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13-15 (D_1) Trisomy Syndrome*

(With special emphasis on pathological findings)

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The cardinal malformations of this syndrome were first described in 1957 by Bartholin, an ophtalmologist, and later on by neuroanatomists Kundrat (1882) and Yakovlev (1959).[1-3] However it was not defined as a specific entity until Patau found that these patients had an extra chromosome in group D (13-15).[4] Today the syndrome is called by different names, such as D trisomy, 13-15 trisomy, or Patau sydrome. Yunis et al (1964) showed by autoradiographic studies that the extra chromosome in this syndrome was a D_1 chromosome, after which this entity has also been called D_1 trisomy syndrome.

This syndrome has not yet been reported in the Turkish medical literature. The purpose of this paper is to discuss briefly D_1 trisomy on the occasion of three patients seen in our clinic.

Case 1: Baby K. a one day old boy, was born by caeserian section as the 11th child to a mother 37 years of age. Physical examination revealed the patient's height to be 46 cm., weight 2200 g., and head circumference 32 cm. The eyes were microphtalmic, the ears were lowset, and there were bilateral postaxial polydactyly of the hands and feet. The nails were hyperconvex (Figure 1). The axial triradii were distally placed. There were 3 radial and 9 ulnar loop patterns on the finger tips (Figure 2). In addition, the infant had omphalocele. X-Rays of the skull, heart, extremities and abdomen were normal. There were no abnormalities in the electrocardiogram.

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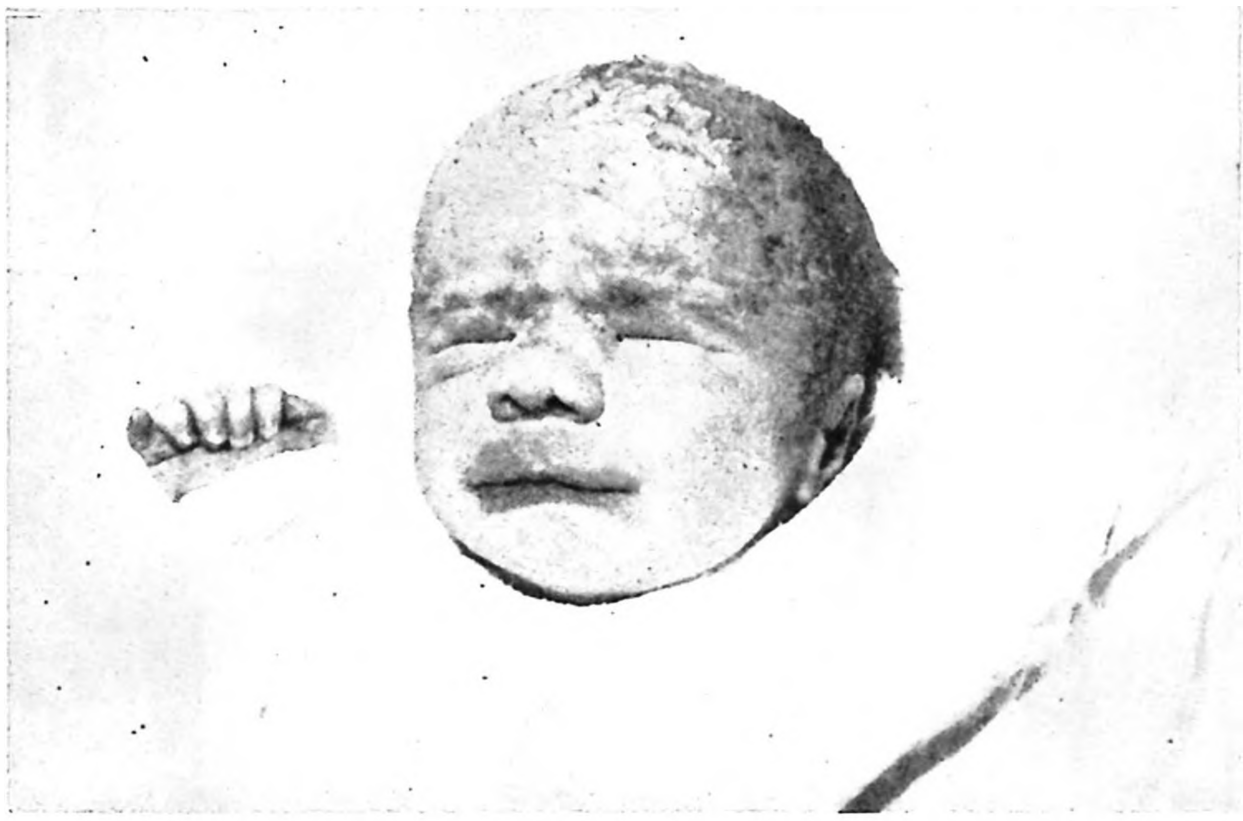

Figure 1. Case 1.

Chromosomal preparations from peripheral blood revealed an extra chromosome in the patient's group D (Figure 3). Surgery was performed to repair the omphalocele. The patient died two days later.

The post-mortem examination further showed an atrial septal defect. Permission to examine the brain was not granted.

Case 2: Baby H. This full-term girl was born as the eleventh child of a mother 40 years of age. The only significant finding in the history was that the mother had spontaneous abortion earlier.

