Xg Groups and Sex Abnormalities in People of Northern European Ancestry

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This paper presents a succession of tables with little comment. We are from time to time asked for the latest Xg score in certain categories of sex chromosome abnormalities and so hope some of the tables may be useful.

The X-linked Xg blood group system was recognized late in 1961 (Mann *et al*, 1962). An account of its application, in the Blood Group Unit, to certain sex chromosome abnormalities in people of northern European extraction from that time until the end of April 1968 was given in the *British Medical Bulletin* (Race and Sanger, 1969). This present paper brings our account up to 7 January 1971, and includes some conditions not summarized in the 1969 account.

Many of the cases out of which the tables are built have been published, so the present list should not be pooled with any previous publication in which the Xg groups were done by the Blood Group Unit.

Xg Frequencies

We have used as a standard the frequencies given by Noades *et al* (1966) which were based on a series of 3418 unrelated people of northern European extraction tested in the Unit:

Alleles	Phenotypes		
		Males	Females
Xg ^a 0.659	Xg(a +)	0.659	0.884
Xg 0.341	Xg(a -)	0.341	0.116

A more recent count (Sanger, Tippett, and Gavin, 1971) brings the total up to 6784 with, curiously and conveniently, exactly the same allele frequencies to three figures.

Notation

We apologize for using the old notation XXY rather than 47,XXY and XO rather than 45,X: just

for our present purpose it seemed clearer to avoid writing, for example, 395 47,XXY patients.

Klinefelter's Syndrome

XXY. In Table I the Xg distribution of the 395 XXY patients differs very significantly from that of males. The distribution also differs, but just significantly, from that of normal females: this was to be expected, for when both Xs are from the mother they will presumably sometimes carry duplicate copies of one of her Xg loci, which will push the Xg distribution a little away from that of the female.

The closeness of the Xg distribution in XXY to that of the female must mean that postzygotic mitotic errors can play little part in their causation.

The Xg distribution of the 113 patients in Table I with more complicated karyotypes does not differ from that of females. There is a slight hint of heterogeneity in Xg distribution between the 395 and the 113 ($\chi^2_1 = 2.97$).

The family Xg information about the 395 XXYs of Table I is given in Table II; when both parents of an XXY man are available the Xg groups will show whether the extra X is of paternal or maternal origin in about one eighth of the cases.

In some families the Xg groups give direct evidence about the site of the accident responsible for the two Xs: for example, there are 7 families in Table II in which the mother is Xg(a -) and the XXY son is Xg(a +); this shows that the extra X is paternal but further shows that disjunction has failed at the first meiotic division of spermatogenesis. There are 13 families in which the father is Xg(a +) and the XXY son is Xg(a -) and these show non-disjunction to have involved a maternal X but do not specify at which cell division.

The families of Table II are the basis for calculations of the relative proportions of XXYs whose extra X is paternal or maternal and, when maternal, what proportion of the pairs of Xs are the same or different. Since, when the two Xs are maternal, it

Received 30 March 1971.

TABLE I

KLINFELTER'S SYNDROME IN 508 NORTHERN EUROPEAN MALES:
DISTRIBUTION OF THE X_g GROUPS

Sex Karyotype	Total Tested	Number X _g (a+)	Proportion X _g (a+)	χ ² Comparison with Normal:		Equivalent Female Proportion*
				Males	Females	
XXY	395	335	0.848	62.87	4.96	0.84
XXXXY	12	11	0.881	14.57	0.01	0.99
XXXXXY	33	28				
XXYY	22	20				
XXY/XY	27	25	0.957	18.13	2.36	1.32
Other mosaics involving XXY†	19	19				
Expected: normal females			0.884			1.00
Expected: normal males			0.659			0.00

* The 'equivalent female proportion' here and in later tables is a way, devised by Professor Edwards, of describing the departure of an observed proportion from that of normal females (Edwards, 1971). Where p_m and p_f are the phenotypic proportions in males and females respectively, and p the proportion in the class considered, it is $(p - p_m)/(p_f - p_m)$. In XXY Klinefelters this is equal to $(1 - c)$ in Fraser's terminology (1963).

