TURNER'S SYNDROME

A PSYCHIATRIC-PSYCHOLOGICAL STUDY OF 45 WOMEN WITH TURNER's syndrome, compared with their sisters and women with normal karyotypes, growth retardation and primary amenorrhoea

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Preface

An investigation like the present one is only possible due to the help, advice and assistance given by many people and institutions.

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The case material must not be reproduced or quoted without written permission from the authors.

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Introduction

A number of psychiatric-psychological studies of women with Turner's syndrome have already been published. No studies, however, have been made of the development of Turner females during childhood and of their education and social adjustment as adults in comparison with their sisters and with women of normal chromosome constitution, growth retardation and primary amenorrhoea. Our main purpose has been to make such a study with the object of procuring as true and realistic a description of women with Turner's syndrome as possible.

We wished furthermore to study and compare certain aspects of the cognitive function of women with Turner's syndrome with those of their sisters and of women of normal chromosome constitution with growth retardation and primary amenorrhoea.

The present study constitutes a part only of the total investigation which will further comprise a number of reports on the clinical-endocrinological, cytogenetic, dermatoglyphic, electroencephalographic and hormonal aspects of Turner's syndrome.

Chapter 1

TURNER'S SYNDROME

Turner (1938) described a syndrome in women characterized by the triad: 1. Short stature with undeveloped secondary sexual characteristics. 2. Webbing of the neck. 3. Cubitus valgus. The only one of these signs which is invariably present in women with Turner's syndrome, is the short stature, while webbing of the neck is only found in approximately 30 per cent and cubitus valgus in approximately 60 per cent of women with Turner's syndrome. *Polani et al.* (1954) and later *Wilkins et al.* (1954) found that most women with Turner's syndrome were chromatin-negative. *Ford et al.* (1959), *Fraccaro et al.* (1959), and *Tijo et al.* (1959) found the chromosome constitution 45,X in women with Turner's syndrome in chromatin-negative cells.

The most common karyotype in Turner's syndrome is 45,X which is found in approximately half of these women. The other half comprises women with a great variation of different chromosome aberrations such as 45,X/46,XX, 45,X/46,X,i(Xq), 45,X/46,X,r(X), 46,X,i(Xq), 46,X,del(Xq), 46,X,del(Xp), other X deletions and translocations as well as mosaics with Y chromosome material as shown in *Chapter 3*.

Chapter 2

MATERIAL AND METHODS

The study comprises all 44 girls with Turner's syndrome and lack of X chromosome material aged 7 to 39 seen at the Children's Hospital Fuglebakken and the Endocrine Clinic at the Queen Louise's Children's Hospital, Copenhagen, during the years 1963-1973, as well as 7 girls from other hospitals.

A letter was written to the 51 probands inviting them to a stay in hospital of one week's duration for research examination.

Three adults and the parents of three younger girls did not wish to participate in the study. The three adults stated that they were healthy, physically and mentally, and that they did not see any reason why they should participate in the study.

It would have been ideal to study an unselected group of Turner probands, but such a group was not available.

The majority of the probands (56 %) grew up in the capital, the expected frequency of an unselected group would have been approximately 20 per cent; 36 per cent grew up in provincial cities, the expected frequency would have been approximately 27 per cent, and 8 per cent of the probands grew up in small towns or rural areas, the expected frequency would have been approximately 53 per cent. The proband sample is thus overrepresented by individuals who grew up in the capital and underrepresented by individuals growing up in small towns or rural areas. The distribution of the probands by paternal social status did not deviate significantly from the expected distribution for Denmark total.

The 25 of the 45 probands aged 7 to 39, who grew up in the capital, comprise approximately 1/3 of the expected number of women with Turner's syndrome in this area and age group when calculating with a prevalence of 1 per 3,000.

Age distribution of the 45 probands and their sisters, with whom they will be compared, is seen in *Table 1.*

Table 1

Age distribution of probands, sisters and controls

Age	Probands	Sisters	Controls
7-14	11	8	4
15-19	10	13	4
20-24	11	7	5
25-29	9	6	2
30-34	1	16	-
35-39	3	6	-
Total	45	46	15

The following examinations were made of the probands who submitted to one week's hospitalization: Clinical-endocrinological, psychiatric-psychological, dermatoglyphic, electroencephalographic, X-ray of bones and joints, hormone studies, glucose tolerance with growth hormone determination, immune electrophoresis of serum proteins, Xg blood typing in probands and parents, cytogenetic and dental investigation.

A control group of children with normal karyotypes, but growth retardation as in Turner's syndrome, was found in a paediatric hospital, and an adult female control group with growth retardation during childhood and adult stature below 162 cm, as well as primary amenorrhoea and a normal karyotype, was found in the diagnostic files of four Danish gynaecological-obstetric departments and two medical wards. The control group comprises a total of 15 girls, the age distribution is shown in *Table 1.*

It was, however, very difficult to find a sufficient number of controls among adults with primary amenorrhoea, normal karyotype and growth retardation during childhood to the extent found in Turner's syndrome. As a second control group we chose sisters of the probands; 21 of the probands had a sister within the age range ± 5 years from the age of the proband, and it was possible to examine 19 of these 21.

In connection with the study we have further estimated the prevalence of patients with Turner's syndrome in all Danish psychiatric institutions (eight patients) as well as in all Danish institutions for the mentally retarded (11 patients). The description of this part of the study is given in *Chapters 9 and 10.* The age distribution of these patients is shown in *Table 2.*

Table 2

Age distribution of patients with Turner's syndrome in Danish psychiatric hospitals and institutions for the mentally retarded

Patients with Turner's syndrome		
Age	In Danish psychiatric hospitals	In hospitals for the mentally retarded
<15	1	1
15-19	–	1
20-24	1	2
25-29	1	2
30-34	–	2
35+	5	3
Total	8	11

Information for the psychiatric record was gathered from the probands and, for girls up to the age of 16, also from the mothers. In 18 of the 45 probands a sister was also interviewed.

The psychiatric interview covered the following items: Family data, disorders in the family, childhood and home, relations with the parents and siblings, nervousness or mental illness during childhood; relations with other children at school and with teachers, information of school record and adjustment at school; relations with fellow workers and friends as an adult; working record, leisure interests; age at attraction to boys, sexual identification, sexual relations in general, marriage and adoption.

All probands and controls aged 16+ were asked to fill out Maudsley Personality Inventory as described in *Chapter 13.*

Information of the school performances of probands and controls was obtained from the relevant schools.

Information of admission to psychiatric hospitals in Denmark for probands, controls, siblings and parents was collected from the Danish Psychiatric Central Register.

The interviews were made during the years from 1971 to 1973, and the manuscript was finished and submitted for publication March, 1975.

Chapter 3

CYTOGENETIC EXAMINATION

The cytogenetic examination was made at the Kennedy Institute, Copenhagen, by one of the authors (G.D.), who had also made the previous cytogenetic examination, before 1970, when the probands had originally been diagnosed as cases of Turner's syndrome.

Several of the available banding techniques were used and skin cultures were made in 15 cases as shown in *Table 3*. A more detailed report of the results of the cytogenetic examination will be published elsewhere by *Dahl et al.* (1977).

The number of cells analysed varied from 20 to 199: 20 to 29 cells were analysed in 4, 30 to 39 cells in 17, 40 to 59 in 15 and above 59 cells were analysed in 9 cases *(Table 3)*.

The differences between skin and blood cultures are shown in *Table 3*.

There were some discrepancies in the percentage of mosaic cell lines between blood and skin cultures, but none of the differences was significant ($P>0.05$). It is seen that three cases (Nos. 1, 15 and 25) had mosaics with 45,X/46,X,i(Xq) in blood and 46,X,i(Xq) in skin, two (Nos. 30 and 34) had 45,X/46,X,i(Xq) in blood and 45,X in skin. One (No. 9) had 45,X/46,X,?del(Y)(q11) in blood and 45,X in skin.

The only significant differences between the results from skin and blood cultures were, however, found in cases No. 15 (P (Fisher) = 0.0014), No. 25 (P (Fisher) = 0.0040) and No. 30 (P (Fisher) = 0.0201).

The information procured by making chromosome analysis on skin cultures was thus not very remarkable; in the three cases with sigificant differences between skin and blood cultures, mosaicism was established by blood culture, but not in skin culture. The possibility of mosaicism in skin culture was, however, not excluded in these three cases by the analysis of 20, 30 and 20 cells, respectively, as seen in *Table 3*.

Table 4 shows the distribution of karyotypes, 21 (47 %) of the 45 probands had karyotype 45,X; 45,X/46,XX was found in two cases. Mosaicism with isochromosome X was found in 9 cases (20 %), 2 of them (Nos. 20 and 32) had dicentric isochromosome in part of their cells as seen in *Table 3*.

Deletion of X chromosome material in some of the cells was found in two cases, one had deletion of the distal part (q26) of the long arms as well as duplication of part of the long arms (q13q26), one had interstitial deletion of part of the short arms (p22p11) as well as deletion of part of the long arms (q11).

Table 3

Karyotypes and number of cells analysed in blood and skin cultures

Case No.	Age	Number of cells analysed in cultures of		Karyotype	Percentage in/second cell line
		Skin	Blood		
1	21	20	50	S: 46,X,i(Xq)	-
				B: 45,X/46,X,i(Xq)	94
2	15	-	35	B: 45,X/46,X,?i(Y)(pter→q11::q11→pter)/?del(Y)(q11)	60*
3	11	-	33	B: 45,X/46,XX	36
4	14	-	34	B: 45,X	-
5	8	-	37	B: 45,X	-
6	30	48	17	S: 45,X/46,X,del(X)(q26),dup(X)(q13q26)	15
				B: 45,X/46,X,del(X)(q26),dup(X)(q13q26)	35
7	9	-	20	B: 45,X	-
8	19	30	15	S: 45,X/46,XX	17
				B: 45,X/46,XX	50
9	19	25	80	S: 45,X	-
				B: 45,X/46,X,?del(Y)(q11)	6
10	22	-	59	B: 45,X	-
11	24	30	50	S: 45,X/46,X,r(X)	16
				B: 45,X/46,X,r(X)	10
12	36	-	30	B: 45,X	-
13	15	-	37	B: 45,X	-
14	24	-	39	B: 46,X,del(Xq)	-
15	38	20	30	S: 46,X,i(Xq)	-
				B: 45,X/46,X,i(Xq)	60
16	27	20	17	S: 46,X,i(Xq)	-
				B: 46,X,i(Xq)	-

Table 3

Karyotypes and number of cells analysed in blood and skin cultures

Case No.	Age	Number of cells analysed in cultures of		Karyotype	Percentage in/second cell line
		Skin	Blood		
17	9	-	30	B: 45,X/46,X,?del(X)(p22p11)del(q11)	13
18	12	-	30	B: 45,X/46,X,i(Xq)	77
19	24	-	50	B: 45,X/46,X,?i(Y)(pter→q11::q11→pter)/?del(Y)(q11)	10*
20	25	-	30	B: 45,X/46,X,i(Xq)/46,X,i(X)(qter→p11::p11→qter)	20/20
21	12	-	25	B: 45,X	-
22	13	-	30	B: 45,X	-
23	14	-	29	B: 45,X	-
24	29	-	50	B: 45,X	-
25	27	30	30	S: 46,X,i(Xq)	-
				B: 45,X/46,X,i(Xq)	73
26	20	-	54	B: 45,X	-
27	16	-	38	B: 45,X	-
28	23	-	50	B: 45,X	-
29	23	-	30	B: 45,X	-
30	27	20	20	S: 45,X	-
				B: 45,X/46,X,i(Xq)	30
31	22	20	33	S: 46,X,i(Xq)	-
				B: 46,X,i(Xq)	-
32	21	-	49	B: 45,X/46,X,i(Xq)/46,X,i(X)(qter→p11::p11→qter)	20/62
33	16	-	50	B: 45,X	-
34	16	30	36	S: 45,X	-
				B:45,X/46,X,i(Xq)	11
35	28	20	30	S: 45,X/46,X,inv(Y)(p11q11)	22

Table 3

Karyotypes and number of cells analysed in blood and skin cultures

Case No.	Age	Number of cells analysed in cultures of		Karyotype	Percentage in/second cell line
		Skin	Blood		
36	26	99	20	B: 45,X/46,X,inv(Y)(p11q11) S: 45,X/46,X,r(X)	40 18
37	15	-	30	B: 45,X/46,X,r(X)	35
38	14	10	28	B: 45,X S: 45,X	- -
39	18	-	38	B: 45,X B: 45,X/46,X,r(X)	- -
40	24	-	30	B: 45,X	35
41	29	20	80	S: 45,X/46,X,r(X) B: 45,X/46,X,r(X)	- 5
42	26	-	48	B: 45,X	11
43	12	-	20	B: 45,X	-
44	35	-	196	B: 45,X/46,X,i(Xq)	-
45	19	-	30	B: 45,X	18

* The percentage of cells with a presumptive isochromosome Y or deleted Y.

The only significant differences between karyotypes from skin and blood cultures were found in case No. 15: P (Fisher) = 0.0014, No. 25: P (Fisher) = 0.0046, No. 30: P (Fisher) = 0.0201.

Table 4

Chromosome constitution

Karyotypes	Probands
45,X	21
45,X/46,XX	2
*45,X/46,X,i(Xq)	9
45,X/46,X,del(X)(q26),dup(X)(q13q26)	1
45,X/46,X,?del(X)(p22p11)del(q11)	1
45,X/46,X,r(X)	4
45,X/46,X,inv(Y)(p11q11)	1
45,X/46,X,?del(Y)(q11)	1
45,X/46,X,?i(Y)(pter→q11::q11→pter)/?del(Y)(q11)	2
46,X,i(Xq)	2
46,X,del(Xq)	1
Total	45

* In two cases 50 and 73-per cent, respectively, of the isochromosome X were dicentric.

45,X/46,X,r(X) was found in four probands (9 %). Two probands had a cell line with presumptive isochromosome of Y chromosome from p-terminal to q11 as well as a cell line with presumptive deletion Y at q11. One proband had a cell line with deletion Y at q11, and another proband had a cell line with a pericentric inversion of a Y chromosome. There were thus, altogether, four cases with a cell line with Y chromosome material of a different kind, giving a frequency of 9 per cent.

There were two probands with 46,X,isochromosome X in all cells, and one proband with 46,X,deletion Xq.

The variation in chromosome constitution was remarkable and greater than that found in cases of Turner's syndrome in previous studies. This variation appeared after the repeated cytogenetic examination with further analysis of cells, usually more than 30 cells, and by the use of banding techniques; this changed the karyotype in 12 of the 45 probands.

The results of the present study indicate that repeated chromosome analyses with more than 30 cells analysed as well as with the use of banding technique might change a considerable number of previous karyotypes in women with Turner's syndrome.

Karyotypes of probands, neither wishing to participate in the one-week clinical examination, nor in the psychiatric-psychological examination, and of patients found in the prevalence study of Turner's syndrome in Danish institutions for the mentally retarded as well as in Danish psychiatric hospitals, are shown in *Table 5*. One of the 45 probands (No. 12) was included among the

patients found in the prevalence of Turner's syndrome in psychiatric hospitals, and one (No. 41) was included among the patients found in the prevalence of Turner's syndrome in institutions for the mentally retarded. There were thus 68 women with Turner's syndrome in these three studies, including the six probands who had not wished to participate in the study.

Table 5

Karyotypes of probands who did not wish to be examined, patients with Turner's syndrome in Danish psychiatric hospitals and institutions for the mentally retarded

Karyotypes	Probands who had not wished to participate in the study	Patients found in the prevalence study in institutions for the mentally retarded	Patients found in the prevalence study in psychiatric hospitals
45,X	4	4	5*
45,X/46,X,i(Xq)	-	1	-
45,X/46,XY	1	-	-
45,X/46,XX	-	1	1
45,X/46,X,r(X)	-	1°	-
45,X/46,X,+mar	1	2	-
45,X/46,XX/47,XXX	-	1	2
46,X,t(X;X)(p21;q13) (Xqter→Xp21::Xq13→Xqter)	-	1	-
Total	6	11	8

° One of the 45 probands (No. 41)

* One of these five is included among the 45 probands (No. 12)

Chapter 4

EDUCATION, OCCUPATION, ACTIVITY, RESIDENCE, MARITAL STATE, SEXUAL RELATIONS, WAY OF DRESSING, GENDER ROLE-IDENTITY, ADOPTION OF CHILDREN, MENTAL STATE IN RELATION TO KARYOTYPE AND ASSOCIATION BETWEEN TURNER SIGNS AND MENTAL STATE

a. Education

Table 6 shows the distribution of school education for all probands and their sisters who had left school. As seen in the Table there was no significant difference in school education between the probands and their sisters. Thirty-nine per cent of both groups had either the school-leaving examination of a Danish »realskole« or university entrance examination, and there was no difference in the frequency of those who left school in the 7th, 8th, 9th or 10th class.

Table 6

School level of probands and sisters who had left school

Stage of leaving school	Probands		Sisters	
7th form	5		4	
8th form	3		8	
9th form	4		8	
10th form	5		2	
Leaving examination of a »realskole«	8	39 %	12	39 %
University entrance examination	3		2	
Total	28		36	

Tables 7 and 8 show that there was no significant difference in school level between probands, matched sisters and controls with 50, 57 and 50 per cent of the three groups, respectively, who got secondary or high school education, and 83, 87 and 75 per cent of the three groups, respectively, who got more than the 7 years' compulsory school education.

Of the 19 probands still attending school at the time of the examination, 6 (32 %) were at a school for secondary or high school education, compared with 47 per cent of their sisters. The total number of girls receiving secondary or high school education in Denmark was, in 1965, 67,151 out of 367,483 girls (18 %).

Table 7

School level of probands, matched sisters and controls who had left school

School leaving level	Probands	Sisters	Controls
7th	2	2	2
8th	1	1	-
9th	1	2	1
10th	2	1	1
School-leaving examination of a »realskole«	4 } 50 %	7 } 57 %	1 } 50 %
University entrance examination	2 }	1 }	3 }
Total	12	14	8

Table 8

School level of probands, matched sisters and controls

School level at the time of examination	Probands	Sisters	Controls
1st - 7th	3	2	7
8th	1	1	-
9th	2	3	1
10th	3	1	1
»Realskole«	6 } 53 %	9 } 63 %	1 } 40 %
Grammar school	4 }	3 }	5 }
Total	19	19	15

Our findings indicate that girls with Turner's syndrome as well as girls with short stature, primary amenorrhoea and normal chromosome constitution attain an educational level similar to that of their sisters and the level which could be expected in their environment.

School work

Eighty-three per cent of the 19 probands worked conscientiously and diligently at school, compared with 28 per cent of their matched sisters (P (Fisher) = 0.002) and 50 per cent of the controls.

Table 9

Special difficulties in school subjects of probands, matched sisters and controls

	Probands	Sisters	Controls
Special difficulties in arithmetic and mathematics	8	3	3
Special difficulties in language subjects	1	1	1
No special difficulties	10	15	11
Total	19	19	15

The differences are not significant

Table 9 shows that 42 per cent of the girls with Turner's syndrome had difficulties in arithmetic, compared with 16 and 20 per cent of their sisters and controls, respectively; the difference is not significant. Difficulties in language subjects were unusual in all three groups.

Girls with Turner's syndrome are usually described as remarkably conscientious and hard-working by their teachers as well as by their parents and other informers. The finding of similar traits in the controls might indicate that such personality traits are associated with short stature and not preliminary genetically determined by lack of X chromosome material. It might to a certain extent be a compensation mechanism due to short stature. On the other hand, mosaicism with a small percentage of cells with lack of X chromosome material in the controls cannot be ruled, and the above mentioned personality characteristics might to a certain extent be genetically determined due to lack of X chromosome material.

Difficulties in arithmetic were not significantly increased when comparing the small groups in the present study, but there were indications that such difficulties were actually more common in girls with Turner's syndrome than in their sisters and controls, and some of the girls with Turner's syndrome were extremely poor at arithmetic.

It was, however, evident that special attention to such difficulties by the teachers and the parents with pedagogical efforts to overcome them, usually were successful.

It is important that teachers and parents to girls with Turner's syndrome as well as the girls themselves are told about the tendency to difficulties in arith-

metic and the possibilities to overcome them to the extent that such girls may choose science line in college.

Attitude towards school

Table 10 shows that 84 per cent of the probands liked going to school, compared with 47 and 67 per cent of the sisters and controls, respectively.

The distribution of the attitude towards going to school for the sisters and controls corresponds well to what was found in a study of 1,488 unselected Danish school girls, 55 per cent of whom liked to go to school, 35 per cent had nothing against it, and 10 per cent did not like it (*Ørum* (1973)).

Table 10

Attitude towards school of probands, matched sisters and controls

Attitude towards school	Probands		Sisters		Controls	
	Total	%	Total	%	Total	%
Liked to go to school	16	84	9	47	10	67
Nothing against it	2	11	7	39	4	27
Did not like it	1	5	3	16	1	7
Total	19		19		15	

The differences are not significant.

Teased at school

Table 11 shows that 84 per cent of the girls with Turner's syndrome were teased at school, compared with 10 per cent of their sisters (P (Fisher) = 0.0001) and 73 per cent of the controls.

Thirty-four of all the 45 probands had been teased at school, 7 of whom quite severely. Most of the other 27 said that teasing did not really bother them very much or not at all, they were able to answer back, and they considered the teasing more as friendly remarks from the other children. There were, however, a few girls with Turner's syndrome who had been teased considerably and had suffered quite a lot from it.

The reason for teasing the probands and controls was mainly short stature and, in some cases, also obesity; girls with obesity and short stature were always teased.

Table 11
Teased at school

Teasing	Probands		Sisters		Controls	
	Total	%	Total	%	Total	%
Teased considerably	3	16	1	5	6	40
Teased	13	68	1	5	5	33
Not teased	3	16*	17	90*	4	27
Total	19		19		15	

* (P (Fisher) = 0.0001).

It was evident that the way the parents and teachers reacted to the teasing had a great effect on the extent to which the probands were affected by the teasing.

The impression gained from the study is that teachers, who were aware of the problem, and who were interested in making the other children in the class accept the girl with short stature without teasing her, could do so quite successfully.

The finding of a remarkably high frequency (83 %) of girls with Turner's syndrome who liked to go to school shows that the teasing in most cases did not interfere seriously with their adjustment at school.

b. Occupation

The educational and occupational profiles of the probands and controls, who had left school, are shown in *Tables 12 and 13.*

Table 12
Education and occupation of probands

Case No.	Age	Education and occupation
1	21	University entrance examination at 18. Language course in England, 3 months. Correspondence school, 3 years' study. Working as a correspondent at the time of the examination.

6		School-leaving examination of a »realskole« at 17.
		Clerical apprenticeship, 3 1/2 years.
		Clerk, 10 years.
8	19	9th class at 18.
		Working at home, 1 year.
		Domestic servant, 1 year.
		Draper's apprentice, 5 months.
		Bookbinder's apprentice, 3 months.
		Applying for a training course as youth leader at a recreation centre, or occupational therapist.
9	19	School-leaving examination of a »realskole« at 17.
		Proprietor of a kennel for Grand Danois dogs from the age of 16.
		Folk high school, 5 months.
		Domestic servant, 6 months.
		Attending a school of domestic science at the time of the examination.
10	22	10th class at 17.
		Junior clerk, 2 1/2 years.
		Clerk, 6 months.
		Domestic servant, 4 months.
		Nursing home attendant, 1 year.
		Obstetric clinic attendant, 6 months.
		Restaurant employee, 6 months.
		Kindergarten attendant at the time of the examination.
		Planning to become an infant school teacher.
11	24	School-leaving examination of a »realskole« at 17.
		Higher commercial diploma, 2 years.
		Could not manage a clerical apprenticeship.
		Rehabilitation centre, 4 months.
		Sheltered clerical employment.
12	36	School-leaving examination of a »realskole« at 17.
		Clerical apprentice, 3 1/2 years.
		Clerk, 2 1/2 years.
		Housewife from the age of 23.
14	24	9th class at 16.
		Clerical apprentice, discharged after 3 months.
		Youth school, 6 months.
		Clerical apprentice, 3 years.
		Clerk in the customs service, 1 1/2 years.
		Clerk in a bank, 1 1/2 years.
		Clerk in an insurance company, 1 year.
15	38	8th class at 15.
		Rehabilitation attempt in office and bookbinding work, 3 months.
		Home for the disabled learning to sew, 2 years.
		Disability pension from the age of 19.
6	30	School-leaving examination of a »realskole« at 17.

16 27 9th class at 16.
Clerical apprentice, 3 1/2 years.
Clerk, 6 years.

19 24 10th class at 17.
Clerical apprentice, 3 1/2 years.
Clerk, 3 years.

20 25 9th class at 16.
Youth school, 5 months.
Domestic servant, 3 years.
Bookseller's apprentice, 1 month, was discharged on account of short stature.
Children's nurse attendant, 7 months.
Rehabilitation workshop, 3 months.
Factory work, 2 1/2 years.
Would like to train as a children's nurse.

24 29 7th class at 14.
Babysitter, 1 year.
Unoccupied, 1 year.
Factory work, 1 year.
Rehabilitation.
Sheltered factory work, 5 years.
Unoccupied, living with her parents, 4 years.
Disability pension, 4 years.

25 27 8th class at 15.
Working in a grocery store, 10 months.
Domestic servant, 4 years.
Kitchen worker in a day nursery, 5 years.
Kitchen worker in an institution for the mentally retarded, 6 months.
Would like to become a nursery attendant.

26 20 University entrance examination at 18.
Studying French and Russian at the university, 2 years.
Is planning to become a grammar school teacher.

28 23 School-leaving examination of a »realskole« at 17.
Clerical apprentice, 2 1/2 years.
Commercial school with English and German correspondence, 2 years.
Clerk, 3 years.

29 23 8th class at 15.
Apprentice in the department of a store, 4 years.
Clerk, 5 years.

30 27 School-leaving examination of a »realskole« at 17.
Apprenticeship in a bank, 2 1/2 years.
Bank assistant, 6 years.
Bank school, 1 year.

		Corresponding course in banking, 2 years. Authorized course of English, 2 years. At present studying law at the university. Got dispensation from the university entrance examination.
31	22	10th class at 18. Folk high school, 6 months. Kindergarten attendant, 1 year. Training as a children's nurse, 3 years.
32	21	9th class at 16. Bookbinding apprenticeship, 1 year. Bookbinder, 4 years.
35	28	School-leaving examination of a »realskole« at 17. Clerical apprenticeship, 10 months. Training as a children's nurse, 1 1/2 years. Children's nurse, 3 years. Clerk, 4 years.
36	26	8th class at 15. Youth school, 6 months. School for handicapped, 3 months. At home without paid occupation, 3 years. Bookbinding in a sheltered rehabilitation workshop, 5 years.
39	18	10th class at 17. Domestic servant, 6 months. School of domestic science, 10 months. Is planning to train as a nursery attendant.
40	24	8th class at 16. Youth school, 6 months. Rehabilitation centre, 3 weeks. Disability pension from the age of 18.
41	29	Normal school till the 5th class at 12. School for the mentally retarded till 18 (IQ = 76). School of domestic science for the mentally retarded, 2 years. Machinist in a private dressmaker's workroom, 7 years. Disability pension from the age of 24.
42	26	University entrance examination at 19. Studied French and philosophy at the university, 2 years. School for medical secretaries, 1 year. Medical secretary, 3 years.
44	35	School-leaving examination of a »realskole« at 17. Clerical apprenticeship in the customs service, 3 years. Clerk in the customs service, 15 years.
45	19	7th class at 14. Working at home, 1 year. Domestic servant, 6 months. Rehabilitation school, 10 months. Clerical apprenticeship, 1 1/2 years.

Table 13

Education and occupation of controls

Case No.	Age	Education and occupation
102	24	9th class at 16. Domestic servant, 5 months. Folk high school, 5 months. Night course, leaving examination of a »realskole«, 2 years. Laboratory assistant course, 5 months. Kindergarten attendant, 5 months. University entrance examination, 2 years. Studying psychology at the university at the time of the examination.
103	25	7th class at 14. Domestic servant, 6 years. Machinist, 5 years. Private day nursery.
104	27	University entrance examination at 18. Studying Russian at the university.
105	24	7th class at 14. Domestic servant, 7 years. Domestic help, 3 years.
110	17	10th class at 17. Rehabilitation workshop. No plans concerning future occupation.
113	21	7th class at 14. Domestic servant, 1 year. Ladies' hairdresser's apprentice, 3 years. Ladies' hairdresser, 2 years.
114	22	School-leaving examination of a »realskole« at 17. Training as a technical assistant, 6 months. Working as a technical assistant, 1 1/2 years. Studying to become a constructional engineer, 2 1/2 years.
115	21	University entrance examination at 18. Studying law at the university, 1 year. Working as an unskilled labourer, 6 months. Student at a folk high school.

Table 14 shows that the distribution of occupation of the probands and their sisters, who had left school, was very similar. The most common occupation was clerk or secretary, this occupation was held by 43 and 42 per cent of the two groups, respectively. The frequency of probands without skilled training was the same as for their sisters.

The two probands, who studied at the university, were studying languages and law, respectively, and the sister was studying pharmacy.

Seven sisters and no probands were employed as shop assistants and hair dressers' assistants; these two occupations are most probably rather distressing for girls with growth retardation as customers will tend to make jokes and remarks or will not wish to be served by persons who are short of stature and who appear considerably younger than their age.

Table 14

Occupation of probands and sisters who had left school

Occupation	Probands	Sisters
Attending a domestic science course	2	-
Commercial school pupil	-	2
University degree student	2	1
In Holy orders	-	1
Correspondent	1	1
Clerk or secretary	12	15
Bookbinder	2	-
X-ray assistant	-	1
Children's nurse	2	3
Shop assistant	-	4
Ladies' hairdresser	-	3
Unskilled labourer	4	5
Disability pensioner	3	-
Total	28	36

(The five probands aged 18+, who refused to be examined, were correspondent, librarian, kindergarten teacher, unskilled labourer and disability pensioner).

Table 15

Occupation of probands, matched sisters and controls who had left school

Occupation	Probands	Sisters	Controls
Folk high school pupil	-	-	1
Attending a domestic science course	1	-	-
Commercial school pupil	-	1	-
Studying to become a constructional engineer	-	-	1
University student*	1	1	2
Correspondent	1	-	-
Clerk or secretary	6	7	-
Ladies' hairdresser	-	1	1
Bookbinder	1	-	-
Model	-	1	-
Unskilled labourer	1	3	3
Disability pensioner	1	-	-
Total	12	14	8

* The proband in this group was studying French, the sister pharmacy and the two controls psychology and Russian, respectively.

As seen in *Table 15* there was no remarkable difference in the type of occupation of the probands, their matched sisters and the controls.

Our findings of no remarkable difference between probands and sisters in type of occupation correspond to our findings of no significant difference in the level of education between these two groups.

Plans of occupation for probands still at school

The probands still at school were asked about their plans for future occupation. Nine of the 16 wished to train for something that had to do with children: Children's nurse, kindergarten teacher or teacher of children at primary school as seen in *Table 16.* Librarian, physician, occupational therapist and teacher of domestic science were also among the wishes of the 16 girls.

Table 16

Plans of occupation of probands still in primary or secondary school

Case No.	Age	Plans of occupation
2	15	Teacher – nurse. Her physician has warned her against her wishes of becoming a physician or a nurse, he thinks she is too handicapped for these two occupations on account of her short stature. She has now ideas of becoming a laboratory assistant.
3	11	Nurse – something which has to do with children.
4	14	Something which has to do with children – teacher. Her plans are to get a university degree in Danish and then take further training to become a librarian.
8	19	Occupational therapist.
9	19	Teacher of domestic science.
10	22	Infant school teacher.
13	15	No plans.
22	13	Kindergarten teacher – nurse.
23	14	Physician.
27	16	Children's nurse.
33	16	Kindergarten teacher or a teacher.
34	16	Children's nurse.
37	15	Nurse – children's nurse – veterinary nurse.
38	14	Occupational therapist.
39	18	Veterinary nurse – nurse.
43	12	Actress – children's nurse – kindergarten teacher.

It was characteristic of the girls with Turner's syndrome, compared with their sisters that they nearly all loved children; already at a very young age, they were said to have been very good and responsible when looking after small children.

They were generally described as hard-working, conscientious and obliging with a good and stable mood, well-liked by everybody and often in request in

their neighbourhood for babysitting and for giving a hand in shops and homes.

Advisers, such as parents, teachers, physicians and elder siblings often advised against the probands' wishes of becoming a physician, teacher, nurse or the like by referring to the handicap of short stature for such professions. There are no reasons for advising girls with Turner's syndrome against any special profession, and one should definitely not advise against any profession by referring to their short stature as a handicap. Short stature is wrongly often equalized with poor strength and endurance, but there is no indication of such a connection in girls with Turner's syndrome.

It is our experience from the present and previous studies of girls with Turner's syndrome that they should be supported in reaching their goals as far as education and occupation are concerned, irrespective of their stature and chromosome aberration.

In girls with Turner's syndrome coupled with considerable mental immaturity and feelings of insecurity, and in girls with a low intelligence level it is, however, of great importance to give advice and support when choosing the occupation and type of training for which they seem best fitted. Very careful rehabilitation for girls in need of rehabilitation is very important as for instance in case No. 11 in the present study. No. 40 is an example of a mentally very immature girl with Turner's syndrome who was not given sufficiently careful instructions and support during the too brief attempt at rehabilitation. She ended as a disability pensioner. There is, however, no doubt that better rehabilitation could have led to satisfactory employment.

If good information, advice and treatment and in some cases special education and training are given, it is our experience that no girls with Turner's syndrome need to become disabled. The main causes of disability, if present in girls with Turner's syndrome, are usually of environmental nature.

c. Activity

The level of activity was evaluated from information given by the proband and her mother or sister as well as from information supplied by the schools. If information derived from several sources indicated that the probands had been very active and more active than her siblings as a child, the term »very active« was used. If the proband appeared to have been normally active and on a level in accordance with her siblings, the term »active« was used; activity level below that of her siblings and below the activity to be expected in her environment, was recorded as »below normal activity«.

There was no significant difference in the level of activity between probands, sisters and controls *(Table 17),* but there was a tendency to a somewhat lower level of activity for the probands, compared with sisters and controls as 5 of the 19 probands (26 %) had a low activity level, compared with 1 of 19 of the sisters (5 %) and 1 of 15 controls (7 %), and only 5 per cent of the probands had a high

level of activity, compared with 26 per cent of the sisters and controls, respectively.

Table 17
Level of activity during childhood

Activity	Probands		Sisters		Controls	
	Total	%	Total	%	Total	%
High level of activity	1	5	5	26	2	13
Normal level of activity	13	68	13	68	12	80
Low level of activity	5	26	1	5	1	7
Total	19		19		15	

The differences are not significant.
Four of the total 45 probands had a high level of activity (8.8 %), 24 a normal level (53.3 %) and 17 a low level of activity (37.7 %).

d. Residence

Table 18 shows that residence with parents, husband, boy friend or alone was very similar for the probands and the controls with 42 and 44 per cent living with husband or boy friend, respectively, compared with 80 per cent of the sisters living with husband or boy friend.

Two of the seven probands aged 18+, who were living alone, did so in an apartment in the same building as their parents, while the others were living in the same city and in the immidiate vicinity of their parents.

Table 18

Residence of probands, matched sisters and controls aged 18+

Residence	Probands		Sisters		Controls	
	Total	%	Total	%	Total	%
Living with parents	4	33	3	20	2	22
Living with husband or boy friend	5	42	12	80	4	44
Living alone	3	25	-	-	3	33
Total	12		15		9	

The differences are not significant.

Table 19

Residence of all probands and sisters aged 18+

Residence	Probands		Sisters	
	Total	%	Total	%
With parents	12	41	5	16
With spouse or boy friend	10	35*	23	72*
Alone	7	24	4	13
Total	29		32	

* (P (Fisher) = 0.0071).

Table 19 shows all probands and sisters aged 18+; 41 per cent of the probands were living with their parents, compared with 16 per cent of the sisters, and 35 per cent of the probands were living with husband or boy friend, compared with 72 per cent of the sisters (P (Fisher) = 0.0071).

There is no significant difference between probands and controls concerning residence, but the frequency of sisters living with parents is lower, and the

frequency of sisters living with husband or boy friend is significantly higher than for the probands.

These differences are accounted for in the following chapter concerning marriage.

e. Marital state

The distribution of marital status among the probands, sisters and controls is shown in *Table 20*. The frequency of those married, cohabiting and divorced was 42 per cent for the probands and 44 per cent for the controls, compared with 80 per cent for the sisters.

Table 20
Marital state of probands, matched sisters and controls aged 18+

Marital status	Probands		Sisters		Controls	
	Total	%	Total	%	Total	%
Single	7	58	3	20	5	56
Married	4		6		3	
Cohabiting	1	42	5	80	1	44
Divorced	-		1		-	
Total	12		15		9	

The differences are not significant.

Table 21

Marital state of all probands and sisters aged 18+

Marital status	Probands		Sisters	
	Total	%	Total	%
Single	21	72*	9	28*
Married	8	28°	20	63°
Divorced	-	-	3	9
Total	29		32	

* (P (Fisher) = 0.0012). ° (P (Fisher) = 0.0126).

Table 21 shows that 28 per cent of all probands aged 18+ were married, none was divorced, compared with 63 per cent married and 9 per cent divorced among their sisters (P (Fisher) = 0.0126). The cohabitation figure is not known among all sisters and is thus omitted in this table.

We found no difference in marital status between probands and controls, but a significantly lower frequency of marriages among the probands, compared with their sisters.

