CHAPTER-V : OBSERVATIONS

OBSERVATIONS

PART-I : AUTOSOMES

Cytogenetic examinations were conducted on 219 patients referred for mental retardation, delayed mile stones and Down's syndrome; and other phenotypic abnormalities like Patau's syndrome, Edward syndrome, multiple congenital anomalies, meningocoele and cleft palate. Under these clinical diagnosis, 133 males and 86 females were studied. Details of all these patients are summarized in Table-1. The Table-2 gives the different clinical features with their cytogenetic findings in Trisomy 21 and in mosaic as well as patients with normal cytogenetic findings. Age and sex of the patients with the complaints of mental retardation, delayed mile stones and Down's syndrome are summarized in Table-3. The Table-4 focussed on the maternal age at the time of birth of 80 patients of Down's syndrome and mosaic patients. The chronological order and maternal obstetrical history of the Down's syndrome and mosaic patients are recorded in Table-5. Dermatoglyphic studies were conducted on 25 patients with clinical complaints of mental retardation, Down's syndrome and delayed mile stones have been shown in Table-6.

(a) In the male patients with Trisomy 21

Clinical features like flat bridge of nose found in 50%, simian crease in 37.50%, short crooked fifth finger in 22.50%, furrowed protruding tongue in 37.50%, narrow high arch palate in 45%, flat occiput in 27.50%, mongoloid slant in 47.50%, mental retardation in 32.50%, undescended testes in 25%, ears deformity/abnormality in 35%, increase distance between big toe and second toe in 22.50%, delayed mile stones in 27.50%, epicanthic fold in 22.50% (Refer Table-2; Fig.6 and Fig.7).

(b) In the female patients with Trisomy 21

Clinical features like flat bridge of nose found in 54.50%, simian crease in 31.80%, short crooked fifth fingers in 27.30%, epicanthus in 13.60%, furrowed and protruding tongue in 22.70%, narrow high arch palate in 22.70%, flat occiput in 22.70%, mongoloid slant in 45.45%, mental retardation in 59%, ears deformity/abnormality in 40.90%, increase distance between big toe and second in 13.60%, delayed miles stones in 50% (Refer Table-2).

(c) In both males and females

With clinical diagnosis of mental retardation, delayed mile stones and Down's syndrome, the cytogenetic findings are found normal i.e. 46,XY and 46,XX. The clinical features like flat bridge of nose : 17.75%; simian crease : 6.45%; short crooked fifth fingers : 2.40%; epicanthus : 5.65%; furrowed and protruding tongue : 8.90%; narrow high arch palate : 29.80% flat occiput : 8.90%; mongoloid slant : 16.10%; mental retardation : 50.80%; ears deformity/abnormality : 17.75%; delayed mile stones : 21.0% (Refer Table-2).

Maximum patients with the clinical diagnosis of mental retardation, delayed mile stones and Down's syndrome are from the age group of 1 to 6 years, 91 cases (43.10%) out of 211 patients. The patients with clinical diagnosis of mental retardation are 45 out of 91 (49.45%), delayed mile stones 17 (18.70%), Down's syndrome 29 (23.40%).

The age group 6-12 years is the next with 36 numbers of patients (17%) out of 211 referred. Out of 36 patients with mental retardation are 23 (63.88%), delayed mile stones 4 (11.10%), Down's syndrome 9 (25.0%) (Table-3).

The third group consists of 34 numbers of patients, out of 211 (16.10%) with the age between 1 month and 12 months. Mental retardation 15 (44.10%), delayed mile stones 7 (20.50%), Down's syndrome 12 (35.30%).

Fourth group of 27 patients out of 211 (12.80%) with the age of 12 years and above. Mental retardation 22 (81.50%), delayed mile stones 1 (3.70%); Down's syndrome 4 (14.80%).

The last group consists of 23 patients below the age of one month.

The Table-4 shows the maternal age at the birth of Down's syndrome and mosaic child. In the present study, it is found that the maternal age is below 24 years at the birth of Down's syndrome child in about 57.50% and 11.25% the mother's age is below 24 years at the time of birth of mosaic child.

Maximum number of Down's syndrome and mosaic children are borned to primi younger mother (Table-5). In the mother, where the patients' chronological order is second, found to have maximum abortions particularly in first trimester. Though the dermatographic pattern could not be studied in all the patients, it is performed only 25 patients (Table-6). In the patients with Trisomy 21 - ulnar loop were present in 70% of the patients. Whorls in 22.85%; simian crease 85.70%.

The patients clinically diagnosed as Down's syndrome but cytogenetically found normal show ulnar loop 72.50% and whorls 20%, simian crease 75%.

In the patients clinical diagnosed as mentally retarded with normal karyotype ulnar loop found in 60% of the patients, whorls in 31.80%, simian crease 45.45%.

In the group referred for delayed mile stones :

Karyotype with Trisomy 21 shows ulnar loop in 60%; whorls in 40%; simian crease 100%.

In patients with normal karyotypes: Ulnar loop 50%; whorls in 30%; simian crease in 66.66%.

If we considered the dermatoglyphic study in all 25 patients, the ulnar loops found on 64.70% fingers; whorls on 28.25%; simian crease was in 65.38%.

Trisomy 18 (Edward's Syndrome)

Under this group 3 males and 1 female were referred to rule out Edward's syndrome. First case (NL) one month old male child with prominent occiput, micrognathia low set ears, short neck, low hair line at neck, flexed extremities with overlapping fingers, hypoplastic fifth finger nail, prominent calcaneous, Rocker bottom feet, small toe nails, dorsiflexed toe, bilateral inguinal hernia, limited hip abduction. He was a 4th child of non-consanguinous parents. He had 3 elder sisters and reported normal. In delayed mile stone patient karyotype showed 47,XY +18.

Second case (GD) 2½ years old male, referred with the complain of cerebral palsy, mental retardation, bilateral flat feet, Rocker bottom feet, clinodactyly. He was one of the child of dizygotic twin. His sister was normal. He started standing with support at the age of 15 months, speak monosyllabus - 18 months but could not walk till today. Incordination of eyes movements. Adductor spasm was there. Shortening of left lower limb by 1 cm. gait lordotic, and walks side ways, incurving of little finger. Height was 86 cms and weight 12.1 kg. Presence of simian crease (Fig.8). His cytogenetic examination revealed 47,XY +18 (Fig.9).

Third patient ( ) aged 2 years old male referred for cytogenetic study had hypertonicity, low set malformed ears, prominent occiput, short overlapping of fingers, Rocker bottom feet, mental retardation, unable to stand, no speech. His cytogenetic examination showed 47,XY +18.

Fourth patient was female (YS) 14 months old. She was the 4th child first abortion at 5th month, the other two were brothers and both were normal. She had a complain of producing noise while taking respiration since birth. Swelling in the neck (small cystic swelling). Since 12 months (s/o thyroglossal cyst), h/o recurrent cough and cold, delayed mile stones, prominent occiput, antimongoloid slant, hypertelorism, low set ears, depressed bridge of nose, high arched palate, flexion of the

fingers with inwardly related thumb, clinodactyly, wide ATD angle, indirect very small inguinal hernia, Rocker bottom feet. Her cytogenetic study revealed 47,XX +18.

Two patients, one male and other female were found to have 47,XY +15 and 47,XX +15 respectively. Male patient (KR) was 4 years old and the second child borned when the mother's age was 21 years old. The patient was mentally retarded, hypospadias present, VSD present, epicanthic fold and hypotelorism were present, delayed mile stones. His cytogenetic finding was 47,XY +15. Clinically diagnosed as Trichotelomenia (Fig.10).

The female patient (DP) aged 20 years, referred with the complaint of mental retardation, mental age was 6 years and I.Q. 37. She was the 4th child of 5 children. Simian crease present on left side. Karyotype was 47,XX +15.

One case (JK) 6 months old male, second child of non-consanguious parents. First pregnancy turned out into abortion at third month of pregnancy. The patient had weak cry accompanied with spasm of the whole body. Rolling of the eye while crying. Large and inverted ear lobules, depressed front and sides of the head, noisy breathing hypospadias, penis fused with the scrotum, hip extension, right lateral squint. Clinically diagnosed as ? cat cry syndrome. Birth weight was 3½ kg, weight at the age of 1 year 6½ kg. height at 1 year 68 cms. Delayed mile stones. The karyotype showed 46,XY/45,XY - F group chromosome (Fig.11).

Table-1 : Cytogenetic findings in 219 patients studied for mental retardation, delayed mile stones and Down's syndrome

Clinical diagnosis	Total No. of cases	Karyotype	Total No. of cases
Mental retardation	Male - 62	46,XY	46
		47,XY, +21	11
		46,XY/47,XY +21	05
	Female - 42	46,XX	32
		47,XX +21	07
		46,XX/47,XX +21	03
Delayed mile stones	Male - 16	46,XY	10
		47,XY +21	03
		46,XY/47,XY +21	02
		47,XY +E	01
	Female - 10	46,XX	07
		47,XX +21	03
Down's syndrome	Male - 41	46,XY	14
		47,XY +21	24
		46,XY/47,XY +21	03
	Female - 25	46,XX	10
		47,XX +21	11
		46,XX/47,XX +21	03
		48,XXX +21	01
	D/G translocation	47,XY +21/46,XY t(15:21)	02
Hypothyroidism	Male - 01	47,XY +21	01

Clinical diagnosis	Total No. of cases	Karyotype	Total No. of cases
Congenital occipital meningocoele with cleft palate	Female - 01	47,XX +21	01
Multiple congenital	Male - 03	46,XX	02
		47,XY +21	01
	Female - 03	46,XX	03
Patau's syndrome	Male - 01	46,XY	01
Mental retardation ? Edward's syndrome	Male - 01	46,XY	01
	Female - 01	46,XX	01
Premature therarchi	Female - 01	46,XX	01
Mental retardation ? Turner's syndrome	Female - 01	46,XX	01
OTHER AUTOSOMAL ABNORMALITIES			
Edward's	Male - 03	47,XY +18	03
syndrome	Female - 01	47,XX +18	01
D group trisomy	Male - 01		02
Patau's syndrome	Female - 01		
F group	Male - 01	45,XX -20	01
anomalies	Female - 01	48,XXX +20	01

Table-2 : Clinical features in the patients with mental retardation, delayed mile stones, Down's syndrome (based on Oster's diagnostic characteristics and with other additional common features (202 cases)

Clinical features	46,XY	46,XX	Karyotype findings	46,XY/ 47,XY +21	47,XX +21	46,XX/ 47,XX +21
			47,XY +21			
	(72)	(52)	(40)	(10)	(22)	(06)
1	2	3	4	5	6	7
Flat bridge of nose	13	09	20(50.00%)	2	12(54.50%)	3
Simian line	05	03	15(37.50%)	-	07(31.80%)	1
Short crooked 5th finger	02	01	09(22.50%)	-	06(27.30%)	1
Short broad hands	02	02	04	1	04	1
Hyperflexibility of joints	07	02	03	-	01	
Oblique palpebral fissures	00	01	-	-	-	-
Epicanthus	03	04	09(22.50%)	1	03(13.60%)	1
Furrowed and protruding tongue	07	04	15(37.50%)	-	05(22.70%)	-
Narrow high arch palate*	24	13	18(45.00%)	4	05(22.70%)	6
Flat occiput	04	07	11(27.50%)	-	05(22.70%)	-
Irregular abnormal sets of teeth	02	00	02	-	-	-

Table-2 : Contd.

1	2	3	4	5	6	7
Mongoloid slant	12	08	19(47.50%)	1	10(45.45%)	2
Mental retardation	38	25	13(32.50%)	7	13(59.00%)	5
Undescended testis	07	00	10(25.00%)	-	-	-
Ears deformity/ abnormality	15	07	14(35.00%)	-	09(40.00%)	2
Increase distance between big toe and second toe	00	03	09(22.50%)	-	03(13.60%)	
Delayed mile stones	19	07	11(27.50%)	1	11(50.00%)	-

Table-3 : Age and sex of the patients in mental retardation, delayed mile stones and Down's syndrome

Patients age	Mental retardation		Delayed mile stones		Down's syndrome		Total
	Male	Female	Male	Female	Male	Female	
Less than one month	04	05	03	00	06	05	23
1-12 months	08	07	06	01	05	07	34
1-6 years	24	21	11	06	21	08	91
6-12 years	15	08	01	03	06	03	36
12 years	16	06	01	00	03	01	27
Total	67	47	22	10	41	24	211

Age was not recorded in eight patients.

Table-4 : Maternal age at the time of birth of Down's syndrome and mosaic patients (80 cases)

Present recorded patient's age	47,XY +21				46,XY/47, +21				47,XX +21				46,XX/47,XX +21			
	Maternal age (in years)															
	Less than 20	20-24	25-30	More than 30	Less than 20	20-24	25-30	More than 30	Less than 20	20-24	25-30	More than 30	Less than 20	20-24	25-30	More than 30
0-1 month	1	-	2	1	-	-	-	-	-	1	-	-	-	-	-	-
1-12 months	-	6	1	-	-	1	-	-	1	1	-	1	-	1	-	-
1-6 years	7	13	4	1	-	-	-	-	1	7	3	1	-	-	-	-
6-12 years	1	3	1	-	-	2	-	1	-	1	-	-	-	2	1	-
12 years and above	-	3	1	4	-	2	1	1	-	-	1	-	-	1	-	-
Total	9	25	9	6	-	5	1	2	2	10	4	2	-	4	1	-
Percentage	11.25	31.25	11.25	7.5	-	6.25	1.25	2.5	2.5	12.5	5.0	2.5	-	5.0	1.25	-

Frequency of Down's syndrome	Mother age below 24 years	Mother age between 25-30 years	Mother age above 30 years
	57.50%	16.25%	10.00%
Mosaicism	11.25%	2.50%	2.50%
Total	68.75%	18.75%	12.50%

Table-5 : Chronological order of Down's syndrome and mosaic patients and maternal obstetrical history

Chronological order of Down's and Mosaic patients	Maternal obstetrical history																													
	Gravida										Para										Abortion trimester			Total number				Still birth		
	1	2	3	4	5	6	7	8	9	10	1	2	3	4	5	6	7	8	9	10	1	2	3	1	2	3	4			
1	21	6	5	1							20	6	4	1							2				2					
2		13	9	2		2					2	1	4	1	1	1					6	2	2		10					
3			9	2							1	8	2								2	1								
4				3								1	3								1									
5					2								1		1						1	1								
6						2									1	1					1									
7							1										1													
8																														
9									1										1											
10										1										1	1									

Table-6 : Dermatographic pattern in Down's syndrome, mental retardation and delayed mile stone (study conducted on 25 patients)

	Down's Syndrome										Mental retardation										Delayed mile stone									
	Trisomy 21 : 7					Normal : 4					Trisomy 21 :					Normal : 11					Trisomy 21:1					Normal : 3				
Simian crease																														
Right hand			6					3									6					1					2			
Left hand			6					3									4					1					2			
	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
Dermal ridges on fingers																														
Ulnar loop (UL) Left hand	4	6	6	-	6	3	2	4	2	2						8	2	7	8	7		1			1		3	2	1	2
Right hand	5	6	7	3	6	2	4	4	3	3						6	3	9	7	9	1	1	1		1	1	2	1	1	1
Radial loop (RL) Left hand				2			1										2													
Right hand																	2													
Whorl (W) Left hand	2		1	4	1	1	1		1	1						2	5	3	4	5	1		1	1		2			2	1
Right hand	2	1		4	1	2			1	1						3	6	2	3	2				1		1	1		1	1
Arch (A) Left hand	1	1		1			1			1							2	1								1		1		
Right hand																1				1						1				

a + d	Rt	Lt	Rt	Lt
Wide	6	6	2	2
Normal	2	2	1	1

One case dermal pattern was found to be under-developed.

Table-6 : Contd.

Trisomy 21		Normal	
UL 70-49	= 70.00%	UL	= 72.50%
RL	= 2.85%	RL	= 2.50%
W	= 22.85%	W	= 20.00%
A	= 4.28%	A	= 5.00%
Simian crease	= 85.71%	Simian crease	= 70.00%

MR : Normal

UL	= 60.00%
RL	= 3.63%
W	= 31.80%
A	= 4.55%
Simian crease	= 45.45%

Delayed Mile Stones		Normal	
Trisomy 21			
UL	= 60.00%	UL	= 50.00%
RL	= -	RL	= 10.00% ?
W	= 40.00%	W	= 30.00%
A	= -	A	= 10.00%
Simian crease	= 100.00	Simian crease	= 66.66%

165/255	UL	= 64.70%
407/255	RL	= 2.75%
72/255	W	= 28.25%
13/255	A	= 5.00%
34/52	Simian crease	= 65.38%

PART-II : SEX CHROMOSOME

Cytogenetic study of 454 patients with abnormal sexual phenotype was conducted. The patients comprising of 228 females, 183 males and 40 individuals with ambiguous sex. The female patients were referred with the complaint of short stature, primary amenorrhoea, delayed menarche, infertility, absence of secondary sexual characters, spontaneous abortions, hersuitism etc. Male patients were referred with complaints of hypogonadism, hypospadias, delayed puberty, sterility, azoospermia, Klinefelter's syndrome etc. Details of the referred cases are summarized in different groups with the age, clinical features, and cytogenetic findings in Table-7 and Table-8. Other 40 cases with ambiguous genitalia and 40 cases of haematological malignancies are summarized in Table-9, Table-16 and Table-17 respectively. The hormonal estimations were done in certain cases of different groups included in the observations of respective patients.

Out of 454 cases studied, 44 cases are showing chromosomal abnormalities and mosaicism. In addition to these, cases of true hermaphroditism, testicular feminization syndrome, gonadal agenesis were also found.

The details of the cases with their clinical data and cytogenetic findings are given below :

Turner's Syndrome

There are 12 patients with Turner's syndrome and Mullerian agenesis. Out of 12, 3 had karyotype 45,X (Table-10 and 5; Patients numbers 7,8,9); 6 had 45,X/46,XX (Patients from 1 to 6); mosaicism. One with 45,X/46,XX marker (Patient No.11) and other showed 46,X, isoX(q) (Patients 10 and 12) chromosomal complement.

Clinical features including age, height, secondary sexual characters, gynaecological and cytogenetic findings are summarized in Table-10 and Table-11. Out of 12 patients, 2 were found mentally abnormal. All were with a normal colour vision. No consanguinity were reported.

Out of the 3 cases of 45,X; one case number 7 (AS) found to have congenital abnormality of external and internal genitalia. She was second child of the two children, other sister was found to be normal genotypically and phenotypically. Hormonal findings indicate hypogonadotrophic hypogonadism (Table-11 - No.7).

The second case (No.8 - RC) with 45,X karyotype showed short stature with short neck, cubitus valgus, low hair line, broad chest with widely spaced nipples. Absence of secondary sexual characters with axillary and pubic hair are sparse. The external genitalia to juvenile type. Simian crease was found in this case. She was the third child and had two brothers and one sister who were all phenotypically normal. Her hormonal essay of S.FSH and SLH were high (FSH 155 mlu/ml; SLH 80 mlu/ml), suggestive of chromosomally incompetent primary ovarian failure (CTOF) (Table-11, No.8, Fig.12 and 13).

Another case-9, only child with 45,X karyotype with short stature bilateral cubitus valgus, shield chest, absence of menstruation. Axillary and pubic hair are scanty, infantile external genitalia. Hypoplastic uterus, and pouch like vagina. Her hormonal levels of S.FSH and S.LH were high (FSH 170 mlu/ml; LH 80 mlu/ml), suggestive of ovarian dysgenesis (Table-11; No.9).

In the present study, 6 patients had 45,X/46,XX type of mosaic line. One patient (BK) with short and webbed neck, spina bifida (cervical), protruding tongue were referred with Turner's stigmata. The ovaries and uterus were not examined. Vagina was present. She was the second child in her family. First was normal phenotypic male. Mother had both full term normal deliveries. Hormonal study could not be conducted (Table-11 No.1; Fig.14).

Second patient (SR) came with the chief complaints of short stature, delayed menarche, infantile external genitalia. No axillary and pubic hair, underdeveloped breast. Ovaries were not examined. Per rectum examination showed presence of rudimentary hypoplastic uterus. Hormonal

findings were S.FSH 125 mIu/ml, L.H. 40 mIu/ml. Testosterone was 0.5 ng/ml. (Table-11; No.2).

Third patient (DH) was referred for primary amenorrhoea with short stature, under-developed breast, absence of pubic and axillary hair. She was the second child in the family having one eldest brother and two younger sisters with normal phenotypic and menstrual histories. Per rectal examination uterus was not felt. Fat distribution was normal. Vagina was normal (Table-11, No.3).

Fourth patient (NK) came with the chief complaint of 4 consecutive first trimester abortions with normal phenotypic features and anthropometric measurements. Her husband karyotype was normal (Table-11, No.4).

Fifth patient (SP) was the case of primary amenorrhoea with short stature. Secondary sexual characters were under-developed. Ovaries were were not examined. Hypoplastic uterus was felt per rectal examination. Family history was not recorded (Table-11, No.5).

The last case with 45,X/46,XX mosaicism was referred for Turner's syndrome. She had hypoplastic uterus. She has three sisters, all were cytogenetically normal. Hormonal study in patients numbers 2, 5 and 6 showed chromosomally incompetent primary ovarian failure (CIOF) (Table11 No.6).

One patient (TA) was referred for short stature, primary amenorrhoea, under-developed secondary sexual characters. Per rectum examination small nodule of uterus was felt. Streak ovaries and absence of uterus were found in laparotomy. Histopathological examination showed few atretic primary follicles with abundant ovarian stroma (Fig.15). However, the clear differentiation of ovarian tissue could not be observed. She had one elder brother and one younger sister. Both were found to have normal karyotype, while the patient (TA) revealed 46,X - X, iso(Xq). Looking to the family study, iso(Xq) origin probably was denovo. Her hormonal profile showed high values of S.FSH and S.LH; suggestive of primary ovarian failure (Table-11, No.10, Fig.16 and 17).

One unmarried girl (LD) was referred with the complaint of primary amenorrhoea, short stature, under-developed secondary sexual characters with absence of axillary and pubic hair, shield chest, cubitus valgus, low hair line and increased distance between big toe and second toe. Per rectum as well as ultrasonographic examination did not reveal uterine and ovarian shadow in pelvis. Her serum gonadotrophin levels were elevated indicating the chromosomally incompetent primary ovarian failure (CIOF). Her cytogenetic study showed mosaic cell line 45,X/46,X + marker. Family study could not be conducted as the patient did not come for follow up (Table-11, No.11, Fig.18).

Last case of iso(Xq) had short stature, primary amenorrhoea, scanty axillary and pubic hair, breast not developed. Ultrasonography examination showed uterine shadow but ovarian shadow was not found. Patient's parents had refused for biopsy of gonad and uterus for histopathological examination. Patient was not available for the study to rule out the origin of isochromosome (Table-11, No.12).

Testicular Feminization Syndrome

One girl aged 19 years (KL) was referred for primary amenorrhoea, short stature, height 160 cms and span 164 cms, height less than span. Breast was not developed, shield-like chest and masculine characters. History of parents gave consanguinous marriage between first cousins. Phenotypic features of external genitalia showed enlarged clitoris, blind pouch of vagina and bilateral undescended testes, left was in the labia and the right one was in inguinal canal. Cytogenetic study showed 46,XY chromosomal constituents. Hormonal profile showed S.FSH 21 mIu/ml, LH 24 mIu/ml. Testosterone 5 ng/ml. Chromosomal study 46,XY and hormonal levels indicated the testicular feminization syndrome.

Other case was a girl (RG) 20 year old, with primary amenorrhoea. The anthropometric measurements were height 160 cms, span 170 cms and weight 44 kg. On clinical examination, she had normal external genitalia, blind vaginal pouch, well developed breast, pubic hair were present with scanty or absence of axillary hair. There was inguinal swelling, inguinal

testes. Ultrasonography showed absence of both uterus and ovaries and confirmed inguinal testes. Histopathology of biopsy from both the sides gonadal tissue confirmed the presence of atrophic seminiferous tubules, thick fibrous and highly vascular tunica vaginalis. There were no signs of active spermatogenesis. The cytogenetic findings were 46,XY. Considering the findings of histopathology and cytogenetic, this was the case of testicular feminization syndrome. Hypertrophy of Leydig cells was found (Fig.19 and Fig.20).

TP was 2 months old baby referred as a case of ambiguous genitalia. She was third child of non-consanguinous marriage. Her height was 53 cms, weight was 4.5 kg, head circumference was 37 cms. Testes were bilaterally palpable in labia majora. External genitalia were female type. Vaginal opening was also found. Cytogenetic findings of this patient were 46,XY. The patient was sex chromatin- (Barr bodies) negative. Genitogram showed presence of vagina, normal size uterus. Her serum testosterone level was undetectable. The 17 OH-progesterone was 4.0 ng/ml (normal range less than 2 ng/ml). This indicates that the undetectable T level is likely to be due to inborn error of metabolism affecting enzymes of testosterone synthesis, 5-reductase or the testosterone receptors. 17-OH progesterone was found elevated suggestive of mild adrenal hyperplasia (Fig.21).

Klinefelter's Syndrome

Thirteen patients were referred for primary sterility, azoospermia and Klinefelter's syndrome. Out of 13 patients, 9 have 47,XXY; 3 with 46,XY/47,XXY; one with 48,XXY, +21 were found. Complete clinical data including age, height, secondary sexual characters, hormonal findings are shown in Table-12 and Table-13. Two patients were found with I.Q. below average. None of them was colour blind. Four patients were married and were azoospermic. All the patients were tall. Six patients were referred for hypospadias and hypogonadism; seven patients with gynaecomastia, azoospermia and Klinefelter's syndrome. Hormonal profile showed high gonadotrophin and low testosterone suggestive of primary testicular failure (Fig.22 and Fig.23).

Sex Chromosome Mosaicism

In 16 cases, chromosome mosaicism were detected. Seven cases were described as Turner's mosaicism and three were described as Klinefelter's mosaic. Other 2 cases include XX/XXX mosaicism in primary amenorrhoea and sterility, one with XX/XY mosaicism in spontaneous abortion, two with XX/XY in ambiguous genitalia and hypogonadism. One with 45,X/46,XX mosaicism in spontaneous abortion.

XX/XY Mosaicism

XX/XY mosaicism was found in a woman with complaint of spontaneous abortions. She was 31 years old female, non-consanguinous marriage with 34 years male. She gave history of 5 an embryonic pregnancies. She had feminine characters with well developed breast and axillary and pubic hairs. Average height, 10% metaphases show XY chromosome constitution. Her husband karyotype was normal. Further endocrinological study and gonadal status could not be performed as patient refused for follow up (Fig.24).

Second case with XX/XY mosaicism was a 10 year old boy with hypospadias. He was second child of non-consanguinous marriage. Anthropometric data show 112 cms, height 20 kg and 106 cms span. Mile stones were normal, external genitalia are of male type, penis normal in size, bifid scrotum with rugosity, pubic and axillary hair present both the testes were not palpable. 100 metaphases were analysed, in 80% of cell with XY constituents and 20% cell with XX constituents were found. The patient refused for follow up. Hence no further tests were conducted.

