	·0046	·0046
$R'R_2$	·0001		

+−++−−+

R_2R_2	·0000	·0000

+++++++−

C^wDe/cDE	·0034		
C^wDe/cdE	·0002	·0036	·0069
C^wde/cDE	·0000		

++−+++−

$(^wDe/$ ~~cde~~	·0113	·0119	~~·0120~~ ·0080
$^wDe/$ cde	·0006		

(χ^2 = 1.11)

−−+++++

De/CDe	·0113		
De/Cde	·0003	·0116	·0126
e/CDe	·0000		

(χ^2 = ·09)

ΔγHΓʷηΓʷΓ

+−−++++−

	EXP	OBS.
C^wDe/C^wde	·0000	
C^wDe/C^wDe	·0002	·0002 ·0000

+−+++++

C^wDe/CDE	·0002	·0002	·0000
C^wde/CDE	·0000		

−−−+++−

C^wde/C^wde	·0000	·0000
~~C^wde/Cde~~		

−++++++−

C^wde/cdE	·0000	·0000

++−++++−

C^wde/cDe	·0000	·0000

−+−+++−

C^wde/cde	·0000	·0000

−−−++++

C^wde/Cde	·9999	·9999

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GRUNE & STRATTON, Medical Publishers, New York

NEWS AND VIEWS

The International Hematology and Rh Conference, November 1946

Perhaps the first International Congress devoted solely to hematologic subjects to be held in the Western Hemisphere took place in Dallas, Texas, and Mexico City in November 1946. It began in Dallas on November 15–16 in affiliation with the second Mexican Congress of Blood Transfusion and then transferred its deliberations to Mexico City, where sessions were held from November 17 to November 23. Thus, the meeting was truly international as to both the participating sections and the meeting places.

The idea for such a meeting developed in December 1945 at a conference between Dr. Eduardo Uribe Guerola of the Juarez Hospital, Mexico City, and Dr. Joseph M. Hill of the Baylor Hospital, Dallas, Texas. Support for the proposal was given by the Mexican Government through the Department of Health headed by Dr. Gustavo Baz and by the Trustees of the Baylor Hospital. Additional financial support in Dallas was offered by various benefactors who had previously shown an interest in Baylor Hospital and its Blood Bank. It was originally planned to limit the program of the meeting to problems of the Rh factor. However, as interest in the proposed meeting rapidly mounted, and as a more general type of program seemed desirable, the final title of the meeting was changed to "International Hematology and Rh Conference."

Chairman of the Conference at Dallas was Dr. Joseph M. Hill, Pathologist at the Baylor Hospital; Secretary, Dr. Sol Haberman of the same hospital. Dr. Eduardo Uribe Guerola was Chairman of the Second Mexican Transfusion Congress and Dr. Alfonso Veléz Orozco, Secretary. There was a large attendance of physicians at the Dallas meeting, representing 21 states and the District of Columbia. In addition several physicians from Canada, Mexico, China, and England were present. Interest in the program which follows was intense:

Philip Levine, New Jersey:	"A Brief Survey of the Rh Factor"
Ernest Witebsky, Buffalo:	"Interrelationship between the Rh System and the A-B System"
Ignacio González-Guzmán, Mexico City:	"The Nuclear Structure of the Blood Cells"
Robert R. Race, London, England:	"The Rh Genotypes and Fisher's Theory"
Joseph M. Hill and Sol Haberman, Dallas:	"Rh Hemolytic Immune Globulins: Evidence for a possible Third Order of Antibodies Incapable of Agglutination or Blocking"

William Dameshek, Boston:	"Hemolytic Mechanisms"
Louis K. Diamond, Boston:	"Physiochemical and Immunological Character of the Rh antibodies"
Israel Davidsohn, Chicago:	"Rh Antibodies"
Mario Salazár Mallen, Mexico City:	"The Frequency of the Rh Factor in Different Groups of the Mexican Population"
Bruce Chown, Winnipeg, Manitoba:	"Variation in the Outcome of the Pregnancies in Which Erythroblastosis Occurs"

The Conference transferred to Mexico City from Dallas by plane at 4:30 A.M., Sunday, November 17, arriving in Mexico City about noon. Formal opening of the Second Mexican Blood Transfusion Congress took place in the Palace of Fine Arts, where addresses of welcome were delivered by, among others, Dr. Salvador Zubirán, Rector of the National University of Mexico and Director of the Hospital for Nutrition, and Dr. Gustavo Baz, Secretary of the Ministry of Public Health. A diplomatic reception was held on the evening of November 21 at the Ministry of Foreign Affairs, the host, a physician himself, being Dr. Francisco Castillo Najéra, Minister of Foreign Affairs. Visits were made to the Hospital de Jesús, the oldest hospital in the Western Hemisphere, in continuous operation since 1554, to the Military Hospital, and to Xochimilco and the Pyramids.

Sessions were held daily, both the Spanish and English languages being used. The program was as follows:

J. M. Hill and Sol Haberman:	"Production and Use of Anti-Rh Serum"
Alfonso Veléz Orozco:	"The A and B Factors as Possible Causes of Erythroblastosis"
Sol Haberman and J. M. Hill:	"Demonstrations of Technics of Rh Testing"
R. R. Race:	"Subgroups of the Rh Factor. Demonstration of the Genetics of Rh and Other New Blood Groups"
A. V. Orozco and Rolando Medina Aguilár:	"Percentages of the Rh Subgroups in Mexico"
Philip Levine:	"The Individuality of Human and Animal Blood"
	"The Importance of the Rh Factor and Historical Development"
R. M. Aguilár:	"Use of A.C.D. Solution in Blood Banking"
I. González-Guzman:	"The Histopathology of Erythroblastosis"
Harry Wallerstein:	"The Treatment of Erythroblastosis by Complete Exchange Transfusion" (motion picture)

The discussions in Mexico City, although often lengthy, were lively and stimulating. At the concluding session* on the morning of November 23, Dr. J. M. Hill, Chairman of the International Hematology and Rh Conference, and Dr. Eduardo Uribe Guerola, President of the Mexican Transfusion Congress, presided as co-chairmen. Discussions were held concerning the following problems:

(1) Organization of an international blood society with particular reference to experimental and immunohematology.

(2) Nomenclature of blood antigens and related antibodies. (3) Technics to be recommended for routine testing for these antigens and antibodies. (4) Availability of sufficient Rh serum for routine typing in transfusions and pregnancies.

After a very active and complete discussion, recommendations and actions were taken by this joint conference. Two committees were appointed with authorization to function as indicated. The first committee was charged with the responsibility for taking the necessary steps to form an international organization to carry on the work begun at this meeting. This committee was also instructed to undertake the standardization of blood typing serums and to promote the production of Rh serums from human sources as a cooperative project. This committee consists of Dr. J. M. Hill, Dallas, Texas, Chairman; Dr. William Dameshek, Boston, Mass.; Dr. Louis K. Diamond, Boston, Mass.; Dr. Luís Gutierrez Villegas, Mexico, D.F.; Dr. Philip Levine, Raritan, New Jersey; Dr. E. A. Mourant, London, England; Dr. W. S. Stansbury, Toronto, Canada; Dr. Eduardo Uribe Guerola, Mexico, D.F.; and Dr. Ernest Witebsky, Buffalo, New York.

The second committee was appointed to study and recommend nomenclatures for blood antigens and technics to be used for routine blood typing and antibody investigations. This committee consists of Dr. Philip Levine, Raritan, New Jersey, Chairman; Dr. Bruce Chown, Winnipeg, Canada; Dr. Israel Davidsohn, Chicago, Illinois; Dr. Sol Haberman, Dallas, Texas; Dr. J. M. Hill, Dallas, Texas; Dr. R. R. Race, London, England; and Dr. Eduardo Uribe Guerola, Mexico, D.F.

In the discussions the advantages of the Chown capillary and Diamond slide technics for routine Rh typing were emphasized. For detection of antibodies the Coombs ("developing") test and the Diamond albumin test received favorable comment. The compatibility test of Witebsky was also highly recommended. Review of these and other technics was referred to the committee.

It was of interest that the Fisher-Race theory of inheritance and the CDE nomenclature suggested by these workers were felt to be most suitable for serologic and genetic study of Rh and Hr subgroups and were recommended for acceptance temporarily until the problem could be more thoroughly reviewed by the committee. The members of the joint meeting also decided to retain, at least for the immediate future, the term "erythroblastosis foetalis" for cases resulting from isoimmunization of mothers by the Rh, Hr, and other blood antigens. The use of the terms "Rh positive" and "Rh negative" along with "homozygous" and "heterozygous" was retained for clinical use. The use of the terms "X-protein" and "conglutination" was rejected on the basis of lack of evidence.

* The report of this session was furnished by Dr. Sol Haberman.

Routine Rh typing for all transfusions and pregnancies was strongly recommended. However, it was suggested that when adequate quantities of anti-Rh serum were not available, only women should be routinely Rh tested. Testing of women only was also recommended when the population or race concerned was known to have a very small percentage of Rh negatives. It was agreed that anti-Rh serum for routine testing should contain the anti-D antibody (85 per cent) or anti-D+C (87 per cent).

The meetings in both Dallas and Mexico City proved highly successful. Their international character was of help in fostering mutual good will among those participating. It was agreed by all that further conferences of this sort, dealing perhaps with other subjects and of a more general character, were worth while. It seemed eminently desirable to initiate by every means possible the formation of an International Society for Hematology. It was also agreed to attempt the publication of the various papers at both sections of the Congress in a special issue of BLOOD.

INTERNATIONAL SOCIETY OF HEMATOLOGY

September 8, 1947

Dr. R. R. Race
Medical Research Council
The Lister Institute
Chelsea Bridge Road
London, S. W. 1.

Dear Dr. Race:

I am writing to ask if you will be kind enough to serve as a representative of your country and your area on our Membership Committee for the International Society of Hematology. If so desired, you may appoint additional subcommittee members from your country to assist you and to serve as a subcommittee in recommending members to the Society. Dr. William Dameshek, 25 Bennett Street, Boston, Massachusetts, is chairman of this Committee on Membership.

Since the next meeting is already set for August 23, 24, 25, 26, 1948 at Buffalo, New York it is essential that work on the program should commence as soon as possible. It would, therefore, be a considerable saving of time if, in your letter of acceptance, you would include any preliminary suggestions in regard to the make-up of the program or outstanding speakers from your region who might have material to present suitable for such an international meeting.

Enclosed is an editorial from Blood: the Journal of Hematology and a brief notation on the aims and progress of the Society to date for your information. Since the success of our Society will be largely determined by the steps taken at the meeting in Buffalo it is of the utmost importance to have a strong program and a good attendance at this meeting.

I am sure that your acceptance of this appointment on the Membership Committee will help assure us of success in this objective.

Sincerely yours,

JMH:ss

J. M. Hill, M.D.
President

P.S. Rob I guess this duplicates my earlier letter, but contains some new information. JH

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MEDICAL RESEARCH COUNCIL
(BLOOD GROUP RESEARCH UNIT)

Council Office :
38 OLD QUEEN STREET,
WESTMINSTER, S.W.1

PRIVY COUNCIL

THE LISTER INSTITUTE,
CHELSEA BRIDGE ROAD,
LONDON, S.W.1

Telephone : SLOane 2181
Tel. Address : BACTERIOLOGY,
KNIGHTS, LONDON.

7th October, 1947.

Dear

I enclose a letter which I have received from Dr. J.W. Hill, the President of the newly formed International Society of Hematology.

This new Society arose out of a Congress last November in Dallas, Texas, and in Mexico City. Although this first meeting was mainly of Rh workers, the Society hopes to have a balanced membership representing all the other branches of haematology.

May I trouble you to bring the enclosed information to the notice of anyone you may consider suitable? I would also be very glad of any help you can give in answering Dr. Hill's request for "suggestions in regard to the make-up of the program, or outstanding speakers from your region (Britain) who might have material to present suitable for such an international meeting".

Yours sincerely,

R.R. Race

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R.R. Race

PROGRESS AND AIMS OF THE INTERNATIONAL SOCIETY OF HEMATOLOGY

This brief note on the progress and aims of the International Society of Hematology is for the purpose of acquainting committee members and prospective members of the Society with certain facts in regard to the origin and aims of the Society and the progress that has been made to date together with future plans.

The International Society of Hematology arose out of the spontaneous expression for the need of some such organization on the part of those attending the International Hematology and Rh Conference held in Dallas, Texas and by the group attending the affiliated meeting of the second Mexican Blood Transfusion Congress in Mexico City. These conferences were held in November, 1946. While the initial enthusiasm was largely in regard to experimental and immunohematology, conferences with many hematologists in the United States soon made it clear that it was desirable to have a more inclusive type of Society in which there would be represented all groups of workers in the broad field of blood. Accordingly the committee on organization appointed at the conferences mentioned undertook the organization of an International Society of Hematology in its broadest aspects. Because of the peculiar difficulties of organizing an International Society it was decided to elect officers by mail through the casting of ballots by those who attended the conferences. Since the election of officers, committees have been appointed and are being appointed to make it possible to have a meeting of the Society next year. In fact, such a meeting has been set for August 23, 24, 25, 26, 1948 in Buffalo, New York. At that time a constitution and by-laws can be approved. A Constitutional Committee working during the year will have recommendations ready in order to facilitate the formulation and adoption of such a constitution. In the meantime, the Program Committee under Dr. Ernest Witebsky and the Membership Committee under the chairmanship of Dr. William Dameshek are already functioning.

The aims of the Society are simple but broad. The first aim is to bring together representatives of all the various phases of hematology for exchange of ideas at meetings held at suitable intervals possibly every two years. In addition to this main objective, the Society may also be useful in advising concerning nomenclature and terminologies, techniques and the encouragement of production of Rh serum, etc. Arrangements have been made for publication of the proceedings of the meeting of the first conference in Dallas as a special issue of the Journal Blood and this Journal will continue as the official organ of the Society.

Eligibility for members is to be determined by the Committee on Membership under Dr. William Dameshek. However, it has been agreed generally that the Society will be composed of those having the Doctor's Degree in Medicine or any of the Sciences or its equivalent who have a definite and continuing interest in some field of hematology. This would naturally include those interested in clinical hematology, pathology in relation to blood disease, transfusions and blood banking, immunohematology, chemistry, physiology, genetics as applied to blood, etc. It is hoped that plans now being made will make it possible to provide the expenses involved in bringing outstanding speakers from continents other than North America.

Society dues have been set at $15.00 a year and will include a subscription to Blood: the Journal of Hematology.

BER	A_1	H	A	B	C	D	E	c	e	f	G	rh_i	hr_i	M	N	S	s	U	K	k	Fy^a	Fy^b	Jk^a	Jk^b	C^w	P	P^k	Le^a	Le^b	Lu^a	Kp^a	Kp^b	Ku

Blood Grouping Laboratory

Boston

Signatures, 195?

To Rob and Ruth with the compliments of the Blood Grouping Lab.
And Pat, if you use this, please think of us.

Boston
195?

Frank Allen
Louis K. Diamond
Cat Corcoran
Mary Walker
Margret Oswald
Judith Weiner
Barbara Plummer
Claire Vitaliano
Virginia Bloom
Lu Kennedy
Gladys Smith
Aaron Kaufer
Hawkins Maddux
Helen E. Fitzgerald
Lucille Rowe
David Levine
Lyn Konigsen
Marilyn Munn
Ann Mathison

NAME	DIAGNOSIS	SENT BY	DAT NUM

No. & Sex	Age in Days	Baby's Blood: Cells — Direct Test	Baby's Blood: Serum — Usual Tests	Baby's Blood: Serum — Indirect Test	Mother's Serum — Usual Tests	Mother's Serum — Indirect Test	Rh and ABO Groups — Baby	Rh and ABO Groups — Mother	Rh and ABO Groups — Father	Preg. Nancy	Clinical Diagnosis	
1 ♀		+	++Δ′	+	Δ′	+	R_1r A	rr A	R_1R_1 A	2	Hemolytic disease	Transfused Recovered
2 ♀	3	+	—	+	+Δ′	+	R_1r A	rr A	R_1R_1 A	6	"	Recovered
3		+	–	++	++Δ	+	R_1r O	rr A	R_1R_1 O	2	"	Not transfused. died
4 ♀	5	+	–	+	+Δ		R_1r O	rr O	R_1R_2 O	3	"	Transfused Recovered
5		+	–		+Δ		R_1r A	rr A	R_1R_2 A	2	"	Transfused
6 ♀	4	+			ΔH		R_2r O	rr O	R_1R_1 O	2	"	died
7 ♀		+	–	+	ΔΔ′		R_1r O	rr A	R_1R_1 O	3	"	Transfused. Recovered
8 ♀	1	+	–	+	Δ′	+	R_1r O	$R''r$ A	[illegible]	3	"	Transfused. Recovered
9 ♂	12 ×39	+	Δ′	+	ΔΔ′		$R'r''$ O	rr O	R_2R_2 A	12	"	See Text
10 ♀	5	+	Δ′	+	++Δ		R_1r A	rr A	[illegible]	3	"	Transfused. Died prematurely
11 ♀	35	— See Over			ΔΔ′		R_1r A	rr A	R_1R_1 A	3	"	Transfused Recovered.
12	3	—					R_1r A	R_1r O	.		Physiological jaundice	Recovered
13 ♂	27	—			—	—	R_1R_1 O	R_1R_2 A	R_1r O	2		2 transfusions Died recovering
14 ♂	21	+	–		–		R_1r O	R_1r O	R_1r O	4		Transfused. Recovered.
15 ♂	8	—	–		—	—	R_2r A	R_1r O		1	non-obstructive jaundice	died.
16 ♂	cord	—	—		—	—	R_2r AB	R_2R_2 AB		2	Normal	
17 ♂	"	—			—		rr O	rr O		2	Stillborn	
18 ♂	"	—			—	—	rr O	R_2r O		1	Normal	
19 ♀	"	—			—	—	R_1R_2 O	R_1R_1 O		3	"	
20 ♀	"	—			—	—	R_2r O	R_1R_2 O	$R''r$ O	2	"	
21 ♀	"	—			—	—	R_1R_2 O	R_1R_1 A		2	"	
22 ♂	"	—			—	—	R_1R_2 O	R_1R_1 A		2	"	
23 ♀	"	—			—	—	rr A	R_1r A		2	"	
24 ♂	"	—			—	—	R_1r B	R_1r A		2	"	
25 ♂	"	—			—	—	R_2r AB	R_2r A		1	"	
26 ♀	"	—			—	—	R_2R_2 O	R_2r O	R_1R_2 O	1	"	
27 ♀	"	—			—	—	R_1r A	R_1R_2 O		1	"	
28 ♀	"	—			—	—	R_1r B	R_1r B		1	"	
29 ♂	"	—			—	—	R_2r A	R_1r O		1	"	
30 ♂	"	—			—	—	R_1r A	rr O		1	"	
31 ♀	"	—				—	R_1r A	R_1r A		1	"	
32 ♂	"	—			—	—	R_2r O	R_2r B	R_2r A	1	"	
33 ♂	"	—			—	—	R_1R_2 A	R_2r A	R_1R_1 A	1	"	
34 ♂	"	—			—	—	R_1r O	rr O	RR_1 O	1	"	

O. 38

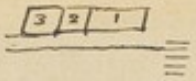
GALTON LABORATORY SERUM UNIT.
DEPARTMENT OF PATHOLOGY,
CAMBRIDGE.
EMERGENCY PUBLIC HEALTH LABORATORY SERVICE

Telephone:

O. 38

GALTON LABORATORY SERUM UNIT.
DEPARTMENT OF PATHOLOGY,
CAMBRIDGE.
EMERGENCY PUBLIC HEALTH LABORATORY SERVICE

Telephone:



(1)

The former letter + parcel arrives & is opened in Room 1 by JEM who pins blank card to the letter, & if necessary ~~makes~~ notes on the letter that the specimens are poor or broken. Preferably before ~~work starts~~ tests are begun (but not when delay would result thereby) RRR or AEM should read the letter & note any brilliant suggestions for tests, on the letter.

JEM does ABO groups in tube (serum check only when there is ~~deplenty~~ plenty of serum)

" Rh groups with absorbed ~~anti-~~ Δ (Δ, 85%)

" Mothers serum v panel

② If mother is Rh− she is put up with ΓΔ & ΔH (Lmt & Tgle) and ~~tested for~~ serum is tested for Δ'

When JEM has finished her tests she records the results on the card eg. " Mrs Coombs (12.8.45 RL Bk VII) O Rh− no aaf (no abnormal antibody found) no Δ' "

The husband also needs a date as his blood may not be received at the same time. Enter him on the next line but two below, so as to leave room for further tests on the mother. He only needs one line. If children are sent first, leave room for the husband. Children only need one line. Dont do serum checks where the serum is scarce. #Test husband & children with anti-A anti-B & Δ absorbed) XAB only

JEM must check the entries on the card as they wont be further checked, but reported directly from the card.

RRR or AEM do genotypes where necessary & Coombs test & record the results on the card preferably with book reference RRR's series of books are St. Bk 1 2 3 4 etc. AEM might use ~~Ho~~ Mo Bk 1 ~~Ho~~ Mo 1 etc. M 1 alone might lead to confusion with groups)

~~The card~~
~~Any preliminary~~

L.L. at a convenient time, as soon as possible in the morning, abstracts the history onto the card. LL pins ~~any~~ the carbon of any preliminary report or telegram to the bundle.

The bundles of ~~papers~~ letters & cards of all tests in progress to be kept, when not ~~in~~ being referred to in a special box in room 3 (kept separate from the other correspondence).

When the tests are completed, ~~& wh~~ if there is no special reply, they are put on LL's desk for her to write the reports. Which done LL pins the report & its carbon copy to the bundle for signing.

At some stage after the completion of the tests L.L. fixes the appropriate coloured tabs to the card, and files the letters, & puts the card in the index box, as soon as ~~possible~~ convenient.

Where a WR is asked for LL is responsible for getting some serum, having asked whoever has it if there is enough, putting it into a small labelled tube & filling in the E.P.H.L.S form.

If anyone does a slide test with anti-A & anti-B this is recorded in pencil on the card, which is inked in when the tube test is done.

Where are the specimens?

JEM takes off the serum of the mother (leaving a little on the clot if there is plenty). The serum tube is dated, & when JEM has finished with it, for the time being it is put in a special small box for sera not yet reported on, in the frig in Room 1. After reporting these are changed into a box of mother's sera waiting to go to the −20°. Father's or older children's sera usually needn't be separated unless there is a specimen from a baby which is treated like the mothers

When JEM has finished, for the time being with the clots & cell suspensions these are put in a specially marked largish block in the frig in room 3. where they stay until reported on, after which they are kept a little longer in a tin.

Control cells

The citrate suspensions, are to be kept in a special block in Room 3, JEM having her own saline suspensions. When DVK gets a fresh citrate suspension he ~~finds~~ discards the equivalent older one.

When any doctor or messenger comes with a specimen a card must be made before he goes, giving the patients name, the doctors name & such details as are ~~available~~ known.

Routine Coombs Test & genotype tests to be done as seldom as possible, & on as many as possible at a time. In order to stop the routine work ~~swamping~~ overwhelming RRR & AEM it may be necessary for them to have some rule such as routine ~~on Tues tests only to be done on Tuesd~~ tests not to be done on Mon, Wed, Friday & as ~~economically~~ quickly as possible on the other days.

There must be no hurry over any ~~investigation~~ piece of research work. (Perhaps for the moment all Coombs tests should be considered research) such work to have absolute priority over all routine work.

VCia

Preparing of bench in room 3. See that RRR & AEM each have ~~tubes~~ clean.

Box of tubes, box of lids, a clean beaker & porcelain dish, a clean water dish with water in it.

Rh Antigens and Antibodies in Man.

A "new" Rh antibody has recently been found[2] which has made possible the recognition of a third allelomorph at Fisher's C-c locus.[2] The antibody has been produced by a hypersensitive recipient of blood transfusions. A detailed account of this case is in the press[3]. The antibody is being called anti-C^W and the corresponding gene or antigen C^W. W stands for Wilke, the name of the donor whose blood stimulated the formation of the antibody. Any remaining doubt as to the appropriateness of recognising three loci seems to be removed by this finding.

The frequency of the three allelomorphs in England is: C 43 per cent., c 56 per cent. and C^W 1 per cent.. C^W can be combined with D or d and E or e in four ways, two of which have been observed — C^WDe and C^Wde. That is to say, two more Rh "allelomorphs" or more properly, combinations of genes have been added to the seven previously found. A further two C^WDE and C^WdE, may be assumed to exist, though both must be rare.

A result of finding the new antibody has been the recognition that about half the sera formerly classified as anti-C (anti-Rh') are in fact mixtures of anti-C and anti-C^W, the remainder being pure anti-C. (Both types may contain the "incomplete" or non-agglutinating form of anti-D). This finding provides the explanation of occasional-

discrepancies of behaviour between different anti-Rh' sera which have been noted during the last two years.

The possible combinations of C, c and C^w in a pair of chromosomes, the calculated frequency of these combinations in England and the reactions which they determine, are shown in Table I. All these combinations have been observed.

Table I.

	anti-Rh' sera				
	"anti-C"				
	50%	50%			
	anti-c	anti-C	anti-C + anti C^w	anti-C^w	frequency
C^wC^w	—	—	+	+	0·01 per cent.
C^wC	—	+	+	+	0·94 "
CC	—	+	+	—	18·40 "
C^wc	+	—	+	+	1·23 "
Cc	+	+	+	—	48·05 "
cc	+	—	—	—	31·36 "
					99·99

Although homozygous C^wC^w blood is very rare in the general population, one example has been found. One daughter of a mating $C^wDe/cde \times C^wDe/CDe$ was C^wDe/C^wDe. Another daughter of this mating was heterozygous C^wDe/CDe. The C^w homozygous blood gave a much stronger reaction on titration against the anti-C^w serum than does heterozygous blood;

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a dosage effect which is also noted with the agglutinin anti-c^4 and anti-e^5. The antigens C, D and E only show a slight dosage effect which is difficult to demonstrate.

The chart of the Rh antigen - antibody interactions, recently published in these columns,[6] can now be extended (Table II).

The 45 genotypes to which the nine known Rh "allelomorphs" give rise, can be divided into 24 serologically distinguishable groups. Considering the Rh groups together with the blood groups of the A_1A_2BO, MN, P and "Lutheran" systems (but ignoring the Levay group as it is extremely rare) there are 1,728 combinations which could be recognised serologically in individuals. These represent 18,225 possible genotype combinations.

R. R. Race
A. E. Mourant
Sheila Callender

Medical Research Council, Emergency Blood Transfusion Service; and Nuffield Department of Clinical Medicine, Oxford.

January 10th, 1946.

1. Callender, Race & Taylor, Brit. Med. J. 2, 83 (1945).
2. Race, Nature, 153, 771 (1944).
3. Callender and Race, Ann. Eugen. Lond., in the press.
4. Race, Taylor, Norman and Dodd, Nature, 152, 563 (1943).
5. Mourant, Nature, 155, 542 (1945).
6. Fisher and Race, Nature, (Jan 12 1946).
7. Race, Taylor, Cappell and McFarlane, Nature 153, 52 (1944).

