

Table. X Chromosome Parental Origin and Metabolic Profile

	Mean (SD)		P Value*
	X ^M	X ^P	
All patients, No.	62	27	
Age, y	30.7 (10.9)	26.7 (11.6)	.11
BMI	27.6 (6.3)	25.2 (6.3)	.15
Fasting glucose, mg/dL	83 (10)	82 (7)	.68
Fasting insulin, μ U/mL	8.2 (7.0)	8.1 (4.6)	.95
Triglycerides, mg/dL	131 (62)	100 (50)	.01
Total cholesterol, mg/dL	208 (40)	189 (43)	.02
LDL-C, mg/dL	137 (41)	113 (44)	.004
HDL-C, mg/dL	58 (13)	61 (17)	.17
Patients aged \geq 18 y, No.	40	16	
Age, y	34.1 (9.3)	32.2 (10.1)	.51
BMI	28.6 (7.8)	27.4 (7.1)	.59
Total body fat by DXA, %	37.1 (7.6)	36.3 (8.1)	.27
Total abdominal fat, mL	78.3 (49.0)	57.7 (36.0)	.005
Visceral abdominal fat, mL	24.8 (19.4)	13.9 (8.0)	<.001

Abbreviations: BMI, body mass index, calculated as weight in kilograms divided by the square of height in meters; DXA, dual-energy x-ray absorptiometry; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; X^M, maternally inherited X chromosome; X^P, paternally inherited X chromosome.

SI conversions: To convert glucose to mmol/L, multiply by 0.0555; to convert triglycerides to mmol/L, multiply by 0.0113; to convert total cholesterol, HDL-C, and LDL-C to mmol/L, multiply by 0.0259.

*Group means were compared by 1-way analysis of variance/analysis of covariance followed by Fisher protected least-significant-difference tests. Age and BMI were used as covariates in comparing metabolic and adiposity measures. Two-sided P values were calculated for age, BMI, fasting glucose, and fasting insulin; all other P values are 1-sided.

that is reduced with testosterone replacement.⁷ Because both Turner syndrome groups in this study had ovarian failure, sex steroids are not likely contributors to the present findings.

Limitations of this study include a relatively small sample size. As an observational study, results could be due to unmeasured confounders. The cross-sectional design limits inferences about causality. While interpretation of the P values should consider that there were 6 comparisons, the parallel increases in plasma lipids and abdominal adiposity are biologically consistent. Additional research is needed to confirm these findings and to extend them to X chromosome effects in normal men and women.

However, these results suggest a role of X chromosome gene dosage in metabolic regulation that could be explained by the imprinting (silencing) of maternally transmitted X-linked genes that normally prevent visceral fat accumulation, or imprinting of paternally transmitted X-linked genes that normally promote visceral fat accumulation. Identification of these putative imprinted X-linked genes and elucidation of the epigenetic mechanisms involved in their differential expression could have implications for cardiovascular health.

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Shyness, Social Anxiety, and Impaired Self-esteem in Turner Syndrome and Premature Ovarian Failure

To the Editor: Shyness and social anxiety are reported in women with Turner syndrome (TS).¹ Possible contributors include physical stigmata, such as short stature and neck-webbing, chromosomally-based deficits in social cognition, and premature ovarian failure with infertility. To investigate the potential role of premature ovarian failure and infertility, we compared measures of psychosocial distress in women with TS, women with spontaneous karyotypically normal premature ovarian failure (POF), and healthy controls.

Methods. Participants in this institutional review board-approved study were recruited through National Institutes of Health (NIH) Web sites and newspapers and provided written informed consent. Inclusion criteria for patients with TS and POF are described elsewhere.² Daily hormone therapy

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was taken by 99% of the women with TS and 90% with POF but was discontinued 2 weeks before evaluation.

Control participants were recruited from the local community and were paid a small stipend. They were required to have regular menstrual cycles, take no medications, and have no current or past medical or psychiatric conditions. Control participants were interviewed during the follicular phase of their menstrual cycle.

