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Serum Immunoglobulin M, G, and A Concentration Levels in Turner's Syndrome Compared with Normal Women and Men

Knud Jensen[1], Per Hyltoft Petersen[1], Elisabeth Lykkegaard Nielsen[2], Gudrun Dahl[3], and Johannes Nielsen[4]

[1] Department of Psychiatry and Department of Clinical Chemistry, Odense University Hospital, Odense, Denmark
[2] Børnehospitalet, Fuglebakken, Copenhagen, Denmark
[3] The John F. Kennedy Institute, Glostrup, Denmark
[4] The Cytogenetic Laboratory, Aarhus State Hospital, Risskov, Denmark

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Summary. Serum concentrations of immunoglobulin G (IgG), immunoglobulin M (IgM) and immunoglobulin A (IgA) were determined in 15 women with a lack of X chromosome material (Turner's syndrome), and compared with the immunoglobulin concentrations in normal men and women. Further, the investigation is supplemented by a comparison of normal women and the Turner group matched according to age.

The serum concentrations of IgG and IgA in women with Turner's syndrome were very close to the concentration in serum from normal men, whereas the concentration of IgM was significantly lower. Compared to normal women the concentrations of IgG and IgM were significantly lower, and the concentration of IgA significantly higher in the Turner group.

Whether these differences in serum immunoglobulins are determined by hormonal factors or under direct genetic control linked to the X chromosomes, is discussed.

In recent years a number of studies have shown that the concentration of serum immunoglobulin M (IgM), is higher in women than in men (Butterworth *et al.*, 1967; Kalff, 1970; Buckley *et al.*, 1971; Weeke and Krasilnikoff, 1971). There is even evidence that women are more resistant to some infectious diseases than men, and that the levels of specific antibodies are higher in women than in men (Washburn *et al.*, 1965).

Wood *et al.* (1970) studied the serum IgM and the immunoglobulin G (IgG) in 18 normal men, 18 normal women, and 27 women with Turner's syndrome who lack X chromosome material. They found that the mean level of IgM in serum was significantly higher in normal women than in normal men and women with Turner's syndrome, but no difference was found between the latter two groups. In the case of IgG, similar concentrations were found for normal females and normal males, but there were lower serum IgG concentrations in women with Turner's syndrome.

Rhodes *et al.* (1969) found higher serum IgM concentrations in 28 women with an additional X chromosome (47,XXX) than in normal women with 46,XX. Similarly men with 47,XXY corresponded to women with 46,XX and men with 48,XXXY were comparable to the women with 47,XXX as far as serum IgM concentrations were concerned.

On the basis of these investigations it has been suggested that genetic control of the synthesis of IgM is related to the X chromosomes.

In the present study we have estimated IgM, IgG and immunoglobulin A (IgA) in serum from normal females, normal males and women with Turner's syndrome who lack X chromosome material. We have, furthermore, made a comparison between women with Turner's syndrome who lack X chromosome material and normal women matched according to age.

The study is part of a more comprehensive investigation of women with Turner's syndrome which will be published by some of the authors.

Method

Blood samples were collected by venipuncture. IgG, IgM and IgA concentrations were determined by electroimmuno assay according to Laurell (1966) and modified by Weeke (1968a, 1968b).

The statistical method used was Wilcoxon's nonparametric test for comparison of two samples (Bliss, 1967). The reason for using Wilcoxon's test was that the group of Turner women was too small to give exact information on the nature of the distribution of concentrations of immunoglobulins.

Material

The material consisted of 100 normal, healthy men aged 18 to 60 years, 20 normal, healthy women aged 18 to 40 years, and 15 females with Turner's syndrome aged 8 to 37 years. The distribution of karyotypes for the women with Turner's syndrome is shown in Table 1.

It is known that the concentration of immunoglobulins in serum varies according to age, and that children have lower values than adults (Uffelman *et al.*, 1970; Weeke and Krasilnikoff, 1972). We found it reasonable, therefore, to exclude the 3 girls under 18 years of age before making the comparison between the matched groups of normal females and women with Turner's syndrome who lack X chromosome material. The value of IgA = 0.0 g/l was excluded in some of the statistical tests, as it might be caused by another genetic variant (Bachmann, 1965).