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A patient called Moore suffering from lupus erythematosus has been given a series of transfusions over a period of about 18 months, and as a result has made, consecutively, three previously unknown agglutinins.

Patient's groups: $Rh_1 Rh_1$ Moore 1, 2 & 3 negative.

Donor's groups

	Date of Transfusion	Rh	Moore 1	Moore 2	Moore 3
1.	2nd Feb. 44	Rh_1 rh	-	-	-
2.	19th Aug. 44	rh rh			
3.	19th Aug. 44	rh rh			
4.	23rd Sept. 44	$Rh_1 Rh_1$	-	+	-
5.	29th Sept. 44	Rh_1 rh	-	-	-
6.	6th Oct. 44	$Rh_1 Rh_1$	-	+	-
7.	7th Nov. 44	$Rh_1 Rh_1$	-	-	+
8.	20th Nov. 44	$Rh_1 Rh_1$	-	-	-
9.					
10.					
11.					

In August 1944 the rare Rh agglutinin called St (y) was found in her serum. (The "incomplete" form of this antibody was also found, the first time this has been recognised).

Moore 1

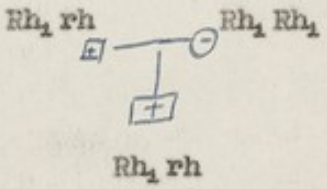
Together with St a new agglutinin unrelated to any previously described was present. This antibody disclosed itself by agglutinating the cells of certain people known to be St negative.(R1,R1) The following figures show the frequency of the Moore 1 antigen in unselected, unrelated people.

	Moore 1 +	Moore 1 -	Total
$Rh_1 Rh_1$	8	97	105
	·08	·92	
Rh_1 rh, $Rh_1 Rh_2$	10	67	77
	·13	·87	

If the Moore 1 antigen was due to a new form of the Rh_1 gene it would only be expected to be found half as frequently

in the Rh_1 rh + Rh_1 Rh_2 group as in the Rh_1 Rh_1 group. The observed figures are quite incompatible with such a state of affairs. (χ^2 = 16 for I.D.F.). This together with the following pedigree I seem to prove that the Moore I gene is not an allele of Rh_1 (or allele of Fisher's C).

Pedigree I



(Hoping such a family will turn up in time)

The Moore I groups are shown within the squares & circles.

The families so far collected are inadequate to show whether linkage exists between Moore I and Rh, and of course the chances are against such a linkage. The Moore 1 antibody is most active at 37°C, and is not anti-M, anti-N nor anti-P. The type of agglutination is often rather striking. The agglutinates are good big ones but more cells than usual are left unagglutinated. The Moore 1 antigen probably arises from a dominant gene. On the two occasions when both parents of a Moore 1 positive person have been tested one of them has also been positive. The count of sibs and children of Moore 1 positive propositi is Moore 1 positive 2, negative 3. It is hoped shortly to improve the family data.

Moore 2

The titre of the St antibody and also that of the special Moore 1 antibody fell, and at the time of the September and October transfusions they were weak. After transfusions 4 and 5 a further new antibody (Moore 2) appeared stimulated by donor 4 and presumably assisted by donor 6. The following are the frequencies of the corresponding Moore 2 antigen:-

Moore 2

	+	-	Total
$Rh_1 Rh_1$	9	101	110
	·082	·918	
$Rh_1 rh$ } $Rh_1 Rh_2$ }	2	91	93
	·02	·98	

The ratios are strikingly disproportional ($\chi^2 = 3{\cdot}6$ for I.D.F.). They suggest a connection between Moore 2 and Rh_1 which is strongly supported by the following pedigree. (Pedigree II). The grandmother is $Rh_1 Rh_2$ Moore 2 positive. Four children and one grandchild have unequivocally received her Rh_1 gene and all of these are Moore 2 positive, five children similarly have received her Rh_2 gene and all of these are Moore 2 negative. The probability of getting this distribution by chance is $\frac{1}{252}$. Consequently it is almost certain that Moore 2 antigen and Rh_1 are connected, probably not linked for so far Moore 2 has not been found without Rh_1, but as third allele at Fisher's C-c locus. Moore 2 antigen appear to be a dominant mendelian character. If has been found in two generations in six families and in three generations in the family shown. No Moore 2 positive person has been found to have both parents Moore 2 negative. The count of ~~parents~~ children and sibs of propositi is Moore 2 positive 10, negative 14.

Moore 3

After about six weeks this Moore 2 antibody faded from the patient's serum, but before it disappeared a further transfusion (No. 7) was given. Once again the blood was recognized as incompatible, the patient producing a third new antibody, Moore 3, rather a weak one. This antibody agglutinates the cells of the donor who stimulated it, but the corresponding antigen must be rare, as so far no other blood has been found that posesses it. Consequently Moore 3 is not of much genetic interest. The family of donor 7

There are two points of general interest in this history. First the patient must be extraordinarily sensitive to antigenic differences, and this is strong support for the hypothesis first suggested by that the symptoms of the disease lupus erythematosus are manifestations of some undetected antigen antibody reaction. Secondly, given such a hypersensitive recipient a glimpse is obtained of the multiplicity of red cell antigens likely to be found in the future. Three new antibodies have been made to 10 pints of blood although considerable care has been taken to use appropriate blood. Landsteiner was of the opinion that blood groups would some day be known to be as individual as finger prints.

An attempt to immunize 4 volunteers to the Moore 2 antigen has so far had no success.

Our thanks are due to Professor Cappell for continued interest and encouragement, and to Professor Wiits for

18/4/45

semifinal

Hypersensitivity to the transfusion of blood.

A patient who is believed to be suffering from the rare disease called lupus erythematosus diffusus required a series of transfusions on account of persistent anaemia. As a result of these transfusions a remarkable succession of antibodies has appeared in her serum. The patient's red cells are group O. M.P. $Rh_1 Rh_1$ and negative with the three "new" antibodies to be described. The patient has never been pregnant.

Transfusions.

	Date	Donor's Name	Donor's Groups			
			Rh	anti-Lutheran	anti-Willis	anti-Levay
1.	2nd Feb. 1944	Marshall	Rh_1 rh	-	-	-
2.	19th Aug. 1944	R.B.	rh rh	unknown		
3.	19th Aug. 1944	Lutheran	rh rh	+	-	-
4.	23rd Sep. 1944	Willis	$Rh_1 Rh_1$	-	+	-
5.	29th Sep. 1944	Mules	Rh_1 rh	-	-	-
6.	6th Oct. 1944	Howes	$Rh_1 Rh_1$	-	+	-
7.	7th Nov. 1944	Levay	$Rh_1 Rh_1$	-	-	+
8.	20th Nov. 1944	Allington	$Rh_1 Rh_1$	-	-	-
9.	31st Jan. 1945	Allington	$Rh_1 Rh_1$	-	-	-

Anti-Lutheran = the patient's serum taken at the end of August 1944
Anti-Willis = the patient's serum taken in October 1944
Anti-Levay = the patient's serum taken in November 1944.

A specimen of serum taken shortly after the Lutheran transfusion was found to contain the ~~Rh~~ Rh agglutinin called St. (Fisher), ~~it~~ the "incomplete" form of this antibody was also present. More interesting, however, was the finding of another separable agglutinin, called anti-Lutheran in the table. The red cells of 8-9% of the English population, irrespective of the ABO, MN, P or Rh groups, are agglutinated by this antibody. The Lutheran antigen is inherited as a dominant mendelian character. The statistical and family evidence will be presented in detail elsewhere.

Insert A

4-7-4

and probably also "a" dominant;
for so far it has been found only
in the blood of ~~the donor~~ Levay,
and in the blood of this donor's
father, but not in several
hundred random bloods
examined

(Ryr & RyR'')

--++ (RyR' & RyRy)

---+ ~~&~~R'R'

The St and anti-Lutheran antibodies gradually disappeared, their titre being low at the time of the September and October transfusions. After the Willis, Mules and Howes transfusions, a second "new" antibody, anti-Willis, appeared. The donor Howes's blood presumably assisted in this immunisation for Howes also has the Willis antigen. The Willis antigen is inherited as a dominant mendelian character independent of ABO, MN or P but not independent of Rh, and it is now practically certain that it is controlled by another allele at Fisher's C-c locus,[1] which may be called C^W. The Willis antigen is present in about 7% of Rh_1Rh_1 bloods, and the relative frequencies of the three alleles in the English population must be about C 43·5%, C^W 1·5% and c 55%. Again the evidence for this interpretation will be presented elsewhere. After some six weeks of existence anti-Willis faded from the patient's serum, but towards the end of this period Levay's blood was given. This blood also proved to be incompatible, for about 14 days later a weak agglutinin, anti-Levay, was evident. The Levay antigen seems to be a rare one, ~~it has been found only in Levay out of 100 people examined, and nothing is known about its inheritance.~~ All three "new" antibodies are more active at 37°C than at lower temperatures. INSERT A

Attempts to immunize one volunteer to the Lutheran antigen and two to the Willis have so far had no success. As the Lutheran and Willis antibodies may not be reproducible, and as the supply of anti-serum is limited, it is proposed to deposit the names and addresses of as many of the Lutheran and Willis positives, ~~who~~ as are willing to help, at the Bureau of Human Heredity, Gower Street, London, W.C.1. It is hoped with the help of Major Moloney of the U.S.Army Medical Corp to make some equivalent arrangement with people whose homes are near New York. If either of these antibodies do turn up again, as they are sure to do sooner or later, it may be possible to correlate the present work.

There are two points of general interest in this history. First the patient must be extraordinarily sensitive to antigenic differences, and this supports the hypothesis that the symptoms of the disease lupus erythematosus are manifestations of some undetected antigen-antibody reaction. Secondly, given such a hypersensitive recipient a glimpse is obtained of the multiplicity of red cell antigens ~~likely to~~ which may be found in the future. One familiar and three "new" antibodies have been made to the blood of eight donors although considerable care has been taken to use appropriate blood. Landsteiner was of the opinion that blood groups would some day be known to be as individual as finger prints.

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Sheila Callender MD. MRCP.
R.R. Race M.R.C.S L.R.C.P.
Z.V Paykoc. M.D. Istanbul.

Nuffield Department of Clinical Medicine, Oxford

and the Galton Laboratory Serum Unit, Medical Research Council.

REFERENCE

1 Race, R.R. (1944) Nature 153, 771.

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TABLE III

SUMMARY OF THE GENOTYPES FOUND IN 50 FAMILIES

TYPE OF MATING	NO: OF MATINGS	CHILDREN							
		R_1R_1	R_1R_2	R_1r	R_2r or R_2R_2	rr	$R'r$	R_0r	$R''r$
$R_1R_1 \times R_1R_2$	4	5	1		1*				
$R_1R_1 \times R_1r$	2			3					
$R_1R_1 \times rr$	9			13					
$R_1R_1 \times R_2r$ or R_2R_2	1			1					
$R_1R_2 \times R_1r$	4	2	1	1	2				
$R_1R_2 \times R_2r$ or R_2R_2	1		2						
$R_1R_2 \times rr$	6			7	8				
$R_1r \times R_1r$	3	3		5		1			
$R_1r \times R_2r$ or R_2R_2	3		2		1				
$R_1r \times rr$	3			4		2			
R_2r or R_2R_2 × R_2r or R_2R_2	3				2	2			
R_2r or $R_2R_2 \times rr$	5				5	2			
$R_1r \times R'r$	1			1		1	1		
$R_1R_2 \times R_0r$	1			1					
$R_0r \times rr$	1							1	
$R_1R'' \times rr$	1								1
R_2r or $R_2R_2 \times R_1R'$	1						2		
$rr \times rr$	1					1			

* EXCEPTION

TO BE PUBLISHED IN FULL IN THE ANNALS OF EUGENICS

A1

✓	Mowlam	N	$R_1 r$	L+	
✓	Wright	MN	rr		
	Tomlinson	?P	rr		
✓	Rolfe		$R_1 R_1$		
✓	Pleasance	MN	rr		
✓	Cole	MN	rr	L-	K-
	Emberley		$R_2 r$		
	Williams	MN	$R_1 R_2$		
	Wilson		$R_1 r$		
✓	Coombs	M P	rr		
✓	A Edwards		$R_1 R_1$		
✓	J.C. Bournell	N P	$R_1 R_2$	w-	K-
Mothers	P. Tate	MN P	rr		
	~~V.M. Wakefield~~	MN P	rr		
✓	Mrs Tunnicliffe		$R_1 r$		
	Sheila Trowell	M	$R_1 R_2$	w-	
	Stewart (student)	MN P	$R_2 R_2$		
✓	Benstead	N P	$R_1 r$	w-	
✓	Waller	MN ?	$R_1 r$	w-	

✓	Hopkins	MN	r	R_1R_2	W−	L−	K−	
	DVK	M	P	R_1R_1	W−	L−	K−	
	JEM	N	P	R_2r	W−	L−	K−	
✓	Vera	MN	P	R_1R_2	W−	L−	K−	
✓	Frank	N	r	R_1R_2	W+	L−	K−	
✓	Burrell	MN	r	R_1R_2	W−	L+	K−	
✓	H.P.H	MN	P	R_1R_1	W+	L+	K+	
✓	R.I.N.G.	M	P	rr	W−			
✓	Patman	MN	P	R_1R_1	W−	L−	K−	Deed +
✓	RAF	N	P	R_1r	W−	L−	K+	Deed −
Lowlands	Barlow	M	r	R_1R_1	W+	L−		
✓	Bowd	N	P	rr	W−	L−	K−	
✓	Robarts.		P	R_2r	W−	L−	K−	
✓	Whitmore		P	R_1R_2	W−	L+		
✓	Hunt	M	P	rr	W−		K−	
✓	Domingo	N		R_1R_1	W−			
	A.E.M.	MN	P	rr	W−	L−	K−	
	Monica	M	P	R_1R_2				
✓ addenb.	Dr Martin	MN	P	R_1R_1	W+	L−		
	H. Dewey	MN	r	R_1r	W−			
	G. Francis	MN	P	$R''r$			K−	
Molteno	T.E. Banks	M	P	R_1R_1	W−			
	~~W.P. Rogers~~	MN		R_1r	W−			Gone to Australia Dec'd
✓	J. Mann	M		R_1R_1	W−	L−		
	Zulveta			R_1r	W−	L−	K−	
	Dorothy Rawlinson			R_1R_2	W−	L−		
	Dennis Muncey	M		R_1R_2	W−			
Molteno	Mulligan			rr	W−			
✓	M. McFarlane	N	P	R_1r	W−	L−	K−	
Camb 4809	Richard Adrian (Student)	MN	r	$R'r$				
	Dr. Dixon	M	r	R_1R_1	W−		K+	
	Mr L. Lax 75 Kendal Way			$R'r$				

A_2

✓	Barrett	MN	P	rr
	George	N		$R_1 r$
✓	Cranfield			$R_1 R_2$
	Limbsell			$R_1 R_1$
	Christie Whitehead	MN		$R_1 R_2$ W–
	Fehrsen			R_2
✓	Edmunds	M		
✓	Matthews	MN	P	$R_1 r$ w–
✓	Dr. Fry	M	P	$R_2 r$ w–
✓	Miss Carey	MN	f	$R_2 r$ w–

B

Low lamp Miss	Smart	MN	$R_1 R_2$	
	F. Fairley	MN	++	
	K.S.	M	$R_2 r$	L–
	L.L.	MN	$R_2 r$	
✓ (Mollers)	B.H Laser		rr	
(Mollers x Obsts)	Simons		rr	

$A_1 B$

✓	Jacobson (Shagaway)	M	++	
	R.R.R.	MN	f	$R_1 R_1$
G.	Owen (Medical Downing)	MN	P	rr L–

$A_2 B$

	Watling	MN	rr	
(Kings)	Mr Powell			
	Miss Oxley (Spindle Cell)	N	$R_1 R_2$	

All mothers sent for whatever reason

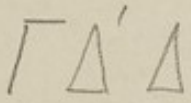
"sent as anti-Rh" excluded.

	Anti-Rh found	D' only found	Neither Rh nor D' found	
			Mother Rh+	Mother Rh neg
June 26. 1945 going backwards	~~Talbot~~ (separated 2D Crink Beasley Fogg Jarvis Thorstensen	Galley Blakeley Bennett Sutton trace D's	Bainbridge Ree Jarvis Lane Snelling Kelley Walters Batty Coles Owen Mckenna McBride Bacon Turner Byrne Murray Mennonites Harding More	Smith CT- Wilkin CT- Wheatley (CT+) Sharp CT- Lake Osbourne Lewis Henderson
Total 36	5	4	19	8
May 45	Bibby Eaton Titchener Ford	Knight Walker Brooks Spackman McDougall	Watson Potter Fairbairn Smith Barlow Nook Jackson Nichols Pedlar Hores Hobson Brady Lewis Harrison Boehan Henry Logan Mead Schiller Nicholson	Parry Marshall Pegg
	4	5	20	3

	Anti Rh found	A' only found	Neither Rh nor A'	
			Mother Rh+	Mother Rh−
April 45 & March–Sept 45	Jackson Loxton Bailey O'Brien, Grace Ratcliffe Collins, Grace Thomas, weak Tellis, weak Eyre	Levy ? (Woolwich) Mould Carolan Hammond	Jenkins, Allison, Lang Seaman, Hill, Dewey Sloan, Clark, Ling Clark, Blowers, Milward Forsyth, Hopkins, Rosen Mann, Lees, Horn Slark, Glover, Allcock Friend, Wood, Griffiths Pander, Mort, Arnell Reynolds, Anisori, Chalk Fox, Nicholson, Regler B'Radley, Motter, Radcliffe Pawcett, Graham, Thomas Hanson, Tomkins, Crouch Haynes, Norton, Lincoln Penn, Gately, Sanders Rooney, Cohen, Johnson Hughes, Allen, Lewis 54	Male Cleary Griffin Saunders Hearn Ashton Hughes Hawes Cobbold Fisher Lydon Davies Day Gregg 14
	(9)	(4)		
Totals for 3 months	18	13	93	25
			118	
			79%	21%

		obs	exp	o−e	$(o-e)^2$	$\frac{(o-e)^2}{e}$
EXP Rh− .15	118 — Rh−	25	17.7	7.3	53.3	3.0
	Rh+	93	100.3			0.5
						3.5

cells 2%
Serum



Δ'

Father

Mother	O	A	B	AB	NOT tested
O	CAROLAN ROBERTS TURNER (CHELMSFORD)	MALE			BOYD HAMMOND (IPSWICH) HAMPTON HARVEY MINGAY SHEPHERD (IPSWICH) SPACKMAN
A	FAIRHEAD McDOUGALL McKENNA OVERTON THOMPSON (GATESHEAD)	DUCKWORTH EMMERSON KENNEDY THORPE		KNIGHT	BENNETT (King's Lynn) BROOKS HAMMOND (Downham Mkt) MOULD PALMER WHITE
B	MOSS (SUNDERLAND)				SPALDING
AB	CADDICK.				

16 / 14
\ 2

$\chi^2 = 3.24$

exp .34

Rh negative mothers typ. O

Rh positive Mothers typ O

	Δ	Δ'	no aaf.		
MAR. 1945.				29·3·45	ANISORENIZ.
29.		CAROLAN		28·3·45	REYNOLDS
				27·3·45	NICHOLSON
26.			HAWES	21·3·45	BRADLEY
				17·3·45	GRAHAM
9			THOMAS	16·3·45	TOMLINSON
				"	HARRISON
6			GREGG	"	HAYNES
				14·3·45	GOOCH
2.	EYRE.			"	LINCOLN.
				12·3·45	MARTIN
				9·3·45	SAUNDERS
				7·3·45	COHEN
				6·3·45	BOLKING.
FEB. 1945.				26·2·45	LUXTON
28.			BIDDLE	"	ROSE
				16·2·45	GILBERT
16.	WILKINS.			"	SMITH
				12·2·45	SPROULE
14			LIGHTFOOT	11·2·45	PIZZEY
				9·2·45	BARWELL
14.			BEVAN	8·2·45	LUMSDEN
				"	BIRD
7.			CONWAY	5·2·45	GOOSE
				1·2·45	ACKLEY-SMITH
JAN. 1945					

Rh negative mothers

Gp O

	A	A'	no agf		Rh + mothers
AUG - 1945				29·8·45	JORDAN
30	WATSON			27·8·45	DOBSON
				21·8·45	BASSETT
				20·8·45	ORLEY
29		TURNER		20·8·45	ALLAN
				17·8·45	KELLECHER
22.	ROLLINS			13·8·45	COOK
				10·8·45	SPARK
10.	SINNOTT			10·8·45	CHILDS.
				10·8·45	TAYLOR
9.			FITZELL	7·8·45	ALLEN
				2·8·45	COX
				2·8·45	RINGROSE
				1·8·45	MILLS
JULY 1945				30·7·45	SIBBETT
31.	MARKS.			30·7·45	HOLLOWAY
				26·7·45	HODSON
23	DAVIS.			25·7·45	PALMER
				21·7·45	WILKINSON
9.			ABBOTT	"	COURTWRIGHT
				18·7·45	PINE
6.		ROBERTS.		"	NEWLY
				16·7·45	SEELEY
3.			HARRISON	10·7·45	COOK
				9·7·45	FOLLHER
2				4·7·45	CLARK
				"	MORROW
1				3·7·45	MANNING
				"	ARMSTRONG
JUNE 1945				28·6·45	DICKINSON
30		HAMPTON	McMILLAN	27·6·45	WOOD
				25·6·45	JAINBRIDGE
25			SMITH	22·6·45	WILKINS
				18·6·45	WATERS
19			SHARPE	"	BATTY
				11·6·45	McKENNA
19.			LAKE	9·6·45	HACON
				8·6·45	TURNER
8.			THOMAS	"	BYRNE
				6·6·45	MURRAY
7.			FOGG	"	MERINOWITCH
				4·6·45	HARDING
MAY 1945				28·5·45	FAIRBAIRN
15			SPACKMAN	18·5·45	BARLOW
				17·5·45	NICHOLLS
10.			THORSTENSEN	"	JACKSON
				15·5·45	HOWES
5	TITCHENER			8·5·45	LEWIS
				5·5·45	HARRISON
				3·5·45	LOGAN
				"	HENRY
APR. 1945				30·4·45	LENG
26.			MALE	"	ALLISON
				24·4·45	DEWEY
18.			JACKSON	21·4·45	SLOAN
				18·4·45	PAGE
14			CLEARY	17·4·45	BLOWERS
				14·4·45	ROSSER
11.		LEVY.		"	HOPKINS
				"	FORSYTH
7			HEARNE	11·4·45	STARK
				"	LEWIS
				9·4·45	WOOD
				"	CHITTOCK
				3·4·45	ARNELL
	6	4	15		65

ATTEMPTED SEPARATION OF ANTI-C AND ANTI-C^W

Either :
Each molecule of the appropriate globulin fraction carries only one antibody group; in this case complete absorption of one antibody should be possible without the other antibody being affected.

or:
Each molecule of globulin carries more than one antibody group (or some molecules carry more than one such group); in this case absorption of one antibody will remove part at least of the other antibody. It is probable that the antibody groups will be allocated at random to the globulin molecules. On this assumption, by determining antibody titres in a serum of the 'Andrews' type for varying degrees of absorption by the two antigens it should be possible to form an estimate of the number of groups on each globulin molecule. For instance, if each molecule carries two groups, then one quarter of the molecules will be pure for each antibody and one half will be mixed, half the total groups of any one antibody being carried on the pure molecules. Thus complete absorption of one antibody will halve the titre of the other.

If the molecules are complex with respect to anti-C and anti-C^W, it is almost certain that they are also complex for anti-C and anti-D (or incomplete anti-D). Thus in absorption experiments carried out to investigate the forms of anti-C it is desirable to eliminate as far as possible any effects due to anti-D. It will probably be best to use cells not containing D, i.e., Cde/cde and C^Wde/cde. There is a particular danger in the case of Andrews that use of cells containing D will absorb incomplete anti-D and unmask a trace of anti-D agglutinin which might tend to be interpreted as one of the forms of anti-C.

Since it has been shown that Andrews serum is difficult to split, the hypothesis of globulin molecules bearing several antibody groups must be considered. If it can be shown that a synthetic mixture of anti-C and anti-C^W is easily and more or less completely split, then the hypothesis is the only one yet proposed which will explain the phenomena, and it ought to be tested with other natural mixtures of Rh antibodies. It should also be tested for other natural mixtures of agglutinins. The ready separation of alpha and beta from the Rh agglutinins and their different behaviour in the anti-globulin test suggest that these occur on different globulin fractions. Fractional separation as above proposed, on the one hand, and the use of highly specific anti-globulin sera on the other may make it possible to analyse the antibody globulins very fully. The physical methods of globulin analysis might also assist.

The following frequencies are an approximate maximum likelihood solution of the data above.

Rh_1	CDe	43·61
rh	cde	37·90
Rh_2	cDE	12·80
Rh_0	cDe	3·05
Rh"	cdE	1·70
Rh'	Cde	·81
Rh_z	CDE	·13
(Rhy)	CdE	probably no more than ·005.

A1

				AR	ST	KJ	And
BCG	A1	MN		-	+	-	-
EWI	A1	N		+	+	-	+
GLT	A1	M		+	+	-	+
Mowlam	A1	N		+	+	-	+
Wright	A1	MN		-	+	-	-
Tomlinson	A1		P (Jam)	-	+	-	
Rolfe	A1			+	-	-	+
Pleasance	A1	MN		-	+	-	
Brackley	A1			+	-	-	
Riley	A1			+	+	-	
Risbeth	A1			-	+	-	-
IMY	A1	MN		+	+	+	+
Bond	A1			-	+	-	
Sivell	A1			+	+	-	
Cole	A1			-	+	-	-
Mcfarlane	A1			+	-	-	+
Maj Wilson	A1			+	-	-	
McCallum	A1			-	+	-	
RT Ross	A1			-	+	-	
Miles	A1			+	-	-	+
Dr Venn	A1	N		-	+	-	
Dunne	A1			+	+	-	
Judy	A1			+	+	-	+
Emberley	A1			+	+	+	-
William	A1	MN		+	+	+	+
Risbeth				-	+	-	-
Dr Wilson				+	+	-	+
(Jam) Mrs Trowell	A1			+	+	+	+
Mrs Tunnicliffe	A1			+	+	-	+
Dr Boomby	A1	MP		-	+	-	-
Mrs Edwards	A1			+	-	-	+

BLOOD GROUP FREQUENCIES - GALTON LABORATORY FIGURES.