† XXY/XXYY, 3; XXY/XY/XXYY, 2; XXY/XX, 4; XXY/XXXXY, 3; XXY/XXXXY/XXXX, 1; XXY/XX/XY, 4; XXY/XO, 1; XXY/XX/XY/XXXXY, 1.

is the X_g locus and not the whole chromosome which is being tracked we shall, on the advice of Professor J. H. Edwards, in this event write X_g for X. Two methods of analysis are available: that of Fraser (1963) which takes account only of the families

We hope we shall continue to be sent samples of blood from XXYs and, when possible, samples also from their parents: one important purpose of this collaborative work is to collect larger figures for Professor Edwards' assessment from these of the map distance of the X_g locus from the centromere of the X.

TABLE II

PARENTAL X_g INFORMATION ABOUT THE 395 XXY MALES WITH KLINFELTER'S SYNDROME LISTED IN TABLE I

X _g Groups			Source of Extra X	No.	X _g Groups			Source of Extra X	No.
F	M	XXY			F	M	XXY		
+	+	+	?	69	+	+	+	?	3
+	+	-	Maternal	5	+	+	-	Maternal	3
+	-	+	Paternal	5	-	+	+	?	2
+	-	-	Maternal	5	-	-	+	?	2
-	+	+	?	31	+	+	+	?	40
-	+	-	?	4	+	+	-	?	2
-	-	-	?	6	+	-	+	Paternal	2
					+	-	-	?	4
					+	+	+	?	183
					+	+	-	?	29
Total				125	Total				270

F = father; M = mother; + = X_g(a+); - = X_g(a-); . = not tested; ? = not disclosed.

in which both parents have been grouped, and the recent computer method devised by Edwards (1971) which makes use also of the families in which one or both parents have not been grouped. Professor Edwards' results are taken from his paper on the subject to which the reader is referred (pp. 434-437). The two estimates are:

	Fraser (1963)	Edwards (1971)
X ^M X ^F Y	27.5%	39.1%
X _g ^{M1} X _g ^{M2} Y	45.7%	42.5%
X _g ^{M1} X _g ^{M1} Y	26.8%	18.4%
X _g ^{M2} X _g ^{M2} Y		

XXXXY. Both parents of only 5 of the 12 XXXYs of Table I were tested for X_g and in only one family were the groups informative: in this case, of Dr H. Zollinger and Dr Gertrud Mürset, all three Xs were maternal, so presumably disjunction had failed at the first and at the second meiotic division of oogenesis.

XXXXY. Thirty-three propiiti (Table I) and both parents of 29 of them were grouped. Four families were informative and showed that all the Xs were maternal: in each of these families the father was X_g(a+) and the mother and XXXY son X_g(a-). (We presume that one X_g^a-carrying X would make detectable X_g^a antigen in face of three X_g-carrying Xs, but this is an opinion based only on tests of artificial mixtures of hemizygous X_g[a+] and X_g[a-] cells.) If all 4 Xs are usually maternal the easiest explanation is that disjunction had failed at the first and the second division of oogenesis, and this fits with the female distribution of the 33 propiiti. The female distribution of X_g is, however, compatible with other theoretically possible backgrounds but does show that two post-zygotic non-disjunctions cannot be a frequent cause of the abnormality for, if they were, the X_g distribution would approach that of males: the observed distribution differs significantly from that of males, χ² being 5.34.

XXYY. The 22 propositi of Table I and both parents of 11 of them were tested for Xg. The groups were informative in two of these 11 families and showed that disjunction must have failed consecutively at first and second meiotic divisions of spermatogenesis: in both families the father was Xg(a+), the mother Xg(a-) and the XXYY son Xg(a+) (de la Chapelle *et al*, 1964; Pfeiffer *et al*, 1966).

XXY/mosaics. The 46 propositi of Table I have a slightly ultra-female distribution of Xg ($\chi^2_1=2.36$) and diverge so significantly from the male distribution ($\chi^2_1=18.13$) that they cannot, except perhaps on rare occasion, result from post-zygotic non-disjunction of an XY zygote: presumably they usually arise from mitotic non-disjunction of an XXY zygote.

XX Males

Both parents of 21 of the 34 propositi of Table IIIb were tested for Xg and in 4 of the families the groups are informative (one ++-, two +- -, and one of the --- families in which the absent father must be Xg[a+] because he has three Xg[a+] daughters) and show both Xs to be maternal. This suggests that XX males arise from XXY zygotes and that the Y, after initiating male development becomes lost, at any rate to the tissues accessible to karyotype testing. An XXY origin gains some further support from the Xg distribution of the propositi which fits the XXY distribution slightly better than the female and much better than the male: from the male the divergence is just significant at the 1 in 20 level of probability. In earlier counts these rare XX males had an Xg distribution more like that of males and this supported Ferguson-Smith's theory (1966) that one of the Xs of these men had interchanged a part of its length with a Y.