Physical examination: At the age of one day, the patient's height was 48 cm., weight 2400 g., and head circumference 30 cm. Other interesting findings included generalized cyanosis and bilateral microphtalmia. Furthermore her ears were low-set and there were hemangioma on the back and the face. Bilateral ulnar polydactyly and flexion deformities of the fingers were seen. The index finger was over-riding the others. The nails were hyperconvex (Figure 4). There was a simian line on the left hand and clinodactyly on the right. The axial triradius was placed intermediately in the right hand and proximally in the left hand. Dermatoglyphic analyses revealed 3 whorls, 4 radial loops, and 1 arch on the finger tips (Figure 5). At the left fourth intercostal space on the midclavicular line the S_1 sound was double. The S_2 sound was

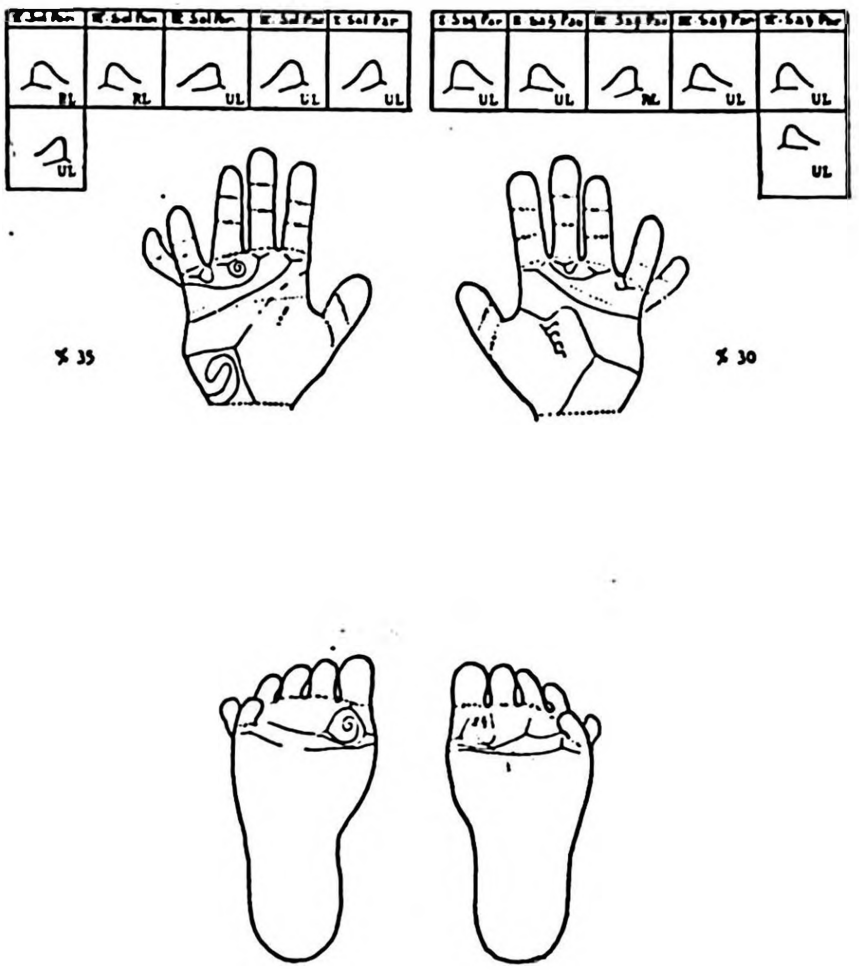

Figure 2
Dermatoglyphic findings of Case 1

normal and there was one aortic component. The liver was palpable 2 cm. below the costal margin. There was no abnormality in the electrocardiogram. In the blood smear 13 percent of the polymorphonuclear leukocytes exhibited one projection, and 16 % showed more than one projection. When the patient was three days old, her fetal haemoglobin was 100 percent, and a week later it was still 80 percent. Chromosome preparations from peripheral blood revealed an extra chromosome in group D. The patient died when she was 12 days old.

The following malformations were found in the postmortem examination.

1. Congenital heart diseases (Figure 6).
   a) Truncus arteriosus (complete),
   b) Single pulmonary artery arising from truncus,