Blood Group	Men	Women	Total	
			Frequency	Percentage
O	1828	818	2646	43·26
A	1887	811	2698	44·11
B	377	183	560	9·16
AB	143	69	212	3·47
Total	4235	1881	6116	100·00

PERCENTAGE GENE FREQUENCY

O .65·86

A 27·61

B 6·53

					Antigena Rh	st	R_2	R_1
Col. Whitmore	O	.	P		+	+	+	+
Mrs Hunt	O	M	P		−	+	−	−
Mrs Williamson	O				−	+	−	−
Dr Martin	O	MN	P		+	−	−	+
Burdon	O				+	−	−	+
Domingo					+	−	−	+
EPH. Miss Cohen					+	−	−	+
MOF Mrs Hawes					+	−	−	+
A.E. Mourant	O	MN	P		−	+	−	−

A_2

AMB.	A_2 MN	P		−	+	−	−
George	A_2 N			+	+	−	+
MEA.	A_2 M	P		+	−	−	+
Miss B.L. Smith	A_2			−	+	−	
Mrs H. Fish	A_2			−	+	−	−
Mrs G.L. King	A_2			+	−	−	+
Mrs D. Lawrence	A_2			+	−	−	
Miss Cranfield	A_2			+	+	+	+
Dr Lindsell				+	−	−	+

B

				Antisera Rh	St	R_2	R_1
Miss Smart	B	MN		+	+	+	+
FF	B	MN		+	+		
K.S.	B	M		+	+	+	−
(rec) Mrs Gilbert	B			+			
Mrs Jenkins	B			+	+	−	+
Miss Margaret Wright	B	M	P	+	+	+	−
Miss Landau		MN		+	+	+	−

A_1B

Jacobson	A_1B	M		+	+		
R_3	A_1B	MN	P	+	−	−	+

A_2B

Watling	A_2B	MN		−	+	−	−
Mrs Powell	A_2B						
Miss Oxley	A_2B		N	+	+	+	+

				Δ RL	St	H KJ	Γ And	? Bruce
Beryl	O	M	P	+	+	−	+	
Arthur	O	MN	P	−	+	−	−	
Hopkins	O	MN	P	+	+	+	+	
DVK	O	M	P	+	−	−	+	
JEM	O	N	P	+	+	+	−	+
Vera	O	MN	P	+	+	+	+	
Frank	O	N	P	+	+	+	+	
Ernest	O	N	P	+	+	+	−	
AMP	O	MN	P	+	+	+	−	?+
Burrell	O	MN	P	+	+	+	+	
ARD	O	MN	P	+				
HPH	O	MN	P	+	−	−	+	
RING	O	M	P	−	+	−	−	
Palman	O	MN	P	+	−	−	+	
RAF	O	N	P	+	+	−	+	
Hubert	O	M		+	+	−	+	
Elliott	O		P	+	+	−	+	
Haines	O			+	+	−		
Barlow	O	M	P	+	−	−	+	
Fall	O			+	−	−	+	
Bowd	O	N	P	−	+	−	−	
Case	O			+	−	−		
Roberts	O		P	+	+	+	−	+
Pollock	O		P	+	+	−		
Tooke	O	MN	P	+	+	+	−	
Mrs Taylor	O	MN	P	+	+	−	+	
Mary Taylor	O	M	P	+	+	−	+	
Monica Race	O	M	P	+	+	+	+	
C. F. Nunn	O			+	−	−	+	
Dr Gosney	O	MN	P	+	+	+	−	
Mrs Leonard	O	N		−	+	−	−	
Dr Ferraira	O	MN		+	+	−	+	
Mrs Rowlatt	O	N	P	+	+	−	+	

R. R. Race.

Born 1907.

Educated at St. Paul's School and St. Bartholomew's Hospital.

1933 M.R.C.S., L.R.C.P.

1935 & 1936 Assistant Pathologist, Hospital for Consumption and Diseases of the Chest, Brompton.

1937-1939 Assistant Serologist, Galton Laboratory, University College, London.

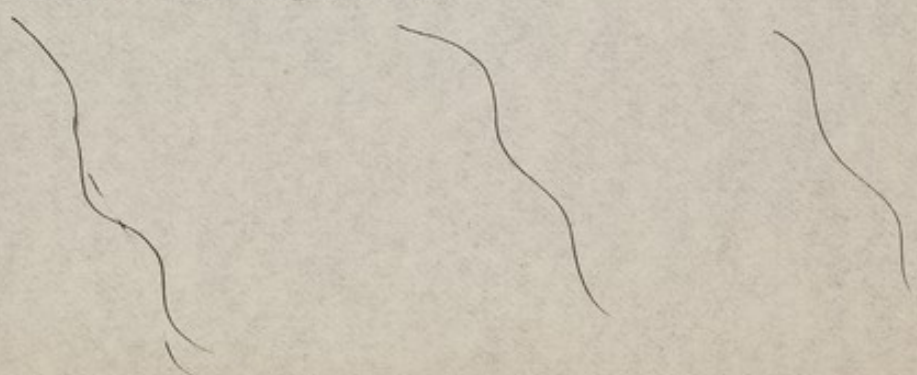
1939-1945 Assistant Director, Galton Laboratory Serum Unit, (Medical Research Council), at the Department of Pathology, University of Cambridge.

SUMMARY OF THE PAPER ON THE SUBGROUPS OF Rh BY R.R.RACE,
MEDICAL RESEARCH COUNCIL BLOOD GROUP RESEARCH UNIT,
LISTER INSTITUTE OF PREVENTIVE MEDICINE, LONDON.

Brief mention is made of the brilliant discovery of the Rh groups by Dr. Levine, the late Dr. Landsteiner and Dr. Wiener, but this paper is mainly concerned with the British work on the subgroups of Rh.

That subgroups of Rh existed was shewn by Landsteiner and Wiener when, as early as 1941, they found a human anti-Rh serum which only agglutinated 70% of European bloods, unlike the earlier anti-Rh sera which agglutinated 85%. The discovery by Levine of a serum called anti-Hr which agglutinated all Rh negative bloods as well as some Rh positives suggested that there were further complications.

In attempting to give an account of the present state of the Rh subgroups I find a historical method the most convenient. British research in this subject began in 1943 when a serum (called St.) from an Rh positive mother of children with haemolytic disease, was found to agglutinate 80% of bloods including all Rh negatives, all heterozygotes (Rr), and some others. Table I shews the distinctions made by the combined use of the original 85% serum and the 80% or St. serum. ~~On the right is our interpretation.~~



A few weeks after work on the St. serum had begun, two further examples of unusual Rh antisera were sent to us. They were both from Rh positive mothers of children with haemolytic disease, and they gave identical reactions, but quite different from those given by the St. serum. These two sera, which were together called K.J., agglutinate about 30% of European bloods. Table II summarizes the advance they made.

It was realised that the 70% serum already described by Landsteiner and Wiener would agglutinate the blood containing what we were calling R_1. Eventually such a serum was found and made the expected major distinctions as well as two unexpected minor ones. Table 3 shews this further step.

SUMMARY

From the reactions of blood, which represents two genes, it was possible to work out what the theoretical reactions of the single genes would be, these are shewn in Table 4. At about the same time Wiener published the result of his work, also shewn in Table 4. It will be seen that as far as Wiener's results went, they were in complete

agreement with ours. We postulated 7 allelomorphs at one locus, and Wiener postulated 6 allelomorphs at one locus.

Professor R.A. Fisher, examining our table, noticed that the 70% serum and the 80% gave antithetical reactions, and he supposed that the antigens recognised by these two sera must depend on allelomorphic genes and these he called C and c. The reactions of the remaining two antisera, the 85% and the 30% were not antithetical, so the antigens they recognised were given separate, but closely linked loci, D and E. Presumably both D and E had alleles, for blood is frequently not agglutinated by anti-D, that is to say it hasn't D, so it must have something which dould

not be recognised and this antigen was called d. Similarly E was given a hypothetical allele e. Fisher supposed that these two hypothetical genes or antigens d and e were each capable of stimulating their own antibodies, like the other genes. If this was the genetic situation, then an Rh chromosome could be assembled in eight different ways - CDe, cDE, etc. (as shewn in Table 5). Seven of these assemblages could be identified in the seven - as we had supposed - allelomorphic genes. The eighth combination CdE has yet to be found. The reactions outside the enclosure are those predicted by Fisher. As they become verified serologically their brackets are removed. In brief the two unknown reactions of Rhz have been found to be as predicted, and Dr. Mourant has found the anti-e serum of prophesy and it has all the reactions it was expected to have, except with Rhy which ~~hasn't yet turned up~~ has not yet been found.

Fisher has made the very ingenious suggestion that crossing-over between these genes may be responsible for some of the rarer combinations in a population, and he has also been able to deduce that the probable

order of genes on the chromosome is DCE.

In 1945 Dr. Callender and I isolated a third allelomorph at the Cc locus, which we called C^W; and early in this year Dr. Stratton of Manchester has isolated a third allele at the Dd locus, which is called D^u. Stratton is of the opinion that D^u is responsible for Wiener's "intermediate"genes. # The recognition by Fisher of the allelomorphisms was absolutely fundamental to our understanding of the subgroups of Rh.

4

4

1939 Levine & Stetson's case

1940 Rabbit e guinea pig anti-Rhesus serum discovered by Landsteiner & Wiener
Coniglio e porcellino — scoperto di

85% European bloods agglutinated
15% " " not agglutinated
non

The antibody of Levine & Stetson found to be the same as the anti-rhesus antibody.
di — trovato — reconosciuto (essere) lo stesso alla
scoperto nello sero

1941 Wiener & Peters found anti Rh in the serum
of transfused human beings
di genere umano transfuso

1941 Levine Katzin & Burnham
Role discovered the role of Rh in haemolytic diseases of the newborn
scoperto la parte di Rh nel — di nuovo nato

A brilliant episode in medical science. Un episodio brillante nella scienza medica.

Pollys translations into Italian

Fisher noticed ~~that there were~~ 3 orders of frequency of

the Rh chromosomes: R_1 R_2 and r above 12%

R_0 R' R'' $2R_2$ 0.2 – 2% and R_y so rare that it

has not yet been isolated. He pointed out

that Cross-overs of the heterozygotes ~~of the frequent group~~,

that is $R_1 r$ $R_1 R_2$ & $R_2 r$ would produce all

4 second order chromosomes, but not R_y

the third order chromosome which would require

a double cross-over.

From the ratio of the frequency of the cross-over chromosomes

to their parent heterozygotes it seems that the most probable

order of the genes on the chromosome is

D C E

(12)

Anti – C^w

Un paziente
A patient ~~R_1R_1~~ CDe/CDe (R_1R_1) era dato sangue
was given blood
pensato essere dello stesso
thought to be of the same genotype ma un
but an antibody
era sviluppato che era riconosciuto all' fine
was developed which was ultimately recognised
asso essendo un Terzo alla
as anti-C^w. , C^w being a third allelomorph at
qualche cosa raro.
the C-c locus, rather a rare one.

Il donatore è riconosciuto ~~ad~~ essere adesso
The donor is now known to be C^wDe/CDe.

I diagramma Seguendo impreandono mostrare come era
The following slides attempt to shew how it was
riconosciuto che questo nuovo era un parte del
recognised that this new antibody was part of
sistema R. e concernito con
the Rh system and ~~directed~~ concerned with
il
the C-c locus.

SVILUPPATO

(10)

Era effettuato ch'il già scoperto
It was realized that the 70% ~~serum~~ serum already found
da
by Landsteiner and Wiener ~~must be used agglutinating~~ would agglutinate
sanguine chi hanno Un ricerca era fatto e eventuale
bloods containing R_1. A search was made and eventually
un esempio di questo sero era trovato. Il da tutti i
an example of this serum was found. It gave all the
reazioni che ~~erp~~ aspettavamo.
reactions expected d'ot
Un sanguine occasionale pensato essere R...
An occasional blood thought to be R_1r ($^{85}_{+}$ $^{80}_{+}$ $^{30}_{-}$) altro
non era agg... da questo sero allora un gene raro
failed to be agglutinated by this 70% serum – so a further rare
adesso chiamato deveva essere postulato
gene, now called R_0, had to be postulated
Anche un sanguine occasionale pensato essere
Also an occasional blood thought to be rr ($^{85}_{-}$ $^{80}_{+}$ $^{30}_{-}$)
eva agg... Ancora un gene nuovo e raro adesso chiamato
was agglutinated. Again a new gene, now called R', had
rare
to be postulated to explain this reaction.
deveva ~~p~~ essere postulato per spiegare questa reazione.

a cominciato a essere complicato Tosto (asso) 1941.

The Rh groups were beginning to be complicated as early as 1941.

5 Landsteiner & Wiener found a human anti-Rh serum which agglutinated the blood of 70% instead of 85% of Europeans.

. Levine, Rad found an a serum called anti Hr which agglutinated all Rh negative bloods and an ill defined group of Rh positive bloods

scoprirò un anti-RH Sero umano che ag.- la sanguine di 70% in luogo di 85% di Eu.

e scoprirò un sero chiamato anti-H che agg- Tutto negativo e un numero indefenito di RH+ sanguine

6 In 1943 we ~~investigated~~ examined a serum (called St.) which agglutinated 80% of English bloods, including all the Rh negatives and all the heterozygotes Rr

Nel

In 1943 abbiamo investigato un sero che agg- 80% di sanguine inglese, compreso Tutti i RH negativi e Tutti i het. Rr.

La distinzione originale fra RH+ e RH- è ancora il più importante della vista clinica.

Sì la RH grouping SEMPLICE SIMPLE è fatto circa 95% della transfusione i pericoli di RH ~~sera~~ sono evitato.

Ma i subgroups a contributato moltissimo ~~molto~~ alla interessa di RH della vista di genetics ~~humanità~~ humano.

L'analisi ~~anatomica~~ adesso possibile di RH è da vero il più fino si può fare ~~sopra~~ sul SUL gene humanità.

The original distinction between Rh+ & Rh− is still for the most important ~~clinically~~ from the clinical point of view.

1 If the simple Rh grouping is performed ± about 95% of the transfusion dangers ~~due to~~ of Rh will be avoided.

But the subgroups have added enormously to the interest of Rh from the ~~go~~ point of view of human genetics.

2 The analysis now possible of Rh is by far the most subtle that can be brought to bear on human genes.

~~Early recognition of heterozygotes.~~

(7)

Tutti negativi sangue deve essere
All St. negative bloods must be homozygous RR.

ma il di sangue che era negativo
but the 20% of bloods negative which were St negative

solo spiega circa metà i RR non- calcolato.
only accounted for about half the calculated

RR homozygotes. Perciò esse devono due sorte di R.
There must therefore be two

Kinds of R ; i.e. R_1 and R_2. Il negativo
varietà chiamano
The St negative Kind we ~~called~~ R_1 and St negative
Sangue preso prendiamo era dell
blood we ~~presumed~~ supposed was of the genotype

$R_1 R_1$.

9

Qualche conferma che la sanguine reagendo antisera
Some confirmation that blood reacting 85% 80% 30%
+ + —
era propria
was really R_1r

può essere riconosciuto senza usando il 30% siero 85% 80%
R_1R_1 could be recognised without using the 30% serum + —
rr " " " " — +

Molti bambini delle nozze chi devono
Many offspring from matings $R_1R_1 \times rr$ who must
essere tutti Rr erano provato i tutti reagivano
all be R_1r were tested. They all reacted

85 80 30
+ + —

Anche la frequenza aspettato di R_1 nella populazione generale, della RR
Also the expected frequency of R_1r in the general population, calculated
calculato era sempre vicinissimo
from the R_1R_1 and rr groups, was always extremely close
alla frequenza observato di sanguine reagendo 85 80 30
to the observed frequency of bloods reacting + + —

13

Il genealogia seguendo mostra il nuovo adesso chiamato o

The following pedigree shews the new antigen (now called C^w)

~~(illegible)~~ following the grandmothers ~~gene~~ chromosome

in quello tempo pensato essere $CDe\ (R_1)$ ma adesso conosciuto essere

then thought to be ~~R_1 = (CDe)~~ but now known to be

C^wDe.

Il The segregation era specialmente fortunato in questa famiglia was particularly fortunate in this family.

La probabilità della coincidenza osservata

The probability of ~~obtaining~~ the observed coincidence

essendo ~~attrib~~ being due to chance is only 1 in 252.

la resultà di fortuna è soltanto ~~uno~~ nel

3

scoprito da in 1939 era chiamata
The antibody discovered by Levine & Sletson was later to be
più tardi
called anti-Rh.

Consolidarono la frequenza del
They established the frequency of the Rh antigen
Mostrarono che era ereditò che può essere causa di
They shewed that it was inherited; that it could cause
de d'una madre e
transplacental immunisation of a mother and
that it could be responsible for severe transfusion
reaction.

che può essere causa di Trasfusione severo
reazione.

(8)

Il prossimo siero di scoprire agg- solo 30%

The next serum to be found agglutinated only 30%

di sangue e dato questa reazione

of bloods and gave the following reactions :-

Tutti quasi

nearly all ~~R₂~~ + * a new gene had to be postulated to explain the occasional + (R″)

nearly all R_1R_1 − " " + (R_2)

Ass questo non a reagito con o il

As this 30% antibody did not react with R_1 nor it

deve essere reagendo con e la frequenza delle sangue agg-

must be reacting with R_2, and the frequency of bloods agglutinated

~~[illegible]~~ concorda bene colla frequenza calcolato

~~[illegible]~~ agreed well with the calculated frequency

of people posessing R_2.

delle gente che hanno R_2.

* un gene nuovo a dovuto essere postulato per esplicare il + occasionale.

LONDO

PROFESSOR R. A. FISHER

Advocates bonuses for babies.

Dressing for old leather.

7 oz anhydrous lanolin
½ oz beeswax
1 oz cedar wood oil
11 oz hexane.

Melt lanolin and beeswax with gentle heat; add cedar wood oil. Before mixture sets add hexane, stirring continually.

Hexane is highly inflammable, and the mixing must be done away from any flame.

Application.

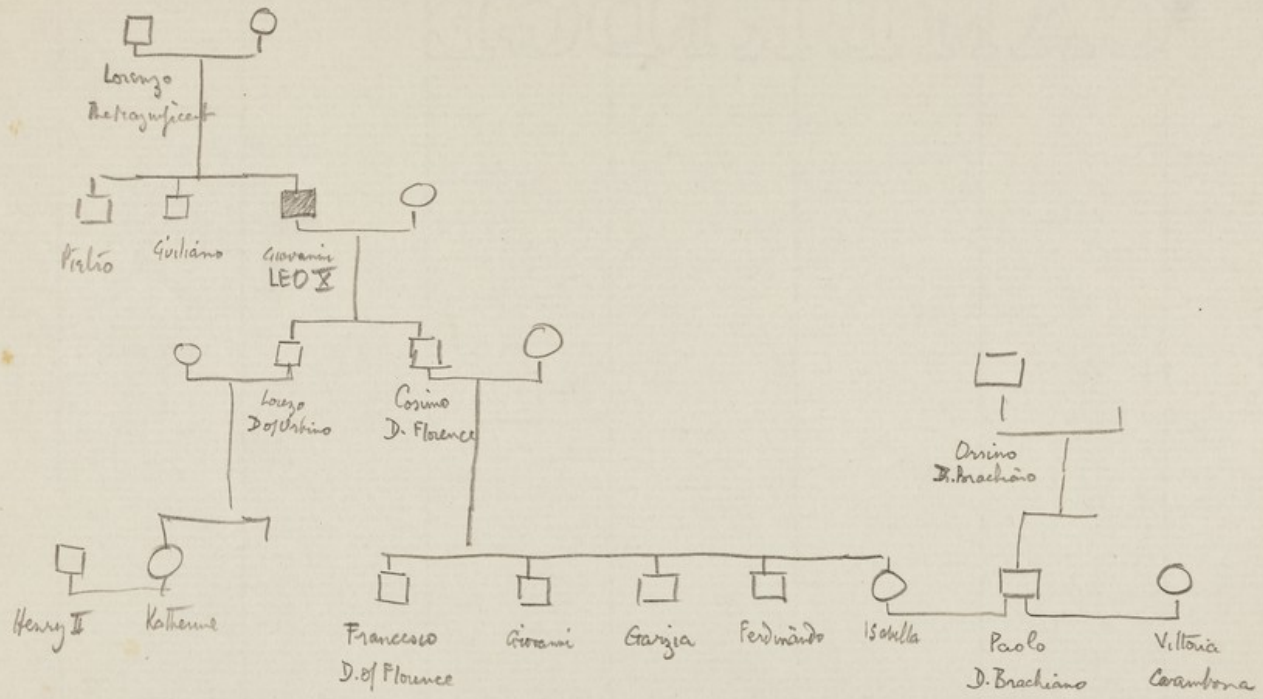
Book leather should be washed with good soap and water, to remove dirt. When book ~~xxxx~~ is dry, apply preservative with a soft brush or muslin rag. About two days after the leather can be polished with a soft cloth.

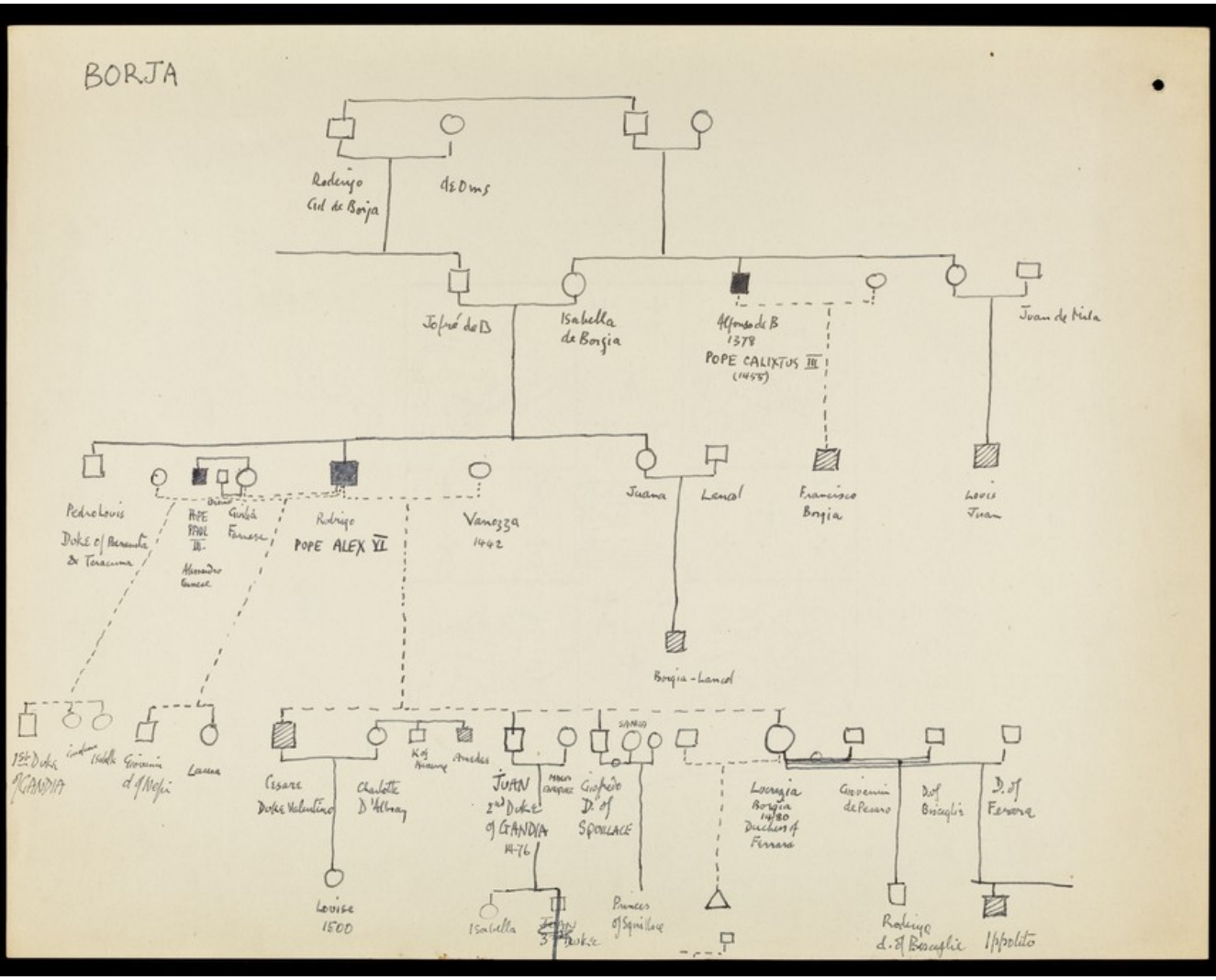
1942 From Mr Mitchell
Dept of Pathology, Cambridge

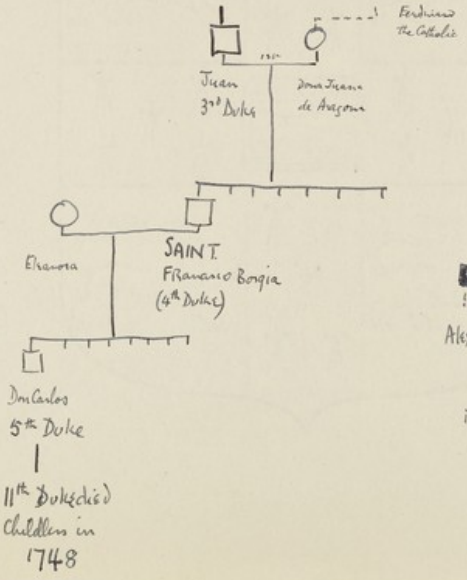
Prof Dean, it presumably was who arranged for Mr Mitchell to be made an honorary MA when he retired at about 65-70 to everyones great satisfaction.

12.