Girls with Turner's syndrome marry later than their sisters, and this also seems to be the case for girls with normal chromosome constitution, growth retardation during childhood and primary amenorrhoea, but no other signs of Turner's syndrome.

Cohabitation is most probably rather unusual for women with Turner's syndrome; in Denmark at the time of the present investigation divorce, too, seems to be rare.

Later marriage for probands and controls is most probably due to several factors, e.g. short stature, retardation in development of secondary sexual characteristics, retardation in development of sexual libido and, to some extent, possibly retardation in mental maturation also. Feelings of sexual insufficiency may to a certain extent be due to lack of information about the fact that the lack of gonadal development does not carry the implication of reduced sexual libido and potency.

Proper hormone treatment as well as good information about the development of sexual libido and ability to have normal sexual relations in spite of infertility given at a sufficiently early age are of great importance for the development of a normal sexual relationship with men.

f. Sexual relations

Fifteen of the 28 probands aged 18+ had never had sexual intercourse, 10 had good sexual relations, and 3 had problems.

Table 22 shows the comparison between probands, sisters and controls. There was no significant difference between probands and controls concerning sexual relations, but the number of sisters with good sexual relations was 87 per cent, compared with 50 and 44 per cent of probands and controls, respectively.

Table 22

Sexual relations of probands, matched sisters and controls aged 18+

	Probands		Sisters		Controls	
	Total	%	Total	%	Total	%
Never intercourse	5	42	2	13	2	22
Good sexual relations	6	50	13	87	4	44
Problems in sexual relations	1	8	-	-	3	33
Total	12		15		9	

The differences are not significant.

In respect of sexual relations, there was no significant difference between probands with karyotype 45,X and those with other karyotypes.

Of the 28 probands aged 18+, 13 had had their first sexual intercourse between the ages of 15 to 31; 10 of these 13 had good and stable sexual relations with no special problems. One had only had intercourse a couple of times, and two had dyspareunia complaining of narrow vagina. One proband, who was mentally retarded, was very scared about having coitus with her boy friend with whom she was cohabiting, and coitus was interfemoral only.

Our findings indicate that, in comparison with their sisters, the age at first sexual intercourse is higher in women with Turner's syndrome as well as in women with growth retardation, primary amenorrhoea and normal karyotype.

Problems concerning sexual relations were found more frequently among the probands and the controls than among the sisters of the probands; such problems were usually not very severe. Only one of the four controls and Turner probands with problems concerning their sexual relations had severe compli-

cations as described in case history No. 41.

When girls with Turner's syndrome are told that they lack normally developed ovaries and have very few chances of giving birth to a child, it is of great importance that they are also told that this aberration, as well as the fact that they need hormone treatment to get satisfactory secondary sexual characteristics, does not indicate any deficiency in respect of their sexual libido, potency and ability to love.

They should be told at a sufficiently early age that they can develop a normal sexual life, marry and adopt children even though their sexual maturity most probably will take place somewhat later than for their sisters and girl friends and usually not till after the cyclic hormone treatment has been started.

It has come out in the present study that most girls with Turner's syndrome have been told that they cannot have children, and that they do not produce ovas and need hormone treatment to develop secondary sexual characteristics and menstruation, but they have usually not been told that they are normal women as far as the ability to love and live a normal sexual life is concerned. This information is also of importance to give to parents of girls with Turner's syndrome; they are often afraid that their daughters will not be able to develop as normal females and not be able to have a normal sexual and married life. Some mothers told that they feared their daughter might become Lesbian due to her lack of ovaries and lack of sex chromosome material. Such misunderstandings on the part of the parents may have a severely traumatic effect through their behaviour towards their daughters with Turner's syndrome, and it is important that parents are as properly informed of all aspects of the development of their daughter with Turner's syndrome as the girls themselves.

g. Way of dressing

Sixty per cent of the girls with Turner's syndrome wore dresses at the interview, compared with only 17 per cent of the sisters. The dresses of the probands were often very feminine; 36 per cent of the probands wore slacks, compared with 61 per cent of the sisters; only 4 per cent of the probands were in jeans, compared with 22 per cent of the sisters.

The jewellery worn by the probands was nearly always very feminine, more so than the jewellery worn by the sisters. Thin gold neck chains with a small heart or medallion and thin gold bracelets were typical of the jewellery worn by the probands.

There was a greater variety in the type of jewellery worn by the sisters, and it was less delicate and less feminine in type. There was no difference in the amount of jewellery worn by the probands, compared with their sisters.

The feminine way of dressing and the jewellery worn by girls with Turner's syndrome support the clinical impression that these girls usually appear very

feminine in their taste, feelings and general behaviour as has also been stressed by other authors and is further discussed in the following chapter dealing with gender role-identity.

h. Gender role-identity

Attempts to distinguish between different types of deviant sexual behaviour have led to the term »gender role« *(Hampson & Hampson* (1961) and *Hampson* (1964)). According to these authors, gender role refers to all those aspects of a person's behaviour and attitudes which serve to disclose the person as having the status of a boy or a man, a girl or a woman. Gender role is one of several components of sex. (According to *Money, Hampson & Hampson* (1957) and *Hampson & Hampson* (1961), these components are: Chromosomal sex, internal anatomic sex, external anatomic sex, hormonal sex, sex of assignment and rearing and gender role-identity).

»Gender-identity« is the sex a person accepts, irrespective of gender role. *Stoller* (1964 a, b, c, 1965) formulated the concept of »core gender identity« for the feeling of »I am a male« or »I am a female« as distinguished from »gender role« for a masculine or feminine way of behaving.

Gender role-identity in girls with Turner's syndrome

Gender role-identity was definitely female in all probands. They had participated in the usual types of girl's games and interests, some of them continued to be interested in playing with dolls somewhat later than their sisters. Most of them loved small children. They were already as children eager to take care of babies in their neighbourhood, and they were considered very good and responsible babysitters. They were very affectionate and had a considerable need for physical contact with their parents.

It was characteristic of them that they were usually more feminine and more neatly and prettily dressed than their sisters with very feminine jewellery; furthermore, their appearance and behaviour during the interview and in the ward, where they spent a week for examination, was always very feminine.

Our findings correlate with previous studies of gender role-identity, e.g. *Ehrhardt et al.* (1970) and *Theilgaard* (1972) who both concluded from their studies that girls with Turner's syndrome were unequivocally feminine in the gender role and gender identity.

Parents, and especially mothers, are often afraid that their daughter with lack of X chromosome material may not become a »real girl«. It is important that they are told that girls with Turner's syndrome usually tend to become even more feminine than their sisters.

i. Adoption of children

Two of the eight probands, who were married, had adopted a child, to one permission for adoption had been granted, to one permission for adoption had been refused, one had sent in an application for permission, and two were planning to apply. One had never considered applying as she was convinced that her application would be turned down on account of her physical handicap of congenital hip disorder.

It was our impression from the psychiatric examination that, with a single exception, all of the married probands were capable of becoming good mothers to whom permission to adopt a child should be granted. Their marriages were good and stable, they were well adjusted in marriage as well as in work, and they lived in comfortable circumstances. They were responsible and conscientious women with strong maternal instincts, they loved children, and in one case only were there signs of mental illness.

The short stature of girls with Turner's syndrome as well as the minor physical aberrations should be no obstacle to adoption. Girls with Turner's syndrome are usually endowed with qualities that make them well-fitted for becoming adoptive mothers, but not seldom they are discriminated against by the adoption authorities on account of their short stature, of their chromosome aberration and occasionally also on account of mental immaturity. In a few cases of Turner's syndrome, mental immaturity is so pronounced that the advisability of granting permission for adoption may be questioned, but such girls will usually not apply at all. It appears in the present study that those who were planning to apply, or who had already applied, for permission to adopt a child were qualified to receive it.

Psychiatrists, psychologists, social workers and others who examine applicants for the adoption af a child usually have too little knowledge of the effect of the chromosome aberration found in Turner's syndrome; this lack of knowledge may easily lead to the conclusion that chromosome aberrations lead to aberrations in personality and intelligence development as well as to difficulties in social adjustment. More knowledge of the personality development in girls with Turner's syndrome would be of great importance for those with whom the decision for or against permission of adoption rests.

k. Occupation, school performance, behaviour and sexual life in relation to karyotype

The distribution of occupation was very similar for those with karyotype 45,X and those with other karyotypes as seen in *Table 23,* and there was no difference in the distribution of school education between the two groups *(Table 24).*

Table 23

Occupation in relation to karyotype

Occupation	Probands with 45,X	Probands with other karyotypes
Unskilled labourer	-	4
Disability pensioner	2	1
Bookbinder	-	2
Correspondent	-	1
Clerk or secretary	5	7
Children's nurse	1	1
Student of domestic science	-	2
University undergraduate	1	1
Total	9	19

Table 24

School education in relation to karyotype
Probands who had left school

Stage of leaving school	Probands with 45,X	Probands with other karyotypes
7 - 8	4	4
9 - 10	3	5
School leaving examination of a »realskole« / University entrance examination	7	5
Total	14	14

School level, school working capacity and difficulties in special subjects were similar in the two groups. There was no significant difference between the two groups concerning attitude towards school and relations with teachers and other children or with regard to behaviour at school.

Half of the 24 probands with other karyotypes had a low activity level, compared with only 24 per cent of those with 45,X, but the difference is not significant.

Half of the probands with 45,X as well as half of the probands with other karyotypes aged 18+ had never had sexual intercourse, and 1/3 of each group had good sexual relations.

A study of the case histories reveals no remarkable differences between girls with Turner's syndrome and 45,X in all cells and those with a cell line having additional X or Y chromosome material.

The girls with 45,X/46,XX had in no way fewer physical or mental signs of Turner's syndrome.

The proband lacking only part of the long arms of X was not significantly different from the probands with isochromosome long arms X lacking the short arms or from the Turner girls with 45,X in all their cells.

l. Association between clinical Turner stigmata and mental aspects

There was no association between the presence of pterygium colli or cubitus valgus and aspects such as intelligence, school education, occupation, social adaption, marital status, sexual life or mental illness. Nor was there any association between pterygium colli or cubitus valgus and stature.

Chapter 5

FERTILITY, HORMONE TREATMENT, STATURE AND WEIGHT, CLINICAL SIGNS OF TURNER'S SYNDROME

a. Spontaneous menstruation in women with Turner's syndrome

Weiss (1971) studied a girl with karyotype 45,X, who had normal secondary sexual characteristics and normal menstruation from the age of 15. Ovarian biopsy showed primary oocytes and primitive follicles.

Weiss (1971) mentioned that several authors have found infants with 45,X with germ cells and primordial follicles (*Carr et al.* (1968), *Frøland et al.* (1963), *Conen & Glass* (1963), *Court Brown et al.* (1964), *Bove* (1970)).

Lindsten (1963) found occasional menstrual discharge in 10 out of 49 adult patients with Turner's syndrome aged 16+, 5 had irregular menstruation for longer periods.

McDonough et al. (1971) found menstruation in three girls with Turner's syndrome, and *Stafford et al.* (1973) studied a 29-year-old girl with karyotype 46,X,i(Xq), she had a grossly normal ovary on one side, in which was found a well developed Graafian follicle lined with a granulosa layer and a theca interna. She had had a spontaneous menstruation period at the age of 19.

The literature contains some 20 examples of females with Turner's syndrome who menstruated fairly regularly as reviewed recently by *Weiss* (1971) and *Lieber & Berger* (1973).

Table 25
Menstruation in women with Turner's syndrome

Case No.	Karyotype	Menstruations
1	45,X/46,X,i(Xq)	2-3 times before the age of 18
15	45,X/46,X,i(Xq)	From the age of 15 to 21
16	46,X,i(Xq)	3 times at the age of 15
39	45,X/46,X,r(X)	2 times at the age of 15
211	45,X/46,XX/47,XXX	*From the age of 16 to 34

* No. 211 gave birth to a boy at the age of 21.

Table 25 shows that 5 of the 51 women with Turner's syndrome aged 15+ and examined in the present study had had spontaneous menstruation (10%), 1 of them from the age of 15 to 21, 1 from age 16 to 34 and in 3 menstruation had occurred from 1 to 3 times. None of these five girls had 45,X in all cells as was otherwise found in 41 per cent of the total group; the differences are, however, not significant (P (Fisher) = 0.0659). The frequency of spontaneous menstruations among those with other karyotypes than 45,X was 17%.

b. Women with Turner's syndrome giving birth to children

Singh & Carr (1966) demonstrated that the gonads of early 45,X embryos appear normal by both macroscopic and microscopic examination with primordial germ cells and pregranulosa cells up to the third month of intrauterine life.

The 45,X female is most probably anatomically and histologically normal at the early stages of gestation and undergoes atrophy and disappearance af the follicles over periods of time that vary from individual to individual; and due to these findings streak gonads should most probably not be included in the definition of Turner's syndrome as also stressed by *Philip & Sele* (1976).

There are several reports of females with a karyotype similar to our patient with 45,X/46,XX/47,XXX, who have given birth to children as surveyed by *Giraud et al.* (1970), and two patients with karyotype 45,X/46,XX have given birth to children *(Bomers-Marres* (1966) and *Kava & Klinger* (1968)). *Lieber & Berger* (1973) studied a woman with karyotype 45,X/46,XX who had an abortion performed at her own request.

Bishun et al. (1964) described a woman with karyotype 45,X/46,XX who had repeated spontaneous abortions of malformed foetuses, and *Predescu et al.* (1969) studied a woman who had four spontaneous abortions, and who gave premature birth to a child with presumptive Down's syndrome.

Mackay et al. (1971) reported pregnancy and childbirth in a 30-year-old woman with karyotype 45,X/46,XX with 66 per cent cells having the karyotype 45,X. She had occasional spontaneous menstruation from the age of 15 to 19. At the age of 30, after cyclic hormone treatment she was given three periods of Clomiphere 100 mg daily for five days in each period. The first two treatment periods produced satisfactory menstrual bleeding, but the monophasic basal temperature curves indicated the absence of ovulation. A third treatment period was subsequently administered, and for 16 days after the end of the therapy the basal temperature remained unchanged. Eight weeks later it was evident that she was pregnant. She had a Caesarean section performed at the 37th week of gestation due to preeclamptic toxaemia, and she delivered a female baby weighing 1,300 grams at birth. The child's progress was complicated by the development of a pulmonary distress syndrome, but when mother and child were finally discharged, they were both well.

Recent literature surveys by *Gilboa & Rosenberg* (1975) and *Reyes et al.* (1976) reveal 54 pregnancies in 22 women with a cell line of 45,X as well as a cell line 46,XX or 47,XXX.

Six women with karyotype 45,X have given birth to seven children *(Bahner et al.* (1960), *Nakashima & Robinson* (1971), *Grace et al.* (1973), *Groll & Cooper* (1975), *Lajborek* (1976) and *Philip & Sele* (1976)). The woman with Turner's syndrome described by *Groll & Cooper* gave birth to two children. The woman described by *Lajborek* (1976) gave birth to a child with Down's syndrome.

Among 60 pregnancies reported in 28 women with Turner's syndrome 18 were spontaneous abortions (33 %), 3 malformed foetuses among 4 stillbirths. Twelwe of the 36 liveborn children (33 %) had some physical abnormalities, 3 of them had Down's syndrome (8 %) and 5 had a 45,X cell line (13 %). Ascertainment bias most probably plays a certain role as background for these high frequencies concerning physical abnormalities and chromosome aberrarations, but pregnant Turner-women should be offered prenatal chromosome examination.

Lieber & Berger (1973) drew attention to the fact that in previous reports of fertile females with karyotype 45,X or 45,X/46,XX, the signs associated with the Turner phenotype appeared, except for short stature, to be either minimal or entirely absent. *Lieber & Berger* (1973) concluded that it would seem advisable to inform such patients that they were potentially capable of conceiving and possibly of having a normal child, or to ensure that unwanted conception does not occur in such patients.

One of the 51 females with Turner's syndrome aged 15+ (No. 211) with karyotype 45,X/46,XX/47,XXX in the present study got a child, a boy who died at the age of 3 months of pyloric stenosis. This woman had had spontaneous menstruations till the age of 34.

Parents of girls with Turner's syndrome, especially those with chromosome mosaicism, and the girls themselves should be told that there is a chance of menstruating spontaneously and hence a possibility of becoming pregnant.

Information given in this way is correct and not nearly so psychotraumatic as to be told that spontaneous menstruation and pregnancy are definitely not possible.

They should never be told that they have no ovaries or no ovas, rather that their ovaries do not function normally, and that hormone treatment is most probably necessary to produce menstruation and to give a normal development of secondary sexual characteristics. They should be urged to apply for the adoption of a child as soon as they marry, and such an application should be supported.

c. Oestrogen treatment

Twenty-five of the 29 probands aged 18+ had received cyclic oestrogen treat-

ment (in nearly all cases the oestrogen treatment was supplemented with gestagen). None of the 45 probands had been given androgen treatment. Eight of the 25 had been given cyclic oestrogen treatment from the age of 14 to 16 (32 %), 14 from the age of 17 to 19 years (56 %) and 3 after the age of 20 (12 %). Hormone treatment was discontinued in 11 of the 25 for reasons varying from case to case as may be seen in *Table 26*. Swelling of feet and legs was the main cause in two cases, obesity in one, nausea in one and anorexia nervosa in one. In three it was not possible to specify any reason for the discontinuation og hormon treatment. Three were not interested in having menstruation when it did not carry with it the possibility of becoming pregnant.

Table 26

Cyclic hormone treatment which was discontinued

Proband No.	Age at beginning of hormone treatment	Age of discontinuation of hormone treatment	Causes of discontinuation of hormone treatment
1	17	17	Swelling of feet and legs
12	20	34	Anorexia nervosa
14	19	21	Obesitas
15	32	36	Unknown cause
16	16	25	Unknown cause
19	17	23	Not interested in having menstruation
24	15	26	Swelling of feet and legs
31	18	22	Unknown cause
35	17	27	Not interested in having menstruation
36	19	20	Not interested in having menstruation
44	17	19	Nausea

Two of those, who had stopped taking hormones, said that they had felt considerably better during hormone treatment, but there was no definite evidence of any beneficial effect of oestrogen hormone treatment on sexual libido, mental maturity or mental and physical health in any of the cases we studied.

It is of importance not to start cyclic hormone treatment before the maximum growth of stature has been attained as hormone treatment tends to stop growth of stature by precocious epiphyseal closure.

Information to girls with Turner's syndrome as well as to their parents of this fact as well as of the effects and possible side-effects of hormone treatment is of great importance.

The cyclic oestrogen treatment, which was started before the age of 17 in 8,

after the age of 20 in 3 and not at all in 4, should most probably ideally have been started between the age of 17 and 19 in all cases and not only in 56 per cent as it was the case in the present group.

Some physicians stress the importance of producing menstruation and secondary sexual characteristics at the same age as in other girls and use this as the main indication for beginning treatment as early as between 14 and 16 years of age as it was done in 32 per cent in the present group. It is, however, our experience that girls with Turner's syndrome, who usually have delayed mental maturity development, do not reach the maturity level of other girls aged 14 to 16 till after the age of 16, and also from a psychological point of view it thus seems advisable to wait with cyclic oestrogen treatment till between the age of 17 and 19.

The effect of cyclic oestrogen hormone treatment is normal menstruations as well as normal development of secondary sexual characteristics. Hormone treatment may have some effect on mental maturation and sexual libido, but the psychological effect of the occurrence of menstruation and the development of secondary sexual characteristics is indication enough for hormone treatment.

Side effects, as mentioned in the present study, need not usually lead to the discontinuation of hormone treatment as these may, in general, be eliminated by a change of hormone preparation or method of administration.

At the time of the interview from 1971 to 1973 we advised all probands aged 18+ to try cyclic oestrogen-gestagen hormone treatment again in order to check whether it had any beneficial effect on their general conditions and sexual libido.

Since the interviews of the probands from 1971 to 1973, we have, however, become aware of some reports concerning endometrial cancer of the uterus in women with Turner's syndrome as surveyed by *Nielsen & Sørensen* (1977). A total of nine such cases has been reported *(Sirota et al.* (1975), *Canlorbe et al.* (1967), *Robert & Wells* (1975), *McCarroll et al.* (1975), *Wilkinson et al.* (1973), *Cutler et al.* (1972), *Dowsett* (1970) and *Scott* (1967)).

The mean age of these nine women was 30 years, compared with an expected mean age of 55 at the time of diagnosing endometrial cancer of uterus in the general female population. Seven of the nine cases were given oestrogen treatment only, and two were given oestrogen-gestagen treatment. The hormone treatment had been given from 5 to 20 years with an average duration of 9 years. All nine were, however, given synthetic oestrogen preparations, diaethylstilboestrol or stilboestrol.

Cutler et al. (1972) made a histological endometrial examination of 24 women with Turner's syndrome who had been given oestrogen treatment for 5 years or more. Two had endometrial cancer of the uterus, and one was a doubtful case.

These findings do not prove a causal relationship between oestrogen treatment and the endometrial cancer of the uterus in women with Turner's syndrome, but on the background of a possible association we believe that one

might consider only to give oestrogen-gestagen treatment for a few years until satisfactory development of secondary sexual characteristics has taken place. Another reason to hesitate to give long-term oestrogen treatment is the finding discussed in *Chapter 13* concerning a poorer cognitive performance found in probands given long-term oestrogen treatment, compared with those not treated or given treatment during a shorter period of time.

However, if one considers continuous oestrogen treatment to be of importance in certain cases, it should always be given as a combined oestrogen-gestagen treatment, and regularly histological endometrial examination should be made, and the findings of cystic glandular hypoplasia should lead to discontinuation of the treatment.

Oestrogen hormone treatment af girls with Turner's syndrome should be initiated at and followed up at endocrinological or gynaecological clinics possessing the requisite experience of such treatment.

A systematic psychiatric-psychological evaluation of the effects on the mental state of continuous and sufficient oestrogen hormone treatment of girls with Turner's syndrome has as yet not been made. Such investigations are called for.

The question of androgen hormone treatment in order to increase stature is discussed in a special section in connection with stature.

d. Height and weight

Birth length and weight

The mean weight of the 45 probands at birth was 2,878 grams with 95% confidence limits 2,734 - 3,023 which was significantly lower than the mean weight of 3,280 grams with 95% confidence limits of 3,262 - 3,298 grams among 4,895 newborn Danish children with normal karyotypes *(Friedrich & Nielsen* (1973) and *Nielsen & Sillesen* (1975)) *(Table 27)* ($P < 0.01$).

Table 27
Length and weight at birth for the 45 probands and 4,895 unselected Danish children

	Mean weight in grams	95 % confidence limits	K-S Dmax	Mean length in cm	95 % confidence limits	K-S Dmax
Probands (n = 45)	2,878	2,734-3,023	0.09	49.1	48.3-49.9	0.15
Controls (n = 4,895)	3,280	3,262-3,298	0.05	50.7	50.6-50.8	0.09

The mean length at birth for the probands was 49.1 cm with 95% confidence limits of 48.3 - 49.9 which was significantly shorter than the mean length of 50.7, 95% confidence limits 50.6 - 50.8, for the 4,895 children with normal karyotypes as seen in *Table 27* ($P < 0.01$).

Birth length and weight below the expected level for children with Turner's syndrome correspond with previous findings. Children with aneuploid sex chromosome as well as autosomal abnormalities in general have birth weight and also often birth length below the expected as found by *Chen et al.* (1971, 1972) and recently reviewed in a survey by *Barlow* (1973). According to *Barlow* the cause of decrease in birth weight in children with aneuploid sex chromosome aberrations might be a retardive effect of heterochromatic chromosomes on cell division. This hypothesis could, however, hardly account for decreased birth weight in girls with Turner's syndrome, karyotype 45,X.

Genetic imbalance with excess or lack of chromosome material might, however, influence nidation and foetomaternal conditions in general and thus lead to a lower birth weight.

The finding of a decrease in urinary oestriol excretion in mothers carrying a child with Down's syndrome or Edward's syndrome (*Jørgensen & Trolle* (1972) and *Blumenthal & Variend* (1972)) indicates that at least certain chromosome aberrations reduce the foetomaternal endocrine activity.

According to *Jørgensen & Trolle* (1972) this might be due to insufficient nidation of the chromosome defect ovum.

Height and weight during childhood

The controls were presented by *Andersen et al.* (1974), they comprise 5,500 randomly selected Danish girls aged 7 - 18 years.

Fig. 1 shows that 14 of the 20 girls with karyotype 45,X were below the third percentile at all ages till the age of 12, and all but 2 till the age of 18.

Fig. 2 shows that 8 of the 12 girls with more than one X in all or part og their cells or Y chromosome material in part of their cells were below the third percentile for normal girls till the age of 12, and all from 12 till 18 years of age.

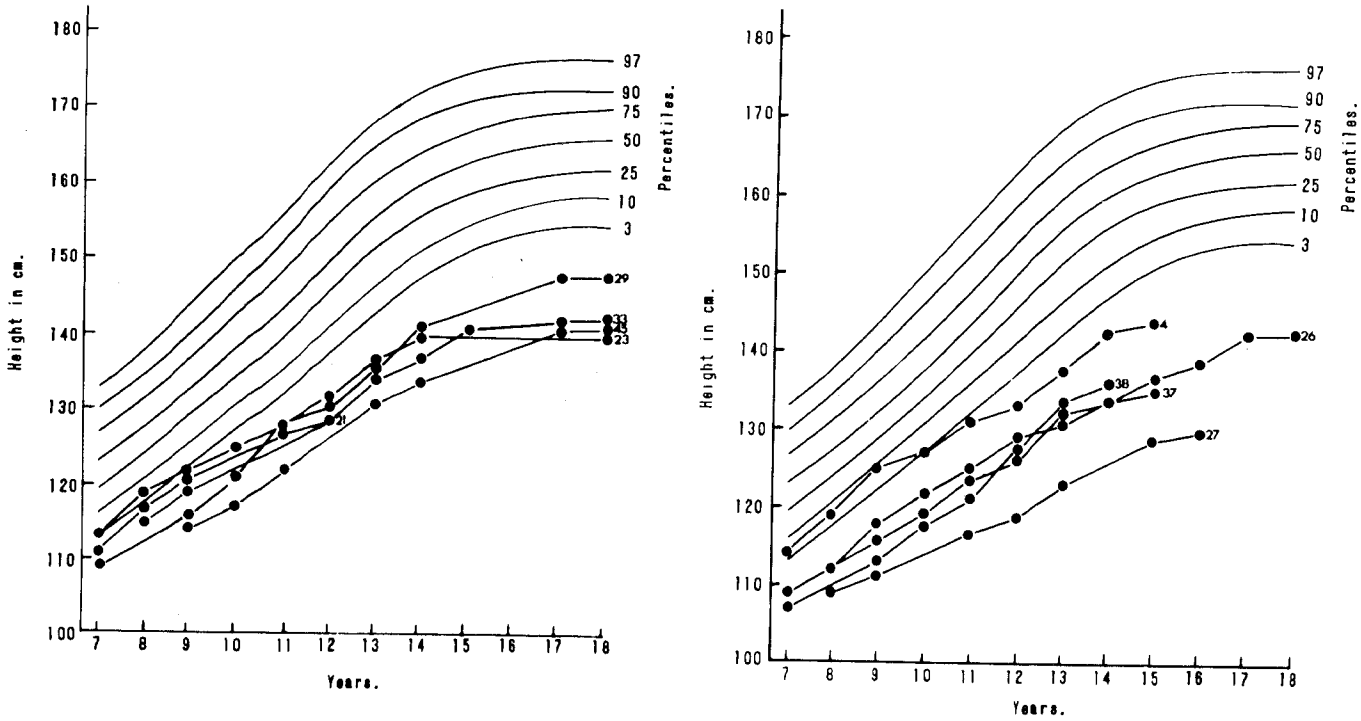
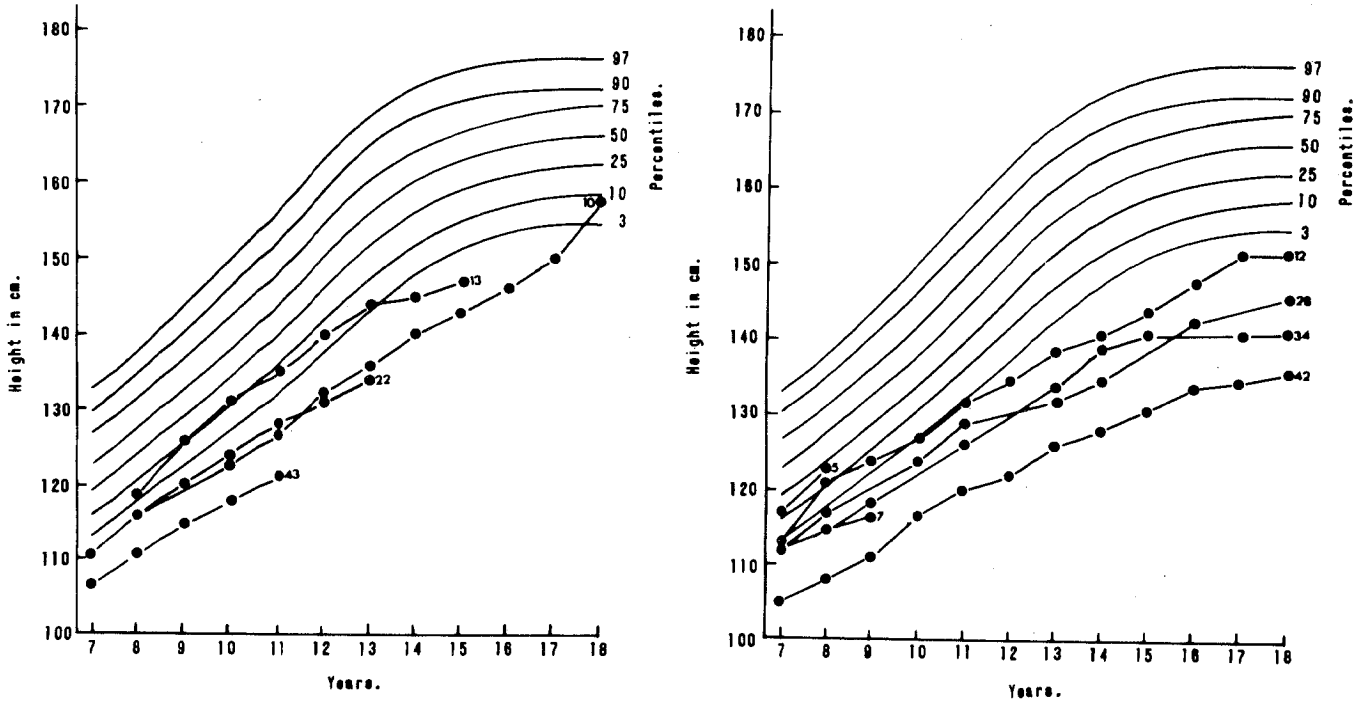


Fig. 1
Height of 10 Turner probands with karyotype 45,X in relation to percentile distribution of 5,500 Danish girls aged 7-18 years



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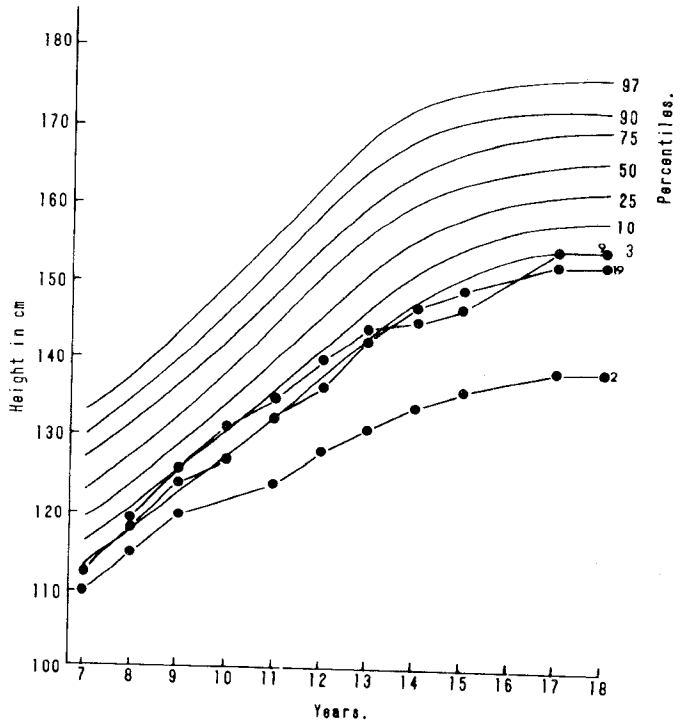

Fig. 2
Height of 3 Turner probands with Y material in part of their cells in relation to percentile distribution of 5,500 Danish girls aged 7-18 years.

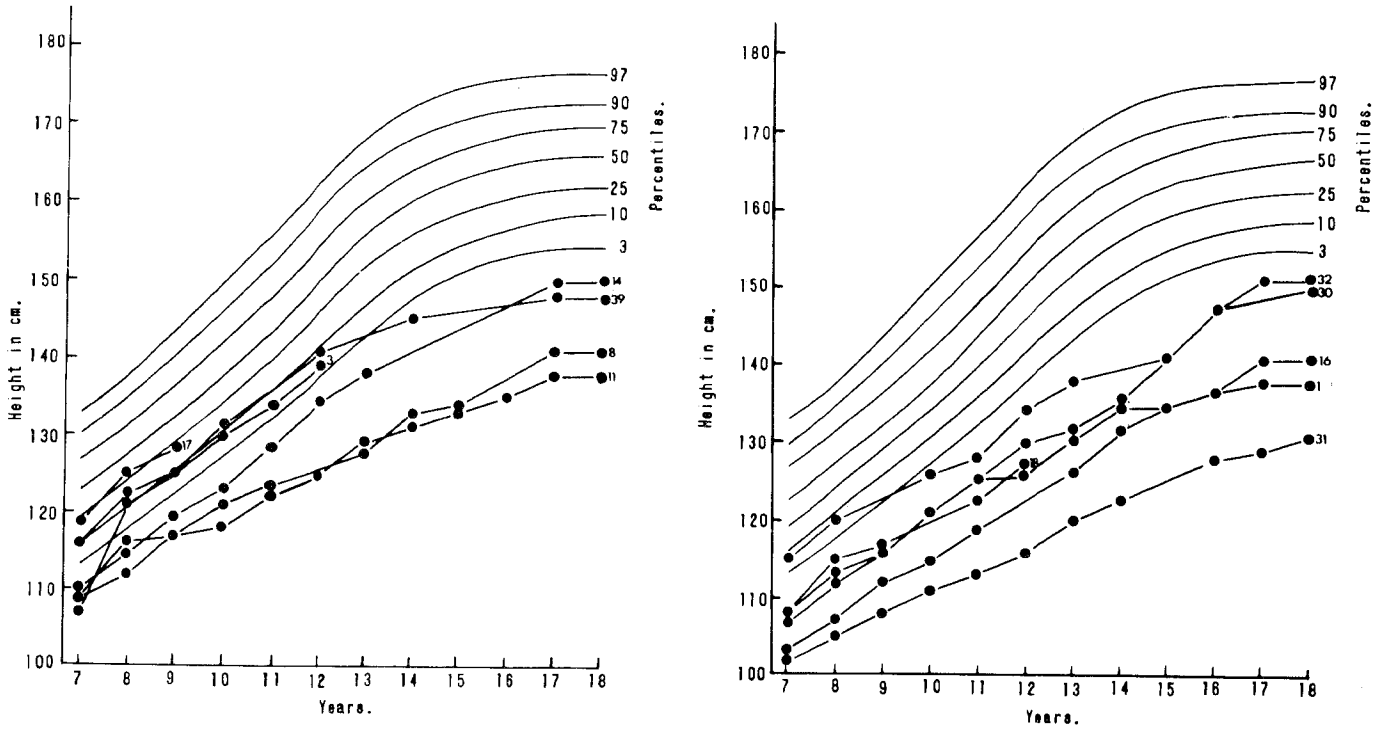

Fig. 2
Height of 12 Turner probands with other karyotypes than 45,X in relation to percentile distribution of 5,500 Danish girls aged 7-18 years.

The difference in growth development between the girls with 45,X in all their cells and the girls with more sex chromosome material in all part of their cells is not significant. As seen in *Fig. 2,* one of the three girls with Y chromosome material in part of their cells had height measurement below the third percentile till the age of 18. The group is, however, small, and the difference compared with the 45,X group is not significant.

The weight in relation to height was above the 50th percentile of normal girls in all but one with a height of 130 cm or above. The only girl with weight slightly below the 50th percentile level was No. 19 with karyotype 45,X/46,X,?i(Y) (pter→q11::q11→pter)/?del(Y)(q11). Thirteen girls had weight measurements above the 97th percentile at one or more measurements above height 130 cm.

The highest frequency of girls with weight above the 97th percentile was found in those with more than one X in all or part of their cells (67 %), compared with only 29 per cent of those with karyotype 45,X, and none of the three girls with Y chromosome material in part of their cells had height measurements above the 97th percentile level.

The mean height with standard deviation and the 95% confidence limits for probands aged 7 to 15 are shown in *Table 28* and the mean ± SD in *Fig. 3*. The height of the majority of girls with Turner's syndrome is below the normal third percentile. The difference between the mean height and the normal third percentile increases gradually from approximately 3 cm at the age of 7 to 12 at the age of 15. The 95% confidence limits are below the normal third percentile from age 7 to 15.

