Detection and Evaluation of Male Reproductive Toxicity

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The potential of drugs and chemicals to cause adverse effects on male fertility is a subject of increasing concern. Early identification of male reproductive toxicants in routine repeat-dose toxicity studies is possible if appropriate endpoints are examined and if the toxicologist and pathologist are experienced in the interpretation of these endpoints. In recent years, methods for identifying male reproductive injury has expanded beyond the traditional endpoints of microscopic examination of formalin fixed testes and fertility assessment in rodent fertility studies. For example, pathologists are expected to examine testes with reference to the stages of the seminiferous epithelium (sperm staging). Assessment of number, motility and morphological abnormalities in epididymal sperm has become routine in rodent fertility studies and measurement of sperm output from the testis (testicular spermatid head) is also frequently conducted. It is important for the toxicologist to understand how to interpret these endpoints with respect to functional effects on fertility and for risk assessment purposes. There are a number of confounding factors that interfere with detecting male reproductive toxicants. These include the use of immature or peripubertal animals in toxicity studies (dogs and monkeys), a high incidence of background pathology in the testes (dogs) and the use of formalin to preserve testes for histopathologic examination (all species). These issues will be discussed with examples of why they can lead to problems for interpretation.