

**Transition From Adolescence to Early Adulthood: Adaptation and  
Psychiatric Status of Women With 47,XXX**

[Articles]

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## ABSTRACT <sup>^</sup>[\\_](#)

**Objective:** To investigate the adolescent and early adult adaptation of a group of 47,XXX women as compared with their siblings, addressing developmental differences in adaptation and psychiatric status.

**Method:** Subjects included eleven 47,XXX women and nine female sibling controls. Interviews during adolescence and during early adulthood were semi-structured and included a psychiatric evaluation. Four areas of inquiry were (1) relationships with other family members, (2) sense of self-esteem, (3) sexual identity and preference, and (4) responses to life stressors. A DSM-IV psychiatric diagnosis was assigned where appropriate. The Schedule for Affective Disorders and Schizophrenia-Lifetime version was also administered, and assessments of overall functioning and adaptation were completed.

**Results:** The 47,XXX women during adolescence and young adulthood were less well adapted; had more stress; had more work, leisure, and relationship problems; had a lower IQ; and showed more psychopathology when contrasted with the comparison group. However, most of the 47,XXX women were self-sufficient and functioning reasonably well, albeit less well than their siblings.

**Conclusions:** This longitudinal study has clarified that previously reported outcomes of severe psychopathology and antisocial behavior in individuals with sex chromosome anomalies are rare and variability in the behavioral phenotype is much larger than originally appreciated. *J. Am. Acad. Child Adolesc. Psychiatry*, 1998, 37(3):286-291.

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**Key Words:** 47,XXX women, adolescence, psychosocial adaptation, sex chromosome abnormality, young adulthood.

Deviations in the number or structure of the 23rd chromosome pair, commonly referred to as sex chromosome abnormalities (SCAs), occur frequently, yet their developmental implications are not well understood. SCAs are found in 1 out of 300 to 400 births, and they most often include the addition of an extra X or Y chromosome in males (the 47,XXY and 47,XYY karyotypes) and the addition or absence of an X in females (the 47,XXX and 45,X karyotypes). The latter

karyotype is responsible for the presence of Turner's syndrome, which can also result from the partial loss of or structural change in one of the X chromosomes. These four karyotype groups constitute the vast majority of SCAB.

An association between SCA conditions and the presence of psychopathology emerged from studies in the 1960s and 1970s, which found a four- to fivefold increased representation of 47,XXY, 47,XYY, and 47,XXX adults in prisons, mental hospitals, and institutions for the criminally insane (Bender et al., 1995; Hook, 1979; Polani, 1977) [3,5,9]. However, the relationship between SCA and psychopathology is less pervasive than first suggested by these early studies and is better understood as a result of more recent studies of unselected children with SCAs identified through programs that screened chromosomes in newborn populations (Evans et al., 1990; Ratcliffe and Paul, 1986; Robinson et al., 1979; Stewart, 1982) [4,10,12,17]. There have been no reports of growth and development of unselected 47,XXX females from adolescence to early adulthood.

Jacobs et al. (1959) [6] described the first 47,XXX karyotype in a woman of average intelligence who had secondary amenorrhea. More than 200 additional 47,XXX women have been reported since that time, but most have been isolated case studies of women ascertained through the presence of another condition. Fewer than 50 47,XXX females have been identified in an unselected fashion through chromosomal screening of newborns and followed longitudinally (Evans et al., 1990) [4]. The information from these prospective studies, which is considered to be more representative and accurate than that from case reports, reveals that 47,XXX girls, unlike most individuals with a chromosomal aneuploidy, have no distinguishing physical features and their pubertal development and reproductive competency are normal. However, as with all groups of individuals with an X or Y chromosome abnormality, they are at risk for developmental delays, particularly language, motor development, and learning disabilities.

The Denver study group has previously reported the childhood functioning of the 47,XXX probands (Bender et al., 1995; Linden et al., 1988) [3,7] and noted that a group of 11 girls demonstrated a greater degree of difficulty than the other SCA karyotypes. All of the girls had speech problems by first grade, and seven of them received speech therapy. Cognitive skills were less than those of the sibling comparison group with a mean Full Scale IQ of 84 (21 points lower than mean IQ score of the comparison group). Ten of the 11 girls received extra assistance during the grade school years, and three of them repeated the first grade. Seven girls had reading skills below grade level, while mathematics was problematic for only three girls and was actually the strongest subject for four of the girls. The 47,XXX group also demonstrated more psychological difficulty and aberrant behavior than any of the other SCA or sibling comparison groups during school age. Three girls experienced recurring bouts of enuresis, one girl had elective mutism and trichotillomania, four girls had multiple somatic complaints, and two girls experienced precocious puberty at approximately 8 years of age, with menses beginning between 9 and 10 years of age. Eight of the girls were noted to be awkward, clumsy, and/or poorly coordinated (Salbenblatt et al., 1989) [14].