Table 28

Height and weight of probands with Turner's syndrome from the age of 7 to 15

n	Age	Mean	SD	95 % confidence limits
		Weight in kilograms		
29	7	20.2	2.8	19.2-21.3
30	8	22.9	3.8	21.4-24.3
29	9	25.2	4.4	23.5-26.9
25	10	27.0	4.6	25.1-28.9
30	11	30.1	5.5	28.1-32.2
24	12	33.8	6.8	31.0-36.7
26	13	35.4	6.4	32.8-38.0
22	14	39.6	8.3	36.0-43.3
19	15	42.1	9.1	37.7-46.5
		Height in cm		
29	7	110.7	4.2	109.1-112.3
30	8	115.6	4.8	113.8-117.4
30	9	118.4	4.9	116.6-120.3
25	10	122.3	5.1	120.2-124.4
30	11	125.9	5.3	123.9-127.9
24	12	130.4	6.1	127.8-132.9
26	13	133.0	5.6	130.7-135.2
23	14	137.1	5.7	134.6-139.5
19	15	139.3	5.5	136.7-141.9

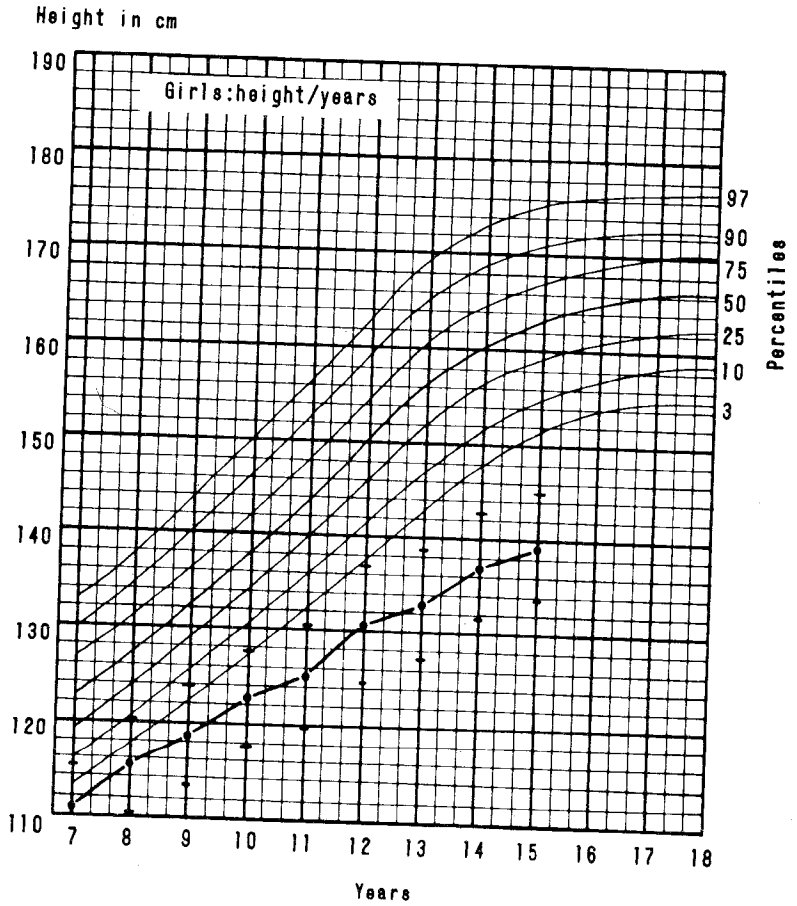

Fig. 3
Mean ± SD for height, weight and mean growth acceleration for the 45 Turner probands in relation to the distribution of 5,500 Danish girls aged 7-18

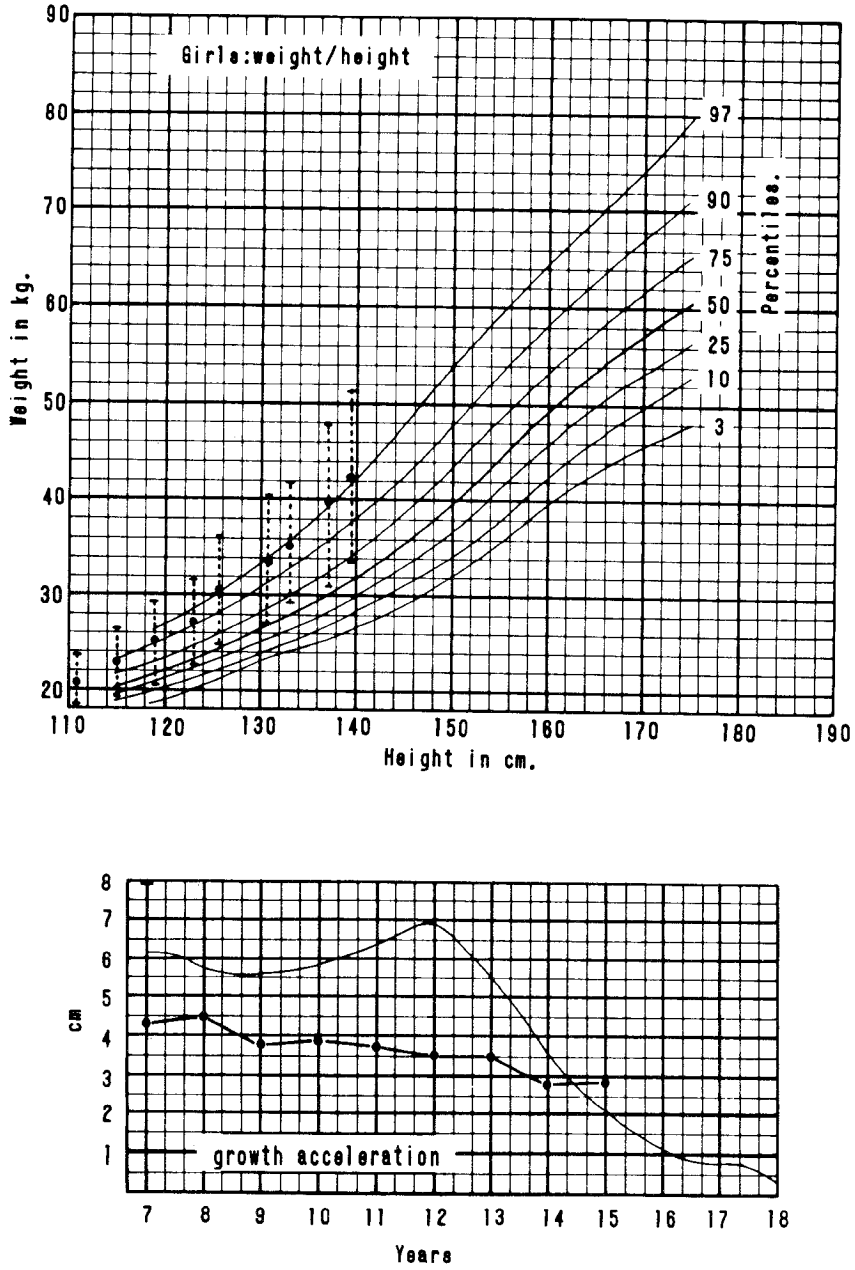

Fig. 3
Mean ± SD for height, weight and mean growth acceleration for the 45 Turner probands in relation to the distribution of 5,500 Danish girls aged 7-18

The pubertal growth spurt was lacking as also shown in *Fig. 5* with the mean growth in cm per year which varied from approximately 4.5 to 3.5 cm per year from the age of 7 to the age of 11, compared with an expected growth rate varying from 5.5 to 6.9 in normal girls during this period as seen in *Fig. 7.*

The growth rate fell from 4.5 to 3 cm per year from the age of 11 to the age of 16, compared with a fall from 6.9 to 2.0 per year in normal girls during this period. *Fig. 5* shows that the mean weight in relation to height was between the 90th and 97th percentile.

The retardation in body height growth in Turner's syndrome thus covers the whole growth period from foetal life to adolescence with a growth rate smaller than normal, especially after 8 years of age and with a decrease in pubertal growth spurt.

Prediction of final height

Table 29 shows the distribution of height for the 24 probands aged 20+. The range was from 138 to 158 cm with a mean of 146 cm.

There was no association between height and karyotype. The 8 girls with karyotype 45,X had a mean height of 148 cm, and the 16 with more X chromosome material and different types of mosaics or 46,X isochromosome X, 46,X ring chromosome X, had a mean height of 145 cm.

The two adult girls with Y chromosome material (isochromosome Y and pericentric inversion Y) in part of their cells were 149 and 153 cm tall, respectively. One girl with karyotype 45,X was 158 cm tall, and one with 45,X/46,X,del(X) was 156 cm tall.

Lindsten et al. (1973) showed that the final body height could be predicted from the time of eruption of the first permanent teeth with a residual standard deviation of 2.33 cm. The final body height in girls with Turner's syndrome could further be evaluated using only body height at the age of 8. *Lindsten et al.* (1973) calculated the final body height for 18 patients with Turner's syndrome and 45,X on the regression line for Y (final height) on H_8 (height at 8 years of age) ($Y = 1.4163\ H_8 - 13.8284$).

We calculated the predicted height in probands aged 20+, on whom we had height measurement at the age of 8, according to the method used by *Lindsten et al.* (1973) according to the regression line of body height for 12 girls with Turner's syndrome ($Y = 1.4163\ H_8 - 13.8284$) and found that the predicted height varied from the observed values from − 3.5 cm to +9.9 cm with a mean of +2.1 cm. Only half of our cases were, however, girls with karyotype 45,X *(Table 30),* compared with all of the cases described by *Lindsten et al.* (1973). It is further questionable whether the measurement of height at the age of 8 as well as the measurement of final height was completely correct, and no conclusion can thus be drawn from this. From the findings by *Lindsten et al.* (1973) it

Table 29

Height of probands aged 20+

n = 24

Case No.	Age	Karyotype	Height in cm
1	21	45,X/46,X,i(Xq)	140
6	30	45,X/46,X,del(X)(q26),dup(X)(q13q26)	156
10	22	45,X	158
11	24	45,X/46,X,r(X)	138
12	36	45,X	152
14	24	46,X,del(Xq)	150
15	38	45,X/46,X,i(Xq)	131
16	27	46,X,i(Xq)	141
19	24	45,X/46,X,?i(Y)(pter→q11::q11→pter)/?del(Y)(q11)	153
20	25	45,X/46,X,i(Xq)/46,X,i(X)(qter→p11::p11→qter)	141
24	29	45,X	144
25	27	45,X/46,X,i(Xq)	150
26	20	45,X	148
28	23	45,X	146
29	23	45,X	148
30	27	45,X/46,X,i(Xq)	150
31	21	46,X,i(Xq)	137
32	21	45,X/46,X,i(Xq)/46,X,i(X)(qter→p11::p11→qter)	151
35	28	45,X/46,X,inv(Y)(p11q11)	149
36	26	45,X/46,X,r(X)	151
40	24	45,X	150
41	29	45,X/46,X,r(X)	138
42	26	45,X	138
44	35	45,X/46,X,i(Xq)	146
Mean			146
Range			137-158
95 % confidence limits			143-148

appears that the method described of final height prediction of girls with Turner's syndrome during childhood either due to body measurement at the age of 8 or time of eruption of the first teeth are very valuable, and they should be used when studying the possible effect of androgen hormone treatment of girls with Turner's syndrome and human growth hormone.

e. Androgen treatment

Ray et al. (1965) found that treatment with Oxandrolone in doses of 0.25 mg per kg per day to children with Down's syndrome during a two-year-period gave a highly significant final increase in stature, compared with a control group. *Danowski et al.* (1967) used Oxandrolone in treatment of three children with

Table 30
Final height and predicted height (Y = 1.4163 H_8 − 13.8284) in probands aged 20+ in whom height at 8 years of age was known

Case No.	Karyotypes	H_8	Y	Y predicted	Y − Y predicted
1	46,X,i(Xq)	107.0	138	137.7	+ 0.3
10	45,X	114.3	158	148.1	+ 9.9
11	45,X/46,X,r(X)	110.5	138	142.7	÷ 4.7
14	46,X,del(Xq)	113.2	150	146.5	+ 3.5
16	46,X,i(Xq)	109.0	141	140.5	+ 0.5
19	45,X/46,X,?i(Y)(pter→q11::q11→pter)/?del(Y)(q11)	118.0	153	153.3	÷ 0.3
26	45,X	110.5	148	142.7	+ 5.3
28	45,X	113.9	146	147.5	÷ 1.5
30	45,X/46,X,i(Xq)	115.0	150	149.0	+ 1.0
31	46,X,i(Xq)	102.0	137	130.6	+ 6.4
32	45,X/46,X,i(Xq)/46,X,i(X)(qter→p11::p11→qter)	112.0	151	144.8	+ 6.2
42	45,X	108.2	138	139.4	÷ 1.4

H_8 = Age at 8. Y = Final height.

Turner's syndrome. Only one of them responded to the treatment with significant increase in growth; no remarkable side-effects were observed. At the beginning of the treatment, the three girls were at the ages of 13, 14 and 19, respectively; the doses were 10 to 40 mg Oxandrolone per day given in 2, 18 and 31 months, respectively.

Johanson et al. (1969) gave Fluoxymesterone in doses of 2.5 to 5 mg daily to 15 girls with Turner's syndrome starting from the age of 9 to the age of 18 and given during 18 to 32 months. Growth rates in cm per year increased from 1.0 to 4.3 cm with a mean of 3.3 cm to 4.1 to 8.1 cm with a mean of 6.6 cm per year during the first year of treatment.

There were, however, several side-effects of such treatment such as: Pedal oedema, varying degress of facial or generalized hirsutism, alteration in character of the voice, hoarseness, »cracking« or actual deepening, some virilization of the external genitals, slight rugation of the labia majora and hypertrophy og the clitoral foreskin, mild glandular breast or areolar development and serious dark-coloured breast secretion.

Lindsten et al. (1973) treated Turner girls with Nandrolone and compared the final height with the predicted height. While untreated girls were lacking a mean of 9.7 cm in reaching the predicted height, the Nandrolone treated girls lacked only a mean of 5.1 cm. The difference is significant ($P < 0.05$). In a personal communication *Lindsten* (1976) reports that he is still treating Turner girls with Nandrolone 25 mg intramuscular every two weeks during one and a half to two years. The side-effects are minimal, and it is the experience of *Lindsten* (1976) that this treatment increases the final height of Turner girls with approximately 5 cm corresponding to what was reported by *Lindsten et al.* (1973).

Rosenbloom & Frias (1973) treated nine girls with Turner's syndrome with Oxandrolone in doses of 0.075 to 0.125 mg per kilo body weight once daily during 4 to 34 months. They began treatment from the age of 9 to the age of 18. Pretreatment growth velocity varied from 0.5 to 3.8 cm per year with a mean of 1.8 cm per year. Treatment with Oxandrolone increased the velocity og growth to an average of 5.3 cm per year with a range of 2.1 to 8.7 cm per year. Osseous maturation progressed no more rapidly than chronologic age or height in any case. The only side-effect of Oxandrolone was a slight deepening of the voice in three of the nine girls.

In a short follow-up report, *Rosenbloom* (1974) confirmed the findings of a significant effect of Oxandrolone; 11 girls with Turner's syndrome treated with Oxandrolone had a mean fourfold increase in height velocity with a mean of 5.1 cm increase in predicted mature height during an average of 27 months' therapy. *Rosenbloom* (1974) mentioned that the dosage should not be increased above 0.125 mg Oxandrolone per kilo body weight per day – according to *Rosenbloom* the choice of anabolic steroid drug may be less important than the dosage used.

A survey of studies reporting on treatment of Turner girls with anabolic steroids has recently been made by *Sørensen & Nielsen* (1977) who concluded

that results obtained with the new anabolic steroids such as Nandrolone and Oxandrolone in low doses seem promising. Precocious epiphyseal closure seems to be avoided by low doses, and side-effects are only weakly expressed. It is further concluded by *Sørensen & Nielsen* (1977) that oestrogen treatment has a growth retarding effect, and it is recommended to postpone it till after one and a hal to two years of treatment with anabolic steroids and usually not before the age of 17 - 18.

Tzagournis (1969) treated three girls with Turner's syndrome with human growth hormone with no significant increase in final height, and *Tanner et al.* (1971) treated five girls with human growth hormone, they had an increase in height velocity from 2.9 cm per year to 3.9 cm, but this increase during treatment was almost entirely lost by posttreatment regulatory deceleration of growth, and it was concluded that human growth hormone had no significant effect on height growth in girls with Turner's syndrome.

Very little is known about the mechanisms behind the genetic regulation of body growth and development. One such mechanism might involve the secretion and/or the action of growth stimulating hormones. *Almquist et al.* (1963) found, however, that growth hormone in patients with Turner's syndrome was normal or high, and the short stature is thus apparently not related to the action of growth hormone.

Turner patients may secrete an altered growth hormone. The retarded growth in patients with Turner's syndrome may be due to peripheral subresponsiveness to the action of growth hormone *(Almquist et al.* (1963) and *Fraccaro et al.* (1960)).

Somatomedin, previously called sulphation factor, mediates or tranfers the effect of human growth hormone, sumatotropin, to the tissues. Preliminary studies have indicated that somatomedin concentration and somatomedin response are normal in girls with Turner's syndrome.

The results obtained by *Johanson et al.* (1969), *Lindsten et al.* (1973) and *Rosenbloom & Frias* (1973) indicate that androgen preparations like Decadurabolin and Oxandrolone increase growth rate and final height with a few cm with very few side-effects, whereas Fluoxymesterone had considerable side-effects.

If one to two years' treatment with Decadurabolin or Oxandrolone increase final height with an average of 4 - 5 cm in girls with Turner's syndrome, such treatment will be of great value as it is often a question of a few cm which determines whether the height reduction is psychotraumatic or not.

Two groups of girls with Turner's syndrome, matched as far as karyotype is concerned, should be studied. One group should be treated with Oxandrolone or Decadurabolin and compared with the untreated group as far as final height is concerned before any definite conclusion concerning the effect of Oxandrolone or Decadurabolin on final height in girls with Turner's syndrome can be drawn.

f. Clinical signs of Turner's syndrome

The results of the physical examination for Turner stigmata are shown in *Table 31*. Only some of the more common signs are included in the Table.

Table 31

Some clinical signs of Turner's syndrome

Clinical signs	Total	%	* Four other studies of 23, 25, 55 and 57 probands	
			Range in per cent	
Low hair level	5	11	64-88	not reported in two studies
Hypertelorism	3	7		not reported
Strabismus	2	4	9	not reported in three studies
Nystagmus	2	4		not reported
Ptosis	5	11	4-20	not reported in one study
Epicanthus	5	11	18-44	not reported in one study
Pterygium colli	17	38	9-52	
Cubitus valgus	27	60	62-78	
Systolic cardiac murmur	9	20	-	
Aortic stenosis	2	4	4-36	
Decreased hearing	11	24	5-49	not reported in two studies

* *Haddad* (1959); *de la Chapelle* (1962); *Lemli & Smith* (1963); *Lindsten* (1963).

Low hair level was found in 11 per cent, hypertelorism in 7 per cent, strabismus in 4 per cent and ptosis in 11 per cent. Pterygium colli was present in 38 per cent and cubitus valgus in 60 per cent. Systolic cardiac murmur was found in 20 per cent, aortic stenosis was found in 4 per cent and decreased hearing in 24 per cent. These frequencies correspond very well with what has been found in previous studies as seen in *Table 31*. Frequency of low hair level (11 %) and epicanthus (11 %) were, however, considerably lower than in previous studies as seen in *Table 31* in which the frequency range of low hair level was from 64 to 88 per cent and of epicanthus from 18 to 44 per cent. The definition of both these signs may, however, be quite controversial as may, however, also several of the other signs of Turner's syndrome such as hypertelorism, pterygium colli and cubitus valgus.

Ferguson-Smith (1965) made a review og 117 patients with karyotype 45,X and 38 patients with 45,X/46,XX and compared certain physical signs between the two groups. The only remarkable difference found was between the frequency of pterygium colli which was found in 54 per cent of the 117 patients and only in

16 per cent of the 38 patients with the cell line 46,XX. He did, however, also find a tendency to increase in stature in the girls with a 46,XX cell line as well as slightly lower frequencies of other Turner stigmata than pterygium colli in girls with a cell line 46,XX.

The only significant difference in physical Turner signs between the 21 probands with 45,X and the 24 with other karyotypes was found for pterygium colli where the frequency among those with 45,X was 52 per cent, while it was only 17 per cent among those with other karyotypes (P (Fisher) = 0.0255) *(Table 32)*.

Table 32
Pterygium colli in relation to karyotype

Karyotype	Pterygium colli		Probands total
	Total	%	
45,X	11	52*	21
Other karyotypes	4	17*	24
Total	15		45

* (P (Fisher) = 0.0255).

These figures correlate well with the finding by *Ferguson-Smith* (1965) of 54 per cent with pterygium colli for Turner girls with 45,X and 16 per cent for those with a 46,XX cell line. We found cubitus valgus in 57 per cent of girls with 45,X and in 50 per cent of those with other karyotypes; there was no significant difference between any other stigmata than pterygium colli between the two groups of probands.

Chapter 6

ELECTROENCEPHALOGRAPHIC EXAMINATION

Previous EEG studies of women with Turner's syndrome

Dumermuth (1961) made an EEG study of seven patients with Turner's syndrome. Three had hypersynchronous EEG aberrations, one of them with epilepsy, one had diffuse dysrhythmia, one had »passagere fortgeleitete rhythmen«, and two had a normal EEG. *Lindsten* (1963) made EEG studies of two patients with Turner's syndrome, one of them had an abnormal and the other a normal EEG. *Gordinova & Verlinskaya* (1966) found an increased frequency of 1.5-3/s delta waves in 34 patients with Turner's syndrome. *Mellbin* (1966) made an EEG study of four patients with Turner's syndrome found in a mental hospital, one had a mild non-specific abnormality in both temporal regions. One had mild paroxysmal abnormalities, slightly more pronounced in the right temporal region; one had a sharp-wave temporal focus in the left side. One had paroxysm activity af the sharp-wave type on the left hemisphere. *Kihlbom* (1969) found mild or moderate paroxysmal abnormalities in five of nine patients with Turner's syndrome. *Poenaru et al.* (1970) made an EEG study of 71 patients with Turner's syndrome, only 8 of whom had a normal EEG, three had EEGs significant for epilepsy. *Poenaru et al.* (1970) concluded that the EEG changes might be related to immaturity of the cerebral cortex or to disorders in the regulatory function of the mesencephalic reticular formation and to well known anatomical nervous anomalies.

Christodorescu et al. (1970) studied three women with Turner's syndrome in a psychiatric hospital. Electroencephalogram showed dysrhythmic bioelectrical activity with dominant slow rhythm 3-6 c/s in one, low voltage bioelectrical activity, dysrhythmic with slow, diffuse theta waves 4-6 c/s mixed with rare delta waves frequency 3 c/s in one, and in the third the occipital leads, predominantly on the right side showed sharp, sinusoidal theta waves and degraded spike-wave complexes were recorded.

Palm et al. (1973) made electroencephalographic studies of 52 women with Turner's syndrome and lack of X chromosome material.

Three of them had suffered from grand mal at the ages of 6, 12 and 15 years of age, respectively. Hypersynchrone activity was found in eight patients. Generalized irregular spike-wave activity was found in two. The authors found an overrepresentation of EEGs with low amplitude, diffuse beta and alpha-beta mixture, and they concluded that it might be due to mild diffuse brain aberra-

tions in girls with Turner's syndrome.

Frenkel & Zarubina (1973) made an electroencephalographic study of 32 patients aged 13 to 18 with Turner's syndrome and 29 patients of the same age group with hypophyseal nanism. They found: »That these two groups had opposite changes in cerebral electroactivity of the brain«. There was a shift of the main EEG rhythms in the direction of slow frequencies in the hypophyseal dwarfs, whereas there was a tendency to rapid frequencies in patients with Turner's syndrome.

The authors concluded that there might be a stimulating effect on the electroactivity of the brain by the increased levels of gonadotropic and somatotropic hormones found in the patients with Turner's syndrome.

Brun & Sköld (1968) reported a case of Turner's syndrome who died from a cerebellar medulloblastoma. Brain autopsy showed disturbance in cortex cytoarchitecture with abnormalities such as indistinct lamination and variations in the width of the molecular layer. The authors concluded that the cortex aberrations indicated mild disturbance of cell migration, presumably occurring late in the histogenetical period of brain development. The IQ of this patient was described as being in the lower end of the normal range, but it was mentioned that she did rather well at school.

Electroencephalographic examination in the present investigation

EEG examination was made in 39 of the 45 probands and the 11 women found in institutions for the mentally retarded.

Three of the 11 women in institutions have had epileptic seizures; in 2 cases, Nos. 61 and 62, they were grand mal seizures, and in No. 59 fits of remoteness with anxiety and vomiting, as well as fits of unmotivated aggression. All three have been treated with antiepileptic drugs.

The three women, who suffered from epileptic seizures, revealed irregular spike-and-wave complex at the occipital area on both sides at rest, and this was increased by photic stimulation. The other two women, Nos. 65 and 66, with EEG abnormalities, had also spike-and-wave complex bi-occipital, but only by photic stimulation. There were thus specific EEG abnormalities in 5 of the 11 women with Turner's syndrome and mental retardation. Unspecific slightly abnormal EEG was found in one patient (No. 67), borderline EEG in two and normal EEG in three of the 11 cases.

None of the 39 women with Turner's syndrome found outside institutions for the mentally retarded had epileptic seizures.

Electroencephalographic examination revealed normal EEGs in 15 (38 %), borderline in 15 (38 %), and slightly abnormal in 9 (23 %). Slightly abnormal EEG in the present study includes sharp waves, high voltage slow wave bursts and dysrhythmia *(Table 33)*. It was of unspecific type in eight and specific in one.

Table 33

Electroencephalographic abnormalities

Case No.	Age	Karyotype	Electroencephalographic abnormalities among the 39 probands examined
1	21	45,X/46,X,i(Xq)	Some sharp-waves diffusely. Slightly abnormal.
8	19	45,X/46,XX	Some 5-7 c/s activity and sharp-waves diffusely. Slightly suspect for epilepsy.
10	22	45,X	Slightly more low frequency 5-7 c/s activity than according to age. Slightly abnormal.
15	38	45,X/46,X,i(Xq)	Some sharp-waves diffusely occasionally appearing bilaterrally synchronously. Suspect for epilepsy.
27	16	45,X	Dominant activity 10 c/s with profusely 14-16 c/s activity, especially bi-occipital with greater amplitude in the right occipital area. Slightly abnormal.
31	22	46,X,i(Xq)	Dominant activity 9-10 c/s with rather too fast activity and low amplitude and some small sharp-waves diffusely. Slightly suspect for epilepsy.
36	26	45,X/46,X,r(X)	Dominant activity 10-12 c/s with fast activity diffusely which gives the curve a spike appearance. Slightly abnormal.
38	14	45,X	Unprovoked normal. Photostimulation provokes universal 4 c/s activity with spikes of 200 μvolt amplitude of $^3/_4$ seconds duration. Slightly abnormal.
40	24	45,X	More fast activity than expected and sharp-waves diffusely. Slightly abnormal.
			Electroencephalographic abnormalities among the 11 patients found in institutions for the mentally retarded
59	25	45,X/46,XX	Bi-occipital posttemporal spike-waves complexes with 3-4 c/s activity with high amplitude and with spreading to the left parietal temporal region. The patient has epilepsy.
61	17	45,X/45,X,+ace	Left occipital and bi-occipital spikes and irregular spike and sharp-wave activity. The patient has epilepsy.
62	24	45,X/45,X,+ace	Bi-occipital spike-foci and paroxysms of 5-6 c/s activity with increased amplitude and numerous spikes. The patient has epilepsy.
65	63	45,X/46,X,i(Xq)	Fast activity 14 c/s diffusely, bi-occipital amplitude greater over the right than over the left side, there are occipital spikes bilaterally. Slightly abnormal.

66	60	45,X	Occipital spike sharp-waves, more pronounced in the right side. Scattered 3 c/s activity occasionally extending to the right parietal area. Runs of sharp 8 c/s with amplitude up to 150 μV. Bitemporal paroxysm runs of 8 c/s sharp-waves and single spikes mainly from the left temporal area. Very suspect for epilepsy.
67	69	45,X/46,XX/47,XXX	Bi-temporo-occipital presumptive paroxystic 3-4 c/s activity with increased amplitude and scattered presumptive spike potentials. Photostimulation provokes 3 c/s spikes biocci-pital radiating bitemporally. Slightly abnormal.

Patients with 45,X in all cells had a slightly higher frequency of paroxysmal EEG abnormalities (specific and unspecific) (7 of 18, 39 %), compared with patients with karyotypes such as mosaics with a 46,XX cell line, isochromosome X or 46,X,ring X (2 of 21, 9.5 %). The difference was significant (P (Fisher) = 0.036).

Seventeen patients (46 %) had an increased amount (more than 50 %) of 14-18/s beta waves in basic pattern. This group comprised 13 patients with diffused beta waves and 4 with frontal dominant beta waves. Alpha wave was found with a mean frequency of 10.5/s, and 26 patients (67 %) had 10-11/s. An increase of theta wave to more than 50 per cent in basic rhythm was found in one patient only. Twelve patients (31 %) revealed spike, sharp wave or dysrhythmia during hyperventilation. Photic stimulation provoked EEG abnormalities in two of nine patients.

The frequency of EEG abnormalities in the present study is 23 per cent among the women with Turner's syndrome found outside institutions (one with specific and eight with unspecific slightly abnormal EEG), and 55 per cent among those found in institutions for the mentally retarded (five with specific and one with unspecific slightly abnormal EEG ($\chi^2 = 4.042$, $P < 0.05$).

Various types of EEG abnormalities have previously been reported in mentally retarded patients. *Dresler et al.* (1967) found 19 per cent of EEG abnormalities, including 12 per cent of 2-3/s spike-and-wave complex, and *Gibbs et al.* (1960) reported spike-and-wave complex in 9 per cent at rest in mentally retarded patients. However, specific abnormalities at the occipital areas such as we have found in mentally retarded women with Turner's syndrome, have not been observed in individuals with other types of mental retardation.

The characteristic findings in the present study of women with Turner's syndrome comprise 1) occipital dominant spike-and-wave complex or spike waves in 5 of the 11 patients who were mentally retarded (45 %) and in 1 of the 39 women with Turner's syndrome found outside institutions, 2) hypersensitivity to hyperventilation with spikes, sharp waves or dysrhythmia in 31 per cent of the cases, 3) an increased amount of 14-18/s beta waves in 46 per cent of the cases.

Our findings correspond to a certain extent with those found by *Gordinova &*

Verlinskaya (1966), *Poenaru et al.* (1970) and *Frenkel & Zarubina* (1973), but we found no loss of alpha waves as reported by *Poenaru et al.* in 46 per cent of the cases; quite contrary, we found normal alpha wave of 10-11/s and we could not confirm the finding by *Poenaru et al.* of a very high frequency of 89 per cent with EEG abnormalities in Turner's syndrome. The frequency of definite EEG abnormalities of 23 per cent found among women with Turner's syndrome outside institutions in the present study is most probably not significantly higher than the expected 12-15 per cent in the general population, but no suitable control group was available. The frequency of borderline aberrations found in 38 per cent might be higher than expected, but no conclusions can be drawn without having a suitable control group.

We do not find that there is evidence enough from EEG studies of women with Turner's syndrome to draw conclusions as done by *Poenaru et al.* (1970), who concluded the EEG changes found in Turner's syndrome might be related to immaturity of the cerebral cortex or to disorders in the regulatory function of the mesencephalic reticular formation and to well known anatomical nervous anomalies, or the conclusions drawn by *Palm et al.* (1973) that the EEG aberrations found in Turner's syndrome might be due to a mild diffuse brain aberration, nor do we agree with the conclusions drawn by *Frenkel & Zarubina* (1973) that there might be a stimulating effect on the electroactivity of the brain by the increased levels of gonadotropic and somatotropic hormones found in patients with Turner's syndrome.

We found no indication of parietal lobe EEG aberrations, but occipital lobe deficits as indicated by the EEG abnormalities with spike-and-wave complex in the occipital area found in the group with mental retardation in the present study might be associated with some of the neuro-cognitional deficits found by psychological tests in women with Turner's syndrome as mentioned in *Chapter 11*. Neuro-psychological investigation ad modum Luria as recently described by *Christensen* (1974) might be helpful to reveal possible occipital and parietal lobe deficits in women with Turner's syndrome, and we have planned to make such an investigation.

Previous studies by among others *Nielsen & Tsuboi* (1974) have indicated that EEG aberrations might be higher than expected in males with Klinefelter's syndrome and XYY syndrome. Women with Turner's syndrome function, however, as far as personality development and intellectual development are concerned, on the same level as their siblings and better than males with XYY or Klinefelter males, and contrary to what has been found in Klinefelter's syndrome and XYY syndrome there is no indication of any increased risk of mental illness in women with Turner's syndrome. A normal pattern of electroencephalographic recordings, or at least a lower frequency, of aberrations than found in Klinefelter's syndrome and XYY syndrome might be expected on the background of the individuals with Turner's syndrome on one hand and males with XYY or Klinefelter's syndrome on the other hand.

Chapter 7

DERMATOGLYPHIC INVESTIGATION

Dermatoglyphic studies of women with Turner's syndrome have previously been made by *Uchida & Soltan* (1963), *Penrose* (1963, 1967), *Holt & Lindsten* (1964), *Forbes* (1964), *Pfeiffer & Kiera* (1968), *Saksena & Kumar* (1968) and *Polani* (1971).

We have studied the dermatoglyphic patterns in 30 of the 45 probands with Turner's syndrome in order to compare dermatoglyphic patterns of cases with 45,X with those having more than one X in all or part of their cells. The group comprises 11 girls with karyotype 45,X and 19 with other karyotypes.

Dermatoglyphic findings in the 30 girls with Turner's syndrome have been compared with patterns in English female controls and a sample of 37 English girls with Turner's syndrome. Tests of significance have not been done as an allowance for ethnic differences, however small it might be, had to be taken into consideration concerning comparison of the Danish girls with Turner's syndrome with an English control group and the English girls with Turner's syndrome.

Patterns on the palms and soles were analysed according to the methods described by *Penrose & Loesch* (1969, 1970).

Dermatoglyphic studies in the present investigation

Fingers

The patterns on the finger-tips were usually large and contained fine ridges. Ridge counts were high, and the mean total finger ridge count was above the average for English female controls. It was rather similar on both Turner karyotype groups, but greater in that consisting of patients with 45,X. The mean total finger ridge count was almost identical for both English and Danish Turners as shown in *Table 34.*

Palms

There was an excess of pattern on both thenar and hypothenar areas of the palms. As a consequence, pattern intensity was above the female average and triradii e, t" and t^b occurred with greater frequency than in English female

Table 34

Percentage frequencies of main dermatoglyphic traits in English and Danish cases of Turner's syndrome and in 100 unrelated English female controls: left and right soles taken together

Karyotypes of cases of Turner's syndrome	Origin	Loops					Triradii			
		I	$\hat{I}$	$\hat{II}$	$\hat{III}$	$\hat{IV}$	e	z	z'	z''
45,X	English	87.5	43.7	15.6	37.5	9.4	43.7	43.7	28.1	12.5
	Danish	85.0	50.0	30.0	55.0	10.0	50.0	65.0	25.0	5.0
Other karyotypes	Danish	90.0	43.3	23.3	46.7	13.3	43.3	60.0	33.3	10.0
(♀) Controls	English	86.5	33.0	15.5	19.5	2.5	36.5	33.5	9.5	2.0

Table 35

Means and standard deviations of the a-b ridge count and percentage frequencies of main dermatoglyphic findings in Englihs and Danish cases of Turner's syndrome and in 450 unrelated English female controls: left and right hands taken together

Karyotypes of cases of Turner's syndrome	Origin	Mean a-b ridge count	S.D.	I	I^r	H	$\widehat{H}$	H^r	e	t''	t^b	Pattern intensity	A-line exit ( )
45,X	English	91.30±2.28	13.85	8.3	11.7	35.0	43.3	5.0	20.0	26.7	48.3	2.1	23.3
	Danish	97.56±3.48	10.45	9.1	13.6	22.7	22.7	13.6	18.2	22.7	40.9	1.8	27.3
Other karyotypes (♀)	Danish	85.89±3.04	12.87	2.6	13.2	13.2	36.8	7.9	13.2	18.4	44.7	1.9	21.1
Controls	English	86.63±0.58*	10.52	4.2	7.6	13.0	30.6	1.7	11.2	7.2	32.2	1.6	9.3

* This figure was obtained from data on 325 English female controls.

controls. The mean of the sums of the ridge counts of the left and right hands in the a-b interval (area between triradii a and b) was greater than in normal females.

The group with karyotypes other than 45,X, i.e. girls with more than one X in all or part of their cells did, however, not show this peculiarity, and the mean a-b ridge count was slightly lower than in female controls.

In both Turner karyotype groups, the A main line showed a tendency to exit on the radial side at the base of the hand. Similar traits were also observed in English girls with Turner's syndrome. The findings for all cases are summarized in *Table 35* showing a characteristic palm pattern of females with Turner's syndrome.

Soles

In the hallucal area the proximal loop $\hat{I}$ and corresponding e triradius were seen more often in the Turner group, compared with the control group. The distal loop I was, more or less, as frequent as in normal females, but the associated f triradius was often placed at or near the thenar distal border of the sole. As a result, the distal loop I was usually large, and the ridge count from the f triradius to the core of this loop was frequently high (well over 35 ridges).

On areas II, III and IV, proximal loops were more common than in female controls, Zygodactyly occurred with greater frequency than in normal females, and this result agreed with the fact that triradii z, z' and z'' are usually associated with proximal loops $\hat{II}$, $\hat{III}$ and $\hat{IV}$. These findings were also observed in the English Turner group as shown in *Table 36*, and they are considered as being typical of Turner's syndrome.