TABLE IIIb

PARENTAL Xg INFORMATION ABOUT THE 34 XX MALES

F	M	XX male	No.	F	M	XX male	No.
+	+	+	13	+	.	+	0
+	+	-	1	+	.	+	0
+	-	+	1	-	.	+	0
+	-	-	2	.	+	+	5
-	+	+	4	.	+	+	0
-	+	-	0	.	-	+	0
-	-	-	0	.	-	+	2
				.	.	+	5
				.	.	-	1
21				13			

F = father; M = mother; + = Xg(a+); - = Xg(a-); . = not tested.

Turner's Syndrome in Females

The commonest cause of Turner's syndrome is the lack of one sex-chromosome to leave a single X; a less common cause is lack of the short arm of one of the two Xs. The Xg groups of the series are given in Table IV. The proportion of XO propositi is probably greater than appears from the Table: rarer karyotypes must often have been selected for Xg grouping.

The patients in section 1 of Table IV have the male Xg distribution. The reason is obvious in the XOs who have a single X on any one of their cells. The distribution to be expected in the XXqi, XO/XXqi, XXp-, and XO/XXp- depends on the answer to two questions—whether the Xg locus is involved in the preferential inactivation of a defective X chromosome (Muldal *et al*, 1963) and whether the Xg locus is sited on the short or the long arm of the X. These questions will be discussed below: here it is enough to say that the Xg distribution in the XXqi etc class is clearly male.

The figures for the XO/XY class are nearly twice as likely to represent a female rather than a male distribution; this is surprising, though the numbers are small.

TABLE IIIa

Xg GROUPS OF XX MALES

Total Tested	Xg(a+)		χ^2 Comparison with:			Equivalent Female Proportion
	Number	Proportion	Males	Females	XXY	
34	28	0.824	4.10	1.22*	0.15*	0.73
Expected normal males		0.659				0.00
Expected normal females		0.884				1.00
Observed in 395 XXY males		0.848				0.84

* The expected Xg(a-) figures in these two comparisons are rather small for the χ^2 test, but a method of Professor C. A. B. Smith for this situation gives the answer:
 The Xg distribution is 5.8 times more likely to be female than male.
 The Xg distribution is 9.1 times more likely to be XXY than male.
 The Xg distribution is 1.6 times more likely to be XXY than female.

The XO/XXr and XO/XXf in section 2 of Table IV have the male distribution of Xg. We feel that the XO/XXr might contribute some guide in the question whether or not the Xg locus is near one end of the chromosome, but we cannot see how to extract it.

In section 3 of Table IV the XX and XX/XXX patients have, as expected, the female distribution of Xg. One could not tell what distribution to expect of the mosaics involving an XO cell line; this would depend on which lines were mostly involved in the imprinting of the red cells. (Buckton *et al* [1971b] for example, describe an XO/XX normal female, who is therefore not included in Table IV, whose lymphocytes were about 33% XO yet whose marrow cells were 90% or more XO.) The observed Xg distribution of these XO mosaics falls somewhat short of the female which suggests that, in a proportion of the patients, a single X was in control of the Xg groups of the red cell precursors.

Both parents of 324 of the 461 patients of Table IV.1 were grouped with the results shown in Table V. In 102, or about a third of the 324 families, Xg shows whether the single normal X of an XO,XXqi, XO/XXqi etc Turner is paternal or maternal; but the Xg groups cannot show, as they may in Klinefelter's syndrome, at just which cell division the causative accident has happened.

The three father-mother-Turner Xg arrangements which can demonstrate a maternal X in the Turner are commoner than the one which can demonstrate a paternal X, so mathematical tests are needed to show what proportion of the normal Xs of XO Turners are indeed maternal and what proportion paternal. Fraser (1963) provided formulae which, when applied to the 234 XO families of Table V where father, mother and Turner have been grouped, give the answer that of the XO patients about 77% are X^{MO} and 23% are X^{PO}. For computer analysis Professor J. H. Edwards