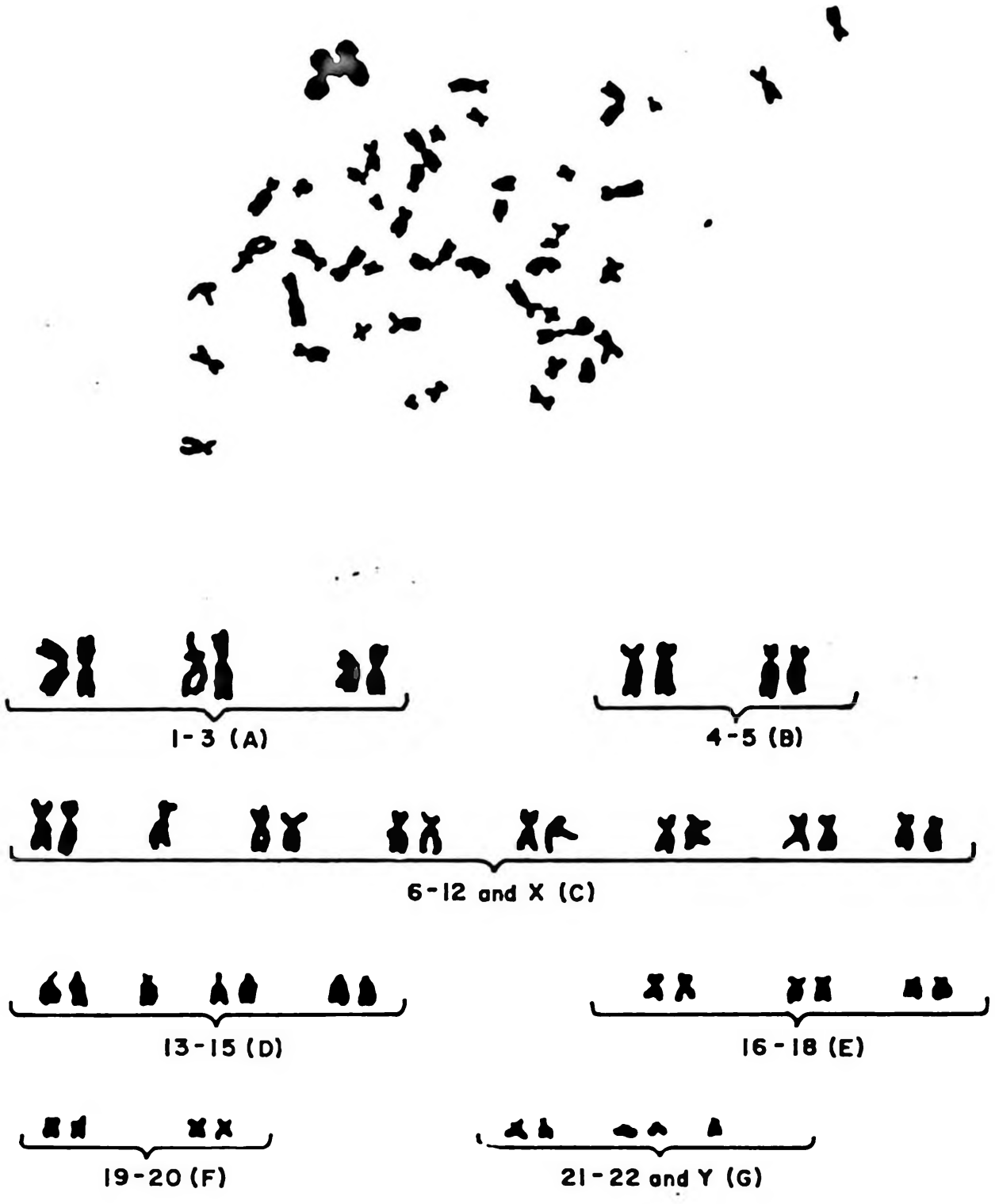

Figure 3
Karyotype of Case 1

c) Right aortic arch,

d) Ventricular septal defect,

e) Fenestration of membrane ovale,

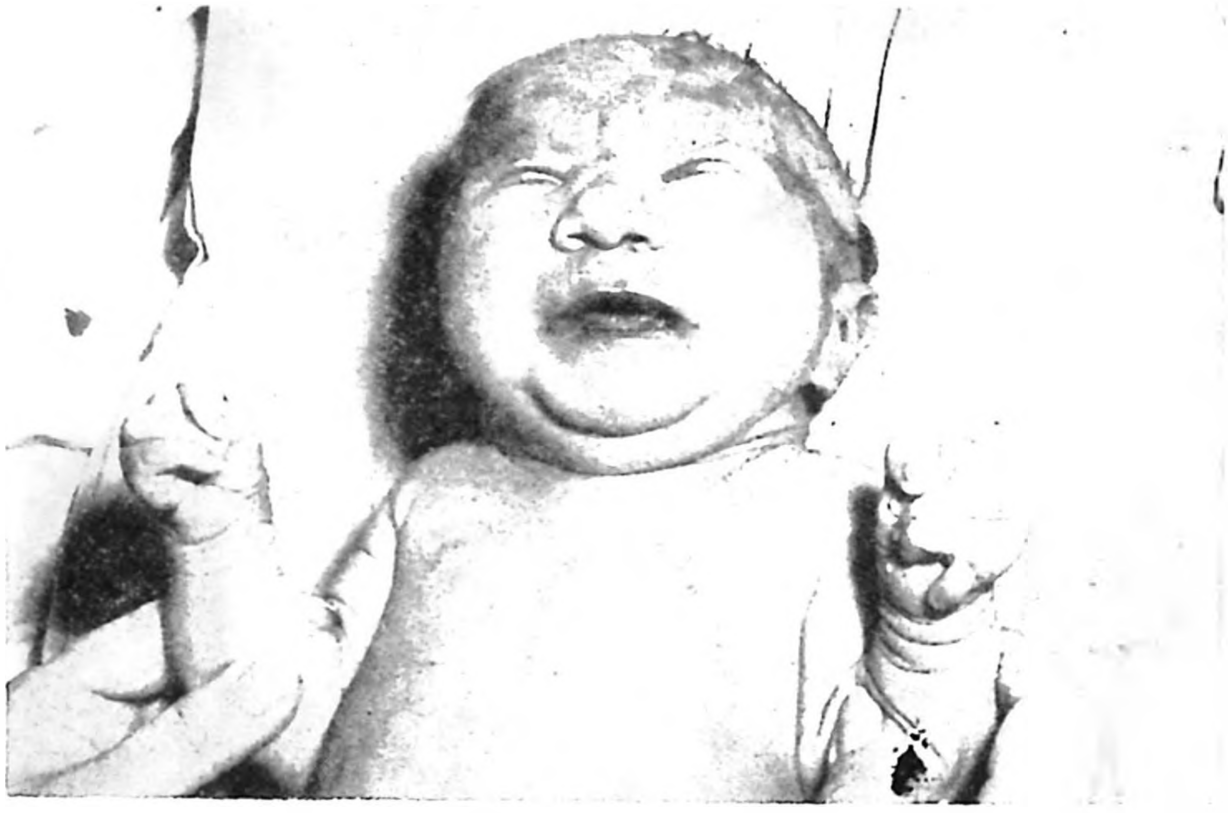

Figure 4. Case 2.

