

## CLINICAL CONFERENCE

# GONADAL DYSGENESIS DIAGNOSED IN INFANCY

Herbert I. Lerner, M.D.

*Sarah Morris Hospital for Children, Chicago*

ONE CAN hardly pick up a medical journal these days without finding one or more articles concerned with chromosomal abnormalities. The case presented here is that of a patient with gonadal dysgenesis (Bonnevie-Ullrich-Turner syndrome), which represents one interesting type of abnormality of the chromosomes.

### CASE REPORT

The patient was a 11½-month-old white female infant, whose mother was gravida III, para III. The pregnancy was entirely normal, with no virus infections or irradiation during the first trimester. The patient had edema of the dorsa of the hands and feet at birth. When she was first seen at 2½ months the edema of the hands had subsided and the skin was very lax. The dorsa of the feet still exhibited pitting edema. In addition, she had a short neck, low set ears, cutis laxa in the neck region, a shield-like chest with widely separated, hypoplastic nipples, a high arched palate, telangiectasia of the cheek and forehead, and hypoplasia of fingernails and toenails. The blood pressure was normal and femoral pulses were palpable. The external genitalia were normal. She was in the third percentile for height and weight on the Stuart growth curve, in contrast to her two older siblings, who had always been in the ninetieth percentile.

Buccal smears revealed a negative sex-chromatin pattern. A diagnostic pneumoperitoneum at 5½ months of age revealed an indication of a small uterus with no demonstrable ovaries. There were no detectable levels of urinary gonadotropins at 4½, 5 and 6 months of age, but at 10 months between 0 and 5 mouse units were reported.

Although these patients usually develop increased urinary gonadotropins at puberty, an investigator has reported<sup>1</sup> three patients with gonadal dysgenesis who excreted increased amounts of gonadotropins in urine before puberty, the youngest being 2 years 8 months old.

Between 2 and 4 months of age the patient developed an infection of the urinary tract that indicated the possibility of a renal anomaly. Intravenous and retrograde urograms revealed normal findings, except for a bifid renal pelvis. A chromosomal count revealed five cells, with a diploid number of 45. Buccal smears from the parents were normal.

### COMMENT

Turner<sup>2</sup> described a syndrome of sexual infantilism, cubitus valgus and webbed neck in post-pubertal females. They had amenorrhea, no breast development, short stature and markedly elevated values for gonadotropins in urine. Diagnostic pneumoperitoneum or laparotomy in patients with this syndrome usually reveals an infantile uterus and tubes, and no ovaries. Various studies demonstrated that fibrous strands along the tubes contained ovarian stroma but no germinal epithelium or follicles. Congenital lymphangiectatic edema of the hands and feet, with cutis laxa and numerous other anomalies (Bonnevie-Ullrich syndrome) was considered a separate clinical entity until a few years ago, when it was found that about 80% of patients in both groups had a negative sex-chromatin pattern.<sup>3</sup> At that time the two syndromes were combined as Bonnevie-Ullrich-Turner syndrome or gonadal dysgenesis.<sup>4,5</sup> (See Table I for associated

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ADDRESS: 29th Street and Ellis Avenue, Chicago 16, Illinois.

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TABLE I  
SOME RECENT DEVELOPMENTS INVOLVING ANOMALIES OF THE SEX CHROMOSOMES