The 47,XXX individual may be at greater risk for poor psychosocial adaptation and psychiatric disorder during adolescence and early adulthood. For all children, adolescence is a critical period during which the individual becomes increasingly independent from family, turns to the peer group for acceptance, and integrates emerging sexuality into a new definition of self. For some SCA adolescents, diminished educational, athletic, and social success, increased self-doubt, and

lowered self-esteem would seem to make the transition to adulthood a particularly difficult period. This article specifically focuses on adolescent and early adult adaptation of this group, addressing developmental differences in adaptation and psychiatric status during the transition from adolescence to young adulthood between the 47,XXX individuals and a sibling comparison group.

## **METHOD<sup>^</sup>**

Beginning in 1964, a total of 40,000 consecutive births at two Denver hospitals were screened for sex chromatin by Barr body analysis of amniotic membranes. Positive findings were confirmed through chromosome analysis of peripheral blood. Of the 68 infants with SCAs thus identified, 12 had 47,XXX karyotypes. Fifty-one of the families agreed to participate in a longitudinal study of their child's development, including 11 families with 47,XXX daughters (one potential subject died from the effects of prematurity). Siblings of the probandi have served as the comparison group. Between the ages of 12 and 19 years, most subjects had an annual visit, which consisted of an extensive interview and discussion to provide detailed information about their life experiences, milestones, successes and failures, and future plans. Physical examination and psychological testing were also completed at these visits. Additional telephone contact was maintained at least twice a year. Between 16 and 19 years of age, the WAIS-R was administered to provide an index of general intellectual competence.

In addition, each subject participated in a semistructured, 1- to 2-hour psychiatric interview conducted by a child psychiatrist who was naive to the chromosomal status of the individual. The interviews focused on four specific areas of inquiry: (1) the relationship between the adolescent/young adult and other family members and the extent to which the subject had separated from the family of origin; (2) the subject's sense of self-esteem, revealed by response to direct inquiry about personal strengths, concerns, and plans for the future; (3) sexual identity and preference; and (4) responses to life stressors. A psychiatric diagnosis from the DSM (American Psychiatric Association, 1987, 1994) [1,2] was assigned where appropriate. A numerical rating based on the Children's Global Assessment Scale (for adolescents) or the Global Assessment of Functioning (American Psychiatric Association, 1987, 1994) [1,2] provided an estimate of overall functioning and adaptation. These scales are used to represent the individual's functioning on a hypothetical continuum of psychological health/illness for the 6-month period preceding the interview. Higher scores indicate higher functioning, with scores greater than 70 reflecting good functioning with family, school, and peers and no more than mild, acute impairment in response to specific stressors. Scores from 61 to 70 indicate slight difficulty in one area, but generally adequate functioning. Scores from 51 to 60 indicate variable functioning with sporadic difficulties or symptoms in several but not all areas. Scores of 50 or less indicate moderate to severe dysfunction.

The Schedule for Affective Disorders and Schizophrenia-Lifetime version was administered, from which a diagnosis(es) was given based on the Research Diagnostic Criteria (Spitzer and Endicott, 1978) [15]. It is a structured interview that reviews lifetime history of symptoms pertaining to affective disorders, schizophrenia, substance abuse, phobias, anxiety disorders, psychosomatic problems, and antisocial behaviors. Finally, the Social Adjustment Scale Interview (Weissman and Bothwell, 1976) [18] was also scored at the end of the interview. These adjustment scales include assessments of work, social/leisure, relationships with extended family, marital adjustment, parental adjustment, and overall adjustment. The scores range from 1

(excellent) to 7 (very severe maladjustment).

The subjects for this study included 11 individuals with 47,XXX karyotype and 9 female sibling controls. Each subject was interviewed during adolescence and during early adulthood. The mean age at the time of adolescent interview was 16 years for the probands (range between 14 and 18) and 16 years for the sibling comparison group (range between 14 and 19). The mean age at the time of the early adult interview was 23.9 for the probands (range between 18 and 29) and 25.5 for the comparison group (range between 20 and 29).