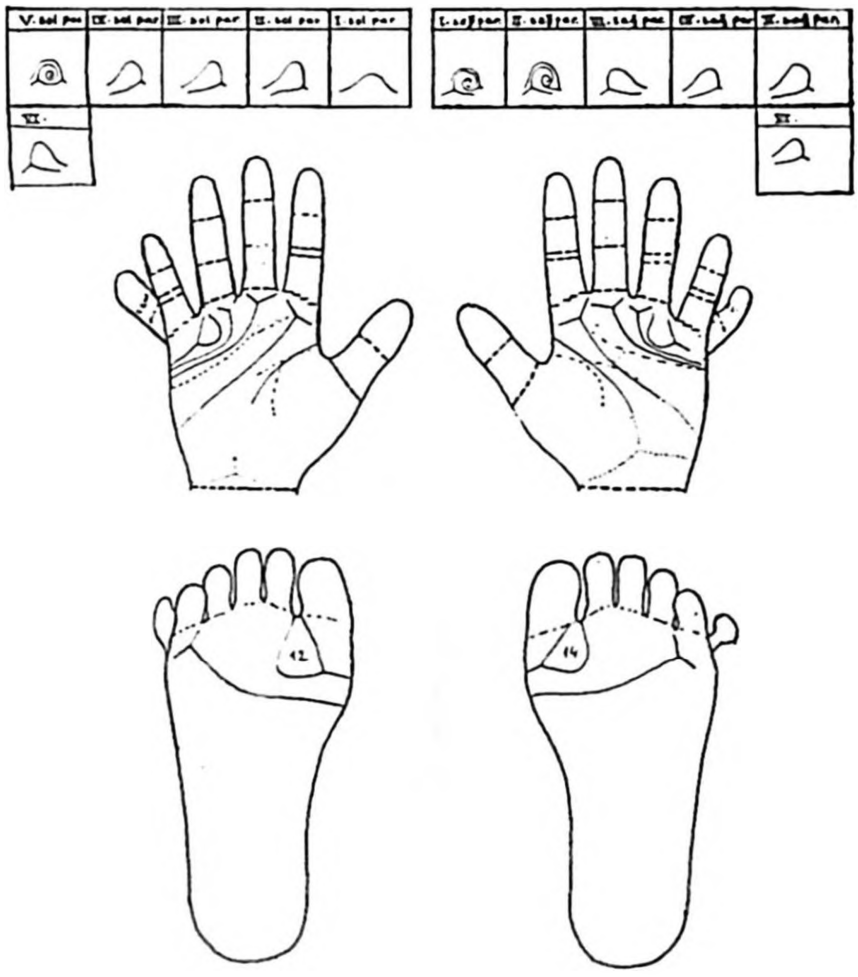

Figure 5
Dermatoglyphic findings of Case 2.

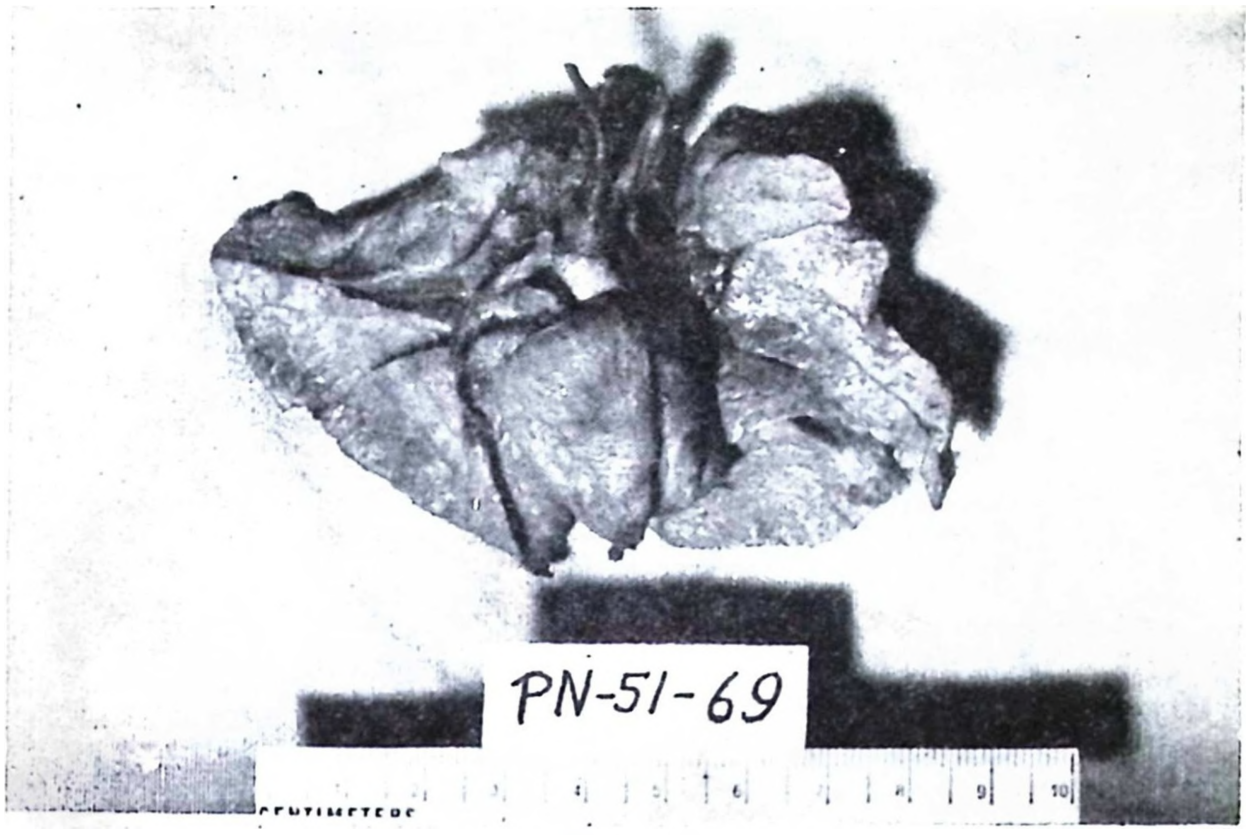

Figure 6

In the foreground is seen single main artery (truncus) deriving from the ventricule. The aortic arch is at the right.

2. Abnormal pulmonary lobulations,
3. Multiple notches and dysfiguration of the spleen,
4. Incomplete, multiple lobulations of the liver,
5. Elongation of the renal pelvises and increase in renal lobulations,
6. Polycystic kidney (Potter type IV),
7. The tail of the pancreas was embedded in the spleen.

Examination of brain revealed no abnormality.

