

REPRODUCTIVE TOXICOLOGY: FROM SCIENCE TO PUBLIC POLICY

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Male reproductive toxicology research substantially influences policies that protect men's health. US policy directs regulatory agencies to ensure environmental protection for vulnerable groups, including boys and men where factors like age- and sex-specific sensitivities are apparent. Regulatory agencies draw from scientific advances to improve the scope and sensitivity of toxicity testing and reduce uncertainties in risk assessment. Computer-aided sperm analysis, quantitative analysis of testis histology, and markers of sexual development added to traditional reproductive test protocols, are providing a more comprehensive picture of adverse effects in both sexes and revealing risks across life stages and generations. Tests for sperm chromatin integrity, while not required in test guidelines, are proving informative in human environmental epidemiology studies. Basic science advances such as gene knock out models and stem cell markers not only help identify genes involved in spermatogenesis, but also are being used to elucidate molecular and cellular mechanisms of testicular toxicity. A revolution in toxicity testing is underway, based on high throughput *in vitro* screening and computational toxicology approaches. It derives from public concern about Endocrine Disrupting Chemicals which, in turn, emerged from reports suggesting that sperm counts may be declining in the Western world, and testicular cancer increasing, potentially due to chemicals in our environment. In this context, basic knowledge about androgen receptor function has been applied to *in vitro* screens for chemicals that interfere with androgen action and thereby impact male reproductive development. The fungicide vinclozolin provides an illustrative example. Thus, as emphasis shifts from adult to fetal sensitivities, knowledge of how early life exposures may impact life-long fertility and cancer risk is expanding. Coming full circle, evidence for epigenetic re-programming during development is extending concerns to risks of obesity, metabolic syndrome and cardiovascular health in adult men, with ever broader public policy implications.

EPA disclaimer: this abstract has been reviewed by the US EPA but does not necessarily reflect EPA policy