<i>Clinical State</i>	<i>Chromatin Pattern</i>	<i>Sex Chromosomes</i>	<i>Autosomes (no.)</i>	<i>Diploid Number</i>	<i>References</i>
Normal female	Pos (40% cells)	XX	44	46	Tjio: <i>Hereditas</i> , 42: 1, 1956
Normal male	Neg (>90% cells)	XY	44	46	Tjio & Puck: <i>Proc. Nat. Acad. Sci.</i> , 44: 1229, 1958.
Gonadal Dysgenesis (Bonnievie-Ullrich-Turner syndrome)*	Neg (80% pts)	XO	44	45	Ford: <i>Lancet</i> , 1: 711, 1959.
	Pos (1 pt)	XO	44	45	Grumbach: <i>Amer. J. Dis. Child.</i> , 100: 548, 1960.
Klinefelters's syndrome†	Pos	XXY	44	47	Jacobs & Strong: <i>Nature</i> , 189: 302, 1959.
With mongolism	Pos	XXY	45	48	Ford: <i>Lancet</i> , 1: 709, 1959.
In identical twins	Pos	XXY	44	47	Holub: <i>J. Clin. Endocr.</i> , 18: 1359, 1958.
Primary amentia and micro-orchidism	Pos (40% double chromatin)	XXXY	44	48	Ferguson-Smith: <i>Lancet</i> , 2: 184, 1959.
Double male (father XYY)	Pos	XXYY	44	48	Muldahl & Ockey: <i>Lancet</i> , 2: 492, 1960.
Triploidy‡	Pos	XXY	66	69	Böök: <i>Lancet</i> , 1: 858, 1960.
Superfemale or metafemale§	Pos in 71% cells; double chromatin in 15% cells	XXX	44	47	Jacobs <i>et al.</i> : <i>Lancet</i> , 2: 423, 1959.
					Frazer <i>et al.</i> : <i>Lancet</i> , 2: 626, 1960.
Testicular feminization,   or hereditary male pseudo-hermaphroditism¶	Neg	XY	44	46	Jacobs: <i>Lancet</i> , 2: 591, 1959.
Sexual mosaics; Klinefelter's syndrome	Pos	XXY/XX	44	46-47	Ford: <i>Nature</i> , 183: 1030, 1959.
Gonadal dysgenesis	Pos	XX/XO	44	45-46	Ford: <i>Amer. J. Human Genet.</i> , 12: 104, 1960.
Gonadal dysgenesis	Pos	XXX/XO	44	45-47	Jacobs: <i>Lancet</i> , 1: 1218, 1960.
True hermaphroditism	Neg	XY/XO	44	45-46	Hirshhorn: <i>Lancet</i> , 2: 319, 1960.

\* Short stature, shield-like chest, overweight, cubitus valgus, abnormal facies, webbed neck, abnormal nails, lymphedema, cutis laxa, mental retardation, aortic coarctation, renal anomalies, telangiectasia and sexual infantilism

† Eunuchoid, small testes, mental deficiency.

‡ 1-year-old boy with lipomatosis, micrognathia, syndactyly of hands and feet, ataxia, retardation and porencephaly.

§ May have sexual infantilism and mental deficiency, ovaries postmenopausal. One mentally defective woman had a normal boy.

|| Testicular feminization is included for comparison with gonadal dysgenesis.

¶ Female habitus, ectopic testes, inguinal hernia, primary amenorrhea, color blindness and mental deficiency.

congenital anomalies.<sup>6)</sup> It was thought that these patients were male pseudohermaphrodites.<sup>7</sup> Recently, chromosomal counts revealed an XO pattern of the sex chromosomes,<sup>8</sup> and this is now interpreted to mean that the patients are incomplete females, lacking the second X chromosome.<sup>9</sup> Recent studies indicate that the sex chromatin body found in female cell-nuclei is probably due to a single X that is heterochromatic, i.e., stains differently from the other X chromosome and the autosomes.<sup>10</sup> Perhaps it is this X that is missing in these patients, accounting for a negative chromatin pattern. However a 12-year-old patient with gonadal dysgenesis, chromatin-positive nuclei and an XO chromosome constitution has been reported.<sup>10</sup> In addition, a female with XO sex chromosome constitution, no stigmata of Turner's syndrome except short stature and late menarche, and who gave birth to a normal male child has been described.<sup>11</sup>

A summary of these variants and other abnormalities of the sex chromosomes is presented in Table I in an attempt to summarize some of the interesting new developments in the understanding of sexual anomalies.

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