Third case was 17 year old female with ambiguous genitalia. The patient was referred as a male upto the age of 13 years. Her external genitalia were female type with enlarged clitoris, vaginal opening with well developed secondary sexual characters and enlarged breast. After the age of 13 years, the patient started regular menstruating cycle every month lasting 4-5 days. She has bifid scrotum and labia majora, penis, phallus present, urethral opening was present. A mass could be palpated in right

labia majora. Her ultrasonography examination revealed the presence of left ovary. The uterus was not seen. Both kidneys and bladder were normal. Cytogenetic finding was 46,XX/46,XY mosaic cell line (95% : 5%). Biopsy was performed for the mass palpated in right labia major. It consisted of two masses. One was testicular tissue with atrophic seminiferous tubules. Some tubules found to have single layer of epithelium, while cell debris found in lumen of other tubules. There was no sign of spermatogenesis. The mass showed ovarian fibrous stroma containing atretic primary follicles and under-developed, undifferentiated ovarian tissue observed. This shows that the tissue mass obtained from the right labia was ovotestis. Few days after the removal of ovotestis serum levels of S. testosterone was found to decrease from 0-65 ng/ml in preoperative condition to 0.5 ng/ml and 17-hydroxy-progesterone from 1.2 ng/ml to 0.09 ng/ml (Refer Table-15; Case-18) (Fig.25 and Fig.26).

Spontaneous Abortions

Seventy couples with repeated (spontaneous) abortions were studied for cytogenetic findings. Two cases, one (NK) with X/XX mosaic discussed as fourth case in mosaic group. Second case is discussed earlier in XX/XY mosaicism.

Third case found to have balanced Robertsonian translocation. Twenty-five year old female, phenotypically normal referred for 3 consecutive abortions. Gynaecological history indicates that commencement of menarche at 14 years of age, gynaecological examination was normal, secondary sexual characters were normal. She got married at the age of 20 years. Her blood culture was repeated twice and 50 G-banded metaphases were analysed each time and 45,XX were found. Robertsonian translocation (RT) (centric fusion) of chromosome 13 and 14 was found. Karyotype was 45,XX - 13-14 (13q; 14q). Proband parents and other family members were also studied. Her father showed 45,XX - 13, -14 + (13q; 14q). Her younger sister has a same translocation. This translocation proved as the paternal origin as proband mother was normal (Fig.27 and Fig.28).

Ambiguous Genitalia

Forty cases with ambiguous genitalia were referred for analysing the genetic sex. Twenty five cases were referred as male and 15 referred as female. On genetic analysis, 29 were having XY male karyotype and 11 with female karyotype (Table-9, Table-15 and Table-16).

Out of 29 cases with male karyotype 6 showed undescended testes on both sides. In 11 cases, left testis was found to be undescended, 5 showed right undescended testis, 6 cases with both sides descended testes. Three showed right descended testis and left inguinal testis.

Case 4 (Table-15), 2 years old baby, referred as female, born to non-consanguinous parents. External genitalia showed hypertrophied clitoris, both sides undescended testes. Baby was operated for inguinal hernia at the age of 1 year. Biopsy showed presence of testicular tissue.

Case-10 (Table-15) was a 10 days old baby referred as male. Testes were not palpated at both sides, phallus was small, no labia majora, no vaginal opening. Under ultrasonography, no uterus or ovaries visualised. Urethral opening was found with phallus. Follow up could not be done.

Case No.18 (Table-15) is already described in detail on XX/XY mosaic group.

Case No.21 and Case No.22, both were brothers referred as male, one (SAK) was 5 years old and other (AAK) was 7 years old. No history of consanguinous marriage. No history of hormonal treatment during pregnancy. Presence of abnormal external genitals - female type with small bilateral testes ? Anthropometric data showed :

SAK (5 years)		**AAK (7 years)**	
Height	= 104 cms	Height	= 116 cms
Weight	= 16 kg	Weight	= 17.5 kg
CC	= 53 cms	CC	= 52 cms

SAK (5 years)		**AAK (7 years)**	
HC	= 50 cms	HC	= 53 cms
$S.T_3$	= 172 (80-230 ng%)	$S.T_3$	= 164 (80-230 ng%)
$S.T_4$	= 15 (4-13 ng%)	$S.T_4$	= 13 (4-13 ng%)
Sex chromatin	= Negative	Sex chromatin	= Negative

The patient (SAK) was given Inj.HCG 1000 U/I.M. and the length of phallus was 10 mm. Ten days after the injection phallus length was 12 mm. S.testosterone (post-HCG) - 0.35 ng/ml (normal less than 1 ng/ml). Karyotype in both cases were 46,XY (Fig.29, 30 and 31).

Case No.4 (Table-16) was a 6 month old baby referred as female, with ambiguous genitalia. Under ultrasonography examination of pelvic region small hypoacholic area was found posterior to bladder which could be small vaginal or uterine shadow. No other pelvic mass seen. Normal urinary bladder was observed by cystogram by catheterization through a single opening between two labia. Vagina could not be seen. Cytogenetic study by performing all G-banding, C-banding showed only 46,XX mosaicism was deleted. 17-ketosteroid in urine was 0.5 ug/24 hours - normal range less than 3 ng/24 hours in urine.

Right gonad biopsy revealed immature seminiferous tubules, ovarian tissue with primordial follicles. One tubular structure found attached to this gonad showed vascular channels, and duct with ciliated columnar epithelium.

On left side the gonadal microscopic examination revealed ovarian stroma with primordial follicles, cord like structure revealed duct, lined by flattened and cuboidal epithelium. Right gonad was diagnosed as ovotestis and the left gonad with ovary. Both the gonads were removed and the hormonal study was done on the blood collected, revealed absence of S.estradiol, S.testosterone, and S.DHES. The absence of hormone suggests absence of hormone secretion at the gonadal level (Fig.32 and Fig.33).

Case No.2 (Table-16) was a 2 year old, referred as female with unidentified external genitalia. Skin was dry. Thyroid function tests were carried out and showed primary hypothyroidism. The treatment Eltroxin was given. Gradually she developed normal external genitalia.

Case No.8 (Table-16) was a 17 years male with male type of external genitalia, bilateral undescended ? testes in scrotal sac. Gynaecomastia present. Ultrasonography shows uterine shadows and also ovaries. Laparoscopy confirmed uterus, fallopian tube and ovaries. The patient was masculine and complaining spotting every month. Karyotype was 46,XX.

XY Agonadism

20 year old male was referred for cytogenetic evaluation with the complain of ambiguous genitalia. No history of consanguinous marriage of parents. He was born as third child at full term normal delivery. He had one brother and one sister. The cytogenetic study could not be performed on them as they were not present. Family history gives no evidence of any abnormal phenotypic features in his relatives. His height was 168 cms, weight was 50 kg and span 190 cms. He was mentally normal and had a male psychological orientation as he had been brought up as a male. He had well developed beard and moustache. No gynaecomastia. Other secondary sexual characters, pubic and axillary hair were normal. Clinical examination showed female type of genitalia, labia majora, labia minora, hypertrophied clitoris and vaginal opening. Bilateral absent of testes. Penile urethra was normal and opening was found below clitoris. On examination, vaginal length was found to be normal with the presence of knob like uterus. Exploratory laparotomy was carried to find out the gonads, but no gonad either testes or ovaries were seen. Biopsy of fibrous fatty tissue was conducted (Fig.34). It showed no evidence of testicular or ovarian tissue - uterus was rudimentary with fibrous band going on both the sides of uterus. Hormonal study showed high levels of F.S.H. and serum L.H. (80 mIu/ml and 45 mIu/ml respectively). S. testosterone was 0.9 ng/ml which was very low. HCG stimulation was carried out by giving intra-muscular injection of profaccy (HCG) to know the functional ability of Leydig cells. Plasma T assay was done at 48

hours and 72 hours and could not find any difference with basal value. These could be because of :

(i) either the Leydig cell does not respond to stimulus, or
(ii) testicular or gonadal dysgenesis of agenesis.

His cytogenetic findings showed 46,XY normal male karyotype (Fig.35).

In other case, three brothers were referred for hypogonadism and absence of secondary sexual characters (Fig.36).

One elder brother (SH) aged 24 years, with the complaint of infantile genitalia, absence of beard and moustache, no axillary and pubic hair, slightly feminine voice, ultrasonography examination revealed absence of testes, uterus and ovaries. Both kidneys were normal. The hormonal studies revealed that he had low levels of S.FSH and LH (1.5 miu/ml and 4.5 mIu/ml, respectively) (normal value adult FSH 3.0-11.0 miu/ml and LH 5.0-28.0 miu/ml); with low testosterone (0.8 ng/ml). The patient's anthropometric measurements were : height 176 cms, weight 75 kgs and span 180 cms. His cytogenetic findings found to be 46,XY male karyotype (Fig.37).

Second brother (Iq) aged 18 years, height 168 cms, weight 68 kg and span 170 cms referred for under-developed external genitalia absence of axillary and pubic hair, undescended (both) tests, no beard and moustache, ? gynaecomastia. Ultrasonographic examination showed both kidneys and urinary bladder were normal, no uterus, no ovaries, absence of testes. Endocrinological profile revealed serum FSH and LH and low level of S.testosterone i.e. 2.3 mIu/ml, 3.4 mIu/ml and 0.6 ng/ml, respectively). There was no elevation of serum testosterone levels following HCG stimulation (72 hours post-HCG levels 0.65 ng/ml); cytogenetic study showed normal, 46,XY chromosome complement.

Third brother (Ak), aged 20 years was referred for under-developed external genitalia with bilateral undescended testes. Height was 165 cms, weight 65 kg and span 170 cms. Absence of axillary and pubic hairs, no

moustache and beard, gynaecomastia + ultrasonography revealed normal, right kidney and absence of left kidney, ureter and bladder normal, urethral opening was found in small ? penis and no echo-images was found from the region of uterus and gonads. Hormonal studies revealed S.FSH 2.5 mIu/ml and LH 5.8 mIu/ml (normal value FSH 3-11 mIu/ml and LH 5.0-28 mIu/ml), low level of S.testosterone 0.8 ng/ml. Intramuscular injection of HCG was given to stimulate Leydig cells. The post-HCG level of T was not found to increase (0.85 ng/ml). His karyotype was 46,XY.

All the above three had male psychological orientation and no history of consanguinous marriage in their parents. Further studies in all these cases are in progress.

Sister's son (Jd), 3 years old (Fig.36) with under-developed genitalia. Penis is little under-developed. Testes were small descended in labio-scrotal fold. S.FSH and LH were 2.0 mIu/ml and 4.0 mIu/ml (normal range 1-9 mIu/ml and LH 3-17 mIu/ml); while S.testosterone was low. Further examination is in progress.

Patient named FR - 17 years old male (Fig.38) referred for cytogenetic examination. He had right descended testis with right side inguino-scrotal hernia since 2 years. While left testis was undescended and could not be located in the scrotum. Initially hernia was reducible and painless but later on it had become irreducible and slightly painful. On clinical examination, it seemed to be right indirect inguinal hernia with left undescended testes. He was operated for hernia. On opening up the hernial sac, it was found ? uterus with fallopian tubes ? testis or ovary or ovotestis. The sac had also an ectopic testis (Fig.39). Histological examination revealed that section of ? uterus showed presence of endometrium and myometrium (Fig.40a). The tissue below the tube ? ovary showed pumpiniform venous plexus. The testis/ovary ? ovotestis section showed testicular atrophy (Fig.40b). The biopsy of right descended testes showed thickening of basement membrane, paucity of germ cells and maturation (Fig.40c). Abnormal presence of uterus and cytogenetic finding 46,XY suggestive of dysgenesis male pseudohermaphrodite.

One girl (PM) 20 years old, born to non-consanguinous parents. Proband was the youngest and 7th child in the family had 3 brothers and 3 sisters, reported phenotypically normal. Mother's age at the time of birth was 30 years. She was referred for primary amenorrhoea and intersex. She had right sided inguinal ? testis (Fig.41) and on exploratory laparoscopy was done and revealed left side fallopian tube and ovary seen, uterus was not seen and felt on per rectum examination. There was blind pouch of vagina (Fig.42), well developed external genitalia with pubic hair female type. Breasts are well developed. Her karyotype was 46,XX . She was operated for right sided hernia and the uterus was found. The uterus was planted near the blind end of vagina. Reconstruction of vagina was done.

XXX and XX/XXX Mosaicism

In the present study, 2 patients found to have XXX syndrome, the other two with XX/XXX mosaicism. They were referred basically with the complain of primary amenorrhoea.

First patient (SM) was 22 years normal phenotype married female with well developed external genitalia, breast and pubic and axillary hair. She was married and was referred for cytogenetic examination for primary amenorrhoea ? Mullerian agenesis. The height was 155 cms and weight 45.5 kg. External clinical examination showed blind pouch of vagina (1½"), cervix and uterus were not felt per rectum examination. Diagnostic laparoscopic examination revealed that both the ovaries were found to be related with big mass on right and small on left side. The hormonal study revealed high levels FSH (135 mIU/ml) and S.LH (60 mIU/ml) and low levels of estradiol and progesterone (10 mg/ml and 0.18 mg/ml) respectively. Cytogenetic finding showed 47,XXX.(Fig.43).

Second patient was 20 years old phenotypic female with primary amenorrhoea was referred for chromosomal study. Earlier she had undergone hormonal therapy but showed no response. Poor breast development with normal axillary and pubic hair. Laparoscopic findings

revealed presence of very small uterus, left ovary was absent, the right ovary was found to be under-developed. Cytogenetic findings revealed 47,XXX. 100 buccal mucosa cells were analysed, 25 cells showed double Barr bodies. Prolactin 9.0 ng/ml, S.FSH 130 mIU/ml, SLH 60 mIU/ml, estradiol 10 ng/ml and 0.20 was progesterone.

XX/XXX Mosaicism

A case (MA) of 16 years old girl with the delayed menarchi with short texture was referred for cytogenetic examination. She had one elder sister and younger brother. Both were normal. She was the second child born after full-term pregnancy to the parents with no consanguinity. Her height was 136 cms, weight was 26 kg. Secondary sexual characters were not well developed. Breast was nodule like. Small nodule was felt on per rectal examination on left side. Ultrasonographic examination revealed presence of uterus, ovaries were not seen. S.FSH 9.5 mIU/ml and SLH 2.2 mIU/ml. Her cytogenetic examination was 46,XX/47,XXX (80:20%).

Second case (SB) was 23 years old married woman. She started menstruating at the age of 15 years. The menstrual cycle was regular and continued for two years. Later on menstrual cycle became irregular and discontinued. Hormonal treatment was given but showed no response. Her height was 151 cms, weight was 38.4 kg. Laparoscopic findings revealed small uterus than normal. Both tubes were normal, both ovaries normal in size and shape, no ovulation point seen.

Biopsy of uterus showed no evidence of secretion i.e. scanty non-secretory endometrium. Her karyotype was 46,XX/47,XXX (95:5%).

Table-7 : Clinical complains, phenotypic features and cytogenetic findings in 228 females studied are given below

Age group (in years)	Clinical features	Total No.of cases	Karyotype	No.of cases
1	2	3	4	5
0-13	Short stature with or without Turner stigmata	09	46,X 46,XX/45,X 46,XX	02 01 06
	Rectovaginal fistula	03	46,XX	03
	Enlarged clitoris	01	46,XX	01
	Inguinal hernia	01	46,XX	01
14-17	Delayed menarche with short stature	13	46,XX 46,XX/47,XXX	12 01
	Delayed menarche with normal stature, hirsuitism	01	46,XX	01
18-30	Primary amenorrhoea with underdeveloped secondary sexual characters and short stature	16	46,XX 46,XX/45,X 46,XX/46,X + marker 46,X - X iso(Xq)	11 02 01 02
	Primary amenorrhoea with normal secondary sexual characters and normal stature	38	46,XX	38
	Primary amenorrhoea with blind vaginal pouch	07	46,XY 46,XX	02 05
	Primary amenorrhoea with Mullerian agenesis	12	46,XX 47,XXX 46,XX/45,X	08 02 02

Table-7 : Contd.

Age group (in years)	Clinical features	Total No.of cases	Karyotype	No.of cases
	Secondary amenorrhoea with irregular menstrual cycle	18	46,XX	13
	Sterility	12	46,XX	11
			46,XX/47,XXX	01
	Spontaneous abortions	70	46,XX	67
			46,XX/45,X	01
			46,XX-13-14 +t (13q; 14q)	01
	Delayed puberty	25	46,XX	25
	Intersex	01	46,XX	01

Table-8 : Clinical complains, phenotypic features and cytogenetic findings of 138 males studied are given below :

Age group (in years)	Clinical features	Total No.of cases	Karyotype	No.of cases
0-13	Hypospadias, bifid scrotum, undescended testes, etc. Hypogonadism	40	46,XY	33
			46,XXY	06
			46,XX/46,XY	01
14-17	Delayed puberty	05	46,XY	05
18-40	Hypogonadism,	35	46,XY	29
	delayed puberty		47,XXY	06
	Gynaecomastia,	33	46,XY	26
	azoospermia,		46,XY/47,XXY	03
	Klinefelter's syndrome		47,XXY	02
			48,XXY +21	01
			48,XXY +15	01
	Spontaneous abortions	70	46,XY	70

Table-9 : Clinical features and cytogenetic findings in 40 cases of ambiguous sex

Age group (in years)	Clinical features	Sex	Total No.of cases	Karyotype	No.of cases
0-13	Palpable descended testes:both sides	F	04	46,XY	04
		M	02	46,XY	02
	One side	M	12	46,XY	12
	Descended testes with female type genitalia	F	02	46,XY	02
		M	02	46,XY	02
	Undescended testes with male type genitalia	M	03	46,XY	03
	Undescended testes with female type genitalia	F	03	46,XY	02
				46,XX	01
		M	01	46,XX	01
	Enlarged hypertrophied clitoris with female type genitalia	F	05	46,XX	05
		M	01	46,XX	01
	Absence of testes, labia, scrotum and vagina not visualized.	M	01	46,XY	01
14-25	Male type genitalia with undescended testes as clitorial hypertrophy	M	02	46,XX	02
		F	01	46,XX/46,XY	01
	Undescended testes with female type external genitalia	F	01	46,XY	01

Table-10 : Phenotypic features of 12 patients with Turner's syndrome and Mullerian agenesis

Clinical features	45,X 3 cases	45,X/46,XX 6 cases	45,X/46,X + marker 1 case	46,X - X iso(Xq) 2 cases
Short stature	3	4	1	1
Normal stature	-	1	-	-
Short and webbed neck	-	2	-	-
Secondary sexual characters, under-developed, breast not developed, axillary and pubic hairs absent	2	3	1	2
Absence of menstruation	2	5	1	2
Cubitus valgus	1	2	1	2
Shield chest with widely spaced nipple	2	3	1	2
Delayed mile stones, mental retardation	-	2	-	-

Table-11 : Age, height, gonadal status and cytogenetic findings in 12 cases of Turner's syndrome

Serial No.	1	2	3	4	5	6	7	8	9	10	11	12
Age (in years)	4 days old	16	19	30	18	21	13	16	16	18	21	19
Height (in cms)	-	130	145	131	131	125	138	128	125	132	140	128
Span (cms)	-	132	130	144	130	128	142	134	132	132	145	130
Ovaries	?	?	?	Normal	?	?	One sided	?	?	Streak like	Not seen	Not seen
Uterus	?	Hypo-plastic Streak like	Absent	Normal	Hypo-plastic	Hypo-plastic	?	Hypo-plastic	Hypo-plastic	Hypo-plastic	Not palpable	Not palpable
Vagina	Present	Present	Normal	Normal	Normal	Normal	Present	Present	Pouch-like	Normal	Normal	Normal
Karyotype	45,X/ 46,XX	45,X/ 46,XX	45,X/ 46,XX	45,X/ 46,XX	45,X/ 46,XX	45,X/ 46,XX	45,X/	45,X/	45,X/	46,X-X iso(Xq)	45,X/ 46,X + marker	46,X-X iso(Xq)
Mosaicism in %	80/20	40/60	30/70	85/15	25/75	20/80	-	-	-	-	50/50	45/55
X chromatin in %	4	7	6	4	8	12	-	-	-	15	-	12

Table-12 : Clinical features of 13 patients with Klinefelter's syndrome, hypogonadism and hypospadias

Clinical features	47,XXY 8 cases	46,XY/ 47,XXY 3 cases	48,XXY +21 1 case	48,XXY +15 1 case
Tall stature	5	2	1	1
Gynaecomastia	3	1	-	1
Obesity	6	2	-	1
Small phallus	6	2	1	1
Small testes (atrophic)	5	1	1	1
Axillary and pubic hair				
- Normal	3	1	-	-
- Scanty	5	2	1	1
Facial hair				
- Absent	6	2	1	1
- Scanty	2	1	-	-
Voice -				
Feminine	4	2	1	1

Table-13 : Age, anthropometric data, cytogenetic findings and hormonal reading in 13 cases of Klinefelter's syndrome

Serial No.	1	2	3	4	5	6	7	8	9	10	11	12	13
Age (in years)	13	32	30	32	28	19	25	29	28	26	18	36	20
Height (in cms)	165	175	170	176	165	162	172	172	175	173	172	162	170
Karyotype	46,XY/ 47,XXY	47,XXY	48,XXY +21	46,XY/ 47,XXY	47,XXY	46,XY/ 47,XXY	47,XXY	47,XXY	47,XXY	47,XXY	47,XXY	47,XXY	47,XXY
Sex cnromatin in %	10%	12%	14%	ND	13%	-	12%	12%	15%	10%	ND	ND	10%
Semen analysis	ND	Azoo-spermia	Azoo-spermia	Azoo-spermia	Azoo-spermia	Azoo-spermia	Azoo-spermia	ND	Azoo-spermia	Azoo-spermia	Azoo-spermia	ND	ND
HORMONES													
F.S.H. miu/ml (1.8 to 20.0)	55.5↑	60.0↑	55.0↑	35.0↑	55.0↑	7.0	90.0↑	40.0↑	35.0↑	30.0↑	ND	45.0↑	ND
L.H. miu/ml (4.0 to 28.0)	31.0↑	30.0↑	29.0	95.0↑	31.0↑	50.0↑	28.0	32.0↑	40.0↑	35.0↑	ND	40.0↑	ND
Testo-sterone (ng/ml)	1.0	2.0	1.5	1.3	1.0	0.5	0.6	2.0	1.0	1.5	ND	2.0	ND

↑ - Increased
↓ - Decreased
ND - Not done

Table-14 : Age, anthropometric measurements, gynaecological findings and cytogenetic results in 7 cases of primary amenorrhoea (PA), Mullerian agenesis (MA), sterility (S) and spontaneous abortions (SA)

Serial No.	1	2	3	4	5	6	7
Age (in years)	16	17	22	23	18	33	30
Secondary sexual characters	Not well developed	Poorly developed	Well developed	Well developed	Poorly developed	Well developed	Well developed
Breast	Under-developed chest ? shield	Under-developed	Well developed	Normal	Not developed	Well developed	Well developed
Uterus	Present	Hypoplastic	Not palpable	Smaller than normal	Hypoplastic	Normal in size	Normal in size
Ovaries	Not seen	Both sides under-developed	Not seen	Both normal	Streak like	Normal	Normal
Karyotype	46,XX/ 47,XXX	47,XXX	47,XXX	46,XX/47,XXX	46,XX/45,X	46,XX/46,XY	45,XX-13-14 +t(13q,14q)
Vagina	Normal	Normal	Blind pouch	Normal	Pouch like	Normal	Normal
% Mosaicism	80:20	-	-	80:20	70:30	-	-
X chromatin	18% : 5%	20%	20%	20% : 10%	10%	-	-
Clinical diagnosis	P.A.	M.A.	M.A.	S	S.A.	S.A.	S.A.

Table-15 : Clinical features of 28 patients with ambiguous genitalia with XY karyotype

Sr. No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Age	2½ yrs	8 months	6 months	2 yrs.	4 months	12 months	8 months	1½ yrs	3 yrs.	10 days	9 yrs	20 yrs	7 yrs.	2 yrs	6½ yrs
Sex of rearing	Female	Female	Female	?Female	Male	?Male	?Female	Male	Male	Male	Male	Male	Male	Male	Female
Ext. Genitalia															
Phallus	Small	Clitoris hypertrophied	Small	Clitoris hypertrophied	Small	Small	Small	Small	Small	Small	Small	Clitoris hypertrophied	Small	Small	Clitoris hypertrophied
Scrotum	Bifid	Labia majora rugosity	Bifid	Labia majora with rugosity	Bifid	Labia majora with rugosity	Labia majora	Bifid scrotum with rugosity	Bifid	Not observed	Bifid	Labia majora rugosity	Bifid	Bifid	Left side labia folded
Testes															
Left	Descended	Undescended	Descended	Undescended	Undescended	Descended	Descended	Descended	Descended	Undescended	Not palpable	Undescended	Descended	Undescended	Descended
Right	Descended	Undescended	Descended	Undescended	Descended	Descended	Descended	Descended	Inguinal	Undescended	Descended	Undescended	Inguinal	Inguinal	Inguinal
Vaginal opening Absent	Absent?	?"	Absent	Present	Absent	Present	Present	Absent	Absent	Absent	Absent	Absent	Absent	Present	Absent
Urethral opening	Perineo scrotal	Perineo scrotal	Perineo scrotal	Peno-scrotal	Perineo scrotal	Perineo scrotal	Perineo scrotal	Single opening for passage of urine and stool	Peno-scrotal	Perineo scrotal	-	Perineo scrotal	Scrotal hypospadias	Perineo scrotal	Perineo scrotal
Pelvic organ	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Uterus	Absent	?	Absent	?	Absent	?	Present	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Ovary	Absent	?	Absent	?	Absent	Absent	?	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent

Table-15 : Clinical features of 28 patients with ambiguous genitalia with XY karyotype (Contd.)

Sr. No.	16	17	18	19	20	21	22	23	24	25	26	27	28
Age	4½ yrs	5 months	14 yrs	12 yrs	8 years	5 years	7 years	8 months	8 years	2½ yrs	4 years	10 months	12 months
Sex of rearing	Male	Male	Female	Male	Male	Male	Male	Male	Male	Male	Male	Male	Male
Ext. Genitalia													
Phallus	Well developed	Small	Clitoris hypertrophied	Small	Small	Small	Small	Well developed	Small	Small	Small	Small	Small
Scrotum	Bifid	Bifid scrotum with rugosity	Bifid	Bifid	Bifid	Bifid	Bifid	Labia majora +ve No minora	Bifid	Scrotum with rugosity	Bifid	Bifid	Labia majora rugosity
Testes													
Left	Inguinal	Inguinal	Undescended	Undescended	Undescended	Descended?	Small descended ?	?	Undescended	Undescended	Undescended	Descended	Undescended
Right	Undescended	Undescended	Descended	Undescended	Undescended	Descended ?	Undescended ?	?	Undescended	Descended	Undescended	Undescended	Undescended
Vaginal opening Absent	Absent	Absent	Present	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Uretnral opening	Perineo-scrotal	Peno-scrotal	Perineo scrotal	Perineo scrotal	Perineo scrotal	Perineo scrotal	Perineo scrotal	At tip	Peno-scrotal	Perineo scrotal	Perineo scrotal	Perineo scrotal	Perineo scrotal
Pelvic Organ													
Uterus	Absent	Absent	Present	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Ovary	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent

Table-16 : Clinical features of 12 patients with ambiguous genitalia having 46,XX karyotype

Sr. No.	1	2	3	4	5	6	7	8	9	10	11	12
Age	2 years	2 years	1½ years	6 months	8 months	8 months	15 years	4 years	2 years	2 months	17 days	3 months
Sex of rearing	Male	Female	?Female	Female	Female	Male	Female	Male	Female	Male	Female	Female
Clitoris	Hypertrophied with scrotal rugosity	?Clitoris	Hypertrophied with pigmentation of labia majora	Normal size	?Clitoris	Enlarged with labia majora, No labia minora	Hypertrophied	Peniel	Hypertrophied	Hypertrophied with scrotal rugosity	?Hypertrophied ?scrotum with few rugae	Enlarged
Vaginal opening	Present	Present	Present	Present	Present	Absent	Present	? opening	Present	Present	Absent	Absent
Uterus	?	?	?	?	Present	?	Present	Present	Present	?	Absent	?
Testes	?	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Undescended	? bilateral palpebral inguinal	?