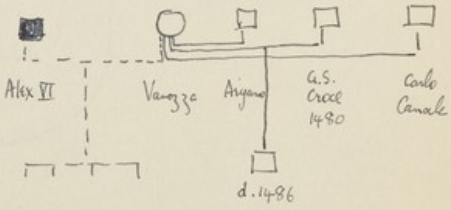
MEDICI

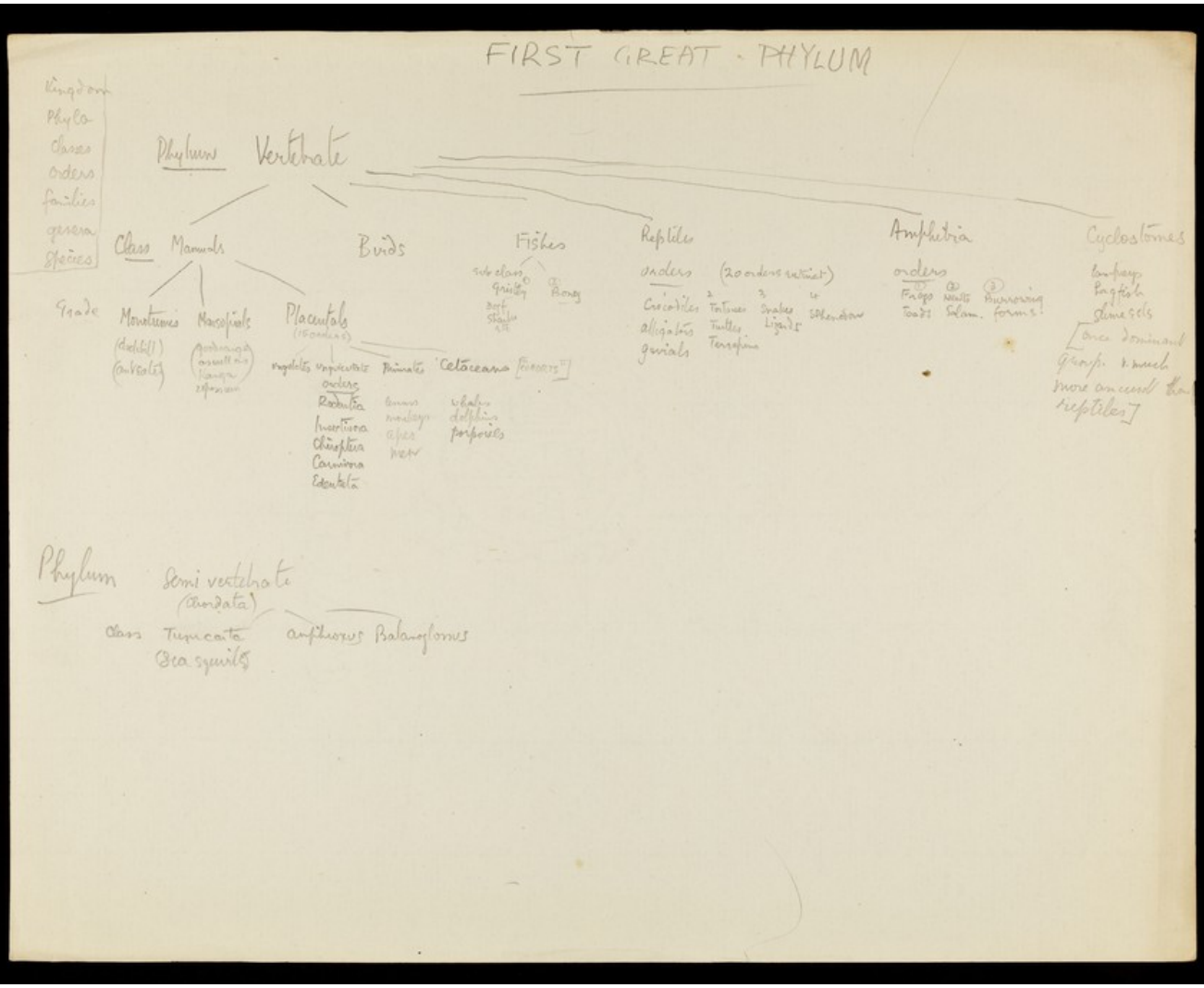

Lorenzo
Il Magnifico
Piero
Giuliano
Giovanni
LEO X
Lorenzo
D. of Urbino
Cosimo
D. Florence
Orsino
D. Bracciano
Henry II
Katherine
Francesco
D. of Florence
Giovanni
Grazia
Ferdinando
Isabella
Paolo
D. Bracciano
Vittoria
Corombona


BORJA
Rodrigo
Cid de Borja
4 Dms
Jofré de B
Isabella
de Borgia
Alfonso de B
1378
POPE CALIXTUS III
(1455)
Juan de Vila
Pedro Luis
Duke of Bernalda
& Teracuna
Rodrigo
POPE ALEX VI
Vanozza
1442
Juana
Lenal
Francisco
Borgia
Loves
Juan
Borgia-Lanol
Cesare
Duke Valentino
Charlotte
D'Albret
JUAN
2nd Duke
of GANDIA
1476
Giofredo
D. of
Squillace
Louise
1500
Princes
of Squillace
Lucrezia
Borgia
1480
Duchess of
Ferrara
Giovanni
de Pesaro
D. of
Bisaglia
D. of
Ferrara
Isabella
Rodrigo
d. of Bisaglia
Ippolito



YANOZZAS HUSBANDS




FIRST GREAT - PHYLUM
Kingdom
Phylo-
Class
orders
families
genera
species
Phylum Vertebrate
Class Mamals
Birds
Fishes
Reptiles
Amphibia
Cyclostomes
Grade
Monotremes
Marsupials
Placentals
orders
Rodentia
Insectivora
Chiroptera
Carnivora
Edentata
Primates
Cetaceans
orders
Crocodiles
alligators
gavials
Tortoises
Turtles
Terrapins
Lizards
Snakes
Amphisbaenians
Fishes
Frogs
Toads
Salam.
Burrowing forms!
Lampreys
Hagfish
Lancelets
Phylum
Semi vertebrate
(Enteropneusta)
Class
Tunicata
Sea squirts
Amphioxus
Balanoglossus

2nd Great phylum

Arthropods

Phylum

Class

Crustacea

lobster
crayfish
prawns
shrimps
crabs
woodlice
Freshwater shrimp

Arachnida

spiders
scorpions
mites & ticks
King crab
Sea scorpions (extinct)
[three dominant groups
before earliest vertebrates]

Insects

(6 sm walking legs)
numerous adult
all of them species

Myriapoda

centipedes
millipedes

Onychophora

genus
Peripatus

the same as the one Miyake identified with $FeCr_2O_4$.

In interpreting the experimental results summarized above, it is natural to consider the oxide formed at lower temperatures as the naturally occurring film, which in the case of stainless steels has now been shown to be α-$(Fe,Cr)_2O_3$.

I wish to express my thanks to Dr. Iitaka for his guidance and encouragement.

TADASI TOKUMITU.

Institute of Physical and Chemical Research,
Tokyo.
Feb. 5.

[1] Miyake, S., *Sci. Pap. Inst. Phys. Chem. Res. Tokyo*, **31**, 161 (1937).
[2] Thomson, G. P., Unpublished observation cited by Thomson and Cochrane in "Theory and Practice of Electron Diffraction", 179 (London: Macmillan, 1939).

Scandinavian Influence in Scottish Ethnology

A FEW months ago[1] we appealed to centres of the emergency blood transfusion service, and in particular to those which we were supplying with testing serum, to allow us to assemble the extensive data on blood group frequencies in Great Britain, then for the first time becoming available. We were confident that such a collection would throw light on the precision with which such extensive groupings can be relied on to determine the gene-ratios in our population, and we hoped further that this precision might be sufficient to detect with certainty any such small variations of ethnographic significance as might exist within our island.

In a preliminary survey, exhibited at the meeting (January 12, 1940) of the Pathological Society at Cambridge, it was shown that a consistent gradient in the frequency of the antigen A is found as we pass from southern England to Scotland. Further data since accumulated bring our totals to 10,969 for Scotland and 8,716 for northern England, which show clearly intermediate frequencies. For southern England our compilation amounts to 106,477.

The values we present are not entirely unselected. A few returns have had to be set aside as apparently anomalous, and only in some cases has the cause of disturbance been ascertained. Systematic errors, not all of which are yet understood, do undoubtedly affect the frequency of the rarest of the four blood-groups (AB). As a further precaution, we have calculated the gene-ratios from the other three groups only, as in this way the effect of grouping errors is diminished.

The contrast between our three main areas, Scotland, England north of the Humber, and southern England, may be shown either in the relative frequencies of the four distinguishable phenotypes, or in those of the three allelomorphic genes:

TABLE 1
PHENOTYPIC FREQUENCIES

	O	A	B	AB
Scotland	52·019	34·233	10·429	3·318
N. England ..	48·600	40·340	8·536	2·524
S. England ..	45·232	43·162	8·508	3·097

The change in the ratio $A : O$ is not, apparently, influenced by the traditional and political Border, but is apparently continuous, and doubtless a cause of heterogeneity, too slight to be detected on the numbers yet available, within the three chosen regions. The corresponding gene-frequencies are as follows:

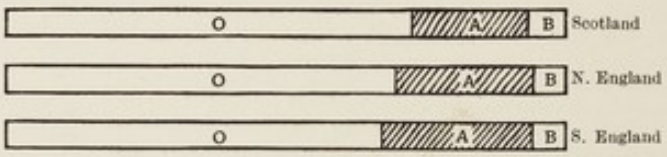
TABLE 2
GENE FREQUENCIES

	O	A	B
Scotland ..	72·247	20·783	6·970
N. England ..	69·587	24·549	5·864
S. England ..	67·207	26·744	6·048

as shown in the diagram below.

It has been customary for ethnologists to suppose that the northern inhabitants of Britain differ from their southern neighbours by reason of a greater infiltration of Scandinavian blood. The modern Scandinavians, however, differ from the English in having not a lower but a higher frequency of A. Thus if, setting aside the small fraction of these populations carrying the gene B, we compare the phenotypic ratios $A/(A + O)$, we find, using the best available series, Norway 58·0, Sweden 58·6, Denmark 50·0, against S. England 48·8, N. England 45·4, Scotland 39·7.

English contact with neighbouring Europe has been extensive since the Roman period; the values for Holland 48·6, Belgium 46·6, France 50·1, and Spain 53·4 are fully in accordance with the view that the English province has been influenced by settlement or intermixture with neighbouring Continental peoples. No Continental population, however, in the north or in the south, comes near to the Scottish ratio.



The only foreign sample we know of comparable to the new Scottish data is from Iceland. A sample of 800 in Wiener's collection gives the ratio $A/(A + O)$ as low as 36·6, slightly more extreme than the Scottish value. Now, Iceland was undoubtedly colonized from Norway, and, though men and women from Scotland and Ireland occur frequently in the Icelandic Sagas, it is not believed to have been extensively colonized from the British Isles. The stock from which the Icelanders sprang would seem to have just the blood-group constitution needed to harmonize with the gradient found in Great Britain, but in recognizing this stock as genuinely Scandinavian, we must distinguish it sharply from the modern Scandinavian peoples, which have evidently changed greatly, by infiltration from central or eastern Europe, since the Viking period. The Scottish and N. English blood-groups show, certainly not modern Scandinavian, but it may well be a proto-Scandinavian influence.

R. A. FISHER.

Galton Laboratory,
Rothamsted.

G. L. TAYLOR.

Galton Laboratory Serum Unit,
Cambridge.
March 14.

[1] *Brit. Med. J.*, Oct. 21, 1939.

A Serum that Discloses the Genotype of some *Rh*-Positive People

THE blood-group antigen *Rh*, present in the red blood cells of about 85 per cent of normal people, called *Rh*-positive, and absent in the rest, *Rh*-negative, plays, with its corresponding anti-*Rh* agglutinin, an important part in the causation of erythroblastosis fœtalis, a familial disease of the new-born. In about 90 per cent of cases of the disease the mother is *Rh*-negative and has made anti-*Rh* which passes through the placenta and damages the red blood cells of her *Rh*-positive fœtus. The *Rh* factor is inherited as a dominant character with three genotypes *RhRh*, *Rhrh* and *rhrh*.

Recently we have found in the serum of the *Rh*-positive mother of an erythroblastotic baby an agglutinin capable of disclosing the genotype of some *Rh*-positive people. This serum, sent to us by Dr. A. J. McCall as containing anti-*Rh* and yet being from an *Rh*-positive mother, we call *St* from the first two letters of the mother's surname. It reacts with the blood of all *Rh*-negative and of all heterozygous *Rh*-positive persons, *Rhrh* (recognized by being *Rh*-positive parents or children of *Rh*-negative subjects), but it fails to react with about 20 per cent of bloods all of which must, therefore, be homozygous, *RhRh*, and represent about half of the *Rh*-positive homozygotes (about 38 per cent of the population). The *St* serum is somewhat similar to the anti-*Hr* serum found by Levine, Javert and Katzin, and referred to by Wiener[1]. The latter serum, like *St*, reacted with all *Rh*-negative bloods, but whereas *St* failed to react with only 20 per cent, the anti-*Hr*, apparently, failed with about 50 per cent of people[2]. Our findings with *St* serum, and family details, are given below.

	St+	*St*—	Total
General population	173	45	218
Rh-negative bloods	100	0	100
Rh-positive heterozygous bloods	32	0	32

Mrs. St.	*O.MN. Rh+. St—.*
Mr. St.	*A_1.MN. Rh+. St+.*
Eldest son	*O.N. Rh+. St+.*
2rd son	Died of erythroblastosis fœtalis.
3rd son	*O.MN. Rh+. St+.*, recovered from erythroblastosis fœtalis.

It follows that certain rules can be formulated concerning parentage in general:

(*a*) An *St*-negative child must have both parents *Rh*-positive. (*b*) All children of an *St*-negative parent must be *Rh*-positive.

In families with erythroblastosis fœtalis due to anti-*Rh*:

(1) All mothers and children must be *St*-positive. (2) The only member who can be *St*-negative is the father. We have found no exception to these rules. (3) The father will be more frequently *St*-negative, since he is always *Rh*-positive, than will fathers of normal children. (4) If a father is *St*-negative he must be homozygous, *RhRh*, and so cannot produce an *Rh*-negative child. His chance of producing a child without the disease is, therefore, extremely remote. (5) If the great majority of fathers of erythroblastotic infants are homozygous, a conclusion to which we and our collaborators have been led by other observations[3], about half of them should be *St*-negative. We have so far found eight out of twenty-one to be *St*-negative. The examination of a larger number should show the extent of any preponderance of homozygous fathers.

There is ample evidence that there occur subgroups of *Rh* somewhat similar to those of the *ABO* system of groups, and to explain the findings that have been reported[1–4], it is certainly necessary to postulate three allelomorphic genes (Rh_1, Rh_2 and *rh*) and almost certainly four (Rh_1, Rh_2, Rh_3 and *rh*). It is tempting to equate the frequency of the genotype Rh_1Rh_1 to 0·20, the proportion of people whose cells fail to react with the *St* serum. If the frequency of the gene Rh_1 is so derived, it may be estimated that people of the genotypes Rh_2Rh_2 and Rh_2rh form about one sixth of all *Rh*-positive persons. It is noteworthy also that Wiener[1], from the behaviour of an anti-*Rh* serum that failed to react with about 16 per cent of *Rh*-positive bloods, thought that one sixth of all *Rh*-positives belonged to the 'subtype' Rh_3.

R. R. RACE.
G. L. TAYLOR.

Galton Laboratory Serum Unit,
Medical Research Council,
Emergency Public Health Laboratory Service.
Aug. 17.

[1] Wiener, *Amer. J. Clin. Path.*, **12**, 302 (1942).

[2] Levine, Katzin, Vogel and Burnham, in "Blood Substitutes and Blood Transfusion", p. 317 (Springfield, Illinois: Mudd and Thalhimer, 1942).

[3] Race, Taylor, Cappell and McFarlane, *Brit. Med. J.* (in the press).

[4] Levine, *J. Hered.*, **34**, 71 (1943).

Vitamin C Requirements of the Syrian Hamster

WHILE engaged in some endocrinological and immunological work on the Syrian hamster, we became interested in the diet of this animal. It was thought of interest to examine the ascorbic acid requirements of the hamster, because if the animal required this vitamin, the hamster might be a useful animal for vitamin C studies since it reproduces and matures so rapidly, and is susceptible to many infections not easily produced in other animals. Since we started this study, Routh and Houchin[1] have concluded that thiamin, riboflavin, pyridoxin, pantothenic acid and nicotinic acid are essential in the diet of the hamster, while Cooper, Waisman and Elvehjem[2] have concluded that biotin and possibly inositol and *p*-aminobenzoic acid, in addition to thiamin, riboflavin, pantothenic acid, pyridoxin, and choline, are essential to the hamster, but that nicotinic acid and ascorbic acid are not. Since no growth curves have been published, we think the present study would be of interest.

The experiments were limited to the single substance ascorbic acid, using a diet containing adequate amounts of other growth essentials.

Procedure: Twenty male hamsters 3–5 weeks old were obtained from a commercial dealer (Henry Bergman, Springfield, Missouri). They were divided into two groups of ten each and of equal weight distribution, average body weight 42 gm., and fed *ad libitum* on a diet with and without added ascorbic acid. The diet was of the following composition:

Dextrose (corn sugar)	50
Casein (vitamin-free)	20
Dried brewer's yeast	10
U.S.P. 11 salt mixture	2
Cod liver oil	2
Corn oil (Mazola)	2
Lard	14
	100

LETTERS TO THE EDITORS

The Editors do not hold themselves responsible for opinions expressed by their correspondents. No notice is taken of anonymous communications.

Recognition of *Rh* Genotypes in Man

IN a recent communication, two of us[1] described a serum which we think discloses the genotype of half the persons who are homozygous for the blood group factor *Rh*. This serum, *St*, agglutinates the red cells of about 80 per cent of people, including the 15–16 per cent who are *Rh*-negative and all the 48 per cent who are heterozygous, *Rhrh*. It fails to react with 20 per cent, all of whom must be homozygous *RhRh* and be about half the total number of homozygotes (about 38 per cent of all people).

It is certain that multiple allelomorphs of the *Rh* gene occur, and to begin with three may be assumed, Rh_1, Rh_2 and *rh*. We suggested that *St* negative (*St*−) people are Rh_1Rh_1. If *St* fails to agglutinate the cells of persons with the Rh_1 gene it must react with all other frequent allelomorphs, Rh_2 and *rh*, in order to make up its 80 per cent of positive reactions.

Recently we have found in the serum of the mother of an erythroblastotic infant a different type of rare anti-*Rh* agglutinin. This serum, which we call *K*, is positive with about 30 per cent of the population, and Dr. C. V. Harrison has sent a second serum, *J*, which gives identical results. We have used *St*, *K*, *J* and normal anti-*Rh* sera to examine the blood of 281 unselected donors (205 at Cambridge and 76 at Sutton) as well as members of families we were investigating for the *Rh* factor in connexion with erythroblastosis fœtalis. The results from the two unselected groups together are :

	St+	*St*−		*KJ*+	*KJ*−		*KJ*+	*KJ*−
Rh+	174	52	*Rh*+	84	142	*St*+	83	146
Rh−	55	0	*Rh*−	2	53	*St*−	3	49

It is seen that (*a*) *Rh*− blood is *St*+ ; (*b*) *Rh*− blood is nearly always *KJ*− ; (*c*) *St*− blood is nearly always *KJ*−. Apart from the five exceptions, it seems that *KJ* can react neither with Rh_1 nor *rh*, and must, therefore, react with Rh_2 to achieve its 30 per cent of positives. (The estimated frequency of the genotypes containing Rh_2 is very near to 30 per cent.) Besides the five exceptions in the 281 unselected bloods, two of them *Rh*−*St*+*KJ*+ and three *Rh*+*St*−*KJ*+, a further example of each type was found in the 139 family samples.

We suppose that the genes so far discussed cause the following reactions :

	Antisera		
	Rh	*St*	*KJ*
Rh_1	+	−	−
Genes Rh_2	+	+	+
rh	−	+	−

If this is true, it follows that Rh_1rh blood must be *Rh*+*St*+*KJ*−. No combination of two of these allelomorphs can make either *Rh*−*St*+*KJ*+ or + − +. The first case, − + +, could be explained by the presence of a rare gene reacting with *KJ* and not with *Rh* ; we may provisionally call this Rh_z. Since it is so rare, it seems certain that in our three examples of this type of exception the gene is not in the homozygous state (for if it was present here in the homozygous state it can be calculated that the frequency of Rh_zrh, −++, would be about 1 in 15 of all persons). The genotype cannot be Rh_1Rh_z or Rh_2Rh_z, since both of these would be *Rh*+ (Rh_zRh_y, see below, would also be much too rare). The genotype must therefore be Rh_zrh.

American workers have described anti-*Rh* sera which react with 2 per cent of people who are *Rh*− with the anti-*Rh* sera most commonly found. It is possible that such a serum would be positive with this genotype Rh_zrh. Although Rh_zrh will be *St*+ by virtue of its *rh* gene, there is evidence that Rh_z also reacts with *St*. If *St* serum is titrated with *rhrh* blood and Rh_1rh blood, the red cells representing the double dose of the *St*-active *rh* gene agglutinate at a much higher dilution (eight times on the average) than do the Rh_1rh cells representing a single dose of the *St*-active gene. Two of our examples of Rh_zrh have been titrated and they are both at the top of the double-dose class.

If the gene Rh_z does react with *St*, as seems likely, then to explain the second class of exception, +−+, a further allelomorph Rh_y which is *St*−*KJ*+ must be postulated. The genotype of the four exceptions of this kind cannot with reasonable probability be Rh_yRh_y. It cannot be Rh_yrh, Rh_zRh_y or the rare Rh_zRh_y, for all these would be *St*+. This leaves only Rh_1Rh_y. It cannot be said at this stage whether Rh_y is *Rh*+, for Rh_1 may be wholly responsible for the *Rh*+ reactions of these four bloods ; no help is given by titration, for anti-*Rh* does not make such a distinction as does *St*. The extended scheme is :

	Antisera		
	Rh	*St*	*KJ*
Rh_1	+	−	−
Rh_2	+	+	+
Genes Rh_z	−	+	+
Rh_y	?	−	+
rh	−	+	−

Only a rough estimate of the frequencies of Rh_z and Rh_y can be made since the total figures are small for such infrequent genes. For what they are worth they may be derived :

$$Rh_zrh = 0{\cdot}007 \text{ and } Rh_z = \frac{0{\cdot}007}{2 \times \text{frequency of } rh} = 0{\cdot}009 \text{ or } 0{\cdot}9 \text{ per cent}$$

$$Rh_yRh_1 = 0{\cdot}011 \text{ and } Rh_y = \frac{0{\cdot}011}{2 \times \text{frequency of } Rh_1} = 0{\cdot}013 \text{ or } 1{\cdot}3 \text{ per cent}$$

The frequency of Rh_z must be deducted in calculating that of *rh*, and the frequency of Rh_y deducted similarly in calculating Rh_1. The proportion of *Rh* negatives among persons examined by us is 722 out of 4,618, or 15·63 per cent. Taking the square root, we have 39·5 per cent as the combined gene frequency of *rh* and Rh_z. Using the frequency estimated above for Rh_z this gives

rh	38·6 per cent
Rh_z	0·9 ,, ,,

Similarly, the proportion of *St* negatives observed is 97 out of 499, or 19·44 per cent. Taking the square root, we have 44·09 per cent as the combined gene frequency of Rh_1 and Rh_y, giving

Rh_1	42·8 per cent
Rh_y	1·3 ,, ,,
leaving Rh_2	16·4 ,, ,,

If we group together as "the rest" all the genotypes which we cannot recognize serologically, we can compare observed and expected frequencies :

	+−− Rh_1Rh_1	−+− $rhrh$	++− Rh_1rh	−++ Rh_zrh	+−+ Rh_1Rh_y	+++ The rest
Observed per cent	17·4	18·9	33·1	0·7	1·1	28·8
Expected per cent	18·3	14·9	33·0	0·7	1·1	31·9

The close fit is good confirmation that the genotypes do react with these three sera as we suppose. The fit of Rh_1rh is particularly important as the expectation could be calculated before *KJ* serum was discovered. Significant also are the children of matings $Rh_1Rh_1 \times rhrh$, since all must be Rh_1rh. We have examined nine such families with sixteen children all

Rh+*St*+*KJ*−. The probability that all sixteen would be *KJ* negative by chance is $0{\cdot}63^{16} = 0{\cdot}0006$ (the chance of an *Rh*+ person being *KJ*− is 0·63). Twenty-five families so far examined have shown no discrepancies. By the use of normal anti-*Rh*, *St* and *KJ* sera the genotypes Rh_1Rh_1, Rh_1rh, *rhrh*, Rh_xrh and Rh_1Rh_y, 68 per cent of the total, can be recognized. This is of prognostic importance in families in which erythroblastosis fœtalis has occurred; and it should increase the usefulness of the *Rh* blood groups in linkage studies.

Since this work has been done, we have received a paper by Wiener and Landsteiner[2] giving frequencies for the genes Rh_1 48 per cent, Rh_2 16 per cent and *rh* 36 per cent. These frequencies were derived from the behaviour of sera quite different from *St* and *KJ*. In a personal communication at the same time, Wiener says that they now have papers in the press demonstrating six distinct allelomorphs. We are at present calling our fourth and fifth allelomorphs Rh_x and Rh_y, in the hope that a name and place is ready for them in Wiener's scheme.

R. R. RACE.
G. L. TAYLOR.
KATHLEEN E. BOORMAN.
BARBARA E. DODD.
Medical Research Council
Emergency Blood Transfusion Service.
Oct. 13.

[1] Race and Taylor, NATURE, **152**, 300 (1943).
[2] Wiener and Landsteiner, *Proc. Soc. Exp. Biol. and Med.*, **53**, 167 (1943).

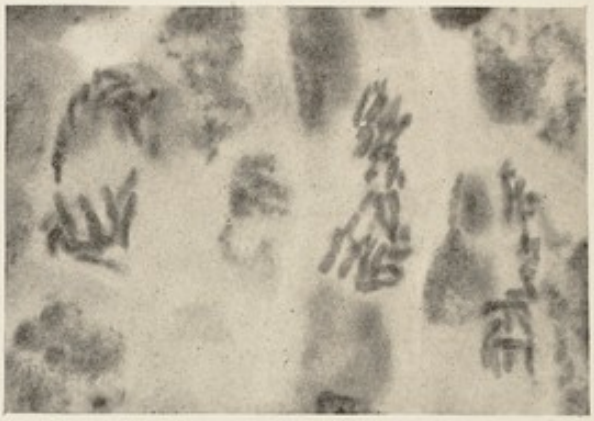
Chemical Control of Mitosis

A CONNEXION between the mode of action of carcinogenic and of polyploidogenic reagents has frequently been postulated[1,2], but the crucial test of the induction of polyploidy in plants by a typical carcinogenic hydrocarbon has so far not been recorded. Patton and Nebel[3], for example, report that dibenzanthracene causes increase in the size of the prophase nuclei in the root tips of Zea, but state that no abnormality of mitosis could be observed. It was therefore with some surprise that we found recently on examining the root tips of rye seedlings, which had been growing in water containing crystals of 1.2.5.6 dibenzanthracene, a striking polyploidogenic effect. This did not occur in the control with water alone.

We repeated the experiment, but found only normal growth, and it was some time before we traced the reason for the first result. At that time we had also been working with organic mercury compounds such as are used for dusting seeds to prevent fungal attack. These compounds are crystalline solids, but some have an appreciable vapour pressure and even at room temperature give off a toxic vapour. This led us to suspect that the laboratory air may have been vitiated and we repeated the first experiment in an atmosphere which was in equilibrium with solid ethyl mercuric chloride. The result was precisely as in the first experiment, namely, definite chromosome doubling.

Further trials showed that a very dilute solution of ethyl mercuric chloride gave the same result and had the great convenience that the dosage could be controlled.

Stock solutions of ethyl mercuric chloride and dibenzanthracene were made by dissolving 1 mgm. of each chemical in alcohol and diluting to the required proportions with tap water. Both substances were difficult to dissolve in water alone and this procedure was necessary to obtain exact dilutions. The final mixtures contained 0·4 per cent alcohol. The dibenzanthracene which is soluble in water only to the extent of 0·001 part per million[4] was a colloidal suspension and therefore saturated; the ethyl mercuric chloride was a clear solution. In a supplementary experiment, as reported by Levan and Ostergren[2] for colchicine, we found that this trace of alcohol showed a slight antagonism and lifted the lower threshold value of action. The accompanying table summarizes our results on the action of these compounds on the root tips of rye seedlings, after 48 hr. treatment at 22° C.



PRONOUNCED POLYPLOIDY IN ROOT TIP OF RYE, GROWN IN A MIXED SOLUTION OF 1·75 P.P.M. DIBENZANTHRACENE AND 0·25 P.P.M. ETHYL MERCURIC CHLORIDE. SEPARATE SOLUTIONS AT THESE CONCENTRATIONS GAVE ONLY DIPLOID NUCLEI ($2n = 14$). (× 750.)