## RESULTS<sup>^</sup>

Scores from the two groups were compared separately from the adolescent interview and the early adult interview using the Kruskal-Wallis test (SPSS Inc., 1988) [16]. There were no significant differences in age between the two groups. However, significant differences favoring the comparison group were found on the Global Assessment of Functioning scale, the number of psychiatric diagnoses, and three of the Social Adjustment Scales (Table 1). The marital and parental scales were not used at this age because few subjects were married and/or parents.

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Table 1. Psychosocial Adaptation Measures

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Similarly, at the time of the early adult interview, there were no age differences between the two groups, but again psychosocial adaptation was better for the sibling comparison group. There were highly significant differences between the two groups in Global Assessment of Functioning, although the number of psychiatric diagnoses showed only a trend toward a greater number of diagnoses in the 47,XXX group. With the addition of a Severity of Psychosocial Stressors scale to the early adult interview, the 47,XXX group described their lives as being more stressful. The Relationship With Extended Family showed a trend ( $p < .08$ ) toward a difference between the two groups, with the probands reporting a less positive relationship. There was also a trend ( $p < .06$ ) toward less positive marital and parental relationships in the 47,XXX group.

Additional information was derived from the psychiatric interview, including age at first sexual experience, number of marriages, number of pregnancies, number of living children, and incestuous experiences. There were no significant differences between the groups on these variables (Table 1). However, the findings that four of the 47,XXX women had consensual intercourse before the age of 13, whereas none of the women in the comparison group had intercourse before the age of 15, and four of them became pregnant while in high school reinforces our general clinical impression of greater sexual promiscuity in our 47,XXX group. It is additionally noted that, although no significant differences emerged on the number of pregnancies, the 47,XXX group appeared to suffer greater reproductive casualty. In the 47,XXX group, one family lost a child through sudden infant death syndrome, and two others elected to have two or more therapeutic abortions; in the comparison group, one woman had two spontaneous abortions. Two of the 47,XXX women have been married twice, in contrast to none

of the women in the sibling comparison group, reflecting again the relationship difficulties reported by this group. Finally, although we had originally hypothesized that the 47,XXX group might be at greater risk for sexual exploitation, this was not the case. It was concerning, however, that a total of 3 (15%) in the total sample of 20 adult women had been subjected to familial sexual abuse.

The frequency of current psychiatric disorders was much higher in the 47,XXX group ([Table 2](#)). There were no clear trends as to a particular psychiatric disorder, although affective and substance use disorders were predominant. The adolescent in whom conduct disorder was diagnosed developed an antisocial personality disorder as a young adult. Another woman, who had not met the criteria for conduct disorder during her adolescent interview, also met the criteria for antisocial personality disorder in adulthood, which seemed to be primarily a reflection of greater candor about her adolescent difficulties. Four of the women were hospitalized during adolescence in psychiatric settings because of suicide attempts ( $n = 2$ ), alcohol and drug abuse ( $n = 1$ ), and psychotic symptomatology ( $n = 1$ ). Thus, although there was only a trend toward a difference between the two groups in number of psychiatric diagnoses, the frequency and, from a clinical perspective, the severity of the psychiatric symptomatology was much higher in the 47,XXX group.

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Table 2. Current Psychiatric Diagnoses

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The second group of comparisons addressed within-group changes over time. All diagnostic and psychosocial adaptation measures were compared using Wilcoxon's  $t$  statistic (SPSS Inc., 1988) [\[16\]](#) for the matched-pair signed-ranks test. For the 47,XXX group, there were no significant differences on any of the measures, except for age across the two times. Strikingly, the means for the remaining measures were almost identical. The only apparent change was a trend in the 47,XXX group toward increased number of psychiatric diagnoses at the early adult interview. For the comparison group, there were no significant differences between the intervals of the interviews except for age.

These results suggest no developmental shift in psychosocial adaptation in either of the two groups from adolescence to early adulthood, with the exception of an apparent increase in psychiatric diagnoses in the 47,XXX: group in early adulthood. At both time periods, the 47,XXX group demonstrated much poorer psychosocial adaptation and more significant psychiatric impairment.

