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RECENT PATHOLOGICAL CONTRIBUTIONS ON THE ORIGIN AND EVOLUTION OF PROSTATIC CANCER.

F. Algaba, I. Trías*, J. Martínez-Hurtado. Fundació Puigvert and *Fundació Plató, Barcelona, Spain.

Recent advances in Pathology on the origin and evolution of prostate cancer (PC) are due to the improvement of classical tehcniques combined with new immunohistochemical and molecular technologies.
Whole-Mount sections.- An accurate sonographic-pathological correlation has been made with this method. The cancer origin by zones (57,6% in the peripherical zone, PZ, 20% in the transitional zone - TZ and 6,8% in the central zone - CZ) has been identified. Eighty-three per cent of incidental carcinomas are in the TZ, whereas 86% of clinical carcinomas are found in the PZ.
The whole section of the prostate has shown that 80% of PC's are multifocal and although evolution is related to the tumoral volume -a 1 cc PC is seldom infiltrating- it also correlates with its localization (capsular infiltration in 61% of PC in PZ and 4% in TZ. Infiltration of seminal vesicles only in PZ PC's).
Classical techniques + new technology. This combination has allowed to confirm that prostatic intraepithelial neoplasia (PIN) appears in 68,8% of PZ, 2,6% in TZ and 28,6% in both of them, correlating with the PC multifocality. Commun changes to the PC are seen with CK.903, Vim, DNA determination and AgNors. Therefore PIN is considered a precursor of the clinical PC.
Future investigation.- is centered in the determination of the relationship between BPH and incidental PC, probably through AAH, as well as the stratification of the incidental cases with or without metastatic ability. Regarding the locally advanced PC molecular (P21 and Myc) changes to foresee the metastatic ability are been searched.

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BIOLOGICAL MARKERS IN THE MANAGEMENT OF UROTHELIAL TUMORS

Dominique K. Chopin, Department of Urology, Hôpital Henri Mondor, 94000 Creteil, France

Bladder cancer is the 7th cause of cancer death and is increasing in frequency. Natural history of the disease has demonstrated two main growth patterns, (i.e.) superficial and infiltrative. With the increasing role of the conservative management there is a need to define biological markers to predict response to intravesical instillation of prophylactic agents such as BCG. In addition, these markers are candidate as target for innovative therapeutic agents. Infiltrative diseases are often far advanced at the time of diagnosis and several multimodal therapeutic schemes are evaluated. Biological markers are needed to improve quality of staging or diagnosis in predefined risk populations. Progress in the biological behaviour of such tumors will allow design of new strategies for the control of metastatic disease. Cell cycle markers and gene products involved in the regulation of the cell cycle, tumor associated antigens, growth factor regulation and signalling pathways, tumor suppressor genes involved in the biology of urothelial tumors will be reviewed. Examples of markers having clinical relevance for diagnosis, response to therapy and drug targeting, worked in our department will be presented.

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BIOLOGICAL MARKERS RELEVANT FOR THE CLINICAL MANAGEMENT OF PROSTATE CANCER.

Mahler Ch.
Dept. of Endocrinology, A.Z. Middelheim, Antwerp, Belgium.

The survival rate for prostatic cancer, provided early diagnosis, can exceed 85 % when treated radically. Early detection might be enhanced if a reliable prostatic cancer marker would be accessible.
The ideal tumour marker needs to be highly specific and sensitive, should be secreted by a tumour of specific histogenetic origin, have a high antigenic potential with a short half-life and be released in fairly detectable amounts.Its levels should correlate with the initial tumour burden,with tumour aggressiveness and response to therapy, thus permitting its use in diagnosis, prognosis and monitoring of follow-up of treatment.
Amid the many available markers that have been proposed in relation to prostatic cancer, none is at present recognized as measuring up to these requirements.
At present Prostate Specific Antigen (PSA) has largely replaced the Prostatic Acid Phosphatase as the most reliable marker for prostatic cancer. In the present paper its relevance in clinical screening, staging and grading, prognostic value and monitoring therapy will be discussed.