Table 1. Distribution by karyotypes

Case No.	Age	Karyotypes
10	22	45,X
12	36	45,X
37	15	45,X
38	14	45,X
40	24	45,X
42	26	45,X
45	19	45,X
11	24	45,X/46,X,r(X)
36	26	45,X/46,X,r(X)
39	18	45,X/46,X,r(X)
41	29	45,X/46,X,r(X)
31	22	46,X,i(Xq)
30	27	45,X/46,X,i(Xq)
35	28	45,X/46,X,inv(Y)(p11q11)
63	8	46,X,t(X;X)(p21;q13)(Xqter→Xp21::Xq13→Xqter)

Table 2. The serum concentration of IgM, IgG and IgA in the women with Turner's syndrome and the normal women matched according to age

Born	Gram per liter					
	Turner's syndrome (XO)			normal women (XX)		
	IgG	IgA	IgM	IgG	IgA	IgM
1937	7.2	1.56	0.24			
1939				10.5	1.00	0.41
1944	9.3	1.60	0.68			
1945	10.1	1.16	0.27			
1946	10.0	0.00	0.18	8.8	1.12	0.59
1947	6.0	1.00	0.23	12.0	0.75	0.74
	5.7	0.66	0.25			
1948	8.0	2.25	0.26	12.8	0.82	0.56
	9.2	1.23	0.35	7.4	1.09	0.52
1949				11.5	2.44	0.44
1950	10.5	2.50	0.33			
1951	5.0	1.28	0.34			
1952				13.0	0.24	1.56
1954	11.0	3.78	0.34	10.0	1.08	0.36
				12.4	0.97	0.76
1955	7.6	1.80	0.28			
1956				11.3	1.00	0.38
1958	8.3	1.46	0.36	The 3 XO cases excluded from the material		
1959	7.3	0.78	0.24			
1967	13.7	0.48	0.20			

In Table 2 the two groups are matched according to age. The group of Turner women consists of 12 women aged 19 to 37 years (mean age 26.3 years), the group of normal women consists of 10 women aged 18 to 35 years (mean 24.7 years).

Results

There was no significant difference in serum immunoglobulin concentrations between the 7 Turner women with 45,X in all cells and the 8 with other karyotypes and all are thus taken together as one group ($P > 0.05$).

The results from the comparison of serum immunoglobulin concentrations between the different groups tested according to Wilcoxon's nonparametric test, are shown in Table 3.

Wilcoxon's test shows significant differences for all immunoglobulins between normal males and normal females ($P < 0.01$). These figures are not tabulated.

When we compare the 15 women in the Turner group with the 100 normal men, we find the level of IgM significantly lower in the former group ($P < 0.01$) but there is no significant difference for IgG or IgA (Table 3).

When the 15 women with Turner's syndrome are compared with 20 normal, healthy women, both IgM and IgG are found to be significantly lower in the Turner group.

When comparing the 12 adult women in the Turner group with the 100 men, only the IgM is significantly lower ($P < 0.05$). Comparison of the 12 adult Turner

Table 3. Comparison of the serum concentrations of IgM, IgG and IgA between the various groups (g/l)

Turner group	Compared with	IgM	IgG	IgA inclusive undetectable case (12)	IgA exclusive undetectable case (11)
All ($n = 15$)	Normal males ($n = 100$)	$P < 0.01$	N.S.*	N.S.	N.S.
All ($n = 15$)	Normal females ($n = 20$)	$P < 0.01$	$P < 0.01$	N.S.	$P < 0.05$
Adults ($n = 12$)	Normal males ($n = 100$)	$P < 0.05$	N.S.	N.S.	N.S.
Adults ($n = 12$)	Normal females ($n = 20$)	$P < 0.01$	$P < 0.01$	$P < 0.05$	$P < 0.01$
Adults ($n = 12$)	Normal females ($n = 10$)[a]	$P < 0.01$	$P < 0.01$	N.S.	$P < 0.05$

* Not significant at the 95% level ($P > 0.05$).
[a] Matched group of women.

women with the 20 normal women shows not only that the IgM and IgG serum concentrations are significantly lower in the Turner group ($P < 0.01$), but also that the IgA is higher for this group ($P < 0.05$). Comparison of the two groups matched according to age, shows significantly lower levels of IgM and IgG for the Turner group.

When a Turner woman with undetectable serum IgA is excluded from the group, a significantly higher level of IgA is found on comparison of the group with the 20 normal women ($P < 0.01$), and also on comparison with the 10 matched, normal women ($P < 0.05$).