Table 36

Means and standard deviations for total finger ridge count in English and Danish cases of Turner's syndrome and in English female controls

Karyotypes of cases of Turner's syndrome	Origin	No. of Cases	Mean total finger ridge count	S.D.
45,X	English	37	175.19± 8.54	51.90
	Danish	11	176.55±14.83	49.07
Other karyotypes	Danish	19	164.95±11.81	51.39
(♀) Controls	English	825	126.97± 1.82	52.33

Control population (after *Holt*, 1963).

Chapter 8

PSYCHOPATHOLOGY

a. Previous psychiatric studies of women with Turner's syndrome

Kihlbom (1969) studied 11 patients with Turner's syndrome. Seven had IQ between 90 and 110, and four were mentally subnormal with IQ between 70 and 74. All patients were psychoinfantile. One was neurotic, one had anorexia nervosa, three had symptoms of minimal brain damage, and one had character disorder of the passive-aggressive type.

Christodorescu et al. (1970) studied three patients with Turner's syndrome found in a psychiatric hospital, one with mental retardation, immature personality and a depressive anxiety state, one with border-line intelligence and infantile personality and one patient with behaviour disorder and a border-line intelligence. *Milcu et al.* (1964) studied a 15-year-old girl with Turner's syndrome and schizophrenia (the diagnosis is somewhat doubtful as judged from the case history). *Slater & Zilkha* (1961) studied a very doubtful case of Turner's syndrome with normal menstruation, normal karyotype in skin culture and possibly 45,X/46,XX in blood culture. She was a 19-year-old girl with schizophrenia and myopathy. *Lynch et al.* (1966) studied two patients with Turner's syndrome with IQ 86 and 82, respectively. They had immature personalities, but no psychopathological symptoms; one had a neutral sexual role and no sexual libido.

Ehrhardt et al. (1970) made a study of gender identity in 15 girls with Turner's syndrome and 15 matched controls. They found that significantly more patients than controls had a strong interest in jewelry, perfumes and hair-styles, and significantly more of the Turner girls had never engaged in childhood fights and more girls with Turner's syndrome had little or no outdoor activity, compared with the controls.

The girls with Turner's syndrome were highly interested in weddings and marriage, in all forms of maternalism from playing with dolls to baby care and in their feminine appearance.

The authors concluded that girls with Turner's syndrome are unequivocally feminine in their gender role and gender identity.

Szczepski et al. (1967) studied 20 patients with Turner's syndrome. All had difficulties in social adjustment, some had neurotic and abnormal personality traits. Conditioning factors for these traits were considered to be among others an inferiority complex due to physical defects such as low stature and retarded sexual development. *Senzer et al.* (1973) studied six patients with Turner's

syndrome, one had anxiety neurosis, and one had a long history of behaviour disorder. All were exclusively feminine in all aspects of their behaviour.

Money & Mittenthal (1970) made a follow-up study of 73 patients with Turner's syndrome. Only 3 of the 73 patients had severe psychopathological symptoms defined as a long-term failure to maintain a minimally acceptable everyday-life. One of these had suffered from a depression, one had tried to commit suicide, and one suffered from a paranoid psychosis. Seven patients had mild psychopathological symptoms defined as a lack of ability to meet the demands of life in a way completely acceptable to family and community, but sufficiently functional to remain participant members of society.

The authors concluded that inertia of emotional arousal may be listed with space-form disability as a psychological concomitant of the syndrome. The authors define inertia as constituting compliancy, phlegmatism, stolidity, equability, acceptance, resignedness, slowness in asserting initiative and tolerance of personal adversity. This, according to the authors, is a protection against stress secondary to the physical handicaps of the syndrome. Short stature and postponement of hormonally induced puberty tend to lower the threshold for retarded social maturation, especially if other people infantilize their relationship with the patient.

The genetic and gonadal anomalies of the syndrome did not interfere with the differentiation of a feminine psychosexual identity in any of the 73 cases. Nine of the 28 adult patients were known to be married, and two had adopted children.

Buckley (1971) studied 12 patients with Turner's syndrome. The mean Full Scale IQ was 92.6, the mean Verbal IQ 98.5, and the mean Performance IQ 85.6. The author concluded that this finding would indicate that all non-verbal items of the intelligence test are contributive towards a significant discrepancy between Verbal and Performance IQ scores previously reported.

Jullien et al. (1973) studied an 18-year-old woman with Turner's syndrome and chromosome constitution 45,X/46,XX with a low frequency of cells with 45,X. The psychiatric diagnosis was schizophrenia, but according to the case history, where she was described as having delirious symptoms, the diagnosis of psychogenic psychosis in a mentally immature person would probably be more likely than the diagnosis of schizophrenia.

b. Psychopathological symptoms

In order to compare certain aspects of our study with that of a similar study by *Money & Mittenthal* (1970) we have used the terms severe and mild psychopathology in the same ways as these authors. Severe psychopathological symptoms have been defined as long time failure to maintain a minimally acceptable everyday-life, and mild psychopathology defined as a lack of ability to meet the demands of life in a way completely acceptable to family and com-

munity, but sufficiently functional to remain a participant member of society.

Only 1 of the 45 probands in our study had severe psychopathological symptoms, and 4 had mild psychopathological symptoms. One of the 45 probands was mentally retarded; this is very similar to what could be expected in the Danish population.

Our finding of 11 per cent with psychopathological symptoms was also similar to the finding by *Money & Mittenthal* (1970) of 10 out of 73 probands with Turner's syndrome having psychopathological symptoms (14 %).

Four of our five probands with psychopathological symptoms had karyotype 45,X, compared with 41 per cent of the total group (P (Fisher) = 0.0349); one had the karyotype 45,X/46,X,r(X). All five with psychopathological symptoms had been exposed to a psychotraumatic childhood environment, compared with 9 of the 40 without psychopathological symptoms (22.5 %) (P (Fisher) = 0.0032).

Our findings indicate that girls with karyotype 45,X are more prone to present psychopathological symptoms than those with other karyotypes and more X chromosome material. The group with mental illness is, however, very small, and we found no other indications that girls with karyotype 45,X were more handicapped physically or mentally than those with other karyotypes. Girls with karyotype 45,X were as intelligent, managed as well at school and were as well adjusted socially as girls with other karyotypes.

Four of the five with psychopathological symptoms were overprotected as seen in *Table 37*, compared with 4 of the 40 without psychopathological symptoms (P (Fisher) = 0.0010), and one had grown up in a broken home.

Table 37

Psychopathological symptoms

Psychotraumatic conditions during childhood	Psychopathological symptoms			Total
	Severe	Mild	None	
Overprotection by parents	1	3	4	8
Broken homes	-	1	2	3
Other psychotraumatic conditions	-	-	3	3
No definite psychotraumatic conditions	-	-	31	31
Total	1	4	40	45

One of the five probands (No. 12) with psychopathological symptoms had been admitted to a psychiatric hospital, but only for two brief periods. She grew up in a home where she had been overprotected to an extreme degree; this, in connection with her Turner personality, was most probably the cause of her anxiety, depression and anorexia nervosa.

No. 24 was, quite contrary to her parents' and her own wishes and without sufficient indication, transferred from a normal school, where she had been very well adjusted, to a school for partially sighted children. This arrested her mental development, she never adjusted to this school and learned hardly anything. This, together with overprotection from her parents, most probably constitutes the main reasons for her present state of anxiety and immaturity that prevents her from finding employment and from leaving her parents.

No. 40, who grew up in a home where she was overprotected, has never tried to earn her own living. Rehabilitation attempts were quite wrongly relinquished after only a few weeks' trial, and she was given a disability pension. She could, no doubt, have been trained for some easy type of work.

The hyperactive, restless state and difficulties in concentration for proband No. 7 were most probably due to her having no father and to her getting so little support from her mother, who had full-time employment away from home.

No. 11 had grown up in an overprotected environment and was too immature and anxious to manage ordinary paid employment, but she has improved quite well in a sheltered job, and her rehabilitation seems to be quite successful. If rehabilitation had been planned with equal thoroughness and care for Nos. 24 and 40, employment might very probably have been found for them in which they would have been well adjusted.

We found no indication of any increase in psychopathology in the women with Turner's syndrome, compared with their siblings or compared with the expected frequency of mental illness in the Danish population.

There was, however, a significant association between overprotection and psychopathological symptoms. Only one of the five probands, who had grown up in broken homes with other psychotraumatic symptoms, developed psychopathological symptoms herself. These findings indicate that as previously mentioned the main aetiological factors of disablement and mental disorders in women with Turner's syndrome are of environmental nature and consequently subject to preventive measures if diagnosis, advice and treatment are given early enough as previously mentioned. Overprotection should definitely be avoided and social stimulation as well as stimulation of independency should be advised.

c. Psychoinfantilism

Lindberg (1950) described psychoinfantilism in the following way: »Psychoinfantilism is a persistence in the adult of mental qualities characteristic of the child. Psychoinfantile behaviour is referable to the helplessness, uncertainty and

desire for guidance and authority distinctive of childhood. The dependence often takes the form of a strong emotional fixation, frequently to the mother or father, but sometimes to other persons, even chance acquaintances. The psychoinfantile person gives the normal adult the same feeling of detachment and the same urge to give protection as to a child. It is the latter attribute which lies behind the terms »naive«, »childish« and »artless« so often used to describe such a personality«.

Girls with Turner's syndrome have often been described as psychoinfantile, but only 2 of the 45 probands in the present study presented the characteristics of psychoinfantilism as described by *Lindberg* (1950); most of the adult probands were, however, or had been retarded in some aspects of social and mental maturation, compared with their sisters. This was also the case for most of the controls with primary amenorrhoea, low stature and normal chromosome constitution.

The finding of no remarkable difference in the mental maturation process between probands and controls might indicate that the lack of X chromosome material is not among the aetiological factors of this aspect; mosaics with a very low percentage of 45,X cells might, however, be present in some of the controls.

The aetiology of retardation in mental and social maturation found in most cases of Turner's syndrome as well as in the controls is most probably mainly due to their short stature as well as to the retardation in sexual maturation; one might expect that these two factors decrease the speed of mental and social maturation as discussed by *Money & Mittenthal* (1970).

In order to prevent retardation of maturity, parents should be advised to avoid overprotection and infantilization and stimulate independence and initiative, they should try to treat their daughter with Turner's syndrome in accordance with her age and not according to her height or degree of physical maturation.

d. Anorexia nervosa

Screening the Danish Psychiatric Central Register revealed the admission of 106 female patients with anorexia nervosa to Danish psychiatric institutions during the years 1970-1974. One of the probands in the present study (No. 12) with Turner's syndrome is among these patients.

According to *Halmi & Rigas* (1973) the possibility of the occurrence of Turner's syndrome with an incidence of 3-4/10,000 and anorexia nervosa with an incidence of 0.45-0.61 per 100,000 in the same patient should be approximately 0.24 per 100,000,000.

The findings in the present study of a girl with Turner's syndrome among 106 with anorexia nervosa as well as the finding of anorexia nervosa in a further seven cases of Turner's syndrome by *Pitts & Guze* (1963), *Lindsten* (1963), *Kihlbom* (1969), *Dickens* (1970), *Forssman et al.* (1970), *Halmi & Rigas* (1973),

Halmi & De Bault (1974) and *Liston & Shershow* (1973) indicate that the occurrence of anorexia and Turner's syndrome may not be pure coincidence.

A possible aetiological connection between Turner's syndrome and anorexia nervosa could hardly be of genetic nature due to loss of X chromosome material. *Forssman et al.* (1970) mention that some specific brain aberrations in Turner's syndrome might be among the aetiological factors of anorexia nervosa.

Our patient with Turner's syndrome and anorexia nervosa had normal electroencephalographic findings and no signs of brain aberration. The growth retardation, retardation in sexual maturity and retardation in mental and social maturity in Turner's syndrome as well as the tendency to be overprotected by parents may very well be the main aetiological factors of anorexia nervosa in Turner's syndrome; such factors could easily explain the atypical anorexia nervosa in our patient. A more detailed investigation of this patient has been published by *Theilgaard & Philip* (1975).

e. Physical and mental disorders among probands, siblings and parents

There was no extremely high frequency of any physical or mental disorders among probands, parents or siblings, but 5 out of the 45 mothers with struma (11 %) is a comparatively high frequency, and so is probably also 5 out of 90 parents with psoriasis as well as 5 with rheumatic fever (6 %) *(Table 38)*.

Table 38

Physical and mental disorders among probands, siblings and parents

Disorders	Mothers n = 45	Fathers n = 45	Probands n = 45	Sisters n = 46	Brothers n = 23
Psoriasis	2	3	1	1	1
Struma	5	-	-	1	-
Diabetes mellitus	-	3	-	-	-
Polyarthritis	2	-	-	1	-
Rheumatic fever	3	2	-	-	-
Mental illness	5	1	2	2	3

The table only comprises physical illnesses which might have aetiological implications for the X chromosome aberrations in the progeny or be associated with an increased risk of such aberrations.

Aortic stenosis was found in 2 of the 45 probands, and systolic murmur was found in further 5; 15 of the 45 probands had decreased hearing.

Only one of these disorders (psoriasis) was present in one of the probands. A question of a possible association between these disorders and the risk of the chromosome aberration leading to lack of X chromosome material should be further studied.

Mental illness was not significantly higher than expected in the probands, siblings or parents. The highest frequency was found among the mothers; five of whom had suffered from mental illness, all however, of different types.

The study comprises too few probands to reach any conclusion concerning the question whether there could be any association between certain physical illnesses and increased risk of X chromosome aberrations in the progeny. Further studies should be made concerning this question.

A person with Down's syndrome was found in 2 of the 45 families: A maternal grandcousin of proband No. 33 with 45,X and a maternal aunt of proband No. 41 with the karyotype 45,X/46,X,r(X), both had Down's syndrome.

Two of the 46 sisters had previously been admitted to a psychiatric hospital as seen in the case histories Nos. 6 and 35, but the admission of one had been for observation for induced abortion as seen in *Table 39*. This correlates with the finding that 1 of the 45 probands (No. 12) and 1 of the 15 controls (No. 105) had been admitted to a psychiatric hospital.

Not all of the 46 sisters were as well known as the 45 probands, but all were checked for admission to psychiatric hospitals through the Danish Psychiatric Central Register, and there was no evidence of present or previous mild psychopathological symptoms according to the definition used for the probands. Four out of the 45 probands had psychopathological symptoms, compared with 2 out of the 46 sisters and 2 out of the 15 controls. The differences are not significant, and we found no evidence of an increased frequency of psychopathological symptoms in women with Turner's syndrome, compared with their sisters and a control group.

In *Chapter 9 b* it is furher seen that there was no indication of any increased prevalence of patients with Turner's syndrome among patients in Danish psychiatric hospitals.

Table 39

Mental disorders among probands, parents and siblings

Case No.	Probands, parents and siblings	Diagnoses
3	Mother	Neurosis anxiosa et depressiva
3	Brother	Character disorder
6	Sister	Observation for induced abortion
12	Proband	Depressio mentis psychogenica Anorexia nervosa Character disorder Neurosis hysteriformis
23	Mother	Neurosis depressiva
24	Proband	Psychoinfantilism Neurosis anxiosa
30	Brother	Character disorder
31	Mother	Tentamen suicidii
33	Mother	Neurosis hysteriformis Character disorder
34	Brother	Behaviour disorder
35	Mother	Depressio mentis psychogenica
35	Sister	Depressio mentis psychogenica
36	Father	Psychosis psychogenica

Chapter 9

PREVALENCE OF TURNER'S SYNDROME IN THE GENERAL POPULATION AND IN MENTAL HOSPITALS

a. Prevalence of Turner's syndrome in the general population

Studies of X-chromatin in newborns by *Mikamo* (1968), *Maclean* (1964) and *Robinson & Puck* (1967) showed a frequency of 0.35 per 1,000 for Turner's syndrome among a total of 17,280 newborn girls.

A later survey by *Fujita et al.* (1972) of 12 previous studies of X-chromatin investigation in newborn children comprises a total of 51,248 newborn girls, 14 of whom had only one X in all or part of their cells; this gives a frequency of 0.3 per 1,000.

Two X-chromatin studies of randomly selected schoolgirls in Japan and USSR, comprising 8,500 girls, showed a prevalence of 0.3 per 1,000 for X-chromatin negative girls *(Fujita et al.* (1972) and *Lavryashin* (1972)).

Friedrich & Nielsen (1973) and *Nielsen & Sillesen* (1975) found 3 girls with one X chromosome in all or part of their cells among 5,387 consecutively newborn girls, and in a survey of 6 chromosome studies of 20,370 consecutively newborn girls the prevalence of girls with lack of X chromosome material in all or part of their cells was 0.39 per 1,000.

The prevalence studies of Turner's syndrome in the general population thus indicate that the prevalence of Turner's syndrome with lack of X chromosome material is approximately 1 per 3,000.

b. Prevalence of Turner's syndrome in psychiatric institutions

Maclean et al. (1968) made an X-chromatin study of 6,241 patients in mental hospitals in Scotland, one of these patients had the karyotype 45,X/47,XXX. *Nielsen* (1973) made a survey of 11 X-chromatin studies of 5,693 female schizophrenic patients, 1 of whom had Turner's syndrome, but *Crandall et al.* (1972) studied 300 girls admitted to a child psychiatric hospital and found that 3 of them had Turner's syndrome with lack of an X chromosome in all or part of their cells.

From prevalence studies of Turner's syndrome in psychiatric institutions, there are, however, no indications that the prevalence of Turner's syndrome in such institutions is higher than in the general population, on the contrary, most

of the studies have indicated that the prevalence of Turner's syndrome in psychiatric institutions may be lower than in the general population.

c. Prevalence of Turner's syndrome in Danish psychiatric hospitals

A letter was sent to the 12 psychiatric hospitals and the 29 psychiatric departments, including adolescent and child psychiatric departments, in Denmark asking for information of patients with Turner's syndrome or patients aged 18+ with primary amenorrhoea. The Danish Psychiatric Central Register was further scanned for patients with the diagnosis of Turner's syndrome. (This Register has previously been described by *Dupont et al.* (1974)). The Danish Cytogenetic Central Register was also checked for women with Turner's syndrome from psychiatric hospitals. This Register has previously been described by *Nielsen et al.* (1973).

Screening of the Danish Psychiatric Central Register for women with the diagnosis of Turner's syndrome admitted to all Danish psychiatric hospitals only revealed three such patients. Only one of whom had not been revealed through the screening by written requests to the psychiatric hospitals.

It is conceivable that most patients with Turner's syndrome admitted to Danish psychiatric hospitals during the past 10 years, would have been diagnosed by reason of the well-known and very characteristic clinical features of these patients coupled with the easy access to cytogenetic examination in Denmark during the past 10 years.

We found that eight patients with Turner's syndrome had been admitted to Danish psychiatric hospitals during the past 10 years. Karyotype distribution is shown in *Table 40.*

Table 40
Karyotypes of patients with Turner's syndrome in Danish psychiatric hospitals

Karyotypes	Patients total
45,X	5*
45,X/46,XX	1
45,X/46,XX/47,XXX	2
Total	8

* One (No. 12) was included among the 45 probands.

The total number of female patients admitted to Danish psychiatric hospitals during the past 10-year-period is difficult to estimate, but first-time admissions would be approximately 7,000 per year. The average number per year of first admissions of Turner patients during the past 10 years was 0.8 per year, and the frequency of patients with Turner's syndrome among first-time admissions would thus be 0.1 per 1,000 per year. The expected prevalence of Turner's syndrome in the general population is approximately 0.3 per 1,000 as described in the present *Chapter a.* If the risk of being admitted to a psychiatric hospital was the same in females with Turner's syndrome as in the general population, one would have expected an average first-time admission frequency of 0.3 per 1,000 per year.

The number of female patients in Danish psychiatric hospitals at any given time is approximately 6,000. With a prevalence of 0.3 per 1,000 for Turner's syndrome, one would expect an average of 2 patients with Turner's syndrome to be in Danish psychiatric hospitals at any given time. At the time of our prevalence estimation of Turner's syndrome in Danish psychiatric hospitals in September, 1973, we found one patient with Turner's syndrome in Danish psychiatric hospitals, and during the 10-year-period the number of Turner patients in Danish psychiatric hospitals varied from 0 to 3.

Our survey of patients with Turner's syndrome admitted to Danish psychiatric hospitals during a 10-year-period as well as previous studies of the prevalence of Turner's syndrome in psychiatric hospitals *(Maclean et al.* (1968) and *Nielsen* (1973)) show that the prevalence of patients with Turner's syndrome in psychiatric hospitals is not increased.

There are no indications that the psychiatric morbidity in women with Turner's syndrome is higher than in the general population, possibly it is even slightly lower, but in order to get any exact measurement of the psychiatric morbidity, women with Turner's syndrome in a very large, unselected population sample should be studied.

The case histories of the eight women with Turner's syndrome, who had been admitted to Danish psychiatric hospitals, are shown in *Chapter 19 c,* and the diagnoses are seen in *Table 41.*

Table 41

Main psychiatric diagnoses

Diagnoses	Patients
Anorexia nervosa	1
Neurosis	2
Psychogenic psychosis	3
Manic-depressive psychosis	1
Mental retardation	1
Total	8

One of the eight patients, a mentally retarded child (No. 54), was admitted to a child psychiatric hospital on account of the diagnostic question, psychosis or mental retardation. She was considered to be mentally retarded and not psychotic as seen in the case history.

One of the seven adult patients with Turner's syndrome, who had been admitted to a psychiatric hospital, only stayed for one day (No. 52) She had a mild depressive reaction, most probably due to her admission to a medical ward for physical examination, and admission to a psychiatric hospital was not really indicated.

The mental disorders of the other six patients were more severe and had entailed a more prolonged stay in psychiatric hospitals, four of them had had several brief admissions, and one patient had remained in the hospital for seven years; she died from meningitis at the age of 58.

Five of these six patients had had a psychotraumatic childhood. Two were overprotected, one grew up as an only child with her paternal grandparents, and the other had very dominating and overprotective parents. One grew up in a home with fanatically religious parents, and her mother developed a paranoid psychosis. One Turner patient grew up in a home where there were constant quarrels and fights between the parents, and the father was hot-tempered and domineering and often hit his children. The financial circumstances of this home were very poor, and the patient had been obliged to leave home at the age of 7 to work for her living. Her three brothers and two sisters have all suffered from mental illnesses of different kinds.

There is no indication of any increased risk of schizophrenia or manic-depressive psychosis in patients with Turner's syndrome from the present or from any previous studies *(Maclean et al.* (1968) and *Nielsen* (1973)). None of the eight patients had any signs of schizophrenia; one had the diagnosis of manic-depressive psychosis during some of the admissions while during other admissions the diagnoses were anxiety and depressive neurosis.

The karyotypes of the eight patients with Turner's syndrome admitted to Danish psychiatric hospitals during a 10-year-period are shown in *Table 40,* five with 45,X, one with 45,X/46,XX and two with 45,X/46,XX/47,XXX. The frequency of patients with 45,X of 63 per cent was not significantly higher than the 47 per cent among the probands found outside psychiatric institutions.

It is remarkable that 2 of the 3 girls with a cell line 47,XXX found among the total of 67 Turner patients studied in the present investigation were admitted to a mental hospital, and the third was in an institution for mentally retarded patients.

Olanders (1974) found 20 women with triple X syndrome among 6,040 female psychiatric patients in Swedish hospitals, giving a frequency of 3.3 per 1,000 which was significantly higher than the expected 0.9 per 1,000. *Olanders* (1974) further found significantly increased frequencies of females with triple X among girls in remedial classes and in the mentally retarded with behavioural compli-

cations or mental disorders whereas he found no increase in the frequency of women with triple X among patients from ordinary institutions for the mentally retarded.

The frequency of mental illness in women with triple X mosaic thus seems to be significantly higher than expected in the general population as indicated by several studies, recently surveyed by *Nielsen* (1973) who found that in 18 studies of 5,693 females in mental hospitals, a total of 26 females with triple X syndrome was found, giving a frequency of 4.6 per 1,000 which is significantly higher than the expected frequency of triple X in the general population of 0.9 per 1,000. Only 1 of these 5,693 patients had Turner's syndrome.

Women with a 45,X cell line as well as a 47,XXX cell line most probably have an increased risk of mental illness. Our findings indicate that the risk is higher than that of women with 47,XXX in all cells; this needs, however, further investigation before any conclusions can be drawn.

Chapter 10

PREVALENCE OF TURNER'S SYNDROME IN INSTITUTIONS FOR THE MENTALLY RETARDED

a. Prevalence of Turner's syndrome in institutions for the mentally retarded in general

Maclean et al. (1962), *de la Chapelle* (1963), and *Harms* (1967) made X-chromatin studies of 4,114 mentally retarded girls and found a prevalence of 1.2 per 1,000 of girls with Turner's syndrome. The range was 0.5-2.0 per 1,000 in the three studies, respectively. *Yanagisawa & Shuto* (1970) made a survey of 24 X-chromatin studies in mentally retarded patients, these studies comprised a total of 12,849 females, 15 of whom had Turner's syndrome which gives a prevalence of 1.2 per 1,000.

Girls with Turner's syndrome, 46 chromosomes and structural aberration of one X as well as some of the mosaics with 46,XX or 46,XX structural abnormal X would, however, not be included in the prevalence made by X-chromatin examination.

b. Prevalence of Turner's syndrome in Danish institutions for the mentally retarded

We have tried to get an estimate of the prevalence of Turner's syndrome under care at institutions for the mentally retarded in Denmark by asking the chiefs of service for information of patients with Turner's syndrome in the 10 Danish centres for the mentally retarded as well as by reference to the Danish Cytogenetic Central Register; this Register has previously been described by *Nielsen et al.* (1973).

There were 11 patients with Turner's syndrome under care at the centres for the mentally retarded in Denmark. A total population of female patients under care at these institutions was 9,608 on April 24th, 1973, as described by *Dupont* (1975).

Seven of the 11 patients with Turner's syndrome were in-patients and the total population of female in-patients comprises approximately 4,000. The prevalence of Turner's syndrome in Danish institutions for the mentally retarded as found in the present investigation was thus 1.8 per 1,000, compared with the expected frequency in the general population of 0.3 per 1,000.

The total prevalence of Turner's syndrome among in-patients as well as out-patients under care at the Danish centres for the mentally retarded was 1.1 per 1,000 as seen in *Table 42*.

Table 42

Prevalence of patients with Turner's syndrome under care at Danish institutions for the mentally retarded on April 24th, 1973

Karyotypes	Patients total: 9,608
	Patients with Turner's syndrome
45,X	4
45,X/45,X,+ace	2
45,X/46,X,r(X)	1*
45,X/46,X,i(Xq)	1
45,X/46,XX	1
45,X/46,XX/47,XXX	1
46,X,t(X;X)(p21;q13)(Xqter→Xp21::Xq13→Xqter)	1
Total	11
Rate per 1,000	1.1

* One (No. 41) was included among the 45 probands.

The prevalence of 1.1 per 1,000 is a minimum figure as it is doubtful whether all patients with Turner's syndrome in Danish institutions for the mentally retarded have been diagnosed. The prevalence we found is, however, as high as the prevalence found in systematic studies using an X-chromatin examination screening method *(Maclean et al.* (1962), *de la Chapelle* (1963), *Harms* (1967), *Yanagisawa & Shuto* (1970)). The real prevalence of Turner's syndrome among patients in institutions for the mentally retarded is most probably somewhere between 1.0 and 2.0 per 1,000.

The finding of a slightly higher prevalence of girls with Turner's syndrome under care at institutions for the mentally retarded does not necessarily indicate that the risk of mental retardation is higher in girls with Turner's syndrome. The combination of short stature and other Turner stigmata as well as a tendency to mental immaturity together with mental retardation might more easily lead to admission to institutions for the mentally retarded than for children with mental retardation alone. No definite conclusion concerning the question of increased risk of mental retardation in girls with Turner's syndrome can thus be drawn from these findings. It is, however, most likely that the prevalence of mental

retardation is slightly higher among girls with Turner's syndrome than in the general population. The exact figures for this can, however, only be derived from investigations of Turner's syndrome from a large unselected population sample.

Chapter 11

INTELLIGENCE IN TURNER'S SYNDROME

a. Full-scale intelligence in Turner's syndrome

The mean FSIQ for women with Turner's syndrome studied by *Lindsten* (1963) (n = 27) was 95, range 72-131. *Money & Granoff* (1965) found a mean IQ of 97 in 46 women with Turner's syndrome, range 50-125, *Bekker & van Gemund* (1968), and *Bekker* (1970) who studied 15 patients with Turner's syndrome found a mean IQ of 97 and a range from 64 to 124. *Buckley* (1970) found a mean FSIQ of 93 in 12 girls with Turner's syndrome.

b. Differences in verbal/performance scores in Turner's syndrome

In most studies on Verbal and Performance IQ in women with Turner's syndrome significant discrepancies above 10 points have been found *(Shaffer* (1962), *Cohen* (1962), *Money & Granoff* (1965), *Buckley* (1971), and *Theilgaard* (1972)). Discrepancies between Verbal and Performance IQ in the WAIS intelligence test $\geq$ 10 points are significant on 0.05 level *(Rapaport et al.,* (1968)), and in such cases it is often best to consider the two IQ-scales as separate.

It was, however, not possible for *Bekker & van Gemund* (1968) to establish that Turner girls score significantly lower on Performance IQ as they found a mean Verbal IQ of 96.8 and mean Performance IQ 95.07. The authors suggest that their observation may be due to the age of the Turner girls studied, because a non-significant tendency for this appeared in their patients above 13½ years of age.

c. Differences between other IQ sub-test scores in Turner's syndrome

By testing 16 girls with Turner's syndrome on the SRA Primary mental abilities Test, *Money & Alexander* (1966) found that verbal meaning was average, the reasoning score, though generally lower, was still within normal limits, but the space score was significantly below the normal level.

Buckley (1971) found that *all* the non-verbal items of the intelligence test contribute to the significant discrepancy between Verbal and Performance IQ, but in different degrees. She found that Object assembly was significantly lower

than that achieved on all other performance sub-tests, and that Block Design was marginally the highest of all the performance sub-tests.

Garron et al. (1973) analysed intelligence score in 44 girls with Turner's syndrome and concluded that the bimodal trends found in the distribution of FSIQ were attributable to the effect on the Full Scale IQ of lower scores on specific non-verbal sub-tests.

d. Specific factor scores in Turner's syndrome

In 1957, Cohen subjected the Wechsler Adult Intelligence Scale (WAIS) to factor analysis. Later (1959) he factor analysed the Wechsler Intelligence Scale for Children (WISC). He derived three specific main factors: Verbal comprehension, Perceptual organization, and Memory, - factors essentially identical with those identified for neuro-psychiatric populations on the Wechsler-Bellevue scale. Two minor factors: Picture completion and Digit symbol were found together with a second-order factor G.

Using Cohen's specific factor quotients as applied by *Shaffer* (1962), *Money* (1964) found that the above mentioned discrepancy between Verbal and Performance IQ in 37 patients with Turner's syndrome is paralleled by a discrepancy between scores for Verbal comprehension and Perceptual organization (M = 11.3; SD = 2.8 versus M = 7.7; SD = 2.6; the difference is significant beyond the 0.1 per cent level).

In a later study, *Money & Granoff* (1965) confirmed - what had also been observed in the Money study from 1963 - that on another specific factor named Freedom from distractibility (derived from Arithmetic and Digit symbol, and, in the factor analysis by *Cohen* (1957), erroneously named »Memory«) the girls with Turner's syndrome scored significantly lower than on Verbal comprehension. The Perceptual organization mean is according to the authors lowest of all, but not markedly different from Freedom from Distractibility, and the discrepancies are more marked at the high levels of IQ than at the average or low.

In line with these results, *Bekker & van Gemund* (1968) observed that compared with a control group of 9 normal girls, 9 Turner girls scored significantly lower on the factor Perceptual organization.

The results have been interpreted in various ways. Low scores on the specific factor of Perceptual organization have been taken to show »a type of dysgnosia for space-form perception« or »a type of space-form blindness«; low scores or Freedom from Distractibility factor were believed to apply specially to numbers and calculation - as »a degree of dyscalculia«; or the low scores were simply interpreted as »a cognitional deficit« *(Money,* 1964).

Alexander & Money (1966) and *Money* (1973) suggested that the deficit is specific to non-linguistic tasks, but not to personal space. Since parietal lesions cause similar impairments, they suggested that the parietal lobes may be abnormal.

e. Critical evaluation of intelligence studies in Turner's syndrome

For various reasons criticism has been raised on the studies of IQ in Turner's syndrome. Thus *Garron & van der Stoep* (1969) stressed the lack of unselected groups of Turner's syndrome as well as the lack of controls in nearly all studies, and they concluded that the increased incidence of slight mental retardation might be attributed to impairment of non-verbal abilities. This impairment might be apparent only in comparison with that person's own verbal ability; these authors suggested tentatively the characterization that persons with Turner's syndrome are poor at tasks which are primarily non-verbal and are unimpaired at all tasks which are primarily verbal. In a later report, *Garron et al.* (1973) argued that because the level and distribution of IQ in any sample with Turner's syndrome will be affected systematically to the degree to which a test contains verbal, numerical, and pictorial items, the reports should note the tests used, and when possible, the intellectual trait structure of the test.

Cohen (1957) concluded from his factor analytic study that the conventional combination of sub-test scores to determine Verbal, Performance and Full scale IQs does not constitute the actual functional unities in intelligence test performance. For example, the Performance IQ was shown to respond to Perceptual organization but also to the minor specific factors D and E. This author also stressed that single sub-test scores do not in general lend themselves to individual interpretation *(Cohen,* 1959).

Buckley (1971) remarked that as *Cohen* (1957) obtained his three factors from a normal group, consideration of the Perceptual organization factor might be of little validity in the Turner group which is abnormal. In the same study, Buckley questioned the validity of considering only the sub-test of Block design and Object assembly involved in the calculation of the Perceptual organization factor because only Object assembly scores were found to be significantly lower than those achieved on all other Performance sub-tests including Block design.

This indicates that the intelligence testing of women with Turner's syndrome should be made and evaluated very carefully. The result should not be evaluated from the Full scale IQ alone, but always in accordance both with Verbal IQ, which will be normally distributed, and with Performance IQ, which may be somewhat lower than expected due to difficulties in certain specific tests. The results of non-verbal tests will to a great extent depend on what kind of non-verbal tests are used and also how carefully and patiently they have been applied by the psychologist.

f. The present study

We made no intelligence testing of our 45 probands with Turner's syndrome.

As shown in *Chapter 4,* the girls with Turner's syndrome did, however, reach

the same educational level and managed as well at school in all aspects as their sisters, and only one of the 45 probands (No. 41) was mentally retarded.

They had a tendency to have greater difficulties in arithmetic than their sisters, but the differences were not significant, and if properly guided and helped, they were usually able to overcome these difficulties. Some of the girls with Turner's syndrome need better teaching and more guidance in subjects like arithmetic than others.

We found, however, no significant difference in intelligence as evaluated by school performance, occupational level and performance between the 45 probands with Turner's syndrome and their 46 sisters. Nor was there any indication of significant differences in intelligence level, occupational level and performance between those with Turner's syndrome and the controls with normal karyotypes, short stature and primary amenorrhoea.

A line in the reviewed IQ research in Turner's syndrome indicates a development from measuring full-scale IQ to measuring more specific factors. Some disagreement is, however, to be found about the specific nature of the factors responsible for the lowered non-verbal score, and it has been argued that even the so-called specific factor Perceptual organization is not »specific« enough in Turner's syndrome.

Nevertheless, there seems to be considerable agreement that one or more cognitive non-verbal and in particular spatial abilities are significantly lower in Turner's syndrome. This situation seems most interesting from an experimental cognitive psychological point of view. In *Chapter 12, 13 and 14* we present the results of an experimental analysis, of performance in Turner's syndrome on tests most of which are supposed to measure spatial aspects and which have some relation to certain parts of IQ sub-test and specific factor scores.

Chapter 12

COGNITIVE PERFORMANCE: I. FIELD DEPENDENCE IN TURNER'S SYNDROME

a. Short introduction to traditional field dependence terminology

If a person shows a tendency to experience parts of a perceptual field as discrete from the field as a whole, she is said to perform in a »field independent« way (or to be »field independent«). If her perception on the other hand tends to be dominated by the organization of the total field in which the item is contained, so that the item cannot easily be disembedded from its context, such tendency is labelled »field dependent« (and the person is said to be »field dependent«) *(Witkin et al.,* 1962).

Field independent or field dependent performance can according to Witkin be measured separately on several indicators, notably in the rod-and-frame test (RFT), the embedded-figures test (EFT), and the human figure-drawing test (HFDT). It has been proposed that if a person performs in a field dependent way in one of these indicators, she will also tend to do so on the other field dependency measures, and similarly will the field independent person show »self-consistency« across various tests. In such cases the performance is indicative of a »perceptual style«.

A person defined perceptually as highly field independent is supposed to find it an easy task to experience items in the intellectual domain as separate from their contexts, and conversely a perceptually very field dependent person would tend to find it difficult intellectually to take some critical elements out of the context in which they are presented *(Witkin et al.,* 1962). This extension of self-consistency from the perceptual domain to the intellectual domain makes Witkin suggest that »cognitive style« is a more appropriate designation than »perceptual style«.

