PART I

THE TESTIS FROM BIRTH TO PUBERTY

FIGURE 1. PREPUBERTAL TESTIS: NEWBORN TESTIS

An important consideration in interpreting biopsies from children is that the testis is a dynamic structure, which changes from birth to puberty. All testicular components undergo waves of proliferation and differentiation prior to puberty (Vilar 1970). There are three waves of germ cell proliferation: in the neonatal period, in infancy, and at puberty (Müller and Skakkebaek 1984; Rey et al 1983). The last wave gives rise to complete spermatogenesis. There also are three waves of Leydig cell proliferation (fetal, neonatal, and pubertal); the last corresponds to the pubertal wave of germ cell proliferation (Svechnikov et al 2010).

A: Newborn testis

This light microscopy section stained with hematoxylin and eosin corresponds to a longitudinal section of a newborn testis. At birth, the testis has about 0.57 ml in volume (Müller and Skakkebaek 1983), and is covered by a thin tunica albuginea (TA) from which the intratesticular septa (S) arise. These divide the testis into lobules (L) (Trainer 1987). Close to the testis is the epididymis (E), which shows multiple sections of convoluted tubules.

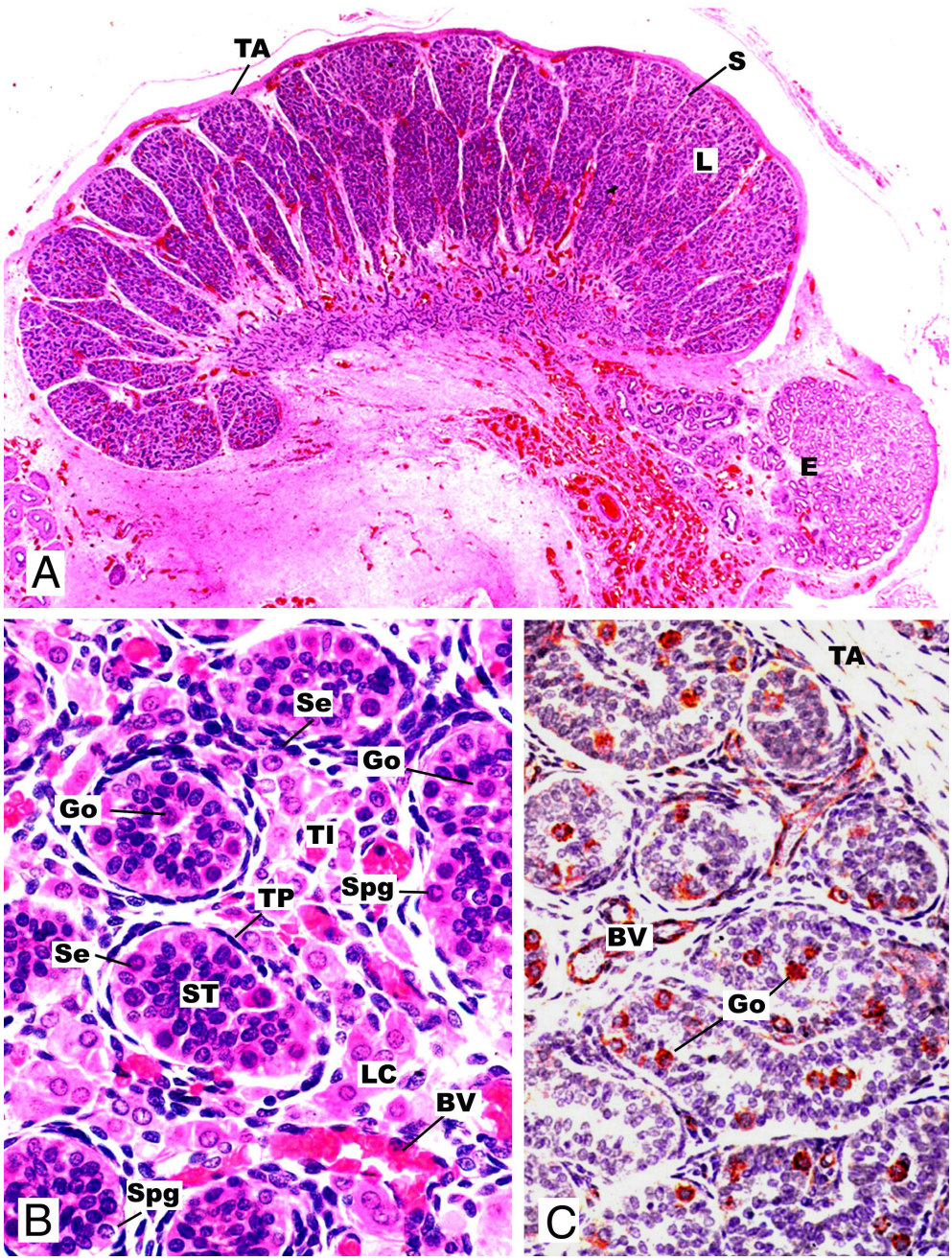
B: Testicular lobule

This his light microscopy section stained with hematoxylin and eosin shows a testicular lobule that contains the seminiferous tubules and the testicular interstitium. The seminiferous tubules (ST) measure 60 - 65 µm in diameter, have no apparent lumen, and consist of the seminiferous epithelium surrounded by the tunica propria. The seminiferous epithelium comprises two cell types: Sertoli cells and germ cells. Sertoli cells (Se) are the most abundant, with 26 to 28 cells per cross-sectioned tubule (Cortes et al 1987). They form a pseudostratified epithelium and have elongated to ovoid nuclei with darker chromatin than that of the adult Sertoli cells, and one or two small peripherally placed nucleoli (Rey et al 2009). Two types of germ cells can be seen at birth: gonocytes (Go), usually in the center of the tubules, and spermatogonia (Spg), which are mainly located at