Case 3: Baby Ç. was born spontaneously after 8.5 months of gestation. She was the 6th child of a mother 36 years of age. Physical examination revealed a height of 46 cm., weight of 2700 gm. and head circumference of 29 cm. at the age of one day. There were enophthalmia, microphtalmia, microcornea and a cloudy cornea in the left eye, and cloudy cornea, leukoma at the middle of the lower quadrant, and coloboma in the right eye. The ears were low-set and external auditory canals were atretic. A cleft-palate and hare-lip were present (Figure 7). Bilateral ulnar polydactyly of the hands and fibular polydactlyly of

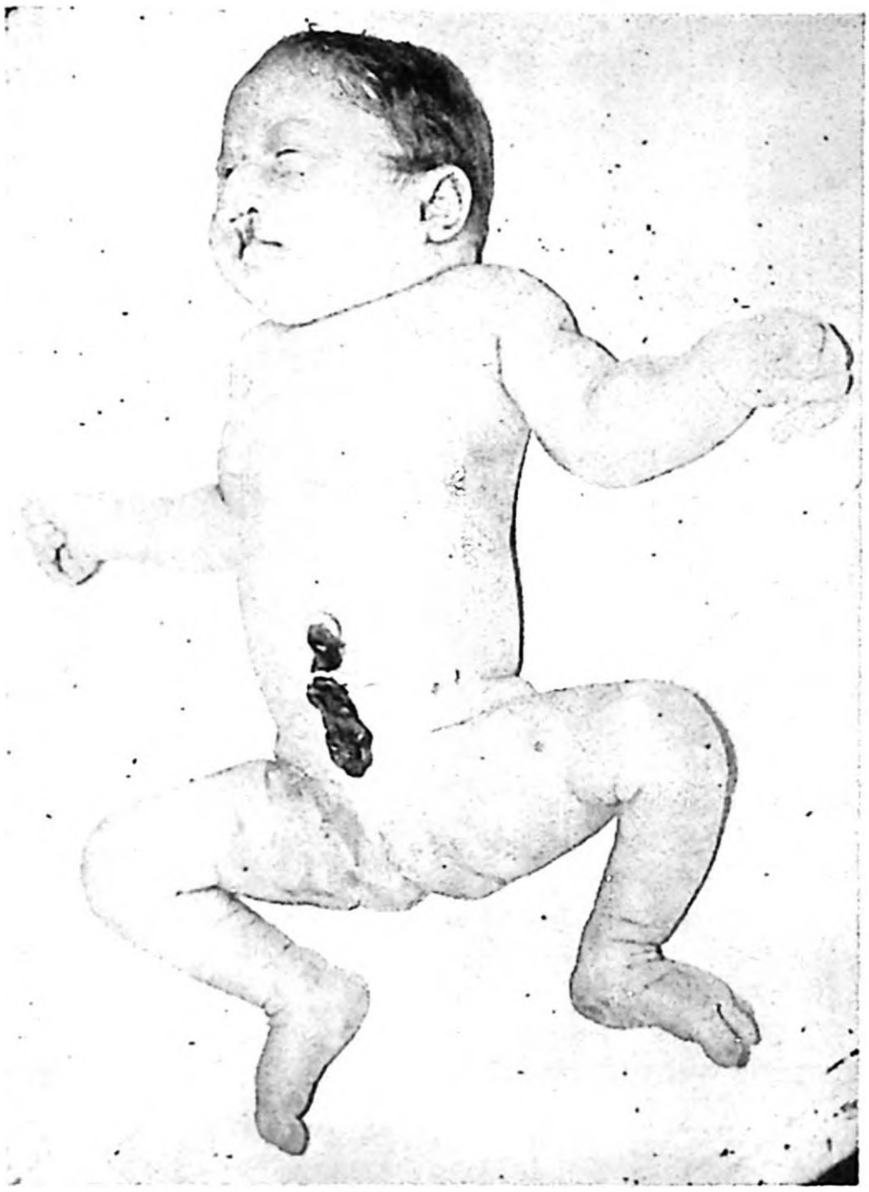

Figure 7. Case 3.

the left foot were seen. By auscultation at the left intercostal space a 3°/VI grade systolic murmur was detected. The axial triradius was placed distally in the left hand and intermediately in the right (Figure 8).

The blood smear showed 14 percent polymorphonuclear leucocytes with a single projection. Those with more than one projection were 20 percent. Fetal haemoglobin was found to be 75 percent on the fourth day of hospitalization.

The patient died when she was five days old.

Post mortem examination showed:

