

Disclosure statement: Nothing to disclose

## Background

Decreased reproductive rates have been reported in men born prematurely (1,2). The underlying cause is unknown and probably multifactorial. The number of Sertoli cells is a significant determinant of the sperm production capacity. Proliferation of these cells during the postnatal hypothalamic-pituitary-gonadal axis activity (minipuberty) has been suggested to have a role in later fertility (3). Whether this process is deranged after preterm birth is not known.

## Objective

The aim was to compare the levels of Sertoli cell markers and testicular volumes between preterm (PT) and full-term (FT) infant boys during the postnatal hypothalamic-pituitary-gonadal activation.

## Methods

Serum AMH and inhibin B (inhB) levels, and testicular volumes (TV) were determined longitudinally at one week (D7) and three months (M3) of calendar age and at 14 months of corrected age (cM14, 14 months from the expected date of delivery) in 33 PT and 29 FT boys. Characteristics of the study groups at birth are presented in Table 1. AMH and inhB levels were measured by ELISA (Beckman-Coulter) and TV by ultrasonography. The length and width of the testis were determined in a single longitudinal plane and the volume was calculated by using the formula length (mm) x width (mm) x width (mm) x  $\pi/6$ . Mixed models analysis was used for the comparisons between the groups and Spearman's correlation for the evaluation of associations between the variables.

## Results

At D7, both AMH and inhB levels were higher in PT than in FT boys (Figure 1;  $p=0.048$  and  $p=0.001$ , respectively). From D7 to M3, AMH and inhB levels increased in both groups ( $p<0.001$ ). AMH levels did not change significantly from M3 to cM14 in either group, but inhB levels decreased in both ( $P<0.001$ ). At M3 and cM14, AMH levels were lower in PT than in FT boys ( $p=0.057$  and  $0.026$ , respectively). InhB levels were not significantly different between groups after D7. TV was significantly smaller in PT than in FT boys at D7, but not after that (at M3  $p=0.055$  and at cM14  $p=0.4$ ).

Both D7 AMH and inhB levels correlated negatively with gestational age at birth ( $\rho=-0.36$ ,  $p=0.007$  and  $\rho=-0.48$ ,  $p<0.001$ , respectively). AMH and inhB levels correlated only at D7 ( $\rho=0.45$ ,  $p=0.001$ ). AMH correlated with TV at cM14 ( $\rho=0.4$ ,  $p=0.015$ ). InhB and TV correlated positively at M3 and cM14, but at D7 their association was negative in PT ( $\rho=-0.49$ ,  $p=0.009$ ) and positive in FT infants ( $\rho=0.45$ ,  $p=0.022$ ).

## Discussion

Postnatal increase in AMH and inhB levels during minipuberty was observed not only in FT but also in PT boys indicating a robust Sertoli cell activity that is also reflected in testicular growth. Higher AMH and inhB levels in PT boys than in FT boys at D7 probably reflect decrease in fetal Sertoli cell activity towards term birth. After minipuberty at cM14, lower AMH levels in PT than in FT boys may indicate early alteration in Sertoli cell function or lower Sertoli cell mass in PT boys.

Table 1. Characteristics of the study groups

	FT	PT
n	29	33
Gestational age (weeks)	39.8 (37.1-42.1)	31.8 (24.7-36.6)
Birth weight (g)	3275 (1910-4420)	1695 (550-2850)
Birth length (cm)	49.1 (42.0-53.0)	41.3 (30.0-48.0)
Birth weight SDS	-0.9 (-3.7-1.5)	-1.25 (-3.7-1.5)
Birth length SDS	-1.0 (-4.7-1.1)	-0.9 (-4.6-2.1)
Maternal smoking (n)		
No	28	27
Yes	1	6 <sup>a</sup>
TTN (n)	1 (3.4%)	5 (15.2%)
Hyperbilirubinemia (n)	0	15 (45.5%)
RDS (n)	0	14 (42.4%)
PDA (n)	0	8 (24.2%)
BPD (n)	0	3 (9.1%)
IVH gradus III-IV (n)	0	2 (6.1%)
NEC (n)	0	2 (6.1%)