Details of the forty patients of haematological malignancies are summarized in Table-17 and Table-18. Out of 40 patients - chronic myeloid leukemia (CML) - 12 patients; chronic lymphocytic leukemia (CLL) - 3 patients; acute myeloid leukemia (AML) - 4 patients; acute lymphocytic leukemia (ALL) - 3 patients; Hodgkin's lymphoma (HL) - 10 patients; Non-Hodgkin's lymphoma (NHL) - 6 patients; and multiple myeloma (MM) - 2 patients.

Table-17 includes age, sex, clinical diagnosis, status of the disease when karyotyped and treatment; prognosis and results.

Table-18 summarizes detailed clinical symptoms, haemogram etc.

TABLE-17 SHOWING SEX/AGE, CLINICAL DIAGNOSIS, STATUS OF THE DISEASE WHEN KARYOTYPED & TREATMENT, PROGRESS IN HAEMATOLOGICAL MALIGNANCIES AND RESULTS

Sr. No.	Name	Sex/Age (years)	Clinical Diagnosis and phase of disease	Status when karyotyped	Treatment	Prognosis and result	Other relevant findings	
							Treatment response	Remission
01.	M N	F/36	CML /CP with early MF	Recurrence	Myleran	Alive/More than 7½ years	Good	Long
02.	J R	M/55	CML / CP	Recurrence	6 MP	Died/after 18 months	Average	Less than 6 months
03.	G K	F/40	CML/CP with early MF	Recurrence	Myleran	Alive/18 months	Good	Long - 18 months
04.	R P	F/24	CML/CP	First diagnosis	Endoxan	? -	Good	Achieved
05.	M K	M/60	CML/CP	Recurrence	Myleran	Alive/More than 2½ years	Good	Long - 18 months
06.	C P	F/55	CML/CP	First diagnosis	Myleran	Alive/ Less than 6 months	Good	For 3 months
07.	S T	F/30	CML/CP	First diagnosis	6 MP	Alive/Less than 3 months	Good	3 months
08.	B A	M/36	CML/AP	First diagnosis	Hydroxyurea	Died/7 days	No response	Not achieved
09.	J C	M/49	CML/CP	First diagnosis	Myleran	Alive/Less than 6 years	Good	2½ years
10.	L U	M/50	CML/CP	First diagnosis	Hydroxyurea	Died/5 days	No response	Not achieved
11.	P C	F/35	CML/CP	Recurrence	Myleran	Alive/2 years	Good	Long
12.	H R	F/58	CML/CP	First diagnosis	Myleran	Alive/6 months	Good	For 4 months
13.	L M	M/52	CLL stage-III	First diagnosis	Leukeran	Died(very short)	Average	No remission
14.	P B	F/58	CLL Stage-IV	First diagnosis	Leukeran + Steroid	Died(14 months)	Average	8 months

TABLE-17 (Contd.)

Sr. No.	Name	Sex/Age (years)	Clinical Diagnosis and phase of disease	Status when karyotyped	Treatment	Prognosis and result	Other relevant findings	
							Treatment response	Remission
15.	K M	M/50	CLL - Stage-IV	First diagnosis	Leukeran + Steroid	Died/Shortly 5 days	Could not observed	Not found
16.	R B	F/25	AML	First diagnosis	Vencristine Prednisolone	Died/after 7 days because of intra-cranial haemorrhage	Nil	Not achieved
17.	L G	M/55	AML	First diagnosis	Vencristine Prednisolone 6-MP	Died/15 days because of septicaemia	Nil	Not achieved
18.	A C	F/18	AML	First diagnosis	Vencristine Prednisolone	Died/10 days because of septicaemia	Nil	Not achieved
19.	S P	M/22	AML	First diagnosis	-	?	Could not be traced	
20.	T K	M/14	ALL (Thrombo-cytopenia)	-	-	Died/1 month Intracranial haemorrhage	Average	Not achieved
21.	U R	M/13	ALL (Thrombo-cytopenia)	-	-	Alive	Good	Complete remission recurrence in 3 months
22.	S K	M/30	ALL (Thrombo-cytopenia)	-	-	Died/1 month	Nil	Not achieved
23.	T V	M/18	HL - IV Mixed cellularity		Mustine Vencristine Prednisolone	Died/15 months	Average	4 months
24.	K P	M/37	HL - II Mixed cellularity		Mustine Vencristine Prednisolone Procarbazine	Not known	Average	-
25.	L B	M/08	HL - I Lympho-cytic predominance		Mustine, Vencristine Prednisolone Cyclophosphamide	Alive/More than 30 months	Good	Complete remission recurrence after 20 months
26.	P M	M/33	HL - III Mixed cellularity		Mustine Vencristine Prednisolone Procarbazine	Alive/12 months	Good	Complete remission
27.	G M	M/44	HL - II Mixed cellularity		Mustine Vencristine Prednisolone	Lost follow up	-	-

TABLE-17 Contd.

Sr. No.	Name	Sex/Age (years)	Clinical Diagnosis and phase of disease	Status when karyotyped	Treatment	Prognosis and result	Other relevant findings	
							Treatment response	Remission
28.	J M	M/34	HL - III Lympho-cytic predominance		Mustine Vencristine Methotrexate	Died/3 months	Poor	Not achieved
29.	D K	F/37	HL - I Lympho-cytic predominance		Mustine Vencristine Prednisolone Methotrexate	Alive/More than 6 months	Good	Complete
30.	B R	M/27	HL - IV Mixed cellularity		Mustine Vencristine Prednisolone Methotrexate	Not known	Average	-
31.	R K	M/34	HL - III Lympho-cytic predominance		Mustine Vencristine Prednisolone Methotrexate	Died/4 months	Poor	Not achieved
32.	U M	F/35	HL - I Lympho-cytic predominance		Mustine Vencristine Prednisolone	Alive/More than 8 months	Good	Complete
33.	S R	M/13	NHL Lympho-cytic	Respiratory infection	C V P	Died/2 months	Poor	Not achieved
34.	L C	M/24	NHL Diffuse histocytic	C N S	C V P	Died/25 months	Good	Remission 15 months
35.	K T	M/51	NHL Follicular histocytic	-	C V P	Not known	Good	Average
36.	B C	M/09	NHL Lymphocytic	-	C V P	Not known	Good	Average
37.	C M	M/12	NHL Lymphocytic	Septicaemia	C V P	Died Poor/7 months	Poor	Partial remission
38.	F H	F/60	NHL Lymphocytic	Septicaemia	C V P	Died Poor/10 months	Poor	Partial remission
39.	I L	M/70	MM/III More than 40% myeloma cells	-	Melphalan	Died/4 years	Good	Achieved twice - 1 year
40.	N P	M/56	MM/III 30-40% myeloma cells	-	Melphalan	Died/3½ years	Good	Achieved twice maintained 1 year

TABLE-18

Clinical Symptoms	Blood Cell Count	Haemoglobin (g/dl)	Last observation
Weakness, bone pains, abdominal swelling with huge splenomegaly	TC : 1,10,000/mm^3 Platelet : 2,00,000/mm^3	Anaemia Hb : 10.5	Blastic crisis
Abdominal swelling, splenomegaly, weakness, malaise, bone pains	Total WBC count : 2,00,000/mm^3 Differential WBC: Myeloblasts : 8-9% Promyelocytes : 6-7% Neutrophils : 28% Basophils : 8-10% Lymphocytes : 3-5% Myelometamyelocytes:20-22% RBC - Hypochromic, microcytic Platelet : 4,12,000/mm^3	Anaemia Hb : 10.0	Did not report at last
Fever, weakness, bone pains, splenomegaly, tenderness	Total WBC : 2,00,000/mm^3 Myeloblasts : 8% Neutrophils : 68% Myelometamyelocytes : 16-18% Basophils : 4% Rest is lymphocytes	Anaemia Hb : 8.0	Trephine biopsy showed myelo-fibrosis
Fever, malaise, weakness, weight loss, abdominal swelling, splenomegaly	Total WBC : 1,80,000/mm^3 Myeloblasts : 3% Myelometamyeloblasts : 45% Neutrophils : 50% Lymphocytes : 2% Platelet : 2,85,000/mm^3	Anaemia(mild) Hb : 10.0	Bone marrow showed myeloid hyperplasia with 5% myeloblasts
Fever, weight loss, bone pains, abdominal swelling with anaemia, splenomegaly, sternal tenderness	Total WB C : 2,90,000/mm^3 Myeloblasts : 5% Myelometamyelocytes : 48% Platelets : 2,55,000/mm^3 Serum uric acid : 5 mg/dl	Anaemia Hb : 7.5	Myeloid series with 8-10% myeloblasts were predominant in bone marrow
Weakness, dyspnoea, abdominal swelling, splenomegaly, sternal tenderness	Total WBC : 3,70,000/mm^3 Myeloblasts: 15% Other immature cells of myeloid series : 80% Platelet : 2,60,000/mm^3	Anaemia (severe) 6.5 g/dl	Trephine biopsy showed myeloid hyperplasia with 8% myeloblasts
Generalised weakness, weight loss, abdominal swelling with splenomegaly, sternal tenderness	Total WBC : 3,500/mm^3 Myeloblasts : 8% Myelocytes : 35% Neutrophils : 35% Basophils : 5% Platelets : 3,40,000/mm^3	Hb : 8.0 Anaemia (severe)	Trephine biopsy showed myeloid predominance with 8% myeloblasts
Weakness, high grade fever, exertional dyspnoea, abdominal pain with splenomegaly, sternal tenderness. Cervical axillary and inguinal lymphadenopathy	Total WBC : 2,10,000/mm^3 Myeloblasts : 21% Premyeloblasts : 8% Myelo & Metamyelocytes : 45% Lymphocytes : 6% Neutrophils : 10% Basophils : 10% Platelets : 75,000/mm^3	Anaemia (severe) Hb : 7.0	Trephine biopsy showed myeloid series predominance with 30% myeloblasts. Last came with blastic crisis
Generalised weakness, malaise, exertional dyspnoea, abdominal pain, splenomegaly	Total WBC : 22,000/mm^3 No blast cells Myelometamyelocytes 20%	Anaemia (moderate) Hb : 10.0	-

TABLE (CONTD.)

Clinical Symptoms	Blood Cell Count	Haemoglobin (g/dl)	Last observation
Generalised weakness, malaise abdominal pain with splenomegaly	Total WBC : 40,000/mm^3 Myeloblasts : 20% Myelocytes : 30% Neutrophils : 35% Basophils : 15% Platelets : 70,000/mm^3	Anaemia (severe) Hb : 6.0	-
Weakness, dyspnoea on exertion, high grade fever, abdominal pain, splenomegaly	Total WBC : 2,00,000/mm^3 Myeloblasts : 25% Promyeloblasts : 5% Lymphocytes : 10% Myelo & Metamyelocytes: 40% Neutrophils : 10% Basophils : 10% Platelets : 80,000/mm^3	Anaemia (severe) Hb : 7.0	-
Abdominal pain, high grade fever, weight loss, splenomegaly	Total WBC : 2,00,000/mm^3 Myeloblasts : 10% Myelometamyeloblasts : 45% Neutrophils : 40% Lymphocytes : 5% Platelets : 2,40,000/mm^3	Anaemia (mild) Hb : 10.0	Bone marrow aspirate showed myeloid hyperplasia with 5% myeloblasts
onic Lymphocytic Leukemia (CLL)			
Swelling on the neck, axillae and inguinal regions, weakness, loss of weight, painful right shoulder movements, X-ray chest showed hilar lymphadenopathy, hepatosplenomegaly	Total WBC : 1,60,000/mm^3 Lymphocytes : 90% Remaining cells were neutrophils. Platelets : 2,50,000/mm^3 During Treatment WBC count had decreased to 30,000/mm^3. Differential Count Neutrophils : 25% Lymphocytes : 75%	Anaemia (moderate) Hb : 8.0	Bone marrow showed 50% lymphocytes
High grade fever, toxic state with patechial haemorrhages all over the body. Swelling in cervical and axillary regions, dyspnoea, weight loss, weakness, lethargy, hepatosplenomegaly, positive Coomb's test	Total WBC : 1,20,000/mm^3 Lymphocytes : 90% Platelets : 40,000/mm^3	Anaemia Hb : 7.0	Later on developed septicaemic shock and died.
Low grade intermediate fever, weight loss, weakness, bilateral, cervical and inguinal lymphadenopathy, hepatosplenomegaly	Total WBC : 1,25,000/mm^3 Lymphocytes small mature 95% Neutrophils : 3% Lymphoblasts : 2% Platelets : 1,00,000/mm^3 Normocytic hypochromic RBCs	Anaemia Hb : 7.8 ESR : 150 mm (1st hour)	Bone marrow showed lymphocytic predominance
AML : Fever, weakness, exertional dyspnoea, weight loss, bone pains rashes all over the body, puffiness of face, bleeding from gums, echymosis over face, arms, legs and back, hepatosplenomegaly	Total WBC : 1,00,000/mm^3 Myeloblasts : 90% Platelets : 1,00,000/mm^3	Anaemia Hb : 7.5	Bone marrow revealed myeloid infiltration with 90% myeloblasts Sudden intracranial haemorrhage and died
AML : Fever, weight loss, abdominal pain, also had pulmonary tuberculosis, mild jaundice, inguinal lymphadenopathy, pulmonary emphysema, splenomegaly	Total WBC : 98,000/mm^3 Blast cells : 55% both myeloblasts and monoblasts; myelo and metamyelocyte 10% Neutrophils : 10% Monocytes : 10% Rest : Lymphocytes Platelets : 2,50,000/mm^3	Hb : 8.0 Anaemia	Bone marrow revealed 80% myeloblasts, monoblasts

TABLE (CONTD.)

Clinical Symptoms	Blood Cell Count	Haemoglobin (g/dl)	Last observation
High grade fever, dyspnoea on exertion, pain and vomiting, cervical and axillary lympnadenopathy, nepatosplenomegaly, patechial haemorrhages	Total WBC : 22,000/mm^3 Myeloblasts : 65% Platelets : 50,000/mm^3	Anaemia (severe) Hb : 4.0	Myeloid predominance in bone marrow aspiration developed septicaemia and died.
AML : Generalised weakness, malaise exertional dyspnoea, weight loss	Total WBC : 3,000/mm^3 Neutrophils : 64% Lymphocytes : 32% ESR : 170 mm in 1st hour Platelets : 3,00,000/mm^3	Anaemia (severe) Hb : 2.0	Trephine biopsy showed myeloid predominance and 70% myeloblasts
ALL : Fever, weakness, exertional dyspnoea, cervical, axillary and inguinal bilateral lymphadenopathy, sternal tenderness, hepatosplenomegaly	Total WBC : 70,000/mm^3 Lymphoblasts : 30% Lymphocytes : 40% Neutrophils : 25% Monocytes : 5% Platelets : 80,000/mm^3	Anaemia (severe) Hb : 5.0	Trephine biopsy showed lymphoid predominance with 80% lymphoblasts. Lymph node biopsy showed lymphocytic infiltration, intracranial haemorrhage and died.
ALL : Bleeding from gums, fever, weight loss, neck swelling, patechial spots all over the body, multiple, bilateral, cervical, axillary and inguinal lymphadenopathy, hepatosplenomegaly	Total WBC : 80,000/mm^3 Lymphoblasts : 70%	Anaemia (severe) Hb : 7.0	Bone marrow aspirate showed more lymphoblasts
ALL : Fever, malaise, dysphagia, swollen gums, puffiness of face,, sternal tenderness, bilateral firm discrete cervical, axillary and inguinal lymphadenopathy, hepatosplenomegaly, right sided Bell's palsy and parotid swelling	Total WBC : 2,00,000/mm^3 Lymphoblasts : 75% Lymphocytes : 20% Rest neutrophils Platelets : 45,000/mm^3 R : decrease in WBC count and number of blast cells	Anaemia (severe) Hb : 6.0	Bone marrow biopsy showed predominance of lymphoblasts. Sudden death.
Neck swelling, pruritus, multiple discrete cervical and axillary lymphadenopathy, hepatosplenomegaly. Later on, he came with complain of superior vena-caval obstructions, pleural effusion, mediastinal lymphadenopathy, headache, vomiting disorientation abnormal behaviour and neck rigidity		Anaemia (moderate) Hb : 9.0	Lymph node biopsy revealed Hodgkin's lymphoma of mixed cellularitis. Pleural fluid cytology confirmed malignant cells. Died soon because of widespread meningeal infiltration and respiratory involvement
Hodgkin's Lymphoma:Fever, weakness, Weight loss, neck swelling, cervical and axillary lymphadenopathy with hepatosplenomegaly	Haematological investigations were within normal limits.	Hb : 10.0	Lymph node biopsy suggestive of Hodgkin's lymphoma
Hodgkin's Lymphoma: Fever, swelling in the neck, weakness, malaise, palpable cervical lymphnode	ESR : 90 mm at 1st hour	Anaemia (moderate)	Lymph node biopsy revealed Hodgkin's lymphoma
Hodgkin's lymphoma: Episodes of fever, weight loss, malaise, neck swelling and weakness, palpable cervical and inguinal lymph node, puffiness of face, hepatosplenomegaly. X-ray chest: showed hilar and peribronchial lymph nodes.	Total Cell Count : 14,000/mm^3 Differential W.B.C. Neutrophils : 20% Lymphocytes : 15% Eosinophils : 65% ESR : 90 mm in 1st hour	Anaemia (mild) 12.0 Hb	Lymph node biopsy revealed Hodgkin's lymphoma
Hodgkin's Lymphoma: Fever, weight loss, neck swelling, weakness, multiple cervical and axillary lymphadenopathy. No hepatosplenomegaly	Normal haemogram	-	Lymph node biopsy suggestive of Hodgkin's lymphoma

TABLE (CONTD.)

Clinical Symptoms	Haemogram	Haemoglobin (g/dl)	Last observation
Hodgkin's Lymphoma: Fever, dyspnoea, weight loss, puffiness of face, exophthalmos and bilateral cervical, axillary and inguinal lymphadenopathy, hepatosplenomegaly. X-ray chest showed enlarged hilar shadow.	ESR : 100 in 1st hr	Anaemia Hb : 9.0	Lymph node biopsy suggestive of lymphocytic predominance. Bone marrow biopsy did not show any infiltration.
Hodgkin's Lymphoma: Low grade fever, swelling at neck region, weight loss, weakness. Right sided cervical lymphadenopathy	Normal	Anaemia (mild) Hb : 10.0	Lymph node biopsy showed infiltration of lymphocytic predominance. Bone marrow biopsy did not show any infiltration.
Hodgkin's Lymphoma: Weakness, weight loss, axillary swelling, hepatosplenomegaly (moderate)	Normal. ESR : 66 mm in 1st hour	Anaemia (mild) Hb 10.5	Lymph node biopsy revealed mixed cellular type lymphoma. Lymphocytic infiltration found in liver.
Hodgkin's Lymphoma: Weight loss, dyspnoea, puffiness of face, axillary, cervical and inguinal lymphadenopathy	ESR : 90 mm at 1st hour	Anaemia (mild) Hb 10.5	Lymph node biopsy suggestive of lymphocytic predominance
Hodgkin's Lymphoma: Weight loss, fever, axillary and inguinal lymphadenopathy, hepatosplenomegaly	Normal, ESR : 70 mm at 1st hour	Anaemia 11.0 Hb	-
Non-Hodgkin's Lymphoma : Low grade fever, exertional dyspnoea, weakness, abdominal swelling, oedema over the limbs, ascites, palpable mesenteric lymph node. X-ray chest : Normal	Total WBC : 8000/mm^3	Hb : 10.0	Trephine biopsy revealed infiltration of lymphoma
Non-Hodgkin's Lymphoma: Low grade fever, malaise, weakness, weight loss; after six months, he developed occipital swelling and later on central nervous system, signs in the form of extensor plantar response developed.	Normal.	Anaemia (moderate) Hb : 5.0	CNS infiltration by lymphoma cells, was considered.
Non-Hodgkin's Lymphoma: Lump in abdomen, low grade fever, weakness, mobile, nodular lump in umbilical region. I.V.P. shows compression of left ureter.	Normal	Hb : 10.0	Histopathology of lymph node showed follicular histocytic lymphoma.
Non-Hodgkin's Lymphoma: Dyspnoea, particularly in lying down position, neck swelling, weakness, dysphagia. Bilateral cervical, axillary and inguinal lymphadenopathy.	Normal	Anaemia (mild) Hb 8.5	-
Non-Hodgkin's Lymphoma: Dysphagia, swelling in the neck and throat, weakness, weight loss, dyspnoea	Other blood cells were normal	Anaemia Hb : 9.0	-
Non-Hodgkin's Lymphoma: Swelling on Rt.arm and Rt.axilla, weakness, weight loss, hepatosplenomegaly. Later on she complained of restricted right shoulder movements due to avascular necrosis of head of the right humerus	ESR : 70 mm at first hour	Hb : 10.0	Developed septicaemia and died.
M.M.: Fever, weakness, weight loss and bone and joints pain	Total WBC: 7000/mm^3 Peripheral bloood smear showed myeloma cells. ESR : 140 mm at 1st hr. S.Ca : 11.0 mg/dl S.creatinine : 1.0 mg/dl	Anaemia Hb : 9.0	Died due to respiratory infection.
M.M.: Pain, respiratory infection, weight loss	Total WBC: 6000/mm^3 ESR : 110 mm at 1st hr. S.Ca : : 11.0 mg% S.Phosphorus : 4.0 mg% S.Creatinine : 1.6 mg%	Anaemia Hb : 8.5	-

Cytogenetic findings of all the patients are tabulated with the complete diagnosis of the disease and its staging.

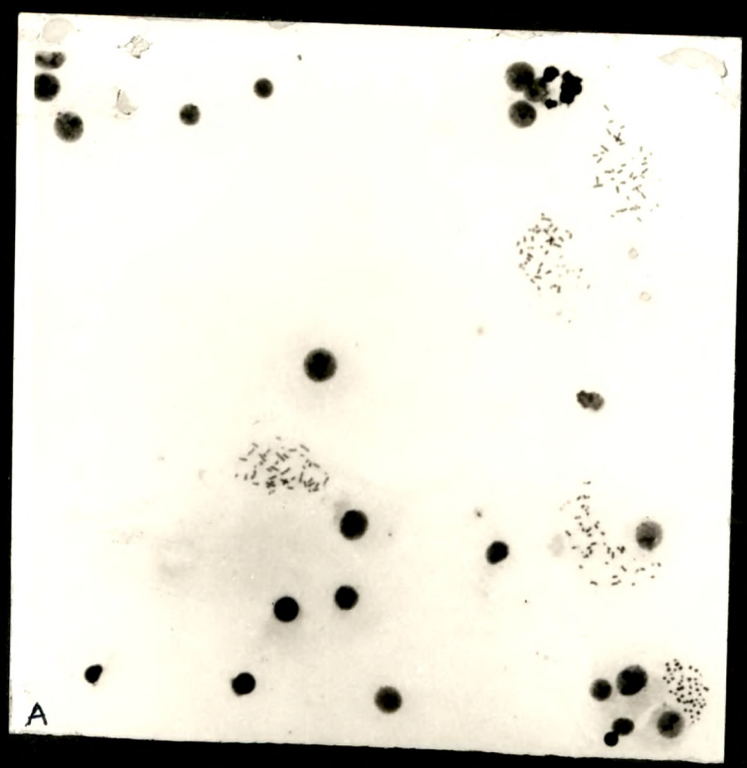
Case No.	Disease stage	Cytogenetic findings
01.	CML	1. 46,XX t(2q+ 22q-)
	CP	2. 45,XX, -15, 22q-/45,XX, -18, 22q-, del(8)(P)
02.	CML CP	47,XY, +8, 22q
03.	CML CP	46,XX, 22q-
04.	CML CP	46,XX, 22q-/43,XO, 22q, 8q-
05.	CML CP	46,XY, t(9q+, 22q-)
06.	CML CP	45,XX, -15, 22q-
07.	CML CP	47,XX, +21, 22q-
08.	CML AP	45,XY, -6
09.	CML CP	45,XY, +21, 22q- (random loss)
10.	CML CP	46,XY, 22q-
11.	CML CP	46,XX, 22q-
12.	CML CP	46,XX / 46,XX, 22q-
13.	CLL, III	46,XY / 47,XY, +20
14.	CLL IV	45,XX, -15
15.	CLL IV	46,XY
16.	AML M1	46,XX
17.	AMMol M4	46,XY/46,XY, -7, +mar
18.	AML M1	46,XX, 22q-
19.	AML M1	46,XY, del(3q-)-20, +22, 22q- / 49,XY, del(6q-, P-), +13, +21, +22, 22q-
20.	ALL	46,XY
21.	ALL	No metaphase
22.	ALL	46,XY/45,XY, -1, +?mar
23.	HL, IVb, MC	45,XY, -18,14q+, diploid cell line
24.	HL IIb MC	No spread
25.	HB Ib, LP	45,XY, -1 triploid cells
26.	HL IIIb	46,XY
	MC	triploid-tetraploid + cells +

Case No.	Disease stage	Cytogenetic findings
27.	HL IIb	45,XY, -2, 14q+
	MC	hyperdiploidy +
28.	HL IIIb	46,XY
	LP	hyperdiploidy +
29.	HL Ib	No spread
	LP	
30.	HL IVa MC	No metaphase
31.	HL III LP	46,XY hyperdiploidy
32.	HL I LP	No good spread
33.	NHL LPD	46,XY, t(14q+, 21q+)
34.	NHL DH	46,XY/46,XY del(3q-)
35.	NHL FH	46,XY
36.	NHL LWD	46,XY
37.	NHL LPD	46,XY
38.	NHL LPD	46,XX
39.	MM III	46,XY/45,XY, -1, -3, -13, -19 +mar, +mar, +mar
40.	MM III	45,XY, -1/44,XY, -1, -2, -4, -17 +marG, +mar, MG

CP	Chronic phase of CML
AP	Acute phase of CML
MC	Mixed cellularity
LP	Lymphocytic predominant
LPD	Lymphocytic poorly differentiated
DH	Diffuse histiocytic
FH	Follicular histiocytic
LWD	Lymphocytic well differentiated

(A) Photomicrograph of human peripheral whole blood culture after 72 hours incubation. The cell division was induced by phytohaemagglutinin and was arrested by Colchicine.