TABLE IV
TURNER'S SYNDROME IN NORTHERN EUROPEAN FEMALES: DISTRIBUTION
OF THE Xg GROUPS

1. Patients with one short arm of the X chromosome

Sex Karyotype	Total Tested	Xg(a +)		χ^2 Comparison with Normal		Equivalent Female Proportion
		Number	Proportion	Males	Females	
XO	326	227	0.696	2.02	111.96	0.16
XXqi	37	22				
XO/XXqi	66	46	0.649	0.05	61.37	-0.04
XXp	7	4				
XO/XXp-	4	2				
XO/XY	21	17				
	461	318	0.690	1.95	169.51	0.14

2. Patients with only one certain short arm of the X chromosome

Sex Karyotype	Total Tested	Xg(a +)		χ^2 Comparison with Normal		Equivalent Female Proportion
		Number	Proportion	Males	Females	
XO/XXr	30	23	0.689	0.18	16.71	0.13
XO/XXf	15	8				

3. Patients with at least some cells with two short arms of the X chromosome; some described as 'Turner's' others as 'probable' or 'possible' Turner's syndrome

Sex Karyotype	Total Tested	Xg(a +)		χ^2 Comparison with Normal		Equivalent Female Proportion
		Number	Proportion	Males	Females	
XX	104	92	0.888	24.95	0.02	1.02
XX/XXX	3	3				
XO/XX	49	41	0.813	6.71	1.33	0.68
XO/XXX	3	1				
XO/XX/XXX	12	10				
More complicated mosaics	8	5				
Expected normal females			0.884			1.00
Expected normal males			0.659			0.00

TABLE V

PARENTAL Xg INFORMATION ABOUT THE 461 FEMALES WITH TURNER'S SYNDROME LISTED IN TABLE IV.1

Xg Groups of			Source of Normal X	Sex Karyotype of the Patient						Total
F	M	T		XO	XXqi	XO/XXqi	XXp-	XO/XXp-	XO/XY	
+	+	+	?	117	16	24	0	1	2	
+	+	-	Maternal	23	4	5	0	1	1	
+	-	+	Paternal	3	1	1	0	0	0	
+	-	-	Maternal	7	0	1	0	0	0	
-	+	+	Maternal	44	2	5	2	0	2	
-	+	-	?	27	4	8	2	0	1	
-	-	-	?	13	5	1	0	1	0	
Total				234	32	45	4	3	6	324
+	.	+	?	2	0	1	0	0	1	
+	.	-	Maternal	1	0	1	0	1	0	
-	.	+	Maternal	1	0	0	0	0	0	
-	.	-	?	0	0	0	0	0	0	
.	+	+	?	28	1	9	0	0	3	
.	+	-	?	5	2	2	0	0	0	
.	-	+	Paternal	1	0	0	0	0	0	
.	-	-	?	3	0	0	0	0	0	
.	.	+	?	32	2	5	2	0	9	
.	.	-	?	19	0	3	1	0	2	
Total				326	37	66	7	4	21	461

F = father; M = mother; T = Turner; + = Xg(a+); - = Xg(a-); . = not tested; ? = not disclosed.

used the same 234 XO families, together with the further 41 XOs of Table V with only one parent tested: the answer came out 78% X^MO and 22% X^PO.

XXX Females

Were non-disjunction at oogenesis the usual cause of XXX, a series of such women would be expected to show an ultra-female distribution of Xg if either there were recombination between the locus and the centromere, or if non-disjunction were at the first meiotic division. If, on the other hand, non-disjunction at spermatogenesis were the usual cause, a normal female distribution of the groups would be expected. Samples of blood from 41 XXX people were sent for grouping, more than half of them from the MRC Clinical and Population Cytogenetics Unit. Table VI shows that all but two were Xg(a+); this suggests but is not yet significant of an ultra-female distribution. Both parents of 13 of the propositi were also grouped, but Xg cannot give direct evidence of the source of the extra X in these families.

XXXX Females

Samples of blood from only four such people were sent for grouping (Table VI) and three of them were Xg(a+): the one Xg(a-) XXXX girl was reported by de Grouchy *et al* (1968); her father was Xg(a+),

her mother Xg(a-), and we have nothing to add to the following comment:

(i) There is very good reason to believe that the legal father is the biological father. (ii) We presume that one Xg^a will make its presence felt in the company of three Xg genes [see XXXXY section above]. (iii) Assuming that (ii) is correct, then the father has contributed no X to the XXXX daughter, and our guess is that all four Xs were present in the egg-cell nucleus. This could come about by successive nondisjunction at the first and second meiotic divisions at oogenesis. If the father's sperm carried a Y, there is no obvious reason why the Y should be rejected from the nucleus of the zygote, for XXXXYs are relatively common compared with XXXXX, which is an extreme rarity; it may be that five Xs are usually too many for the mitotic divisions of the zygote to cope with and that one is rejected. (Race and Sanger, 1969.)

