Serum AMH levels are lower in healthy boys who develop pubertal gynaecomastia

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BACKGROUND

40-60% of boys experience breast development (gynaecomastia) around puberty (**ILLUSTRATION A**). Though often self-limiting, it can have profound effect on the individual boy. The main mechanism is thought to be an imbalance between androgens and estrogens. However, in most cases no underlying endocrinopathy can be identified.

In boys, Anti-müllerian hormone (AMH) is produced by immature Sertoli cells, and circulating level decreases as testosterone increases during pubertal maturation. But the function of AMH in boys are far from understood.

In a previous cross sectional study we found significant lower levels of AMH in boys with pubertal gynaecomastia (Mieritz et al, Clin Endocrinol, 2013).

In a unique longitudinal set-up we aim to evaluate serum AMH in boys developing pubertal gynaecomastia, and to explore the influence of two SNPs encoding AMH and the AMH-receptor, respectively.

METHODS

99 healthy Danish boys (aged 5.8 to 16.4 years) were followed in a prospective cohort over 8 years with semi-annual examinations (total examinations, n=951), with clinical evaluation of height, weight, pubertal development (genital stage, pubic hair stage and testicular volume), presence of gynaecomastia and blood samples.

Serum AMH concentrations were analyzed by immunoassay (Beckman Coulter).

Furthermore, we analyzed two single nucleotide polymorphisms (SNPs) located in exon 1 of the gene encoding AMH (AMH rs10407022 T>G) and in a putative enhancer of the AMH-receptor (AMHR2 rs11170547 C>T), respectively.

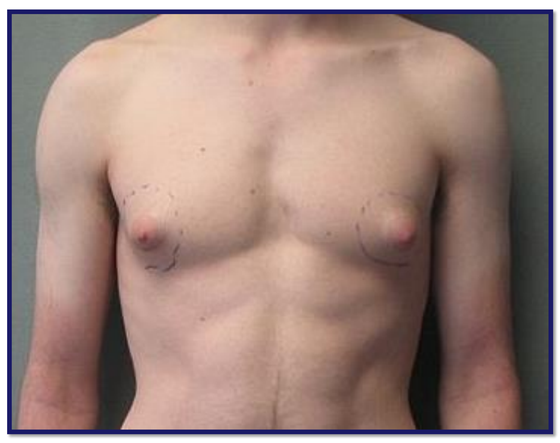
RESULTS

Pubertal gynaecomastia was observed in 47/95 (49%) of the boys during follow-up. Circulating levels of AMH were significantly lower in boys with pubertal gynaecomastia compared to boys without during pubertal transition - even after controlling for pubertal stage ($p<0.001$)(**ILLUSTRATION B**).

Lower levels of serum AMH after pubertal onset was associated with the presence of the minor allele (T) of the AMH-receptor SNP (age 13-15 years, median 359.0 vs 305.0 pmol/L, $p=0.008$)(**ILLUSTRATION C**). No association between AMH SNPs and serum AMH was found.

Pubertal gynaecomastia was not associated with AMH SNPs (GG+GT vs TT, $p=0.324$, Chi2) or AMH-receptor SNPs (CC vs CT, $p=0.963$).

To our knowledge this is the first longitudinal study to find an association between low serum levels of AMH and the development of pubertal gynaecomastia. We speculate that this might be due to impaired testicular function in these boys.



