Bilateral Orchiectomy with or without Flutamide for Metastatic Prostate Cancer

Reviewers: Kenneth Blank, MD

Background
The treatment of metastatic prostate cancer is controversial. Radiotherapy plays a critical role in palliating bone pain and preventing local symptoms; hormonal therapy palliates pain and can increase survival and chemotherapy remains investigational when hormonal therapy fails. Controversy exists over when to initiate these treatments and what type of hormonal therapy to use.

Prostate cancer is a hormone sensitive tumor in that prostate cancer cells need the hormone testosterone to grow and divide. When testosterone is removed the majority of cells die. However, a few prostate cancer cells remain and these can grow without the stimulation provided by testosterone (these are termed hormone insensitive). With time these few cells grow into a large tumor and eventually metastasize (spread to other places in the body) leading to the patients decline.

The testis produces ninety percent of the body's testosterone and the other 10% is secreted by the adrenal glands. Several strategies have been devised to rid the body of testosterone and therefore slow down the growth of prostate cancer. These include surgical removal of the testes (orchiectomy) and prescribing oral medications called leutenizing hormone releasing hormone (LHRH) agonists. One potential problem with these therapies is that they only effect testosterone made by the testis not the adrenal gland. Another class of medications called anti-androgens function to block uptake of testosterone into the cell. The use of LHRH agonists or orchiectomy in combination with an anti-estrogen is called combined androgen (androgen is the generic term for testosterone) blockage as both adrenal and testicular testosterone are removed from the cancer cell.

Materials and Methods
One controversy in the treatment of metastatic prostate cancer is whether or not the addition of an anti-androgen provides additional benefit to just orchiectomy or just LHRH therapy. Theoretically, combined androgen blockage makes good sense but clinical testing is always warranted to determine the efficacy of a treatment.

The October 8, 1998 issue of the New England Journal of Medicine reports on a trial examining this issue. 1387 men underwent surgical removal of their testes and were then randomly assigned to either receive a placebo or an anti-androgen (flutamide).

Results
There were no differences in major toxicities in either arm but there was more anemia and diarrhea with the flutamide. Unfortunately, the addition of flutamide had no effect on survival or progression free survival. This finding was surprising in light of a prior study by the same group of physicians demonstrating a significant survival advantage to flutamide when dosed with LHRH agonist versus LHRH agonist alone. The authors provide an explanation for the discrepancy in that it is possible that patients were not compliant with the LHRH agonist.

Conclusion
The controversy remains as to what constitutes the best therapy for patients with metastatic prostate cancer. The results of this study suggest that the use of combined androgen blockade provides no benefit over orchiectomy alone.