Testicular Feminization Syndrome, XY Females

Of 66 propositi of northern European extraction 36 were Xg(a+) (Table VI). As expected, this distribution differs very significantly ($p=1$ in many millions) from that of females and does not differ significantly from that of males.

The distribution is, in fact, somewhat ultra-male ($\chi^2=3.78$) and we can only suppose that this is due to chance: it will be interesting to see whether the disturbance persists.

Many members of the families of the propositi with the syndrome were grouped in the hope that

TABLE VI
Xg GROUPS IN FURTHER KINDS OF SEX ABNORMALITIES

Abnormality	Sex Karyotype	Total Tested	Number Xg(a+)	Proportion Xg(a+)	χ^2 Comparison with Normal		Equivalent Female Proportion
					Males	Females	
Females	XXX	41	39	0.951	15.58	1.81	1.30
Females	XXXX	4	3				
Testicular feminization	XY	48	27	0.545	3.78	73.72	-0.51
Testicular feminization	nk	18	9				
Male pseudo-hermaphrodites	XY	16	8	0.625	0.21	26.17	-0.15
Male pseudo-hermaphrodites	XO/XY	5	4				
Male pseudo-hermaphrodites	nk	19	13	0.577	0.78		-0.36
Hypospadias	XY	12	9				
Hypospadias	nk	14	6				
Reifenstein's syndrome	XY	1	1				
Reifenstein's syndrome	nk	2	2				
Kallman's syndrome	nk	2	1				
Pure gonadal dysgenesis	XX	14	13				
Pure gonadal dysgenesis	XO/XXX	2	2				
Pure gonadal dysgenesis	XY	14	9				
Pure gonadal dysgenesis	nk	13	11				
True hermaphrodites	XX/XY	9	7	0.895			1.05
True hermaphrodites	XX	6	4				
True hermaphrodites	XX/XXY	2	2				
True hermaphrodites	XX/XY/XXY	2	2				
True hermaphrodites	XY	6	2				
True hermaphrodites	XO/XY	2	1				
True hermaphrodites	nk	7	6				
Intersex	XY	7	6				
Intersex	XX	1	1				
Intersex	XO/XX/XXX	1	0				
Intersex	nk	1	1				
Male Turner's syndrome	XY	6	3				
Male Turner's syndrome	XX/XY	1	1				
Male Turner's syndrome	nk	1	1				
Bonnevie-Ullrich syndrome	XX	12	12				
Bonnevie-Ullrich female	XX+r	1	1				
Bonnevie-Ullrich male	XY	3	2				
Primary amenorrhoea	XX	9	8				
Primary amenorrhoea	XO/XXX	2	2				
Primary amenorrhoea	XO/XX/XXX	1	1				
Primary amenorrhoea	nk	1	1				
Females with Xq-	XXpi	2	1	0.5200	Over 1000 times more likely to represent a male than a female distribution		-0.71
Females with Xq-	XXq-	8	4				
Females with Xq-	XO/XXq-	8	4				
Females with Xq-	XX/XXq-	1	0				
Expected: normal females				0.884			1.00
Expected: normal males				0.659			0.00

nk = karyotype not known to us.

measurable linkage with Xg would establish the *testicular feminization* locus as X-borne, which it probably is (Lyon and Hawkes, 1970), but this hope was not realized: if it be on the X it is not within direct measurable distance of Xg (Sanger *et al*, 1969).

Male Pseudo-Hermaphroditism and Related Conditions

Again the Xg distribution of this group differs, as expected, very significantly from that of females but not from that of males.

Pure Gonadal Dysgenesis

The number of propiti in this category is small: the Xg groups look appropriate to the karyotype. Practically all the samples were sent by Professor Polani, Dr Boczkowski, or Dr Ferguson-Smith.

True Hermaphrodites

From the point of view of the autosomal blood groups the XX/XY are the most interesting of this class: we have tested 9 northern European samples and 5 of them had two separate populations of red cells thus showing them to have a dispermic origin.