Parts per million of water		Effects*		
Dibenz-anthracene	Ethyl mercury chloride	*c*-Mitosis	Toxicity	Polyploidy
1	*0*	—	—	—
0	*1*	+	++	—
1	*1*	—	++	—
1·5	*0·5*	+	++	—
0	*0·5*	+	+	+
1·75	*0*	—	—	—
0	*0·25*	—	—	—
1·75	*0·25*	+++	—	++

* The *c*-mitosis column shows the degree of spindle disturbance—the toxicity is measured in inverse proportion to the number of accumulated active nuclei after 48 hours.

It will be noticed that only very minute concentrations of the reagents are involved and that there is a limited range of effectiveness. Dibenzanthracene alone has no effect on mitosis at any concentration while ethyl mercuric chloride alone has a slight effect at 0·5 part per million. Ethyl mercuric chloride alone has no effect at 0·25 part per million, but in conjunction with dibenzanthracene the polyploidogenic effect is pronounced (see accompanying illustration).

Evidently the ethyl mercuric chloride is the direct polyploidogenic agent and the dibenzanthracene facilitates its action. The observation by Lisle[5], which we have confirmed, that dibenzanthracene reduces the ability of lipoids to inhibit the oxidation of fats, may show how this comes about.

It is too early to decide the exact role of these two reagents, and systematic study of pairs of similar

LETTERS TO THE EDITORS

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Recognition of a Further Common *Rh* Genotype in Man

SINCE the publication of a recent communication[1] on the subject of *Rh* genotypes certain advances have been made. The point had been reached, as described in that communication, where by the use of three different forms of anti-*Rh* sera, the genotypes of about 68 per cent of the population could be recognized, and five allelomorphs could be distinguished. Since then we have found a serum, described at a meeting of the Royal Society of Medicine on November 2, 1943, which, when used in combination with the other three, makes recognizable the genotype of about 80 per cent of people and defines two further allelomorphs, making seven in all. More recently a letter (see below) has come from Wiener describing all these allelomorphs except Rh_y. We will use Wiener's names, which are Rh_1, Rh_2, *rh*, *Rh′* (*rh* dot), *Rh″* (Rh_x), but for the gene Wiener calls *Rh* (Rh_1 bar) we prefer Rh_0, for *Rh* has for so long had a much wider meaning. The names we have used[1] and are now abandoning are given in brackets. Rh_y we will continue to use.

The new serum agglutinates the red cells of people who have the frequent gene Rh_1 or the rare gene *Rh′*. It is undoubtedly the type of serum called by Wiener[2] anti-Rh_1. Perhaps its greatest use is in separating the genotypes Rh_1Rh_2 (12 per cent), Rh_1Rh'' (1 per cent) and Rh_2Rh' (0·2 per cent) from the serologically indistinguishable group called "the rest" in our previous communication. "The rest" group now contains only Rh_2rh (12 per cent) and Rh_2Rh_2 (2 per cent) of common genotypes while, ignoring the rare ones, the genotypes of about 80 per cent of people can be recognized.

We were first made aware of the existence of the forms Rh_0 and *Rh′* when the blood of 154 unselected donors was tested with *Rh St KJ* and anti-Rh_1 sera. Of these, 57 gave the reaction of Rh_1rh (++−), all of them being positive with the new anti-Rh_1 serum except one. The presumption that the factor responsible for this unexpected reaction, now called Rh_0, is allelomorphic is supported by its occurrence in two generations of a family (father *rhrh*, mother Rh_0rh, daughter Rh_0rh). Rh_0rh cells give the double dose effect[1] when titrated with *St* serum, showing that Rh_0 is St^+. Twenty of the 154 bloods gave the reaction of *rhrh* (−+−); of these all were negative with the anti-Rh_1 serum except one; the gene responsible for the exception is now called *Rh′*. In one family (No. 15, Race *et al.*[3]) this allelomorph has been found in two generations (mother's sister *Rh′rh*, mother *Rh′rh*, father Rh_1rh, first child Rh_1rh, fourth child *Rh′rh*). *Rh′rh* cells give the single dose effect when titrated with *St* serum, showing that *Rh′* is St^-.

The total number of unselected bloods examined with *Rh*, *St* and *KJ* is now 435, and the last 154 of these have also been tested with the anti-Rh_1 serum. This latter serum is supporting the general theory put forward in the previous communication, for in the group $Rh^+St^+KJ^+$ called "the rest", it can be calculated that 47 per cent should have either the gene Rh_1 or *Rh′*. In the 154 bloods there were $48^{+}{+}{+}$, and of these 20, or 42 per cent, were positive with the anti-Rh_1 serum ($\chi^2 = 0{\cdot}49$ for 1 *D.F.* Probability about 0·5).

The results with the three sera are:

	−+−	+−−	++−	−++
Mainly	*rhrh* (96%*)	Rh_1Rh_2 (96%)	Rh_1rh (97%)	*Rh″rh* (97%)
	75	75	149	4
Per cent	17·24	17·24	34·25	0·92

	+−+	−−−	+++	Total
Mainly	Rh_1Rh_y (100%)	*Rh′Rh′* (100%)	The rest	
	3	0	129	435
Per cent	0·69	0	29·66	

* The figure in brackets shows, in the first case for example, the percentage of bloods reacting −+− which are in fact *rhrh*; the remaining 4 per cent are *Rh′rh*.

The gene frequencies given in the previous communication need slight alteration. Before calculating the frequency of *rh*, a deduction must be made from the 17·24 per cent −+− bloods, since one person in 154, or 0·65 per cent, previously thought to be *rhrh*, is now known to be *Rh′rh*. The gene frequency of *rh* is $\sqrt{0{\cdot}1724 - 0{\cdot}0065} = 0{\cdot}4073$; *Rh′rh* = 0·0065; therefore $Rh' = \dfrac{0{\cdot}0065}{2 \times 0{\cdot}4073} = 0{\cdot}0080$. The frequency of Rh_1 can be calculated from the +−− group, of which Rh_1Rh_1 makes up 96 per cent, the remaining 4 per cent consisting of Rh_1Rh' (see Table 2), consequently:

$(Rh_1)^2 + 2(Rh_1Rh') = 0{\cdot}1724$, and since $Rh' = 0{\cdot}0080$, then $Rh_1 = 0{\cdot}4073$, by chance the same as *rh*. $Rh_1Rh_y = 0{\cdot}0069$.

$$\therefore\ Rh_y = \frac{0{\cdot}0069}{2 \times 0{\cdot}4073} = 0{\cdot}0085;\quad Rh''rh = 0{\cdot}0092$$

$$\therefore\ Rh'' = \frac{0{\cdot}0092}{2 \times 0{\cdot}4073} = 0{\cdot}0113;\quad Rh_0rh = 0{\cdot}0065$$

$$\therefore\ Rh_0 = \frac{0{\cdot}0065}{2 \times 0{\cdot}4073} = 0{\cdot}0080,$$

and by difference $Rh_2 = 0{\cdot}1496$.

Based on these gene frequencies, the expectation for the group ++− and for the group called "the rest" can be calculated, and the theory tested by comparison with observation.

	++−	"The rest"
Expected	34·50%	28·63%
Observed	34·25%	29·66%

The frequency of the commonest six genotypes as calculated from our sample are given below. These frequencies are only approximate for the community as a whole, the proportion of *Rh* negative being slightly higher than we have found in a much larger sample.

TABLE 1.

	Per cent	*Rh*	*St*	*KJ*	Rh_1
rhrh	16·59	−	+	−	−
Rh_1Rh_1	16·59	+	−	−	+
Rh_1Rh_2	12·19	+	+	+	+
Rh_1rh	33·18	+	+	−	+
Rh_2rh	12·19	+	+	+	−
Rh_2Rh_2	2·24				

These total 93 per cent; the remaining 22 rarer genotypes make up 7 per cent, and ignoring these we are able to distinguish serologically between all the 93 per cent, except that we cannot make the distinction between Rh_2rh and Rh_2Rh_2. Examination of thirty families has so far revealed no exception to this scheme of allelomorphs.

This was the state of our work when a letter, dated October 11, 1943, came from Wiener enclosing the typescript of a paper then in the press, in which is described the behaviour of six allelomorphs of the *Rh* gene. In Table 2 is a comparison of Wiener's scheme and our own:

Table 2.

Genes	Wiener Antisera *Rh*	(*St*)	*Rh*$_2$	*Rh*$_1$	*Rh′*	*Rh″*	Genes	Race, *et al.* Antisera *Rh*	*St*	*KJ*	*Rh*$_1$
Rh$_1$	+	0	—	+	+	+	*Rh*$_1$	+	—	—	+
Rh$_2$	+	0	+	—	+	+	*Rh*$_2$	+	+	+	—
Rh	+	0	—	—	+	+	*Rh*$_y$	+	+	—	—
Rh′	—	0	—	+	+	—	*Rh′*	—	—	—	+
Rh″	—	0	+	—	—	+	*Rh″*	—	+	+	—
rh	—	0	—	—	—	—	*rh*	—	+	—	—
							Rh$_y$	?	—	+	?

The two schemes show complete agreement, save that Wiener has not met the *Rh*$_y$ allelomorph because he has not had an *St* serum. The results are so strikingly similar that the probability of their being correct must be very high. We were stimulated by Wiener's letter to attempt to identify his types of sera with those we have used, and have found all of them represented in our collection. Among sera which have occasionally given anomalous reactions, we have been able to identify anti-*Rh′* and anti-*Rh″*. That we had not employed these two types of serum regularly does not seem to matter since the distinctions they make are already made by anti-*Rh*, *St*, *KJ* and anti-*Rh*$_1$. The great value of *St* serum is made clear, for ignoring those that are very rare, it raises the proportion of people whose genotypes are recognizable from approximately 30 to 80 per cent. While these schemes cover the great majority of our findings occasional anomalous results suggest that other very rare forms may exist.

R. R. RACE.
G. L. TAYLOR.
D. F. CAPPELL.
MARJORY N. MCFARLANE.
Medical Research Council
Emergency Blood Transfusion Service;
and University of St. Andrews.
Dec. 1.

[1] Race, Taylor, Boorman and Dodd, NATURE, **152**, 563 (1943).
[2] Wiener, *Amer. J. Clin. Path.*, **12**, 302 (1942).
[3] Race, Taylor, Cappell and McFarlane, *Brit. Med. J.*, **2**, 289 (1943)

Phenogenetic Evidence for the Amphidiploid Origin of New World Cottons

THE genus Gossypium may be divided cytologically into four main groups:

(1) Asiatic diploids .. .. .. ($n = 13$)
(2) American diploids .. .. .. ($n = 13$)
(3) Australian diploids .. .. .. ($n = 13$)
(4) New World 'tetraploids' .. .. ($n = 26$)

Cytological evidence[1,2] suggests strongly that New World cottons have been evolved by amphidiploidy from hybrids between Asiatic and American diploid cottons. It is supported by artificial syntheses of amphidiploids which produce partly fertile hybrids when crossed with New World types[2,3]. Phenogenetic evidence leading to the same conclusion is presented here.

It is known that Asiatic and New World cottons each have a series of multiple alleles which control the shape of the leaf. That a similar series occurs in American diploid cottons is highly probable, though critical data are not yet available. If New World cottons are amphidiploids of Asiatic × American diploid parentage they should have (at least initially) *two* leaf-shape loci, one homologous with the Asiatic alleles, the other homologous with the corresponding series in American diploids. Phenogenetic studies of the action of the leaf-shape alleles on the development of the leaf led to the suggestion[4] that the joint action of an entire (unlobed) leaf gene from the

FIG. 1. TOP ROW: ASIATIC PARENTS, (*a*) ***l*** (*herbaceum*), (*b*) ***L^A*** (*arboreum*); SECOND ROW: ASIATIC × AMERICAN F_1s, (*c*) ***l*** × *raimondii*, (*d*) ***L^A*** × *raimondii*; THIRD ROW: NEW WORLD AMPHIDIPLOIDS, (*e*) ***l*** (*hirsutum* VAR. *taitense*); (*f*) ***L^E*** (*barbadense* VAR. *darwinii*); BELOW: AMERICAN PARENT, (*g*) *raimondii*.

American diploid parent and a lobed leaf allele from the Asiatic parent might reproduce a type of leaf development which is characteristic of New World cottons. In other words, the New World allelomorph series might be regarded as a series of Asiatic alleles acting in conjunction with an entire leaf gene at the other locus. No duplicate leaf-shape genes are known in New World cottons, so it was postulated, on this hypothesis, that the entire leaf gene is quite stable and common to all New World cottons.

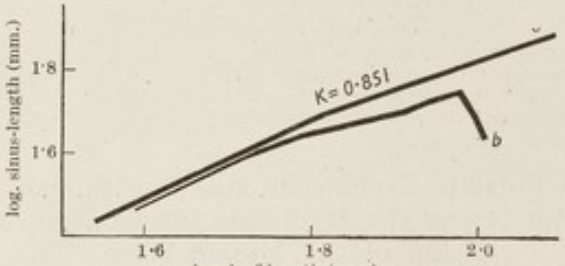

FIG. 2. DEVELOPMENTAL TRACKS OF ASIATIC × *raimondii* F_1 HYBRIDS: (*a*) ***l*** × *raimondii*, (*b*) ***L^A*** × *raimondii*.

Crosses between Asiatic and American diploid cottons very rarely set viable seeds (less than 0·5 per cent in my experience). However, two hybrids have so far been obtained:

Asiatic		American
(1) *G. arboreum* (***L^A***)	×	*G. raimondii*
(2) *G. herbaceum* (***l***)		

The symbols refer to the leaf shape alleles carried by the Asiatic parents. The American species has entire leaves. Leaf outlines of the parents and hybrids are compared with standard New World types in Fig. 1. It can be seen that the leaves of F_1, ***L^A*** × *raimondii*, and F_1, ***l*** × *raimondii*, show a marked resemblance to the New World ***L^E*** and ***l*** leaf types, respectively. This resemblance is not a chance superficial one since the course of development is remarkably similar. Developmental tracks* of the F_1 compounds closely resemble those of the corresponding New World types (Figs. 2 and 3). The corresponding ***l*** × *raimondii* (Fig. 2) and ***l*** (Fig. 3) tracks are almost linear and

* Graphical representations[4] of the progressive change in leaf shape from node to node during the juvenile stages.

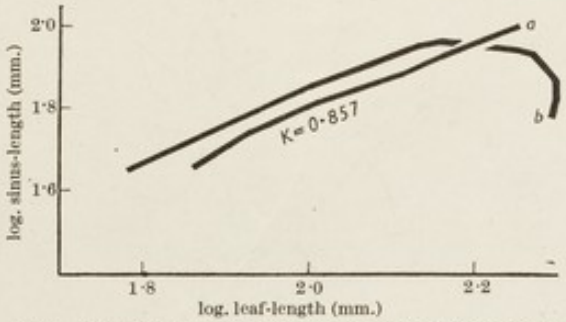

Fig. 3. DEVELOPMENTAL TRACKS OF NEW WORLD AMPHIDIPLOID TYPES: (*a*) *l*, (*b*) L^E. COMPARE WITH SYNTHESIZED TYPES IN FIG. 2.

can therefore be expressed as allometric developmental constants (K values). As shown in the figures, the two K values are practically identical.

Subject to confirmation by orthodox genetic analysis—which awaits the successful synthesis by colchicine treatment of a set of amphidiploids which will cross with New World types—the data suggest that two alleles of the New World series, L^E and l, are identical with $L^A + X$, $l + X$ respectively, where X is an entire leaf allele from an American diploid entire leaved ancestor. Four American diploid species with entire leaves still exist: *G. aridum*, *G. armourianum*, *G. klotzschianum* (including *davidsonii*) and *G. raimondii*. General morphological considerations suggest that either of the two last-named in combination with *G. arboreum* would produce a hybrid showing considerable similarity to present-day New World cottons.

S. G. STEPHENS.

Empire Cotton Growing Corporation,
Cotton Research Station,
Trinidad.

[1] Skovsted, A., *J. Genet.*, **34**, 97 (1937).
[2] Beasley, J. O., *Genetics*, **27**, 25 (1942).
[3] Harland, S. C., *Trop. Agric.*, **17**, 53 (1940).
[4] Stephens, S. G., *J. Genet.* (in the press).

Acid-labile Carbon Dioxide in Mammalian Muscle and the Hydrogen Ion Concentration of the Muscle Fibre

FOR the isolated sartorius muscle of the frog it was found[1] that over a wide range of concentration of external potassium and chlorine ions the following relation applied (in accordance with the Donnan principle):

$$\frac{[K]_1}{[K]} = \frac{[Cl]}{[Cl]_1},$$

where $[K]_1$,$[K]$ are the potassium concentrations within and without the fibre, and similarly for [Cl]. It may be assumed that the following would likewise apply:

$$\frac{[K]_1}{[K]} = \frac{[H]_1}{[H]} = \frac{[Cl]}{[Cl]_1} = \frac{[HCO_3]}{[HCO_3]_1}$$

since H is a smaller cation than K, and HCO_3 about the same size as Cl.

Recently Wallace and Hastings[2] published data for the total carbon dioxide in mammalian muscle, finding therein about 11 mM. carbon dioxide per kilo—and allowing the free carbon dioxide to be in approximately equal concentration across the membrane, and the remainder to be altogether HCO_3 ion, it follows that the ratio $\frac{[HCO_3]_1}{[HCO_3]}$ would then be far higher than $\frac{[K]}{[K]_1}$. Therefore, either the mammalian muscle fibre has a much different electrolyte distribution and a different membrane permeability than frog muscle, or the fraction of the total carbon dioxide assigned by Wallace and Hastings to the HCO_3 ions is much too high.

The latter is the true explanation, as shown in recent work in this laboratory. The total carbon dioxide in mammalian muscle was determined by extraction in alkali solution and subsequent measurement of the carbon dioxide liberated on acidification. The figure of Wallace and Hastings was confirmed. It was found, however, that if to the alkaline extract saturated barium chloride was added, and the mixture centrifuged for about 90 minutes at 3,000 rev./min., in many cases a clear solution was obtained, and this contained more than half the total acid-labile carbon dioxide. The leg muscles of very young rabbits, and the abdominal muscle in general, were found to be the most satisfactory for the purpose.

For rabbit abdominal muscle the total carbon dioxide was found to be 11·4 mM. per kilo and the barium-soluble fraction 5·2. For the leg muscle of rabbit and cat the total was found to be 10·6 and the barium soluble fraction 7·0 mM. per kilo. The reality of a true barium-soluble fraction of such magnitude was proved by the following facts. (*a*) Additions of HCO_3 (as potassium bicarbonate) to the alkali extracts before addition of barium chloride were fully precipitated. (*b*) A curve of turbidity against HCO_3 present before addition of barium chloride was obtained by first evacuating abdominal muscle for hours in the cold, and then extracting with alkali, and adding graded amounts of HCO_3 to similar volumes of extract. The turbidity on adding the barium chloride was measured in the Pulfrich turbidimeter, and expressed in absolute numbers. A value of 0·10 in the extract would about correspond to the barium-soluble carbon dioxide in extract of fresh muscle, whereas either no opacity was present after the barium chloride addition and centrifuging (90 min.) or so little that the total average value was 0·008, or only 8 per cent of the turbidity for the equivalent amount of HCO_3.

Nature of the barium-soluble fraction. From the researches of Henriques[3], Faurholt[4], Meldrum and Roughton[5], it might be expected that some at least of this barium-soluble fraction is carbamino carbon dioxide. We have investigated the time curve of carbon dioxide loss from evacuated guinea pig muscle, and obtained the mean curves as shown in the accompanying figure. It will appear that a 2–3 mM. fraction only of the barium-soluble quantity is given off rapidly, and the greater fraction, 3–4 mM. per kilo, is emitted very slowly. Only 2–3 mM. can therefore be regarded as likely to be carbamino carbon dioxide, the remainder being a still unknown compound.

The pH in the muscle fibre. The free carbon dioxide plus the HCO_3 ion in leg muscle is $10·6 - 7·0 = 3·6$, and allowing for the interspace values, etc., the true value of the bicarbonate content in the water of the muscle fibre becomes 0·9 mM. per litre, whereas the carbon dioxide in the extracellular water is approximately 1·2 mM. per kilo. Therefore the pH is given by

$$p\text{H} = 6·1 - \log 1·2/0·9 = 6·0.$$

If, on the other hand, we consider the ratio

$$\frac{[K]_1}{[K]} = \frac{[H]_1}{[H]},$$

LETTERS TO THE EDITORS

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Mutation and the Rhesus Reaction

IN his interesting letter[1] on genetics of the *Rh* antigen in man, Prof. L. T. Hogben advances two hypotheses. The first is that the frequency of the *rh* gene, determining the absence of the antigen, is approximately constant from one generation to another in human populations. The second is that this constancy is due to the formation of new *rh* genes by mutation, at a rate which replaces those eliminated by the deaths of heterozygotes from erythroblastosis fœtalis. Thus such populations as those of England and the United States are thought to be in equilibrium.

Prof. Hogben does not refer to the earlier work of Wiener[2] and Haldane[3] on this question, perhaps because the latter at least requires some revision in the light of later observations. Neither Wiener nor Haldane believed that the present frequency of the *rh* gene was stable, and they ascribed it to the formation of the Western European people by (geologically) recent crossing between a race in which the *rh* gene was very rare, as it is[4] in American Indians, and one in which it was very common. Haldane calculated that selection at its present intensity would reduce the frequency of *Rh*-negative individuals from its present mean American value of 14 to 1 per cent in about six hundred generations.

Whether or not the theory of racial crossing is accepted, there is a sound reason for rejecting Prof. Hogben's theory, namely, that the equilibrium which he postulates would be unstable. Let t be the time measured in generations, p the frequency of the *rh* gene, $1 - k$ the ratio of the mean viability of *Rh rh* children of *rh rh* mothers to that of other babies, and μ the frequency with which *Rh* (or a group of dominant allelomorphs) mutates to *rh* per generation. Then it follows from the argument given by Haldane[3] that

$$\frac{dp}{dt} = \mu(1-p) - kp^2(1-p)\left(\tfrac{1}{2} - p\right) + O(k^2).$$

Hence at equilibrium $\mu = kp^2\left(\frac{1}{2} - p\right)$. Among American whites $p = 0{\cdot}39$, so if they are in equilibrium $\mu = 0{\cdot}016731k$. If p is slightly increased, say, to $0{\cdot}40$, $\frac{dp}{dt} = +\,0{\cdot}0004386k$, so it will tend to increase further. If it is slightly diminished to $0{\cdot}38$, $\frac{dp}{dt} = -\,0{\cdot}000370k$, so it will tend to diminish further. If $\mu = 0{\cdot}016731k$ the only stable equilibria are given by $p = 1$ and $p = 0{\cdot}27$.

In general, the condition for stability is that $\frac{d}{dp}\left(\frac{dp}{dt}\right)$ should be negative in the neighbourhood of the equilibrium. It can readily be shown that this is only possible, whatever the mutation-rate, if $p < 1/3$. The existence of unstable equilibria between selection and mutation was pointed out by Haldane[5], and it is always desirable to investigate the stability of postulated equilibria of this kind.

While it would seem that Prof. Hogben's theory must be rejected, I do not wish to suggest that my own should therefore be accepted. Its acceptance must depend, among other things, on research into the frequency of different allelomorphs at the *Rh* locus in various populations, and I fully support Prof. Hogben's plea for more such research. This is particularly desirable in Asiatic populations where, if anywhere, a high frequency of *rh* might be expected.

J. B. S. HALDANE.

Department of Biometry,
University College, London.

[1] Hogben, NATURE, **152**, 721 (1943).
[2] Wiener, *Science*, **96**, 407 (1942).
[3] Haldane, *Ann. Eug.*, **11**, 333 (1942).
[4] Landsteiner, Wiener and Matson, *J. Exp. Med.*, **76**, 73 (1942).
[5] Haldane, *Proc. Camb. Phil. Soc.*, **23**, 838 (1927).

IN NATURE of December 18, Prof. L. Hogben has discussed the question of gene equilibrium in the Rhesus blood-group factor, and draws the conclusion that a mutation-rate from Rhesus-positive to Rhesus-negative genes of quite unprecedented magnitude can be inferred from what is at present known of the genetic situation and the medical facts.

With the importance of obtaining direct and unbiased data of the vital statistics of marriages between different genotypes we are in most hearty agreement; and, indeed, have already taken preliminary steps toward a direct ascertainment of these factors. The situation in some respects, however, does not appear to us to have been correctly stated by Prof. Hogben; in particular, we would dissociate ourselves from the statement that "Levine's hypothesis postulates a form of adverse selection. . . ." It appears to us, on the contrary, that the evidence for Levine's theory of the causation of hæmolytic disease of the newborn is completely independent of any such postulate, and would be equally convincing whether there is or is not any such selective influence at work. It would also be wrong to infer a selective elimination of the rarer gene from a demonstrable elimination of heterozygotes, unless we knew, as we do not know, that fertility is not concurrently affected.

Finally, we do not think that Prof. Hogben's theory of an abnormal mutation-rate gains any confirmation from the rather extensive system of multiple allelomorphs of the Rhesus factor recently demonstrated at the Galton Laboratory Serum Unit and elsewhere. Speaking of his mutation-rate, Hogben says: "on the other hand, its value is not inordinately high if we interpret μ to signify the rate of mutation at the *Rh* locus from *any one of a series* of 5 or more dominant alleles". Of the seven allelomorphs we now postulate, not more than four are Rhesus-positive, while three are Rhesus-negative. Moreover, we do not see that the mutation theory is aided by the supposition that the hypothetical mutation is derived from any one rather than equally from all of the possible sources.

R. A. FISHER.

Department of Genetics,
Cambridge.

R. R. RACE.
G. L. TAYLOR.

Galton Laboratory Serum Unit,
Department of Pathology,
Cambridge.

The Human Side of Anthropology

THE recent editorial in NATURE[1] made out a very strong case for the importance of the social sciences as a scientific contribution to the welfare of the community; and in the same issue, Prof. Le Gros Clark directed attention to some of the rich and interesting

Healing Stage. It may be useful here to detail the exact instructions to be given to the patient as soon as an ulcer has been diagnosed. He should (1) stay in bed; (2) avoid tobacco and alcohol; and (3) adhere strictly to the diet outlined: each hour, when awake and also if awake during the night (whether or not in pain) take one of the following: cup of milk, flavoured with tea, coffee or cocoa; porridge and milk; sieved vegetable soup; bread and milk; custard, milk jelly, junket or blancmange; thin crustless bread and butter; plain chocolate; soft biscuits; raw egg in milk. He should be given a certificate entitling him to two pints of milk per day and to extra eggs whenever these are issued, and he should also make use of his rations of household milk, sugar, dried egg, honey and treacle, all of which will increase the caloric value of the diet and make for variety; (4) It is wise to give vitamin C tablets 50 mgs. daily.

It will be found that on the above regime the great majority of patients will lose their pain within a few days, and within a fortnight will be clamouring for more licence—to be allowed up, for more food, the occasional cigarette, etc. These demands must be resisted, and it should be explained that ulcers become silent long before they heal, while indulgence at this stage will inevitably lead to relapse.