Testing was performed in the NIH Clinical Research Center between January 2001 and January 2004. Participants completed 4 rating scales previously validated in community populations: the shyness scale,^{3,4} social anxiety scale,⁵ Rosenberg's self-esteem scale,⁶ and the Center for Epidemiologic Studies–Depression Scale.⁷ From an initial sample of 103 women with TS, 100 fully completed all the surveys; and from an initial sample of 128 women with POF, 100 completed all surveys. Age and marital status did not differ significantly between participants and nonparticipants.

Group means were compared using analysis of variance with age and body mass index (calculated as weight in kilograms divided by the square of height in meters) as covariates. Multiple linear regression was used to examine the effects of age, years of education, years of hormone therapy (as a measure of duration of ovarian failure), and marital status on scores. For comparisons of rating scale scores between women with TS and those with POF, sample sizes of 96 to 104 women per group provided 90% power to detect a difference of 10% or greater on any of the rating scales with $\alpha = .05$. Analyses excluding women with TS younger than 18 years showed similar results and are not reported. All analyses were performed using Stat View 5.0.1 (SAS Institute Inc, Cary, NC).

Results. There were group differences in the percentage of participants taking thyroid or antidepressant medication (TABLE 1). However, all women were euthyroid, and these medications were continued during the study. More women with POF were married, likely reflecting their initial presentation of infertility.

Turner syndrome and POF groups scored significantly higher on the shyness scale, social anxiety scale, and the Center for Epidemiologic Studies–Depression Scale, and lower

on the self-esteem scale compared with controls (TABLE 2). However, there were no significant differences between the TS and the POF groups for the scores on any of these scales. Age, years of education, years of hormone therapy, and marital status did not contribute to score variations in TS or POF.

Comment. In this study population, 2 dissimilar groups of women who had experienced premature ovarian failure had similar psychosocial profiles, with increased shyness, social anxiety, and depression, and decreased self-esteem compared with women with healthy ovarian function. These results are not likely to be due to ovarian hormone deficiency because the majority of women in both groups were taking hormone therapy. Short-term cessation of hormone therapy should not result in changes in these scales that measure chronic social distress. Although our results do not pro-

Table 1. Characteristics of Women With Turner Syndrome, Karyotypically Normal Premature Ovarian Failure, and Healthy Controls

	Turner Syndrome (n = 100)	Premature Ovarian Failure (n = 100)	Healthy Controls (n = 35)
Age, mean (SD) [range], y	34.7 (11.6) [16-61]	30.9 (5.7) [19-42]	35.8 (9.6) [19-50]
Ethnicity, No. (%) [*]			
White	91 (91)	85 (85)	23 (66)
Black	1 (1)	8 (8)	9 (26)
Asian	3 (3)	3 (3)	2 (6)
Hispanic	5 (5)	4 (4)	1 (2)
BMI, mean (SD)	27.6 (6.5)	23.6 (4.4)	23.2 (4.0)
Height, mean (SD), cm	146.2 (10.0)	165.0 (7.5)	160.8 (6.2)
Hormone therapy duration, mean (SD), y	14.6 (10.7)	4.9 (4.4)	NA
Taking thyroid medication, No. (%) [†]	33 (33)	7 (7)	0
Taking antidepressant medication, No. (%) [†]	14 (14)	13 (13)	0
Education, mean (SD), y	16.3 (2.1)	17.0 (2.8)	17.0 (2.6)
Currently married, No. (%)	31 (31)	85 (85)	15 (43)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); NA, not applicable.

^{*}Race/ethnicity based on patient self-identification using National Institutes of Health categories.

[†]All women were euthyroid. Antidepressant and thyroid hormone medications were continued during this study.

