testosterone, DHT, androstanediols, prolactin, LH and FSH.

The reported changes in plasma hormone levels before and after prostatectomy will be discussed.

3. Prostatic tissue measurements: The levels of testosterone and DHT in normal, benign and malignant tissue will be reviewed. The levels of zinc in prostatic diseases and the relationship of zinc to hormone uptake by the tissues is examined.

11. Plasma testosterone (T), dihydrotestosterone (DHT), androstenedione (A), free testosterone fraction (FTF) and sex hormone binding globulin capacity (SHBG) in prostatic adenocarcinoma, F. SCIARRA, C. PIRO, V. TOSCANO, E. PETRANGELI, S. CAIOLA, F. DI SILVERIO[1], U. BRACCI and C. CONTI, Istituto di Clinica Medica Generale V, Università di Roma, [1]Clinica Urologica, Università di Chieti, Italy

T, DHT, A, FTF and SHBG in patients with prostatic adenocarcinoma and aged 52 to 65 years were within the normal range for subjects of that age. After orchidectomy a dramatic fall in T (16 ng ± 1.6 SD/dl), DHT (5.4 ng ± 0.8/dl) and FTF (0.8 ± 0.1%) was observed, whilst SHBG increased ($8.8 \pm 1.4 \times 10^{-8}$ M) and A showed no significant modification (160 ng ± 80/dl). After 200 mg/day cyproterone acetate (CPA) without orchidectomy the decrease in plasma androgens was less significant (T = 148 ng ± 73/dl; DHT = 17 ng ± 6/dl; FTF = 1.54 ± 0.26%), whilst A was not modified (160 ± 70/dl) and SHBG showed a slight increase ($7.3 \pm 0.9 \times 10^{-8}$M). All these parameters were evaluated every day for 5-12 days immediately after orchidectomy or CPA treatment, and restudied after 2-3 months. The effect of orchidectomy in association with CPA was also studied. As CPA has an inhibitory action on target tissue, its administration in prostatic carcinoma may potentiate the effects of castration.

12. Hormone receptors in prostatic tissue, N. BRUCHOVSKY and P.S. RENNIE, Department of Cancer Endocrinology, Cancer Control Agency of British Columbia, Vancouver, Canada, V5Z 3J3

The success of the estrogen receptor test in predicting the hormonal status of breast cancer has fostered mounting interest in the potential use of androgen receptors in the medical and surgical management of prostatic cancer. In breast cancer, patient selection with the estrogen receptor test increases response rates from 15-35% to 60% or slightly higher. Since the response rate in unselected patients with prostatic cancer is already 60-80%, the impact of a receptor test on this predetermined high rate is unlikely to be very important. Nevertheless, it remains possible that the receptor test might be useful in identifying the small percentage of nonresponders in the group of patients with untreated metastatic disease, and, furthermore, it might be applied to the selection of the minority of patients who will benefit from endocrine therapy of reactivated disease.

Unfortunately, the measurement of the concentration of androgen receptor in the cytoplasm of the human prostate is hampered by several problems. From a conceptual standpoint, one of the more serious of these is the strong possibility that most of the receptor is localized in the nucleus owing to the elevated concentration of dihydrotestosterone, especially in hyperplastic and carcinomatous tissue. We were persuaded by this line of reasoning to measure the quantity of receptor in highly purified nuclei. The following results, expressed in terms of molecules per nucleus, were obtained; normal prostate 900 ± 180 (mean ± S.E.M., n = 7); hyperplastic prostate, 1600 ± 260 (17); well-differentiated carcinoma, 1800 ± 160 (7). The 2-fold increase in the amount of receptor in carcinomatous nuclei appeared to be explained by the chance finding that such nuclei contained twice as much DNA as nuclei from normal tissue. We infer, therefore, that the concentration of receptor in carcinomatous tissue is elevated in proportion to the DNA content of the nucleus.

In an extension of this work, the nuclear concentration of dihydrotestosterone was measured by radioimmunoassay and compared to the amount of receptor. The number of molecules per nucleus of dihydrotestosterone was 11,000 ± 3000 (mean ± S.E.M.), 50,000 ± 6000 and 36,000 ± 7000, respectively in normal, hyperplastic and carcinomatous prostates. Thus, irrespective of the normal or abnormal condition of the prostate, the nucleus of the prostatic cell is characterized by an apparent capacity to accumulate dihydrotestosterone in excess of the quantity of receptor. This feature is most pronounced in hyperplastic prostate.

In view of the direct relationship between the amounts of nuclear receptor and DNA, we investigated the binding reaction between the two molecules in more detail. Extracts of nuclei from rat ventral prostate were digested with micrococcal nuclease to yield receptor-chromatin complexes of varying sizes; the complexes were separated in linear 7.6-76% (v/v) glycerol density gradients. With extensive digestion of DNA, receptor labeled with radioactive dihydrotestosterone was released from the chromatin. After 5% digestion of DNA to acid soluble products only a trace amount of labeled receptor was detected in the unbound form. In the latter instance most of the receptor was recovered from the gradients in association with five A_{260} peaks representing oligomeric and monomeric nucleosomes with a repeat length of 182 ± 3 (mean ± S.E.M.) base pairs. The concentration of receptor was highest in the A_{260} peaks which contained large oligomers of nucleosomes and lowest in fractions containing monomers, Similar experiments were performed with chromatin from nuclei of normal and hyperplastic human prostates; free receptor was recovered only after the chromatin was digested with micrococcal nuclease. We conclude from these observations that the androgen receptor is bound to linker DNA in