

Role of apoptosis in seasonal involution and recrudescence of testis

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Transitions between total arrest and recrudescence of spermatogenesis occur in several mammals with seasonal cycles of testicular activity. The involution of testicular parenchyma could result from a cessation of proliferation in seminiferous tubules. However, the significant decrease in testicular weight and function – an efficient mechanism to adjust physiology and behaviour of the animals to the needs of the non-breeding season – can not be explained exclusively by such a process. A second mechanism of regulated, programmed reduction of tissue such as apoptosis (programmed cell death) must be involved. Apoptosis is an active, genetically governed, signal-induced process of selective cell elimination (SCHWARTZMAN and CIDLOWSKI 1993; TENNISWOOD et al. 1992). Apoptosis seems to be activated and inactivated at different times in the annual cycle as an antagonist of seasonal testicular proliferation. Thus, changes in levels of apoptosis could contribute to involution and reactivation of the testis and to fluctuations in sperm production. Therefore, quantitative measurements of both the proliferation-specific antigen TPS and apoptotically produced nucleosomes have been compared with sperm and testosterone production during the transition from breeding to non-breeding seasons in testes from 80 adult roe deer, *Capreolus capreolus* (May 1994–October 1995) and from 50 brown hares, *Lepus europaeus* (June 1993–February 1994).

Testes of the animals investigated, were removed immediately after hunting. Testis weights were measured. The number of testicular spermatozoa was counted in prepared homogeneous suspensions of spermatogenic cells with a hemocytometer and calculated as sperm/g testis parenchyma and sperm/testis. The value of proliferation-specific TPS in testicular parenchyma was measured using a monoclonal antibody by an immunoradiometric assay (TPS-IRMA, Beki, Stockholm) as described by BLOTTNER et al. (1994) and was given in units/g testis (U/g). Apoptosis of testicular cells was measured in the same homogenised tissue samples according to the method of HINGST et al. (1995) using a cell death detection ELISA (Boehringer-Mannheim) and expressed in units/mg tissue (U/mg). Testicular testosterone was measured by EIA as described by MEYER and HOFFMANN (1987).

In roe deer the highest testicular and epididymal weights were found in the rutting period in late July and early August (27.2 ± 8.6 g and 3.3 ± 0.8 g, respectively). Gonadal size corresponded with the numbers of testicular spermatozoa/g parenchyma and spermatozoa per testis, respectively (Fig. 1). The most intensive apoptosis (60.4 ± 34.2 U/mg testis) was found during the period of testicular involution. The amount of testicular apoptosis was negatively correlated to gonadal weight ($r = -0.5268$, $p < 0.05$). The number of testicular spermatozoa/g parenchyma was highly correlated to testicular proliferation.

Changes in apoptosis and proliferation showed inverse correlation. The highest testicular proliferation (108.7 ± 58.9 U/g testis) was found during the rutting period in early

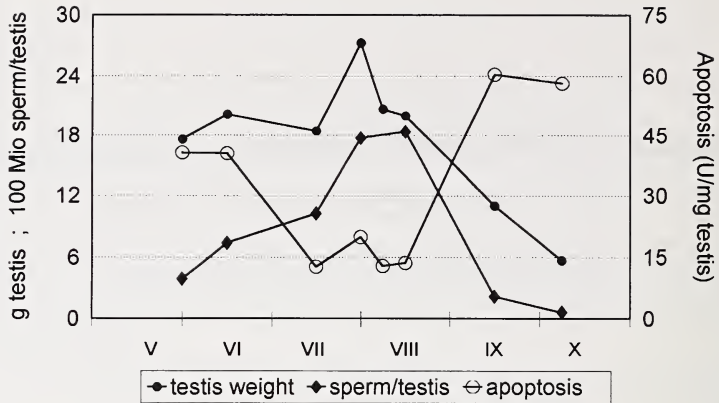


Fig. 1. Testis weight, total testicular spermatozoa and the level of testicular apoptosis in roe deer during the transition from pre-rutting to post-rutting period (May–October).

August coinciding with the lowest amount of apoptotic nucleosomes (13.7 ± 1.2 U/mg testis). In contrast, the activated apoptosis during the post-breeding period was associated with a low rate of proliferation (32.3 ± 29.7 U/g testis). Differences in apoptosis and proliferation were significant between breeding and non-breeding periods ($p < 0.001$ and $p < 0.01$, respectively). Testosterone production increased during the pre-rutting period and showed a peak in the first half of August (1.2 ± 0.6 $\mu\text{g/g}$ testis). Its concentration dropped to 0.3 ± 0.3 $\mu\text{g/g}$ in September.

Also in brown hare the testicular weight showed a cyclic involution and recrudescence. The regression of the testes in August/September is associated with the most active apoptosis and a diminished sperm production per gram of parenchyma and per testis (Fig. 2).

The maxima and minima of testicular apoptosis and proliferation during involution and reactivation of testes were inversely related. The highest apoptotic level was found

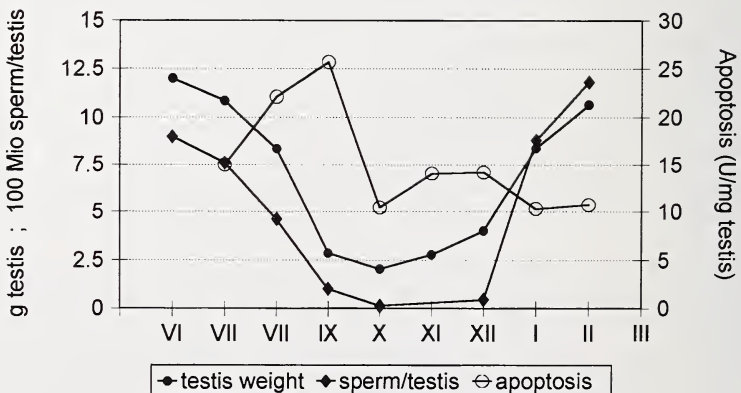


Fig. 2. Testis weight, total testicular spermatozoa and the level of testicular apoptosis in European brown hare during the transition from the breeding to non-breeding season and then again to the breeding season (June–February).

when proliferation was low (0.06 ± 0.06 U/g testis; $n = 10$). Proliferation was newly activated in November/December (0.85 ± 0.34 U/g testis; $n = 10$), preceding the increase in testicular size. At this time, apoptosis showed low levels. The differences were highly significant between the compared stages for both parameters ($p < 0.001$). Testosterone level in July/August was 12.0 ± 10.4 ng/g testis and 67.5 ± 86.4 ng/g testis in November/December ($p < 0.05$).

The results as presented from two seasonal breeders with different periods of reproduction within the annual cycle, indicate that apoptosis as an antagonist to proliferation plays an important role in seasonal regulation of testicular activity. The highest testosterone concentrations occurred simultaneously with highest proliferation and lowest apoptotic levels. This result is in accordance with the assumption that gonadotropins and androgens play an essential role in prevention of apoptosis in the testis (TAPANAINEN et al. 1993; TENNISWOOD et al. 1992). Recent report from a tropical bat demonstrated also that the sexual dormancy is characterized by a marked apoptosis (ONYANGO et al. 1995). The counteraction of proliferation and apoptosis seems to be a general phenomenon in seasonal breeders. The characterisation of proliferation and apoptosis by simultaneous quantification could be a valuable approach to study seasonal changes on the gonadal level and its dependence on different conditions.

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