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Urological Research

Report

1st Prostate Workshop Subject: Prostatic Hyperplasia on 28–29 January, 1983, in Frankfurt/Neu-Isenburg

The 1st workshop on the complex of subjects "prostatic diseases" took place under the chairmanship of *W. Vahlensieck* (Bonn), *Th. Senge* (Herne), and *B. Helpap* (Singen).

Twenty urologists, anatomists, pathologists, internists, and biochemists discussed basic research and clinical aspects of benign prostatic hyperplasia (BPH).

The term "benign prostatic hyperplasia" characterizes the clinical picture sufficiently so that any other nomenclature such as prostatic hypertrophy, adenoma of the vesical cervix, etc. should in future be given up.

Vahlensieck reported on the epidemiology.

The incidence increases continuously with age, and from the age of 70 BPH is nearly always found. There is little new information available, and figures vary greatly depending on the methods of examination and on the questions asked. Transabdominal and rectal sonography might contribute to a more accurate picture of the incidence. A classification in 4 stages is suggested, stage 1 being prostatic hyperplasia without micturition difficulties which does not require treatment and which may for instance be found in a preventive check-up, and stages 2–4 corresponding to the former stages 1–3.

The morphology of the normal prostate and experimental models of prostate research were explained by *Aumüller* (Marburg).

Amongst animals BPH appears mostly in the dog and the disease seems to be most common in domestic animals. The causal impact of endocrinological factors is uncontested. According to *Altenähr* the prostate is divided into a masculinely determined causal outer zone and a bisexually determined periurethral mantle zone and a cranial internal zone. *Aumüller* described the structural element, which consists of the glandular acinus and the periacinous tissue of mesenchymal origin and is similar in all parts, as the functional prostatic unit.

It could be demonstrated with immunohistochemical methods (acid phosphatase activity) that the prostatic epithelium does not reach complete functional maturity before the age of 19. A comparison with experimental results from the rat shows that the basal cells do not function as parent cells and that growth is caused by the glandular cells. The dependency of prostatic growth on hormones was tested on castrated male beagles which were given different combinations of androstandiol, oestradiol, cyproteronacetate, and tamoxifen, three characteristic structural reaction patterns were found: regression, atrophy, and metaplasia.

Immunohistologically, the individual cells of the prostatic epithelium react very differently to hormones and antihormones, a fact that might be attributed to the individual receptor pattern.

Aumüller set up the following hypothesis on the proliferation of the prostatic epithelium:

Prostatic proliferation is regulated by the quantity and the composition of the glandular secretion. A reduction of the secretion is the signal for the formation of daughter cells. This process is, however, dependent on a sufficient supply of testosterone. A disturbance of the transport chain of stroma/basal cell/glandular cell results in functional decompensation and the basal cells divide as a kind of functional substitution.

In his contribution on the morphology of prostatic hyperplasia *Helpap* proposed an exact classification of BPH similar to that of the carcinoma of the prostate. He commented on the various proposals made on the classification of BPH and suggested the following simple subdivision which takes into account urological as well as pathological and anatomical requirements:

1. Primary typical nodular hyperplasia, mature or immature, glandular or stromatic form

2. Primary atypical hyperplasia

3. Secondary hyperplasia

The author illustrated this classification with instructive typical histophotograms. Atypical hyperplasia was detected only in about 4% of the 6,000 tissue biopsies of the prostate, but in 55% of 660 manifest carcinomas. It occurs in all

parts of the prostate. As in almost every second case a carcinoma was found after resection a grading is suggested in which grade III is to be considered as precancerous and requires comprehensive after-care.

Morphologically, BPH is an androgen-oestrogen/induced epithelial and mesenchymal, ordered proliferation in connection with a hormonal imbalance.

Hormone metabolism and receptors were reviewed by *Senge*. The central role in the biology of the prostate is played by androgens. The organ is influenced by the peripheral hormone plasma pool as well as by the hormone utilisation or the endogenous hormonal metabolic processes in the prostatic cell. The author draws the following conclusions from comprehensive experimental data and tests on man:

1. The prostate is the target organ for metabolized androgens. The enzymes 5-α-reductase and 3-α-Beta-steroid-dehydrogenase are necessary catalysts for the androgen metabolism in the prostate.

2. In BPH 5-α-reductase activation leads to an excessive enrichment of dihydrotestosterone which has a high affinity for an androgen receptor within the prostate.

3. The normal prostate is protected against this dihydrotestosterone accumulation by a higher 3-α-(Beta) diol bond.

4. The enzyme acitivity for 5-α-reductase is higher in the stroma of BPH than in the epithelium.

5. The BPH stroma is responsible for increased production and concentration of dihydrotestosterone in BPH.

6. The preferred oestrogen bond and, possibly, activation of the fibromuscular stroma comes from the stroma.

Thus, the fibromuscular stroma is the dynamic tissue structure for the development of BPH.

Endocrinological aspects of the pathogenesis of prostatic hyperplasia was the subject dealt with the by *Thunn* (Herne).

Frick and *Bartsch* detected the age-related behaviour of the serum testosterone/17-β-oestradiol concentration. Both hormones increase until puberty. Whereas testosterone decreases in the course of life, the oestradiol concentration remains constant. What is decisive for the development of BPH are the changes of intraprostatic hormone concentration. Increased 5-α-reductase activity is largely tied to the stroma of BPH and has a pacemaker function. 60% of the prostate volume in BPH is stroma and only 18% is glandular cells. In the periurethral area the stroma proportion is as high as 75%. How far BPH is caused by intraprostatic hormone changes can up to now be studied only in animal experiments. The only suitable animal is the dog in which spontaneous hyperplasia occurs as a diffuse epithelial and not as a stromal proliferation. The classification can be made with the aid of a relative enzymatic index which is seen as the sum of the enzyme activities forming dihydrotestosterone minus those decomposing dihydrotestosterone.

The relative index is 1 for animals without BPH; with an index of over 3, 80 to 100% of the animals developed BPH.

Morphologically, stereologically, histochemically, and biochemically, three forms of steroid-induced prostatic hyperplasias can be distinguished in the castrated dog, which the author characterized in detail. The antiandrogen cyproteronacetate can be used to block effectively androgen effects in the reacting organ and to prevent experimental prostatic hyperplasia of types I and II.

In the discussion *Voigt* (Hamburg) added that oestrogens stimulate the 5-α-reductase. Oestrogen-effective androgens also occur in larger quantities in BPH. The biochemist, too, focuses his attention on the stroma of BPH.

In the clinical part, *Sommerkamp* (Freiburg) discussed diagnosis, *Bichler* (Tübingen) the conservative therapy, and *Potempa* (Mannheim) the operative therapy of BPH.

The interdisciplinary composition of the participants and the large proportion of discussion time contributed to the value of this workshop.

The papers and discussions will be published in a brochure.

The subject of the second workshop in 1984 will be "carcinoma of the prostate".

H.-J. Schneider, Giessen