(B) Karyotype of cultured chromosomes (extreme left and right) are compared with diagramatic representation of G- and R-banding (by ISCN) in the centre. Each chromosome shows characteristic banding patterns.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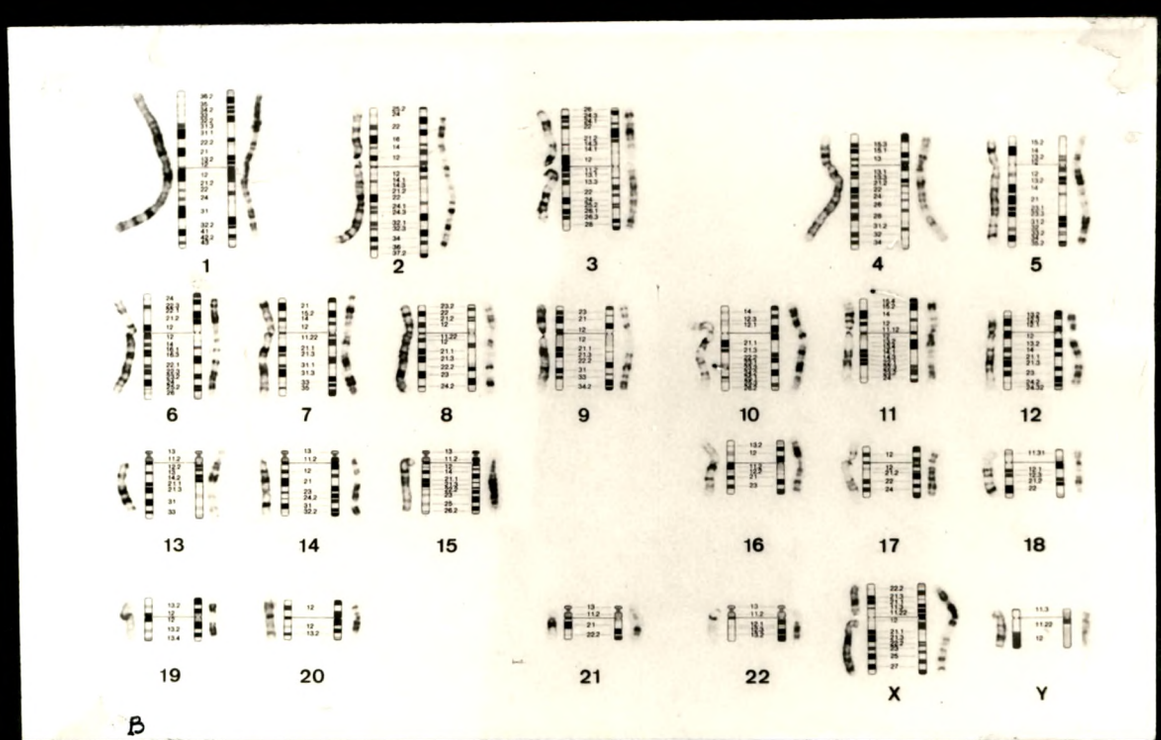
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Fig.6(a)

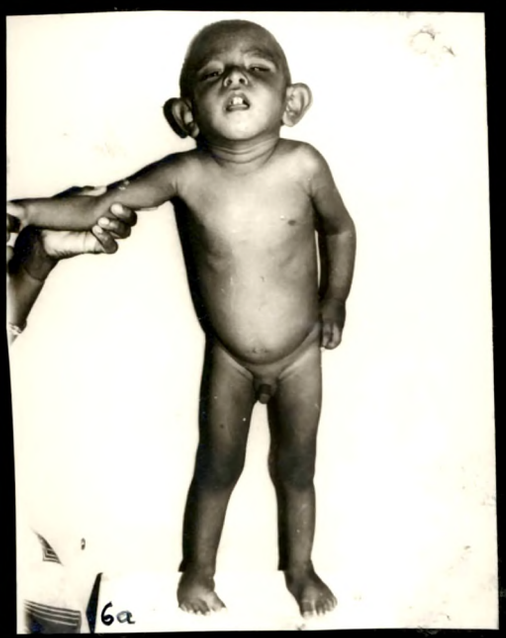
A male patient with typical facies of mongolism. Note the flat bridge of nose, large low set ears, protruding tongue and mental retardation.

(b)

Photograph showing short broad hand palmer surface with simian crease (SC).

Fig.7

(a) Giemsa stained karyotype of a patient showing Trisomy-21, Down's syndrome.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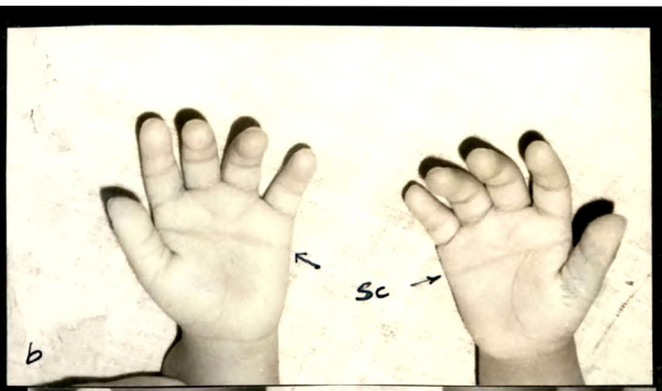
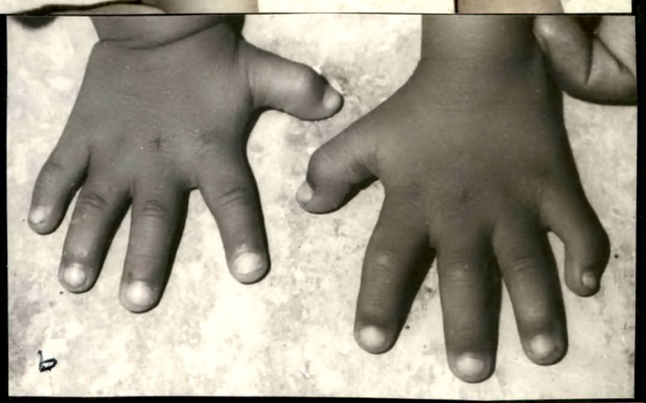
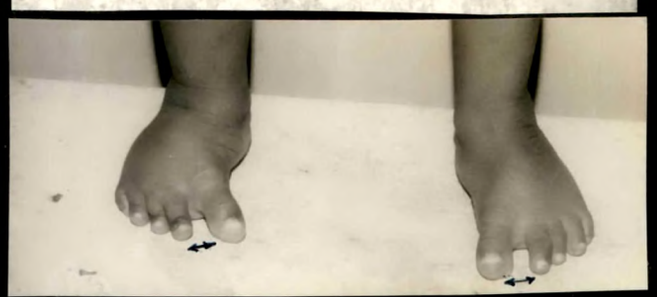
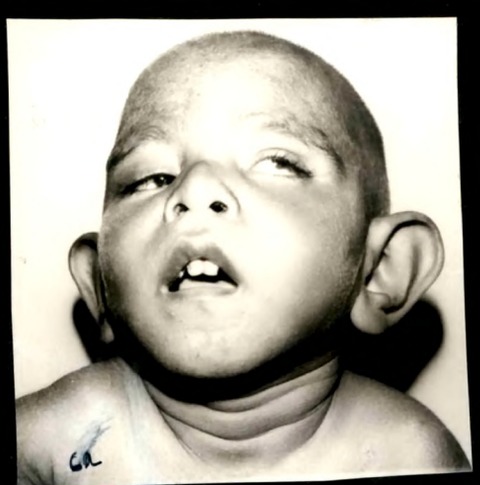

Sc
b


b





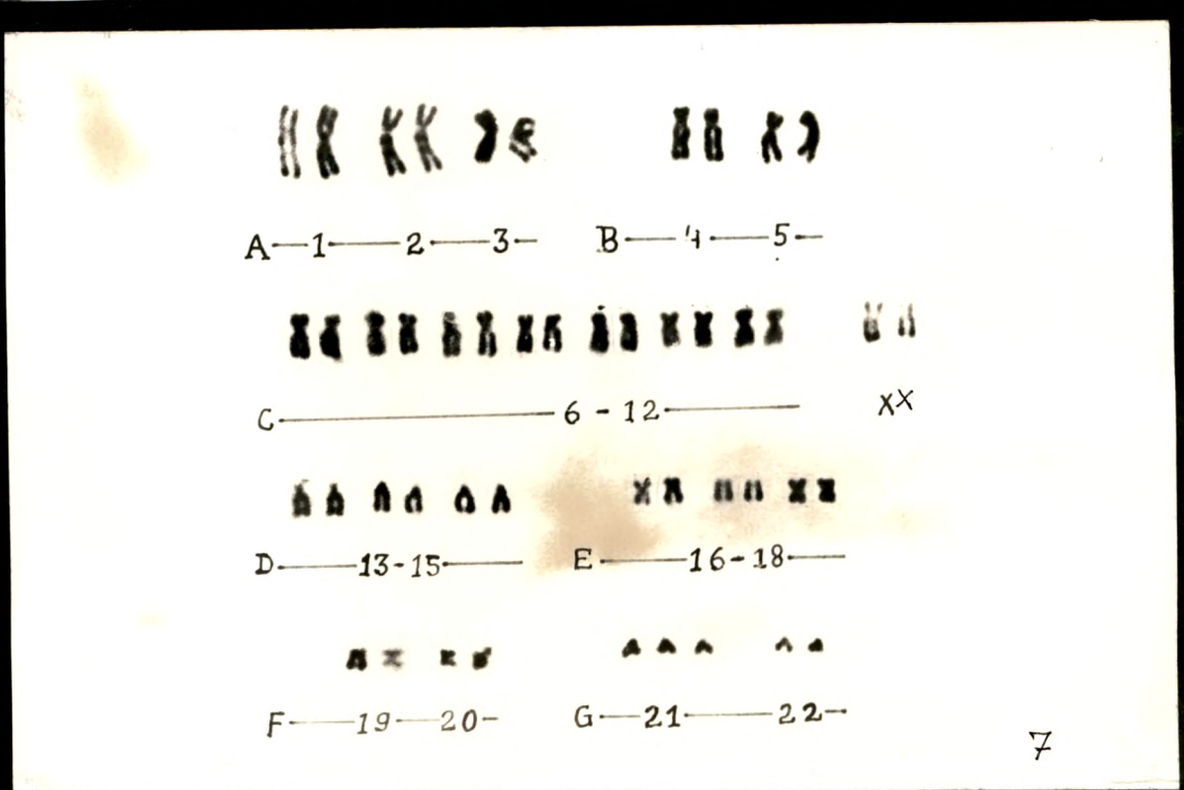

A—1——2——3—
B——4——5—
C——————6 - 12————
XX
D——13-15——
E——16-18——
F——19—20—
G—21——22—

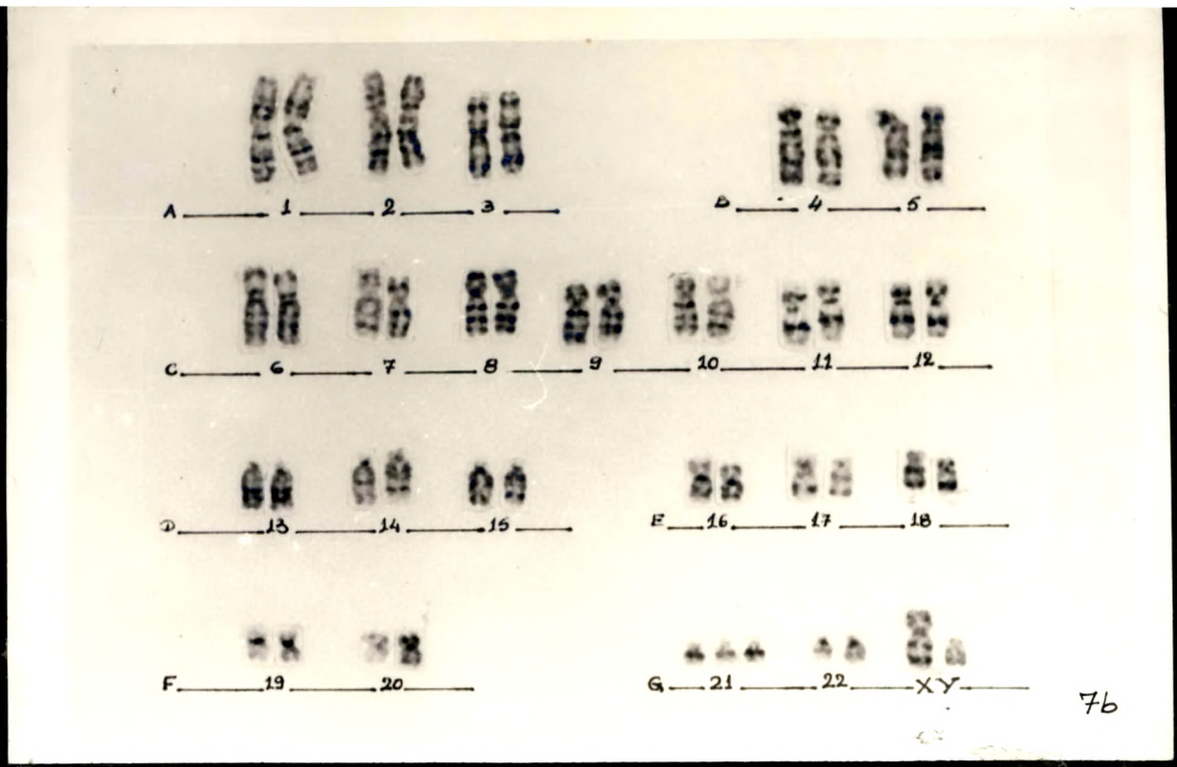
Fig.7(b)

G-banded karyotype of Down's syndrome patient with Trisomy-21.

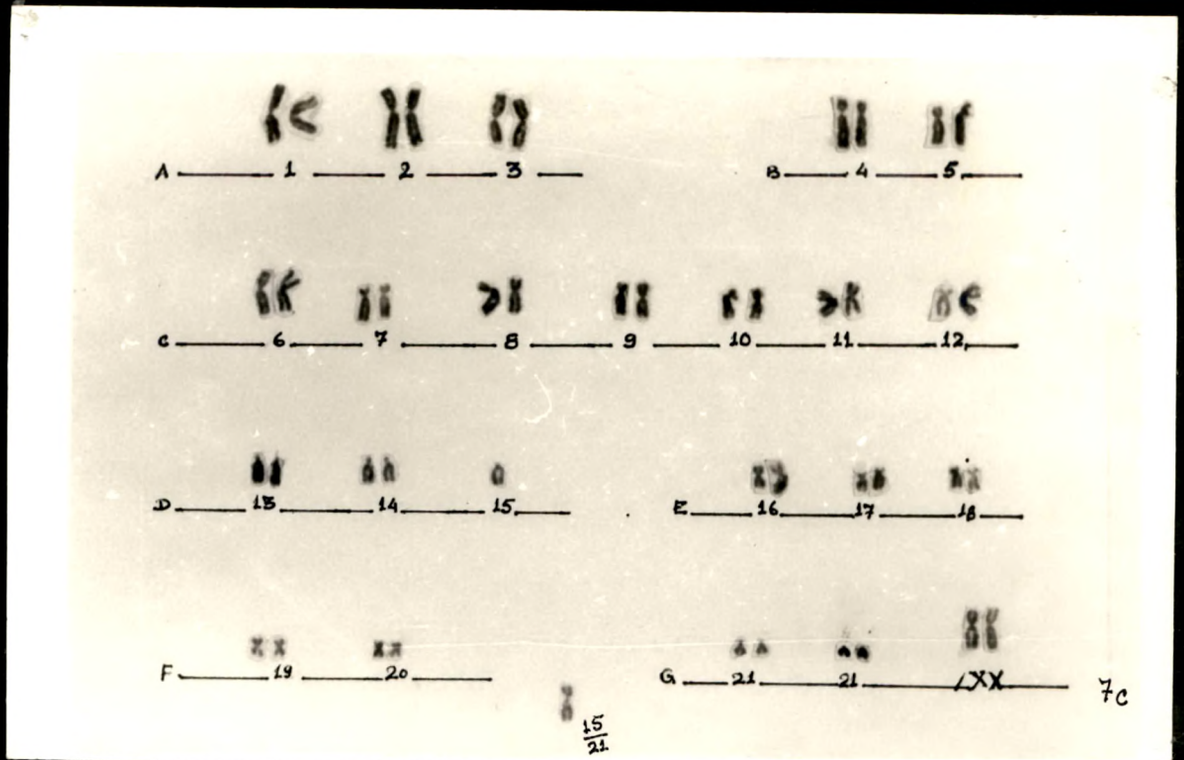
(c) Giemsa stained karyotype shown D/G translocation (in centre) mongol showing 46 chromosomes including the abnormal chromosome, which resembles members of the $^{C}_{6\text{-}12}$ group.

Fig.8

Clinical photograph of patient with E-18 trisomy. Rocker-bottom foot syndactyly of 2nd and 3rd toes; low set ears.


A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 XY

7b


A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 21 XX

7c

15/21

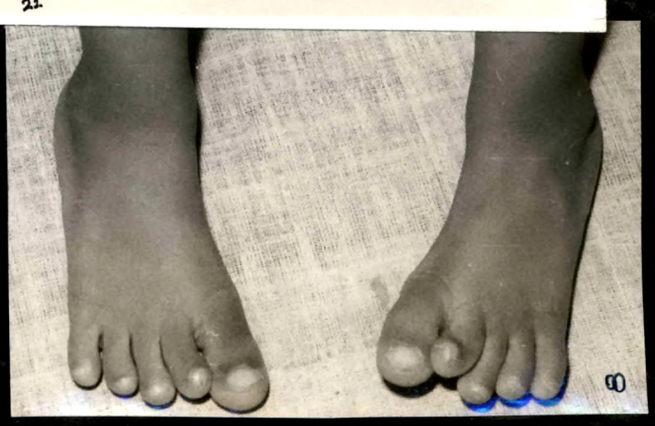
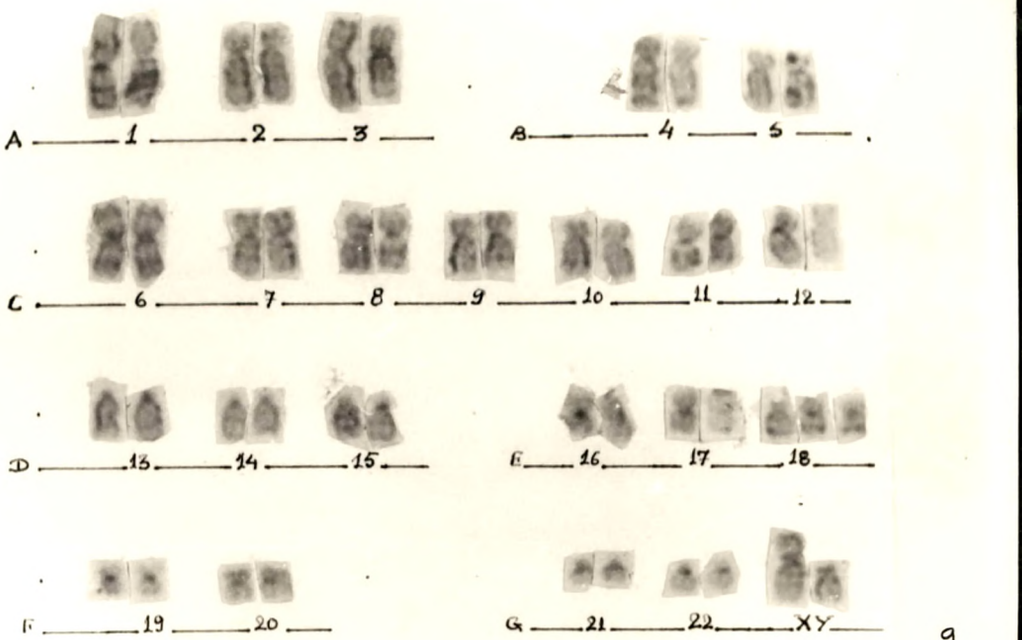


Fig.9

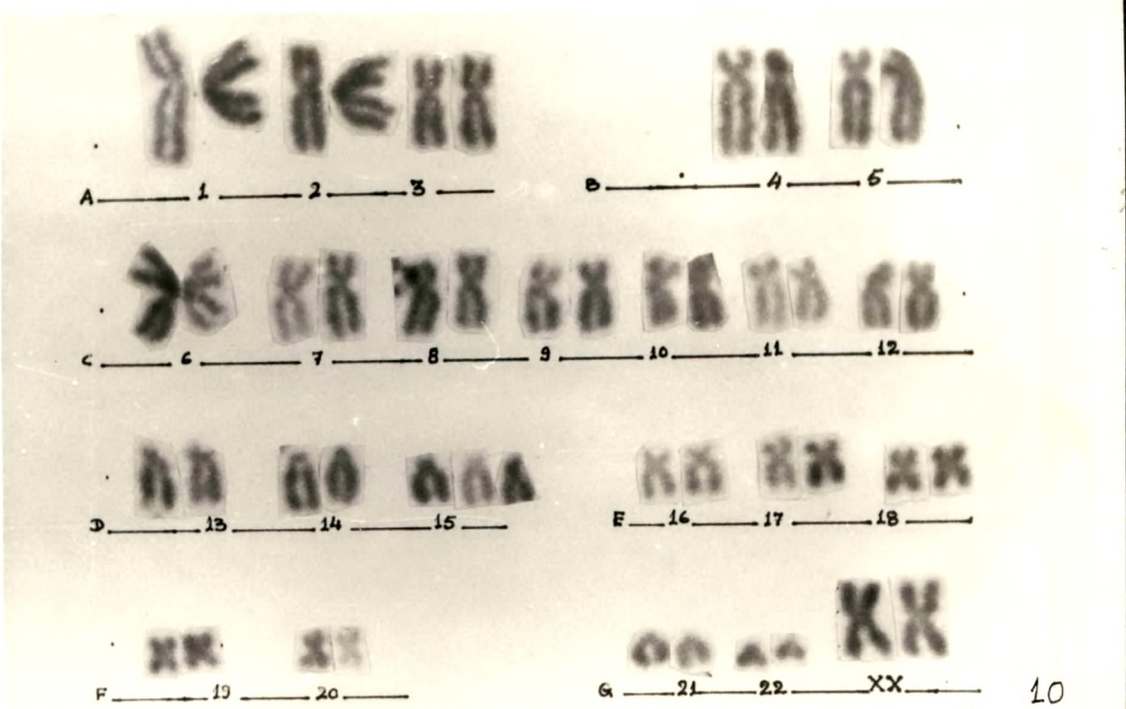
Giemsa banded karyotype of a patient with E-18 trisomy syndrome (Edward's syndrome).

Fig.10

Giemsa stained karyotype of a patient showing E-15 trisomy syndrome (Patau's syndrome).


A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 XY

9

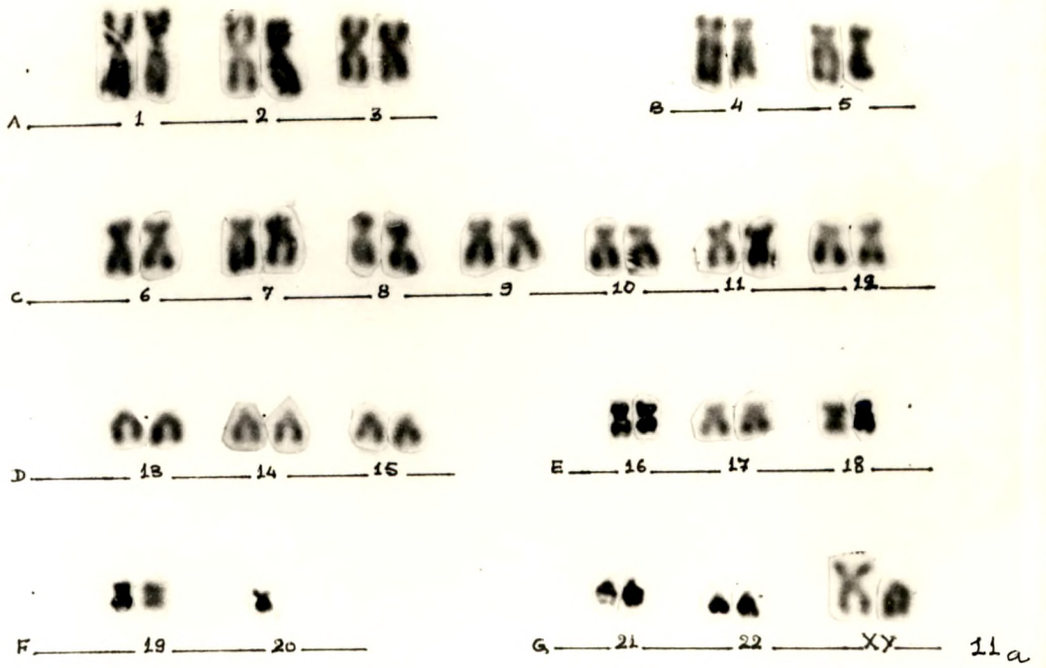

A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 XX

10

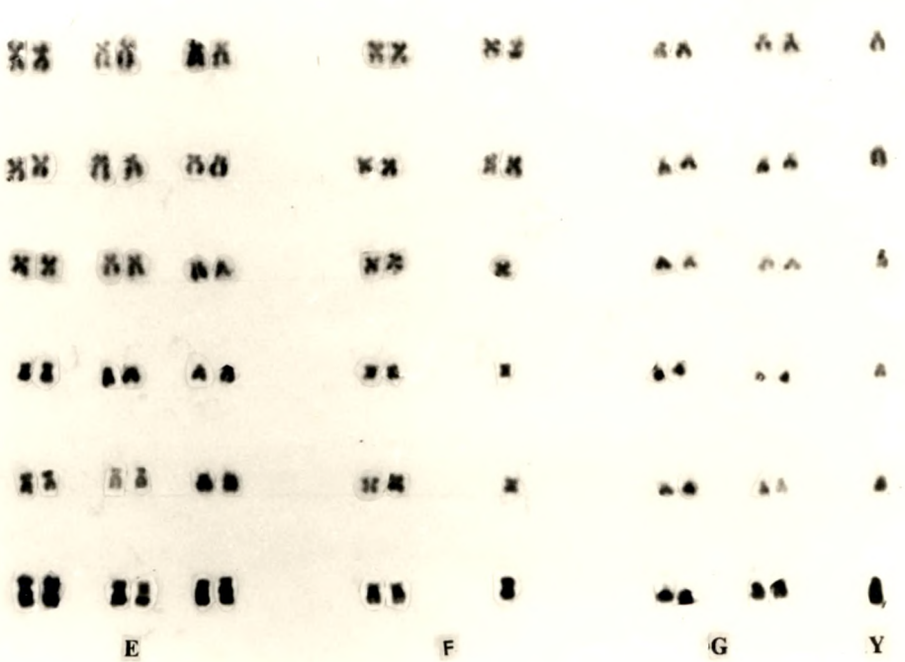
Fig.11 (a)

Giemsa stained karyotype of patient showing 45,XY -20 (F group monosomy) chromosome.

(b) Partial karyotype showing F group monosomy, with G group and sex chromosomes.