To link these and other concepts theoretically, Witkin considers it likely that the degree of field dependence measured in one or the other domain indicates a broader underlying dimension of a given person's greater or lesser *psychological differentiation.* The extent of psychological differentiation can be measured in domains other than the above mentioned; of these only the »articulation-of-body-concept« aspects will also be discussed in some detail in connection with the presentation of the human figure-drawing test results.

b. Field dependence in Turner's syndrome

It has been shown *(Shaffer,* 1962) that girls with Turner's syndrome score

remarkably low on the analytic triumvirate (Block design,Picture completion, and Object Assembly) of Wechsler's sub-tests. According to Witkin such performance signifies field dependence, and Shaffer's observation made Witkin suggest that field dependent behavior might be at least in part under genetic control *(Witkin,* 1965).

The only study of Turner girls involving one of the original measures of field dependence – the RFT – was made by *Bekker* (1969). He found no significant difference between the Turner girls and a control group. The number of subjects (n = 9) in the groups was, however, rather small.

In order to test the hypothesis put forward by Witkin and in the light of the interesting theoretical perspectives e.g. possible genetic influence on cognitive style, we decided to study a group of girls with Turner's syndrome by means of a battery of field dependence indicators. As controls were included a group of sisters to the Turner girls and a group of growth-retarded girls with primary amenorrhoea, and normal karyotype.

Furthermore we wished to study possible differences between 1) Turner girls with karyotype 45,X and girls with other karyotypes within the Turner syndrome, 2) Turner girls and their sisters, 3) Turner girls and growth-retarded girls with normal karyotypes. We also wished to inspect how »self-consistent« the Turner girls are with regard to field dependence. In this way, we hoped to learn more about what Shaffer has called a »cognitive deficit« in Turner's syndrome in order to help these girls as far as possible to overcome such a »deficit«.

Besides these matters we also aimed at examining in more detail the possible relation between growth-retardation and field dependence and in this way present basic material for more theoretical considerations about possible agents for field dependent performances.

These early intentions for the study have been supplemented with an increasing need for a re-analysis of the empirical basis of one of the indicators of field dependence, namely, the rod-and-frame test. This re-analysis we see as a natural extension of the original intentions of the present study, because it serves to give a more detailed picture of the cognitive performance in Turner's syndrome. Such work cannot, however, be presented within the present spatial limitations and will be presented elsewhere *(Nyborg & Nielsen,* (1977,a); *Nyborg,* (1976)).

c. Methods

In the study we included the rod-and-frame test (RFT) and the embedded-figures test (EFT) to measure field dependence together with the human figure-drawing test (HFDT) scored according to *Witkin's* (1962) 5-points »articulation-of-body-concept« scale.

We had several reasons for choosing these three tests. It has for example been

argued that observation with only one of Witkin's perceptual tests hardly gives an adequate basis for the safe estimation of a given person's degree of field dependence *(Arbuthnot,* 1972). Furthermore we preferred to study more »directly« the degree of field dependence in Turner's syndrome by applying Witkin's original perceptual tests (RFT and EFT). The human figure-drawing test performance has been found to relate significantly to the analytic triumvirate of Wechsler's sub-tests mentioned above *(Goodenough & Karp,* 1961; *Karp,* 1963), and to perceptual scores from the RFT and EFT *(Witkin,* 1965). In the present study we included the HFDT in the battery partly in order to make more complete the picture of the probands' degree of field dependence. We also wanted to correlate the ABC-ratings in the HFDT with the RFT and EFT scores to study the subjects' degree of self-consistency over tests.

Finally the HFDT was chosen because, in other studies using the human figure-drawing technique, it has been found that women with Turner's syndrome draw unrealistic, little detailed figures with minimal or completely lacking sexual characteristics; these projective studies used techniques, however, of scoring the human figure-drawings other than Witkin's. We wished to see if the Turner girls would get a low score on Witkin's non-projective »articulation-of-body-concept« (ABC) ratings.

d. Procedure

The experimenter had no access to cytogenetic, physical, psychiatric or anamnestic data prior to testing. The experimental protocols were assigned a code number specific to the given person before scoring. The quantitative analysis was performed blindly, i.e. without knowledge of the person in question or of the group to which she belonged.

The total test procedure took for every single person between $1^3/_4$ to $2^1/_2$ hours, and the succession of the tests was always: RFT, EFT, Porteus Mazes test, Money's Road-Map test, and HFDT. The same examiner was responsible for the individual collection of data throughout the study.

Some of the tests were administered untraditionally on minor points. Deviation from the traditional administration of the tests is described in the relevant sections.

The performance scores were analysed mainly in terms of group mean scores partly due to a decision taken several years ago when starting the investigation and partly to allow for comparison with results from earlier studies, in which mean scores dominate. In a work to be published elsewhere a more individ-specific analysis will be made *(Nyborg & Nielsen* (1977,a)).

e. Hypotheses

As the score of Turner girls with karyotype 45,X is not significantly different from that of Turner women with karyotypes other than 45,X with regard to Full-scale IQ score, Sub-test IQ score or Specific factor IQ score, we expected that these groups would not differ significantly on RFT, EFT, and HFDT performance.

We knew from the *Shaffer* (1962) study that women with Turner's syndrome scored significantly lower than a control group on those parts of Wechsler's sub-tests which may indicate field dependence. This may according to the differentiation theory raise the expectation that the Turner girls in the present study would show typically field dependent performance in the RFT, EFT, and on the »articulation-of-body-concept« scale in the HFDT, relative to their sisters.

Given a high degree of field dependence in the Turner groups it might tentatively be argued that such characteristic performance of the probands is primarily related to their chromosome abnormality. From this point of view it could be expected that the observed high degree of field dependence in Turner girls could be contrasted to a relatively low degree of field dependence in the control group of women with normal karyotype, growth-retardation and primary amenorrhoea. In fact, the control group of growth-retarded girls with karyotype 46,XX could on this basis be expected to perform in much the same way as the sisters of the Turner girls.

Out of these expectations grew the following hypotheses:

1. Turner girls with karyotype 45,X will not perform differently from a group of Turner girls with karyotypes other than 45,X on indicators of field dependence.

2. Women with Turner's syndrome will perform with a greater degree of field dependence than their sisters on all indicators herefore.

In case that hypotheses 1 and 2 were confirmed it was furthermore hypothesized that

3. The relatively high degree of field dependence in the Turner group is contrasted by a relatively low degree of field dependence in the growth-retarded controls with normal karyotype 46,XX.

In accordance with Witkin's differentiation hypothesis we finally hypothesized that

4. A person scoring high or low on the field dependence-independence continuum in one test will also do so on the other tests of field dependence, thereby showing a high degree of what Witkin calls »self-consistency«.

These hypotheses we tested. The reports are presented in the following way: each of the three measures of field dependence is first described with regard to the physical appearance and the »nature« or »rationale« of the test; the traditional procedure is roughly outlined and the remarks on deviations from it are

made; results are then reported and compared with earlier studies. Then correlations between Witkin's three tests of field dependence have been calculated.

When the results of these analyses are inspected, the reader should keep in mind that the number of subjects – although considerable compared with many other chromosomal studies – is small. Also some distributions were more or less skew; we nevertheless refrained from more technical transformations of the data. Whenever the term »significant« is used, we mean »statistically significant« and at least on 5 per cent level.

The presentation of the test results is as follows:

1. test for difference between probands with karyotype 45,X and probands with other karyotypes;
2. tests for differences between probands total and sisters, and between sisters total and controls; and
3. tests for differences in the distributions of scores in the just mentioned order.

Before the hypotheses-testing took place, we had to consider a developmental aspect in the material.

f. Developmental trends in field dependence

It is generally agreed that most cognitive functions undergo marked changes during childhood and adolescence. Such changes have relevance also for field dependent performance, and developmental aspects in the field dependence-independence dimension have accordingly received extensive attention from *Witkin et al.* (1962). Their studies, as well as those of others, showed that 8-10-year-old children generally perform relatively field dependently in the classical indicators herefore (RFT, CHEF, EFT). But it was observed that the degree of field dependence gradually decreased to an individ-specific minimum up to puberty to a rise again at about, or shortly after, puberty and more so for girls.

These age-related differences in degree of field dependence could be an important variable in the present study, as about one third of the probands had not reached their fifteenth year of age at the time of cognitive testing. We therefore controlled whether the probands could be regarded as a homogenous group with regard to age on the field dependence dimension.

The probands were divided in five age-groups:

1. one group of subjects fifteen years or younger at time of testing (n = 14);
2. another group with ages between fifteen and nineteen (n = 7);
3. a third group aged 20-24 years (n = 11);
4. one group with ages between 25-29 years (n = 9); and finally;
5. a group of probands aged 30 years or more (n = 4).

We tested for differences between group means, linearity, and tilt of regression lines for all cognitive scores. Results of such analyses of the field dependence-independence scores are presented in this section (the analyses of

developmental aspects in the other scores are presented in the proper sections later).

Results of the developmental analysis of field dependent performance

With probands divided in five age-groups we found no statistically significant differences between means as seen in *Table 43.* Neither was statistically significant linearity found between scores in the age-groups. Accordingly no tests for tilt of lines were calculated. From this we concluded that age-differences in the field dependence-independence scores do not play a considerable role in the next following analysis. It should, however, be remembered that the number of subjects in age-group 1 ($\leq$ 15 years) with relatively high mean score tends to elevate the probands' total group mean score. (Closer inspection of the *pattern* of data revealed interesting trends in the material, to be considered elsewhere *(Nyborg & Nielsen* (1977,b)).

Table 43

Analysis for age-related differences in field-dependence-independence performance in probands

Age in years:		Rod-and-Frame Test (RFT); unsigned deviation of the rod in degrees		Embedded-Figures Test (EFT); number of seconds per figure		Human Figure Drawing test (HFDT); ABC-ratings	
	n	Mean	SD	Mean	SD	Mean	SD
1) $\leq$ 15	14	15.04	7.23	137.76	38.33	3.79	1.05
2) 15-19	7	10.23	7.40	88.74	58.00	3.57	1.62
3) 20-24	11	9.30	8.29	98.02	44.80	3.18	1.47
4) 25-29	9	9.29	8.12	123.05	40.19	3.89	1.17
5) $>$ 30	4	12.00	8.93	97.15	41.41	4.00	0.82
Total group mean	45	11.47	7.90	113.87	45.80	3.64	1.25

The differences between means
in the RFT ($F = 1.16$; $p > .2$; $F_{lin} = .78$; $p > .2$)
and in the EFT ($F = 2.27$; $p > .2$; $F_{lin} = 2.37$; $p > .2$)
and in the HFDT ($F = .58$; $p > .2$; $F_{lin} = .76$; $p > .2$)
are not significant.

g. The rod-and-frame test (RFT) scored ad modum Witkin

We applied a transportable rod-and-frame test (RFT) furnished from Darro Scientific. It consists of a semi-transparent box. When the subject's head was arrested in the head-rest at one end of the box she no longer saw the test room but was confronted with a frame painted in black on a white background at the other end of the box. The frame was tilted stationary 28 degrees either to the right or to the left of physical vertical. Within it was a black rod. This rod could be tilted independently of the frame and its position was measured in degrees and direction relative to physical vertical.

The subject was required simply to direct the experimenter to adjust the initially tilted rod to a position which appeared to her to be physically vertical within the stationary tilted frame. Considerable individual differences have been found in numerous studies on this task. It is generally believed that persons who adjust the rod exactly to or near physical vertical show capacity to perceptually »extract« the rod out of its context and handle it without being unduly distracted by the frame tilt (characteristic field independent behavior); persons who on the other hand find themselves troubled with the task of adjusting the rod to physical vertical under the presence of the frame are said to show inability to keep an item (the rod) out of its context (the frame) (characteristic field dependent behavior).

We followed the traditional procedure for the transportable RFT *(Oltman,* 1968). In short: no indication of tilt was apparent to the subject when she placed her head in the head-rest before the cloth curtain which prevented her from seeing the preparatory settings of the rod and the frame in the beginning of the first and subsequent trials. She was then told that her task was to adjust the rod to physical vertical under a number of tilt combinations of the frame and the rod which were explained to her. The concept of physical vertical was carefully outlined and it was ensured that she understood it clearly. The rod and the frame were alternately tilted 28 degrees to the left or to the right of physical vertical, which gives four tilting combinations: these four tilting combinations were repeated twice thus giving eight measures of each subject's rod tilting deviations in degrees off vertical. Occasionally some subjects' behavior in the RFT situations seems to indicate that they had either after all misunderstood the instruction, or they were spatially disoriented. In Witkin's standard instructions for the RFT reference is made to a »disorientation test«.

This test we modified. In the case of »strange« responses to the test we simply - after the series of eight trials - asked the subject to take her head out of the RFT apparatus with the frame tilted and the rod in its last adjusted position. In all cases the subjects were now able to adjust the rod to physical vertical within zero to two degrees as long as they could see the walls and ceiling of the test room. Whenever it became clear that the subject had misunderstood the instruction the trials were repeated. This happened in two cases only, and the last

obtained data were incorporated in the present study. In other cases the subjects still performed »strangely« even after this experience. In such case we interpreted the »strange« behavior as not due to misunderstanding of the instructions *(Nyborg & Nielsen* (1977,a)).

According to tradition *(Witkin et al.,* (1954)), the values of these eight measures were added, and the sum was divided by the number of observations thus giving a rough over-all error score. This score has been called the »unsigned deviation score« (USD). Most studies to date have this USD score as the basis for the evaluation of the subjects' performance in the RFT. When the present study was initiated some years ago we also decided to apply this method of scoring.

Results and discussion

The probands were divided according to 1) karyotype 45,X and 2) other karyotypes within Turner's syndrome for analyses of possible differences in their perceptual performance. As seen in *Table 44* the two groups did not differ to any notable extent with regard to mean USD error score in the RFT. We could thus not find any perceptual differences between these chromosomal different groups when the mean group deviation in the RFT of the rod in degrees off physical vertical was calculated unsigned (i.e. without considering to which side the rod deviated from physical vertical (clock-wise or counter-clock-wise) and also without considering the direction of the tilt of the frame in the calculations, and finally unweighed (i.e. without taking into account the subject's degree of response consistency to comparable trials in the test)). This observation on perceptual performance in Turner's syndrome is in accordance with results from most other studies in which attention has been paid to possible differences between the two chromosomal different groups in phychological function other than those studied here (see *Chapter 9).* Accordingly, we treated the two subgroups of probands as one in the next following statistical analyses.

When the mean USD error score of the unified group of probands was compared with that of the group of sisters, a pronounced difference was observed: while the probands' mean USD error score amounted to as much as 11.47 degrees with a deviation of (SD 7.90) in their attempts to set the rod to exact physical vertical, the sisters had a much lower mean USD of 4.59 degrees (SD 4.70) as seen in *Table 45.* The difference is highly significant ($p < .001$).

The controls could be found in an intermediate position between the probands and the sisters with a mean USD error score of 7.67 degrees (SD 8.14). The difference between the sisters' USD and that of the control group was, however, not significant. It can be noted that the SD of the probands and of the controls are approximately twice as high as those of the sisters.

Occasionally somewhat arbitrarily chosen cut-off points on the field dependence-independence score continuum is seen in the literature. Thus some authors

Table 44

Group scores of field dependence in the Rod-and-Frame test ad modum Witkin: mean unsigned, unweighed deviation scores (USD) for probands [1) 45,X; 2) other karyotypes; and 3) probands total]

Probands:	n	unsigned, unweighed deviation score, USD	
		Mean	SD
45,X	21	11.82	8.58
other karyotypes	24	11.16	7.62
Probands total	45	11.47	7.90

The difference is not significant ($t = .27$; $p > .2$).

divide subjects on the basis of their USD error score into groups as follows: 1) persons with USD less than two degrees (and call them extreme field independent persons); 2) persons with USD between two and eight degrees; and 3) subjects with more than eight degrees of mean USD error score (extreme field dependent persons). Applying this classification to our own subjects we found as seen in *Table 46* nearly identical distributions of Turner girls with karyotype 45,X and Turner girls with other karyotypes.

Table 45

Group scores of field dependence in the Rod-and-Frame test ad modum Witkin; mean unsigned, unweighed deviation scores (USD) for probands, sisters, and controls

Groups	n	unsigned, unweighed deviation score, USD	
		mean	SD
Probands	45	11.47	7.90
Sisters	19	4.59	4.70
Controls	15	7.67	8.14

The difference between probands and sisters is significant ($t = 3.53$; $p < .001$)
The difference between sisters and controls is not significant ($t = 1.38$; $.2 > p > .1$)

Table 46

Distribution of field dependence scores in the Rod-and-Frame test ad modum Witkin; unsigned, unweighed deviation scores (USD) for probands [1) 45,X; 2) other karyotypes; and 3) probands total]

Probands	USD = 0 - 2° (the field independent group)		USD = 2.01 - 8°		USD > 8° (the field dependent group)		Total
	n	%	n	%	n	%	
Karyotype 45,X	2	9	9	43	10	48	21
Other karyotypes	2	8	10	42	12	50	24
Probands total	4	9	19	42	22	49	45

The difference is not significant ($\chi^2 = .035$; $p > .2$)

When data of the probands, sisters and controls were distributed in this way we found an interesting difference. Nearly half of the total number of probands (49 per cent) could be identified in the group of so-called extreme field dependent persons according to *Table 47*. This is in contrast with the observation that only eleven per cent of the sisters, and 27 per cent of the controls could be classified in the same way as extreme field dependent. Conversely, in the category of field independent persons (with USD less than 2 degrees) we found less than one tenth only of the probands but more than one quarter of the sisters and also of the controls.

Compared with most earlier studies with the RFT the overall observed proportion of field dependent persons (USD higher than eight degrees) is of remarkable size in the present study. This was due primarily to the strong representation of Turner girls in the extreme field dependent group, and secondarily to the growth-retarded control-group. The probands were on the other hand relatively underrepresented in the field independent group while in this category the percentages of sisters and controls were identical and as could be expected from an unselected group.

These observations support Witkin's suggestion that very field dependent performance could be found in the RFT for girls with Turner's syndrome; it contrasts on the other hand with Bekker's observation that Turner girls were not more field dependent than a control group.

Bekker also studied groups of girls with growth-retardation greater than that of his Turner girls. They scored interestingly enough more field dependent than »normal« (which in this case means not-growth-retarded) girls. Bekker

Table 47
Distribution of field dependence scores in the Rod-and-Frame test ad modum Witkin: unsigned, unweighed deviation scores (USD) for probands, sisters, and controls

Groups	USD = 0 - 2°		USD = 2.01 - 8°		USD > 8°		Total
	n	%	n	%	n	%	
Probands	4	9	19	42	22	49	45
Sisters	5	26	12	63	2	11	19
Controls	4	26	7	47	4	27	15
Total	13		38		28		79

The differences between probands and sisters are significant
($\chi^2 = 9.34$; $.01 > p > .001$)
The differences between sisters and controls are not significant
($\chi^2 = 1.65$; $p > .2$)

suggested that field dependence could be more »bound« to growth-retardation than to chromosome anomalies. This interesting possibility was further studied in the present work and will be discussed more thoroughly later in this report. Here we just note that our control group of growth-retarded girls tended to score more field dependent in the RFT (i.e. obtained higher mean USD score) than the sisters but not as pronounced as the probands.

h. The embedded-figures test

The embedded-figures test *(Witkin,* (1950)) is made of a set of complex geometric figures in which a particular, simple figure is embedded. In the present study we used the *Jackson* (1956) short form of the test in which twelve of the originally 24 figures are used. The test was administered and scored according to Witkin's procedure. In the RFT the subject is required to separate an item (the rod) from its context (the frame); the embedded-figures test (EFT) is supposed to require comparable capacity for analysing perceptually an item (the simple figure) out of its context (the more complex design in which it is embedded). The subject's score in the test is simply the time it takes her to locate the simple figures within the more complex. In the present study we calculated the group mean time the subjects required per figure. Rapid solution time scores are taken to indicate field independent performance, while slow solution time is characteristic of field dependent performance.

Results and discussion

As for RFT scores we also tested for possible differences in EFT performance between probands with karyotype 45,X and other karyotypes within Turner's syndrome; we found a non-significant difference as seen in *Table 48*. As for the group mean RFT score, the group mean EFT score also tended to be slightly higher for the group with karyotype 45,X than for other karyotypes (116.37 vs. 111.68).

Table 48
Group mean scores of Embedded-Figures test for probands [1) 45,X; 2) other karyotypes; and 3) probands total]

Probands	Number of seconds per figure	
	Mean	SD
1) 45,X	116.37	50.25
2) Other karyotypes	111.68	42.50
Probands total	113.87	45.80

The difference is not significant ($t = .33$; $p > .2$)

The sisters found it a fairly easy task to locate the simple figures in their embedded context as is seen from their group mean score of 61.25 seconds per figure; in comparison the probands total required approximately twice that time to locate the simple figures (113.87 seconds per figure) as seen in *Table 49*. The difference between probands and sisters is highly significant ($p < .001$). The score of the controls lay between that of the sisters and the probands with regard to EFT performance (82.91 seconds per figure). The difference between the sisters and the controls was not significant.

From *Table 50* can be seen that probands 45,X do not differ from other karyotypes within the Turner group with regard to distribution of EFT time score (Fisher's exact test for 2x2 tables; $p \sim .75$).

Table 49
Group mean scores of Embedded-Figures test for probands, sisters, and controls

Groups	Number of seconds per figure	
	Mean	SD
Probands	113.87	45.80
Sisters	61.25	23.68
Controls	82.91	49.27

The difference between probands and sisters is significant ($t = 4.73$; $p < .001$)

The difference between sisters and controls is not significant ($t = 1.68$; $.2 > p > .1$)

Table 50
Distribution of number of seconds per figure in the Embedded-Figures test for probands [1) 45,X; 2) other karyotypes; and 3) probands total]

Number of seconds per figure	Probands					
	45,X		Other karyotypes		Probands total	
	n	%	n	%	n	%
0 - 44	2	10	2	8	4	9
45 - 89	4	19	6	25	10	22
90 - 134	8	38	11	46	19	42
135 - 180	7	33	5	21	12	27
Total	21	100	24	100	45	100

The differences are not significant ($\chi^2 = 1.01$; $p > .2$).
Neither is the distribution over the two highest and the two lowest quartiles significant (Fisher's exact test for 2×2 tables; $p \sim .75$).

When, on the other hand, the distribution of the probands total was compared with the sisters' we found, as seen in *Table 51,* considerable differences: almost 70 per cent of the probands took 90 seconds *or more* to locate the simple figures while for the majority (79 per cent) of the sisters 90 seconds *or even less* sufficed. More than a quarter of the sisters could on an average find the simple figure within the first 44 seconds while less than one tenth of the probands could be so

classified. Test of the distribution over the two highest and the two lowest quartiles was highly significant (Fisher's exact test of 2x2 tables; $p \sim .0004$).

Table 51
Distribution of number of seconds per figure in the Embedded-Figures test for probands, sisters, and controls

Number of seconds per figure	Probands		Sisters		Controls	
	n	%	n	%	n	%
0 - 44	4	9	5	26	6	40
45 - 89	10	22	10	53	2	13
90 - 134	19	42	4	21	5	33
135 - 180	12	27	0	0	2	13
Total	45	100	19	100	15	99

The differences between probands and sisters are significant ($\chi^2 = 13.57$; $.01 > p > .001$).
The differences between sisters and controls are not significant ($\chi^2 = 4.57$; $p > .2$).
Tests of the distributions over the two highest and the two lowest quartiles were significant for the probands and sisters while not for the sisters and controls (Fisher's exact test for 2×2 tables; $p \sim .0004$ and $p \sim .14$, respectively).

Somewhat surprisingly in the light of their former perceptual performances in this study, 40 per cent of the control group appeared in the lowest scoring group; compared with the sisters a considerable part of this group thus found it relatively easy to localize the simple figures in the complex. On the other hand, while none of the sisters needed more than 135 seconds per figure in the EFT task, thirteen per cent of the controls did so. Twice as many (27 per cent) of the probands could be found in this group of persons who found the EFT a really difficult task. Test for differences between the two highest and the two lowest quartiles showed, however, no difference (Fisher's exact test of 2×2 tables; $p \sim .14$).

The EFT performance of the probands could not be compared with EFT results from other studies with Turner girls because none such had been made. We therefore decided to refer to »normative« data in the EFT for women with ages between 30-39 (mean age 33.7; $n = 32$) presented by *Witkin* (1968). The women in Witkin's study obtained a mean score per figure of 84.24 (SD 34.35) (as calculated from full series score); the sisters in the present study took 61.25 seconds per figure (SD 23.68), and appeared thus to be more field independent than could be expected from Witkin's data ($t = 2.57$; $.02 > p > .01$). But even if

we compared Witkin's »more field dependent« results from his »normal group« with the performance of the Turner girls in the present study, the difference between these two groups is still significant ($.01 > p > .001$). We concluded that girls with Turner's syndrome clearly perform in a very field dependent way in the EFT. We also noted that the growth-retarded girls with primary amenorrhoea tended to score field dependent but not significantly different from the sisters.

i. The human figure-drawing test

As the fifth test in the battery we asked the subjects to draw human figures. The procedure was as outlined by *Witkin* (1962) with one exception. According to Witkin the subject is asked to draw the first figure without requirement as to the sex of the drawing; the next drawing to be of the opposite sex. In the present study we asked the subject first to draw a male and then a female figure.

Drawings of human figures are considered by *Witkin et al.* (1962) to be an index of the drawer's conception of her own body. Although Witkin admits that the drawn representation of the conception of the body is multi-determined, he suggests that all the relevant factors are organized around the conscious or unconscious experiences of the body. Indirect knowledge of the body conception can be obtained through inspection of the subject's drawings of the human body. Witkin has been specifically concerned with the degree of »articulation-of-body-concept« defined by the extent to which the drawings mirror the body as experienced to have definite limits (boundaries) and to what extent the »parts« within these limits are experienced as separate although kept together in a »gestalt».

These characteristics were judged in a single global evaluation based on a number of specific criteria that were read directly from observable characteristics in the drawings rather than bound to a more traditional projective interpretation. After all identification marks had been removed, the drawings were rated by two independent judges with previous experience in evaluating drawings. The judges applied the adult version of the »articulation-of-body-concept« scale (the so-called ABC-scale). In short, they looked for three main indicators of degree of articulation: 1) fair integration of reasonably formed parts of the body and articulation in representation of body and face expressions; 2) identity and sex differentiation where the role and the articulation of the sex characteristics of the figures drawn were evaluated, and finally 3) the degree of detail in the drawings. This last category overlaps the foregoing and was relatively decisive in the differentiated estimation of the drawings. In principle the adult version of the scoring is very much like the first developed children's version except that the standards of estimation are considerably raised.

The most primitive, immature, undetailed and disintegrated drawings were rated five points (indicative of field dependence). The most articulated drawings

with emphasis on many details in face, head, clothing, expression, forms and sex characteristics consistent with rational integration of body and clothing were rated one point (indicative of field independence). Drawings which could neither be categorized in the very primitive nor in the highly articulated groupings were placed in between. In the case of disagreement in the estimation of the drawings, the two judges solved the problem by talking to agreement.

Results and discussion

When probands with karyotype 45,X were compared with other karyotypes within the Turner group we found no significant difference as seen in *Table 52.* Probands with 45,X tended, however, to draw slightly less articulated figures than the other probands.

Table 52
Group mean ratings of Witkin's »articulation-of-body-concept« (ABC-ratings) in Human-Figure-Drawing test for probands [1) 45,X; 2) other karyotypes; and 3) probands total]

Probands	ABC-ratings	
	Mean	SD
1) 45,X	3.71	1.27
2) Other karyotypes	3.58	1.25
Probands total	3.64	1.25

The difference is not significant ($t = .34$; $p > .2$).

When the probands total was compared with the group of sisters, we found a highly significant difference ($p < .001$; see *Table 53).* The probands achieved a mean score of 3.64 (SD 1.25) for their relatively poor drawings while the sisters scored 2.53 (SD .84).

As with the RFT and EFT performance the growth-retarded group again was found in an intermediate position with a mean group rating of 3.00 (SD 1.07) between the sisters and the probands. Their score did not, however, differ significantly from the sisters'.

From *Table 54* can be seen that scores of the probands with karyotype 45,X were very similarly distributed to those of the other probands (Fisher's exact test for 2×2 tables; $p \sim .70$).

Table 53
Group mean ratings of Witkin's »articulation-of-body-concept« (ABC-ratings) in Human Figure-Drawing test for probands, sisters, and controls

Groups	ABC-ratings	
	Mean	SD
Probands	3.64	1.25
Sisters	2.53	0.84
Controls	3.00	1.07

The difference between probands and sisters is significant ($t = 3.54$; $p < .001$).

The difference between sisters and controls is not significant ($t = 1.43$; $.2 > p > .1$).

Table 54
Distribution of Witkin's »articulation-of-body-concept« scores (ABC-ratings) in Human Figure-Drawing test for probands [1) 45,X; 2) other karyotypes; and 3) probands total]

Degree of articulation	Probands					
	45,X		Other karyotypes		Probands total	
	n	%	n	%	n	%
1 (high)	2	9	2	8	4	9
2	2	9	3	12	5	11
3	2	9	4	17	6	13
4	9	43	9	38	18	40
5 (low)	6	29	6	25	12	27
Total	21	99	24	100	45	100

The differences are not significant ($\chi^2 = .67$; $p > .2$).

Fisher's exact test for 2×2 tables over the two highest and the two lowest quartiles (group 3 divided with half to the lowest and half to the highest) gave no significance; $p \sim .70$).

When the distribution of all the probands was compared with that of the sisters and controls (see *Table 55*) it was somewhat surprising, in the light of their earlier perceptual performance, to find that while ten per cent of the sisters were in the group classified as most articulated performing persons, nine per cent of the probands also performed at this very high level. It was furthermore unexpected that the growth-retarded group excelled over both the other groups in this respect, as thirteen per cent were represented in the most articulated drawers' group; they did not, however, score significantly different from the sisters (Fisher's exact test for 2×2 tables; $p \sim .40$).

Table 55
Distribution of Witkin's »articulation-of-body-concept« scores in Human Figure-Drawing test for probands, sisters, and controls

Degree of articulation	Probands		Sisters		Controls	
	n	%	n	%	n	%
1 (high)	4	9	2	10	2	13
2	5	11	7	37	4	27
3	6	13	8	42	4	27
4	18	40	2	10	2	13
5 (low)	12	27	0	0	3	20
Total	45	100	19	99	15	100

The differences between probands and sisters are significant ($\chi^2 = 18.59$; $p < .001$).
The differences between sisters and controls are not significant ($\chi^2 = 4.75$; $p > .2$).
Fisher's exact test for 2 × 2 tables over the two highest and the two lowest quartiles (group 3 divided with half to the lowest and half to the highest) showed significant difference between probands and sisters; $p \sim .002$, but not between sisters and controls; $p \sim .40$.

When on the other hand the groups were compared with regard to most primitive drawings, this picture changed: no sisters were found in this category while 20 per cent of the controls and 27 per cent of the probands made drawings of this poor standard.

These tendencies were more exaggerated if the drawings rated in the intermediate category 3 were divided with half to a relatively high articulation category, together with category 1 and 2, and the other half was combined into a relatively low articulation category, together with category 4 and 5, signifying relatively high or poor articulated drawings, respectively. So analysed, we found

26.5 per cent of the probands in the relatively high articulated group compared to 68 per cent of the sisters and 53.5 per cent of the controls. In the relatively poor articulated category 73.5 per cent of the probands were to be found, compared to 31 per cent of the sisters and to 46.5 per cent of the controls.

As no other studies with Turner girls have used Witkin's »articulation-of-body-concept« rating of the human figure drawings we could not relate our results directly to those of others. In the following chapters, the drawings were rated also according to the Goodenough-Harris scoring. These results are related to observations in other studies of Turner girls using this score. Drawings rated according to Witkin's scale have been shown in some studies to correlate fairly high with Goodenough-Harris score of the same drawings; for this reason the results and discussion presented in the next chapter on the drawings may have some relevance for the present discussion.

From the present material we observed that: 1) possible differences with regard to human figure-drawing test performance scored ad modum Witkin between karyotype 45,X and other karyotypes within Turner's syndrome are small; 2) girls with Turner's syndrome as a group draw considerably less articulated human figures than those of their sisters; 3) girls with growth-retardation tend as a group to draw less articulated drawings than the group of sisters in this study (while, on the other hand, the number of highly »articulated« drawers were higher in the growth-retarded group than in the group of sisters).

k. Consistency in Witkin's measures of field dependence

According to one of Witkin's basic hypotheses a person who performs in a given field dependent way on one indicator is also likely to do so on another test sup-

Table 56

Correlations between performance on various indicators of field dependence (i.e. the Rod-and-Frame test: RFT; the Embedded-Figures test: EFT; and the Human Figures-Drawing test: HFDT) for all persons included in the present study (N = 79)

Field dependence tests	Pearson product-moment correlation coefficients					
	RFT		EFT		HFDT	
	r.	p <	r.	p <	r.	p <
RFT			.61	.001	.41	.001
EFT					.65	.001
HFDT						

posed to measure field dependence; in doing so, her performance is said to be »self-consistent».

In order to study this suggested self-consistency tendency in performance across the various tests of field dependence, we correlated the field dependence measures obtained in our study, namely the RFT, the EFT, and the HFDT scores. We simply analysed the data of all persons in the study without regard to group placement and calculated the Pearson correlation coefficients (r.s.).

From *Table 56* can be seen that the correlation coefficient between the RFT and the EFT data (r. = .61) and between RFT and HFDT (r. = .41), and between EFT and HFDT data (r. = .65) are all highly significant (on .001 level).

This supports Witkin's basic assumption that a person performing in a field dependent or field independent way in one test also tends to do so in other tests of field dependence.

1. Discussion of field dependence in Turner's syndrome

The results of the human figure-drawing test ad modum Witkin are in good accordance with group results from the other tests supposed to measure the subjects' degree of field dependence, namely the RFT and the EFT. A definite pattern could be found in the data. Comparing the RFT, EFT, and the HFDT-results, we observed that Turner girls with karyotype 45,X did not behave significantly differently from girls with karyotypes other than 45,X but were still within Turner's syndrome on these tests of field dependence. In other words, field dependent performance is very similar in the two groups. Examination of the data suggests, nevertheless, a slight difference. The group of girls with karyotype 45,X performed on *all* tests slightly more field dependent than girls with other karyotypes. Furthermore, the SD of the girls with karyotype 45,X in *all* cases exceeded that of the other probands. The differences were, however, small. In this connection it should be mentioned that although not significant the sub-group of probands aged 15 years or less at the time of the cognitive testing (n = 14) tended to raise the total group mean score (see *Table 43);* 12 of these 14 young probands had karyotype 45,X while the other two had other karyotypes. The over-representation of young probands with karyotype 45,X relative to probands with other karyotypes might be responsible for the observed differences in mean scores between the two groups. This stresses once more the necessity of being alert to the age of the Turner girls studied as a potentially important variable in cognitive performance (see also next chapter).

Without exception we found that the combined group of probands performed more field dependently on all indicators herefore than the group of sisters; the differences were in all cases highly significant. Growth-retarded girls as a group consistently got scores on the RFT, the EFT, and the HFDT that placed them in

the field dependence-independence continuum between the group of probands and the group of sisters (although on HFDT a number of them drew highly articulated drawings). They tended in general to perform in a more field dependent way than could be expected relative to the performance of the sisters; the difference was, however, only borderline significant.

In short we might say that the group of Turner girls performed extremely field dependently as defined by Witkin in all the tests applied, while the growth-retarded girls tended to be field dependent in their performance.

The first hypothesis set forth in the present study stated that Turner girls with karyotype 45,X will perceptually not perform differently from a group of Turner girls with karyotypes other than 45,X. This hypothesis was tested by observing how these two groups performed on the rod-and-frame test (RFT), the embedded-figures test (EFT), and the human figure-drawing test (HFDT). Without exception the results confirmed the hypothesis. In other words, the lack of differences in intellectual performance (full-scale IQ, sub-test IQ, and specific factor IQ) between girls with karyotype 45,X and other karyotypes within Turner's syndrome found in a number of other studies can in the present study be paralleled to a convincing degree in the perceptual domain by showing that the two groups do not differ in their performance on three original indicators of field dependence.

The second hypothesis was based on 1) the observation that Turner girls in general have difficulties with the »analytic triads« in the Wechsler IQ test and 2) on Witkin's self-consistency hypothesis which in this connection states that girls with such difficulties would also perform in a very field dependent way on other tests for that dimension. The second hypothesis was fully confirmed: the perceptual performance of the group of Turner girls was more field dependent than that of their own sisters on the same tests. Bekker's observation that Turner girls are not more field dependent than a control group was not supported by this result.

Hypothesis three stated that given confirmation to hypotheses one and two, the field dependent performance in Turner's syndrome could be contrasted by relatively »normal« field dependent performance in growth-retarded girls, with karyotype 46,XX. If confirmed one might speculate whether the demonstrated high degree of field dependent behavior in Turner girls is due primarily to their chromosome abnormality and not primarily to retarded body growth, as found in both groups. The hypothesis appeared to be difficult to test because although the growth-retarded girls performed less field dependently than the Turner girls, they nevertheless tended to perform more field dependently than the group of sisters.

Hypothesis four stated that a person scoring high or low on the field dependence-independence continuum in one test will tend to do so on the other tests of field dependence also. As seen from the fairly high correlations in *Table 56* this

hypothesis was confirmed signifying that within the traditional field dependence terminology there is meaning in the designation »self-consistency« across various indicators of field dependence.

Hypothesis one, two, and four were thus confirmed while hypothesis three was not tested.