1. Congenital heart disease (Figure 9).
   a) Hypoplastic aortic arch,
   b) Aneurismal dilatation of ductus arteriosus,

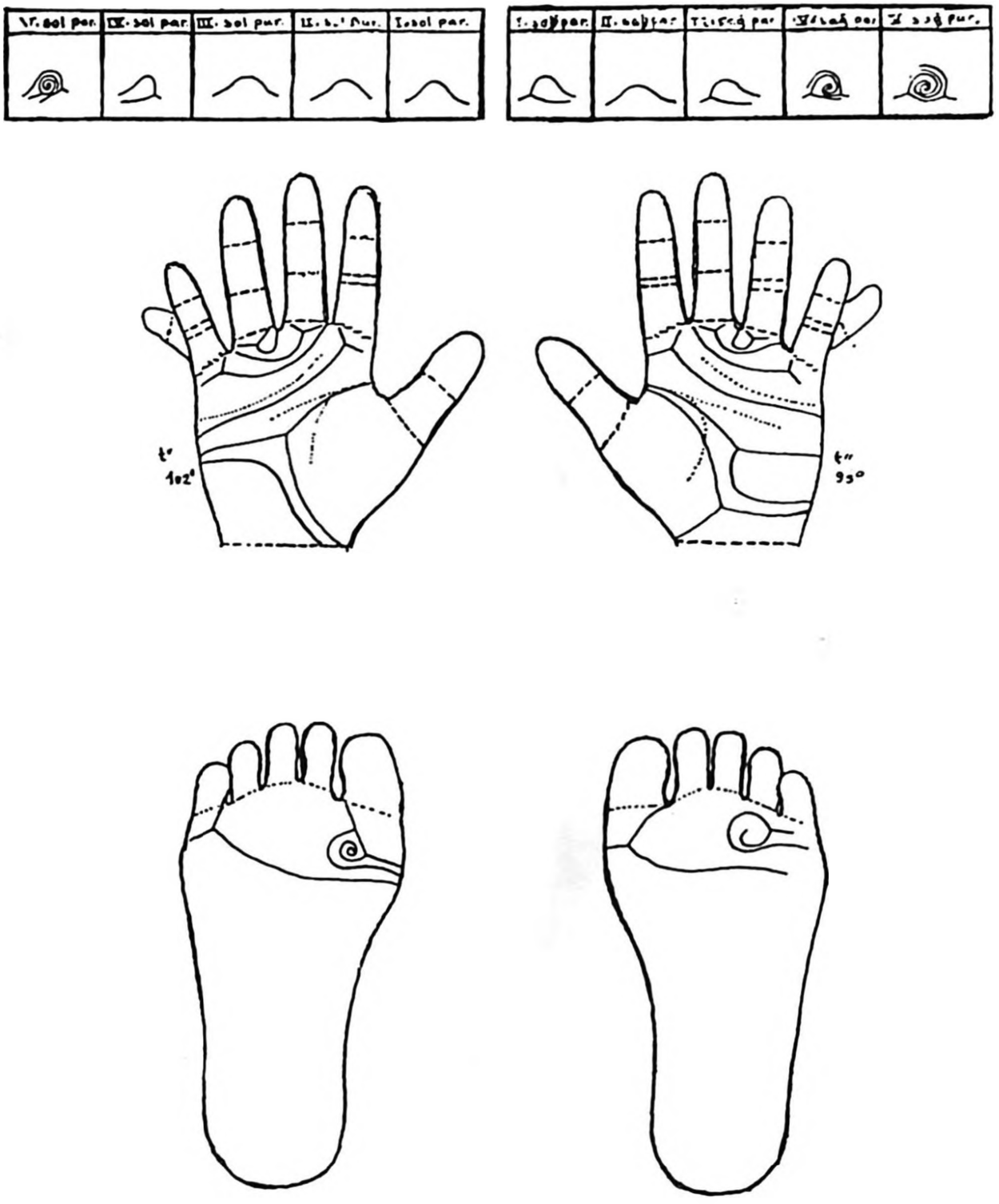

Figure 8
Dermatoglyphic findings of Case 3.

c) Fenestration of the ovale membrane,
d) Ventricular septal defect (membraneous),
e) Hypoplastic left atrium,
f) Severe stenosis of the mitral valve.

Figure 9

In this figure the heart and lungs are seen together. The hypoplastic aortic arch is marked by two arrows and aneurismal dilatation of the ductus arteriosus with a single arrow.

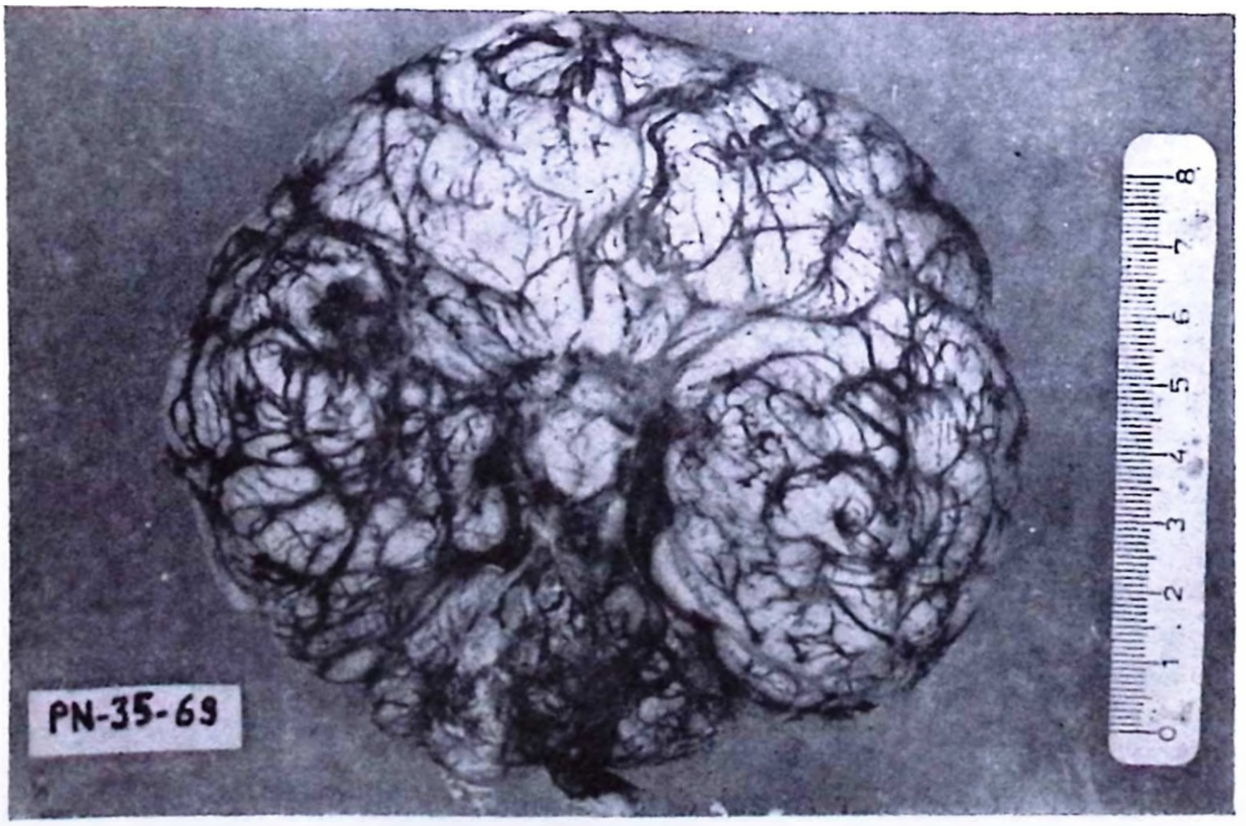

Figure 10

The brain is spherical. The olfactory bulbus are absent and cerebral hemispheres were not separated frontally.