11a



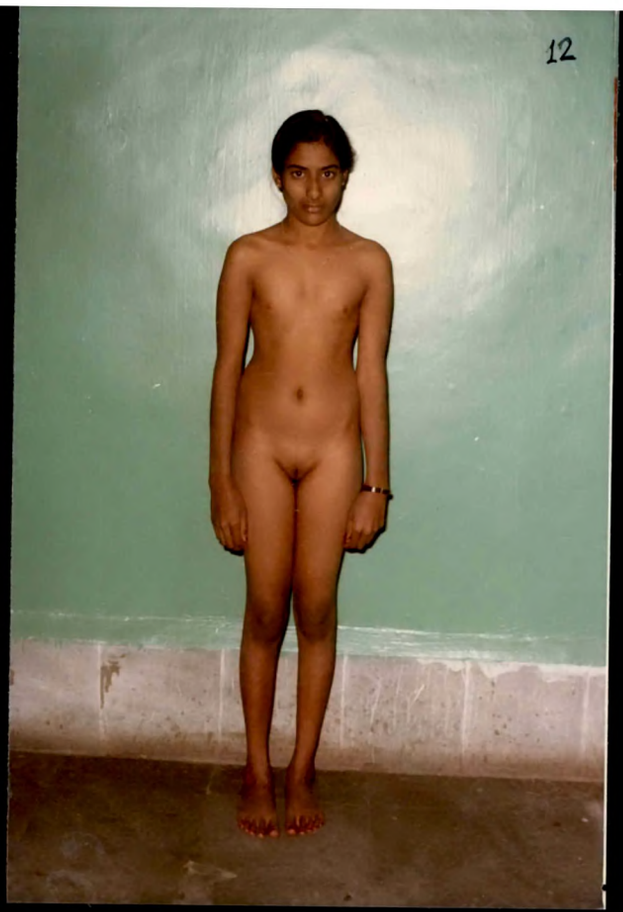
11b

Fig.12

Clinical photograph of the patient with primary amenorrhoea showing broad flat (shield) chest, widely spaced nipples. Absence of secondary sexual characters with almost absent or sparse axillary and pubic hair, under developed external genitalia.

Fig.13

G-banded karyotype of patient referred for primary amenorrhoea, showing 45,X Turner's syndrome.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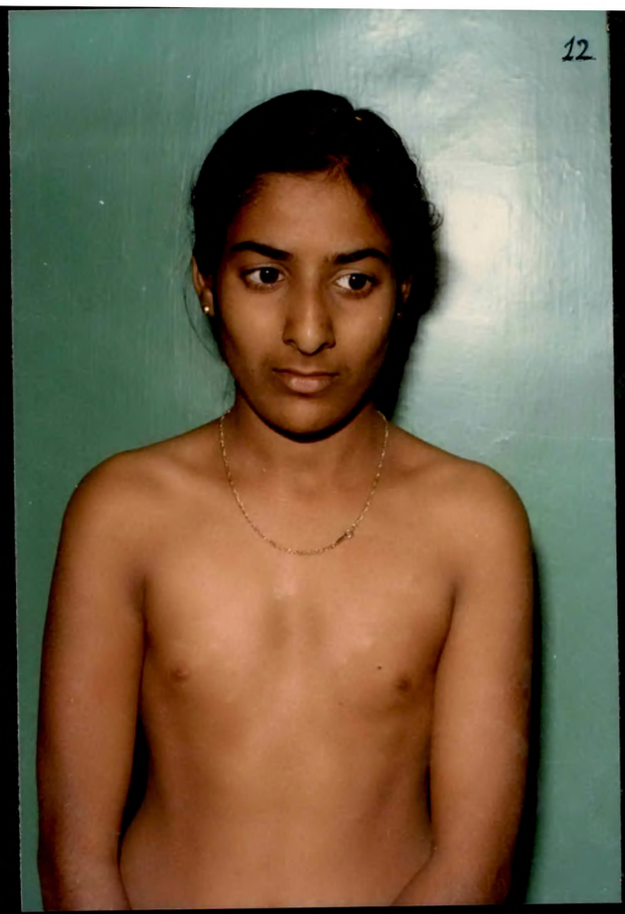

12

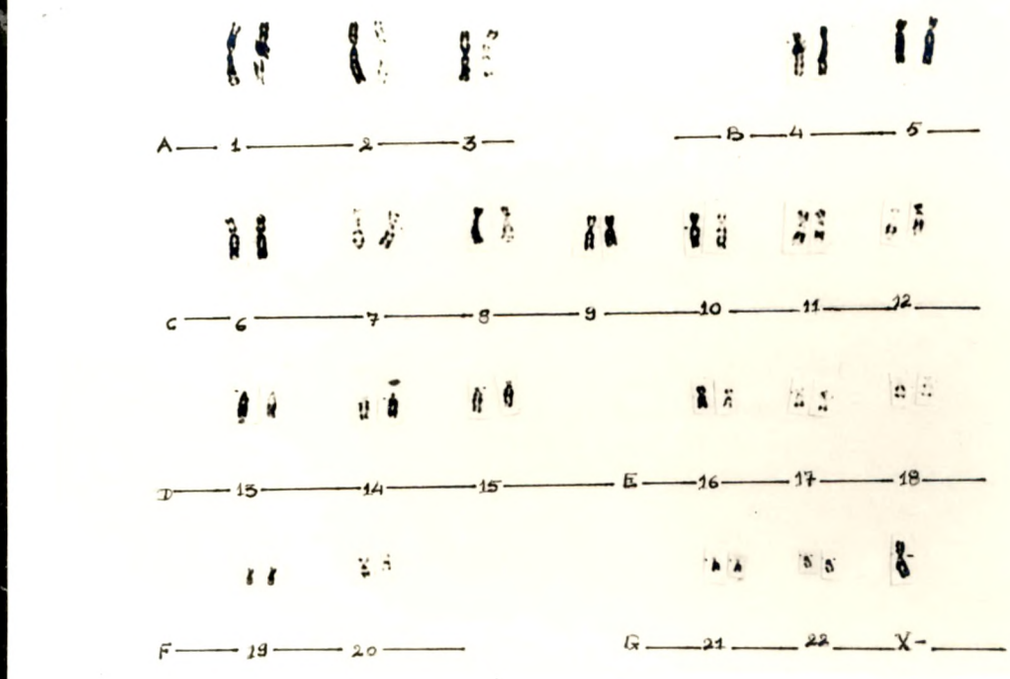
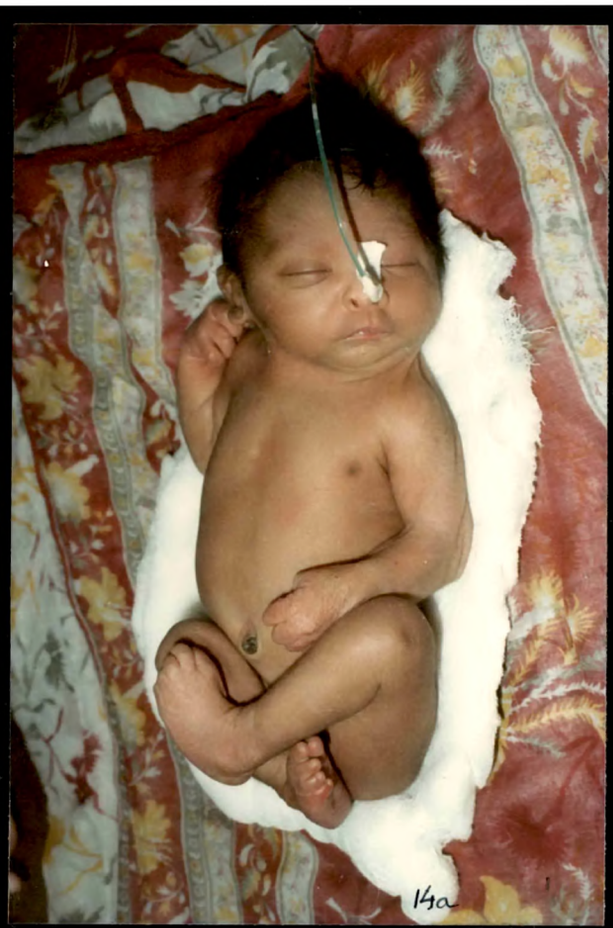
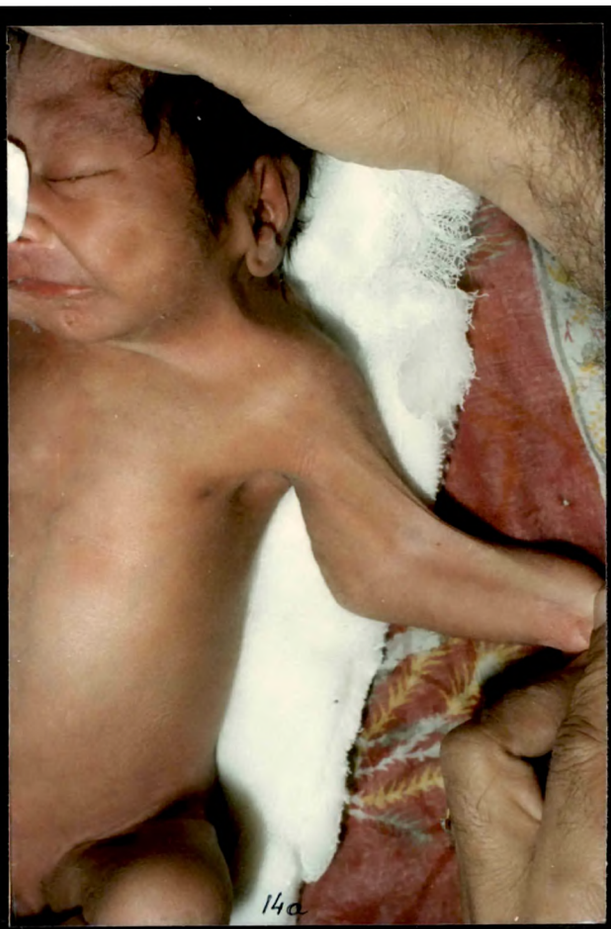

A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 X
13

Fig.14

(a) Clinical photograph of patient with short and webbed neck, spina bifida. The skin fold extends from occipital region to scapula and from arm to cubital fossa also.

(b) Photograph of Turner patient showing presence of simian crease.


14a


14a

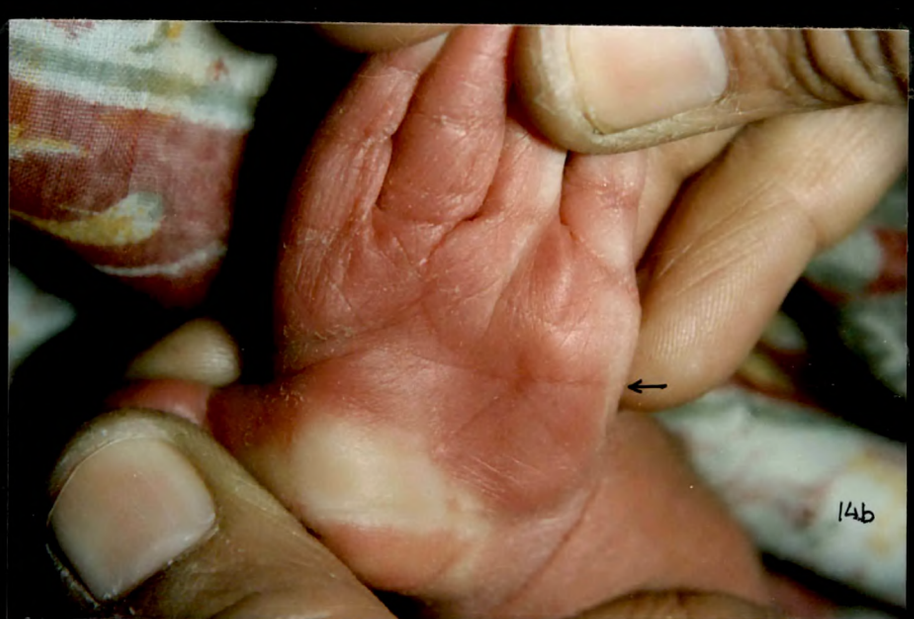

14b

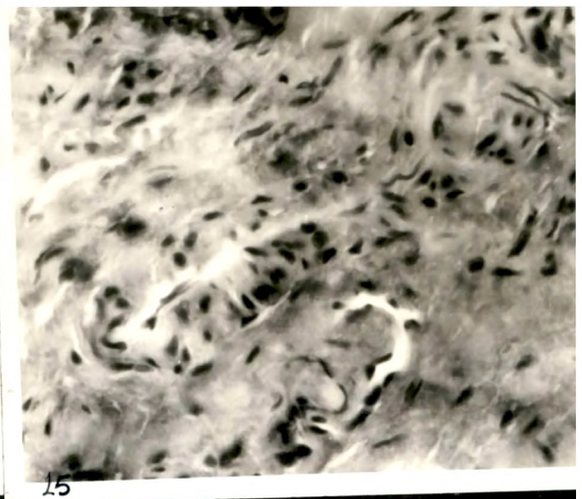
Fig.15

Photomicrograph shows ovarian stroma with very few atretic follicles (AF) and blood vessels, in the patient of 46,X iso(Xq).

Fig.16

Clinical photograph of patient referred for primary amenorrhoea. She has under-developed breast, scanty pubic and axillary hair, short stature and under-developed external genitalia. Her cytogenetic findings show 46,X, iso(Xq).


AF
15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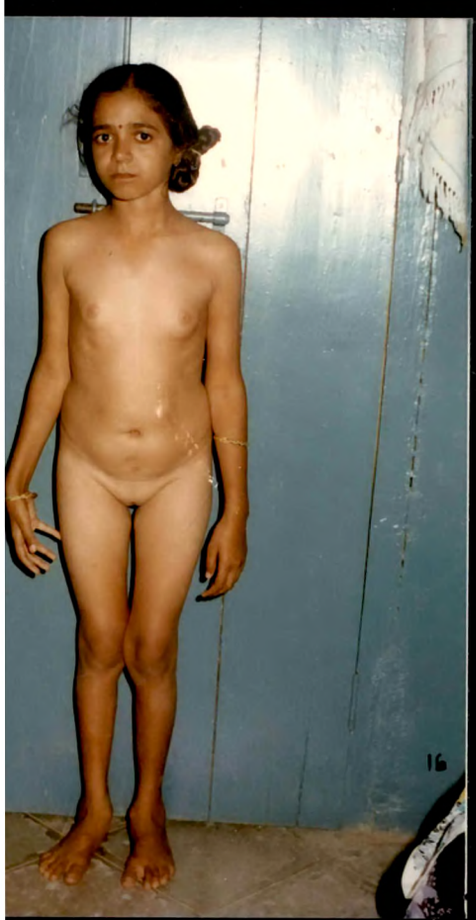
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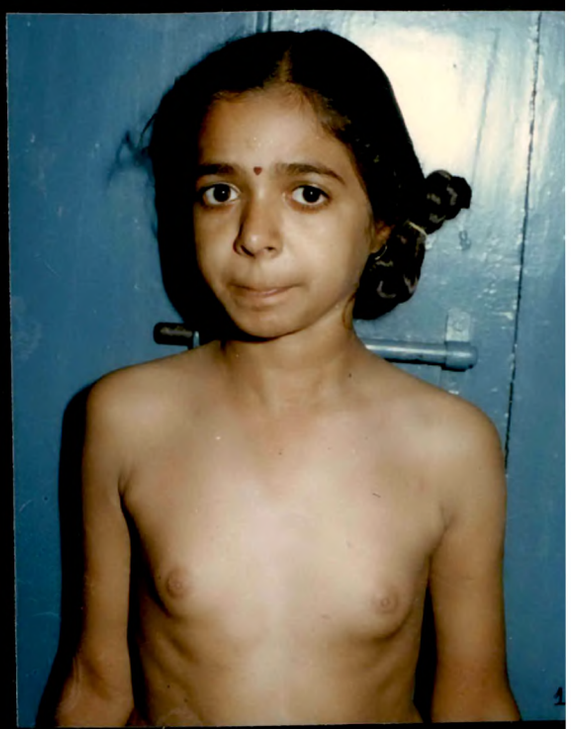


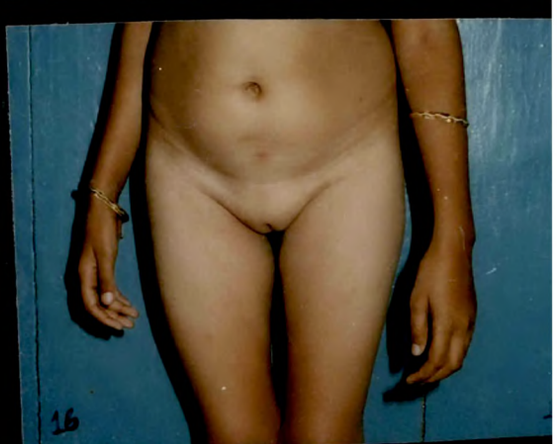

16

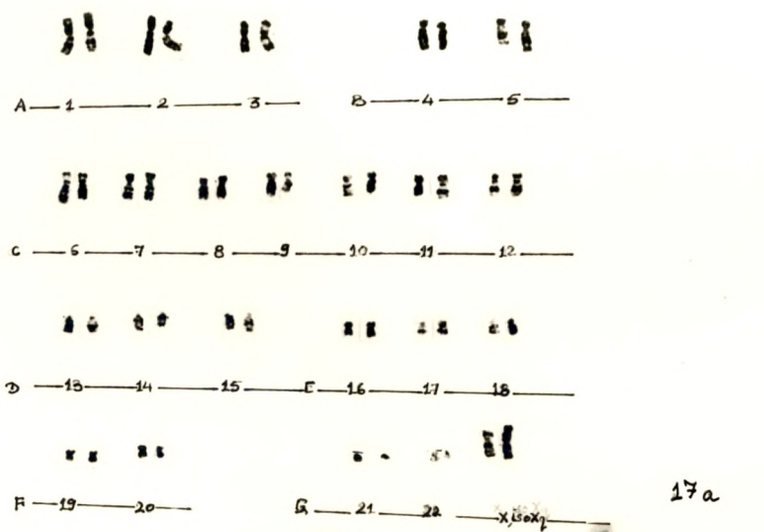
Fig.17

(a) G-banded karyotype of patient with primary amenorrhoea. Karyotype revealed 46,X, iso(Xq).

(b) (i) Partial G-banded karyotype with G group chromosomes, normal X chromosome and one isochromosome of Xq region.

(ii) C-banding of X and isoXq chromosome showing two different clear bands near the centromere.

(iii) A comparison of normal X chromosome with the iso,Xq chromosome by late replicating banding. iso Xq was located at the periphery of metaphase.


A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 X,isoXq

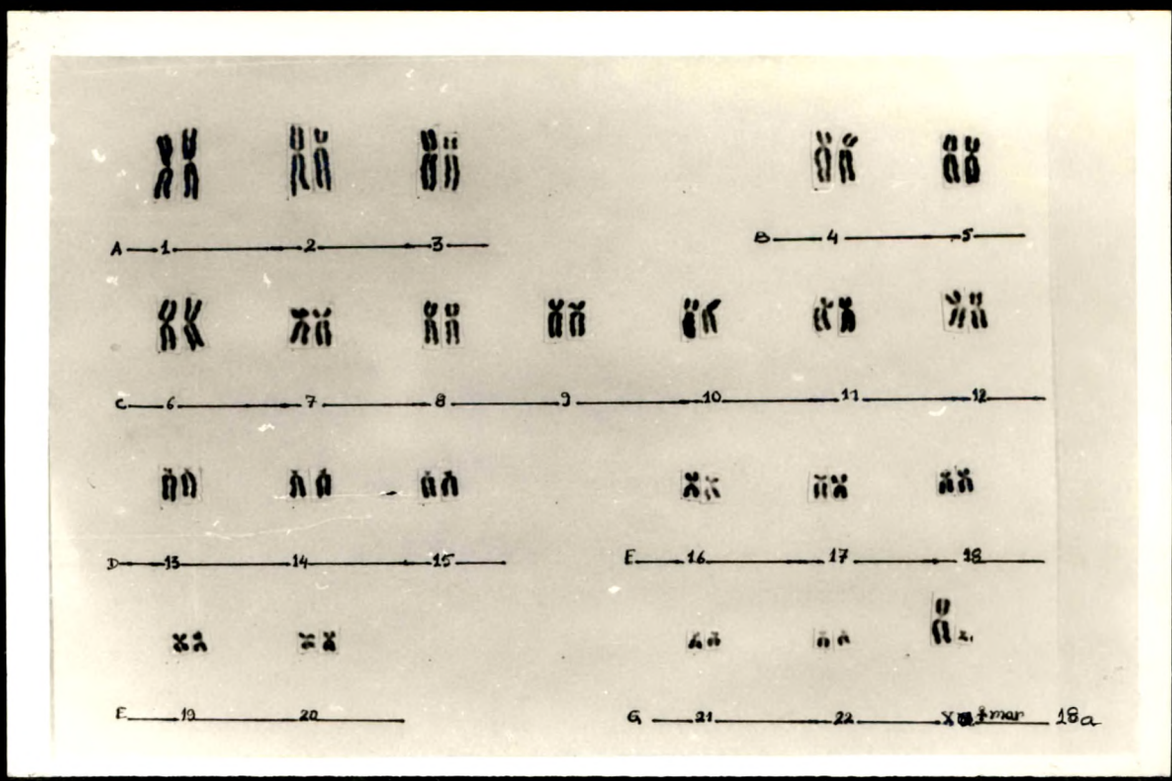
17a


21
22
Q-Banding
X, isoXq
C-Banding
X isoXq
Late Replicating
X Chromosome

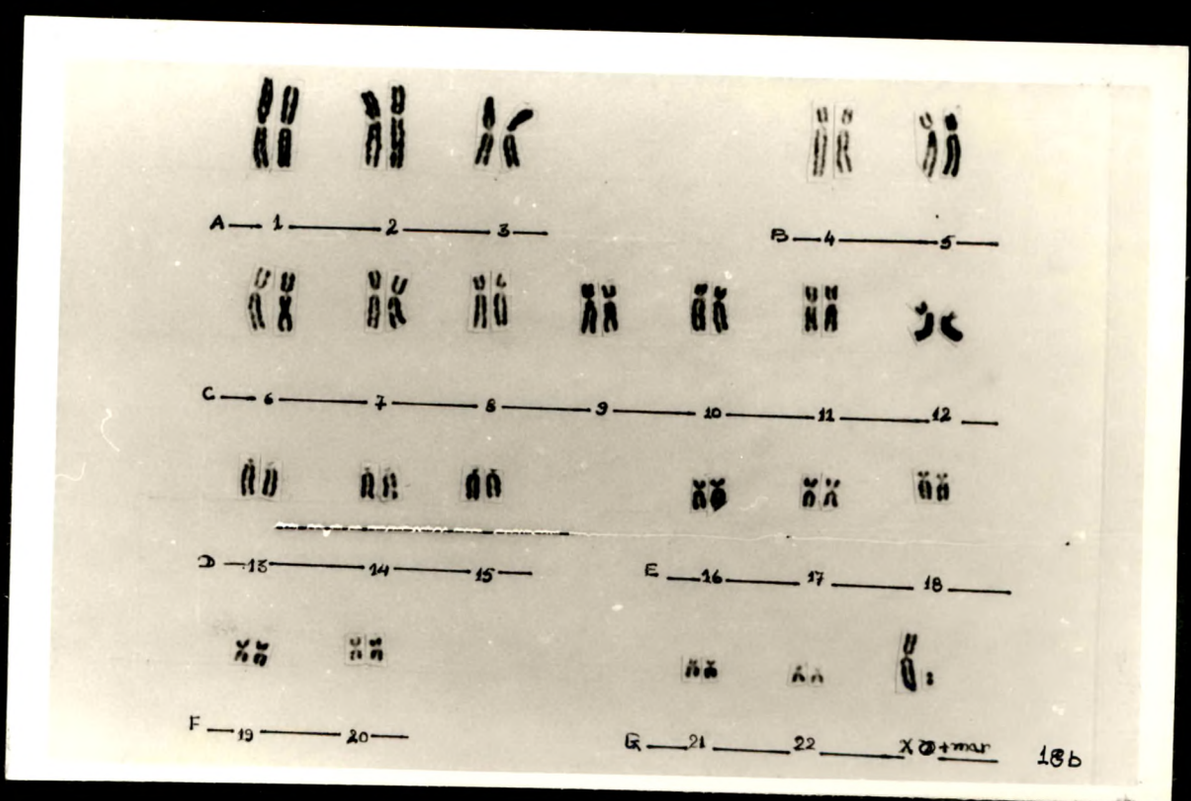
17b

Fig.18 (a) and (b)

Both karyotype (Giemsa stained) showing 46,X +marker (small metacentric) chromosome of the patient with primary amenorrhoea.


A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 X +mar

18a

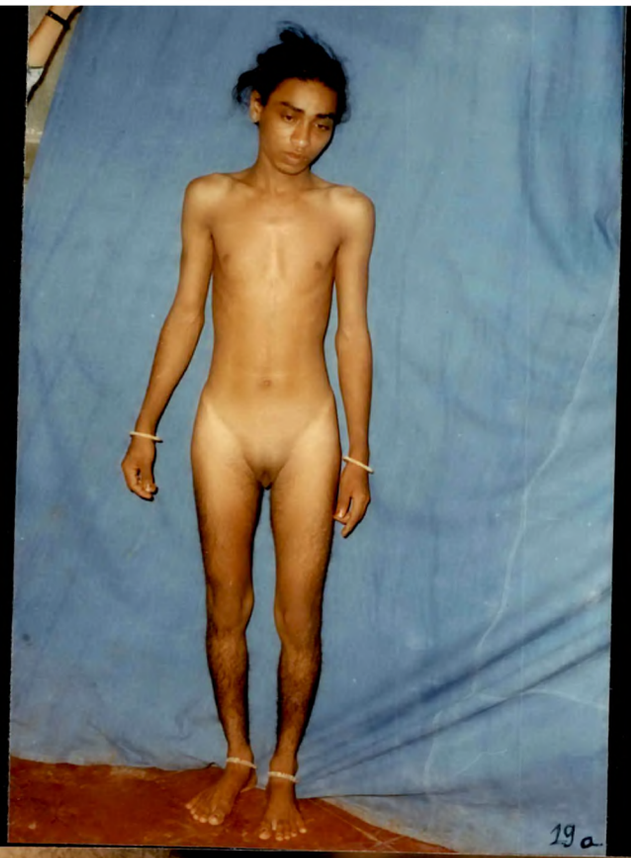

A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 X +mar

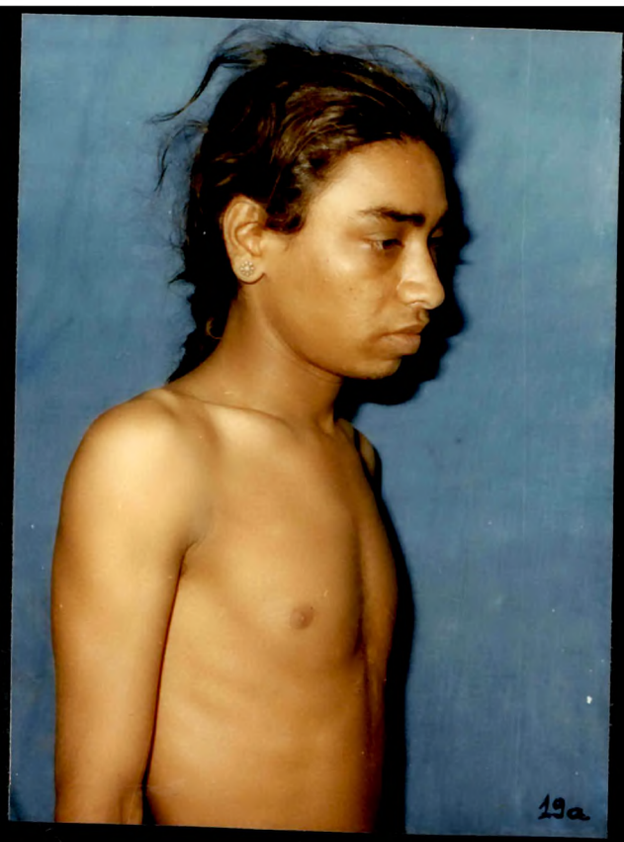
18b

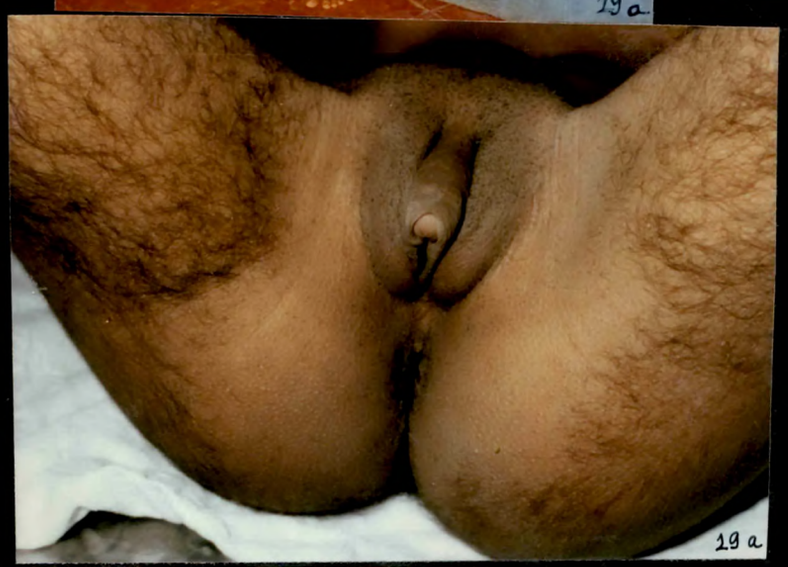
Fig.19

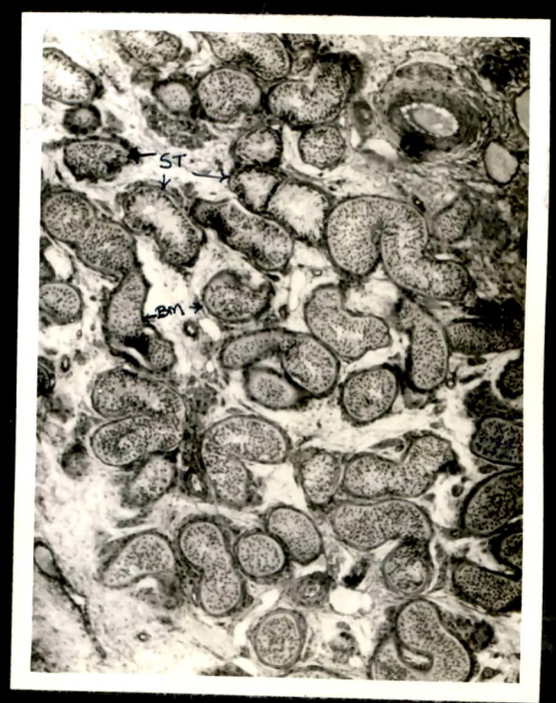
(a) Clinical photograph of patient referred for testicular feminization with the complaint of primary sterility. Presence of hair all over the body hersuitism, no breast development, ? enlarged clitoris, presence of vaginal opening (Vo) leads into pouch, bilateral palpebral masses (? testes) in labia majora.