## **DISCUSSION<sup>^</sup>**

In summary, this group of 47,XXX women during both adolescence and young adulthood were less well adapted; described their lives as more stressful; had more work, leisure, and relationship problems; had a lower IQ; and showed evidence of more psychopathology when contrasted with the comparison group composed of female siblings. Propositi with lower IQs tended to demonstrate poorer psychological adaptation, as reflected by lower Global Assessment

of Functioning scores. However, psychiatric status was not determined solely by intelligence; psychological dysfunction occurred even among women with IQs in the average range. Although these women seem to have more difficulty, most of them are self-sufficient and functioning reasonably well, albeit less well than their siblings. Previous case reports have emphasized severe psychopathology and antisocial behavior in individuals with sex chromosome anomalies. However, this longitudinal study, along with others (Evans et al., 1990) [4], has clarified that such extreme outcomes are rare and that variability in the behavioral phenotype is much larger than originally appreciated. Thus, while many 47,XXX women have lower levels of psychosocial adaptation and a higher incidence of psychiatric disorder than their siblings, some have adapted reasonably well, have finished high school and attended college, have married and raised children, and have successfully maintained competitive employment. The apparent trend toward increased psychiatric diagnoses over time must be confirmed or refuted by this and other longitudinal studies of 47,XXX women.

Of concern related to these findings is the representativeness of this small sample of 47,XXX women. In a recent publication of another longitudinal study, the adaptation of 47,XXX women was better than that described in this study (Rovet et al., 1995) [13]. Although subjects in that study were identified through the consecutive chromosome screening of a cohort of newborns, much as subjects were identified in this study, subjects in that study were from families who were of high socioeconomic status and had higher IQ scores. Because their findings on adaptation were anecdotal and did not include formal psychiatric evaluations, they cannot be compared directly with the findings from this study. In a small-sample prospective study of prenatally diagnosed sex chromosome aneuploidy (Robinson et al., 1992) [11], young 47,XXX girls appeared to have more successful adaptation than those represented in this report. The prenatally diagnosed sample (Robinson et al., 1992) [11], however, was a self-selected group who called our research team for guidance about continuing or terminating a pregnancy of a child with a chromosome anomaly. Most of these families, having chosen not to terminate their pregnancy, were of higher socioeconomic status and appeared to be higher-functioning as a group than the families in our longitudinal study. As was the case in the Rovet et al. (1995) [13] study, the group had higher IQs than represented in this report and likely reflect a bias toward the upper end of the distribution of 47,XXX females.

Finally, we should note that participation in this study may have influenced the outcome measures. Almost all of the participants and their families have commented on the positive effects of being examined almost yearly by the clinical research team. In particular, referrals for medical and psychiatric treatment, when indicated, the development of long-term relationships with research team members, and a sense of being "special" are routinely expressed during the psychiatric interview. On the other hand, the families also state that they have not treated their SCA children (now adults) any differently than their other children. Most of the siblings agree with this statement when interviewed. However, the potential for research participation to have had an ameliorating effect on the sequelae of the 47,XXX condition must be acknowledged.

### Clinical Implications<sup>^</sup>

Sex chromosome anomalies are not rare, occurring in about 1 out of 300 to 400 births. Although in some cases they will remain undiagnosed, these conditions are relatively common in any urban setting. Thus, individuals with SCAs may present themselves for psychiatric treatment. Given the higher incidence of diminished psychosocial adaptation and psychiatric disorder,

47,XXX women in particular may be candidates for psychiatric intervention. Increased awareness of the implication of this diagnosis will improve both understanding of and intervention with individuals having this karyotype. In particular, the psychiatrist presented with a 47,XXX patient must understand the developmental risks associated with this condition while at the same time maintain an appreciation for its variability. Treatment plans must, as always, be based on an assessment of the individual's strengths and weaknesses, and under no circumstances should it be assumed that the genetic effects imposed by the additional X chromosome are immutable to psychiatric treatment.

An additional important application of the results of this longitudinal study is found in the field of genetic counseling (Linden et al., 1996) [8]. A variety of health professionals are commonly called upon to provide prognoses for prenatally diagnosed 47,XXX fetuses. Psychiatric consultation may be sought both in aiding couples faced with the decision about continuation of a 47,XXX pregnancy and in preparing for developmental risks after the child is born. Our group has repeatedly advocated for "anticipatory guidance," which emphasizes the child's normal development but remains prepared to identify and provide early intervention when developmental deviation occurs. Appropriate speech/language therapy, physical/occupational therapy, educational remediation, and child psychiatry treatment are thus recommended immediately when their need is identified. The variability in the psychological phenotype of 47,XXX women and their developmental outcome indicates the potential positive impact of psychiatric intervention.

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