the tubular periphery, resting on the basement membrane, and have smaller nuclei and nucleoli and less cytoplasm than gonocytes (McLaren, 2000). The tunica propria (TP) surrounds the seminiferous epithelium and consists of fibroblastic peritubular cells and collagen fibers. The testicular interstitium (TI) contains fetal Leydig cells (LC) (Hadziselimovic 1977; Prince 1990; Griswold and Behringer 2009). Blood vessels (BV), mainly blood capillaries, are abundant. Additionally, mast cells, macrophages, and hematopoietic cell can be present (Nistal et al 1984).

C: Seminiferous tubules

This is a light microscopy section of part of the tunica albuginea (TA) and the subjacent testicular parenchyma, immunostained to c-kit (nuclear proliferation antigen) for demonstration of gonocytes (G) (Figueira et al 2014). These cells are clearly identified by their large size and their location, in the center of the tubules. Their nucleus is spherical and possesses a voluminous, centrally located nucleolus (Gondos and Hobel 1971; Niemi and Ikonen 1965). The gonocyte cytoplasm contains a well-developed Golgi complex, lipid droplets, short rough endoplasmic reticulum cisternae, and numerous filaments. These latter are mainly beneath the cell surface. Gonocytes immunostain to placental alkaline phosphatase, c-kit proto-oncogene, and the antibodies TRA-1-60 and M2A (Jorgensen et al 1995). C-kit is a receptor that is primarily expressed in the cell surface of primordial germ cells and is involved in the migration of these cells to the gonad (Orth et al 1997) and their adherence to the Sertoli cells (Pesce et al 1997), since the latter express the c-kit ligand (known as Steel-factor) (Rossi et al 1991; Tajima, et al 1991). Gonocyte migration is probably favored by several cell adhesion molecules including P cadherin, which is detected on the immature Sertoli cells (Bendel-Stenzel et al 2000; Lin and De Philip 1986). Blood vessels (BV) appear also immunostained to c-kit.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