As the distribution of immunoglobulins seems to be "log-normal" (Weeke and Krasilnikoff, 1972; Buckley *et al.*, 1971), the concentrations of immunoglobulins in the groups are illustrated as cumulative percentage frequency in the form of probits on a logarithmic concentration scale (Bliss, 1967) and shown in Fig. 1. The figure shows the distribution of IgM and IgG for the 100 men, the 20 normal women, and the 12 adults with Turner's syndrome. With regard to the distribution of IgA this is shown for the 100 normal men, 20 normal women, and for the 11 adults with Turner's syndrome where IgA was detectable.

Discussion

It is shown in Fig. 1 that the distribution of IgA values for the Turner group and the normal male group coincide, whereas the distribution of IgA in the normal females differs from the other two groups.

The difference in IgA concentrations between both normal females and normal males as well as between normal females and Turner females is significant. The higher IgA concentrations found for the normal male group in comparison with that of the normal female group are in accordance with the finding of Buckley *et al.* (1971) and Weeke and Krasilnikoff (1971). Rhodes *et al.* (1969) found that means of IgA for normal men and women are almost identical, but the XXX, XXY, and XXXY groups all had lower means of IgA concentrations.

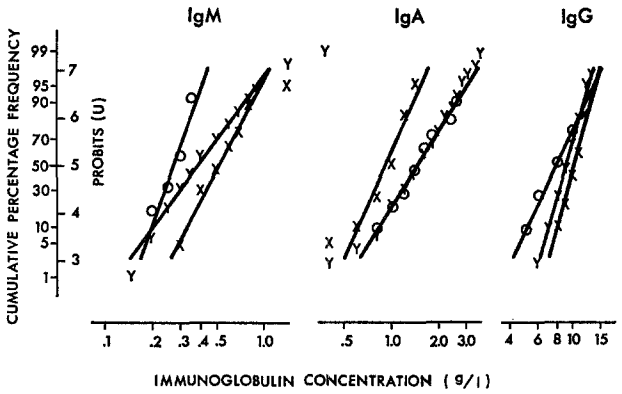

Fig. 1. Distributions of IgM, IgA and IgG for normal men: *Y*, normal women: *X*, and adult women with Turner's syndrome: *O*. Ordinate: cumulative percentage frequency and correspondent probits. Abscissa: concentrations in logarithmic scale

The IgG distribution for the normal females shows the highest values with a geometric mean of about 10% higher than that of the normal male group (Fig. 1). Wood *et al.* (1970) found a similar slight difference and Rhodes *et al.* (1969) found the highest IgG values in XXX, XXXY, and XXY types, whereas Lyngbye and Krøll (1971), Buckley *et al.* (1971) and Weeke and Krasilnikoff (1971) did not find any difference between females and males.

All 3 groups differ significantly from each other ($P < 0.01$) in the serum concentrations of IgM (Table 3 and Fig. 1). Wood *et al.* (1970) found a mean value for IgM concentrations in serum from normal women that was approximately 60% higher than the mean for women with Turner's syndrome, and Rhodes *et al.* (1969) suggested that IgM levels were dependent on the number of X chromosomes.

The IgM concentration in normal women changes throughout life with the highest concentrations occurring between the ages of 20 and 40 years (Lyngbye and Krøll, 1971), which is also the age range of the Turner group in this investigation. Furthermore they found that the IgA level of normal women reaches the level normal for men around the age of 60 years.

Differences in sex hormone concentrations, which are mainly determined by the X chromosomes in the fertile age, may be etiological factors for the higher IgM and lower IgA serum concentration in normal fertile women as compared to women with Turner's syndrome and normal men. It should be expected that regular use of oral contraceptives should influence the serum level of immunoglobulins. Laurell *et al.* (1967, 1969) were, however, unable to find any significant effect when normal fertile women are given oral contraceptives containing synthetic estrogens and gestagens.

In the present study we have been able to demonstrate that the serum concentrations of IgG and IgA in women with Turner's syndrome are close to the concentration in serum from normal men, whereas the concentration of IgM is significantly lower. Women with Turner's syndrome show significantly lower serum concentrations of IgG and IgM and significantly higher serum concentration of

IgA when compared with normal women. Whether this difference in serum immunoglobulins is determined by hormonal factors or is, under direct genetic control, linked to the X chromosomes is still an open question, and further investigations are needed before any conclusions on the etiology of these differences in serum immunoglobulin concentrations can be drawn.

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Knud Jensen
Department of Psychiatry and Department
of Clinical Chemistry
Odense University Hospital
Odense, Denmark