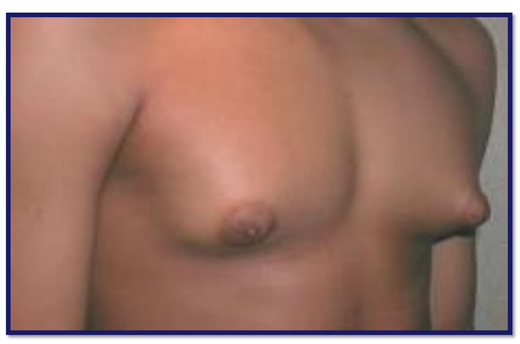


ILLUSTRATION A
Pubertal gynaecomastia in normal weight boys

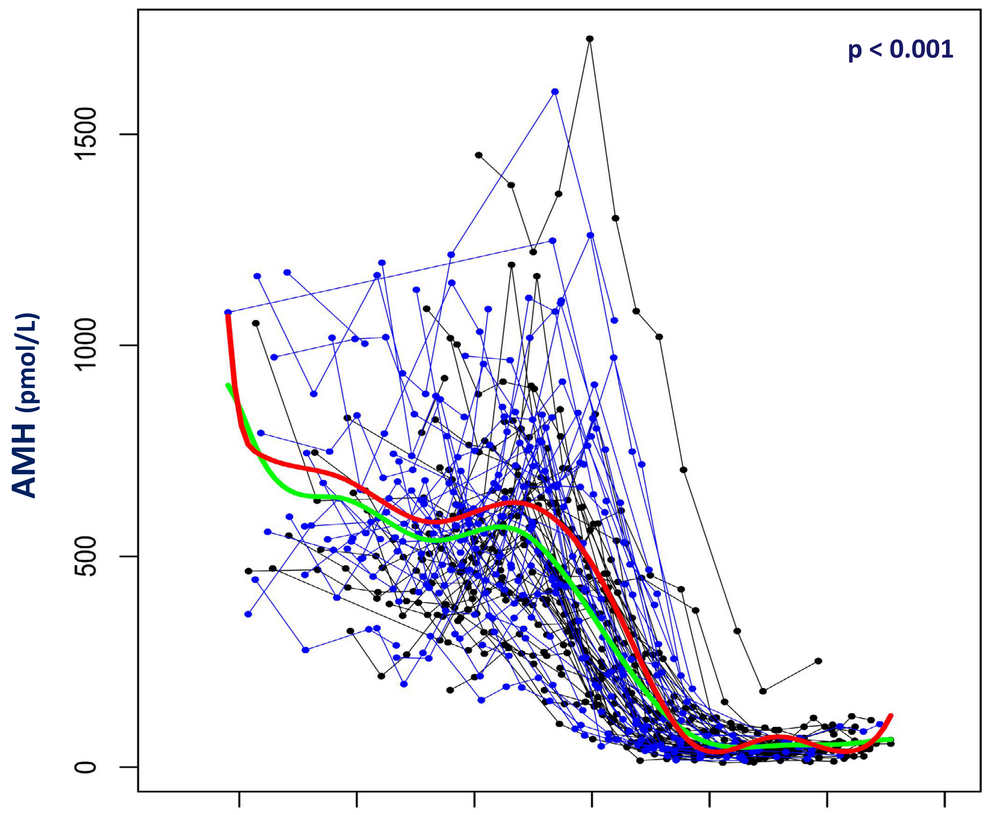


ILLUSTRATION B
Decreased serum AMH according to age controlled for pubertal development in boys with gynaecomastia (individual lines in black, mean in green) compared to controls (individual lines in blue, mean in red).

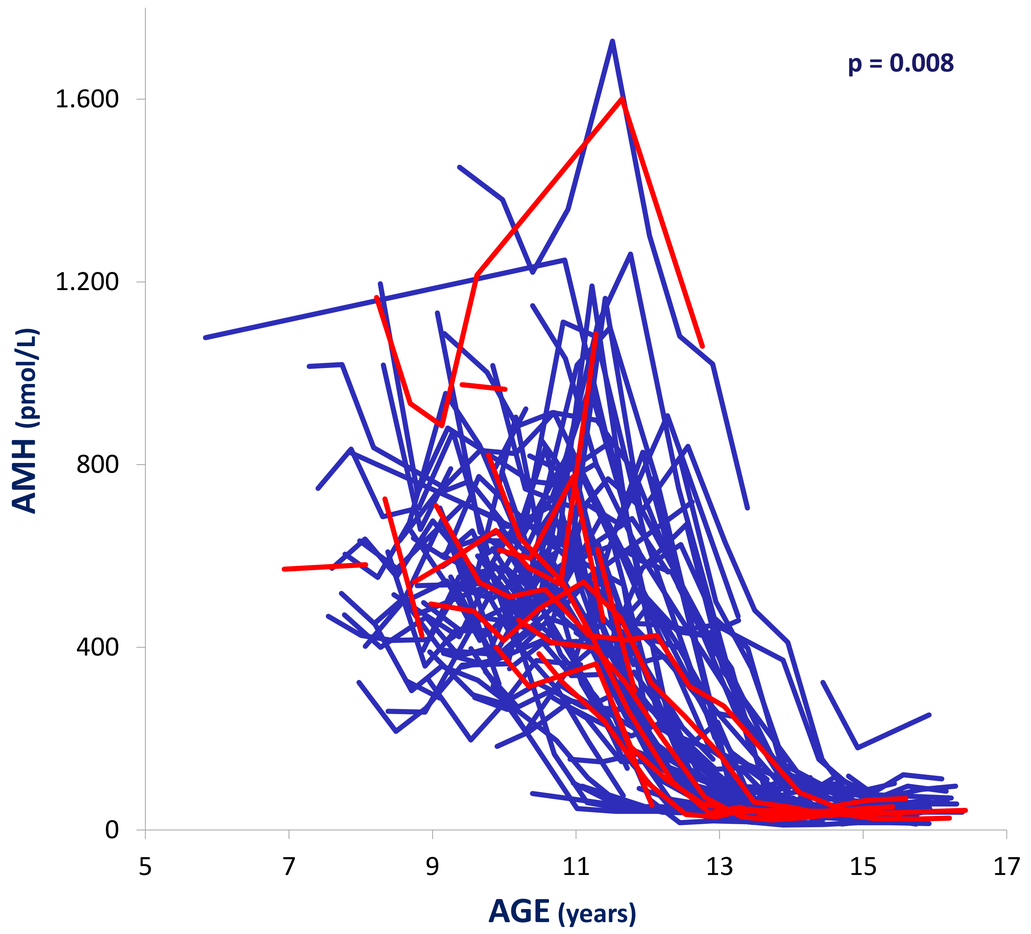


ILLUSTRATION C
Serum AMH levels according to age and AMH receptor SNPs (CC in blue, CT in red).

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