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ANATOMICAL APPROACH IN UROLOGICAL ONCOLOGY SURGERY

G. Bartsch and S. Poisel
Department of Urology and Anatomy, University of Innsbruck, Austria

In collaboration of the Department of Urology and the Institute of Anatomy of our University the project "Anatomical approach of Urological Surgery" was performed over the period of 2 years and will recently be published by the Thieme Medical Publishers Stuttgart.
The surgical procedures were "cut" by the surgeon, "prepared and dissected" by the anatomist and afterwards painted by an artist (H. Lechenbauer) in 42 cadaver specimens; the original instruments, especially retractors were used; all coloured paintings were drawn in the position of the surgeon.
Out of this project the special chapters regarding urologic oncology are demonstrated: thoraco-abdominal approach in kidney cancer with caval thrombus, abdominal approach in bulky-testicular disease, radical anterior exenteration in the male and female, symphysis resection in cancer of the female urethra, radical prostatectomy in the retropubic and perineal approach.
Special attention in these anatomical approaches is given to the aspect of reducing the morbidity in cancer surgery : preservation of ejaculation and erection. Clinical results are demonstrated.

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MOLECULAR GENETICS IN PROSTATE CARCINOMA

P. Ekman, Karolinska Institute, Stockholm, Sweden

We have used RFLP and Southern blotting techniques to study chromosomal deletions in prostate cancer. The mean number of chromosomal deletions, in localized cancers were 0.7 in lymph node metastases 2.0, and in brain metastases 3.5 deletions per tissue studied. The most commonly deleted chromosomal parts were located on the long arm of chromosome 16 (16q, 60%), and on the short arm of chromosome 8 (8p, 50%). Also both arms of chromosome 10 and the long arm of chromosome 18 (18q) were often deleted.
When in detail studying the deletion pattern, it became clear that the short arm of chromosome 8 was involved quite early in the malignant process of prostate cancer. Only a few localized cancers had retained 8p. The second most common step was losses on chromosome 16q, whereas 10p seemed to be involved in the metastatic potential of the tumour. The long arm of chromosome 10 seemed to be of less importance. Apart from losses on 18q, other chromosomal deletions seemed to be occurring only in very advanced cases.
When trying to relate the chromosomal deletion pattern to clinical outcome for the patients in localized prostate cancer, patients with the losses on 8p and 16q seemed to be still in curable state, whereas losses on 10p invariably indicated a poor outcome.

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SURGICAL INNOVATIONS IN UROLOGICAL CANCER

Frans M.J. Debruyne, University of Nijmegen, Department of Urology

Surgery remains a very important therapeutic modality in the management of malignant Urological diseases. Especially curation can be achieved by removing surgically the urological organ affected. In recent years surgery continued to improve and innovative surgical approaches have been developed.
In kidney cancer the role of nephron sparing surgery has been reemphasized. Indeed more and more small renal cell cancers are detected by the wide and liberal use of abdominal ultrasound. Therefore it is crucial to investigate whether in all these cases a radical nephrectomy, has to be performed or whether a partial resection, including the (small) tumor and a 1 cm margin of healthy kidney suffices, allowing to preserve the greatest part of the kidney tissue and its function.
More locally advanced renal cancers with massive caval involvement are now surgically curable. Even supradiaphragmatic and intra-atrial tumor thrombi are now treated surgically (with or without the use of extracorporeal circulation). The results obtained are more than acceptable with low surgical mortality.
In bladder cancer surgery, differentiated transurethal resection of (a) superficial tumor(s) has now become standard practice within the urological community. This is the only way to obtain optimal pathological classification of the tumor. For more invasive bladder cancer, in the absence of CIS in the prostatic urethra, bladder replacement surgery after radical cystectomy has now become more standard practice. With the use of segments of intestine (preferably ileum a low pressure reservoir can be constructed and anastomosed to the urethral stump, providing a functional bladder substitution with excellent voiding and continence. Moreover, the preservation of the neurovascular bundles to the penis will also maintain postoperative erection and potency. This is also the case when a nerve-sparing radical prostatectomy is performed for localised prostate cancer.
The most innovative approach in the treatment of urological tumors is the introduction of laparoscopic techniques. Laparoscopic pelvic lymphadenectomy is now advocated and performed in patients with localised prostate and bladder cancer with suspicion of micro-metastases in the regional lymph nodes. This minimal invasive approach has substantially lowered the morbidity of the intervention. Even laparoscopic retroperineal lymphadenectomy for low-stage non-seminomatous testis cancer has been successfully performed.
Other minimal invasive techniques such as laser, shock wave energy with high intensity ultrasound although perspectful, remain still largely experimental in the management of urological tumors.