Intersexes

Seven of the 10 samples were sent by Professor Edwards or Dr Ferguson-Smith. The Xg groups were informative in one family, as no paternal X was evident in the XO/XX/XXX male patient of Dr J. Insley.

Male Turner's Syndrome

All but 2 of the 8 samples were sent by Professor Polani. The Xg groups fit the prevailing XY karyotype.

Bonnevie-Ullrich Syndrome

All 16 samples were sent by Professor Polani. The 13 females were all Xg(a+) which fitted their XX karyotype. The three males look as if they are shaping towards the expected male distribution of Xg.

Primary Amenorrhoea

Nine of the 13 samples were sent by Professor Polani or Professor Edwards. The Xg groups would fit the expected female distribution.

Females Lacking the Long Arm of an X

In Table VII details are given about the females summarized in the last category of Table VI. The Xg arrangement in 4 of the families (PRU 748/98), Di., R.H., and De., is informative and shows the

normal X of all 4 patients to be maternal. (Asterisks indicate propositi included in the analysis by Polani *et al* [1970].)

There is an excess of Xg(a-) propositi, 9 out of 18 (leaving out the one XX/XXq-): this distribution does not differ significantly from that expected of males but does so, very significantly, from that expected of normal females; it is, we think, 1165 times more likely to represent a male than a female distribution. (If only the 10 XXpi and XXq- are considered then their Xg distribution is 50 times more likely to be male than female.) This category of patients is involved in the questions of inactivation and location of the Xg locus to be discussed below.

Xg Groups of the Parents of Propositi

In Tables I, III, IV, and VI 1547 propositi are recorded with a variety of abnormalities of sex. Both parents of 756 of them were available for grouping with the results shown in Table VIII.

There is no obvious reason why the parents of the propositi should differ in Xg distribution from random matings, and they do not. There is a non-significant shortage of father Xg(a+) × mother Xg(a-) matings which can be traced to the XO, XXqi etc category of Table V where 24.75 matings were expected though only 13 were observed: probably a striking departure from expectation only to be expected by chance when making so many counts.

TABLE VII
Xg GROUPS OF 19 PATIENTS WITH AN X LACKING A LONG ARM

Father	Mother	Propositus	Identity	Case of
XXpi -	+	-	U.R.*	Lindsten
.	.	+	PRU 752/2065*	Polani
XXq-				
+	+	+	PRU 126/100*	Polani
+	+	-	PRU 748/98*	Polani
-	+	+	Di.	Van Went
-	+	-	H.F.*	Philip
+	.	+	Lo.	Richards
.	.	+	Boy.	Lucas
.	.	-	17/59*	Court Brown
.	.	-	Z.C.*	Crawford
XO/XXq-				
+	+	+	34/62*	Court Brown
+	+	+	H.L.*	Lindsten
+	+	+	PRU 4604	Polani
+	+	+	Le.	De Grouchy
+	-	-	R.H.*	De la Chapelle
+	+	-	De.	Ferguson-Smith
-	+	-	L.P.*	Grove-Rasmussen
-	+	-	Bog.	Dahl
XX/Xq-				
.	-	-	L.H.*	Davidson

+ = Xg(a+); - = Xg(a-); . = not tested.

* The 12 of these cases included in Polani *et al* (1970).

TABLE VIII

Xg GROUPS OF BOTH PARENTS OF 756 OF THE
1547 PROPOSITI OF THIS PAPER

Father	Mother	Proportion Expected	Expected in 756	Observed in 756
Xg(a+)	Xg(a+)	0.5826	440.44	449
Xg(a+)	Xg(a-)	0.0764	57.76	48
Xg(a-)	Xg(a+)	0.3014	227.86	226
Xg(a-)	Xg(a-)	0.0396	29.94	33
Total		1.0000	756.00	756

Two Informative Families not Fitting into Previous Lists

In a random survey of general practitioners' patients the MRC Clinical and Population Cytogenetics Unit found a normal fertile female whose peripheral blood karyotype was mosaic, 33% XO/66% XX, and who was by pedigree evidence heterozygous Xg^aXg . Nevertheless, her red cells gave the reaction $Xg(a-)$ and this was subsequently explained when her marrow was found to be about 90% XO (Buckton *et al*, 1971a).

Dr Patricia Jacobs raised the question whether the XO cell lines in mosaics preferentially colonize the marrow; but this can hardly be a common event because the 49 XO/XX of Table IV.3 have an Xg distribution which differs significantly from that of males.