Chapter 13

COGNITIVE PERFORMANCE IN TURNER'S SYNDROME. II

a. Introduction

Money and associates: Shaffer (1962), *Alexander & Money* (1962), *Money* (1964), *Money & Alexander* (1966), *Alexander & Money* (1966), and *Alexander et al.* (1966) have reported poor ability to draw geometric designs from memory in patients with Turner's syndrome. They found no »deficit« in identifying personal left and right or in the ability to name parts of the body, but difficulty in identifying left and right on others was frequent. The ability to change direction on command while drawing a line is unimpaired, but pointing with closed eyes and labelling turns on a street map are impaired.

Garron & van der Stoep (1969) criticized that only two of the studies concerning spatial abilities of patients with Turner's syndrome used any controls, one used fortuitously chosen, somewhat younger girls in a comparison of figure drawings *(Cohen* (1962)), and the other used student nurses, whose age range is less and average education probably higher, to study direction sense *(Alexander et al.* (1966)); children and adults have often been included in the same analyses. *Shaffer* (1962) compared small samples of older and younger persons, finding no differences in intellectual pattern. *Bekker & van Gemund* (1968) compared girls with Turner's syndrome with »normal« girls matched for age and IQ and confirmed most results of the Money-group.

In the present study we examined the Turner girls as well as the sisters and the growth-retarded girls with the road-map test and scored the human figures drawing test according to Goodenough-Harris. *Alexander & Money* (1966) suggested that the so-called cognitive deficit in Turner's syndrome is specific to non-linguistic tasks involving extrapersonal, but not personal space. Since parietal lesions cause similar impairments, they suggested that the parietal lobes may be abnormal. Porteus Mazes test – it has been argued – is sensible to at least some form of brain damage *(Porteus* (1967)) and can be used for assessing certain personality qualities especially relevant for the study of Turner's syndrome. We therefore also included the Porteus Mazes test in the present investigation.

b. Left-right discrimination in Turner's syndrome

Money's road-map test is devised to study direction discrimination. It requires orientation to right and left simultaneously with orientation towards and away from the subject on a flat surface resembling part of a city map. Heavy lines on the map indicate a standard test route which is laid out in such a way that there are eight different turn types (turning right after going up, down, right, and left; turning left after going up, down, right, and left) with a total of thirty-two turns. A shorter heavy line indicates a preliminary practice route of three turns. Both practice and test routes were traced on the map by the Examiner while the subject looked on. The subject was then requested to retrace the routes saying whether she turned right or left at the corners *(Alexander, Walker & Money,* 1964; *Money, Alexander & Walker,* 1965). All subjects were tested individually. The subjects were corrected for errors on the practice route only.

Money, Alexander & Walker (ibid.) have shown that responses to the test are correlated with age. As we have in the present study a number of young Turner girls (i.e. $\leq$ 15 years) and a few in this age-group in the other groups studied, we examined a possible relation between age and road-map test scores. As with »field dependence«-scores we calculated the group mean score in the Money's road-map test for the five age-groups of Turner girls and tested for differences.

Results and discussion

With probands divided in the five age-groups we found a significant difference ($p = .001$) between group means as seen from *Table 57.* There was no significant linearity between mean scores for the age-groups; accordingly no tests for tilt of lines were calculated. The scores related in a patterned way to age; this pattern will be discussed in another work *(Nyborg & Nielsen* (1977,b)).

From *Table 57* can also be seen that the group mean score of group 1 (Turner girls aged fifteen years or less) compared with each single mean of the age-groups 2, 3, 4 and 5 is considerably higher. We found that groups 2, 3, 4 and 5 could be considered as one homogenous group with regard to the function of age on direction discrimination performance ($p > .05$). We then compared the group mean score of the young probands in group 1 with the combined group mean score for the age-groups 2-5 and found the difference to be highly significant ($p < .0001$) as seen in *Table 58.* Apparently Turner girls aged fifteen years or younger have not established left-right discrimination. *Alexander, Walker & Money* (1964) concluded that right-left spatial discrimination in »normal« girls becomes well established between the ages of eleven and fourteen. The Turner girls aged fifteen years or younger as well as the sisters and the growth-retarded girls with normal karyotype in the same age-group were therefore excluded from the following analyses.

Table 57
Group mean scores in the »road-map test of direction sense« as a function of age in Turner's syndrome

Age in years	n	Money's road-map test scores	
		Group mean number of errors	SD
1) ≤ 15	14	11.57	6.72
2) > 15-19	7	4.86	3.29
3) 20-24	11	2.45	2.98
4) 25-29	9	6.44	4.93
5) > 30	4	5.25	5.32
Total group mean	45	6.71	6.00

The differences between means are significant ($F = 5.52$; $p = .001$).

Table 58
Group mean scores in the »road-map test of direction sense« as a function of age in Turner's syndrome

Age in years	n	Money's road-map test scores	
		Mean number of errors	SD
1) ≤ 15	14	11.57	6.72
2-5) 15+ - 38	31	4.52	4.15
Total group mean	45	6.71	6.00

The difference between means is significant ($F = 18.71$; $p = .0001$).

Thus considering in the following only probands older than fifteen years, we compared ten such girls with karyotype 45,X with 21 Turner girls with other karyotypes and found no significant differences ($p > .2$) as seen in *Table 59*.

Table 59

Group mean scores in the »road-map test of direction sense« for probands > 15 years broken down by karyotypes: 1) 45,X; 2) other karyotypes; and 3) probands total

Probands > 15 years	n	Money's road-map test scores: Mean number of errors	SD
1) 45,X	10	3.90	4.77
2) other karyotypes	21	4.81	3.91
Probands total	31	4.52	4.15

The difference is not significant ($t = .54$; $p > .2$).

The direction discrimination scores of these 31 probands were then combined into one group mean score (4.52 errors; SD 4.15) and compared with the group mean score of the eighteen sisters (1.78 errors; SD 4.68). The difference was not significant ($p > .05$) (see *Table 56*).

When the group mean score of the sisters was compared with that of the growth-retarded girls (5.55 errors; SD 7.12) we found no significant difference ($p > .05$) as seen in *Table 60*.

Table 60

Group mean scores in the »road-map test of direction sense« for probands, sisters, and controls, older than 15 years

Groups	n	Money's road-map test scores: Mean number of errors	SD
Probands > 15 years	31	4.52	4.15
Sisters > 15 years	18	1.78	4.68
Controls > 15 years	11	5.55	7.12

The differences between probands and sisters ($t = 1.65$; $p > .05$) and between sisters and controls ($t = 1.73$; $p > .05$) are not significant.

Distribution of errors in the »road-map test of direction sense« was very similar for probands with karyotype 45,X and for those with other karyotypes,

as seen in *Figure 4.* When the distribution for probands was compared with those of the sisters and the growth-retarded girls *(Figure 5)* some differences could, however, be noted. While less than half of the probands obtained fewer than four errors in the direction discrimination test, approximately 65 per cent of the growth-retarded girls did so; some 90 per cent of the sisters obtained fewer than four errors. Ten per cent of the sisters had error scores higher than four, as also had about 35 per cent of the growth-retarded girls, as well as a little more than half of the probands. The differences, however, did not reach significance.

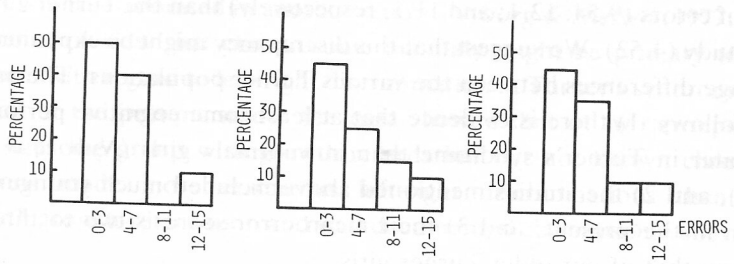

Fig. 4

Errors in the »road-map test of direction sense« for probands aged > 15 years: 1) karyotype 45,X; 2) other karyotypes and 3) probands total

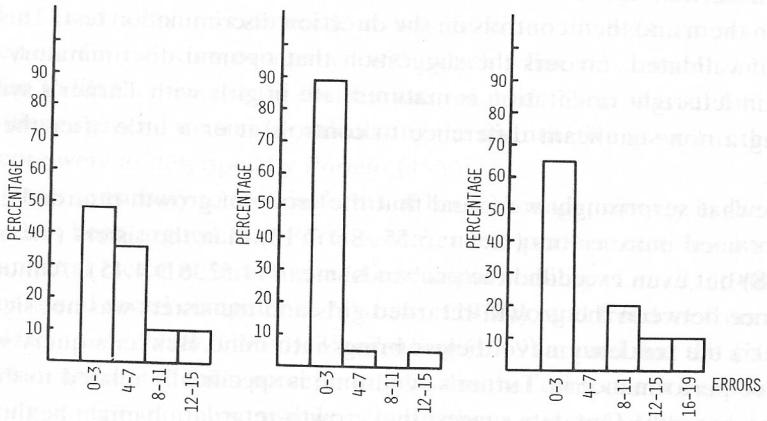

Fig. 5

Errors in the »road-map test of direction sense« for probands, sisters and controls aged > 15 years

The errors in the road-map test can be divided into four main types: 1) »go away and turn«; 2) »come back and turn«; 3) »left errors«; 4) »right errors«. Probands, sisters, and growth-retarded girls did not differ with regard to percentile distribution of types of errors, and all three groups made approximately twice as many errors of the »come back and turn« type as of any other type.

Alexander, Walker & Money (ibid.) studied thirteen Turner girls with the road-map test and found a mean group score of 9.54 (SD 5.21). *Bekker & van Gemund* (1968) tested eleven Turner girls, who scored 12.1 errors on an average. Later *Bekker* (1969) tested ten Turner girls who made an average score of 11.1.

It can be noted that in all these studies the Turner girls made a much higher number of errors (9.54; 12.1; and 11.1, respectively) than the Turner girls in the present study (4.52). We suggest that this discrepancy might be explained on the basis of age differences between the various Turner populations. The argument goes as follows: 1) there is evidence that at least some cognitive performances mature later in Turner's syndrome than in »normal« girls *(Nyborg & Nielsen* (1977,b)), and 2) the studies mentioned above included much younger Turner girls than in the present, and 3) their mean error score is two to three times higher than that of our older Turner girls.

Our suggestion of age-related differences in cognitive maturation rate between the Turner girls and their controls is also supported by the following data. *Bekker & van Gemund* (ibid.) and *Bekker* (ibid.) studied girls with a mean age of about 14 ranging from approximately 8 to 22; the mean age of the Turner girls in *Alexander, Walker & Money's* study was about 19.4 (range 13-26). In the present study we only analysed data for Turner girls older than fifteen years (with an upper limit of 38 years) and with mean age of 24.4 years. It is interesting to note that the older the Turner girls studied the less the discrepancy between them and their controls on the direction discrimination test. This observation if validated, favours the suggestion that optimal discriminatory performance in left-right orientation is matured late in girls with Turner's syndrome reaching a non-significant difference to controls at or a little after the age of twenty.

Somewhat surprisingly we found that the group of growth-retarded girls not only obtained more errors (mean: 5.55; SD 7.12) than the sisters (mean: 1.78; SD 4.68) but even exceeded the probands' mean (4.52; SD 4.15). Although the difference between the growth-retarded girls and the sisters was not significant ($p > .05$) the tendency nevertheless brings into mind Bekker's query whether cognitive performance in Turner's syndrome is specifically related to the chromosome anomaly. Our data suggest that growth-retardation might be thought of as a variable related to direction discriminatory performance. It might certainly also be taken into consideration whether some, not yet recognized but related, factors might be responsible for both growth-retardation and for left-right dis-

crimination performance. Clearly, the time has not come for a definite conclusion.

From the foregoing it was concluded that the considerable differences between Turner girls and controls observed in other studies with the road-map test and the lack of difference in the present study are not necessarily contradictory and can possibly be explained on the basis of differences in the rate of maturation of certain aspects of cognitive functioning among the groups: the older the Turner girls, the less the difference. A developmental view seems central for a deeper understanding of performance which hitherto has been taken to reflect a »cognitive deficit« in Turner's syndrome; it is apparently a realistic possibility that a »developmental delay«-terminology suffices. These thoughts will be elaborated in another report: *Nyborg & Nielsen* (1977,b).

The point of view that chromosome anomaly might be primary to growth-retardation with regard to left-right discrimination in Turner's syndrome was not supported in the present study: the data showed that of two groups of comparable ages the group with growth-retardation but not known chromosomal aberrations made more erroneous left-right discriminations than did the group with growth-retardation and well documented chromosome aberrations.

c. Porteus Mazes test performance in Turner's syndrome

The maze test was originally devised by *Porteus* (1918) in order to make more accurate diagnoses of feeble-mindedness. The test consists of a number of city-map like diagrams. The subject was told that the lines could be considered as solid stone walls, which were not to be crossed; she was to imagine that she was driving a car through the streets, from the entrance, through the maze, to the exit. If a blind alley was entered, it was forbitten to back or reverse the imagined car (in the form of a pencil with which a line was traced), and it was forbidden to lift the pencil until the exit was reached. There was no time limits. Other rules of procedure and for calculating the quantitative as well as the qualitative score were as descriped by *Porteus* (1967).

Besides its sensitivity to certain forms of brain damage, namely in the frontal lobes, it has been argued that Porteus Mazes test performance involves some temperamental factor of initiative and emotional stability *(Cattell,* (1948)), impulsiveness and social competence *(Porteus,* (1918)), and freedom from neuroticism *(Macfarlane Smith,* (1964)). *Vandenberg* (1969) argued that the mazes call for a certain amount of form perception, plus another component like »foresight or looking ahead of one's pencil«. Vandenberg concluded (based on twin studies) that the mazes test has a hereditary component, commom to other visuo-spatial tests. The argument that this visuo-spatial test performance may have genetic components has also been advocated by *Stafford* (1961), and *Garron*

Table 61
Group mean quantitative and qualitative scores in Porteus Mazes Test for probands [1) 45,X; 2) other karyotypes; and 3) probands total]

Probands	Quantitative test score		Qualitative test score	
	Mean	SD	Mean	SD
1) 45,X	35.52	17.45	92.48	22.51
2) Other karyotypes	50.79	34.81	98.29	13.14
Probands total	43.67	28.83	95.58	18.14

The differences are not significant
($t_{quant.} = 1.81$; $.1 > p > .5$) ($t_{qual.} = 1.07$; $p > .2$).

(1970), who proposed that visuo-spatial ability is carried on the X-chromosome.

Results and discussion

When the total Turner population was broken down by the previously mentioned age-groups, we found no significant differences between the sub-groups and accordingly we treated all Turner girls, sisters, and growth-retarded girls as complete groups, respectively, in the analyses of Porteus mazes performance.

As seen in *Table 61*, neither in the quantitative nor in the qualitative score did we find significant differences ($p > .2$) between probands with karyotype 45,X and probands with other karyotypes.

When girls with Turner's syndrome were compared with their sisters with regard to quantitative mazes test performance, we found no significant difference (means: 43.67; SD 28.83 versus 32.37; SD 24.78 ($.2 > p > .1$)); the group of growth-retarded girls obtained scores (mean: 30.20; SD 22.80) much like those of the sisters on the quantitative scale ($p > .2$) (see *Table 62*).

Regarding the interpretation of the quantitative mazes score *Porteus* (1967) remarks that low score signifies a special kind of intelligence – an intelligence which may be described as »common sense« ability to use prudence and foresight in dealing with concrete, visually present situations »... mazes are thus valuable in predicting how an individual will get along in everyday life.« (p. 40). As the probands in our study did not score significantly differently from their sisters on the Porteus quantitative score, we may according to such interpretation expect that girls with Turner's syndrome get along in everyday life as well as their sisters. This inference coincides with what we found from the school

Table 62
Group mean quantitative and qualitative scores in Porteus Mazes test for probands, sisters, and controls

Groups	Quantitative test scores		Qualitative test scores	
	Mean	SD	Mean	SD
Probands	43.67	28.83	95.58	18.14
Sisters	32.37	24.78	111.26	10.03
Controls	30.20	22.80	110.07	19.50

The differences in quantitative scores between probands and sisters ($t_{quant.} = 1.49$; $.2 > p > .1$) and between sisters and controls ($t_{quant.} = .26$; $p > .2$) are not significant.
The differences in qualitative scores between probands and sisters are significant ($t_{qual.} = 3.53$; $p < .001$) but the differences between sisters and controls are not ($t_{qual.} = .23$; $p > .2$).

reports of the Turner girls, from interviews with them, their parents, and sisters, and from all other available sources as reported in *Chapter 4* in this study: i.e. we found no remarkable differences between the probands and the sisters with regard to type of occupation, level of education or other everyday aspects. Regarding social competence, which the mazes according to Porteus measures, the results are also in accordance with what we found earlier, namely, that the Turner girls get along well with other people in spite of their often being teased at school, and in spite of their being to some extent discriminated in occupational choice due to low stature, and other problems characteristic of their situation. Parents and school authorities often report that their behavior is good, that they are very good and responsible at taking care of small children, they are diligent and conscientious and so on. The »objective« Porteus mazes test quantitative score thus confirms earlier observations made in the present study and similar clinical observations made by others.

While no difference could be observed between the sisters and the growth-retarded girls with regard to quantitative score in the mazes, we found, however, in the qualitative score, a significant difference between the sisters and the probands: the probands got a much lower error score (mean: 95.58; SD 18.14) than the sisters (mean: 111.26; SD 10.03) ($p < .001$).

The qualitative scoring consists of a system of weighed penalties which are recorded for a number of slips in the execution of the mazes. The principle upon which it is based is that each person has her own characteristic way of approaching and executing the run through the mazes. Poor subjects disclose signs of impulsiveness (such as starting into the blind alleys and then stopping the pencil

just in time), increased emotional tension (shown by wavy pencil-lines), and loss of self-control (seen in many line-crossings and corner-cuttings in the subject's tracing of the maze pathways). In these qualities of performance there was a possible measure of the emotional instability which was blocking the subject's intellectual ability in maze-solving (*Porteus* (1967)).

Money & Mittenthal (1970) noted on the basis of a study of 73 girls with Turner's syndrome that »inertia of emotional arousal« was a concomitant of the syndrome. Among other characteristics of this were equability, acceptance, resignedness, and slowness in asserting initiative. Apparently, all these terms might more or less express degree of emotional stability and accordingly be measured in the mazes test. And in fact, as expected, the Turner girls scored remarkably differently from their sisters on the emotional stability indicator ($p < .001$), signifying, according to the interpretation of Porteus, that their behavior in the test situation was much more conscious, less impulsive, without undue emotional tension and with a remarkable degree of self-control. The result is also in accordance with the experimenter's subjective impression of the Turner girls, having tested all 45 persons: although not measured exactly practically all the Turner girls sat quietly, listening carefully to the test instructions, eager to conform to the expectations of the experimenter, apparently not becoming frustrated when they could not solve the problems they were required to face – as often happened. In this respect their behavior in general contrasted with that of some of their sisters!

Thus, the present psychiatric-psychological investigation, as well as a number of other studies, has shown that Turner girls usually appear emotionally remarkably stable; this coincided with the results of psychological testing from the Porteus mazes test.

The growth-retarded girls (mean: 110.07; SD 19.50) did not differ from the group of sisters on the qualitative score ($p > .2$).

d. Human figures drawing performance ad modum Goodenough-Harris in Turner's syndrome

The human figures rated according to Witkin's non-projective technique in Chapter 10 were also scored ad modum Goodenough-Harris who prescribes a projective interpretation (*Harris* (1963)). As the upper range of Harris' normative data is limited to 15 years all drawers older than that were scored as 15 years. The ratings were performed blindly by two independent judges as when scoring the drawings ad modum Witkin. Discordant ratings were pooled and the judges talked to agreement. In a few cases the ratings differed by more than four points mainly due to disagreement on how to rate modern Danish clothing in accordance with the somewhat old-fashioned style expressed in the manual.

Results and discussion

As we found neither significant differences between the previously mentioned age-groups ≤ 15 vs. > 15 years ($p > .2$), nor between the five age-groups ($p > .1$), we proceeded with the analyses without breaking down any group by age.

Table 63
Group mean scores of Goodenough-Harris Human-Figure-Drawing test for probands [1) 45,X; 2) other karyotypes; and 3) probands total]

Probands	Mean perceptile Goodenough-Harris drawing score	
	Mean	SD
1) 45,X	26.0	31.04
2) Other karyotypes	30.83	31.42
Probands total	28.58	30.98

The differences are not significant ($t = .52$; $p > .2$)

From *Table 63* can be seen that the probands with karyotype 45,X did not differ from probands with other karyotypes (mean percentile: 26.0; SD 31.04 versus 30.83; SD 31.42, respectively; $p > .2$). The united group of probands got, however, a lower mean percentile score (28.58; SD 30.98) than the group of sisters (54.0; SD 27.23) and the difference was significant ($.01 > p > .001$) (see *Table 64*). The difference between sisters and controls (46.47; SD 33.41) was not significant ($p > .2$).

The pattern in the data was very much like that of the data obtained by scoring the drawings according to Witkin.

The overall correlation for all subjects in the present study ($n = 79$) between the drawings scored ad modum Witkin and ad modum Goodenough-Harris amounted to $r. = -.77$ ($p < .001$) signifying an association between the two tests as firmly as could be expected from other reports in the literature (e.g., *Witkin et al.* (1962)). Probands with karyotype 45,X do not draw human figures that are much poorer than are those drawn by probands with other karyotypes, except for the slight difference possibly explainable by age differences previously mentioned.

While the drawings of the probands were significantly lower than those of the sisters, the growth-retarded girls could be placed between these two groups but were not significantly different from the sisters.

Table 64

Group mean scores of Goodenough-Harris Human-Figure-Drawing test for probands, sisters, and controls

Groups	Mean perceptile Goodenough-Harris drawing score	
	Mean	SD
Probands	28.58	30.98
Sisters	54.0	27.23
Controls	46.47	33.41

The differences between probands and sisters are significant ($t = 3.10$; $.01 > p > .001$).
The differences between sisters and controls are not significant ($t = .72$; $p > .2$).

Table 65

Percentile distribution of the Goodenough-Harris Human-Figure-Drawing test for probands [1) 45,X; 2) other karyotypes; and 3) probands total]

Percentile	Probands					
	45,X		Other karyotypes		Probands total	
	n	%	n	%	n	%
1-24	15	71	13	54	28	62
25-49	3	14	5	21	8	18
50-74	1	5	1	4	2	4
75-99	2	10	5	21	7	16
Total	21	100	24	100	45	100

The differences are not significant (Fisher's exact test for 2×2 tables used with distributions divided into two parts around the 50 percentile; $P_{\text{one-tailed}} > .2$).

The percentile distribution of Turner girls with karyotype 45,X and probands with other karyotypes did not differ as seen in *Table 61*. Neither the difference between the sisters and the growth-retarded girls according to *Table 66*, nor the difference between probands and sisters reached significance as tested by a χ^2-test, stressing that the before mentioned differences between group means

Table 66
Percentile distribution of the Goodenough-Harris Human-Figure-Drawing test for probands, sisters, and controls

Percentile	Probands		Sisters		Controls	
	n	%	n	%	n	%
1-24	28	62	4	21	6	40
25-49	8	18	6	32	3	20
50-74	2	4	5	26	3	20
75-99	7	16	4	21	3	20
Total	45	100	19	100	15	100

The differences between probands and sisters are not significant ($\chi^2 = 4.14$; $p > .2$).
The differences between sisters and controls are not significant ($\chi^2 = .82$; $p > .2$).

are not so very convincing. (Fisher's exact test for 2x2 tables showed, however, significance when the distributions were divided into two parts around the 50 percentile; $p \sim .04$ between probands and sisters, but not between sisters and controls; $p \sim .69$).

We concluded that there seems to be a tendency for probands and growth-retarded girls to draw slightly poorer human figures than the group of sisters.

This result is in fair accordance with that of other studies. Thus, *Cohen* (1962) found, based partly on subjective impressions, that the drawings of Turner girls seem more immature, lacking femininity, with few trends to express movements of arms, legs or body, and a marked tendency to omit hands and fingers. The omission of hands and fingers in the present study was, however, nearly equal for the Turner group (28 %) and the group of sisters (24 %), but was somewhat higher for the growth-retarded girls (60 %).

Lynch et al. (1966) studied two Turner girls who both drew poor and immature figures. *Ehrhardt et al.* (1970) asked fifteen Turner girls to draw human figures using the sex of the first drawing to indicate gender identification as other authors have done, and found that all their subjects first drew a female figure; the percentage of female first drawings in their Turner group was slightly higher than in large normal samples indicating - according to the authors - definite feminine gender identity. *Christodorescu et al.* (1970) tested three Turner girls; two of them performed the Draw-a-Person test very poorly,

drawing figures far below the expected age-standard. *Senzer et al.* (1973) investigated 6 girls with Turner's syndrome two of whom refused to take the human figures drawing test; two drew low-quality figures, and the remaining two performed at least on an average level.

Based on his studies with Turner girls, *Money* (1970) discussed whether the often grossly distorted and defective drawings could be ascribed to distortion of the body image. This possibility was discounted with reference to the fact that girls with Turner's syndrome also have difficulties with geometric figures. Money therefore suggested that the human-figure distortion is correctly attributed to what he calls »space-form disorientation«.

Alexander et al. (1966) and *Bekker & van Gemund* (1968) observed percentile distributions in the Goodenough-Harris ratings much like the present. The observed distribution for the Turner girls did not, however, amount to significant difference from the distribution of their sisters in our study, while in the other studies the score of the Turner girls was significantly different from the controls.

e. Discussion of cognitive performance in girls with Turner's syndrome

We might here call attention to our observation that the considerable differences in some cognitive scores between our very young Turner girls and their age-matched controls seem to diminish progressively the older the compared persons were. This might possibly give hope for a very slow cognitional maturation rate in girls with Turner's syndrome rather than a definite and insuperable cognitive defect.

If confirmed, it does not seem unreasonable to regard a late mature cognitive functioning in certain areas to be responsible for the considerable number of girls with Turner's syndrome who meet troubles at school in arithmetic and in the »new maths« where spatial representations are widely applied. A comparison of Turner girls with difficulties in arithmetic and certain cognitive scores will be presented in the next chapter. It does, however, seem to have very little, if any effect on general intellectual capacity at school and as far as occupation is concerned, in as much as the probands with Turner's syndrome in the present study reached the same educational and occupational level as their sisters and managed as well at school as their sisters in most subjects.

The present study demonstrates that it is usually possible to overcome the handicap with arithmetic and the »new maths« and reach the expected level. If a delayed maturational rate is a fact in Turner's syndrome, one might also find it reasonable in cases where such girls meet serious troubles in non-verbal school disciplines to delay the introduction of such subjects into the curriculum as long as possible. At all times, teachers should be alert to the possibility that girls with Turner's syndrome may need better teaching and more help in subjects like arithmetic than other pupils.

Chapter 14

COMPARISON OF SOMATIC AND PSYCHIATRIC DATA WITH COGNITIVE PERFORMANCE TEST SCORES

a. Introduction

This chapter comprises a number of analyses of cognitive performance test scores reported on in chapter 10, and 11 broken down by selected somatic and psychiatric variables presented in earlier chapters.

Preliminary analyses of the total material showed that the age distribution in a number of cases was rather skew with many very young probands in one or more of the categories of analyses. As this may have special implications in studies of girls with Turner's syndrome, as mentioned earlier, we eliminated as far as possible this age factor by excluding all 14 girls with Turner's syndrome below the age of 15 from the analysis.

Thus cognitive performance scores in: 1) the RFT (i.e. USD group mean error scores); 2) the EFT (i.e. group mean number of seconds per figure); 3) the HFDT (i.e. group mean ratings for »articulation-of-body-concept« scale ad modum Witkin); and in 4) the Money's »Road-map test of direction sense« (i.e. group mean numbers of errors) were broken down by the following variables: a) presence of Y-chromosome material; b) birth weight; c) birth length; d) pterygium colli; e) cubitus valgus; f) level of behavioral activity; g) cyclic hormone treatment; h) overprotective behavior of the mothers of the probands; i) special difficulties in certain school subjects; j) skeletal retardation; k) 8/12 years mean growth-retardation; and finally l) retarded stature at time of testing.

b. Y-chromosome material and cognitive performance in Turner's syndrome

Group mean scores for the 4 probands with Y-chromosome material in part of their cells (numbers 2, 9, 19, and 35) were compared with scores for 27 probands without Y-chromosome material but we found no significant difference.

c. Birth weight and cognitive performance in Turner's syndrome

Information of weight at birth was forthcoming for 30 probands older than fifteen years at the time of testing. Turner babies weighing less than 3000

grammes were compared with those weighing more. There was a tendency for the heavier babies to score more errors, but the tendency was not significant.

d. Birth length and cognitive performance in Turner's syndrome

Fourteen of the 22 girls had a body length at birth below 50 cm and 8 were 50 cm or longer. The longer babies got higher error scores and in two tests the differences were significant (mean USD 12.84 (SD 9.37) vs. 6.15 (SD 3.70), p = .03; and EFT mean score 130.51 (SD 34.83) vs. 84.85 (SD 42.33) p = .02) as seen in *Table 67*. The differences cannot be explained on the basis of skew distribution of young Turner girls because the mean age was greater in group 2 with the highest error score (25^0; SD 3^3 vs. 23^9; SD 6^{11}, respectively).

Table 67

Comparison of cognitive performance in probands older than fifteen years with body length at birth less than 49 cm or greater than 50 cm on three tests of field dependence and one test of direction sense

Body length	Probands					USD		EFT		HFDT		Road-map	
		Birth length		Age									
at birth	n	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
1. < 49 cm	14	47.93	1.07	23^9	6^{11}	6.15	3.70	84.85	42.33	3.36	1.50	4.07	3.50
2. ≥ 50 cm	8	51.63	1.06	25^0	3^3	12.84	9.37	130.51	34.83	4.25	0.71	6.00	5.16
Total and means	22	49.27	2.10	24^2	5^9	8.59	6.97	101.45	44.94	3.68	1.32	4.77	4.16
Test of significance						F = 5.76 p = .03		F = 6.68 p = .02		F = 2.48 p = .13		F = 1.10 p > .2	

e. Pterygium colli and cognitive performance in Turner's syndrome

We found no association between pterygium colli and cognitive performance. While some error scores were high in the group of probands with pterygium colli others were lower and none of the differences were significant.

f. Cubitus valgus and cognitive performance in Turner's syndrome

In three out of four tests probands with cubitus valgus made more errors than those without. Only in the EFT, however, did the difference approach statistical significance (111.89; SD 44.42 vs. 89.13; SD 44.98, respectively; p = .18) and in the RFT the tendency was reversed.

g. Level of behavioral activity in childhood and cognitive performance in Turner's syndrome

In chapter 4 we reported a tendency, in respect of behavior, for probands to be less active than the sisters and the controls. The level of activity was determined on the basis of self-reports of the proband and of information given by her mother and sisters as well as of information given by the school. The information from several sources was compared for coincidence and evaluated in relation to her sibling. As seen in *Table 17 (chapter 4)*, we found four probands with high level of activity, 24 with »normal« level of activity and 17 with low activity.

In the actual analysis we excluded the four probands with high level of activity because their number was too small and selected probands older than fifteen years at the time of testing from the two other groups. This procedure gave 16 probands with normal level of activity (mean age 25^5; SD 6^7) and 14 low activity probands (mean age 23^6; SD 3^{10}). As seen in *Table 68*, the Turner girls in the low ativity group consistently scored more errors than the probands with »normal« level of activity, and in one case the difference was highly significant. Although the mean age in the low activity group is lower than that of the »normal« activity group, this age difference cannot explain the differences, as an analysis has shown that Turner girls in general can be placed on a non-tilted regression line with regard to developmental changes in cognitive performance in the time span indicated by the two mean ages *(Nyborg & Nielsen* (1976,b)).

Table 68

Comparison of cognitive performance in probands older than fifteen years with »normal« or »low« level of behavioral activity (as compared with their sisters) on three tests of field dependence and one test of direction sense

Level of activity	Probands			USD		EFT		HFDT		Road-map	
	n	Age	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
2. »Normal«	16	25^5	6^7	7.52	6.87	79.05	34.54	3.31	1.49	3.06	3.53
3. Low	14	23^6	3^{10}	12.89	8.13	136.56	29.93	4.0	1.04	6.50	4.11
Total and means	30	24^6	5^6	10.02	7.84	105.89	43.25	3.63	1.33	4.67	4.13
Test of significance				F = 3.84 p = .05		F = 23.40 p < .0001		F = 2.08 p = .16		F = 6.08 .02>p>.01	

h. Cyclic hormone treatment and cognitive performance in Turner's syndrome

When we compared the cognitive performance of 24 probands, who received

cyclic hormone treatment, to those who did not, we found no differences as seen in *Table 69*. If the mean age of the non-treated probands (19^{8}; SD 5^{0}) is compared with that of the treated probands (25^{8}; SD 5^{1}), one might, however, suspect that the number of errors in the non-treated group actually might be lower if corrected for age.

Table 69

Comparison of cognitive performance in probands older than fifteen years that received or did not receive cyclic oestrogen hormone treatment on three tests of field dependence and one test of direction sense

Hormone treatment		Probands				USD		EFT		HFDT		Road-map	
		Duration		Age									
	n	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
1. Cyclic Hormone treatment	24	6.04	4.37	25^{8}	5^{1}	9.95	8.00	105.31	43.50	3.54	1.35	4.38	4.41
2. No Hormone treatment	7	0	0	19^{8}	5^{0}	9.57	7.46	110.25	42.51	3.71	1.38	5.43	2.70
Total	31					9.86	7.76	106.42	42.62	3.58	1.34	4.61	4.07
Test of significance						$F = .01$ $p > .2$		$F = .07$ $p > .2$		$F = .9$ $p > .2$		$F = .01$ $p > .2$	

This impression is supported by the observation that we found differences when we compared cognitive performance for probands who had received cyclic oestrogen treatment for less than four years (mean: 1^{2}, SD 0^{11}) with those who had received treatment for a longer period (mean: 8^{1}; SD 3^{6}).

Table 70

Comparison of cognitive performance in probands older than fifteen years that received cyclic oestrogen hormone treatment for less than four years or more than four years, on three tests of field dependence and one test of direction sense

Duration of cyclic hormone treatment		Probands				USD		EFT		HFDT		Road-map	
		Duration		Age									
	n	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
1. 0^{1} - 3^{11} years	7	1^{2}	0^{11}	24^{7}	5^{6}	7.20	7.14	60.81	26.47	2.57	1.72	2.00	1.63
2. 4+ years	17	8^{1}	3^{6}	26^{1}	5^{1}	11.08	8.25	123.63	35.14	3.94	0.97	5.35	4.85
Totals and means	24	6.04	4.37	25^{8}	5^{1}	9.95	8.00	105.31	43.50	3.54	1.35	4.38	4.41
Test of significance						$F = 1.19$ $p > .2$		$F = 18.12$ $p < .01$		$F = 6.29$ $p < .05$		$F = 3.15$ $p > .2$	

For probands that had received the relatively long-term treatment it was observed that they on all four tests obtained a higher error score than probands so treated for less than four years. In two tests the differences were significant, as seen in *Table 70*. The differences could not be attributed to developmental differences as the mean age was higher in the group with the greater mean error score (26^{1}; SD 5^{1} vs. 24^{7}; SD 5^{6}, respectively).

i. Overprotective behavior of the mothers and cognitive performance in Turner's syndrome

Of the probands older than fifteen years, eight could (according to the procedure also applied in the estimation of level of behavioral activity mentioned in section g. in this chapter) be classified as overprotected in childhood by their mothers. The childhood conditions of 23 were estimated as not overprotective. As we were interested in the possible effects of overprotection we compared the cognitive performance of the two groups. From *Table 71* can be seen that the overprotected girls consistently got higher error scores than the girls not overprotected; the differences were, however, small. It is not very likely that the differences would be much greater if we were able to compensate for the mean age difference between the groups in as much as cognitive development in Turner's syndrome does not seem much further matured in the mean age span considered.

Table 71

Comparison of cognitive performance in probands older than fifteen years that were overprotected or not overprotected in their childhood by their mothers on three tests of field dependence and one test of direction sense

Level of protection	Probands			USD		EFT		HFDT		Road-map	
	n	Age	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
1. Overprotected	8	26^{11}	4^{7}	11.52	9.36	124.91	40.78	3.88	1.25	5.88	4.55
2. Not overprotected	23	23^{4}	5^{9}	9.28	7.28	95.49	45.13	3.48	1.38	4.04	3.99
Total and means	31	24^{3}	5^{7}	9.86	7.76	103.08	45.31	3.58	1.34	4.52	4.15
Test of significance				$F = .49$ $p > .2$		$F = 2.64$ $p = .12$		$t = .63$ $p > .2$		$F = 1.17$ $p > .2$	

k. Special difficulties in certain school subjects and cognitive performance in Turner's syndrome

Eighteen probands had special difficulties in arithmetic and mathematics while ten had not difficulties in these school subjects. For probands that met troubles in these subjects we found as seen in *Table 72* that they made more errors in all cognitive tests except HFDT; the differences were, however, not significant.