In a minority of cases, the above steps will be insufficient to produce total alleviation of symptoms, and other measure are required.

If the patient continues to complain of pain at night, interfering with sleep, so that he cannot get off or is awakened in the small hours, he should be given, before settling down for the night, i.e., between 10 and 11 p.m. half an ounce of a preparation of colloidal aluminium hydroxide (e.g., Aludrox or Collumina), together with 20 minims of tincture of belladonna, in a wineglassful of water.

If the pains during the day, although lessened, continue after one week, and there is no doubt that the patient is resting, not smoking, and keeping strictly to the diet, it is necessary to use other means for reinforcing the neutralisation of the gastric contents. This means, in effect, the employment of regular doses of an antacid, given between each feed, so that there is an alternation of food and drug entering the stomach each half-hour. There is no doubt that the safest, most reliable and pleasant preparation to take is an aluminium gel—thus, for every 50 ulcer patients obtaining complete relief of pain after the administration of colloidal aluminium hydroxide only five obtained complete relief with calcium carbonate, the remainder being improved, but having a residue of pain. Further, because of the risk of producing alkalosis, it is wiser to use only those preparations in which this risk is absent, viz., an aluminium gel or magnesium trisilicate. The latter carries the disadvantage of feeling gritty to the taste, its action is not always effective and it occasionally appears to stimulate acid secretion. The only disadvantage of an aluminium preparation is one of expense. To summarise, one might say that preferably colloidal aluminium hydroxide (or phosphate) should be given in doses of 1-2 drachms between feeds—failing this, magnesium trisilicate in the same dosage.

If there is evidence of anæmia following repeated small hæmorrhages from the ulcer, iron should be given in full doses, e.g., Ferri. et Ammon. Cit. gr. 30-40 T.D.S. p.c.

Convalescent Stage. It is essential that the healing stage should be adhered to until the patient has been completely free of symptoms for a period of at least three weeks, giving a total on this stage of about four weeks. During the next fortnight, while still in bed most of the day, but allowed to sit out in a chair for a few hours, by an increase of the interval between meals and the allowance of a more liberal diet, a dietary is arrived at to which the patient must adhere for the next two years. It is best to give him a written copy of this diet, together with the necessary instructions, as follows:

FIG. 1.—Gastric Ulcer. Healing Stage Diet.
FIG. 2.—Duodenal Ulcer. Healing Stage Diet with aluminium gel between feeds.

FIG. 3.—Duodenal Ulcer. Hourly Citrated Milk.
FIG. 4.—Gastric Ulcer. Intragastric Drip feeding.
Examples of ulcers, with treatment required for healing. (X-rays by courtesy of Dr. F. R. Berridge).

On waking:	Milky tea.
Breakfast:	Milky tea or coffee. Bread or thin toast. Porridge with milk and sugar. Egg, or boiled or steamed fish, or fish cakes.
Mid-morning:	Milk or vegetable soup or soft biscuits.
Lunch:	Vegetable soup. Boiled or steamed fish, or chicken, rabbit, liver or minced meat. Mashed potatoes, sieved vegetables. Milk pudding or custard, milk jelly, junket, blancmange or steamed sponge pudding.
Mid-afternoon:	Milk or plain chocolate, or soft biscuits.
Tea:	Milky tea. Bread or thin toast. Sponge or Madeira cake.
Supper:	As for lunch.
Bed-time:	Milk flavoured with tea, coffee, cocoa.

Use your rations of butter, margarine, jam, honey, treacle, marmalade, dried eggs, household milk, sugar and chocolate, to supplement the above. Keep to this diet for at least two years. Never go more than two hours without food. Always carry biscuits and chocolate with you. Only smoke immediately after meals. Take alcohol sparingly and only with meals. Never use strong purgatives. Go back to the Healing Stage diet and see your doctor if you get any return of pain.

During the final fortnight the patient should be allowed to return to full activity and, after gastroscopic or radiological confirmation of healing of the ulcer has been obtained, he may return to work at the end of eight weeks.

Failure to Heal. A small percentage of ulcers fail to heal despite strict attention to the regime outlined above, and for these cases other methods are available.

A trial should be given of hourly feeds of five ounces of citrated milk (gr. one of Sod. Cit. to one ounce of milk) with two drachms of colloidal aluminium hydroxide between each feed, and half an ounce of aluminium hydroxide together with 20 minims of tincture of belladonna last thing at night. Few ulcers do not respond to this, but those which are resistant may yield to continuous intragastric drip milk feeding. A Ryle's Tube is passed into the stomach and attached to a drip apparatus, filled with citrated milk, to each pint of which has been added one ounce of colloidal aluminium hydroxide and one ounce of sugar or glucose. This is allowed to run into the stomach at the rate of 40 drops a minute (one pint in four hours, or six pints in 24) day and night, ensuring complete neutralisation of the gastric contents throughout the 24 hours. This method is highly successful, healing four out of six otherwise resistant ulcers, but clearly can only be used at those times of the year when milk is not rationed, or when plenty of household or other dried milk is available. It requires fairly constant attention and is undoubtedly a procedure more readily carried out in hospital, but it should be borne in mind, for by such ancillary methods the total number of ulcers remaining unhealed by medical means can be reduced to under two per cent.

Hæmorrhage. It must be borne in mind that hæmorrhage from an ulcer always carries serious potentialities—with this proviso mild cases, as judged by the amount and duration of bleeding, general condition, pulse rate and, if possible, hæmoglobin estimation, can be treated at home, by rest in bed, morphine, small hourly feeds of milk and water for the first 24 hours and, subsequently, the healing stage diet and iron.

More severe cases, requiring continuous drip blood transfusion, can either be treated at home or in hospital, according to the facilities available.

Surgery. Surgical intervention is indicated, whether in peace or war, for perforation, stenosis, hourglass deformity, malignant degeneration and those ulcers which fail to heal under medical treatment. The type of operation required for each condition is outside the scope of this article.

In conclusion, it may be said that despite wartime restrictions, it is possible to devise healing and convalescent types of ulcer diets which give excellent results and produce healing in the large majority of cases of peptic ulcer.

ORIGINAL PAPERS

THE Rh BLOOD GROUP FACTOR—I

By G. L. TAYLOR,* M.D., Ph.D., M.R.C.P., and R. R. RACE,* M.R.C.S., L.R.C.P.

The Galton Laboratory Serum Unit, Department of Pathology, Cambridge.

THE fascinating story of the discovery of the new blood-group antigen Rh by Landsteiner and Wiener (1940 and 1941) and its relationship to hæmolytic reactions following blood transfusion and to hæmolytic disease of the newborn (erythroblastosis fœtalis) has aroused great interest in the profession. These two workers found that the serum of a rabbit injected with the red blood cells of the Rhesus monkey agglutinated the red cells of 85 per cent. of white people in America and failed to agglutinate those of the other 15 per cent. The two classes are called Rh-positive and Rh-negative respectively. The population in our island is distributed in the same proportions. We have examined samples sent from all parts of the United Kingdom, with the following results:

Rh+	Rh—	Total
3896	722	4618
84.37%	15.63%	100.00%

But there are marked racial differences, as there are in the distribution of the A-B-O groups. Landsteiner and Wiener soon noticed that the proportion of Rh-positive people was higher amongst the negroes than amongst the whites in America, and since then Landsteiner, Wiener and Matson (1942) have found only one Rh-negative amongst 120 pure-bred American Indians. The distribution of the Rh factor is the same in the two sexes and appears to be quite independent of the other known blood-group antigens, A, B, O, M, N and P. Rh is present at birth; in cord bloods we found:

Rh+	Rh—	Total
285	45	330
86.36%	13.64%	100.00%

Not long after the discovery of the Rh factor Wiener and Peters (1940) found agglutinins which were identified as anti-Rh in the sera of certain persons who had hæmolytic reactions following transfusion of blood which, according to the A-B-O groups, was compatible. These recipients were all Rh-negative, and either had received previous transfusions or were women who had recently been pregnant. The first group had been immunised by an earlier transfusion of Rh-positive blood, the second by Rh antigen which was present in the fœtus and inherited from the father. As six donors

* Working on behalf of the Medical Research Council.

out of seven are Rh-positive, a person who has made the antibody is likely, if transfused, to be given incompatible Rh-positive blood, and when an antigen such as Rh and its corresponding antibody are brought together in the circulation, hæmolysis of the injected cells will nearly always occur. When transfusion reactions shown to be due to anti-Rh were found in the mothers of babies suffering from hæmolytic disease of the newborn, the connection between immunisation of the mother and this disease of the baby was quickly realised. According to Levine, Burnham, Katzin and Vogel (1941) it results from the iso-immunisation of the mother by a red cell antigen which she lacks, but which the child has inherited from the father, and the subsequent passage through the placenta of the resulting antibody to act on the susceptible blood of the fœtus. Iso-immunisation is the immunisation of one member of a species by an antigen absent in himself, but present naturally in another member of the species.

In three large series of cases, involving 251 mothers, described by Levine, Burnham, Katzin and Vogel (1941), Boorman, Dodd and Mollison (1942), and Race, Taylor, Cappell, and McFarlane (1943), it has been found that 90 per cent. of the mothers of erythroblastotic babies are Rh-negative, and that the sera of a large proportion of these Rh-negative mothers contain an antibody to the Rh factor. Whenever it has been possible to test the blood of an affected child of an Rh-negative mother the child has been Rh-positive. That 90 per cent. of these mothers are Rh-negative, when only 15 per cent. of the normal population are negative, is in itself so overwhelmingly significant statistically, that a connection between the Rh factor and the disease can scarcely be doubted, even apart from the evidence provided by the finding of the antibody in many of the cases. In some women anti-Rh persists for years after the last pregnancy, and may cause trouble if Rh-positive blood is transfused.

In the 10 per cent. of cases where the mother is Rh-positive it seems that some other red cell antigen such as A, B, O, M, N or P must be responsible. Of the antibodies to these antigens only anti-A and anti-B occur regularly in human sera under normal conditions, and there is evidence that their strength may be increased in a woman bearing a fœtus containing the appropriate antigen. The sub-group antibody alpha$_1$ occurs, usually in small amount, in the sera of 25-30 per cent. of A_2B, and in something like 2 per cent. of A_2 persons (Taylor, Race, Prior and Ikin, 1942a). The other sub-group antibody anti-O, often and unfortunately called alpha$_2$, because it clumps the cells of most A_2 donors, occurs but very rarely in human sera, and the same is true of anti-P, which is Landsteiner's extra-agglutinin No. 1. As far as we know only nine (or perhaps ten) human sera containing anti-M, and one with anti-N, have so far been met (see special list of references). In seven the anti-M appears to have occurred spontaneously; whilst in two it arose from iso-immunisation to blood transfusion, as did the anti-N. Any of the above antigens, or some unknown and uncharted one, may possibly give rise to iso-immunisation and lead to a transfusion reaction, or to erythroblastosis fœtalis. Even when a mother is Rh-positive she and her children are not certain to be free from trouble due to Rh. Erythroblastosis fœtalis has been caused by an Rh-positive mother making a sort of anti-Rh which clumps the red cells of all Rh-negative and those of many Rh-positive persons, including her child's. This unusual type of agglutinin, because it works, as it were, the other way round from anti-Rh, has been called anti-Hr. Some workers have found a high proportion of Rh-negative men among the husbands of Rh-positive mothers of affected children, and it is possible that many cases with positive mothers are due to anti-Hr, but to produce an antibody which reacts with Rh-negatives the father need not be Rh-negative; it has arisen when the father and fœtus were Rh-positive (Race and Taylor, 1943). One person in seven is Rh-negative; in one mating in eight the mother is Rh-negative and the father positive; and in one pregnancy in ten the mother is Rh-negative and the fœtus positive; whilst in one pregnancy in five the mother's serum contains an agglutinin for an antigen of the A-B-O groups present in her fœtus; and in such a heterospecific pregnancy the mother's natural iso-agglutinins might, perhaps, destroy her child's red cells. Hæmolytic disease seems to occur once in about 400 pregnancies; that is in only a very few where the blood groups make it possible; so other factors, not yet understood, must be concerned. First-born children usually escape, perhaps because the antigenic stimulus of more than one pregnancy may, in most cases, be needed to produce enough antibody. Race, Taylor, Cappell and McFarlane (1943) found that of six Rh-positive mothers four had first children with the disease, and they suggested that the earlier onset in this group might be due, if the A-B-O system of groups were responsible, to the iso-agglutinins being already present in the mother's serum.

It has been suggested that the naturally occurring maternal iso-agglutinins anti-A and anti-B do not regularly damage fœtal red blood cells which contain the corresponding antigens, because A and B occur not only in the red cells, but also in many of the tissue cells, and in most body fluids including plasma, and this extra-corpuscular store of antigen takes the strain from the red cells by neutralising most of the iso-agglutinins which normally pass across the placenta to the fœtus. People may be divided into two types according to whether the saliva contains in considerable amount the antigens of the A-B-O group to which they belong (secretors), or lacks them almost entirely (non-secretors). In secretors the group antigens are present in most other body fluids besides saliva, e.g., tears, urine, semen, milk, but not in cerebro-spinal fluid; in non-secretors the body fluids contain practically none. According to Hartmann (1941) the antigens occur in alcohol-soluble form in the red cells and in most tissues of both secretors and non-secretors, and also in a water-soluble form in secretors only: this explains their absence from the body fluids of non-secretors. The ability to secrete

A, B or O is a dominant character and its inheritance is quite independent of that of the groups themselves. It is not generally realised that O is itself antigenic and more than merely an absence of A and B; O is secreted in the saliva, but it is only a poor antigen, and anti-O occurs in human serum very rarely.

American workers have failed to find the Rh antigen outside the red cells and have attributed to this absence of extra-corpuscular Rh the damaging effects of anti-Rh on the fœtal blood. But Boorman and Dodd (1943) state that the Rh substance is widely distributed in the tissues and almost entirely absent from body fluids. They suggest that the neutralisation of maternal iso-agglutinins which cross the placenta depends, for the most part, on antigens in the fœtal body fluids and little, if at all, on those in the tissues, and ascribe the destruction caused by anti-Rh to the scantiness of the Rh-antigen in the body fluids.

It appears likely that the lack of A and B antigens in the body fluids of non-secretors may be concerned in the causation of those cases of hæmolytic disease due to the A and B factors. About one person in five is a non-secretor and, as mentioned above, in one pregnancy in five the mother has an antibody for A or B present in her fœtus, so the combination of heterospecific pregnancy and non-secretor fœtus happens once in about twenty-five times.

A total of 100 normal families have been tested by Landsteiner and Wiener (1941), and by Wiener and Sonn (1943). They showed that the Rh factor is inherited as a Mendelian dominant character with three genotypes RhRh, Rhrh and rhrh, the first two of which appear as Rh-positive since the gene Rh determining the presence of the factor is dominant to rh that determining its absence, whilst rhrh is Rh-negative. A question asked with increasing frequency nowadays concerns the chances of an unaffected child being borne by an Rh-negative mother who has had one or more erythroblastotic children. If the Rh-positive husband is homozygous (RhRh) all subsequent children will be almost certainly affected, for they will be Rh-positive; very occasionally a later Rh-positive child is born apparently normal. If the father is heterozygous (Rhrh) each child will have an even chance of being Rh-negative and of escaping the disease. But in families in which the disease occurred, Race, Taylor, Cappell and McFarlane (1943) have noted a marked scarcity of Rh-negative children, which may be, they think, explained by the majority of the fathers being homozygous. The mother is more likely to be immunised when every pregnancy provides the antigenic stimulus, as it does with a homozygous husband, than when he is heterozygous and some of the children are positive and others negative. If the father has been shown to be heterozygous by his producing an Rh-negative child, or by having an Rh-negative parent, the chance of the next child being negative and unaffected is one in two, but in the absence of this indication the outlook is very unfavourable.

There exist Rh sub-groups, somewhat similar to those of the A-B-O groups, and the variants of the Rh factor seem to be determined by a series of allelomorphic genes. Whilst the position is not yet fully elucidated it is proving possible to recognise, by serological tests, the genotypes of a large proportion of people, and so increase considerably the knowledge on which to base an estimate of the chances of unaffected children being born to couples who have had erythroblastotic babies (see Race and Taylor, 1943; and Race, Taylor, Boorman and Dodd, 1943).

Transfusion Reactions

The Rh factor is of great importance and it is being shown to be the cause of many transfusion reactions which would previously have gone unexplained. But incompatibility is far from being the only cause of transfusion reactions, and Rh is not the only cause of incompatibility. The antigens and antibodies of the A-B-O system of groups are potentially far more dangerous, and will lead to far more reactions unless the grouping is accurate. It seems that A and B are regularly antigenic for man, and that when, owing to some mistake, a recipient is given blood cells with an antigen for which his plasma contains the antibody, there will be a reaction ranging in intensity from the very mildest, which may not be noticed, to one severe enough to kill. In any case, if the recipient survives, the antibody in his plasma will, within a week or ten days, almost certainly be enormously increased so that another transfusion from the same, or another donor of like group will be fraught with the gravest danger. Similarly, a recipient may be immunised against a sub-group antigen and trouble arise at a later transfusion, although first-transfusion reactions, due to the sub-groups, are not of much importance, because the antibodies concerned are seldom present in large amounts. The antigens M and N can be regarded as practically non-antigenic for man. As mentioned above, only two cases of human anti-M and one of anti-N, due to transfusion, have been found. Anti-P is Landsteiner's extra-agglutinin No. 1, and occurs but rarely in human serum. As a cause of incompatibility Rh is much commoner than the sub-group and the M, N and P antigens. When Rh-positive blood is given to some Rh-negative recipients the body seems to recognise it as foreign and eliminates it. At a first transfusion the hæmolysis may be so gradual as to be unsuspected, but following this "silent" reaction Rh antibodies may be formed and cause at a later transfusion the most serious reaction.

What has been said makes obvious the need for the following procedures:

(1) Most careful and complete A-B-O grouping in every case.
(2) Avoidance of using the same donor more than once for any one recipient, because of the possibility that the latter may make an antibody to some rare and irregular antigen in the donor's cells.
(3) Careful direct matching of the recipient's serum and the cells of intended donors, and when this cannot be done adequately only group O (universal donor) blood should be given.

(4) When the recipient has been transfused before, or is a woman in whose blood there is reason to suspect there may be anti-Rh, the blood should, if possible, be examined for the Rh factor and its antibody, and if it is Rh-negative only Rh-negative blood of suitable A-B-O group should be given. Ideally, the recipient's serum should be tested against the cells of any intended donor by a tube method similar to that to be described.

In connection with testing the blood of a patient recently transfused, it should be remembered that the transfused cells may be of different group from those of the recipient and lead to a grouping error; thus anti-Rh serum will agglutinate Rh-positive donor cells in an Rh-negative person's blood, whilst the donor cells may neutralise any anti-Rh in the recipient's serum. The cause of an incompatible transfusion may, in this way, be masked. Examination of a sample of the patient's blood taken before the transfusion, and of the blood transfused, should clear up a case of suspected incompatibility. Nearly always, unfortunately, these specimens are not available; they should be kept until it is certain that the transfusion has been entirely satisfactory. Examination of the post-transfusion blood of the recipient alone may, by the method of differential agglutination (see Wiener, 1942, and Mollison, 1943), show that blood of more than one sort is present and disclose incompatibility. Antibody removed from the recipient's serum by donor cells may be again detectable in samples taken a week or ten days after the transfusion.

(5) When the need for transfusion is urgent, and the position as regards compatibility is uncertain, it may be a good plan to begin a transfusion of serum or plasma whilst the necessary tests are being made.

To deal with the risk of incompatibility due to the Rh factor, it has been suggested that only Rh-negative blood should be given to women transfused in connection with pregnancy. This would eliminate the risk almost entirely, but knowledge of the recently discovered anti-Hr agglutinins shows that Rh-negative blood would not be compatible for some women.

(To be continued)

CRITICAL DIAGNOSIS

By S. WATSON SMITH, M.D., F.R.C.P.(Edin.), F.R.C.P.(Lond.),
Hon. Consulting Physician, Royal Victoria and West Hants Hospital, Bournemouth.

"Ad sanitatem gradus est novisse morbum."

"It is a step towards health to know what the disease is." If all diseases were commonplace, diagnosis would present little difficulty; but it is not so, and though obstacles will occur to be overcome, it takes courage on the part of the clinician to refuse to commit himself to any diagnosis. The wisest among doctors will not label a particular patient where doubts and questionings occur to forbid it; and rightly so, because it is nobler this than to risk being at fault or wrong, so to add to the patient's troubles. To affix a misleading or uncertain diagnostic label is more often than not unpardonable, even if forced by the importunity of an anxious relative demanding to know "what's wrong" before the medical man has had time and opportunity to possess himself of all the facts of the case upon which to make a decision.

The science and art of diagnosis is toilsome and perplexing at times. For bedside work—the most important part of the doctor's day's work—a good knowledge of clinical medicine is necessary, and an acquaintance with the elements of logic will repay itself. In most instances of mistaken or wrong diagnosis, the underlying error is found to be one of omission rather than of commission, from lack of method with failed attention and observation in the taking of the case. On occasions, the haste and hurry that pursues all doctors, may well have consequences little short of lamentable.

Casting one's thoughts backward brings into mind a number of instances where diagnosis proved to be erroneous. Fortunately, these have not perhaps been many, but are imprinted on the memory when other presumably correct diagnoses are forgotten.

Although we know that medical men are no more infallible than others, in our innermost consciences we feel blameworthy, even guilty, refusing to adopt the attitude of excusing ourselves for giving insufficient time and care to the work.

In infancy and childhood, acute infection commonly gives rise to sudden sharp reaction and illness with much anxiety on the part of parents who, in their fear, demand to be told "what is wrong" before signs and symptoms have made any diagnosis possible. A provisional diagnosis of pyrexia, symptom only as this is, often satisfies, giving the doctor time to marshal all the clinical facts of the case. Yet, even if the truth is blunt, it should be told.

One great error of omission in dealing with children is failure to complete the physical examination by inspecting tonsils and pharynx, taking a throat swab if any departure from the normal is discovered.

Then, again, in young children, tracheo-bronchial adenitis has to be kept in mind as a possible cause of acute illness—not a clearly defined disease by any means. It is surprising, too, how an appendix abscess in a child can be missed by failure to examine per rectum—too common an omission at any age in any patient.

No patient is properly examined unless the urine is tested, and a blood film taken for staining and microscopic examination.

Even eosinophilia will indirectly disclose the presence of parasitic disease or of incipient spasmodic asthma. Where in the child there is abdominal colic, the skin should be examined for purpura; laparotomy has been inadvertently done even in Henoch's purpura.

In later childhood, acute rheumatism may be subtle in its manifestations: vague pains, malaise, disinclination for effort, and persistent tachycardia, with a fluctuating temperature, may be indicative of an established rheumatic pancarditis.

In the adolescent, tuberculous disease may excite a persistent tachycardia which, even taken alone, will differentiate from any of the typhoids where, in the uncomplicated, there is slowing of the pulse rate. At the same time, general tuberculosis may present a critical problem in differentiation until a deepening cyanosis with late appearance of physical signs in the lungs settles the diagnosis.

In the adult, care should be taken these days to enquire as to the previous taking of drugs, because herein may lie the explanation of cyanosis, of unusual skin eruptions, even of agranulocytosis. Self-medication with the sulphonamides is known these days; or, it may be that the drug has been taken for a recent illness, ordered by another doctor.

In stout middle-aged women, complaint of high abdominal pain and of flatulence will suggest the commonest abdominal trouble at that time of life, namely, cholecystitis; and here it should be mentioned that an X-ray diagnosis of gall-stones, without clinical evidence, may prove to be wrong when cholecystostomy is done.

In any patient, at any age, we would offer a plea for clinical proof, using laboratory or X-ray evidence only for confirmation or otherwise, not as a short cut to diagnosis. It is a well-known fact that X-ray evidence in any patient, taken alone and acted upon, invites disaster.

Again, diaphragmatic pain which is referred to the abdomen may wrongly be ascribed to appendicitis (and operation done) when in reality the cause is a right thoracic empyema.

Some time ago, a patient presented himself with the complaint that he had felt ill for a week, during which time he had continued his employment as a commercial traveller, moving from town to town. He had felt himself becoming gradually weaker in the few days, and had had several attacks of nose bleeding. He was a stout man of 40 years, with "pink and white" complexion, and was found to have a large, soft spleen. Suspecting blood disease, an immediate blood examination was made, only to disclose an acute lymphatic leukæmia from which he died some ten days later.

On one occasion a young farmer came who presented all the signs of spinal cord compression. After determining the level of the likely neoplasm, I asked a surgeon to do laminectomy, indicating the level at which this might be done. At operation, when the theca was exposed and incised, no tumour was found. On my request that the incision might be extended upwards, a medium marble-sized tumour extruded itself on to the surface at the upper angle of the incision. With healing of the operation wound, recovery was complete. In locating a lesion, the fact of spinal cord segments lying at a level higher than the corresponding vertebræ is to be remembered.

A not uncommon mistake which may have very serious consequences for both doctor and patient is to declare a young or middle-aged unmarried woman to be pregnant when, in fact, she has a large, more or less centrally placed, ovarian cyst. One has even seen the opposite happen—when a pregnant uterus has been believed to be an ovarian cyst. The error may only be discovered on laparotomy. If there is the shadow of doubt, examination under an anæsthetic or by X-ray photography will speedily decide the truth. The possibility of such a mistake happening has to be borne in mind.

In uræmia, before the onset of coma, complaint of intense pain in the epigastrium is not unusual. In men past middle life abdominal pain with persistent vomiting, and absence of other signs, even with a blood urea within normal limits and a urine clinically not unhealthy, may result from a latent uræmia: in one such case known to me, laparotomy was done which only hastened the patient's death; nothing was found to be amiss at operation.

Certain hernias are not easily diagnosable. A small, strangulated femoral hernia may be mistaken for an enlarged lymphatic gland, and valuable time lost; but that most difficult to diagnose is the rare obturator hernia. The only example I ever saw was promptly diagnosed by a senior surgeon who remembered having seen a similar case many years before. This same surgeon, wise in his generation, never by any chance did a laparotomy without first venturing a diagnosis; he was never known to say: "Oh! Wait till we get inside."

In the elderly, failure of structure, so of function, sometimes sudden, more often gradual, is to be expected; particularly after the sixth decade of life, long-lasting chronic infections and degenerative processes, commonly cardio-vascular in the beginning, are to be looked for. Diagnosis here is not "cut-and-dry"; it is not enough to name the disease, but underlying pathological processes must be watched and followed from day to day if treatment is to have any degree of success. Even the patient's general strength should be estimated by noting his decubitus, ability to help himself, and *strength of voice*. A weakening or failed voice is of value, too, as a reliable bad prognostic.

There are two conditions affecting the elderly not always at once obvious, namely, cerebral thrombosis in local areas, and degenerative myocarditis. Patients suffering from either of these may need close observation for several days before a confirmed diagnosis can be made. At ages 50-60 commonly, local arterio-sclerosis in the coronary vessels of the heart may precipitate a coronary thrombosis which, because of "angina abdominis" may be mistaken for indigestion—a fatal mistake.