A family found in another Edinburgh survey, of hospital patients, gave information about Xg, a family in which the short arm of an X is translocated to the long arm of a No. 14 (Buckton *et al*, 1971b). A male member of the family demonstrates that Xg^a can express itself, though more weakly than normal, when carried on one or the other part of the severed X. In female members carrying the translocated X it is, surprisingly, the normal and not the translocated X that is late-labelling. A female in the family appears to give direct evidence that the Xg^a carried on her normal, late-labelling, X can express itself, though more weakly than normal. We wrote 'appears to give' because Buckton and her colleagues are careful to consider another theoretically possible interpretation of the woman's Xg genotype.

X Chromosome Abnormalities and the Questions of Xg Inactivation and Location

There is growing evidence that Xg when carried on a structurally normal X chromosome is not subject to inactivation (Gorman *et al*, 1963; Race and Sanger, 1968; Fialkow, 1970; Fialkow *et al*, 1970; Lawler and Sanger, 1970). The only evidence in favour of Xg in-

activation (Lee *et al*, 1968) has been called in question (Weatherall *et al*, 1970).

If, in consequence, we suppose that Xg is not subject to inactivation when carried on an abnormal X we are faced with a paradox. In Table V there are 13 XXqi or XXp- patients, with or without XO cell lines, who are $Xg(a-)$ with $Xg(a+)$ fathers and they would seem to place the Xg locus on the missing short arm: in Table VII, on the other hand, there is one XXq- and two XO/XXq- patients who are $Xg(a-)$ with $Xg(a+)$ fathers, and they would seem to place the missing Xg locus on the long arm. Polani *et al* (1970) concluded that this contradiction could only be resolved by assuming that, in the known preferential inactivation of an abnormal X (Muldal *et al*, 1963), the Xg locus is also inactivated.

Inactivation of Xg would also explain the unquestionably male distribution of Xg in the 114 XXqi, XXp- etc, of Table IV and the 18 XXq- etc of Table VI. The evidence provided by the XXp- etc and XXq- etc when mosaic with an XO cell line was realized to depend on the proportion of the two cell lines in the marrow of the mosaic (Polani *et al*, 1970). This possible complication was recently illustrated by the family reported by Buckton *et al* (1971a) mentioned in the previous section. However, excluding the demonstrable mosaics does not alter the picture: in Table IV the XXp- and XXqi that remain have a male distribution of Xg which differs very significantly from the female; in Table VI the 10 XXpi or XXq- that remain have an Xg distribution 50 times more like male than female.

The present evidence is therefore that the Xg locus is not subject to inactivation when carried on a normal X, and probably is subject to inactivation when carried on a deleted X.

There is nothing definite to say about the long or short arm location of Xg. However, X translocations, now that the fluorescent technique makes their recognition more certain, may, before long, plot the position of Xg.

Of course, we shall be very glad to group for Xg people with X translocations, or, indeed, with X chromosome abnormalities of any other kind.

Summary

Eight tables condense the results of testing 1547 patients, of northern European extraction with various abnormalities of sex for the Xg blood groups, a greater number of their relatives were also tested.

The Xg groups contribute to knowledge in several classes of abnormality, such as Klinefelter's

and Turner's syndromes, XX males, XXX and XXXX females, and others. Some abnormal karyotypes contribute to questions of Xg inactivation and may ultimately disclose the position of the Xg locus on the chromosome.

Much the greater part of the work on which this account is based has not, of course, been the authors' but that of more than a hundred physicians and cytogeneticists and their helpers who, over the 9 years since the recognition of the Xg blood group system, sent samples of blood from their patients.

The majority of the samples came from: P. E. Polani (London), M. A. Ferguson-Smith (Glasgow), W. M. Court Brown, W. H. Price, J. Aitken, and M. Newton (Edinburgh), J. H. Edwards and J. Insley (Birmingham), A. Frøland (Copenhagen), J. Lindsten (Stockholm), H. van den Berghe (Louvain), K. Boczkowski (Warsaw), A. de la Chapelle (Helsinki), J. de Grouchy (Paris), G. Dahl (Copenhagen), V. A. McKusick and P. Bowen (Baltimore), J. J. van Went (Leiden), J. Philip (Copenhagen), and J. L. Hammerton (Winnipeg).

