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A morphologic, ultrasonographic and endocrinologic study in rats undergoing Fowler-Stephens-procedure for cryptorchidism

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Undescended testis is a common problem in childhood. Fowler-Stephens (FS) procedure is often the surgical intervention especially in cases of a high intra-abdominal location of the testis. A postoperative examination of the operated testis including histological evaluation as well as fertility tests can not be performed in humans. Ultrasonographic, and endocrinological parameters might be an option, however these examinations could not be correlated to histomorphometric parameters. Because of similarities in testicular anatomy, Wistar rats were used to simulate and evaluate this operative procedure. In the present study the size, blood supply, function and morphology of the right testis were investigated at different time intervals after laparoscopic FS-procedure (unilateral right testis or combined with left side orchiectomy) performing a fertility test, an ultrasonographic and histomorphometric analysis as well as the determination of inhibin-βB in serum and in tissue, the latter by immunolabeling.

I. The fertility test showed, that from 9 animals undergoing unilateral FS-procedure plus orchiectomy only one rat was fertile (11%).
II. Massive atrophy of the right testis after ligature of the testicular artery was detected in 23 animals from a total of 30 rats. Ultrasonographic analysis revealed a marked reduction in testicular size and minimal blood supply. These data correlated: *1.* with a striking decrease in serum inhibin βB to 50% of the control in the LV-group in the first 40 days and a total absence in the LVO-group and *2.* with a complete collapse and disorganisation of the germinative epithelium of the seminiferous tubules, showing apoptotic processes not only in all spermatogenic cells but also in Sertoli cells. In dependency upon the time interval after unilateral FS-procedure progredient microlithiasis in the central zone of the right testis could be clearly demonstrated by sonography which is paralleled by neoangiogenesis in the peripheral zone of the right testis. The detailed histological analysis revealed that these alterations were

accompanied by mast cell accumulation and Leydig cell proliferation in the peripheral testicular zone

III. Partial atrophy of the right testis was observed in 6 out of 21 animals in the LV-group. The seminiferous tubules showed a reduction of the height of the germinative epithelium which contained large vacuoles as an expression of a beginning atrophy.

IV. Unilateral FS-procedure in combination with left sided orchiectomy revealed that in dependency of the time interval after the surgical intervention in addition to central core microlithiasis, parallel to peripheral neoangiogenesis and mast cell accumulation in the right testis Leydic cell nodule formation was induced, resulting in Leydic cell adenoma at a time interval of 12 months after surgery.

Our data reveal a close correlation between initial testicular atrophy resulting in adenoma formation. In the future we have to focus our attention on neoangiogenesis in the peripheral zone of the atrophic testis, however, our findings provide evidence that there is a functional correlation between central microlithiasis and peripheral mast cell accumulation, neoangiogenesis and tumour development. Consequently, following FS-procedure in humans, we propose a detailed monitoring protocol including initial ultrasonographic analysis during the first two p.o. weeks and half yearly and a biochemical analysis of hormone levels, particularly of the inhibin βB serum level.

Due to the close correlation of the presented data the proposed protocol seems suitable to minimise the risk of malignant transformation in the testis and for early diagnosis of neoplasm formation. Furthermore, following the protocol, the number of testicular biopsies in cryptorchid patients would reach a desirable low level.