A senile disability about which comparatively little has been said or written is senile paraplegia, which is of commoner occurrence than is generally supposed, happening at any age after 60 years. The chief deciding factor in the diagnosis here is the loss of muscular power and of balance, and a feeling of weakness and insecurity in the lower limbs with consequent shuffling or faltering gait. The signs, though often equivocal, are those of a progressive lower motor neurone paresis or paralysis, with failing sensation. The mischief appears to have its beginning in a degenerative arterio-sclerosis of spinal vessels.

In the practice of clinical medicine, without correct diagnosis—which is not always by any means easy—all else fails. Only with sure and certain diagnosis can treatment succeed. How can

In the cookery classes, the number of girls who could weigh half a pound of sugar correctly was not 50 per cent., whilst the number of those who could weigh and mix three ingredients correctly was not 25 per cent.! These are the future men and women, the fathers and mothers of the future, regarding whom such wonderful statements have been made in connection with their needs, desires and capacities for choosing their own "panel" doctors, to say nothing of their teachers and preachers.

It is well known that most husbands have their "doctors" chosen for them by their wives who, on the advice of female friends, call in so-and-so because he is so nice, or his bedroom manners are so good.

When 50 per cent. of the people are incapable of measuring things by a physical standard, how can they be expected to do so by abstract moral or religious standards? In days gone by we used to be warned against judging cigars by the picture on the box, and a similar warning might be issued regarding the purchase of patent foods and medicines with which this country has been flooded.

Personally, I hold that the control of the national health should be in the hands of a Ministry where agricultural, veterinary and medical officers formed a special section to superintend the health of the land, animals and human beings. In order to secure a good national body of such officers, admission to each of the professions should be by means of one State examination in agriculture, veterinary or medical science. Teachers in secondary schools are required to hold good honours degrees, and if such a good standard is necessary for teaching purposes surely a still higher one is needed for those who have to deal with the "National Health." As long as the national health of land, animal and man depends on professional competition, to secure in the first place an adequate income and, as a consequence, to knock other practitioners out of the running, so long will our national health remain on an unsatisfactory basis. Such a state of things means that the first few years of a medical practitioner are spent in striving for this financial foothold, instead of utilising his recently acquired knowledge to the best advantage. If, however, we place the members of these three professions on a sane and sound financial footing, so that they can combine to raise our national health, I am convinced that an increased percentage of the population will be able to rearrange its present-day rhythm, and to live much more sane, healthy and happy lives.

THE Rh BLOOD GROUP FACTOR—II

By G. L. TAYLOR,* M.D., Ph.D., M.R.C.P., and R. R. RACE,* M.R.C.S., L.R.C.P.

The Galton Laboratory Serum Unit, Department of Pathology, Cambridge.

(*Continued from page* 89)

Hæmolytic Disease of the Newborn

No method is known of preventing anti-Rh in an Rh-negative mother's serum from harming her Rh-positive fœtus. If in future a poylsaccharide responsible for the specificity of the Rh antigen can be isolated, its injection into the mother may neutralise the antibody and prevent or diminish its harmful effects on the fœtus. Although no treatment is possible before delivery, steps can be taken during pregnancy to ensure that proper treatment is available, if it is needed, for either baby or mother after the confinement. Ideally, the Rh position would be investigated in every pregnancy. The discovery of anti-Hr agglutinins has shown that an Rh-positive woman and her children are not certain to be free from trouble caused by Rh. Nevertheless, 90 per cent. of erythroblastotic babies have Rh-negative mothers, and when a woman is Rh-negative it is wise to remember this. It should not be forgotten that an Rh-negative person may be immunised to some antigen other than Rh. At present, investigations are confined almost entirely to families where erythroblastosis has occurred, or is suspected, or where there has been a series of miscarriages or stillbirths. Samples of blood from the mother and, if possible, from the father and all the children should be tested for the A-B-O and Rh factors, and the mother's serum examined for anti-Rh and other irregular agglutinins. When the history is suggestive, and the mother Rh-negative, and father positive, trouble is likely, and finding anti-Rh in her serum makes it almost certain. Failure to find anti-Rh on one occasion does not mean that it will not be present later in pregnancy, and it is a good plan to test for it at intervals. After confinement it may be undetectable for a few days and be found after a week or ten days and then disappear, but it may persist for months or years. In a few cases it can be detected in the child's blood for a short time after birth. When the tests show that the mother's serum may contain an irregular agglutinin it should be arranged that blood of suitable group is available, in case it is needed either for the newly-born baby or the mother. Most commonly, Rh-negative blood will be needed and, since before birth the baby's group will not be known, universal donor blood (group O), either in the blood bank or in a donor readily accessible, should be available; this blood would also be suitable for the mother.

Knowledge of the connection between isoimmunisation of the mother, and hæmolytic disease of the newborn, has suggested the treatment of the child by transfusion of blood lacking the antigen for which the mother has made the agglutinin, and this treatment seems full of promise. In the past, attempts to replace by transfusion the child's blood destroyed by lysis, have not been very successful. Nearly always it is the Rh factor which is involved, and the lysis is due to the baby's Rh-positive cells reacting with the antibody made by its Rh-negative mother, and as six out of seven donors are Rh-positive and untested blood was used, mostly positive blood was given, and this, like the child's own, was liable to be destroyed. As soon as hæmolytic disease is diagnosed—and with a previous or suggestive history, cord blood should be examined for erythroblastosis—the child should be transfused

* Working on behalf of the Medical Research Council.

with O Rh-negative blood, into the veins, not into the muscles. Successful transfusions into the bone marrow of the tibia have been recently reported. The mother's whole blood, although Rh-negative, should not be used, as the plasma will almost certainly contain the harmful antibody. If no other negative blood is available, and the A-B-O groups permit, the mother's cells washed free from plasma may be given. If Rh-negative blood cannot be obtained, and the need for transfusion is urgent, blood from an O donor, taken at random, can be used, but it will probably be Rh-positive and may cause a transient jaundice. The father should not be the donor, and Rh-negative blood is more likely to be found amongst the wife's, than amongst the husband's, relatives. As anti-Rh can be found in the mother's milk, the child should be taken from the breast. Gimson (1943) has been able to compare a series of affected babies treated with Rh-negative blood with a very similar series given blood which, untested for the Rh factor, would nearly always be Rh-positive. In 14 of the 18 cases treated with negative blood the results are described as "perfect"; the other four regained and maintained normal blood pictures; no more than two transfusions of negative blood were needed in any case. Of 17 treated with blood not tested for Rh, six died from the disease or from transfusion, four were kept alive, but without improvement in the blood condition, and only seven did satisfactorily, although they received much more blood —up to six transfusions in some cases—than the 18 cases treated with negative blood. Moreover, no reactions followed the giving of negative blood, but in the other series, more often than not, there was a rise of temperature and some constitutional disturbance with increase of jaundice and size of liver and spleen. When Rh-positive blood was given there was an initial rise in hæmoglobin and red cells, but lysis went on and, within a few days, further transfusion was needed. Rh-negative blood does not prevent hæmolysis of the child's own cells, it merely provides cells which will not be destroyed more rapidly than normal, and on which the child may live until the lytic process ends. Some babies were given a mixture of Rh-positive and negative blood; the negative cells survived normally, whilst the positive were often destroyed within a few days. It is well known that some cases, even of icterus gravis, recover without treatment, but the mortality seems to be about 75-80 per cent. (Gimson, 1943; Race, Taylor, Cappell and McFarlane, 1943). Treatment with Rh-negative blood is most encouraging, and if a baby lives long enough to receive it, there is an excellent chance of its survival. Gimson is not hopeful that transfusion will influence kernicterus, which, it is suggested by McIntosh (1941), occurs in 10 per cent. of affected children, and which may be followed by mental and other afflictions.

The principles governing the management of transfusion and hæmolytic disease where isoimmunisation of an Rh-negative person to Rh has taken place, should be applicable to cases where some antigen other than Rh is responsible.

Tests for the Rh Factor and its Antibody

The presence of Rh antigen is detected by the red blood cells containing it being agglutinated when they are mixed with a serum in which there is the corresponding anti-Rh agglutinin. There are two sources of grouping sera:

(1) animal sera: serum of an animal injected with the red blood cells of the Rhesus monkey, and so far rabbits and guinea-pigs have been used. The preparation and use of animal sera is difficult.

(2) Human sera: anti-Rh may be found in the serum of the mother of an erythroblastotic baby and in the serum of a person who has had a hæmolytic transfusion reaction due to Rh and, if people who had been given transfusions, or women who had ever been pregnant were examined, some might be found in whose serum there was anti-Rh in amount large enough to make it a good reagent. Only a small proportion of human anti-Rh sera are strong enough to be used as reagents, for some Rh-positive cells react very weakly and unless a good serum is used they may be recorded as negative. Human sera will probably prove the most convenient reagents and most of them will come from mothers of erythroblastotic babies.

Detecting anti-Rh in serum. Our present procedure is:

Serum is heated for 15 minutes at 56°C., as Wiener recommends, for some sera before heating fail to react properly with some Rh-positive cells. The serum is tested with cells from at least two positive donors chosen to cover the range of the different forms of Rh and the other known irregular agglutinins, those for O, M, N and P, with negative cells, and with cells from the donor of the serum; some sera agglutinate their own cells and this is a necessary control. Known positive and negative cells should be of group O to avoid the possibility of reactions due to the A-B-O system of groups. Most workers make grouping tests on a slide, tile or plate, but although very strong sera may give a slight reaction after fifteen to twenty minutes on a slide, tubes are essential for Rh work. With a Pasteur pipette and an india-rubber teat we deliver known volumes of reagents. The stem is marked rather crudely with grease pencil or waterproof ink to deliver about 0.04 c.c. Our tubes are 2in. by ¾in. diam., without lip, and in them we make series of falling dilutions of serum. In the first tube the serum is undiluted; in the second, 1 :2, in the third, 1 :4 and so on for 4 or 5 tubes. Into every tube except the first we place a volume of physiological saline solution; the first receives a volume of undiluted serum. With the saline in tube 2 we mix a volume of serum, getting two volumes of 1 :2, one of which we add to tube 3 getting two volumes of 1 :4, and continue this doubling up until every tube gets its dilution. One of the two volumes in the last tube is discarded. To each tube we add a volume of red cell suspension (1-2 per cent. whole blood) of a strongly positive donor. Cells and serum are mixed by flicking the tube with

the finger, and on each tube is placed a glass cap to prevent evaporation and serve as a place-marker in reading tests. To other identical series are added cells from a second positive person, negative cells and the cells of the donor of the serum. If the donor is the mother of an erythroblastotic baby, and if the A-B-O groups permit, and if we have the cells we also titrate the serum with cells from the baby and the father. The tests are stored at room temperature and an identical set in the incubator at 37°C. Some human anti-Rh sera are said to work better at room, others at body, temperature. The great majority are better at body than at room temperature.

After an hour, or better after two, the tests are read. Whilst they have been standing the red cells have settled to the bottom of the tube, and the shape and nature of the sediment give a good idea as to whether clumping has taken place or not. Positive sediments present a variety of appearances: granularity, waviness, irregular or serrated margin, etc., whilst negative sediments are small and compact with a regular margin, and occasionally with a bull's-eye appearance. The cap is taken from the tube and the sediment may be examined with a hand lens in a good light, but the final diagnosis is based on a microscopic examination of the sediment, and the greatest care and gentleness are needed in transferring some to a microscope slide because the slighest roughness may be enough to undo a weakly positive reaction, and a false negative may be recorded. A little of the sediment and of the overlying fluid is transferred with the pipette to a slide and touched very lightly with the stem of the pipette just enough to make it readable under a low power of the microscope. When good reactions have taken place there is no difficulty in seeing them; it is the more weakly reacting cells which cause trouble and doubt. An inexperienced reader may diagnose a negative as positive. In sedimenting, the cells have aggregated, but not in the specific way we associate with agglutination. There may be under the microscope a smear or drift of aggregated cells with perhaps lumps which may suggest a positive reaction. The field on either side of the drift will be quite negative and the drift will gradually break up. Or there may be biggish aggregates in a sea of unagglutinated cells, but they are quite different from the clumps of true agglutination. A little experience will enable a worker to differentiate these aggregates from true agglutination. It is, however, possible to record false positives in Rh work due to the same causes as false positives met in grouping for other factors, e.g., some anti-Rh sera may lead to rouleaux formation and it may be necessary to add a volume of saline to the volumes of serum and cell suspension.

Some set up only the top tubes of a series, but we prefer titration, because: (1) it indicates the strength of any antibody present; (2) Taylor, Race, Prior and Ikin (1942b) have found a serum which, undiluted, failed to react with some positive cells, but which, in titration, gave definite reactions in some dilutions. Without titration, incompatibility between such a serum and the cells of intended donors might be missed.

When tests suggest that anti-Rh is present we mix the serum with positive cells from four or five other donors, and with one or two lots of negative cells, and if it reacts with all, or nearly all, the positives, and not with any negatives, it seems certain that anti-Rh is present, and, indeed, when all the positives react and the negatives fail to, a simple sum gives exactly the odds that the serum contains anti-Rh. When the reactions given by a known and an unknown antibody and the same panel of red cells are identical, the probability that the apparent identity of the two antibodies is due entirely to chance is given by the formula $\frac{a!\,b!}{n!}$*, where n is the number in the panel and a and b the numbers of positive and negative reactors. We advise this titration technique in direct compatibility tests between recipient's serum and potential donors' cells, and we would not use any donor whose cells gave the slightest sign of a reaction.

With good sera, red cells can be grouped for Rh by methods similar to those described. Titration is not needed, and a serum which required titration would not be used. A volume of serum is mixed with a volume of red cells, and to avoid any tendency a serum may have to give false agglutination, a volume of saline is added. Tests are stored at room or incubator temperature according to which is better for the sera in use. Bringing together antibodies and antigens of the A-B-O groups should be avoided, otherwise the Rh grouping cannot be done. Anti-A or anti-B in a serum can be absorbed by mixture with appropriate cells, e.g., group A Rh-negative cells will remove anti-A and leave anti-Rh. Mixing the serum with the saliva of a person who secretes the appropriate antigen will also remove the A-B-O antibodies. About 80 per cent. of people secrete in the saliva the A-B-O antigens present in their red cells. With a supply of Rh sera from all the four blood groups a worker need not absorb, he can choose those appropriate for the cells he is testing.

No cells should be diagnosed as negative unless they have been tested with at least three strong anti-Rh sera. Some sera react well with all but a few Rh-positive cells. One may react well with the cells of x and poorly with those of y, whilst another does well with y and badly with x. If a serum tends to give slight false positive reactions, reference to the reactions given by other sera will help diagnosis.

Rh testing is tricky and needs considerable experience, but it will become less troublesome when we get good supplies of really strong sera, and for these we must look to the clinicians who are in charge of the mothers of erythroblastotic babies.

*(6! = 6 x 5 x 4 x 3 x 2 x 1 = 720).

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THE COMMON COLD

By SYDNEY LINFOOT, B.Sc.(Gen.), B.Sc.(Phys.), A.M.I.Chem.E.

Director, The Lexden Laboratories, London.

(Accepted as a thesis for the degree of Ph.D.)

THE common cold is the cause of more ill-health in this country than all other diseases, yet its very frequency and the rarity of a really serious outcome occurring has tended to cause most people to ignore the seriousness of the disease and its effect on our general health, our mental ability and our well-being.

There have been quite well-defined lines of attack, most of them based on the assumption that the origin is bacterial, and the cold caused by a germ. We will consider these approaches to the subject. A tremendous amount of work in the laboratory has been performed. Most of it has been directed to discover some particular organism which can justifiably be blamed for producing the symptoms we know so well.

Organisms isolated from the respiratory tract which have shared the blame to a greater or less degree include micrococcus catarrhalis, bacillus Freidlander, pneumococci, streptococci of all types, B. influenza (Pfeiffer) and many others. No one organism has yet been stated to be the sole culprit. If no one organism could be blamed, then it was assumed with apparently some justification that it might be, and probably was, any one of a very large number. As it was obviously impossible to attempt to isolate from each individual commencing with a cold the particular organism responsible, and make an autogenous vaccine, it seemed sensible to prepare some type of a vaccine which could be used to protect against colds, having their origin in the presence of one or more of these organisms. This was the start of the vaccine theory of treatment. A polyvalent vaccine was prepared from all the organisms isolated from the respiratory passages of a large number of people suffering from colds. The vaccine has been somewhat of a disappointment, however, because it was found that although a few cases did improve, they were only a small percentage. It was, therefore, hoped that the vaccine would prove to be an efficient prophylactic. In a few, but again only a few, cases, some measure of protection was obtained. The protection was, however, uncertain and doubtful in the length of time it would exist. Varying doses were given, ranging in the average case where prophylaxis was to be assured, from one million organisms per c.c. to one thousand or one thousand five hundred million per c.c. The course of treatment in most cases necessitated a large number of injections, although some physicians assumed hopefully that three doses of one hundred, five hundred, and one thousand million organisms would be satisfactory. All these methods have been, unfortunately, doomed to fail.

The next step was the discovery of an "influenza virus." The discovery of the virus of influenza was hailed as a real step forward. Unfortunately, the treatment, which has been based on the discovery of the alleged cause, has not proved markedly more successful than the "vaccine cure," and it is doubtful if any permanent and satisfactory cure has been obtained from the use of preparations made from the influenza virus. The only remaining hope now seems to be that:

(*a*) Either a new method of administration can be introduced, or

(*b*) that a new and unsuspected causal germ be discovered.

Both these hopes appear to me to be certain to fail. The question has been approached at the beginning from false grounds, with the assumption that an organism existing in the respiratory tract is the cause in every case. We must, therefore, make a fresh beginning from a different basis. If we ignore the respiratory organisms as a possible root cause, it seems that the only other cause can be organisms which live and increase in the intestinal canal.[8] Let us assume that such an organism or organisms do exist. How could they produce the symptoms which are familiar to all? They could perhaps produce a toxin which would be released into the blood-stream. The cold would then be simply a poisoning effect carried in the blood-stream to the mucous membrane of the nose and throat. The toxin could with some justification possibly be blamed for the sore throat, the coryza, the sore eyes, the hoarseness of the voice. Unfortunately we do not know of any pathogenic organism in the bowel, which is only present in patients suffering from a cold, except the common Esch. Coli. Regretfully we must relinquish this theory. There is, however, another method by which these effects could be produced. If the blood-serum of an individual be examined under the microscope with an oil immersion lens, nothing is seen except an adventitious blood-cell or piece of fibrin. Let this examination be now performed with dark ground illumination. At once there are seen to be a large number of particles in Brownian

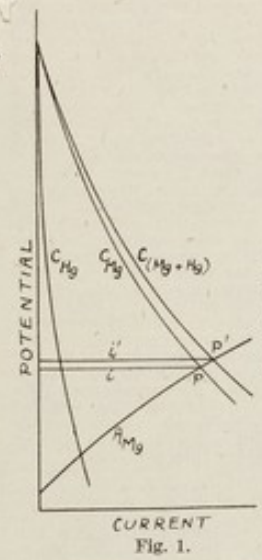

Fig. 1.

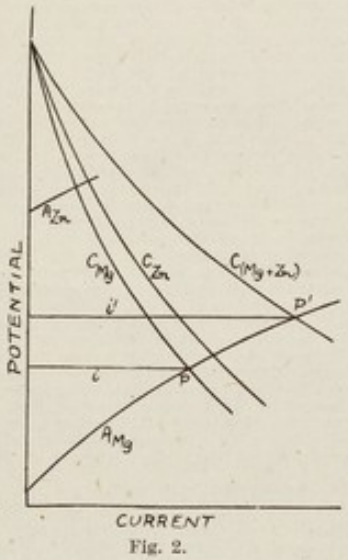

Fig. 2.

greater than i. In Fig. 2, the corresponding case for a zinc-magnesium couple is shown. Here, the much less easily polarizable (low-overvoltage) zinc cathode, curve C_{Zn}, causes a relatively large increase in magnesium corrosion.

In both the above cases, the anodic polarization curves representing the metal dissolution of mercury and zinc respectively—the positions of which depend on the single electrode potentials of the metals—do not need to be considered, because the corroding potential of magnesium is so much less noble (of the order of −1·2 to −1·5 v. on the hydrogen scale[6]) than even the equilibrium single potentials of mercury and zinc (E_H°, +0·799 and −0·762 v. respectively). For metal couples where the two anodic curves are close together, we may sum these in the same way as the cathodic curves and obtain a graphical representation of the more complicated case where anodic and cathodic reactions occur on both metals simultaneously. We may also make allowance for the resistance of the circuit where this is not very small, as here assumed. These constructions and others showing (*a*) the conditions at a pore in a metal-on-metal coating, (*b*) the reason why cadmium (E_H° = −0·402 v.) is usually *anodic* towards iron (E_H° = −0·440 v.) under corrosive conditions, are given in my original paper. The yet more complicated case of trimetallic systems—important in practice where, for example, a zinc protector is used to counteract the harmful action of a cathodic metal in a couple—may also be usefully treated along the same lines; I hope to elaborate this matter elsewhere.

The remark by Messrs. Le Brocq and Cocks that presence of oxygen reduces hydrogen overvoltage may perhaps be more accurately stated: oxygen at a cathode diminishes the total cathodic polarization at any given current-density, by providing the alternative *net* cathodic reactions

$$\tfrac{1}{2}O_2 + H_2O + 2e \rightarrow 2OH^- \text{ or } \tfrac{1}{2}O_2 + 2H^+ + 2e \rightarrow H_2O,$$

which begin at more noble potentials than the reduction of H^+ to H_2. At an oxygen-reduction cathode, there need be no intermediate formation of H or H_2.

T. P. Hoar.

Metallurgical Laboratories,
Cambridge.
Nov. 16.

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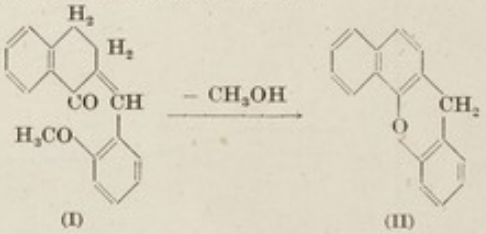
3 : 4-Benzxanthene

o-Methoxybenzaldehyde condensed with α-tetralone in alcoholic potassium hydroxide to give 2-(*o-methoxyben:ylidene*)-*α-tetralone*[1] (I) in faint yellow plates, m.p. 110–111°. When (I) was refluxed with phosphorus pentoxide in xylene for twenty hours, it gave in a poor yield a colourless product (II), m.p. 91–92°, thought to be 8-methoxy-3 : 4-benzfluorene. (II) gave in absolute alcohol a red picrate, m.p. 125–126°.

This compound (II) can be obtained in a much better yield by heating (I) with a fused mixture of potassium hydrogen sulphate and sodium sulphate at 260–270° for three quarters of an hour.

Analysis showed that (II) contains neither methoxyl nor hydroxyl groups. This was supported by the fact that it was insoluble in alkalis and was recovered unchanged on being refluxed with hydriodic acid (d., 1·96) in glacial acetic acid for five hours. It was easily oxidized by different oxidizing agents (selenium dioxide, cold or hot sodium dichromate or potassium permanganate in acetic acid, alkaline potassium ferricyanide and cold chromic acid in acetic acid) to give the same colourless product, m.p. 161–162° (III). This cannot be a 3 : 4-benzfluorenone, as all these compounds are coloured. On drastic oxidation of (II) with a boiling solution of chromic acid in glacial acetic acid, an orange-red compound, m.p. 348°, insoluble in most organic solvents, was obtained; this compound is under investigation.

We found that the melting point and the physical properties of (III) resembled those of 3 : 4-benzxanthone. This identity was ascertained by the fact that no depression of the melting point was observed on admixture with an authentic specimen[2].



(I) (II)

This shows that ring (I) closed under the influence of phosphorus pentoxide or the pyrosulphate, with the elimination of methyl alcohol, to give 3 : 4-benzxanthene (II), which gave on oxidation 3 : 4-benzxanthone (III).

This new method is now applied for the synthesis of substituted 3 : 4-benzxanthenes.

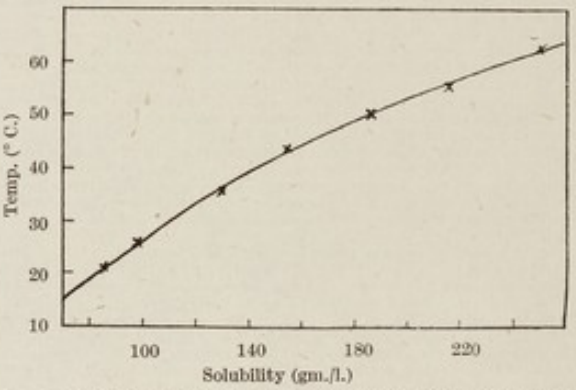
Fawzy Ghali Baddar.
Munir Gindy.

Fouad I University,
Abbassia, Cairo.
Nov. 11.

[1] Rapson, W. S., and Shuttleworth, R. G., *J. Chem. Soc.*, 638 (1940).
[2] Knapp, W., *J. Prakt. Chem.*, **146**, 116 (1936).

Solubility of Pyrocatechol in 1, 2, 4-Xylenol

Local deposits of lignite were worked up under the Germans by low-temperature carbonization and subsequent hydrogenation of tar by means of converted water gas. The water which formed in the course of this process was extracted for phenols and other organic substances by means of isobutyl acetate and the extract worked up by distillation. Phenol and the cresols were obtained in an impure state, the heavier phenolic substances being returned to the hydrogenation process.



In an attempt to obtain pyrocatechol in a pure form it was found that it could only be recrystallized with considerable loss from benzene, but that we had at hand a more efficient solvent in the mixture of xylenols constituting the fraction which distilled before pyrocatechol.

The solubility of pyrocatechol in 1,2,4-xylenol (Merck) was measured and expressed in the accompanying graph. The presence of homo- and isohomo-pyrocatechol does not interfere. Pyrocatechol crystallizes in small plates of a melting point of 102–103° C.

A paper on the composition and separation of the above-mentioned mixture of phenols is in preparation.

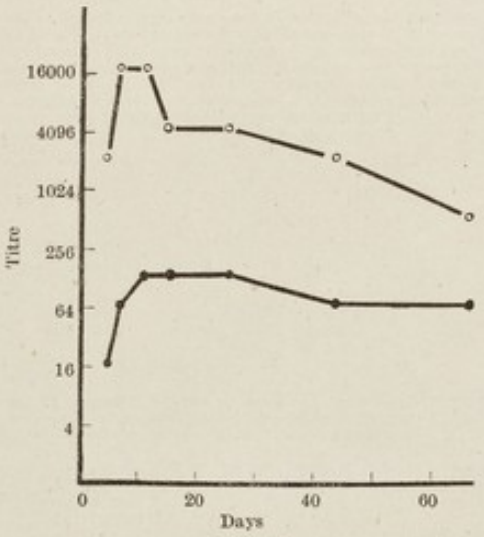
W. Lowenstein.

Czechoslovak Works for the Manufacture of Synthetic Fuels,
By-products Department,
Zaluzi, near Most,
Czechoslovakia.
Dec. 1.