Table 72

Comparison of cognitive performance in probands older than fifteen years with or without special difficulties in arithmetic and mathematics on three tests of field dependence and one test of direction sense

Difficulties in arithmetic and mathematics	Probands			USD		EFT		HFDT		Road-map	
		Age									
	n	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
1. Special difficulties	18	25[3]	6[1]	10.67	8.17	107.63	49.09	3.39	1.50	4.94	4.62
2. No difficulties	10	24[2]	4[7]	8.28	6.02	101.43	39.12	3.80	1.14	3.30	3.37
Total and means	28	24[10]	5[6]	9.82	7.45	105.41	45.13	3.54	1.37	4.36	4.23
Test of significance				F = .66 p > .2		F = .12 p > .2		F = .57 p > .2		F = .97 p > .2	

l. Growth-retardation and cognitive performance in Turner's syndrome

The last three variables to be considered here all have that in common that they are concerned with growth-retardation but measured in three different ways. The first is an estimation of skeletal maturation; the second is based on measured body height of the probands when they were eight years old and again when they were twelve; the third variable was simply calculated on the basis of the body height of probands aged 20+ years at the time of testing. It should be mentioned that the three variables are not necessarily equivalent measures of stunted growth.

Skeletal maturation: Ten of the seventeen probands aged more than fifteen years that were studied showed no skeletal retardation (group 1) as estimated by a comparison of roentgenological representation of the probands' right hand and arm with *Greulich & Pyle's standards* (1959). Seven probands had a mean skeletal retardation of six years ten months (SD 2[6]; group 2), as seen from *Table 73.*

We found that the probands with no skeletal retardation consistently made

more errors in the tests while only in the HFDT did the difference approach significance. If it were possible to correct for the considerable mean age difference between the groups (group 1 = 25^{2}; SD 5^{6} and group 2 = 21^{0}; SD 3^{4}) the error scores of group 1 might be elevated while that of group 2 might be lowered.

Table 73

Comparison of cognitive performance in probands older than fifteen years with or without developmental skeletal retardation on three tests of field dependence and one test of direction sense

Skeletal retardation in years and months (*)	Probands					USD		EFT		HFDT		Road-map	
		Retardation		Age									
	n	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
1. 00^{00}	10	0^{0}	0^{0}	25^{2}	5^{6}	9.51	5.84	106.38	45.09	3.90	0.88	4.30	5.23
2. 00^{01} - 10^{05}	7	6^{10}	2^{6}	21^{0}	3^{4}	8.79	8.19	99.93	32.31	3.00	1.63	4.29	3.30
Total and means	17	2^{10}	3^{10}	23^{6}	5^{1}	9.21	6.67	103.72	39.31	3.53	1.28	4.29	4.41
Test of significance						F = .05 p > .2		F = .11 p > .2		F = 2.19 p = .16		F = .0 p > .2	

(*) Calculated as difference between probands' actual skeletal maturation and standards of Greulich & Pyle (1959).

8/12 years' mean growth-retardation: Information of body height at eight years of age and again at twelve years of age was forthcoming for 21 probands aged more than fifteen years at the time of the cognitive testing. A mean of the probands' eight and twelve years measures of body height in centimetres was compared with the hypothetically graphically interpolated mean body height of the same age groups from a recently published Danish normative study of normal girls *(Andersen et al.* (1974)). The negative differences between the values of the probands and the values of the normal girls (i.e. 138 cm) were designated the »8/12 years growth retardation in cm«.

The values of such growth-retardation estimations in Turner's syndrome were divided into two categories: I) differences from the normal population ≤ 15 cm (group 1, n = 11; mean: 11.73; SD 2.97); II) differences from the normal population > 15 cm (group 2; n = 10; mean: 19.60; SD 3.53). The two groups were then compared for possible cognitive differences. The mean ages in the two groups were much alike (22^{5}; SD 5^{8} vs. 21^{6}; SD 3^{5}, respectively).

Table 74

Comparison of cognitive performance in probands older than fifteen years with 8/12 years mean growth-retardation (see text for explanation) ≤ 15 cm or > 15 cm on three tests of field dependence and one test of direction sense

Comparison with »normal« population	Probands					USD		EFT		HFDT		Road-map	
	Retardation			Age									
	n	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
1. Difference from the normal population mean ≤ 15	11	11.73	2.97	22^{5}	5^{8}	7.25	5.01	91.19	31.97	3.82	1.17	3.45	3.56
2. Difference from the normal population mean > 15	10	19.60	3.53	21^{6}	3^{5}	8.80	8.49	87.02	55.43	3.0	1.56	3.40	2.72
Total and means	21	15.48	5.12	22^{0}	4^{8}	7.79	6.76	89.20	43.57	3.43	1.40	3.43	3.11
Test of significance						F = .27 p > .2		F = .05 p > .2		F = 1.87 p = .19		F = .0 p > .2	

As seen in *Table 74* the differences in cognitive performances between the groups were small. But in three out of four tests we found that the probands with the smallest growth-retardation made most errors.

Retarded statures at time of testing: As the last measure of growth-retardation in Turner's syndrome we noted the body height of all Turner girls aged 20+ years at the time of the cognitive examination. The probands were divided into two groups on the basis of being 1) < 150 cm (group 1; n = 12; mean height: 140.75; SD 3.12), and 2) 150+ cm (group 2; n = 11; mean height: 152.10; SD 2.66). The mean ages of the two groups were nearly equal. As seen from *Table 75* the differences between the groups were non-significant.

m. Discussion of the comparisons

As mentioned in Chapter four we found seventeen probands with low level of activity; fourteen of these were older than fifteen years. The relatively pronounced degree of low level activity in Turner's syndrome has also been reported by others. Among these *Shaffer* (1963). *Ehrhardt, Greenberg & Money* (1970) stressed that girls with Turner's syndrome scored low on athletic interests, rough outdoor games and aggressive fighting behavior.

According to *Witkin et al.* (1962) a relation between level of activity and »field dependence« (i.e. between activity and RFT, EFT, and HFDT scores in the present study) could be expected. Although these authors admit that a clear-cut

Table 75

Comparison of cognitive performance in probands older than twenty years with different body heights at time of testing on three tests of field dependence and one test of direction sense

Body height at time of testing	Probands					USD		EFT		HFDT		Road-map	
		Height		Age									
	n	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
1. < 150 cm	12	140.75	3.12	26^{3}	4^{5}	8.99	8.34	118.85	40.86	3.67	0.87	5.50	5.74
2. 150+	11	152.10	2.66	26^{9}	5^{0}	10.99	8.57	102.80	34.16	3.73	1.35	3.45	2.77
Total and means	23	146.17	7.09	26^{6}	4^{8}	9.95	8.13	111.17	37.59	3.70	1.18	4.52	4.49
Test of significance						F = .33 p > .2		F = 1.06 p > .2		F = .02 p > .2		F = .06 p > .2	

definition of the term »activity« is not at hand they were mainly interested in the facet of activity that can be characterized by assertiveness, striving and interest in being active, or, an »active attitude«, which they believe was related to field dependence, rather than simply motorically expressed energy expenditure (p. 187).

In the present study we found in fact a relation between the level of behavioral activity and cognitive performance in Turner's syndrome; in all four tests the Turner girls with low activity made more errors: in one case the relation was highly significant. It is not clear, however, whether field dependent persons in general behave in a less active way, or whether less active persons bcome field dependent, or whether a third factor is responsible for both low level of activity and field dependent performance. Therefore, it is at present not advisable unequivocally to mention low behavioral activity of the Turner girls during childhood as *the* aetiological factor of field dependence or vice versa.

Whether the probands received cyclic hormone treatment or not, did not apparently affect the cognitive performance of our Turner girls. The age difference between the two groups compared was too great, however, to allow for a definite decision in this matter. According to our developmental study of cognitive performance in Turner's syndrome mentioned earlier, a correction for age between the groups would most probably lower the error scores for the probands not treated, thus giving relatively higher error scores for the treated group. The observation that probands, who had been given cyclic treatment for a period of an average of eight years with oestrogen, consistently made more errors than those who had been so treated for at little more than one year on an average, suggests a relation between a cyclic oestrogen treatment and cognitive performance. More specificly: the two field dependence indicators, the EFT and

the HFDT, seem especially sensible to the effect of long term cyclic oestrogen treatment. This could tentatively be taken as an indication of a sex hormone as accessary to field dependence. In *Chapter 5* it is mentioned that long-term oestrogen treatment may increase the risk of uterus cancer in women with Turner's syndrome. If long-term oestrogen treatment further interfere with cognitive performance as indicated in the present study, it should most probably only be given for a few years until satisfactory development of secondary sexual characteristics has taken place as discussed in *Chapter 5*. It will, on the other hand, be remembered that: the groups studied are small and of unequal size. A more thorough investigation of this problem is needed.

Turner girls are often in the literature reported to be overprotected by their mothers (e.g., *Sabbath, Morris, Menzer, Benaron & Sturgis,* 1961; *Bekker,* 1969; *Money & Mittenthal,* 1970). In the present study we found eight probands older than fifteen years that according to our classification deserved the characterization »overprotected«.

According to *Witkin et al.* (1962) overprotective mothers may tend to have field dependent children. In the present study we found no significant differences between the field dependent performance in the two groups although the error scores were consistently higher for the overprotected group. The differences shown in *Table 71* might actually be somewhat greater if we corrected for age. Nevertheless it would be hazardous to claim on the basis of our present knowledge that overprotective mothers »educate« their children to behave in a field dependent way or that overprotective mothers give birth to field dependent children. We can and should certainly advise mothers of Turner girls not to overprotect their daughters, but degree of overprotection does not in the present study seem to affect the cognitive performance.

Of the probands older than 15 years we found 18 to have special difficulties with arithmetic and mathematics. Such difficulties may possibly be due, at least in part, to some special impairment in Turner's syndrome. The new mathematics according to modern methods is to a considerable extent illustrated by diagrams and geometric pictures, hence most elementary arithmetic must also be conceived of in spatial representations. As the cognitive tests applied in the comparisons comprise spatial elements we expected some relation between the groups with difficulties in arithmetic and the cognitive scores that would not show up in the other group. Although in most cases the group with special difficulties also made more errors, the differences were small. The cognitive tests applied had thus no diagnostic value for difficulties in these school subjects for the Turner girls studied.

None of the comparisons between the three measures of growth-retardation and cognitive performance gave substance to the idea that the more stunted growth the more impaired cognitive performance could be observed. Quite the contrary, we found in a number of tests that Turner girls with the most exag-

gerated growth-retardation made relatively few errors while the less growth-retarded made more.

This result can be seen in the light of a remark by *Money & Pollitt* (1966) that the degree of psychomaturation in general tended to parallel age and *not* size in 17 dwarfs. It can on the other hand not be analogized to *Bekker's* (1969) suggestion that the cognitive »defect« commonly ascribed to girls with Turner's syndrome may be considered as a deviation related to growth-retardation.

The observation that the less growth-retarded girls on a number of tests made more errors than the more growth-retarded can possibly be paralleled by the observation that the Turner girls, heavier and longer at birth, late in life tended to make more errors. If confirmed, such observation speaks directly against the idea that growth-retardation automatically entails retarded cognitive performance. This problem should be subjected to a more thorough investigation.

From the comparisons we might say in conclusion that the only parameters which appeared to have importance for cognitive performance in girls with Turner's syndrome in the present study were birth length (and to some extent birth weight), level of behavioral activity in childhood, and duration of cyclic oestrogen treatment. Cubitus valgus, overprotection and special difficulties in arithmetic may possibly be of some importance while the presence of Y-chromosome material and pterygium colli according to our results do not seem to have any relation to cognitive performance in Turner's syndrome.

Chapter 15

NEUROTICISM AND INTROVERSION IN TURNER'S SYNDROME

a. Introduction

In *Chapter 11* it was mentioned that Porteus Mazes test is assumed to involve factors of emotional stability, impulsiveness and freedom from Neuroticism, observable in the qualitative score. We found that the girls with Turner's syndrome scored remarkably different from their sisters on the qualitative scale: they scored considerably more emotionally stable. This result is in accordance with the clinical observations of most other investigations as well as with our own. Thus Turner girls often exhibit a phlegmatic, compliant, equable and accepting manner, with high tolerance for adversity. *Money & Mittenthal* (1970) stressed the stolidity, the resignedness and the slowness in asserting initiative of girls with Turner's syndrome.

It is interesting to note how well such characterization fits with a description of one end of a personality dimension – Neuroticism-Stability – proposed by *Eysenck* (1962). The description of the extreme stability end of this dimension is considered appropriate for a person exhibiting extraordinarily stable emotions, she is not easily aroused, is calm and even tempered, she exhibits a high degree of tolerance for stress. Such description seems relevant for a general account of girls with Turner's syndrome. The other end of this dimension: Neuroticism – can, according to *Eysenck*, be considered as opposed to Stability; it refers to the general emotional instability of a person with labile, strong and easily aroused emotions. An emotionally instabile person is said to be moody, touchy, anxious and restless. None of these terms seems relevant for girls with Turner's syndrome.

We therefore hypothesized that girls with Turner's syndrome would score low on the Neuroticism-Stability scale (i.e. low N-score) of Maudsley Personality Inventory (MPI) developed by *Eysenck* (1962). Such expectation was furthermore supported by *Eysenck's* statement that »... better adjustment is associated with low Neuroticism score ...« (*Eysenck*, (1962)); Turner girls are usually remarkably well adjusted despite their low stature and other handicaps.

Eysenck also states that besides low N-score better adjustment is associated with middle to above average Extraversion scores (E-score). Accordingly we might expect Turner girls to score middle to above average on the Extraversion-Introversion scale (a scale assumed to be orthogonal to the Neuroticism-Stability scale). A person with high E-score has, however, according to *Eysenck*,

many friends, craves excitement, is generally an impulsive person and generally likes change, is carefree and easygoing. This description seems far from perfect for Turner girls. The typical introvert is on the other hand quiet, introspective, reserved and distant, except to intimate friends, not impulsive etc.; such a description seems more readily applicable to girls with Turner's syndrome although it is still not perfect. Thus the remarkable adjustment of Turner girls speaks, according to *Eysenck*, for average or above average E-score while the description of the extravert person seems unfit for Turner girls. We therefore made no hypothesis concerning the possible score of Turner girls on the Extraversion-Introversion scale.

b. Methods

In order to test our hypothesis we examined 31 probands, 16 of their sisters and 9 growth-retarded girls with normal karyotype and primary amenorrhoea with the MPI which was applied individually. This test, *Eysenck* (1962) claims, isolates the two pervasive and relatively independent dimensions of personality in question: 1) Neuroticism-Stability (N), and 2) Extraversion-Introversion (E). N and E is measured by means of a scale with 24 questions, each with a maximum of zero. High N-score indicates Neuroticism, high E-score Extraversion.

c. Results and discussion

In the following will be given only a short account of some main results with the MPI; a more detailed account will be presented later *(Bækgaard, Nyborg & Nielsen*, (1977)). As seen in *Table 76* the differences in group mean score of the probands, sisters and controls with regard to the E-score were 26.84 (SD 9.08), 26.63 (SD 7.15) and 31.22 (SD 9.11), respectively; the differences between probands and sisters and between sisters and controls were insignificant.

The score for Neuroticism (N-score) on the other hand gave significant differences between probands and sisters (mean: 16.87 (SD 9.26), versus 23.87 (SD 10.94); $F = 5.34$, $P_{\text{one-tailed}} = .01$). The difference between sisters and controls was not significant.

In the scatterplot in *Fig. 6* the mean N-scores of the probands, sisters and controls were related to an American and an English normative material. We furthermore plotted in the data of 19 Danish nurses in an attempt to »anchor« our test results with the MPI which is not standardized in Denmark; these data can, of course, not be considered as representative. From *Fig. 6* will be seen that the N-scores of this group nevertheless come quite near to the scores from the representative American and English studies, as well as did the N-scores of our control group of growth-retarded girls with primary amenorrhoea and

Table 76
Group mean Extraversion score (E) and Neuroticism score (N) as measured by the Maudsley Personality Inventory (MPI) for probands, sisters, and controls

Groups	n	E-score		N-score	
		Mean	S.D.	Mean	S.D.
1. Probands	31	26.84	9.08	16.87	9.26
2. Sisters	16	26.63	7.15	23.87	10.94
3. Controls	9	31.22	9.11	21.56	7.25

The differences in E-score between probands and sisters and between sisters and controls are not significant on a two-tailed F-test.
The difference in N-score between probands and sisters is significant ($F = 5.34$; $P_{\text{one-tailed}} = .01$) while the difference between sisters and controls is not significant.

normal karyotype. The sisters were found somewhat higher on the N-scale, but not significantly different from the controls while the probands scored lower than all other groups, and significantly so ($p = .01$).

From these results we concluded that the sisters of the probands as well as our controls scored not significantly different from what was to be expected by chance, as measured by the N-score in the MPI, although the sisters tended to do so. In comparison, girls with Turner's syndrome appeared remarkably emotionally stable as they obtained a low N-score. This observation confirmed our hypothesis. It also complies with subjective clinical impressions of Turner girls as well as with our results with the Porteus Mazes.

d. Comparison of somatic and psychiatric data with N- and E-scores

In order to observe any relationship between the somatic and psychiatric data of the probands on one hand and Neuroticism and Extraversion on the other, we broke down the N- and E-scores by the following variables: 1) birth weight, 2) birth length, 3) pterygium colli, 4) cubitus valgus, 5) level of behavioural activity in childhood, 6) onset and duration of cyclic hormone treatment, 7) overprotective behaviour of the mothers of the probands, 8) special difficulties in certain school subjects, 9) psychotraumatic conditions in childhood, 10) skeletal retardation, 11) 8/12 years mean growth-retardation and finally 12) retarded stature at time of testing.

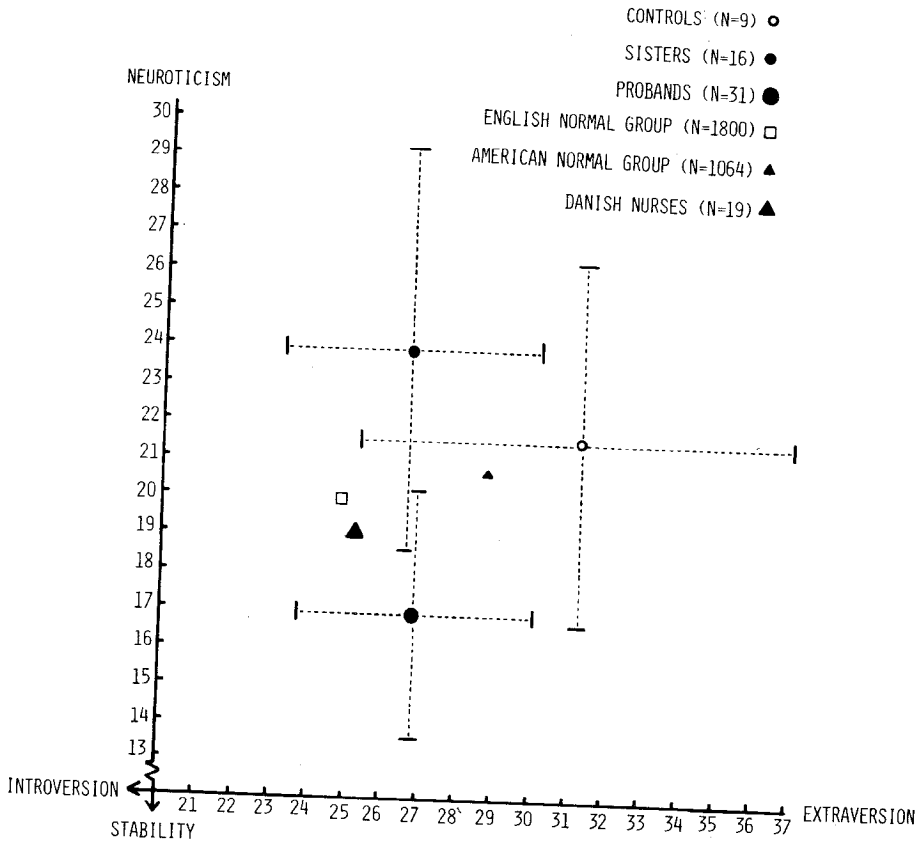

Fig. 6
Mean N- and E-scores for probands, sisters, controls, and selected »normative« data in the two orthogonal dimensions of personality: Neuroticism-Stability and Extraversion-Introversion as measured by Maudsley Personality Inventory (MPI)

Results and discussion

We found no relation between Extraversion and any of the above mentioned variables for Turner girls.

When the N-scores were similarly broken down, we found significant relations to birth weight and to birth length only.

The significant difference between the two groups of probands with birth weight under or over 3000 grammes was due to the group with karyotypes other than 45,X; in this group the means were 13.00 (SD 5.90) for babies < 2.999 grammes, and 27.11 (SD 7.17) for heavier babies, and the difference was clearly significant ($F = 19.32$; $p = .0005$). This difference may possibly be paralleled to

the observation that Turner girls with birth weight > 3000 grammes tended to make more errors in tests of field dependence (see *Chapter 14).*

In the group with karyotype 45,X there was no significant difference between means, 13.88 (SD 5.87) and 8.00 (SD 4.85), respectively, and, contrary to the group with karyotypes other than 45,X, those who weighed less than 3000 grammes at birth obtained the highest N-score.

On this basis nothing general about a possible association between birth weight and N-score could be concluded.

In the group of probands with karyotype 45,X, those with a body length at birth $\geq$ 50 cm got a significantly lower N-score than those with birth length < 50 cm ($p = .03$). Such difference could not be found in the group of probands with other karyotypes; the groups are, however, small and no conclusion can be drawn concerning a possible association between birth length and N-score.

Summarizing our results with the Maudsley Personality Inventory it can be said that girls with Turner's syndrome are no more extraverted than their sisters, but more emotionally stable as revealed by their low Neuroticism score. The remarkable emotional stability confirmed the earlier observation made by us as well as by others. We found no consistent association between somatic or psychiatric data of the Turner girls and scores of the Extraversion or the Neuroticism dimensions.

Chapter 16

TURNER'S SYNDROME WITH UNUSUAL KARYOTYPES

a. Turner's syndrome with deletion long-arm-X

One of the 45 probands (No. 14) had the karyotype 46,X,del(Xq). As seen in the case history she presented no remarkable differences from the other probands, physically or mentally. Her height was 150 cm.

Previous studies of girls with Turner's syndrome and deletion long-arm-X have not indicated any remarkable differences from Turner girls with 45,X in physical appearance, except for a tendency to slightly higher stature *(Melin & Samuelson* (1969), *Hecht et al.* (1970), *Bocian et al.* (1971), *Stevenson et al.* (1971), *Boczkowski & Mikkelsen* (1973) and *Stoll et al.* (1973)).

The six Turner girls with 46,X,del(Xq) studied by the above mentioned authors were all described as having a normal intelligence, none of them was studied from a psychiatric-psychological point of view, but the girl described by *Bocian et al.* (1971) was tested by a psychologist, and found to have considerable difficulties in spatial relations and discrepancy between Verbal and Performance IQ with a comparatively low Performance IQ as characteristic of girls with Turner's syndrome and karyotype 45,X.

From the studies of girls with karyotype 46,X,del(Xq), including the present case, there are thus no indications of any remarkable differences from cases of Turner's syndrome with karyotype 45,X.

Autoradiography was not made, but it might be expected that the deleted X was inactive as found by *Boczkowski & Mikkelsen* (1973) in a similar case and in accordance with the findings in other cases of X chromosome deletion *(Fraccaro & Lindsten* (1964), *Atkins et al.* (1965), *Steinberger et al.* (1966), *Gianelli* (1970) and *Kikuchi & Oishi* (1970)).

The Turner signs in cases with deletion short-arm-X and long-arm-X are thus most probably not due to lack of specific genes in the short or long arms, but rather due to lack of genetic influence from the heterochromatic inactivated deleted X.

Xg blood type was not made; it might, however, have given evidence about the possible inactivation of the Xg locus in structurally abnormal X chromosomes as suggested by *Polani et al.* (1970) after finding Xg (a-) daughters of Xg (a+) fathers in cases of Xg-probands.

b. Turner's syndrome with presence of Y chromosome material

There were four probands with 45,X and a cell line which contained presumptive Y chromosome material, one with 45,X/46,X,?del(Y)(q11), two with 45,X/46,X,?i(Y)(pter→q11::q11→pter)/?del(Y)(q11) and one with 45,X/46,X, inv(Y)(p11q11).

These four girls had no remarkable clinical signs which deviated from the rest of the group, they were typical girls with Turner's syndrome, and they did not deviate mentally from the other girls with Turner's syndrome.

Birth weights were 3,600, 2,350, 3,000 and 3,000 grams, respectively, which was above the mean of 2,878 in three cases, but within the 95 % confidence limits 2,734-3,023 for three of the four cases. Birth lengths were 51, 48, 51, and 51, respectively, compared with a mean of 49,1 in all girls with 95 % confidence limits 48.3-49.9; three of the four had thus a birth length which was above the expected 95 % confidence limits for the whole group.

Stature did not deviate significantly from the rest of the group, it was 153, 149 and 155 cm for the three adults. These values were all above the mean of 146 for all adults, but there were cases of 45,X with stature 158, 152, 153 and 150 cm.

The Y chromosome material might have some increasing effect on birth length and stature, but the group is too small for any conclusions to be drawn. There were no indications that the Y chromosome material had any effect on phenotype or mental development.

In the cases with Y chromosome material where Xg blood type was made (two cases), the results showed lack of paternal X which would be expected in all four cases.

c. Interstitial deletion and duplication of X chromosomes

The girl with presumptive interstitial deletion of a short part of short-arm-X as well as deletion long-arm-X at q11 in part of her cells (karyotype 45,X/46,X,?del (X)(p22p11)del(q11)) and the girl with 45,X/46,X,del(X)(q26),dup(X)(q13q26) did not deviate remarkably from girls with 45,X which could hardly be expected if the structurally abnormal X was inactive as would be expected from previous autoradiographic studies of cases with structural aberrations of the X chromosome.

d. X/X translocation

One of the patients found in the prevalence of Turner's syndrome in institutions for the mentally retarded was originally diagnosed as a case of 46,X,i(Xq), but repeated cytogenetic examination with banding technique showed that the

presumed isochromosome long-arm-X was: Xqter→Xq13::Xp21→Xqter dating from a reciprocal translocation (X;X)(p21;q13).

This girl was severely mentally retarded with several congenital abnormalities, bilateral simian crease and a few signs of Turner's syndrome such as growth-retardation and pterygium colli as seen in the case history No. 63 in *Chapter 19 d.*

The Turner signs present are most probably due to the combination of the inactive chromosome Xqter→Xq13::Xp21→Xqter as shown by autoradiography, and the incompletely active X: Xpter→Xq13::→Xp21→Xpter with lack of long-arm-A material. The lack of long-arm-X material in the active X might further be the main aetiological factor for the mental retardation as well as the congenital abnormalities of this patient.

A case of 45,X/46,X,t(Xp+Xq−) of similar type has been described by *van den Berghe et al.* (1973). This girl was a typical case of Turner's syndrome with no mental retardation and no congenital abnormalities, but she had a cell line with an active complete X besides the cell line with an active deleted X. Autoradiography showed that the X, to which a considerable part of the long arms from the other X was translocated, was inactive.

Further studies of cases with Turner's syndrome with (X;X) are, however, needed to reach any conclusion concerning this problem.

Chapter 17

AETIOLOGY OF TURNER'S SYNDROME

The aetiology of the loss of X chromosome material leading to the karyotypes found in Turner's syndrome is unknown. There is no parental age effect on the frequency of loss of X chromosome material.

Xg blood type studies *(Race* (1970)) have shown that the loss of X chromosome material in girls with karyotype 45,X is due to loss of paternal X chromosome in 75 per cent of the cases, and maternal loss of X is only found in 25 per cent of the cases. The loss of paternal X could occur either at the first or second meiotic division of spermatogenesis, but non-disjunction and loss of X chromosome material could also take place at fertilization or earliest cleavage. Another possible origin of the 45,X chromosome complement is mitotic secondary non-disjunction which most probably only accounts for mosaic formation.

The finding that most Xqi chromosomes are paternal indicates that the paternal X is more susceptible to structural rearrangement and isochromosome formation.

The tendency to mitotic errors leading to mixoploid and structural aberrations in X chromosomes could be inherited in the genome of the cell *(Krooth* (1971)). There might be an association between this tendency and the tendency to twin formation.

a. Parental age

Parental age was very similar for the probands and their sisters. The mean maternal age was 27.5 for the 45 probands, compared with 27.0 for their 46 sisters. Paternal age was 30.3 for the probands, compared with 30.9 for their sisters. The parental age corresponds well with the expected parental age for Denmark total, and there were no indications of any parental age effect on the aetiology of the X chromosome aberrations found in Turner's syndrome.

Xg blood type was examined in 27 cases by *Race and Sanger,* paternal abnormal or lacking X was found in 9 and maternal in 1; in 17 cases no information was gained. This supports the finding by *Race* (1970) that in the majority of Turner cases found, the lacking or structurally abnormal X was paternal. Two of our nine cases with paternal X were isochromosome long-arm-X, and one was a ring chromosome X.

b. Seasonal variation in birth

A study of all women with a 45,X chromosome constitution registered in the Danish Cytogenetic Central Register in 1972 showed a seasonal variation deviating considerably from the expected, analysis with a chi square test with 11 degrees of freedom showed no significant deviation (χ^2, 11 df = 12.536, $0.30<P<0.40$) as reported by *Nielsen et al.* (1973) and shown in *Fig. 7.* There was, however, a significantly higher frequency of children with Turner's syndrome born during the months from February to May than expected (χ^2 (Yates) = 7.048, $P< 0.01$) which corresponds with month of conception from May to August.

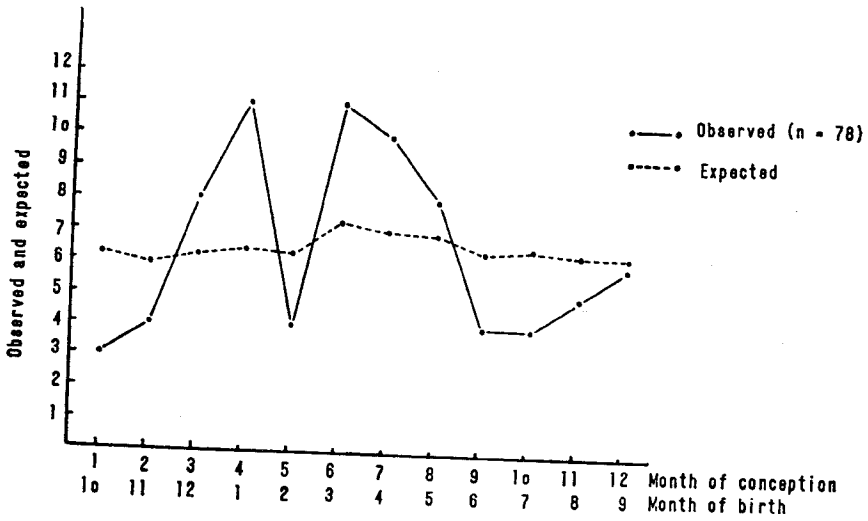

Fig. 7
Women with karyotype 45,X. Distribution by month of birth and month of conception. From Nielsen et al. (1973)

The present group of Turner probands is small, but 69 per cent of the 45 probands were born during the months from February to July, compared with 41 per cent of their 90 siblings, which corresponds to month of conception from May to September (χ^2 (Yates) = 8.320, $P< 0.01$).

The finding of seasonal variation in the birth of girls with Turner's syndrome indicates that there are certain environmental factors among the aetiological factors that lead to the lack of X chromosome material in girls with Turner's syndrome. Such environmental factors might be virus infections or other types of infections with seasonal variation, but there is a great number of possibilities of environmental aetiological factors which would vary with season as

mentioned by *Nielsen et al.* (1973). The phenomenon of seasonal variation in the birth of children with different chromosome abnormalities should be studied in different parts of the world and compared in order to ascertain any association between such variation and the variation of different disorders or factors which might be of aetiological nature for sex chromosome aberrations.

c. Twin births in the sibships and parental sibships

Table 77 shows the distribution of twin birth frequency in the sibships of the 45 probands in relation to karyotype 45,X or other karyotypes with lack of X chromosome material. The frequency of twin births in the sibships of the 21 probands with karyotype 45,X was 3.7 % which is not significantly higher than the expected as shown in *Table 77*.

Table 77
Twin births in the sibships of girls with Turner's syndrome in relation to karyotype

Karyotype	Probands	Births in the sibships			
		Total	Twin births		
			Total	%	95 % confidence limits
45,X	21	54	2	3.70	0.45-12.75
45,X/46,XX	2	6	-		
(1) 45,X/46,X,i(X)	9	24	1		
(2) 45,X/46,X,del(X)	2	7	1		
45,X/46,X,r(X)	4	13	-		
45,X/46,X,inv(Y)(p11q11)	1	4	1	5.71*	1.58-13.99
(3) 45,X/46,X,i(Y)/del(Y)	2	5	-		
45,X/46,X,del(Y)(q11)	1	4	-		
46,X,i(X)	2	5	1		
46,X,del(Xq)	1	2	-		
Total	45	124	6	4.83	2.10-12.10
Danish population 1900-1974, mean and 95 % conf. limits				1.38*	1.37-1.39
Highest frequency in 1929				1.66	1.56-1.76
Lowest frequency in 1972				0.91	0.84-0.98

(1) In five cases 25 to 75 % of the isochromosome X were dicentric.
(2) 45,X/46,X,del(X)(q26),dup(X)(q13q26)
(2) 45,X/46,X,del(X)(p22p11)(q11)
(3) 45,X/46,X,?i(Y)(pter→q11::q11→pter)/?del(Y)(q11)
(*) ($\chi^2 = 4.016$, $P < 0.05$)

Table 78
Twin births in maternal and paternal sibships in relation to karyotype

Karyotype of probands	Births in the sibships of the mothers				Births in the sibships of the fathers			
	Total	Twin births			Total	Twin births		
		Total	%	95 % confidence limits		Total	%	95 % confidence limits
45,X (n = 21)	73	1	1.37	0.03- 7.40	63	1	1.59	0.04-8.53
Other karyotypes (n = 24)	89	7	7.87*	3.22-15.54	134	3	2.23	0.45-6.13
Total	172	8	4.65	2.04- 9.10	197	4	2.03	0.55-5.04
Danish population 1900-1974, mean and 95 % confidence limits							1.38*	1.37-1.39
Danish population, highest frequency mean and 95 % confidence limits							1.66	1.56-1.76
Danish population, lowest frequency mean and 95 % confidence limits							0.91	0.84-0.98

* $\chi^2 = 11.382$, $P < 0.001$

In the sibships of the 24 probands with other karyotypes, we found a twin birth frequency of 5.7 % which is significantly higher than the expected mean frequency of 1.4 % in the Danish population from 1900 to 1974 ($\chi^2 = 4.016$, $P < 0.05$) *(Table 77)*.

Table 78 shows that the frequency of twin births in the maternal sibships of the 21 probands with karyotype 45,X was 1.4 %, and in the paternal sibships the twin frequency was 1.6 %, both of these frequencies correspond well with the expected mean frequency of 1.4 % in the Danish population from 1900 to 1974.

In the maternal sibships of the 24 probands with other karyotypes than 45,X *(Table 78)*, we found a twin frequency of 7.9 % which is significantly higher than the expected frequency ($\chi^2 = 11.382$, $P < 0.001$). The twin frequency in the paternal sibships was 2.2 % which corresponds with the expected 1.4 %.

The twin frequency in the sibships of all 45 probands was 4.8 % which is significantly higher than expected and similar to the pooled frequency of 3.2 % in the sibships of 165 women with Turner's syndrome and different karyotypes described by *Boyer et al.* (1961), *Lindsten* (1963) and *Nance and Uchida* (1964).

We found that the twin frequency was normal in Turner sibships and parental sibships of probands with karyotype 45,X, while the twin frequency was significantly increased in Turner sibships as well as maternal sibships of probands with mosaics and structural aberrations of the X chromosome such as deletion X, ring X or isochromosome X. This correlates to a certain extent with the findings by *Lindsten* (1963) that the twin frequency in sibships of Turner cases studied by him was only significantly increased when cases of isochromosome X were included, as well as with the findings by *Soltan* (1968) who found no increase in twin frequency in the sibships of girls with Turner's syndrome and 45,X.

The maternal age distribution for all probands was normal as expected for Turner's syndrome, and the increased twin frequency could thus not be due to increase in maternal age.

Our findings of a very similar and highly increased twin frequency in proband sibships as well as maternal sibships of Turner females with X chromosome mosaics or structural aberrations of the X chromosome, but not in those with karyotype 45,X indicate that there might be some association between the increased risk of such X chromosome aberrations in the progeny due to mitotic non-disjunction, deletion, isochromosome or ring chromosome formation on one hand, and twin formation on the other hand. Such X chromosome aberrations and twin formation might thus have some common aetiological factors.

The treatment of certain types of female sterility with FSH increases the risk of multiple births, and *de George* (1969) found indications of increased chorion-gonadotropic levels preceding twin conception in a high frequency of 329 mothers of twins. Such aberrations in the hormone levels might also increase the risk of certain aberrations in mitosis as well as the risk of X deletion, ring formation and isochromosome formation.

Increased frequency of twin births in the sibships of males with Klinefelter's syndrome has also been reported *(Ferguson-Smith* (1966), *Nielsen* (1966), *Soltan* (1968) and *Nielsen* (1970)). Further studies to explore the possible association between twin conception and certain sex chromosome aberrations and the possible common aetiological factors are needed.

We found paternal abnormal or lacking X in 9, and maternal in 1 of the 27 probands on whom Xg blood typing was made. The Xg blood type studies have indicated that most structural X chromosome aberrations in mixoploids are found in the paternal X. The tendency to mitotic errors leading to mixoploids and structural chromosome aberrations in the X chromosome could, however, be inherited in the genome of the maternal cell or be due to some hormonal aberrations in the mother.

