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, µU/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 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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1. Carr MC, Hokanson JE, Zambon A, et al. The contribution of intra-abdominal fat to gender differences in hepatic lipase activity and low/high density lipoprotein heterogeneity. J Clin Endocrinol Metab. 2001;86:2831-2837.
2. Cooley M, Bakalov V, Bondy CA. Lipid profiles in women with 45,X vs 46,XX primary ovarian failure. JAMA. 2003;290:2127-2128.
3. Wilkins JF. Genomic imprinting and methylation: epigenetic canalization and conflict. Trends Genet 2005;21:356-365.
4. Skuse DH, James RS, Bishop DV, et al. Evidence from Turner's syndrome of an imprinted X-linked locus affecting cognitive function. Nature. 1997;387:705-708.
5. James RS, Coppin B, Dalton P, et al. A study of females with deletions of the short arm of the X chromosome. Hum Genet. 1998;102:507-516.
6. NIH Clinical Center Test Guide. Available at: http://cclnprod.cc.nih.gov/dlm/testguide.nsf. Accessed February 11, 2006.
7. Wu FCW, von Eckardstein A. Androgens and coronary artery disease. Endocr Rev. 2003;24:183-217.

## 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