(b) Photomicrograph of a section of masses showing presence of seminiferous tubules (ST) with thick basement membrane.


19a


19a


19a


ST
BM

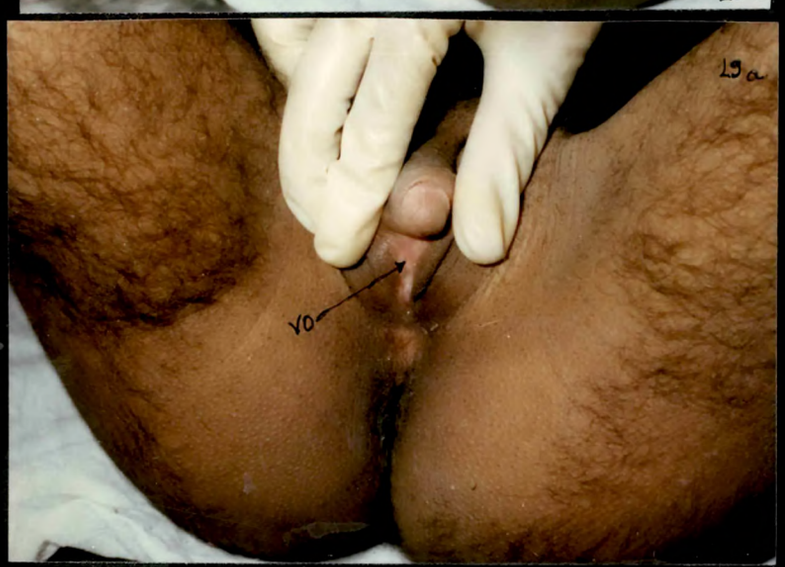

19a
VO

Fig.19

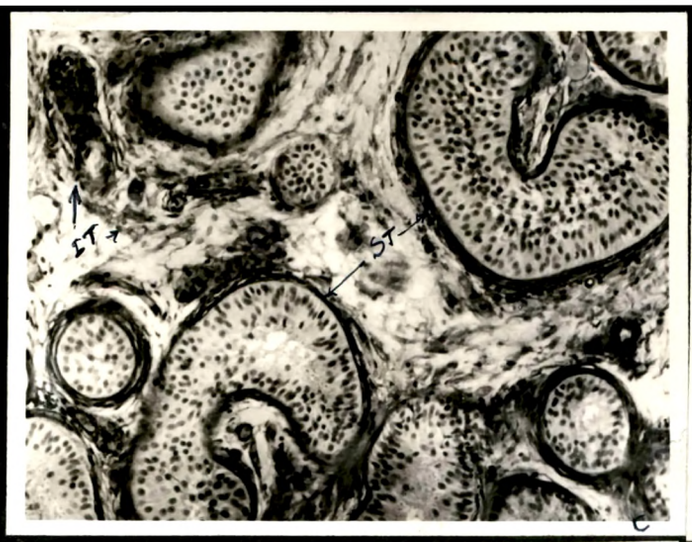
(c) High power view of section (19b) seminiferous tubules (ST) with interstitial (IT) tissues.

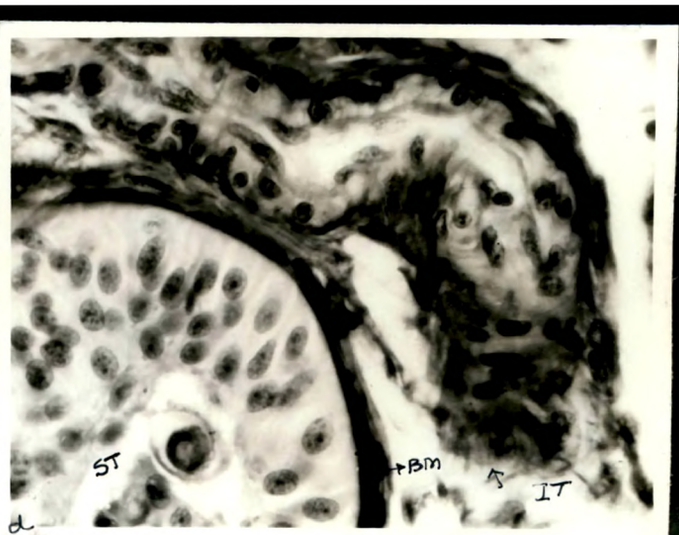
(d) Magnified view of single seminiferous tubules (ST) with clear basement membrane (BM) and interstitial cells (IT). Spermatogenia with predominantly sertoli cells (S) are seen.

(e) The photomicrograph of section showing presence of vas deference in the patient with testicular feminization. The lumen (L) is present with muscularis externa (ME) and numerous blood vessels are also seen.

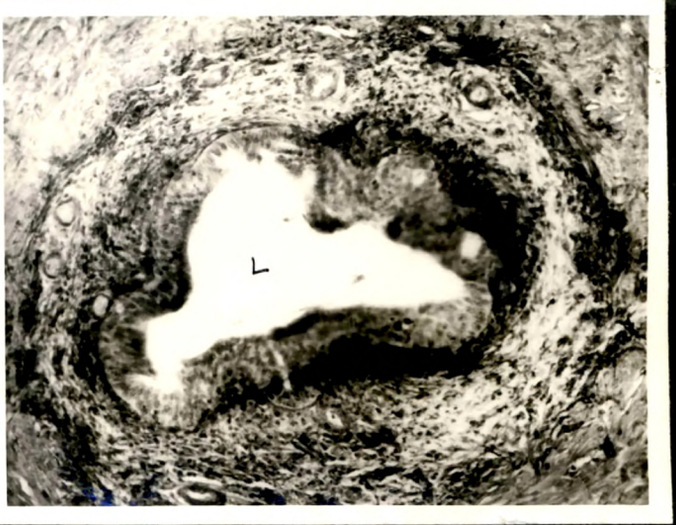
Fig.20

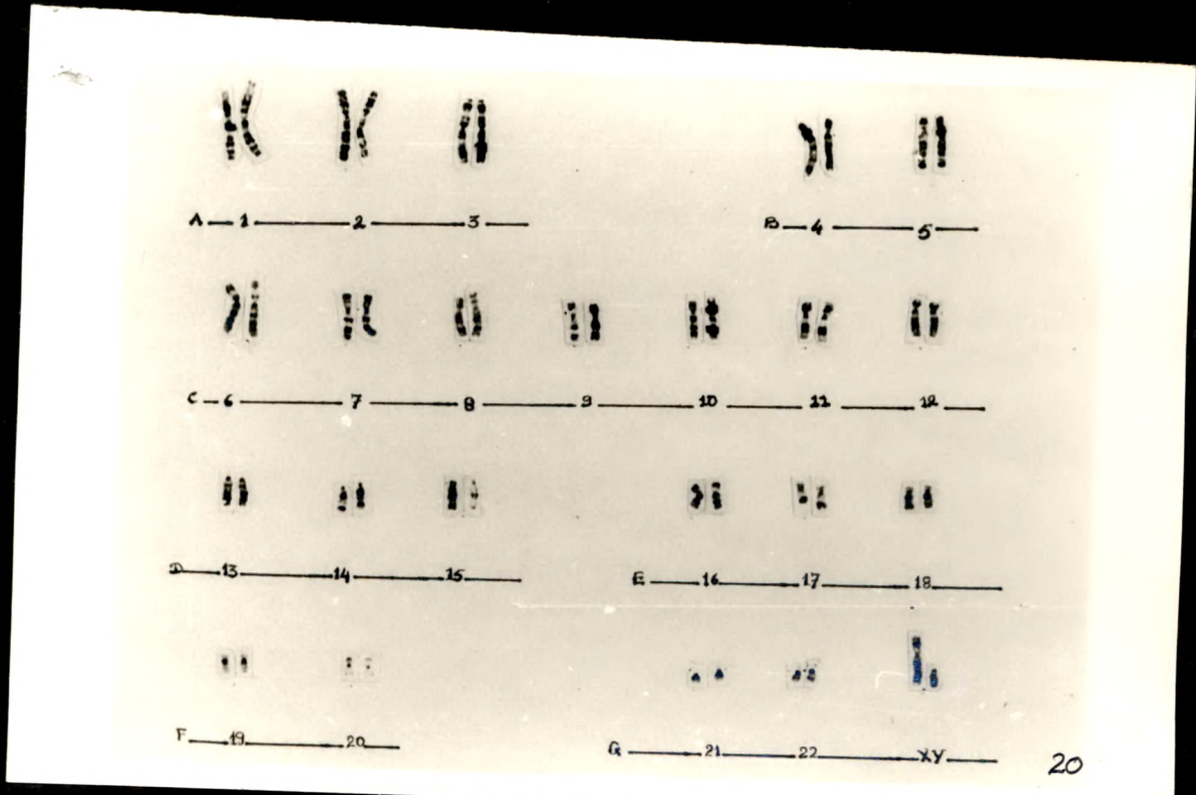
G-banded karyotyping in the patient of testicular feminization syndrome showing 46,XY chromosomal constituents.


IT
ST
c


ST
BM
IT
d


L


L


A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 XY

20

Fig.21

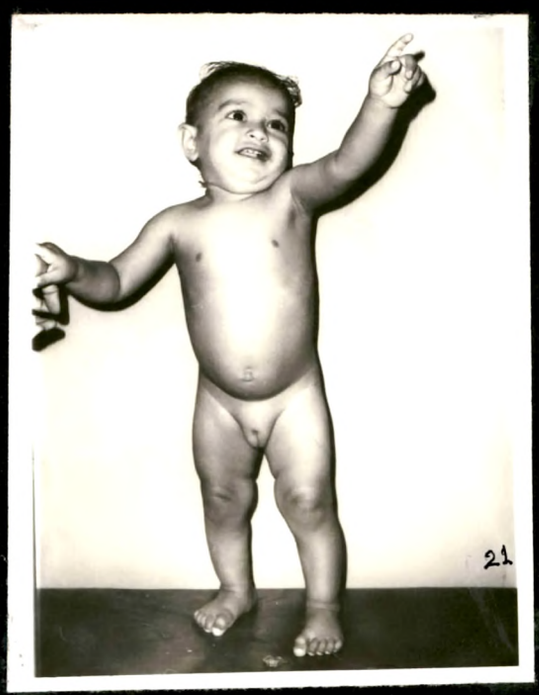
The clinical picture of the patient with bilateral palpebral testes in labia majora having 46,XY chromosome.

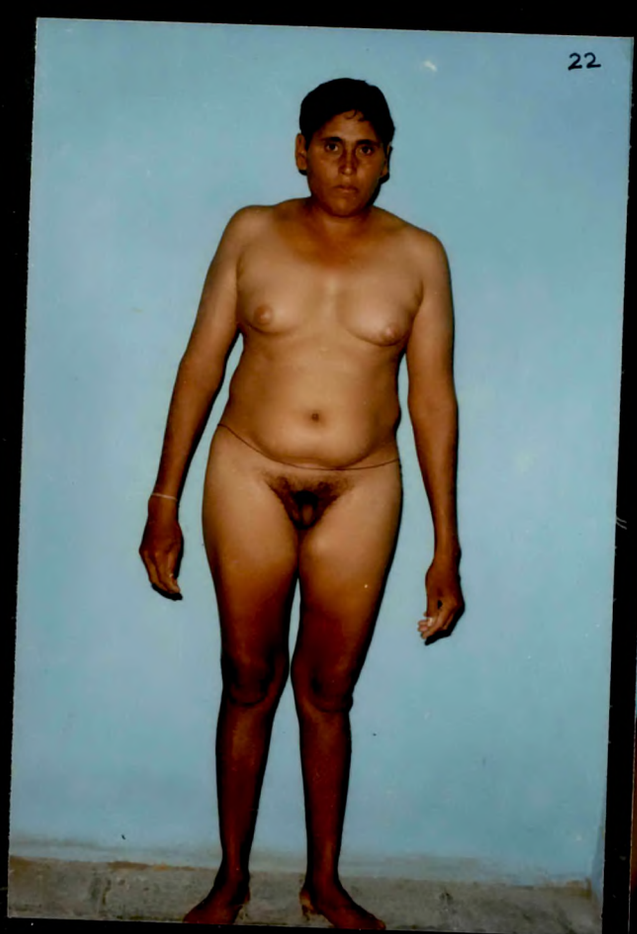
Fig.22

(a) A 32 year old male patient referred for Klinefelter's syndrome with complaint of azoospermia and primary sterility. No secondary sexual characters, fat distribution is feminine type.

(b) Close up of chest showing presence of gynaecomastia, absence of mustache, beared. No male pattern hair line at chest.

(c) Close up of external genitalia, which is under-developed and presence of scanty feminine type pubic hair.


21


22

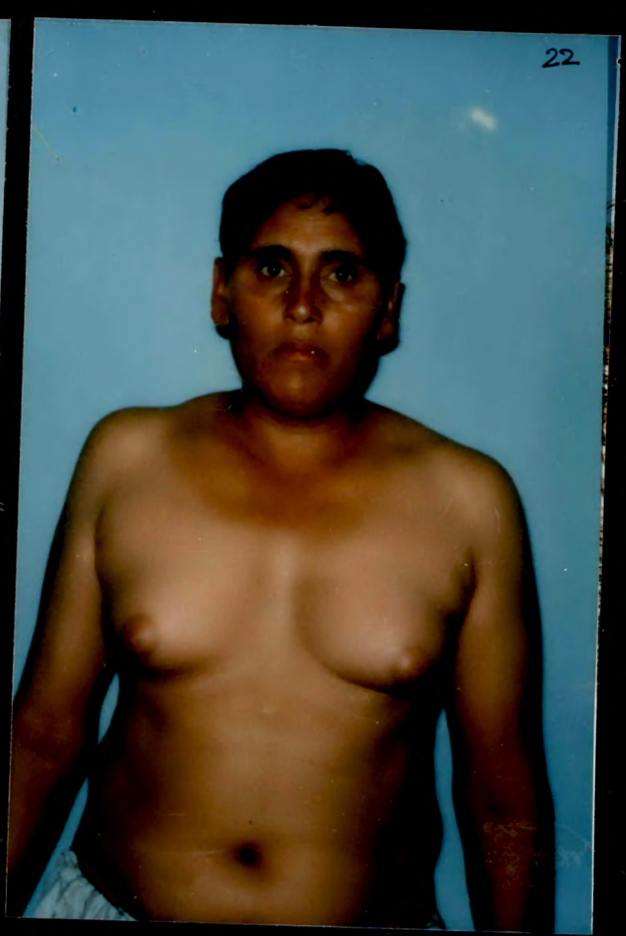
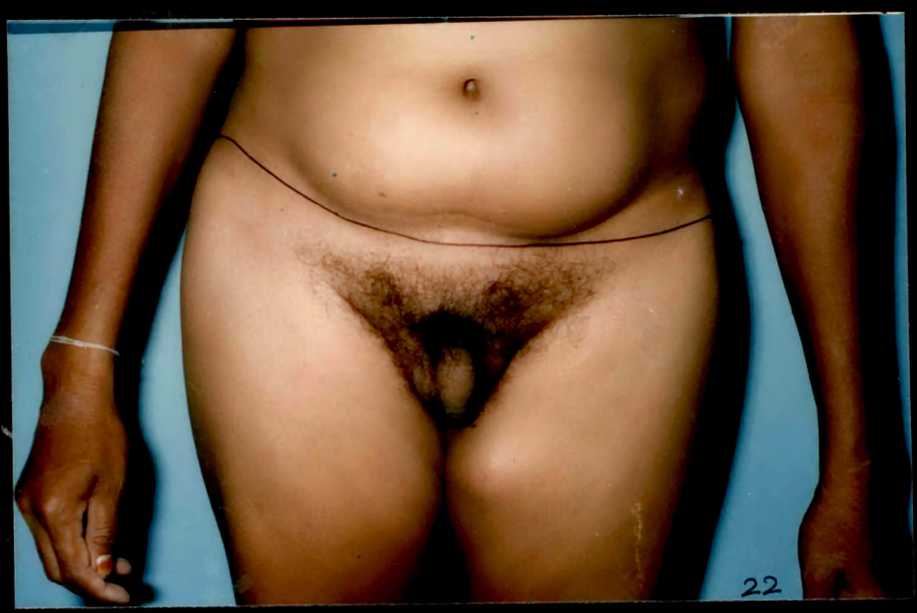

22

Fig.23

(a) Photomicrograph of testicular biopsies shows characteristic picture of Klinefelter's syndrome with hyalinization of seminiferous tubules and relative predominance of the interstitial (Leydig) cells.


22

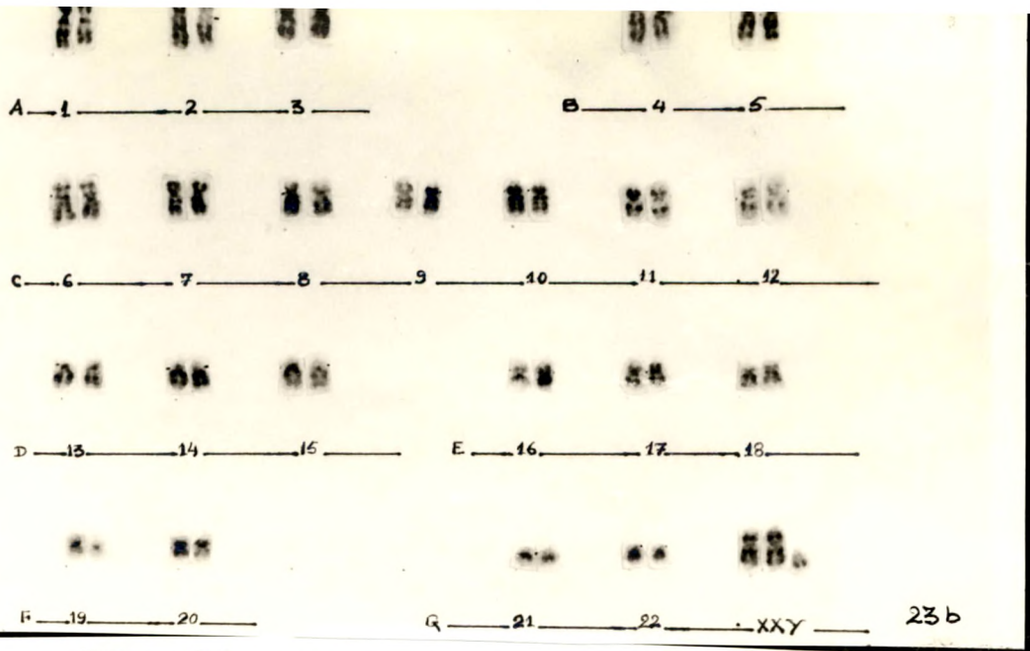

Epy.C
ST
23

Fig.23

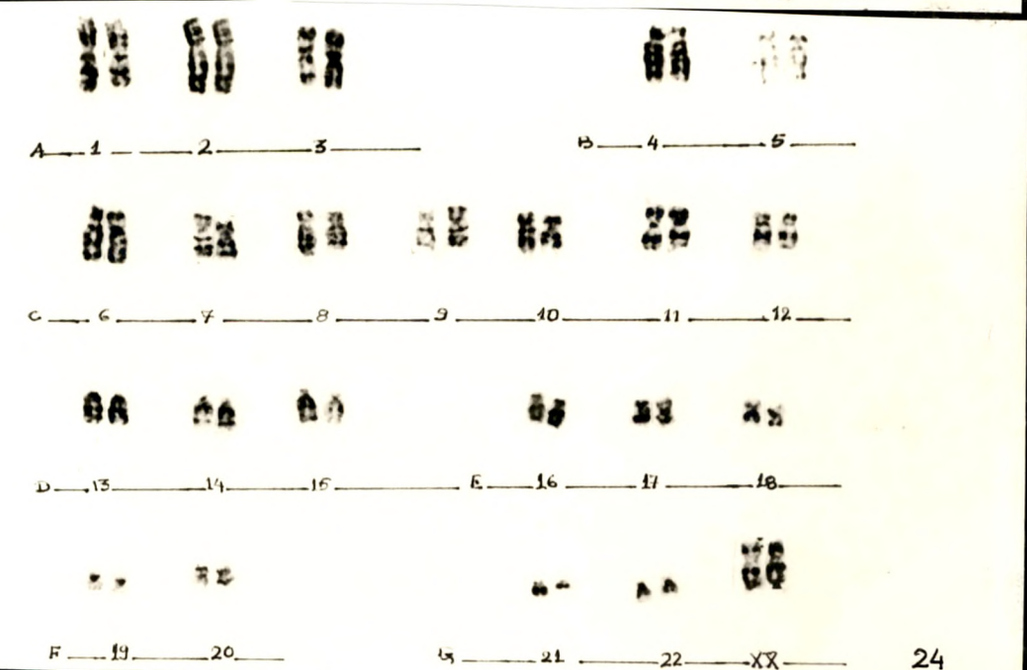
(b) G-banded karyotype of a Klinefelter's syndrome showing a 47,XXY sex chromosome complement.

Fig.24

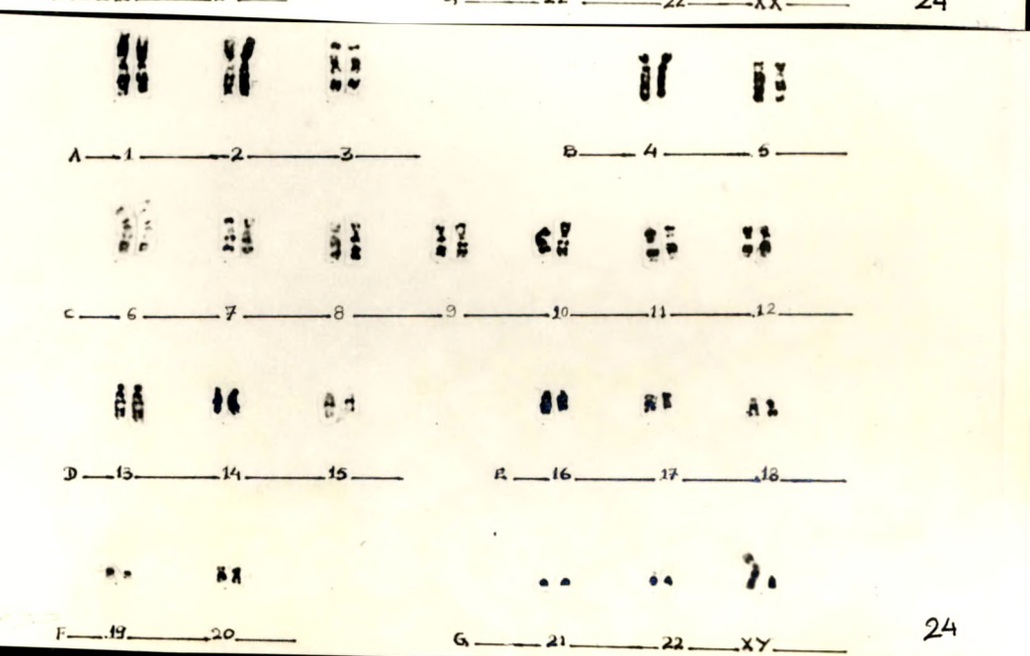
G-banded karyotype with 46,XX and 46,XY chromosome complements in the true hermaphrodite patient.


A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 XXY

23 b


A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 XX

24


A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 XY

24

Fig.25

Photomicrograph of testicular tissue in case of true hermaphrodite with seminiferous tubules (ST), containing Sertoli cells and few germ cells. Cytogenetic finding was 46,XX/46,XY.

Fig.26

Ovarian fibrous stroma with possibly atretic primordial follicle; undifferentiated ovarian tissue may be infantile ovarian tissue.

Fig.27

G-banded karyotype of patient referred for spontaneous abortions - 45,X, -13, -14 t(13q/14q).

Fig.28

Partial G-banded karyotype showing t(13q 14q) in (a) proband; (b)sister of proband and (c) father of proband. Partial karyotype suggests paternal origin of the balanced Robertsonian translocation.