If the paternal X is more susceptible than the maternal X to mitotic X chromosome aberrations as indicated by the Xg blood type studies, the tendency to mitotic errors leading to mixoploids and structural X chromosome aberrations could very well be found in the mother, but affect the X chromosome of the father.

Chapter 18

INFORMATION AND ADVICE

a. Information and advice to girls with Turner's syndrome as well as to their parents

It is more important that the diagnosis of Turner's syndrome is made during childhood in all cases so that information and advice can be given to the parents. Information, in particular, of the very good aspects of mental development should be stressed for parents of girls with Turner's syndrome, and so should the great importance of the avoidance of overprotecting and infantilizing such girls.

The behaviour of parents and siblings to a family member with Turner's syndrome should preferably be according to her age and mental development and not according to stature and physical development.

The overprotecting and infantilizing of girls with Turner's syndrome will tend to retard mental development with increased mental immaturity, anxiety and feelings of insecurity as results.

It is the experience from the present study that proper information to girls with Turner's syndrome at the time of expected menstruation is as important as the early diagnosis and the information to the parents during childhood. At the time of expected menstruation, girls with Turner's syndrome should be told that they will not get menstruation because of the lack of X chromosome material and consequently deficient gonadal development, but they should further be told that menstruation and the development of secondary sexual characteristics will follow cyclic hormone treatment. They should also be told that this treatment should not be started till height growth has stopped as it tends to decrease height growth.

It is of great importance to tell the parents of girls with Turner's syndrome, and later also the girls themselves, that in spite of the fact that they usually cannot have children, they can have a completely normal sexual life, marry and adopt children. They do not need to have any doubt about their femininity or ability to become good wives and good mothers to adopted children.

It appears in the present study, as has also appeared in a study of 25 other girls with Turner's syndrome, that those who have adopted children, have become excellent mothers. It is of great importance that the authorities that examine applications and grant permission for adoption are made aware of this fact.

In connection with the present study, we have told the probands that we would be willing to support their application for the adoption of a child by

means of a recommendation to the adoption authorities.

The age at which the probands were informed about their aberration in gonadal development varied from childhood to the late twenties, and many had, in our opinion, not been given sufficient information of all the aspects of their condition, especially in respect of the many positive aspects of personality development. Girls with Turner's syndrome have in fact no increased risk of physical or mental illness, and they possess good possibilities of acquiring sufficient education and training to fit them for most occupations and to become well adjusted as far as work and social conditions are concerned.

Turner girls lack X chromosome material, and on this account they have certain physical handicaps: Low stature, usually primary amenorrhoea and sterility and sometimes other physical aberrations as shown in *Table 31*. They function well as far as intelligence and personality are concerned, and they have a number of positive qualities in their personality such as a good ability for contact with others and an eagerness to use this ability as well as to help and understand other people. They are usually diligent and conscientious with a good and stable mood.

They are sensitive and may, if not supported and stimulated in their environment, be rather late in becoming mature adult women. Their tendency to retardation in maturity and independence may be a certain handicap which, however, they usually overcome quite well, especially if the parents and the environment in general support and stimulate them in their maturity and independence development, and if overprotection and infantilizing are avoided.

Turner's syndrome with lack of X chromosome material is a good example of the fact that a chromosome aberration does not necessarily lead to deviations in personality and intelligence development associated with a handicap. A certain deviation in personality may even become an advantage in overcoming some of the physical handicaps as in the cases of Turner's syndrome. It is evident that many of the qualities of personality and behaviour pattern of girls with Turner's syndrome would be judged very valuable by most people.

b. Advice to parents with reference to diagnosis of a foetus with lack of X chromosome material at neonatal chromosome analysis

Amniocentesis will eventually become easily available to all women aged 35 years and above due to the increased risk of non-disjunction and chromosome aberrations with maternal age.

It is of great importance to have a good knowledge of the mental and physical development and the possibilities for social adjustment of girls with Turner's syndrome, as of persons with all other types of sex chromosome aberrations, in order to give thorough information to the parents of a foetus with such a chromosome aberration.

Some geneticists might be of the opinion that individuals with a major chromosome aberration should rather not be born, and that abortion is indicated in all such cases. In the case of Turner's syndrome where there are so good and positive personality traits, normal intelligence and such excellent possibilities of good social adjustment as is indicated in the present study that there can hardly be any indication for abortion.

Advice of abortion of a Turner foetus would further be an act of discrimination against the approximately 900 women with Turner's syndrome in this country and the thousands in other countries, most of whom live a normal life and are well adjusted.

Summary

Introduction

The main purpose of the investigation has been to study the development of Turner females during childhood, their education and social adjustment as adults in comparison with their sisters and with a control group of women of normal chromosome constitution, but growth retardation and primary amenorrhoea. It has further been the purpose to compare certain aspects of the cognitive styles of women with Turner's syndrome with that of their sisters and controls.

Chapter 1

Brief definitions of Turner's syndrome according to the original description by *Turner* and according to the one used in the present study: Females with lack of X chromosome material.

Chapter 2

The study comprises 45 girls with Turner's syndrome found outside institutions, 15 controls, 18 age-matched sisters, 8 patients with Turner's syndrome found in a study of patients with Turner's syndrome in all Danish psychiatric hospitals and 11 patients with Turner's syndrome found in a prevalence study of Turner's syndrome in Danish institutions for the mentally retarded. The methods of the investigation are described.

Chapter 3

Cytogenetic examination of the 45 probands on chromosomes from blood cultures in all, as well as skin culture in 15 cases, and the use of banding techniques showed a great variety of karyotypes, 21 with 45,X, two with 45,X/46,XX – 9 with 45,X/46,X,i(Xq) – 1 with 45,X/46,X,del(X)(q26),dup(X)(q13q26) – 1 with 45,X/46,X,?del(X)(p22p11)del(q11) – 4 with 45,X/46,X,r(X) – 1 with 45,X/46,X,inv(Y)(p11q11) – 1 with 45,X/46,X,?del(Y)(q11) – 2 with 45,X/46,X,?i(Y)(pter→q11::q11→pter)/?del(Y)(q11) – 2 with 46,X,i(Xq) and 1 with 46,X,del(Xq).

There was no significant difference in education between probands, sisters and controls, and girls with Turner's syndrome reached the same level of school education as Danish girls in general. Girls with Turner's syndrome were more frequently described as conscientious and diligent at school, compared with their sisters. The girls with Turner's syndrome had considerably greater difficulties in arithmetic than their sisters. A higher frequency of girls with Turner's syndrome, compared with their sisters, liked to go to school in spite of the fact that more of them were teased on account of their short stature and/or obesity.

There was no significant difference in type of occupation between girls with Turner's syndrome, their sisters and the controls. There was a preference for future jobs that had to do with children for the girls with Turner's syndrome still at school.

It is concluded that girls with Turner's syndrome should be supported in reaching their goals as far as education and occupation are concerned, irrespective of their low stature and chromosome aberration.

The girls with Turner's syndrome had a slightly lower level of activity, compared with the controls and their sisters during childhood.

More of the girls with Turner's syndrome aged 18+ still lived with their parents, compared with their sisters, and fewer were married or living with a boy friend. There was no difference between girls with Turner's syndrome and controls in this respect.

Age at first sexual intercourse was higher in girls with Turner's syndrome than in their sisters, but there was no significant difference in problems in sexual relations between girls with Turner's syndrome, controls and sisters.

The girls with Turner's syndrome were more feminine than their sisters in behaviour, in their style of dressing and in the jewellery they wore. The gender role-identity was definitely feminine in the girls with Turner's syndrome.

The possibility of adoption is discussed, and the conclusion derived from the study is that the women with Turner's syndrome, who had applied for the adoption of a child, were all qualified to get it. Women with Turner's syndrome are usually well fitted to become mothers.

There was no significant difference in school performance, education or type of occupation and behaviour between women with Turner's syndrome, karyotype 45,X, and those with Turner's syndrome and other karyotypes with more than one X. Nor was there any significant difference in clinical Turner stigmata between these two groups, except for pterygium colli which was found to a significantly higher degree among Turner girls with 45,X. There was no difference in height between the two groups.

Chapter 5

Spontaneous menstruation was found in 5 of the total 51 women with Turner's syndrome aged 15+, 1 of them, a women with karyotype 45,X/46,XX/47,XXX had given birth to a child.

Twenty-four of the 29 probands with Turner's syndrome aged 18+ had received cyclic hormone treatment, in 10 the treatment had been discontinued for various reasons. Women with Turner's syndrome should be given cyclic oestrogen hormone treatment at an appropriate age until satisfactory development of secondary sexual characteristics has taken place. If further treatment is needed, it should always be given as a combination of oestrogen and gestagen and associated with regular control as there may be a slightly increased risk of endometrial uterus cancer as discussed further later in this Chapter.

There are indications from some recent studies that androgen treatment should be given for a period prior to the instigation of oestrogen treatment, i.e. before the age of 17; such treatment may increase height by a few cm which can be of great importance, especially for some of the girls of very short stature.

The birth length and weight were significantly lower than expected, and height during childhood remained below the expected level. There was further a lack of the puberal growth spurt in height. The height of the 24 probands aged 20+ was 138 to 158 cm with a mean of 146 cm, and there was no significant difference between women with 45,X and those with other karyotypes. The tallest girl with a stature of 158 cm had the karyotype 45,X.

The clinical signs of Turner's syndrome in the 45 probands are presented. Cubitus valgus was found in 60 per cent and pterygium colli in 38 per cent. The only sign, which was considerably higher in probands with 45,X than in girls with other karyotypes, was pterygium colli.

Chapter 6

Electroencephalographic examination was made in 39 of the 45 probands with Turner's syndrome found outside institutions and in all 11 patients with mental retardation. The characteristic findings were: 1) occipital dominant spike-and-wave complex or spike waves in 5 of the 11 patients who were mentally retarded (45%) and in 1 of the 39 women found outside institutions, 2) hypersensitivity to hyperventilation with spikes, sharp waves or dysrhythmia in 31 per cent and 3) an increased amount of 14-18/s beta waves in 46 per cent of the cases.

Definite EEG abnormalities were found in 23 per cent of the probands found outside institutions and 55 per cent of the patients found in institutions, borderline EEG aberrations were found in 38 per cent of probands found outside institutions and 18 per cent of those with mental retardation.

It is concluded that the spike-and-wave complex in the occipital area found in

a group with mental retardation might be associated with some of the neurocognitional deficits found by psychological tests in women with Turner's syndrome. The finding of 23 per cent with definite EEG abnormalities among those found outside institutions is not considered to be significantly higher than expected.

Chapter 7

Dermatoglyphic examination was made of 30 probands with Turner's syndrome. The mean total finger ridge count was above the average for controls and greater in the group consisting of probands with 45,X in all cells. There were further palm and sole patterns characteristic of Turner's syndrome with some differences between the Turner group with 45,X in all cells, compared with the group having other karyotypes.

Chapter 8

A survey is given of previous psychiatric studies of women with Turner's syndrome. We found psychopathological symptoms in 5 of the 45 probands (11%) which is similar to what could be expected in a normal population this age. All five probands with psychopathological symptoms had been subjected to a psychotraumatic environment during childhood, four of them had been overprotected, compared with only 4 out of the 40 without psychopathological symptoms. Only 1 of the 45 had been admitted to a psychiatric hospital.

There was no increase in the frequency of psychopathology in women with Turner's syndrome, compared with what was expected in the Danish population. Most of the probands had a later mental maturation than their sisters, but only 2 of the 45 probands in the present study presented a characteristic psychoinfantilism as described by *Lindberg* (1950). As preventive measures of immaturity parents should be advised to avoid overprotection and infantilization and to stimulate independence and initiative.

Atypical anorexia nervosa was found in one woman with Turner's syndrome, and a possible association between Turner's syndrome and anorexia nervosa is discussed.

The frequency of mental disorders was similar among the women with Turner's syndrome and near relatives. There was no remarkably high frequency of physical disorders in parents and siblings of the girls with Turner's syndrome, but a prevalence of 11 per cent of the mothers with struma and 6 per cent of parents with psoriasis as well as 5 per cent with previous rheumatic fever are comparatively high frequencies, and a possible association between these disorders and risk of chromosome aberration leading to lack of X chromosome material should be further studied.

Chapter 9

A survey of prevalence studies of Turner's syndrome in the general population is presented. The prevalence in the general population is approximately 1 per 3,000.

Investigation of Turner's syndrome in Danish psychiatric hospitals showed a frequency of 0.1 per 1,000 for first-admissions to all Danish psychiatric hospitals per year during a 10-year-period, compared with an expected frequency of approximately 0.3 per 1,000. The figures observed were minimum figures, but there was no indication of any increased frequency of patients with Turner's syndrome among patients in Danish psychiatric hospitals. The mental illnesses of the eight patients, who had been admitted to Danish psychiatric hospitals during the past 10 years, are discussed.

Chapter 10

Previous psychological investigations of the intelligence level of women with Turner's syndrome are presented. We found no difference in intelligence as evaluated by school performance, occupational level and performance in general between the 45 Turner probands and their 46 sisters or between the probands and the controls.

A survey of prevalence studies of patients with Turner's syndrome in institutions for the mentally retarded is presented. We found a prevalence of 1.1 per 1,000 among the 9,608 female patients under care from Danish institutions for the mentally retarded. The finding of a slightly higher prevalence of girls with Turner's syndrome under care from institutions for the mentally retarded than expected does not necessarily mean that the risk of mental retardation is higher in girls with Turner's syndrome, and the reason for this is discussed.

Chapter 11

A critical survey is given of previous studies of intellectual functioning in women with Turner's syndrome. According to these there seems to be no general intellectual retardation in women with Turner's syndrome. In the present study we found no difference in intelligence as evaluated by school performance, occupational level and performance in general between the 45 probands and their 46 sisters, or between the probands and the controls. Most earlier studies found the WAIS performance IQ score to be significantly lower than could be expected by chance while the verbal score seems within normal limits. In some studies was observed remarkably low score in certain specific factors, interpreted as a »cognitional deficit« in girls with Turner's syndrome.

Chapter 12

The probands, sisters and controls were studied by the Rod-and-Frame test, Embedded-Figures test, and Human Figure-Drawing test, which tests according to Witkin indicate degree of »field dependence«. We found no differences between probands with karyotype 45,X and probands with other karyotypes. The probands as a group scored extremely field dependent on all tests herefore, compared to their sisters, while the controls performed moderately field dependent. Developmental trends in the data seem to indicate a delayed rate of maturation in cognitive functions in girls with Turner's syndrome.

Chapter 13

Although the probands made more errors on Money's Road-Map test signifying a tendency for a less developed left-right direction discriminatory ability in Turner's syndrome than that of their sisters, the difference was not significant, as was neither the error score of the controls. The absence of difference in our study between girls with Turner's syndrome and their controls to be found in most other studies may possibly be explained in terms of a developmental delay. On the Porteus Mazes test the girls with Turner's syndrome made no more errors on the quantitative scale. On the qualitative scale they, on the other hand, made considerably less errors which is taken as an indication of a predominant emotional stability in girls with Turner's syndrome.

The Human Figure-Drawing test scored ad modum Goodenough-Harris gave results essentially comparable with those obtained by scoring the drawings ad modum Witkin (see *Chapter 10),* i.e. most Turner girls drew poor human figures while the growth-retarded group tended to do so too. On basis of the cognitive test results it was considered reasonable to regard a late matured cognitive functioning in certain areas as a reality to overcome later in the cognitive development rather than a definite and insuperable cognitive defect.

Chapter 14

Some of the cognitive performance test scores were broken down by the following variables: presence of Y-chromosome material, birth weight, birth length, pterygium colli, cubitus valgus, level of behavioral activity in childhood, cyclic hormone treatment, overprotective behavior of the mothers of the probands, special difficulties in certain school subjects, skeletal retardation, 8/12 year mean growth-retardation, and finally retarded stature at the time of testing. The only parameters which appeared to have importance for cognitive performance in girls with Turner's syndrome were birth length, level of behavioral activity in childhood, and duration of cyclic oestrogen treatment. Some aspects of this were shortly discussed.

Chapter 15

In this chapter is reported the results of testing 31 girls with Turner's syndrome with the Maudsley Personality Inventory (MPI) as well as of 16 sisters and 9 growth retarded girls. We found no differences between probands, sisters and controls on the Extraversion-Introversion scale. A hypothesis that Turner girls would score low on the Neuroticism-Stability scale was on the other hand confirmed, indicating exceptional emotional stability. Such result coincided with our clinical impression of girls with Turner's syndrome as well as with their score in the qualitative part of Porteus Mazes test. We found no consistent associations between somatic or psychiatric data of the Turner girls and scores of the Extraversion or the Neuroticism dimensions.

Chapter 16

Cases of unusual karyotypes are presented and compared with previous studies of such cases.

Chapter 17

Possible aetiological factors of Turner's syndrome are presented and discussed.

Chapter 18

The importance of giving information and advice to parents of girls with Turner's syndrome and the girls with Turner's syndrome themselves is discussed, and the question of advice on finding a foetus with Turner's syndrome by prenatal examination is briefly discussed.

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many friends, craves excitement, is generally an impulsive person and generally likes change, is carefree and easygoing. This description seems far from perfect for Turner girls. The typical introvert is on the other hand quiet, introspective, reserved and distant, except to intimate friends, not impulsive etc.; such a description seems more readily applicable to girls with Turner's syndrome although it is still not perfect. Thus the remarkable adjustment of Turner girls speaks, according to *Eysenck*, for average or above average E-score while the description of the extravert person seems unfit for Turner girls. We therefore made no hypothesis concerning the possible score of Turner girls on the Extraversion-Introversion scale.

b. Methods

In order to test our hypothesis we examined 31 probands, 16 of their sisters and 9 growth-retarded girls with normal karyotype and primary amenorrhoea with the MPI which was applied individually. This test, *Eysenck* (1962) claims, isolates the two pervasive and relatively independent dimensions of personality in question: 1) Neuroticism-Stability (N), and 2) Extraversion-Introversion (E). N and E is measured by means of a scale with 24 questions, each with a maximum of zero. High N-score indicates Neuroticism, high E-score Extraversion.

c. Results and discussion

In the following will be given only a short account of some main results with the MPI; a more detailed account will be presented later *(Bækgaard, Nyborg & Nielsen*, (1977)). As seen in *Table 76* the differences in group mean score of the probands, sisters and controls with regard to the E-score were 26.84 (SD 9.08), 26.63 (SD 7.15) and 31.22 (SD 9.11), respectively; the differences between probands and sisters and between sisters and controls were insignificant.

The score for Neuroticism (N-score) on the other hand gave significant differences between probands and sisters (mean: 16.87 (SD 9.26), versus 23.87 (SD 10.94); $F = 5.34$, $P_{\text{one-tailed}} = .01$). The difference between sisters and controls was not significant.

In the scatterplot in *Fig. 6* the mean N-scores of the probands, sisters and controls were related to an American and an English normative material. We furthermore plotted in the data of 19 Danish nurses in an attempt to »anchor« our test results with the MPI which is not standardized in Denmark; these data can, of course, not be considered as representative. From *Fig. 6* will be seen that the N-scores of this group nevertheless come quite near to the scores from the representative American and English studies, as well as did the N-scores of our control group of growth-retarded girls with primary amenorrhoea and

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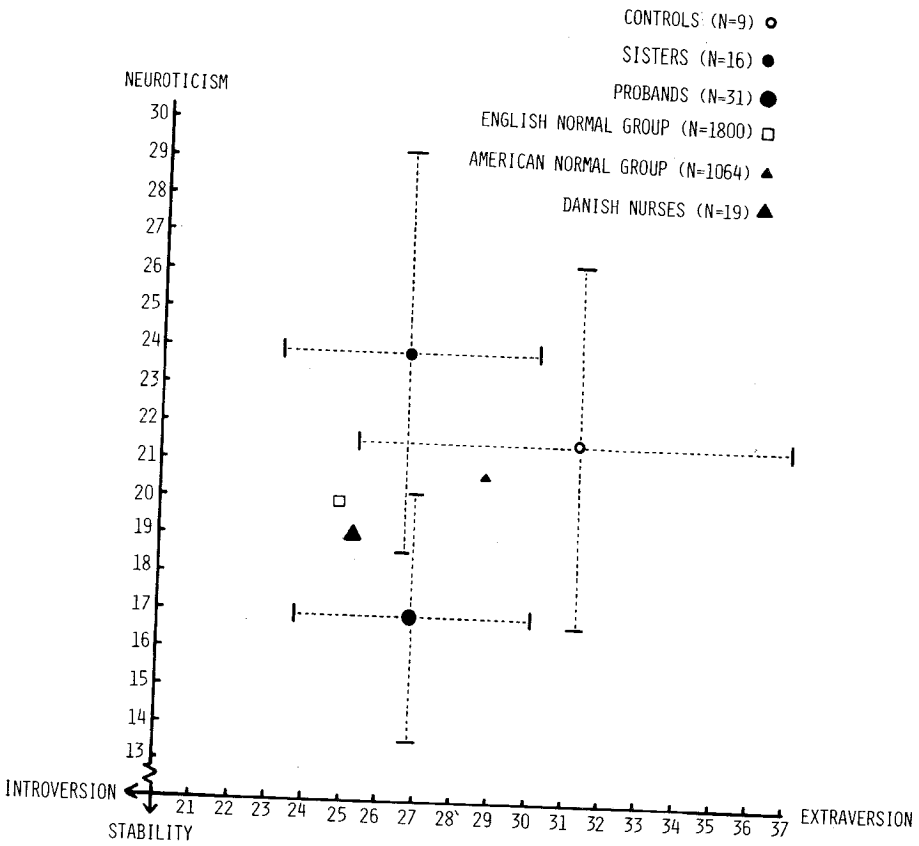

Fig. 6

Mean N- and E-scores for probands, sisters, controls, and selected »normative« data in the two orthogonal dimensions of personality: Neuroticism-Stability and Extraversion-Introversion as measured by Maudsley Personality Inventory (MPI)

Results and discussion

We found no relation between Extraversion and any of the above mentioned variables for Turner girls.

When the N-scores were similarly broken down, we found significant relations to birth weight and to birth length only.

The significant difference between the two groups of probands with birth weight under or over 3000 grammes was due to the group with karyotypes other than 45,X; in this group the means were 13.00 (SD 5.90) for babies < 2.999 grammes, and 27.11 (SD 7.17) for heavier babies, and the difference was clearly significant ($F = 19.32$; $p = .0005$). This difference may possibly be paralleled to

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b. Turner's syndrome with presence of Y chromosome material

There were four probands with 45,X and a cell line which contained presumptive Y chromosome material, one with 45,X/46,X,?del(Y)(q11), two with 45,X/46,X,?i(Y)(pter→q11::q11→pter)/?del(Y)(q11) and one with 45,X/46,X, inv(Y)(p11q11).

These four girls had no remarkable clinical signs which deviated from the rest of the group, they were typical girls with Turner's syndrome, and they did not deviate mentally from the other girls with Turner's syndrome.

Birth weights were 3,600, 2,350, 3,000 and 3,000 grams, respectively, which was above the mean of 2,878 in three cases, but within the 95 % confidence limits 2,734-3,023 for three of the four cases. Birth lengths were 51, 48, 51, and 51, respectively, compared with a mean of 49,1 in all girls with 95 % confidence limits 48.3-49.9; three of the four had thus a birth length which was above the expected 95 % confidence limits for the whole group.

Stature did not deviate significantly from the rest of the group, it was 153, 149 and 155 cm for the three adults. These values were all above the mean of 146 for all adults, but there were cases of 45,X with stature 158, 152, 153 and 150 cm.

The Y chromosome material might have some increasing effect on birth length and stature, but the group is too small for any conclusions to be drawn. There were no indications that the Y chromosome material had any effect on phenotype or mental development.

In the cases with Y chromosome material where Xg blood type was made (two cases), the results showed lack of paternal X which would be expected in all four cases.

c. Interstitial deletion and duplication of X chromosomes

The girl with presumptive interstitial deletion of a short part of short-arm-X as well as deletion long-arm-X at q11 in part of her cells (karyotype 45,X/46,X,?del (X)(p22p11)del(q11)) and the girl with 45,X/46,X,del(X)(q26),dup(X)(q13q26) did not deviate remarkably from girls with 45,X which could hardly be expected if the structurally abnormal X was inactive as would be expected from previous autoradiographic studies of cases with structural aberrations of the X chromosome.

d. X/X translocation

One of the patients found in the prevalence of Turner's syndrome in institutions for the mentally retarded was originally diagnosed as a case of 46,X,i(Xq), but repeated cytogenetic examination with banding technique showed that the

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b. Seasonal variation in birth

A study of all women with a 45,X chromosome constitution registered in the Danish Cytogenetic Central Register in 1972 showed a seasonal variation deviating considerably from the expected, analysis with a chi square test with 11 degrees of freedom showed no significant deviation (χ^2, 11 df = 12.536, $0.30<P<0.40$) as reported by *Nielsen et al.* (1973) and shown in *Fig. 7.* There was, however, a significantly higher frequency of children with Turner's syndrome born during the months from February to May than expected (χ^2 (Yates) = 7.048, $P< 0.01$) which corresponds with month of conception from May to August.

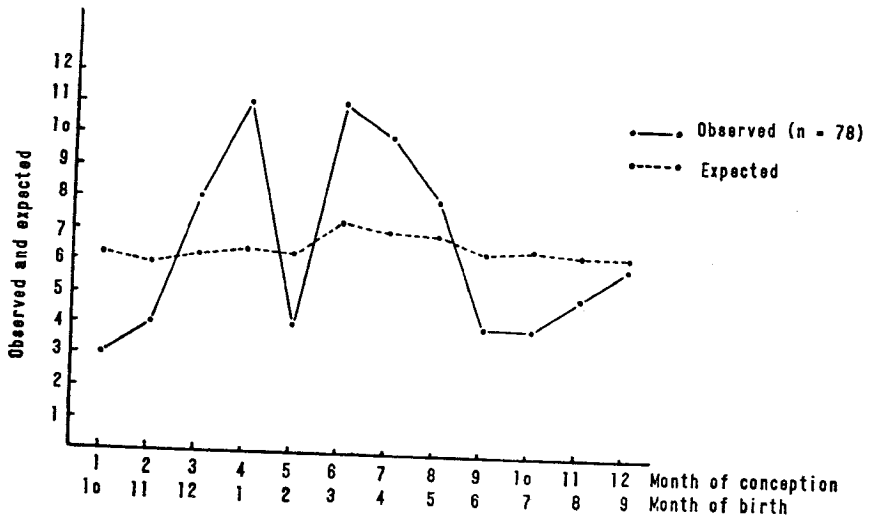

Fig. 7
Women with karyotype 45,X. Distribution by month of birth and month of conception. From Nielsen et al. (1973)

The present group of Turner probands is small, but 69 per cent of the 45 probands were born during the months from February to July, compared with 41 per cent of their 90 siblings, which corresponds to month of conception from May to September (χ^2 (Yates) = 8.320, $P< 0.01$).

The finding of seasonal variation in the birth of girls with Turner's syndrome indicates that there are certain environmental factors among the aetiological factors that lead to the lack of X chromosome material in girls with Turner's syndrome. Such environmental factors might be virus infections or other types of infections with seasonal variation, but there is a great number of possibilities of environmental aetiological factors which would vary with season as

Table 78
Twin births in maternal and paternal sibships in relation to karyotype

Karyotype of probands	Births in the sibships of the mothers				Births in the sibships of the fathers			
	Total	Twin births			Total	Twin births		
		Total	%	95 % confidence limits		Total	%	95 % confidence limits
45,X (n = 21)	73	1	1.37	0.03- 7.40	63	1	1.59	0.04-8.53
Other karyotypes (n = 24)	89	7	7.87*	3.22-15.54	134	3	2.23	0.45-6.13
Total	172	8	4.65	2.04- 9.10	197	4	2.03	0.55-5.04
Danish population 1900-1974, mean and 95 % confidence limits							1.38*	1.37-1.39
Danish population, highest frequency mean and 95 % confidence limits							1.66	1.56-1.76
Danish population, lowest frequency mean and 95 % confidence limits							0.91	0.84-0.98

* $\chi^2 = 11.382$, $P < 0.001$

In the sibships of the 24 probands with other karyotypes, we found a twin birth frequency of 5.7 % which is significantly higher than the expected mean frequency of 1.4 % in the Danish population from 1900 to 1974 ($\chi^2 = 4.016$, $P < 0.05$) *(Table 77)*.

Table 78 shows that the frequency of twin births in the maternal sibships of the 21 probands with karyotype 45,X was 1.4 %, and in the paternal sibships the twin frequency was 1.6 %, both of these frequencies correspond well with the expected mean frequency of 1.4 % in the Danish population from 1900 to 1974.

In the maternal sibships of the 24 probands with other karyotypes than 45,X *(Table 78)*, we found a twin frequency of 7.9 % which is significantly higher than the expected frequency ($\chi^2 = 11.382$, $P < 0.001$). The twin frequency in the paternal sibships was 2.2 % which corresponds with the expected 1.4 %.

The twin frequency in the sibships of all 45 probands was 4.8 % which is significantly higher than expected and similar to the pooled frequency of 3.2 % in the sibships of 165 women with Turner's syndrome and different karyotypes described by *Boyer et al.* (1961), *Lindsten* (1963) and *Nance and Uchida* (1964).

We found that the twin frequency was normal in Turner sibships and parental sibships of probands with karyotype 45,X, while the twin frequency was significantly increased in Turner sibships as well as maternal sibships of probands with mosaics and structural aberrations of the X chromosome such as deletion X, ring X or isochromosome X. This correlates to a certain extent with the findings by *Lindsten* (1963) that the twin frequency in sibships of Turner cases studied by him was only significantly increased when cases of isochromosome X were included, as well as with the findings by *Soltan* (1968) who found no increase in twin frequency in the sibships of girls with Turner's syndrome and 45,X.

Chapter 12

The probands, sisters and controls were studied by the Rod-and-Frame test, Embedded-Figures test, and Human Figure-Drawing test, which tests according to Witkin indicate degree of »field dependence«. We found no differences between probands with karyotype 45,X and probands with other karyotypes. The probands as a group scored extremely field dependent on all tests herefore, compared to their sisters, while the controls performed moderately field dependent. Developmental trends in the data seem to indicate a delayed rate of maturation in cognitive functions in girls with Turner's syndrome.

Chapter 13

Although the probands made more errors on Money's Road-Map test signifying a tendency for a less developed left-right direction discriminatory ability in Turner's syndrome than that of their sisters, the difference was not significant, as was neither the error score of the controls. The absence of difference in our study between girls with Turner's syndrome and their controls to be found in most other studies may possibly be explained in terms of a developmental delay. On the Porteus Mazes test the girls with Turner's syndrome made no more errors on the quantitative scale. On the qualitative scale they, on the other hand, made considerably less errors which is taken as an indication of a predominant emotional stability in girls with Turner's syndrome.

The Human Figure-Drawing test scored ad modum Goodenough-Harris gave results essentially comparable with those obtained by scoring the drawings ad modum Witkin (see *Chapter 10),* i.e. most Turner girls drew poor human figures while the growth-retarded group tended to do so too. On basis of the cognitive test results it was considered reasonable to regard a late matured cognitive functioning in certain areas as a reality to overcome later in the cognitive development rather than a definite and insuperable cognitive defect.

Chapter 14

Some of the cognitive performance test scores were broken down by the following variables: presence of Y-chromosome material, birth weight, birth length, pterygium colli, cubitus valgus, level of behavioral activity in childhood, cyclic hormone treatment, overprotective behavior of the mothers of the probands, special difficulties in certain school subjects, skeletal retardation, 8/12 year mean growth-retardation, and finally retarded stature at the time of testing. The only parameters which appeared to have importance for cognitive performance in girls with Turner's syndrome were birth length, level of behavioral activity in childhood, and duration of cyclic oestrogen treatment. Some aspects of this were shortly discussed.

a group with mental retardation might be associated with some of the neurocognitional deficits found by psychological tests in women with Turner's syndrome. The finding of 23 per cent with definite EEG abnormalities among those found outside institutions is not considered to be significantly higher than expected.

Chapter 7

Dermatoglyphic examination was made of 30 probands with Turner's syndrome. The mean total finger ridge count was above the average for controls and greater in the group consisting of probands with 45,X in all cells. There were further palm and sole patterns characteristic of Turner's syndrome with some differences between the Turner group with 45,X in all cells, compared with the group having other karyotypes.

Chapter 8

A survey is given of previous psychiatric studies of women with Turner's syndrome. We found psychopathological symptoms in 5 of the 45 probands (11%) which is similar to what could be expected in a normal population this age. All five probands with psychopathological symptoms had been subjected to a psychotraumatic environment during childhood, four of them had been overprotected, compared with only 4 out of the 40 without psychopathological symptoms. Only 1 of the 45 had been admitted to a psychiatric hospital.

There was no increase in the frequency of psychopathology in women with Turner's syndrome, compared with what was expected in the Danish population. Most of the probands had a later mental maturation than their sisters, but only 2 of the 45 probands in the present study presented a characteristic psychoinfantilism as described by *Lindberg* (1950). As preventive measures of immaturity parents should be advised to avoid overprotection and infantilization and to stimulate independence and initiative.

Atypical anorexia nervosa was found in one woman with Turner's syndrome, and a possible association between Turner's syndrome and anorexia nervosa is discussed.

The frequency of mental disorders was similar among the women with Turner's syndrome and near relatives. There was no remarkably high frequency of physical disorders in parents and siblings of the girls with Turner's syndrome, but a prevalence of 11 per cent of the mothers with struma and 6 per cent of parents with psoriasis as well as 5 per cent with previous rheumatic fever are comparatively high frequencies, and a possible association between these disorders and risk of chromosome aberration leading to lack of X chromosome material should be further studied.

means of a recommendation to the adoption authorities.

The age at which the probands were informed about their aberration in gonadal development varied from childhood to the late twenties, and many had, in our opinion, not been given sufficient information of all the aspects of their condition, especially in respect of the many positive aspects of personality development. Girls with Turner's syndrome have in fact no increased risk of physical or mental illness, and they possess good possibilities of acquiring sufficient education and training to fit them for most occupations and to become well adjusted as far as work and social conditions are concerned.

Turner girls lack X chromosome material, and on this account they have certain physical handicaps: Low stature, usually primary amenorrhoea and sterility and sometimes other physical aberrations as shown in *Table 31*. They function well as far as intelligence and personality are concerned, and they have a number of positive qualities in their personality such as a good ability for contact with others and an eagerness to use this ability as well as to help and understand other people. They are usually diligent and conscientious with a good and stable mood.

They are sensitive and may, if not supported and stimulated in their environment, be rather late in becoming mature adult women. Their tendency to retardation in maturity and independence may be a certain handicap which, however, they usually overcome quite well, especially if the parents and the environment in general support and stimulate them in their maturity and independence development, and if overprotection and infantilizing are avoided.

Turner's syndrome with lack of X chromosome material is a good example of the fact that a chromosome aberration does not necessarily lead to deviations in personality and intelligence development associated with a handicap. A certain deviation in personality may even become an advantage in overcoming some of the physical handicaps as in the cases of Turner's syndrome. It is evident that many of the qualities of personality and behaviour pattern of girls with Turner's syndrome would be judged very valuable by most people.

b. Advice to parents with reference to diagnosis of a foetus with lack of X chromosome material at neonatal chromosome analysis

Amniocentesis will eventually become easily available to all women aged 35 years and above due to the increased risk of non-disjunction and chromosome aberrations with maternal age.

It is of great importance to have a good knowledge of the mental and physical development and the possibilities for social adjustment of girls with Turner's syndrome, as of persons with all other types of sex chromosome aberrations, in order to give thorough information to the parents of a foetus with such a chromosome aberration.

There was no significant difference in education between probands, sisters and controls, and girls with Turner's syndrome reached the same level of school education as Danish girls in general. Girls with Turner's syndrome were more frequently described as conscientious and diligent at school, compared with their sisters. The girls with Turner's syndrome had considerably greater difficulties in arithmetic than their sisters. A higher frequency of girls with Turner's syndrome, compared with their sisters, liked to go to school in spite of the fact that more of them were teased on account of their short stature and/or obesity.

There was no significant difference in type of occupation between girls with Turner's syndrome, their sisters and the controls. There was a preference for future jobs that had to do with children for the girls with Turner's syndrome still at school.

It is concluded that girls with Turner's syndrome should be supported in reaching their goals as far as education and occupation are concerned, irrespective of their low stature and chromosome aberration.

The girls with Turner's syndrome had a slightly lower level of activity, compared with the controls and their sisters during childhood.

More of the girls with Turner's syndrome aged 18+ still lived with their parents, compared with their sisters, and fewer were married or living with a boy friend. There was no difference between girls with Turner's syndrome and controls in this respect.

Age at first sexual intercourse was higher in girls with Turner's syndrome than in their sisters, but there was no significant difference in problems in sexual relations between girls with Turner's syndrome, controls and sisters.

The girls with Turner's syndrome were more feminine than their sisters in behaviour, in their style of dressing and in the jewellery they wore. The gender role-identity was definitely feminine in the girls with Turner's syndrome.

The possibility of adoption is discussed, and the conclusion derived from the study is that the women with Turner's syndrome, who had applied for the adoption of a child, were all qualified to get it. Women with Turner's syndrome are usually well fitted to become mothers.

There was no significant difference in school performance, education or type of occupation and behaviour between women with Turner's syndrome, karyotype 45,X, and those with Turner's syndrome and other karyotypes with more than one X. Nor was there any significant difference in clinical Turner stigmata between these two groups, except for pterygium colli which was found to a significantly higher degree among Turner girls with 45,X. There was no difference in height between the two groups.