<sup>a</sup> Two mothers quit smoking during the 1st trimester

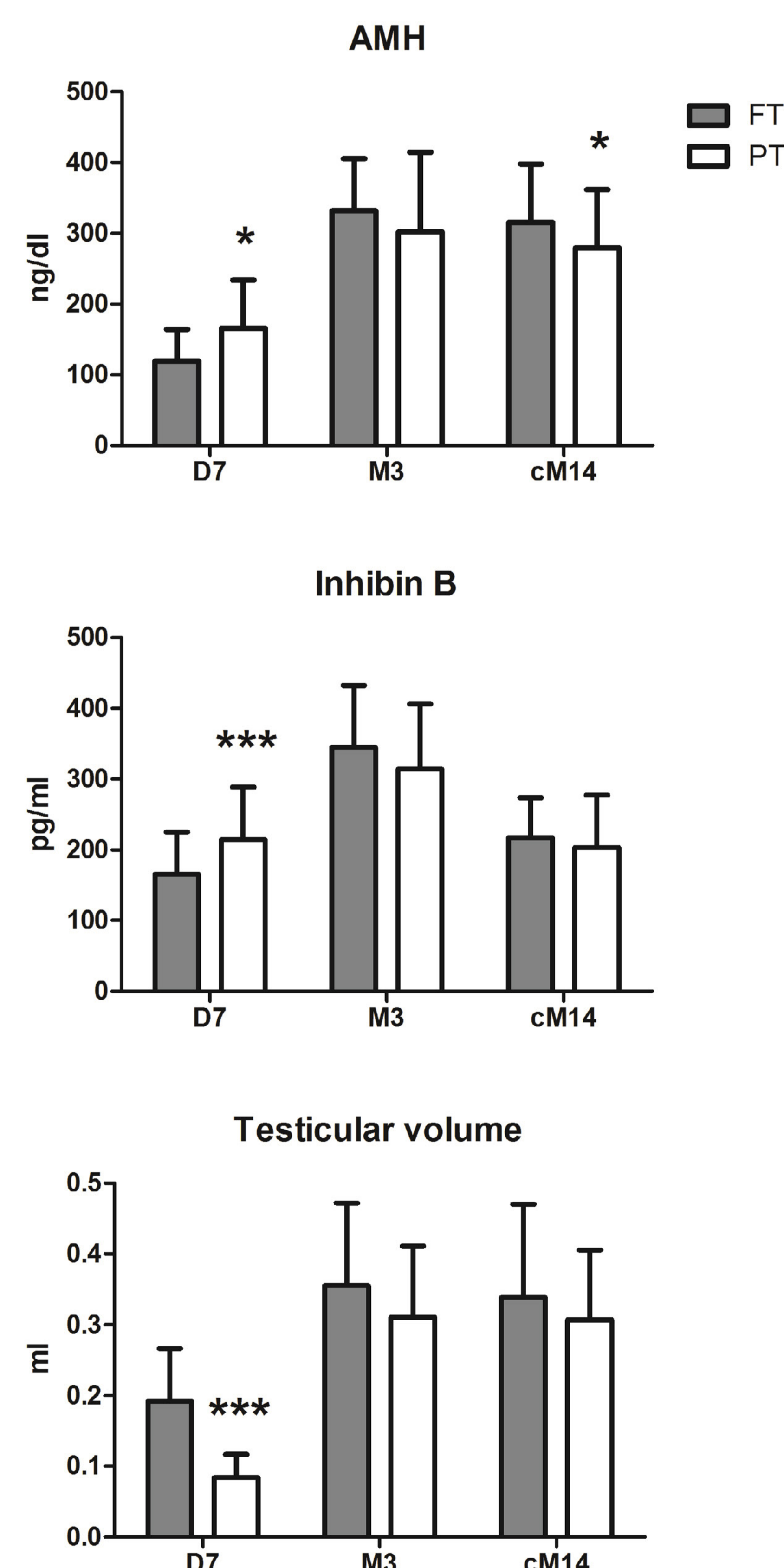


Figure 1. AMH and inhibin B levels, and testicular volumes at one week (D7) and three months (M3) of calendar age and at the corrected age of 14 months (cM14) in full-term (FT) and preterm (PT) boys.  $*p<0.05$ ,  $***p<0.001$

## References

1. Association of preterm birth with long-term survival, reproduction, and next-generation preterm birth. Swamy et al. *JAMA* 2008
2. Premature birth and low birthweight are associated with a lower rate of reproduction in adulthood: a Swedish population-based registry study. deKeyser et al. *Hum Reprod* 2012
3. Proliferation and functional maturation of Sertoli cells, and their relevance to disorders of testis function in adulthood. Sharpe et al. *Reproduction* 2003