2. Arrhinencephaly (Figures 10 and 11)

   a) Failure of separation of the cerebral hemispheres,

   b) Absence of olfactory bulbus,

   c) Absence of cribriform plate.

3. Polycystic disease in various organs (kidney, pancreas, sublingual and salivary glands).

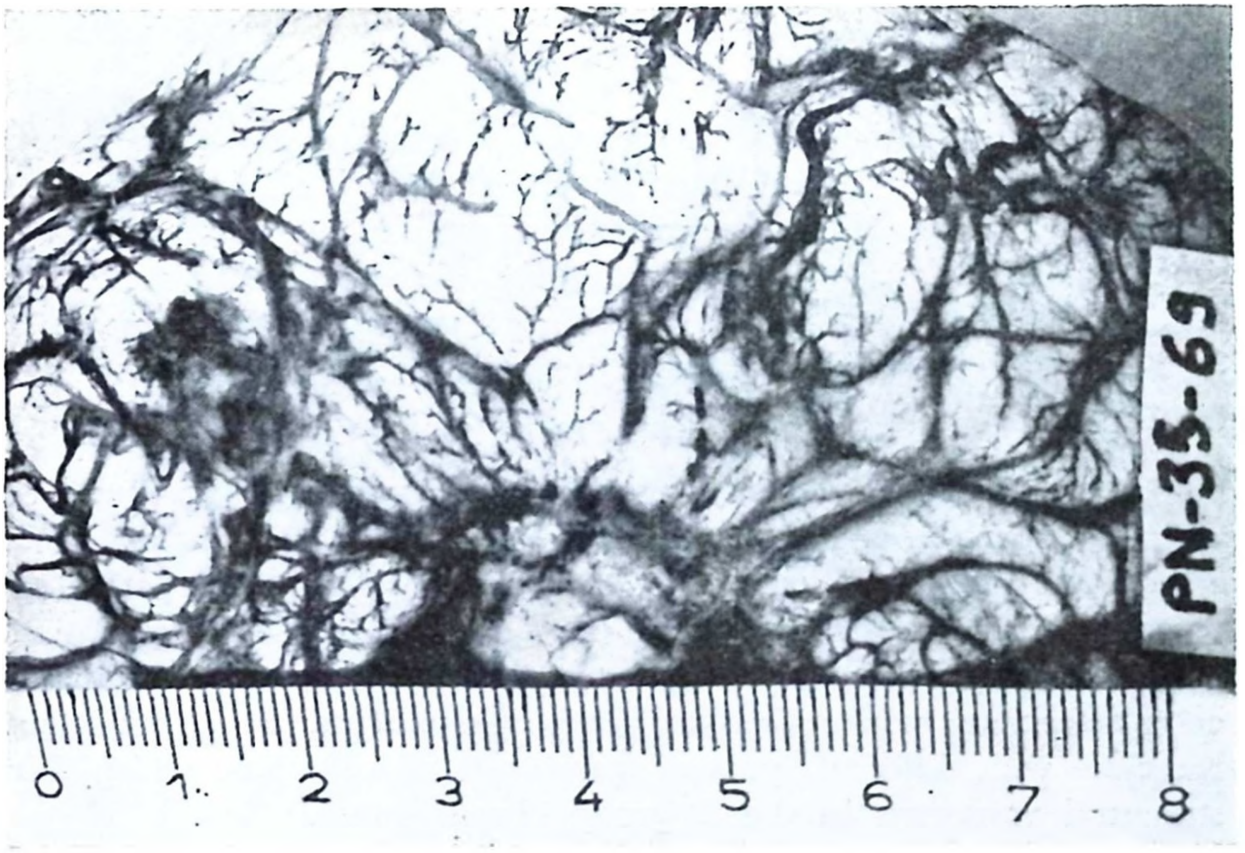

Figure 11

The frontotemporal region in the base of the brain is seen under high magnification. In the middle the sagittal fissure and on either side the olfactory bulbus are not formed.

Discussion

Since simple chromosomal culture techniques have been available, two more autosomal trisomic syndromes besides Down's syndrome have been recognised: trisomy 13-15 and trisomy 18. In both conditions in spite of the fact that no single pathognomonic malformation exists, a combination of certain defects usually enables one to reach the correct diagnosis. However, for definite diagnosis chromosome analysis is essential.

According to Smith's work (1964), which was done on 10,000 newborns, the incidence of D_1 trisomy syndrome was found to be two per ten thousand.[6] Conen and Erkman, on the other hand, reported an incidence of 0.68 per ten thousand[7] (1966). In a recent survey we found two cases of 13-15 trisomy in 10,000 newborn babies,[8] which correlates with the frequency of Smith et al.

It is quite likely that the incidence of this syndrome is much higher than these figures indicate. Carr reported 6 cases of D_1 trisomy among the chromosomal aberrations in 200 spontaneous abortions.[9] This indicates that many of the cases may be lost during fetal life through spontaneous abortions.

In most cases the cause of the chromosomal aberration is meiotic nondisjunction. It has been determined that there is a relation between the incidence of nondisjunction of D chromosomes and the mother's age, similar to that seen in Down's syndrome. The ages of the mothers of 13-15 trisomic children are above 35 in 40 percent of the cases; where as the mothers above this same age constitute 11 percent of the normal population.[6]

Apart from this frequent form of trisomic syndrome, there are cases with 46 chromosomes, having a D/D translocation. No statistical difference has been found between the maternal ages of translocation and trisomic children. The clinical findings of D/D translocation patients also do not differ form the straight trisomic ones except that cardiovascular defects are more serious in the trisomic patients.[7] In addition there are cases with different types of translocations and those which show structural variations in the D group chromosomes.

