

Does the male infertility clinical evaluation adequately assess toxicologic exposures?

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At this summit, we have learned about the effects of environmental exposures on reproductive health among animals in the wild and in the laboratory setting. In humans, the effects of high-level exposure to specific populations as well as low-level, widespread exposures in large populations were also reviewed. From this discussion an important question is raised: how good is the standard clinical evaluation of male infertility at detecting toxicologic exposures? Another way to ask this is whether this evaluation, performed on infertile men who may be at higher than ambient risk for exposures, is a reasonably good toxicologic assessment.

The answer to this question is determined in part by the type of clinician responsible for assessing male infertility. A male reproductive health specialist, generally a urologist, will routinely perform a thorough history, physical examination, two semen analyses, and a pituitary–gonadal hormone assessment, if indicated (1). Gynecologists and female reproductive endocrinologists who routinely assess the female partner will generally ask simple questions about the male partner and obtain a semen analysis. Given the increasing popularity of assisted reproductive techniques such as in vitro fertilization and intracytoplasmic sperm injection that bypasses much of male factor infertility, I believe a real consequence of this is that most male partners are being “shunted” directly toward technology and never receive an adequate infertility evaluation. In an era in which male infertility is increasingly being shown to be a “window” into men’s health, this is an unfortunate occurrence.

Those individuals who receive a standard male factor evaluation undergo a unique assessment for occupational exposures and social habits in addition to a routine history that reviews medical problems and medication use. As reviewed in this summit, however, among 80,000 new chemical compounds introduced to human civilization in the last 100 years, only a handful ($n = 145$) have been rigorously assessed for

their reproductive health effects. We simply know very little or nothing about the rest. Not only that, exposures as common as hot baths or hot tubs that have been suspected to cause male infertility for decades have only recently been formally assessed for reproductive toxicity (2). Our experience with the physical examination suggests that loss of testis volume or atrophy is the single most important predictor of impaired semen quality in men. However, although semiquantitative in nature, the semen analysis correlates remarkably poorly with fertility potential, largely because of the inherent biologic variability within and among individuals and the fact that the most widely accepted measures of “normal” semen quality are determined not by biologic correlation but by expert consensus (3, 4). Additionally, adjunctive testing such as antisperm antibody, seminal leukocyte testing, or sperm morphology do not have well-defined specificity for reproductive toxicity. Finally, the assessment of pituitary–gonadal hormones in male infertility, although important for defining several specific pathologic conditions such as hyperprolactinemia and hypoandrogenism, lack sensitivity for even established reproductive toxins such as estrogen or cannabis exposure. Thus, even when properly performed, the male infertility evaluation is likely to be, at best, a “blunt” instrument in the detection of most toxicologic exposures.

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