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*Editorial*

# Marker Substances and Prostate Cancer

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Ten years ago when Cooper and Foti [1] published their very optimistic results on the clinical application of the immunological assay for prostatic acid phosphatase (PAP) the arrival of a new tumor marker was hailed. Early detection of tumor growth even within the prostate gland seemed at hand. Association of serum PAP concentration with the progress of tumor growth, analogous to the experiences with AFP and β-HCG in case of teratocarcinoma, was expected. Unfortunately the hope that the immunological PAP determination would serve as a screening test was not fulfilled as was soon recognised by numerous groups. True, the specificity of the immunological quantifikation of PAP was greatly enhanced and only very few cases were reported on other carcinomas secreting PAP-like substances into the circulation, giving rise to false positive results [2]. In addition, the detection limit of the test was lowered and healthy male populations exhibited only very low serum concentrations of PAP, well separated from those of the carcinoma patients.

A clinically different population, that of the adenoma patients, exhibits PAP serum concentrations slightly higher than normal. This decreases the value of PAP as a tumor marker since the discrimination limit has to be set at such high levels that prostate carcinomas with low concentrations of PAP could well go undetected by this test.

Other substances were simultaneously and subsequently brought forward in order to serve as prostate tumor markers. In this connection one very interesting protein with an as yet unknown function but which is physicochemically defined – Prostate specific Antigen (PSA) – has to be discussed [3]. It is distinct from PAP but shows the quality of being secreted into prostatic fluid and is reported to enter the circulation. This latter capacity is somewhat different from that of PAP or other tumor marker proteins in that normal males also show detectable levels of PSA in serum. However the analysis of PAP in combination with PSA in serum yielded surprisingly good results. Early stages of prostate tumors were detected as well [4]. On the other hand, following the same line of thinking, we were unable to increase the number of prostate carcinomas detected by biochemical means when we measured other tumor markers such as tissue polypeptide antigen (TPA) [5] or creatine kinase BB [6] in combination with PAP. However, we must await further results from other groups to duplicate these very promising results published by Wang and coworkers [4]. The other substances postulated as tumor markers have been widely reviewed by Pontes [7] and all have in common with the aforementioned, that unless the carcinoma breaks through the capsule of the prostate gland no enhanced concentrations of tumor marker can be found. The additional common feature of these substances is their suitability for monitoring therapy.

After intensive efforts over a number of years to find a substance characteristic for prostatic tumor growth, we have to admit that the substance which deserves the qualification of the "true prostatic tumor marker" has still to be found.

Thus the search has to go on, but meanwhile the clinician is well advised to use the immunological detection of PAP instead of the enzymatic activity measurement. The reason being the higher specificity of the test and the lower likelihood of a false-negative result from an ill-handled blood sample. Also most commercial companies take pains to keep the quality of their reagents high. It is important that within each laboratory large populations be tested to establish normal ranges so as to be quite certain of being able to distinguish elevated PAP concentrations caused by malignant growth from those caused by adenomas. We feel that in the field of prostate tumor markers a lot of basic research is still necessary. The study of tumor growth in cell culture might be fruitful, in that induced proteins which are shed in the culture medium might later serve as probes to monitor tumor growth. The research done in other areas such as in carcinoma of the breast should be closely followed to learn more about possible growth mechanisms. Another field of research is the chemical analysis of the prostatic fluid, which might bring insights to evolving malignant growth. Since it is so difficult to distinguish between carcinoma and adenoma it is imperative

to study the growth conditions of adenomas and to look for possible adenoma – "messengers" in prostatic fluid.

Increased levels of such "markers" as PAP, PSA, TPA or CKBB in serum of patients with metastatic growth might well help to direct the therapy given to the patient, even though these substances are present in low levels even when the tumor is in an advanced stage. We suggest two measures to assure the diagnosis of metastases. First, the radioimmunological detection of PAP in bone marrow serum [8] and second, the immunohistochemical detection of prostatic tumor cells in histological sections of the periopheral tissue.

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