The following sent occasional selected samples:

J. D. Allan (Macclesfield)	J. Leisti (Helsinki)
L. Aubert (Toulon)	F. J. W. Lewis (Bristol)
D. Bartlett (Oxford)	M. Lucas (London)
C. E. Blank (Sheffield)	L. Massimo (Genoa)
M. Bobrow (Oxford)	W. Mellman (Philadelphia)
W. R. Breakey (Belfast)	M. Mikkelsen (Copenhagen)
J. Brocteur (Liège)	C. Moraine (Tours)
L. J. Butler (London)	A. G. Motulsky (Seattle)
N. Carlon (Marseilles)	R. Mundo (Barcelona)
C. O. Carter (London)	J.-D. Murken (Munich)
R. Ceppellini (Turin)	G. Mürset (Zürich)
H. Chimenes (Paris)	A. Netter (Paris)
H. G. Close (Dartford)	J. Opitz (Madison)
P. J. L. Cook (London)	L. S. Penrose (St. Albans)
M. Crawford (London)	H. Perrimon (Marseilles)
D. Dain (Edinburgh)	R. A. Pfeiffer (Münster)
W. M. Davidson (London)	A. Prader (Zürich)
C. Davison (Oxford)	S. Rampini (Zürich)
L. De Carli (Pavia)	M. J. Ree (Bristol)
O. Dubois (Arras)	B. W. Richards (Caterham)
T. Emerit (Paris)	M. A. C. Ridler (St. Albans)
M. Faed (Dundee)	C. Ropartz (Rouen)
P. Ferrier (Geneva)	C. Salmon (Paris)
M. Fischer (Århus)	G. Sansone (Genoa)
C. E. Ford (Harwell)	J. S. Scott (Leeds)
G. L. Foss (Bristol)	M. S. Seabright (Salisbury)
M. Fraccaro (Pavia)	P. Seringe (Paris)
J. V. Garrett (Birmingham)	A. Serra (Rome)
E. R. Giblett (Seattle)	P. M. Sheppard (Liverpool)
S. Gilgenkrantz (Nancy)	I. Shine (Oxford)
J. E. Gray (Newcastle)	W. Shutt (Oxford)
M. Grove-Rasmussen (Boston)	M. Siniscalco (Leiden)
P. Grütznér (Freiburg)	G. Stalder (Basle)
K.-H. Gustavson (Uppsala)	A. C. Stevenson (Oxford)
E. Gutí (Sienna)	J. S. S. Stewart (Dundee)
P. Hellriegel (Cologne)	R. L. Summitt (Madison)
W. Hirsch (Berlin)	A. J. Therkelsen (Århus)
L. Holmberg (Malmö)	H. C. Thuline (Washington)
A. Jamin (Nantes)	R. Tourneur (Paris)
J. Jancar (Bristol)	A. C. Turnbull (Aberdeen)
A. W. Johnston (Aberdeen)	R. Turpin (Paris)
H. W. Jones (Baltimore)	J. Vague (Marseilles)
N. H. Kemp (London)	R. Walbaum (Lille)
C. Kerr (Oxford)	S. Walker (Liverpool)
B. Kjellström (Eskilstuna)	J. Wennström (Helsinki)
M. Lamy (Paris)	W. G. Whyte (Glasgow)
C. Laurent (Lyon)	J. H. Williams (Newcastle)

Much involved in the Xg testing were past members of the Unit: Miss Jean Hamper, Miss Jean Noades, Mrs Ann Gooch and Mrs Joan Whittaker.

The original anti-Xg^a serum from Mr And was used on nearly every sample in the series: this was the magnificent gift of Dr Amos Cahan, of The Knickerbocker Foundation, New York and of its successor Pfizer Diag-

nostics Division. We also received princely gifts of another excellent anti-Xg^a from Dr Edward Shanbrom of Hyland Laboratories, Los Angeles and yet another from Dr F. H. Allen of the New York Blood Center. These antisera were much used in confirming critical results.

Anti-Xg^a is eclectic in the antiglobulin serum it requires: many examples were sent by the English and Scottish Blood Transfusion Services for assay: the most suitable for our special purpose were given by Dr C. C. Bowley of Sheffield, Dr J. Wallace and Mr G. R. Milne of Glasgow, and Professor P. L. Mollison, FRS of St Mary's Hospital Medical School, London.

Professor J. H. Edwards and Professor P. E. Polani have given us encouragement and advice throughout the whole investigation.

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