SC
ST

25

OVARY
F. TUBE

26

A
1
2
3
B
4
5
C
6
7
8
9
10
11
12
D
13
14
15
E
16
17
18
F
19
20
G
21
22
XY

27

A]
13 (13q/14q) 14
15
X X
B]
13(13q/14q) 14
15
X X
C]
13(13q/14q) 14
15
X Y

28

Fig.29

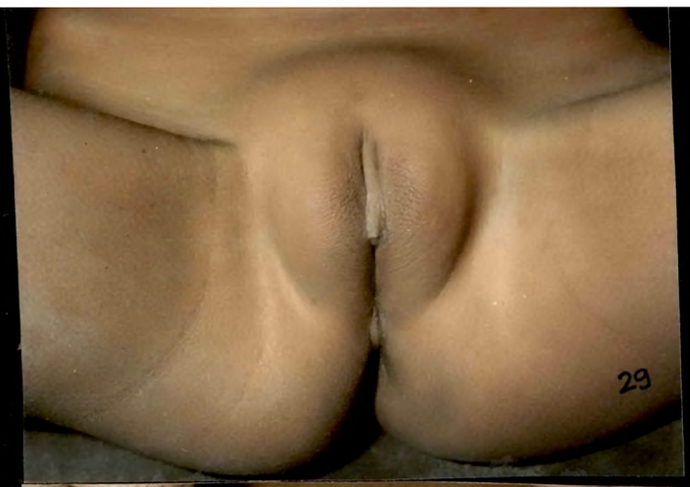
Clinical photograph of one brother referred for ambiguous genitalia with very small mass (? testes) palpated and under-developed phallus.

Fig.30

Clinical photograph of second brother having ambiguous genitalia, microorchidism, small under-developed penis.

Fig.31(a) and (b)

Photomicrograph of bilateral palpated mass showing infantile testicular tissues, in both brothers. Both have 46,XY.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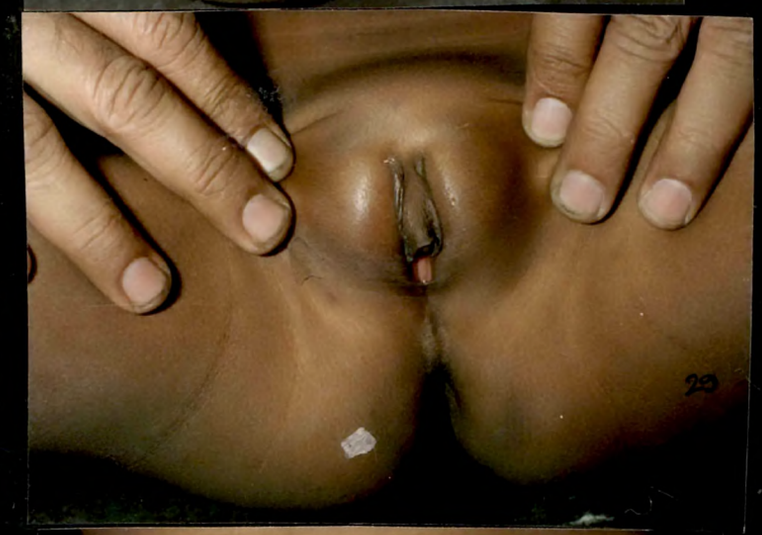
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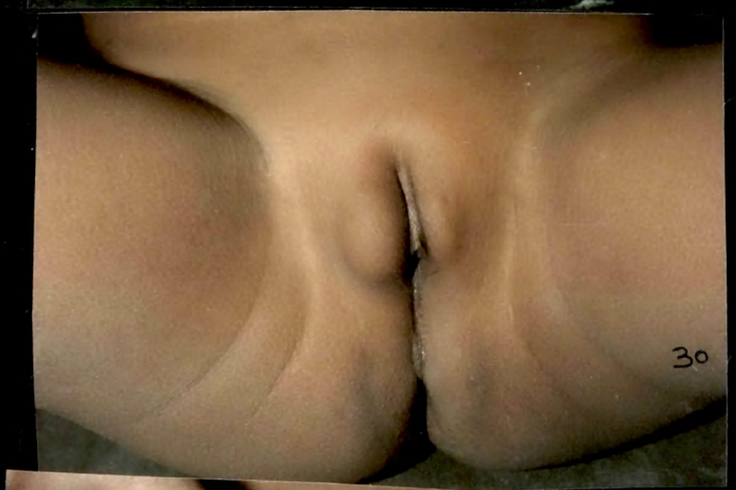
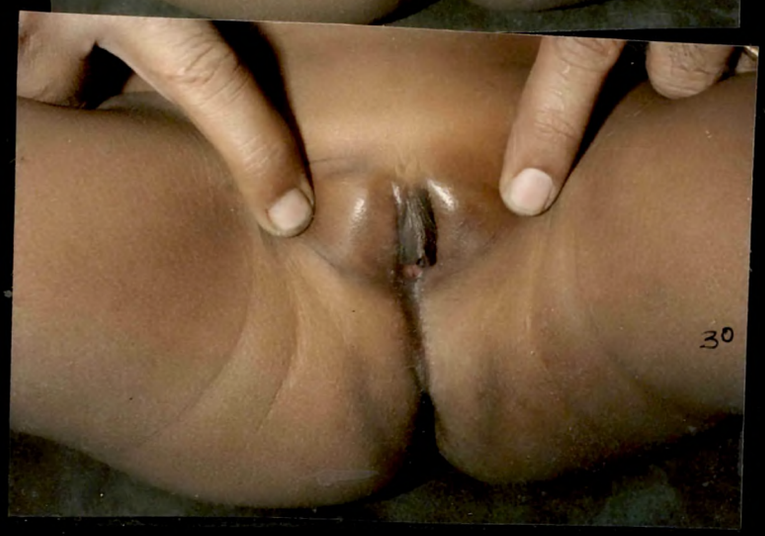

30


30


SM
31a

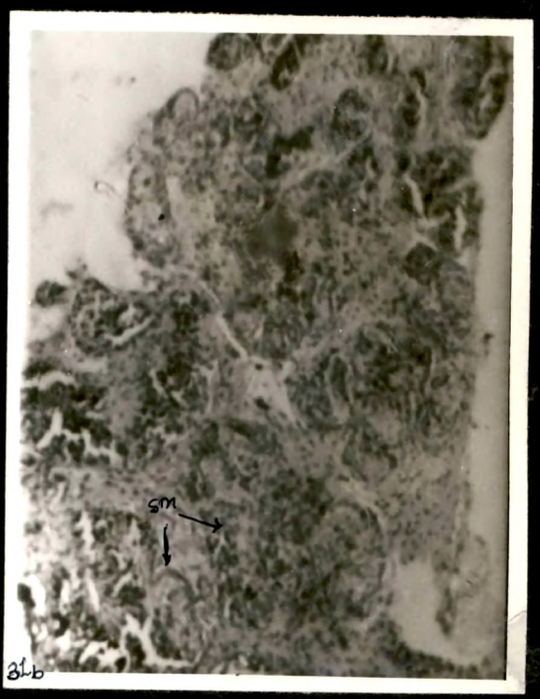

SM
31b

Fig.32

Photomicrograph of biopsy tissue showing on left side testicular tissue with seminiferous tubules and on right side ovarian stroma with atretic follicles, hence ovotestis.

Fig.33

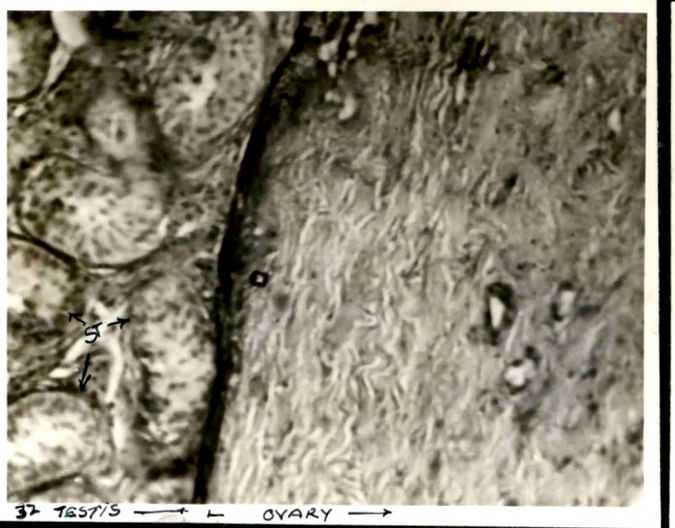
The biopsy tissue of other side shows only ovarian stroma with atretic primordial follicles.

Fig.34

Photomicrograph of section shows fibrous tissue, no evidence of developing gonads either testes or ovaries in patient of 46,XY gonadal agenesis.

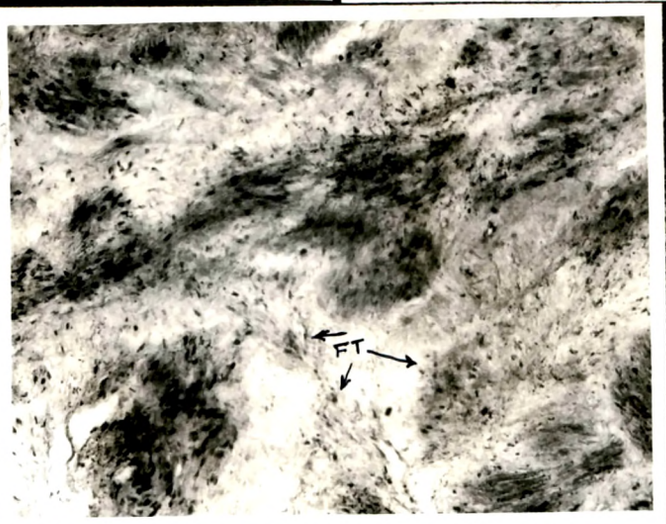
Fig.35

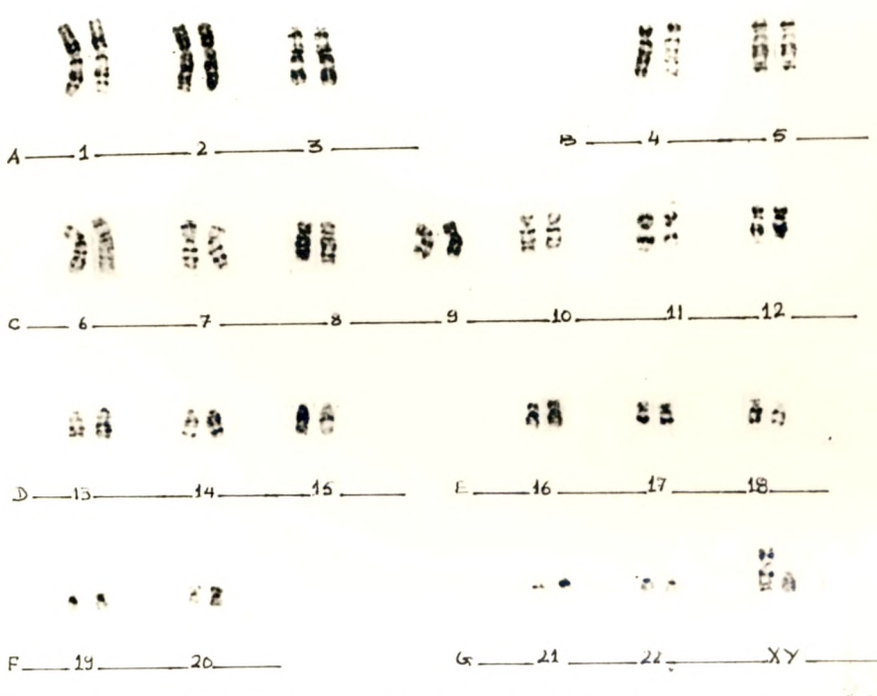
G-banded karyotype of 46,XY gonadal agenesis.



32 TESTIS ⟶ ← OVARY ⟶

33 OVARY





35

Fig.36

(I) Clinical photographs of two brothers (Iq) and (AK) with hypogonadism, ? labio scrotal folds with rudimentary penis, no mustache, no beared with feminine voice, absence of any testis/mass in the labio scrotal folds.

(II) CLinical photograph of a patient, son of the sister of above brothers showing same characters but has small palpated bilateral masses (? testis) in the labio scrotal folds. He has 46,XY.

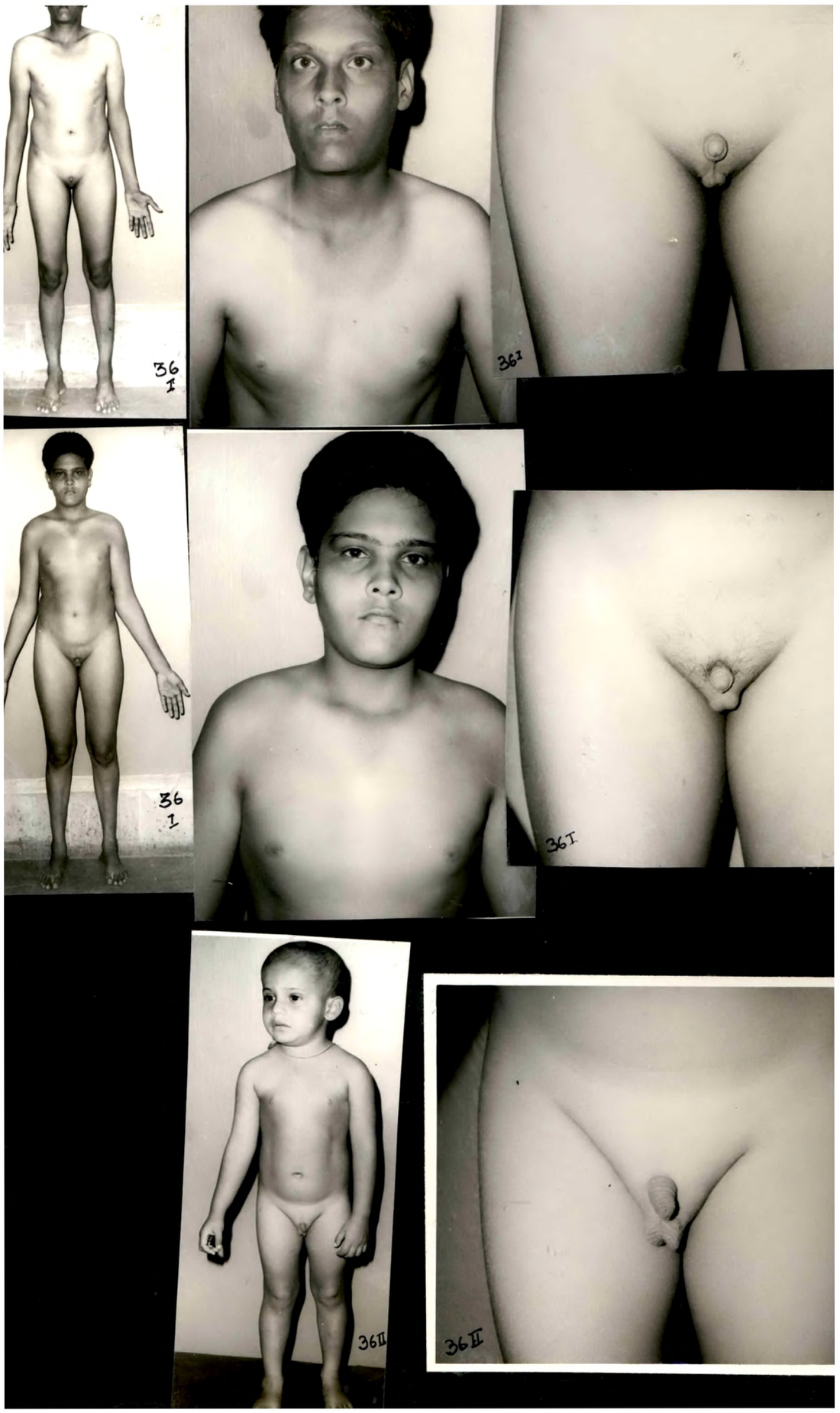
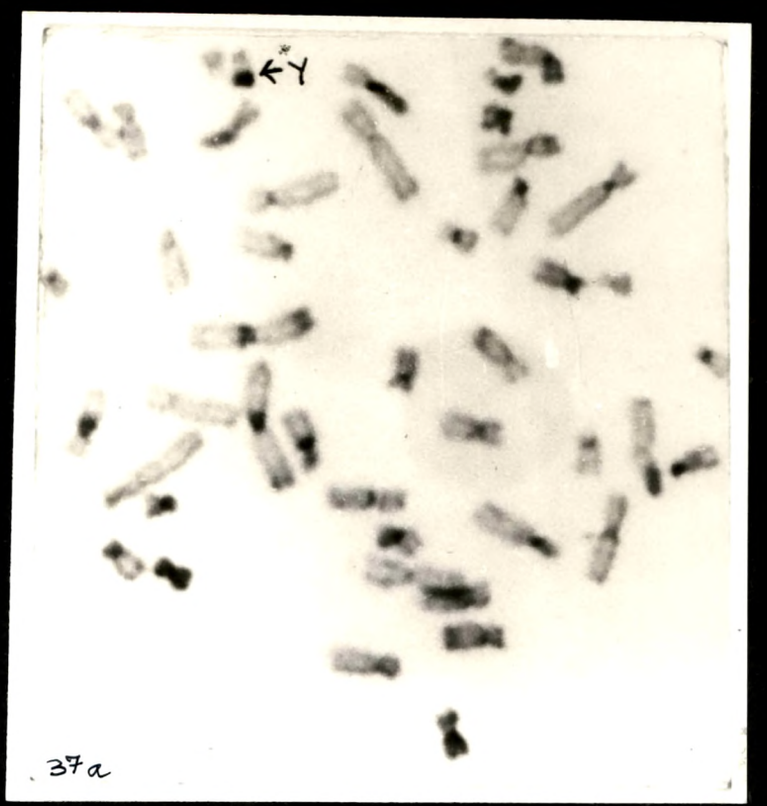

36 I
36I
36 I
36I
36II
36II

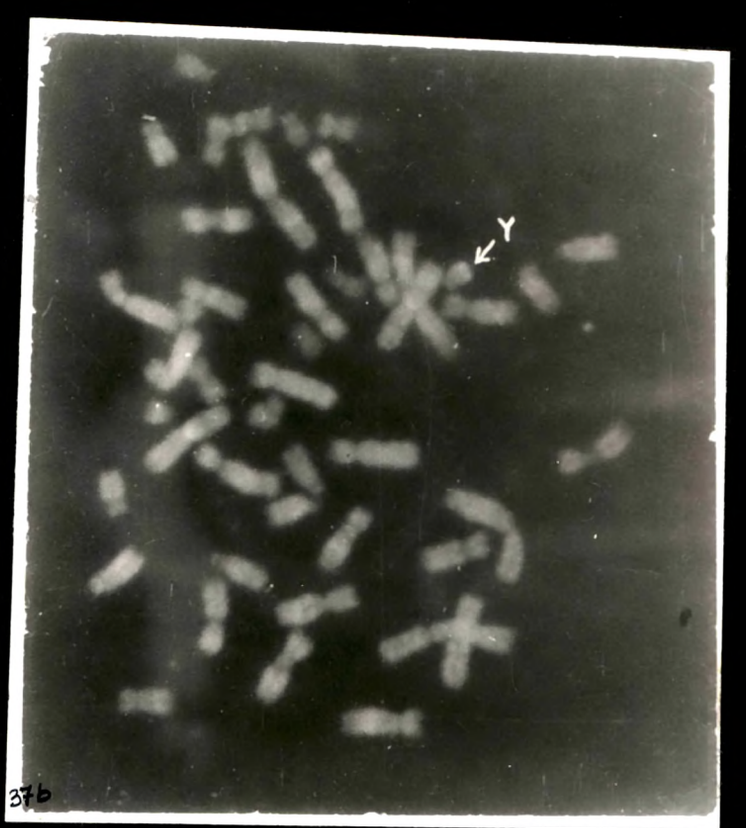
Fig.37

(a) C-banded metaphase showing 46,XY (arrow - Y chromosome) pattern in one brother (Iq).

(b) Q-banded metaphase showing 46,XY (arrow Y chromosome) pattern in other brother (AK).



37a



37b

Fig.38

Clinical photograph of genotypically and phenotypically a normal male with normal height, external genitalia and unilateral undescended testis. Arrow (A) indicates the site of operation for hernia during which whole sac was removed and later opened up. Cytogenetic finding was 46,XY.

Fig.39

Photograph of uterus (ut), fallopian tube (FT), Testes (T), vas deference (VS) found after opening of hernial sac.

Fig.40

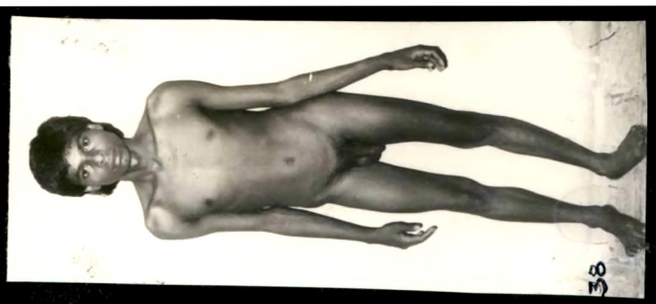
(a) Photomicrograph of uterus with endometrium and endometrial gland.

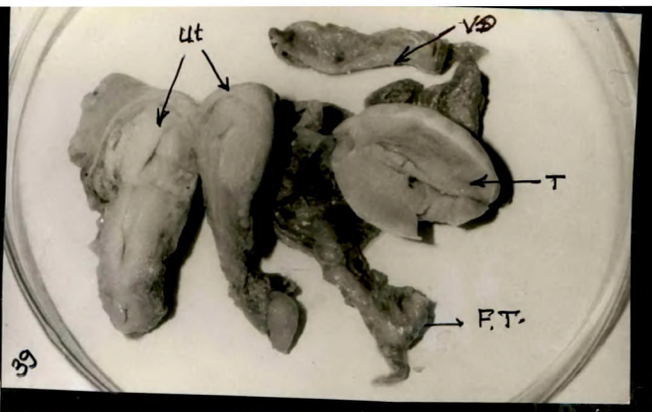
(b) Photomicrograph of testis showing normal spermatogenesis. Seminiferous tubules are normal in size.

(c) Photomicrograph of testis showing thickening of basement membrane, marked depletion of germ cells population. Some of the tubules are atrophied.

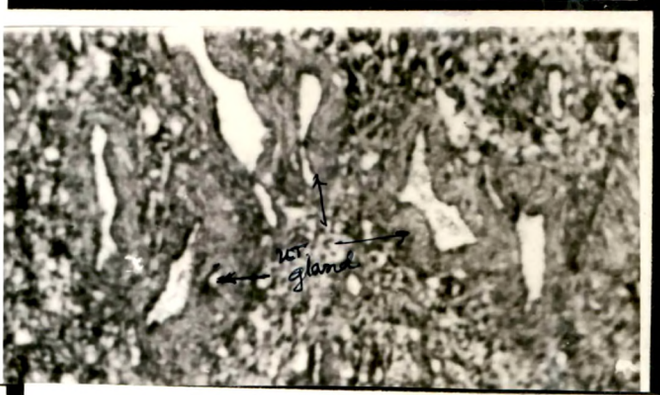
(d) Photomicrograph of vas deference with muscular coat.

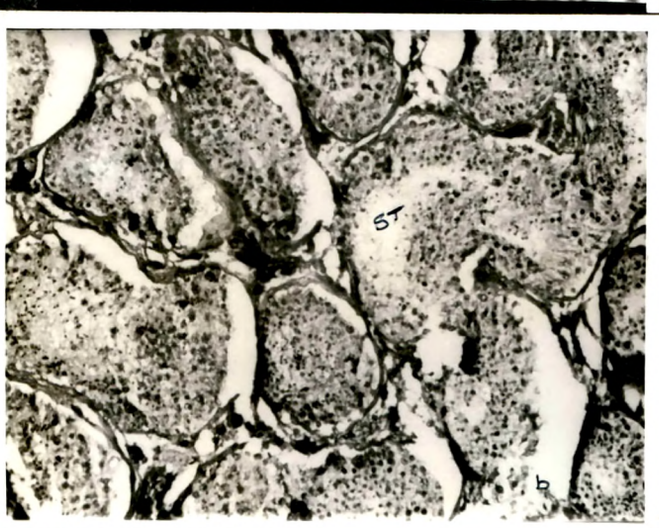
(e) Photomicrograph of fallopian tube ampullary region with muscularis externa.

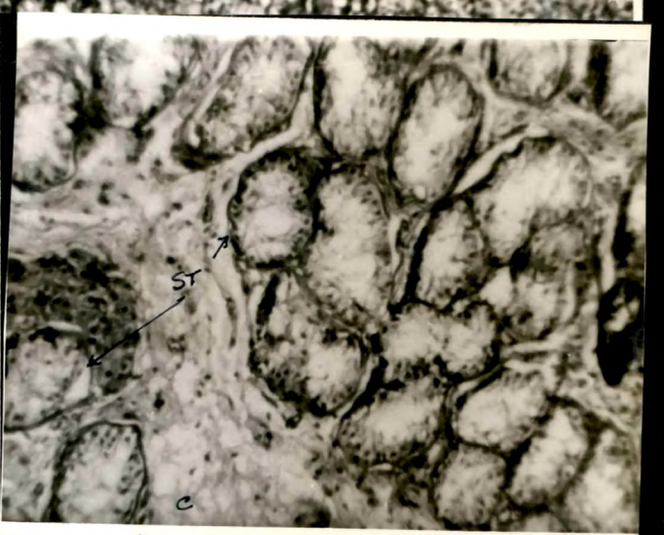


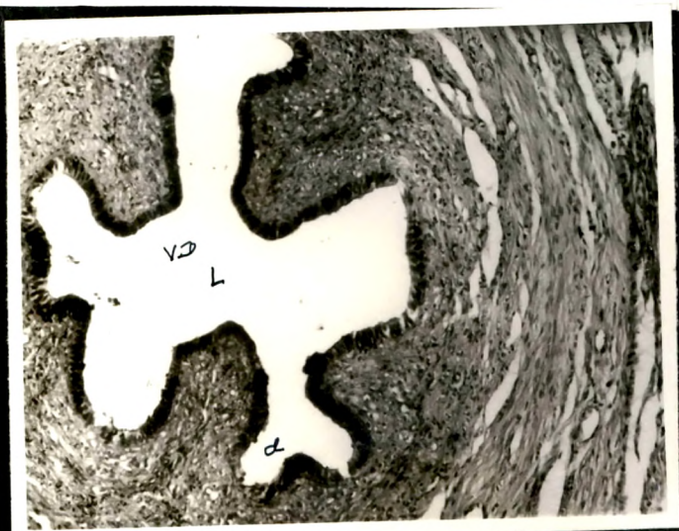

Ut
V.D
T
F.T.
39


UT
150 a


UT
gland


ST
b


ST
c


V.D
L
d

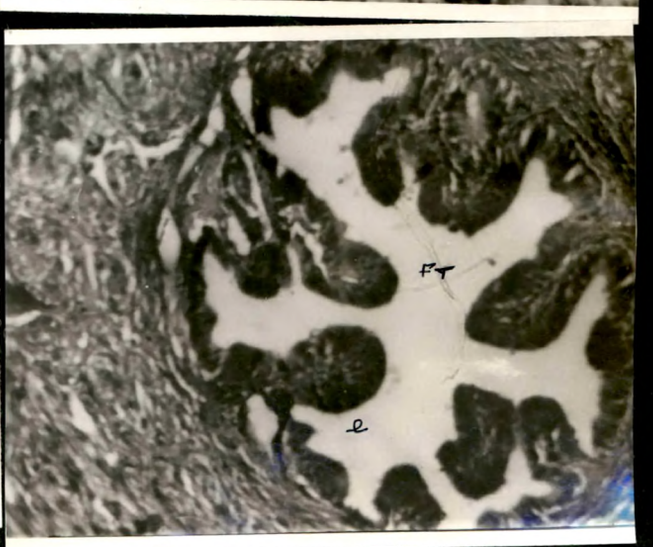

FT
e

Fig.41 (a)

Clinical photograph of female patient referred for intersex and primary amenorrhoea. She has well developed breast. Secondary sexual characters are well developed.