Table 2. Results of Psychological Tests

	Mean Score (95% CI)			P Value [*]		
	TS	POF	Healthy Controls	TS vs Healthy Controls	POF vs Healthy Controls	TS vs POF
Shyness scale [†]	34.4 (32.3-36.6)	31.9 (29.3-33.3)	23.8 (20.8-26.8)	<.001	<.001	.11
Social anxiety scale [‡]	23.0 (20.3-25.8)	21.9 (18.8-23.7)	10.8 (8.7-13.5)	<.001	<.001	.58
Rosenberg's self-esteem scale [§]	31.6 (30.5-32.6)	32.5 (31.7-33.7)	36.4 (35.0-37.6)	<.001	<.001	.20
Center for Epidemiologic Studies–Depression Scale	10.1 (8.6-11.9)	11.9 (9.7-13.9)	3.3 (1.8-4.3)	<.001	<.001	.13

Abbreviations: CI, confidence interval; POF, premature ovarian failure; TS, Turner syndrome.

^{*}Comparison of group means by analysis of variance with age and body mass index as covariates.

[†]Scale ranges from 14 to 70, with scores of higher than 35 indicative of clinically significant shyness.^{3,4}

[‡]Scale ranges from 0 to 80, with higher scores indicating more severe social anxiety.⁵

[§]Scale ranges from 10 to 40, with higher scores indicating greater self-esteem.⁶

^{||}Scale ranges from 0 to 60, with scores of 16 or higher consistent with major depression.

vide an explanation for this symptom profile, uncontrolled studies⁸ suggest infertility as a factor.

Study limitations include the use of self-selected groups that were primarily white, relatively well-educated, and took the initiative to participate in NIH protocols; as such, they may not be representative of other women with premature ovarian failure. Control participants were screened for the absence of psychiatric illness so their rating scale scores could have been biased toward less distress than those from a general population. As a cross-sectional study, conclusions about causality cannot be made and, as an observational study, associations could be due to unmeasured confounding. To confirm these findings, it is important to study other groups, such as young women with ovarian failure secondary to cancer or cancer therapy. Nevertheless, these results suggest that clinicians should consider these psychosocial issues in addition to the medical consequences for patients with premature ovarian failure.

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Depression Among Pregnant Rural South African Women Undergoing HIV Testing

To the Editor: Rates of human immunodeficiency virus (HIV) infection in southern Africa are high, with up to 45% of pregnant women being HIV-positive.¹ Depression is associated with lowered adherence to antiretroviral medication² and poor use of antenatal care.³ It frequently persists into the postnatal period, raising the risk of adverse child outcomes.³ Because little is known about the rates of depression among women undergoing HIV testing in prevention of mother-to-child transmission programs (PMTCT), we undertook this prevalence study. A secondary aim was assessment of perceptions among these women about adverse consequences of an HIV diagnosis, and whether these perceptions were related to depression status.

Methods. This study was conducted in rural northern KwaZulu-Natal, South Africa, a region with a very high HIV prevalence.¹ A consecutive sample of women offered PMTCT during routine antenatal care at 3 representative clinics⁴ was invited to participate. Women were eligible if this was their first HIV test in the current pregnancy and they had not previously tested HIV-positive. Written informed consent was obtained and approval was granted by the Ethics Review Board of the University of KwaZulu-Natal and the Oxford Tropical Research Ethics Committee. Enrollment was obtained from 242 (82%) of the eligible women. Reasons for nonparticipation included insufficient time, nonreturn after requesting opportunity to discuss with family, and unwillingness to participate in research. Ethics boards did not permit collection of any other comparison data from nonparticipants.

Depressive symptoms were assessed with the Edinburgh Postnatal Depression Scale (EPDS). It has specificity and sensitivity greater than 76%,⁵ has been validated antenatally and postnatally,⁶ and has been validated in a black South African population.⁷ Depression was defined by a score of 13 or above.⁶ Any patient reporting recent thoughts of self-harm was referred for intervention. A 9-item questionnaire scored in 3 domains (health care access, financial resources, and social support) was used to elicit women's perceptions of the consequences of an HIV