The birth weight of D_1 trisomic patients is low but not low as that of 18 trisomic patients. A series of 30 cases were categorized according to birth weight and a mean value of 2480 gr. was found. In this series, in only 7 cases was the gestational period less than 38 weeks.[10]

The common malformations seen in this syndrome are shown in Table I.[11]

All three cases reported here showed the classical findings of D_1 trisomy syndrome in these patients maternal age was above 35 years, and birth weight of the patients varied around 2200 gm. Findings such as microcephaly, microphthalmia, low set ears, polydactyly, hyperconvex finger nails and congenital heart disease which were found in our three cases are the ones most frequently seen in this condition.

TABLE I

D_1 (13-15) TRISOMY SYNDROME[11]

Area	Common 50 % or More of Patients	Less Common
General	Apneic spells, death within 3 months	Intrauterine growth deficiency
Central nervous system	Developmental deficiency	Hypertonia, hypotonia, fusion of frontal lobes, agenesis of corpus callosum, cerebellar hypoplasia, cyclancephaly, cebocephaly, meningomyelocele
	Minor motor seizures Agenesis of external olfactory lobes	
Cranium	Sloping forehead	Microcephaly,
Eyes and adjacent structures	Microphthalmus or colobomata	Shallow supraorbital ridges, slanting palpebral fissures, absent eyebrows, hypertelorism
Auricles	Abnormal helices+/–low-set	
Mouth and mandible	Cleft in lip or palate	Micrognathia, narrow palate, cleft in tongue
Skin	Capillary hemangiomas	Localized scalp defect, loose skin at neck,
Hands and feet	Distal palmar axial triradii	Retroflexible thumb, ulnar deviation of hand, synostosis 5th finger, high frequency of low arch digital dermal pattern
	Hyperconvex narrow fingernails Flexion of fingers+/–overlapping	
	Polydactyly, hands and feet Posterior prominence of heel Fibular S-shaped hallucal arch dermal pattern	Syndactyly, hypoplastic toenails, equinovarus
Cardiac	Ventricular septal defect	Rotational anomaly, atrial septal defect, patent ductus arteriosus, anomalous venous return, bicuspid aortic valve, overriding aorta, pulmonary stenosis, hypoplastic aorta, atretic mitral and aortic valves
Abdominal	Incomplete rotation of colon, accessory splenic tissue	Umbilical hernia, inguinal hernia, hiatus hernia, omphalocele, heterotopic pancreatic tissue; excess tissue of liver, pancreas, and mucosa of small intestine
Renal	Abnormality	Polycytic with cortical renal cysts, saccular tubules, hydronephrosis, horseshoe kidney, duplicated ureters
Genitalia Male	Cryptorchidism, abnormal scrotum	Hypospadias
Female	Partially bicornuate uterus	Duplication of fallopian tubes and upper vagina, anomalous insertion of fallopian tubes,
Hematologic	Unusual nuclear projections of neutrophils Unusual persistence of fetal type hemoglobin	Thrombocytopenia (neonatal)
Other	Single umbilical artery	Small areolae, situs inversus of lungs, cysts of thymus, limited hip abduction, myelogenous leukemia (still-born), absence of radius diaphragmatic defect

In addition, scalp defects, capillary hemangioma, flexion contractures of fingers and polycystic kidney which were found in the post-mortem examination of the second case, and arrhinencephaly, coloboma, cleft palate and cleft lip, distal axial triradius and polycystic kidney in the third case, are findings which are seen in more than 50 percent of the cases. Omphalocel, seen in the first case, and atresia of the external auditory canal in the third case have also been described in D_1 trisomic patients.

In the second and third cases the level of fetal haemoglobin was above 75 percent and nuclear projections in the neutrophils were much higher than normal.

Among dermatoglyphic findings distal axial triradius is frequently seen. We found it in two of our patients. Again in two patients, the number of radial loops were increased. However we did not observe a fibular arch pattern on the hallucal area which is reported as a frequent finding.

We found some other defects such as aneurismal dilatation of the ductus arteriosus, polycystic disease of the pancreas and sublingual salivary gland, truncus arteriosus, multiple and incomplete lobulation of liver. Another interesting and uncommon finding seen in one of our cases was the insertion of the tail of the pancreas in the spleen.

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REFERENCES

1. Warburg, M. and Mikkelson, M.: A case of 13-15 trisomy or Bartholin-Patau's syndrome, Acta Ophth. 41: 321, 1963.
2. Kundrat, H.: Arhinencephalic als typische Art von Missbildung, Graz: Von Leuschner and Lubensky, 1882.
3. Yakovlev, I.: Pathoarchitectonic studies of cerebral malformations. III. Arhinencephalies, J. Neuropath. and Neurol. 18: 22, 1959.
4. Patau, K., Smith, D. W., Therman, E., Inhorn, S. L. and Wagner, H. P.: Multiple congenital anomaly caused by an extra autosome, Lancet 1: 790, 1960.
5. Yunis, J. J., Hook, E. B. and Mayer, M.: Deoxyribose-nucleic-acid replication pattern of trisomy 18, Lancet II: 286, 1964.
6. Smith, D. W.: Autosomal abnormalities, Amer. J. Obst. and Gynec. 90: 1055, 1964.

7. Conen, P. E., and Erkman, B.: Frequency and occurrence of chromosomal syndromes: I-D_1 Trisomy II-E. Trisomy, Amer. J. Hum. Genet. 18: 374, 1966.
8. Say, B., Tunçbilek E., Balcı, S., Yalçın, Z.: Türk Halkında Çeşitli Konjenital Malformasyonların Görülme Sıklığı, Hacettepe Üniv. Yayın. No C-12, 1971.
9. Carr, D.: Chromosome studies in spontaneous abortions, Obstet. Gynec. 26: 308, 1965.
10. Warkany, J., Passarge, E. and Smith, L. B.: Congenital malformations in autosomal trisomy syndromes, Amer. J. Dis. Child. 112: 502, 1966.
11. Gardner, L. I.: Endocrine and Genetic Disease of Childhood, W. B. Saunders Co., Philadelphia and London, 1969.