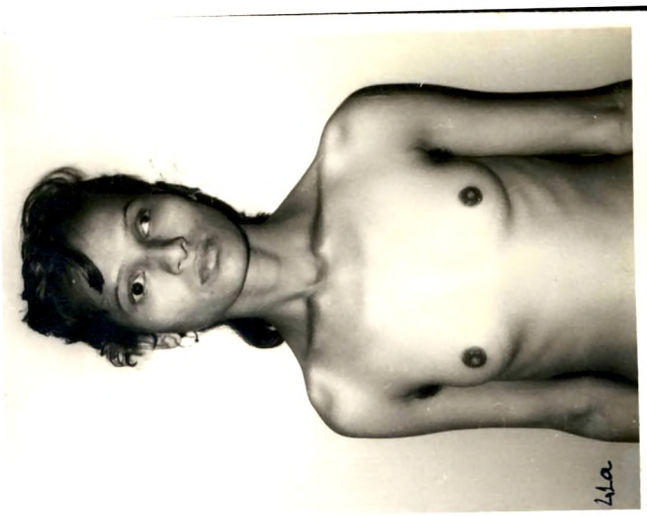
Fig.42

Photograph showing blend pouch of vagina and hernial region (Arrow). Her cytogenetic finding was 46,XX.

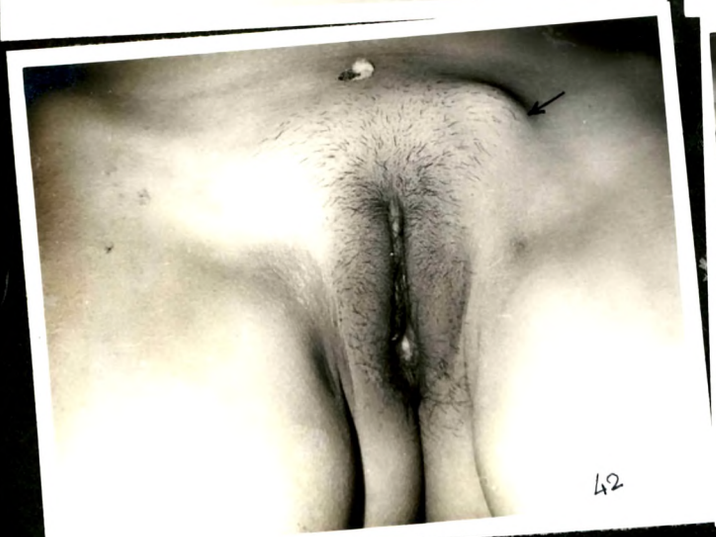
Fig.43

G-banded karyotype shows 47,XXX in the patient of primary amenorrhoea.

41a

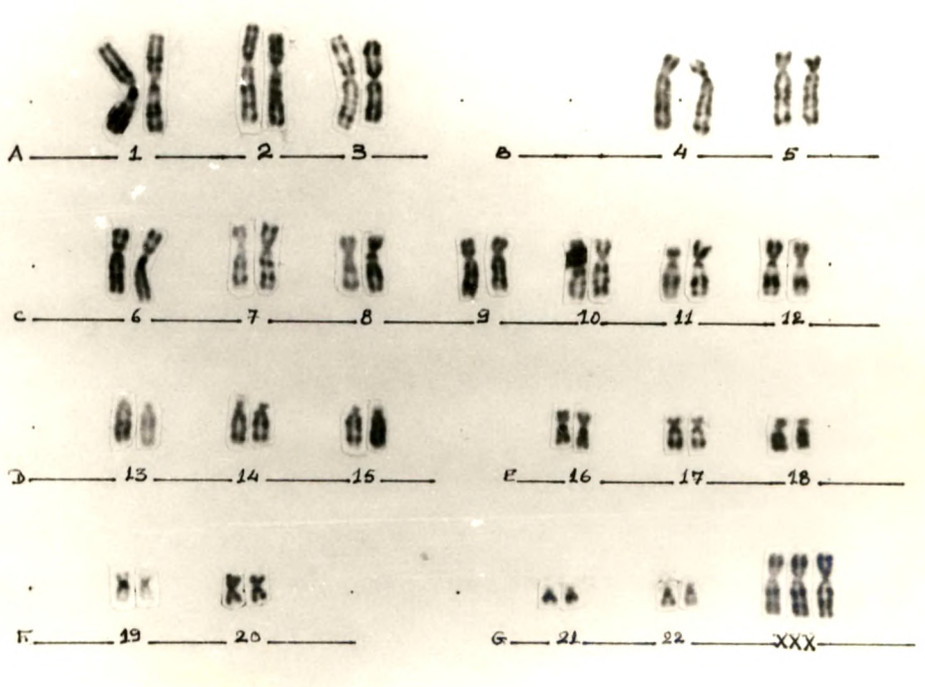


41a



42

42



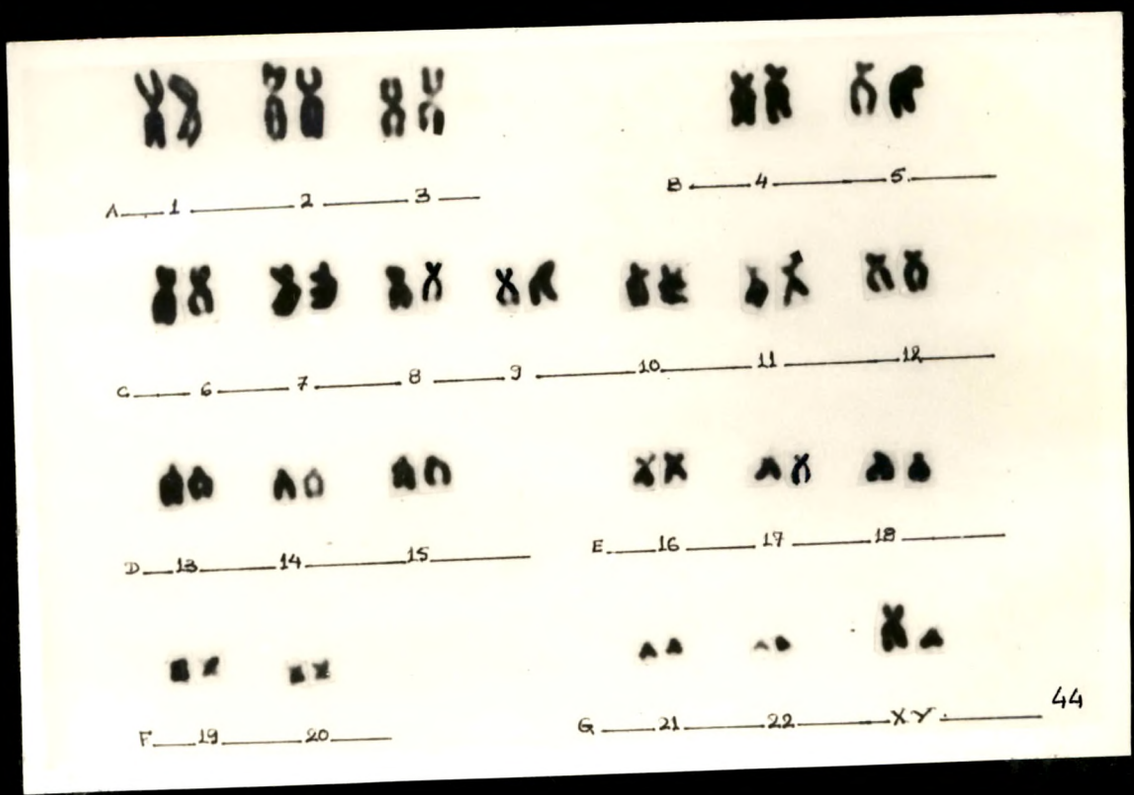
43

Fig.44

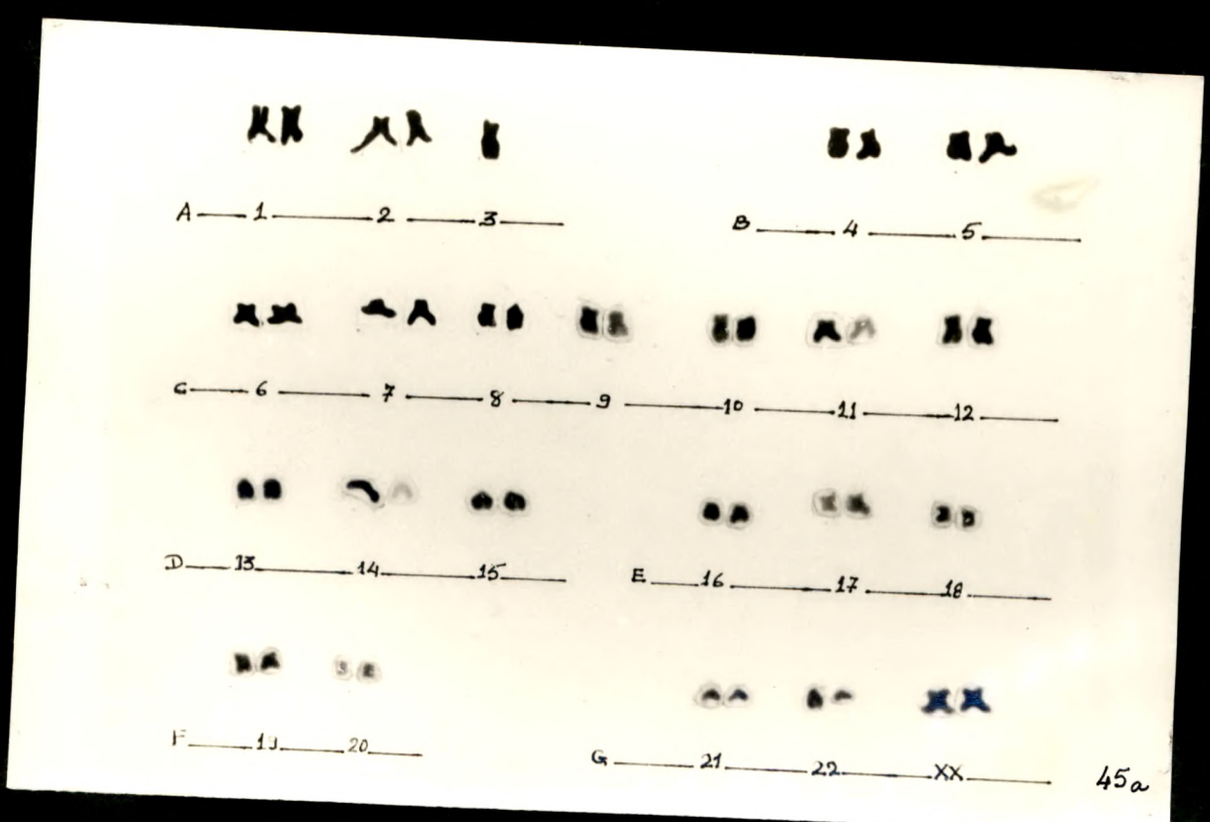
Giemsa stained karyotype of chronic myeloid leukemia (CML) showing 46,XY t(9q +22q) - Classical Ph^1 translocation.

Fig.45 (a)

Giemsa stained karyotype of CML patient showing possible translocation between long arm of chromosome 2 and long arm of chromosome 22 i.e. t(2q+, 22q-).


A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 XY

44


A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 XX

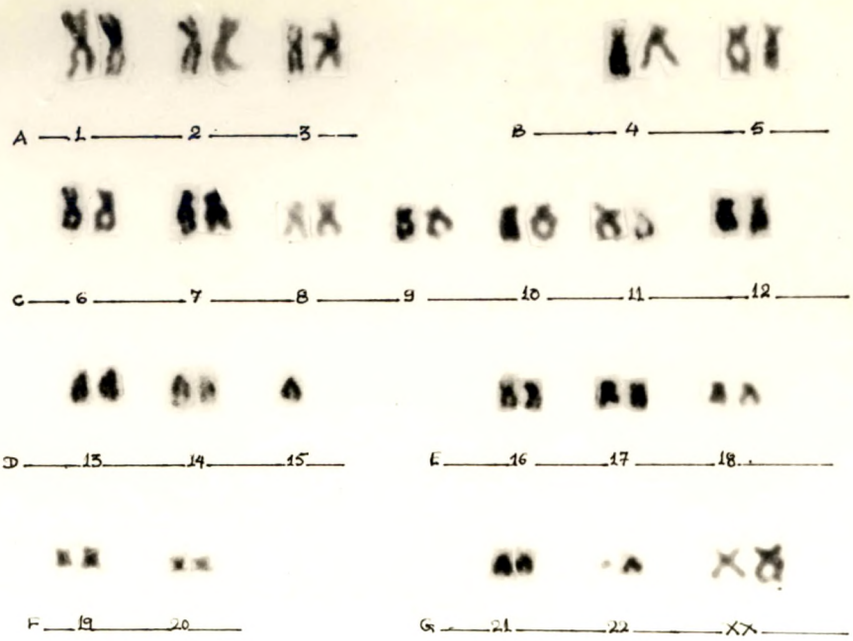
45a

Fig.45 (b)

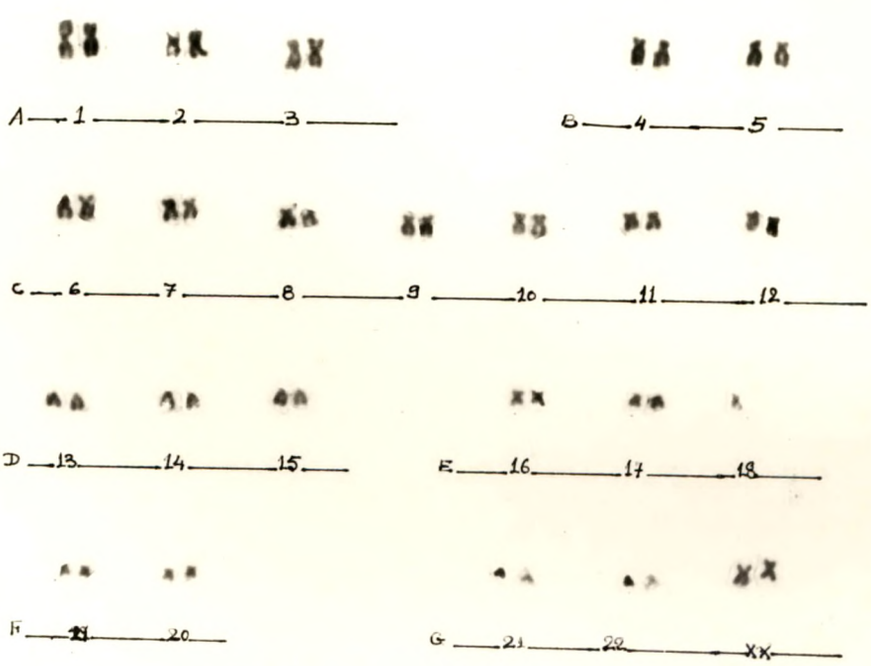
The same patient in follow up showed loss of chromosome 15 and deletion of long arm of 22q-.

Fig.45 (c)

Photograph of karyotype of the same patient during follow up, shows loss of chromosome 18 and long arm of 22q-. There may be possible deletion of short arm of chromosome 18.


A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 XY

45b


A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 21 20
G 21 22 XX

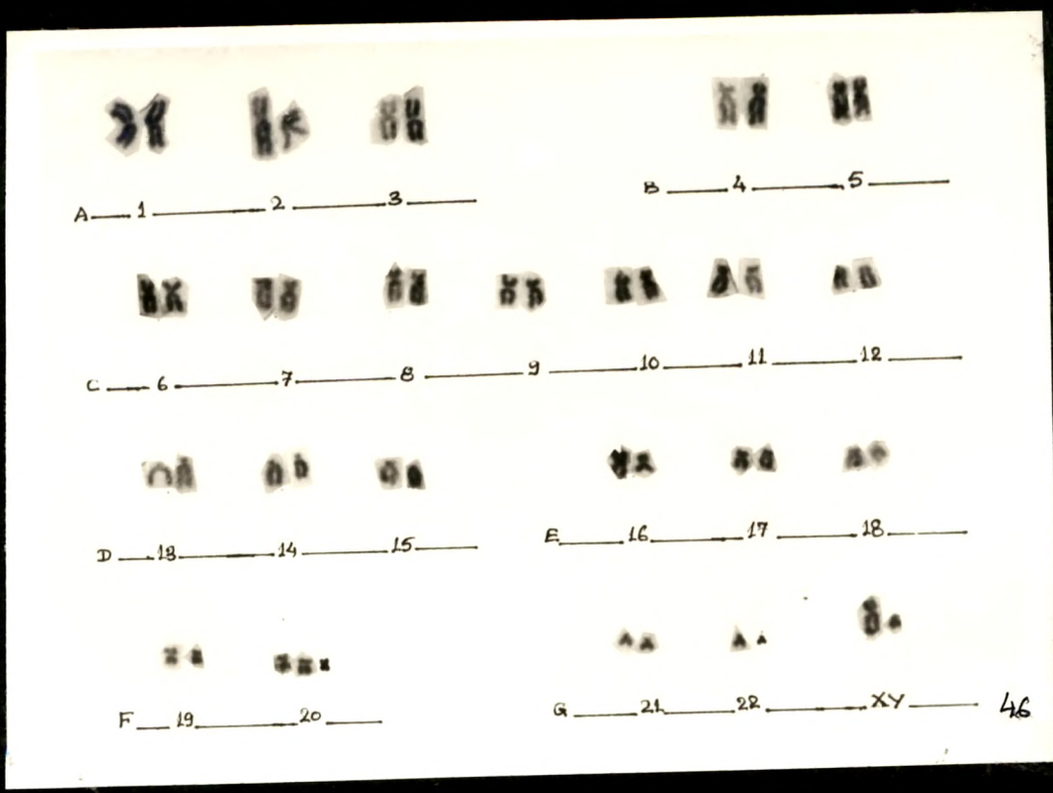
45c

Fig.46

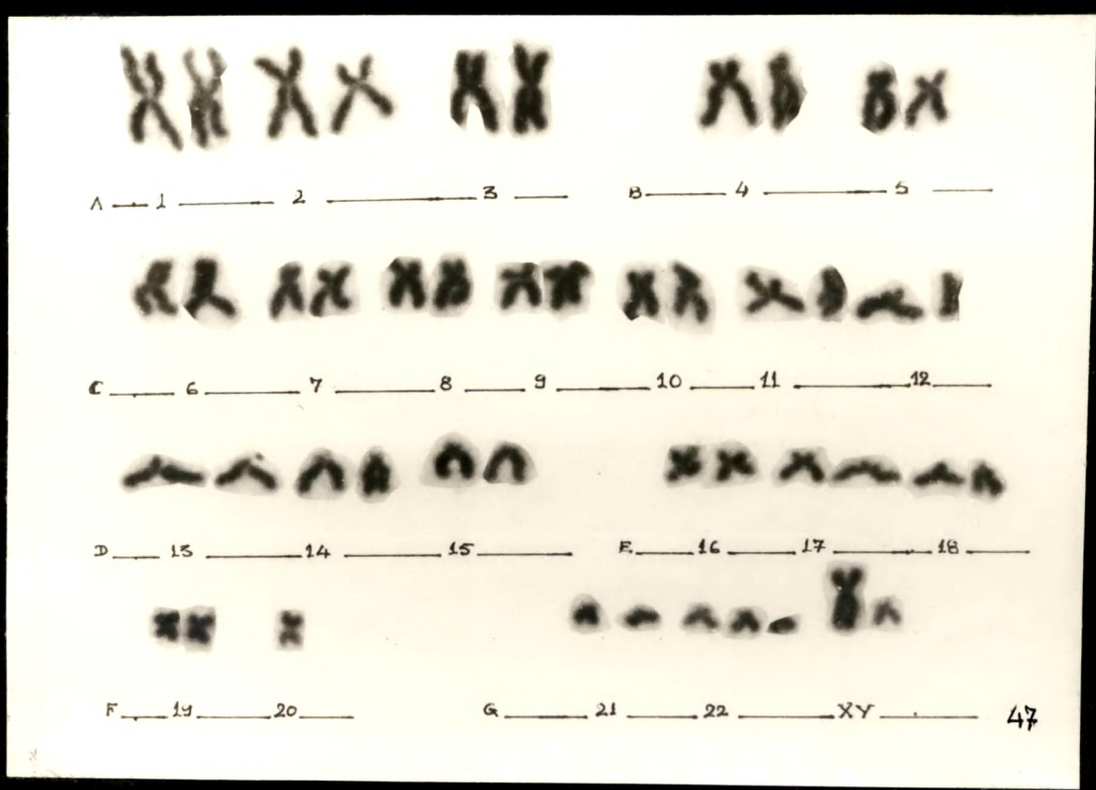
Giemsa stained karyotype of CLL patient showing 47,XY +20. There is trisomy 20 with random loss of 18th chromosome, in few.

Fig.47

Photograph showing 46,XY, del (3q-) -20, +22, 22- Trisomy of G group and Ph^1 chromosome are seen. Ph^1 positive acute leukemia.


A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 XY

46


A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 XY

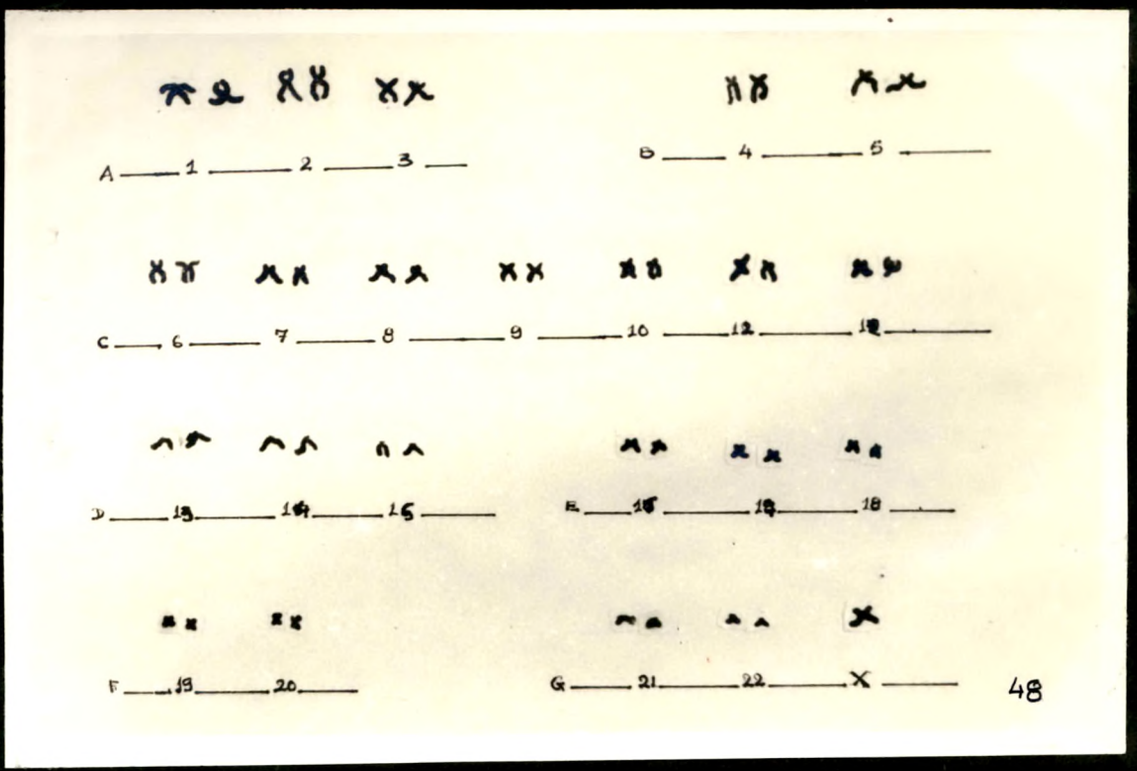
47

Fig.48

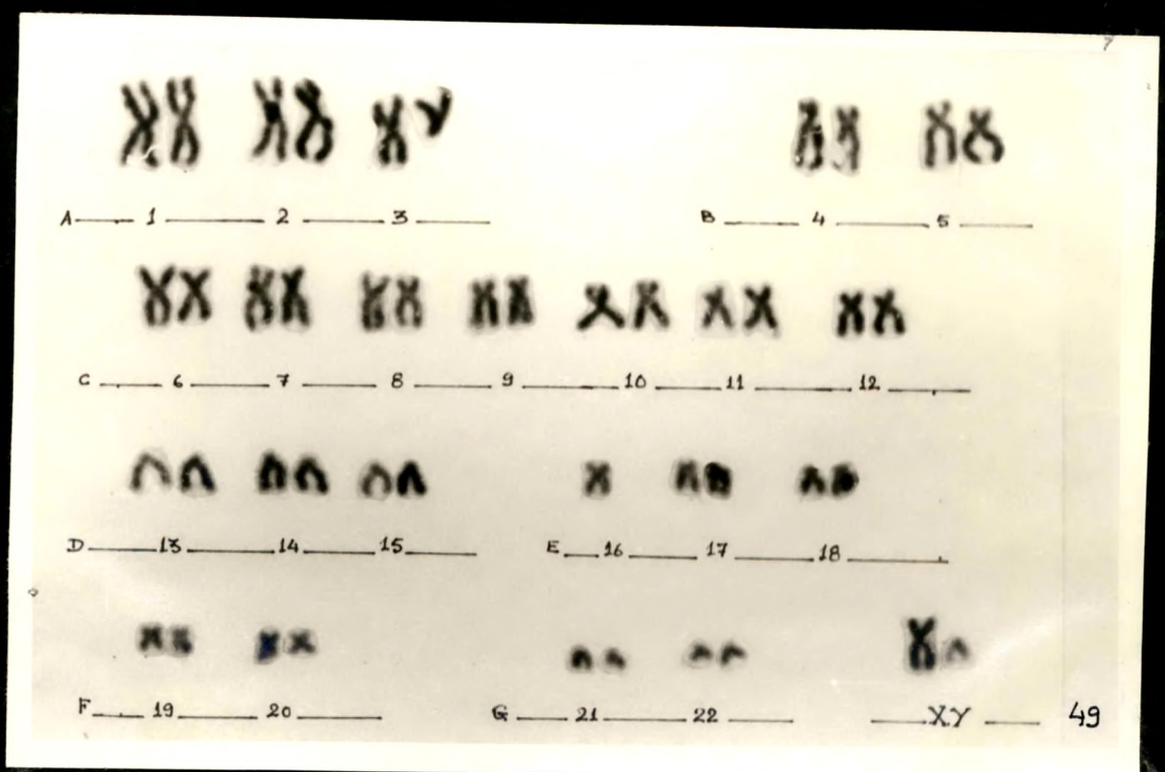
Karyotype of patient of non-Hodgkin's lymphoma showing 46,XY, t(14q +, 21q-).

Fig.49

G-stained karyotype of patient of non-Hodgkin's lymphoma showing 46,XY, del(3q) and random loss of chromosome 16.


A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 X

48


A 1 2 3
B 4 5
C 6 7 8 9 10 11 12
D 13 14 15
E 16 17 18
F 19 20
G 21 22 XY

49