Rh Blocking Antibodies

The detection of *Rh* sensitization in a patient often depends on the detection of *Rh* antibodies. *Rh* agglutinins are most commonly sought, but in certain cases where *Rh* sensitization is anticipated they are not found. In some of these sera, 'incomplete'[1] or 'blocking'[2] antibodies are found.

A mother received 1,000 c.c. of *Rh*-positive blood and was subsequently delivered of a stillborn child affected with congenital hydrops. Samples of blood were first obtained on the fifth day after transfusion. The mother was *Rh*-negative. The maternal serum was examined



●, blocking; ○, 'conglutination'. Blood transfusion at 0 days.

and *Rh* agglutinins were detected in the first two samples, although there was marked zoning. The samples of serum were preserved since 1943 at − 20° C., and later titrated for blocking antibodies (using an anti-Rh_0 test serum titre 1 : 16) and by the 'conglutination' method[3]. The results are shown in the accompanying graph. The two curves are roughly parallel, but do not show a marked peak; this may in part be due to the time elapsing between the examination of samples. The persistence of a high-titre blocking antibody for a long period is shown, since after 18 months it was still 1 : 8.

Rh agglutinins have been known to persist in maternal sera for twelve or more years. In the case cited above, blocking antibodies of titre 1 : 4 were detectable 2½ years later; in another instance they have been known to persist for 18 months.

In 1942 a serum was examined which was known to react with cells eventually classed as Rh_1 and failed to react with Rh_2 type, in fact an anti-Rh_1 serum. Blocking antibody was detected in this serum but was only weakly present in the last sample obtained three months after birth of the affected child. In 1944 a further specimen of maternal serum (there having been no intervening pregnancy) was examined and found to be of anti-*Rh'* variety. This latter serum had a titre of 1 : 16 with the Rh_2 donor's cells with which the 1942 sample failed to react. Blocking activity seems to have disappeared from the serum revealing the presence of anti-Rh_0 agglutinins. This confirms the specificity of the blocking antibodies here as anti-Rh_0. That these antibodies have this action is put to practical use in preparing specific anti-Rh_1 and anti-Rh_2 typing sera from the commoner anti-*Rh'* and anti-*Rh"* varieties. The suppression of agglutinating activity may be due to the more rapid and complete reaction between the blocking antibody and the antigen, but this is probably not the whole explanation.

Baar[4] has described the presence of blocking antibodies in the blood of babies affected with hæmolytic disease. I have seen a child affected with congenital hæmolytic anæmia whose blood, examined on the eighth day after birth, was found to have erythrocytes which failed to react with anti-Rh_2 serum. A strong agglutination reaction was given using an anti-Rh_1 typing serum and a negative one with anti-Rh_2 serum. The cells thus appeared to be of type *Rh'*. Re-examination of this child's erythrocytes at the age of 18 months showed them to be of type Rh_1, giving a strong reaction with the anti-Rh_2 typing serum. The maternal serum contained strong *Rh* blocking antibodies on both occasions. Wiener[3] mentions this phenomenon, but this is the only case I have so far observed, though this may be accounted for by the high-titre anti-Rh_2 typing serum (1 : 2,000) used as a routine.

Eight other samples of blood from babies affected with hæmolytic disease have recently been tested for blocking antibodies by the original method[1,2]; one case gave a positive and two doubtful results.

The sample of blood containing blocking antibodies was obtained from an affected child 24 hours old. There were no *Rh*-agglutinins in the child's serum, but it gave a positive 'conglutination test'. The erythrocytes were of Rh_1 type and reacted strongly with anti-Rh_2 serum. The erythrocytes were washed with saline and added to a serum from a group *AB* mother and containing Rh_2 blocking antibodies. The erythrocytes were allowed to remain in contact with the serum at 37° C. for 30 minutes. They were then separated and washed with saline. These treated babies' cells now failed to agglutinate when mixed with an anti-Rh_2 typing serum. Moreover, the cells before treatment gave a positive Coombs–Mourant–Race test (*vide infra*), but after treatment this was very strongly positive.

The evidence in this particular case points to the infant's cells being incompletely saturated with Rh_0-blocking antibody whereas this latter was present in its own blood. It must be remembered, however, that the blocking antibodies in the child's blood were difficult to detect and much weaker than those normally encountered in maternal sera.

Coombs, Mourant and Race[5] introduced a test for *Rh*-sensitivity by detecting globulin absorbed on to erythrocytes with an anti-human globulin precipitin serum. Using this test on the blood of seven of the eight children affected with hæmolytic disease referred to above, all seven babies' erythrocytes gave positive results. (The reagent was kindly supplied by Dr. Race.) By the use of this test and the 'conglutination test', information will be obtained concerning the affected child's blood which will be of value in the diagnosis and treatment of hæmolytic disease of the newly born.

F. Stratton.

Regional Transfusion Service,
Royal Infirmary, Manchester, 13.

[1] Race, R. R., *Nature*, **153**, 771 (1944).
[2] Wiener, A. S., *Proc. Soc. Bio. Med.*, **56**, 173 (1944).
[3] Wiener, A. S., *J. Lab. and Clin. Med.*, **30**, 662 (1945).
[4] Baar, H. S., *Nature*, **155**, 789 (1945).
[5] Coombs, R. R. A., Mourant, A. E., and Race, R. R., *Lancet*, ii, 15 (1945).

Rh Antigens and Antibodies in Man

A 'new' *Rh* antibody has recently been found[1] which has made possible the recognition of a third allelomorph at Fisher's *C*−*c* locus[2]. The antibody has been produced by a hypersensitive recipient of blood transfusions. A detailed account of this case is in the press[3]. The antibody is being called anti-C^w and the corresponding gene or antigen C^w. *W* stands for Willis, the name of the donor whose blood stimulated the formation of the antibody. Any remaining doubt as to the appropriateness of recognizing three loci seems to be removed by this finding.

The frequency of the three allelomorphs in England is: *C*, 43 per cent, *c*, 56 per cent and C^w, 1 per cent. C^w can be combined with *D* or *d* and *E* or *e* in four ways, two of which have been observed, namely, C^wDe and C^wde. That is to say, two more *Rh* 'allelomorphs' or, more properly, combinations of genes have been added to the seven previously found. A further two, C^wDE and C^wdE, may be assumed to exist, though both must be rare.

A result of finding the new antibody has been the recognition that about half the sera formerly classified as anti-*C* (anti-*Rh'*) are in fact mixtures of anti-*C* and anti-C^w, the remainder being pure anti-*C*. (Both types may contain the 'incomplete' or non-agglutinating form

Table 1.

	Anti-*Rh'* sera 'anti-*C*'				
	anti-*c*	50% anti-*C*	50% anti-*C* + anti-C^w	anti-C^w	frequency
C^wC^w	−	−	+	+	0·01 per cent
C^wC	−	+	+	+	0·94 ,,
CC	−	+	+	−	18·40 ,,
C^wc	+	−	+	+	1·23 ,,
Cc	+	+	+	−	48·05 ,,
cc	+	−	−	−	31·36 ,,
					99·99 ,,

Table 2.

Antibodies	Genes and antigens										
	R_0 *cDe*	*r cde*	R_2 *cDE*	*R"* *cdE*	R_1 *CDe*	*R'* *Cde*	R_z *CDE*	R_y *CdE*	C^wDe	C^wde	C^wDE	C^wdE
Anti-*C*	−	−	−	−	+	+	+	(+)	−	−	(−)	(−)
Anti-*D*	+	−	+	−	+	−	+	(−)	+	−	(+)	(−)
Anti-*E*	−	−	+	+	−	−	+	(+)	−	−	(+)	(+)
Anti-*c*	+	+	+	+	−	−	−	(−)	−	−	(−)	(−)
Anti-*d*	(−)	(+)	(−)	(+)	(−)	(+)	(−)	(+)	(−)	(+)	(−)	(+)
Anti-*e*	+	+	−	−	+	+	−	(−)	+	+	(−)	(−)
Anti-C^w	−	−	−	−	−	−	−	(−)	+	+	(+)	(+)

The left upper compartment shows the interactions known before Fisher's theory was postulated[2]. The middle compartment shows the extension demanded by Fisher's hypothesis, now in part confirmed serologically. The right and lower compartment shows the extensions made and those suggested by the anti-C^w serum. Reactions which have not yet been confirmed serologically are shown in brackets. In this table anti-*C* means pure anti-*C* and not anti-*C* + anti-C^w which, as already mentioned, is the constitution of about half the anti-*Rh'* sera.

of anti-*D*.) This finding provides the explanation of occasional discrepancies of behaviour between different anti-*Rh'* sera which have been noted during the last two years.

The possible combinations of *C*, *c* and C^w in a pair of chromosomes, the calculated frequency of these combinations in England and the reactions which they determine, are shown in Table 1. All these combinations have been observed.

Although homozygous C^wC^w blood is very rare in the general population, one example has been found. One daughter of a mating $C^wDe/cde \times C^wDe/CDe$ was C^wDe/C^wDe. Another daughter of this mating was heterozygous, C^wDe/CDe. The C^w homozygous blood gave a much stronger reaction on titration against the anti-C^w serum than does heterozygous blood; a dosage effect which is also noted with the agglutinins anti-c^s and anti-c^t. The antigens *C*, *D* and *E* only show a slight dosage effect which is difficult to demonstrate.

The chart of the *Rh* antigen – antibody interactions, recently published in these columns[6] can now be extended (Table 2).

The 45 genotypes to which the nine known *Rh* 'allelomorphs' give rise can be divided into 24 serologically distinguishable groups. Considering the *Rh* groups together with the blood groups of the A_1A_2BO, *MN*, *P* and 'Lutheran' systems (but ignoring the Levay group as it is extremely rare) there are 1,728 combinations which could be recognized serologically in individuals. These represent 18,225 possible genotype combinations.

R. R. Race.
A. E. Mourant.
Sheila Callender.

Medical Research Council,
Emergency Blood Transfusion Service;
and Nuffield Department of Clinical Medicine,
Oxford.
Jan. 10.

[1] Callender, Race and Paykoc, *Brit. Med. J.*, ii, 83 (1945).
[2] Race, *Nature*, **153**, 771 (1944).
[3] Callender and Race, *Ann. Eugen., Lond.*, in the press.
[4] Race, Taylor, Boorman and Dodd, *Nature*, **152**, 563 (1943).
[5] Mourant, *Nature*, **155**, 542 (1945).
[6] Fisher and Race, *Nature*, **157**, 48 (1946).
[7] Race, Taylor, Cappell and McFarlane, *Nature*, **153**, 52 (1944).

Incidence of the *Rh* Factor in Indians

Levine[1] has shown that the incidence of erythroblastosis fœtalis in any race is directly proportional to the frequency of negative reactions with anti-Rh_0 serum. Racial differences in the incidence of *Rh* agglutinogen have already been described, and clinical observations have confirmed the existence of a close correlation between the distribution of the *Rh* factor and the frequency of hæmolytic disease of the newborn.

In India there have been no reports of the occurrence of hæmolytic disease of the newborn, even during the last few years after the discovery of the *Rh* factor by Landsteiner and Wiener[2]. Similarly, reports are lacking of hæmolytic transfusion reactions due to *Rh* iso-immunization.

The number of blood transfusions given in India is much smaller than in other countries, for example, England or the United States, and the number of patients receiving multiple blood transfusions, fewer still. This might perhaps explain in part the lack of reports of hæmolytic transfusion reactions due to iso-immunization against the *Rh* factor.

The poor antigenicity of the *Rh* antigen may be another factor. DeGowin[3] has shown that iso-immunity against the *Rh* factor was the cause of hæmolytic transfusion reactions in only 0·1 per cent of 5,386 consecutive transfusions given to recipients without regard to the *Rh* type or obstetric history of female patients. In a group of 1,717 recipients who received from one to three transfusions, none was sufficiently sensitized to the *Rh* factor to give clinically significant reactions.

No satisfactory explanation has been forthcoming to account for the non-occurrence of erythroblastosis fœtalis in India. It was therefore considered of interest to study the incidence of the *Rh* factor in the population.

Lack of *Rh* typing serum and of known *Rh* positive and *Rh* negative bloods was the initial difficulty. Anti-*Rh* sera produced by immunization of laboratory animals against Rhesus monkey cells have not been satisfactory in our hands. We were able to obtain a supply of immune human anti-Rh_0 serum from England. One hundred and forty-five specimens of blood from an unselected population, most of them blood donors, were examined. Of these 123 were from Hindus, 13 Muslims, 8 Indian Christians and one Anglo-Indian. There were 139 (95·9 per cent) *Rh* positives and 6 (4·1 per cent) *Rh* negatives, the latter being all Hindus.

There are significant differences in the published figures relating to the distribution of the *Rh* factor in Indians. Greval and Chowdhury[4] place it at 90 per cent at Calcutta, while Khanolkar and Sanghvi[5] have reported a frequency of 98 per cent *Rh* positives in Bombay. The figure for the present series is 95·9 per cent. It is probable that the above differences are due to the small number of bloods examined in each series. Further, the Calcutta workers employed immune animal serum for *Rh* typing. It will be necessary to examine some thousands of bloods with reliable anti-*Rh* typing sera before statistically accurate figures can be obtained. Nevertheless, the above findings suggest the probability of a higher incidence of the *Rh* factor in Indians than in white individuals, and a lower one than that in the Chinese and the Japanese. They would also appear to suggest that erythroblastosis fœtalis may not be so rare in Indians as it is supposed to be. It is now known that immunization of even an *Rh* positive person can occur, and a person of one *Rh* subgroup can form antibodies against the antigen of another subgroup. A factor favourable for the causation of hæmolytic disease of the newborn in Indians is the large number of children born in each family. This may be expected to offset to some extent any tendency to low frequency of hæmolytic disease of the newborn, due to a higher incidence of the *Rh* factor in the population.

A systematic investigation of all cases of suspected hæmolytic disease of the newborn, unexplained stillbirths, hæmolytic transfusion reactions, etc., would appear to be called for in order to prove beyond doubt the occurrence or otherwise of clinical manifestations of iso-immunization against the *Rh* factor.

Our thanks are due to Dr. G. L. Taylor, of the Galton Laboratory Serum Unit, Cambridge, and to Dr. Janet M. Vaughan, for the supply of anti-*Rh* sera, and to Dr. C. G. Pandit, director of the King Institute of Preventive Medicine, Guindy, Madras, for permission to publish this note.

K. S. Ranganathan.
C. S. Ramachandra Rao.
N. R. Ratnakannan.

Madras Blood Bank,
King Institute of Preventive Medicine,
Guindy, Madras.
Nov. 29.

[1] Levine, P., *Science*, **96**, 452 (1942).
[2] Landsteiner, K., and Wiener, A. S., *Proc. Soc. Exper. Biol. Med.*, **43**, 223 (1940).
[3] DeGowin, Elmer L., *J. Lab. Clin. Med.*, **30**, No. 2, 99 (1945).
[4] Greval, S. D. S., and Roy Chowdhury, A. B., *J. Ind. Med. Assoc.*, **13**, 65 (1943).
[5] Khanolkar, V. R., and Sanghvi, L. D., *Nature*, **155**, 427 (1945).

Rh-negative Rate for Indians

The *Rh*-negative rate for Indians in our first series of 200 cases in Calcutta was 10 per cent[1]. In a second series it fell to 7·85 per cent[2]. Wiener's[3] rate in a series of 200 cases is 7·1 per cent. This rate contains all types of *Rh*, including 2·6 per cent *Rh'*, which would be missed by animal/(anti)serum. By the use of the latter serum alone, therefore, the rate would be 9·7 per cent, which is not materially different from our first rate.

The rate of Khanolkar and Sanghvi[4], at least the one based on the findings in 70 Hindus and 5 Muslims none of whom was found to be *Rh*−, is materially different: 14 Parsees—possibly an ethnological group—and 11 Indian Christians—definitely not an ethnological group—gave one *Rh*− subject in each group. These workers admit the difference, but impute it to the animal serum used by us. We justify the use of our serum on the following grounds: (1) The *Rh* antigen is named after the brown monkey *Macacus rhesus* in the red blood corpuscles of which it is found. Its presence in man was and could only be determined by an animal antiserum prepared against the red blood corpuscles of the monkey. (2) The serum was compared with the same human serum with which Khanolkar and Sanghvi worked (standard, anti-Rh_0 serum, supplied by the late Dr. George Taylor and brought to India by Dr. Janet Vaughan). Of 54 cases tested with both the human serum and the animal serum, 5 were found to be negative. As the human serum came from group *A* and the subjects tested also belonged to group *A*, the question of over/under absorption of the co-existing iso(hæmaggluti)nin did not arise. Incidentally, none of the human anti-*Rh* sera (for detecting Rh_0, Rh_1, Rh_2 and *Rh'*, according to nomenclature used by Taylor on October 26, 1944) showed a particular affinity for the red blood corpuscles of the monkey.

We use both slides and test tubes, and the two sets of results agree on the whole. Incidentally, at least one other team of workers[5] has found the slide satisfactory. The use of the slide and the test tube, and the preparation and appropriate dilution of animal serum, will be discussed elsewhere.

The animal serum yields a certain percentage of doubtful, ±, reactions which we include with +. A suggestion, however, emerges: ± reactions (with animal sera) should be taken as + for a donor but as − for a recipient, in transfusion of blood.

As in Bombay, cases of erythroblastosis fœtalis have not yet been found in Calcutta (population three millions), although a lookout has been kept since 1943. The reason may be the absence of chilling, which presumably also lowers the incidence of paroxysmal hæmoglobinuria in Calcutta to 0 (no case has yet been seen by the senior writer, who first made his request to the clinicians for contacting one in 1934).

On the data so far available, we are inclined to think that the *Rh*− rate for Indians lies between 7 and 10 per cent. Going by the incidence of A_2 and *Rh*− rate, Wiener[3] puts Asiatic Indians among Caucasian races.

Incidentally, *Rh* is a 'character' genetically and an 'antigen' immunologically: 'factor', essentially a mathematical term, is scarcely necessary. (Factors in physiology—for constituents, fractions, parts, etc.—are equally unnecessary.) We determine the *Rh*+/− state of a subject, not his *Rh* factor.

S. D. S. Greval.
A. B. Roy Chowdhury.

Laboratory of Imperial Serologist and
Chemical Examiner to the Govt. of India,
School of Tropical Medicine,
Calcutta.
Dec. 29.

[1] Greval, S. D. S., and Roy Chowdhury, A. B., *J. Med. Assoc.*, **13**, 65 (1943).
[2] Greval, S. D. S., Roy Chowdhury, A. B., and Banerjee, B., *J. Ind. Med. Assoc.*, in the press.
[3] Wiener, A. S., *J. Immunol.*, **50**, 341 (1945).
[4] Khanolkar, V. R., and Sanghvi, L. D., *Nature*, **155**, 427 (1945).
[5] Simmons, R. T., Graydon, J. J., Jakobowicz, Rachel, and Bryce, Lucy M., *Med. J. Aust.*, **2**, 496 (1945) (abstracted in *Brit. Encyc. Med. Prac., Med. Progress*, 129 (1945).

STEDMAN Mrs — Anti-Hr present — Dr Mc Call

Delivered Jan 20 1943 — Baby in hosp at first, readmitted later

5.2.43 (p 98) Mrs. Group O MN Rh+ Pourtney negative — Strong Antibody at 37° — less strong at lower temps (p 107) for Donor (O) Bab (O) & for 9 other O's no antibody at all for her own cells nor those of DUK (eg Mrs St.'s serum gave ++ c Arthur)

Father "4/5 A" (22.2.43 p 114) A_1MN Rh+ R_2+

Child Group OMN Rh+? (p 107. 14.2.43) Had had blood from Meredith 150cc Pourtney negative MN confirmed ( ) 2 specimens

Donor Meredith Group O_N Rh− (gave became Rh−) about 150 cc of whole blood given to baby − good result before babies first specimen taken

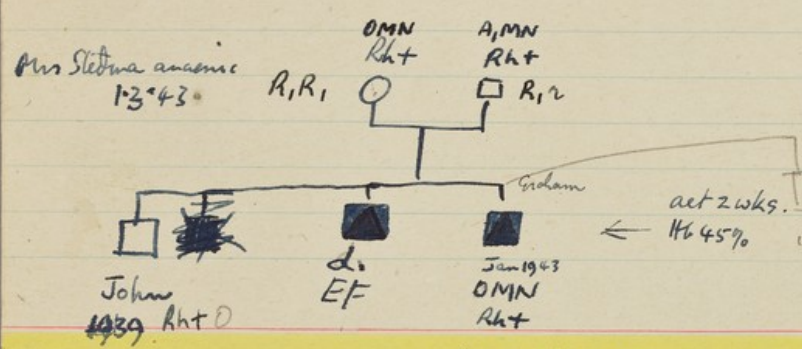
McCall has obtained Mrs Stedmans serum c Rh− cells

8.2.43 More asked for & details asked for

Father Stedman +.

v. letter 30.3.43 re Forssmann antigen.

"No abnormal sheep cell agglutinins"
AMB 4.4.43



P. T. O

John Steadman 14.5.43 (p. 38. bk 2) O N Rh+ P− Std+

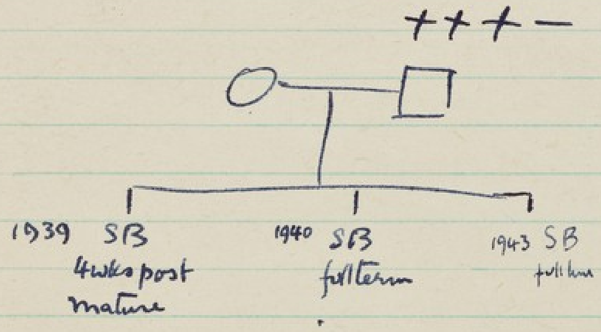
Fresh specimen from Mrs. St. 14.5.43 " antibody still present.

25.2.44 "Mrs St. 6 months preg. coming into hospital for delivery"

Mrs O.B. Harrisson — Dr Harrisson.

Serum examined (− ? BCG) — presumably A — 29.10 43. — 26.11.43 — 29.1.44

Dr C.V. Harrison 5.11.43 St book. O Rh+ St+ KJ+ And ∓ OBH+ ~~[illegible]~~



R_2r or R_2R_2 (or R_2R_{z}) $R_2\bar{R}_1$ R_2R_4

P.T.O

Some of the more informative matings

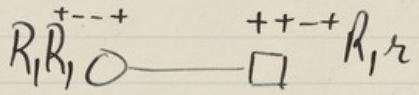
Mating type	Number	Children Observed	Children Expected
$Rh_1Rh_1 \times rh.rh$	8	14 R_1r	all Rh_1rh
$Rh_1rh \times Rh_1rh$	3	R_1R_1 : rr : R_1r 1 : 2 : 5	Rh_1Rh_1 : $rh.rh$: Rh_1rh 1 : 1 : 2
$Rh_1Rh_1 \times Rh_1rh$	2	R_1r 3	Rh_1Rh_1 : Rh_1rh 1 : 1
$Rh_1rh \times rh.rh$	3	R_1rct : rr 2 : 2	Rh_1rh : rh/rh 1 : 1
$rh.rh \times$ one of the rest			mostly Rh_1rh & Rh_2rh
$Rh_xr \times$ one of the rest			a variety of genotypes

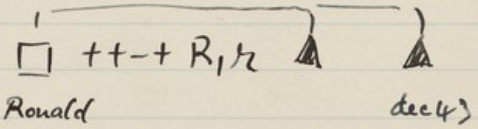
Gould Mrs Rose (A:2473) Dr Hirsch

Mrs.	R_1R_1	A_1	MN
Mr Fred	R_1r	O	M
Ronald	R_1r	A_1	M

Strong St. antibody 18.2.44 (RL iv & St ii)
(suggestive grouping of single & double dosers)

B/16





2 f ♀ deliveries both ♂ passed in 1st fortnight last Dec 1943

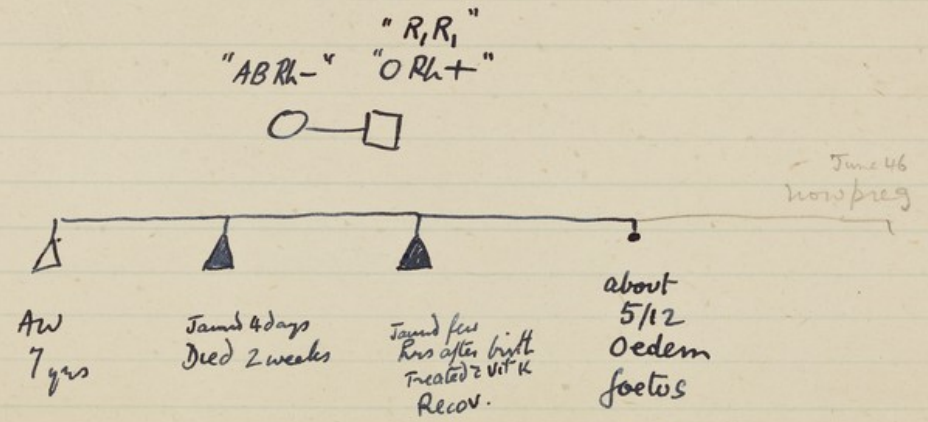
sex ratio ♂ preponderated

Mrs Bastow — Sent as Anti-R_1 — Dr Leitlin

"AB Rh neg, her serum agglutinates 165 bloods out of 241, i.e 68·5%"

10.1.45 (serum) Δ' present (St-IV book) Confirmed Γ type ≡ DVK w/32

Δ' present



Sent as St.

Moore Nancy Lupus erythem. Dr Callendar

"O R_1R_1"

4.10.44 Still dosage

age 25, never been pregnant

2.2.44 Transfused 1 pint O R_1r no reaction (Marshall donor)

19.8.44 Transf 2 pints O rr a bit yellow a few days later 33745, 33751. (Rh- Anti-)

28.8.44 First sample taken "good agglutination for R_2 & rr cells & R_1r (low titre)

7.9.44 the max titre reached at this time, r → . Dr A.C.F. Callendar then went away

double dose max titre 1/120 1/16 single

~~9.9.44 Transf.~~ R_1r agg. missed on X watching Bad reaction

23.9.44 Trans 1 pint "R_1R_1" L rigor at end WILLIS 46653

29.9.44 Trans "R_1r or R_1R_2" stopped after 50 cc donor 10110. MULES R_1r 7.12.44

6.10.44 Trans R_1R_1 (tested by us) "carefully matched" Rigor at end, no other symptoms of incomp.

HOWES

7.11.44 Trans. LEVAY (+--+) no reaction

20.11.44 Trans Allington (+--+) no reaction

29.11.44 Donor Marshall R_1r Donor Willis R_1R_1 Donor Howes R_1R_1

Blank verse "v. without rhyme esp. the heroic v. of 5 feet."

Heroic verse – classic: hexameter | 1 dactyl — ∪∪ / spondee — — | 2 — ∪∪ | 3 — ∪∪ | 4 — ∪∪ | 5 — ∪∪ | 6 — — |

– English: iambic pentameter or heroic couplet – | ∪ — |

– French: alexandrine

anapaest | ∪∪ — |

Trochee | — ∪ |

Turner, J.C. Box 8

Development of cold agglutinins in Atypical pneumonia.

Nature, Vol.151,p.419, Apr. 10, 1943.