

All 844 patients diagnosed with localized prostate cancer between 1 January 1989 and 31 December 1998 in Geneva, Switzerland, were enrolled in this study; 47 patients were later lost to follow-up. In total, 158 patients underwent prostatectomy, 205 underwent radiotherapy, 378 were managed using a strategy of watchful waiting, 72 received hormone therapy, and 31 were managed using other treatment regimens. The mean duration of follow-up was 6.7 years. Cox proportional hazards analysis, adjusted for age, sector of care, period of diagnosis, method of detection, lymph-node status, clinical tumor stage, tumor differentiation, and PSA value, revealed that management strategy influenced 5-year prostate-cancer-specific mortality only slightly. By contrast, long-term prostate-cancer-specific mortality was strongly influenced by treatment option. In comparison with patients who underwent prostatectomy, significantly increased risks of death from prostate cancer at 10 years were seen in patients who underwent radiotherapy (hazard ratio [HR] 2.3, 95% CI 1.2–4.3; $P < 0.05$), hormone therapy (HR 4.4, 95% CI 2.2–8.8; $P < 0.001$) or watchful waiting (HR 2.0, 95% CI 1.1–3.8; $P < 0.05$). The long-term cancer-specific survival benefit associated with surgery was even more apparent in those patients younger than 70 years old and in those with poorly differentiated tumors.

Original article Merglen A *et al.* (2007) Short- and long-term mortality with localized prostate cancer. *Arch Intern Med* 167: 1944–1950

The histone demethylase JHDM2A is essential for spermatogenesis in mice

A research group at the Howard Hughes Medical Institute has described a critical role for JHDM2A (JmJC-domain-containing histone demethylase 2A) in spermatogenesis. Okada and colleagues used a loss-of-function mouse model to characterize the expression patterns and protein interactions of JHDM2A.

The group found that mice lacking the functional *Jhdm2a* gene were infertile and had smaller testes and lower sperm counts than normal mice. The sperm found in the epididymis of mutant mice all had abnormal head shape and nuclear structure, and 98.5%

of sperm were immotile. Mice possessing the mutant *Jhdm2a* gene were also found to show deficient chromatin condensation, an essential stage of sperm maturation; the expression of TNP1 (transition nuclear protein 1) and PRM1 (protamine 1), which have been shown to be required for chromatin condensation, was decreased in *Jhdm2a*-mutant mice. Chromatin immunoprecipitation analysis showed that JHDM2A was specifically recruited to the *Tnp1* and *Prm1* gene regions, suggesting a vital role for JHDM2A in the transcription of these two post-meiotic proteins.

The authors conclude that JHDM2A is essential for viable spermatogenesis in mice, and suggest that the *Jhdm2a* gene might be important with respect to human infertility syndromes such as azoospermia and globozoospermia.

Original article Okada Y *et al.* (2007) Histone demethylase JHDM2A is critical for *Tnp1* and *Prm1* transcription and spermatogenesis. *Nature* 450: 119–123

Hemastix[®] is a useful diagnostic tool for urinary schistosomiasis control programs

Urinary schistosomiasis is particularly prevalent among schoolchildren in sub-Saharan Africa. The infection is a common cause of hematuria, and disease sequelae include bladder damage and kidney dysfunction. Rapid and accurate diagnoses are crucial to measure the effectiveness of control programs for this infection. French *et al.*, therefore, evaluated Hemastix[®] (Bayer, Elkart, IN)—diagnostic reagent strips that detect microhematuria—during a 3-year period of a control program aimed at schoolchildren on Zanzibar, Tanzania.

A subset of schoolchildren among the 135,000 who were administered praziquantel for schistosomiasis and albendazole for soil-transmitted helminthiasis were surveyed at treatment baseline in 2004 ($n = 2,002$), and at annual follow-up with re-treatment in 2005 ($n = 3,278$) and in 2006 ($n = 3,993$). The urine samples of the children surveyed were graded for microhematuria by use of Hemastix[®], and parasite burden was assessed microscopically by the egg-count method.

Hemastix[®] scored highly for sensitivity, specificity, positive predictive value and negative predictive value for the whole 3-year

period, even as prevalence and parasitic burden decreased as a result of chemotherapy; the scores for girls, however, were not quite as good as those for boys, probably because menstrual blood was a confounder. The method was diagnostically superior to patient-reported blood in the urine and pain upon urination.

The authors recommend Hemastix® for use in future control programs because it is rapid, cost-effective, and its ease of use could increase screening coverage.

Original article French MD (2007) School-based control of urinary schistosomiasis on Zanzibar, Tanzania: monitoring micro-haematuria with reagent strips as a rapid urological assessment. *J Pediatr Urol* 3: 364–368

COX-2 overexpression might predict treatment failure in patients with prostate cancer

Cyclo-oxygenase-2 (COX-2) is overexpressed in some types of human cancer, including prostate cancer, and the overexpression of COX-2 might also be involved in tumor resistance to chemotherapy and radiation therapy. Khor and colleagues analyzed data from the Radiation Therapy Oncology Group (RTOG) 92-02 trial to identify the association between COX-2 and prostate cancer outcomes.

The study population included 586 patients (median age 70 years, range 43–88 years) with locally advanced (T2c–T4) prostate cancer who were randomly assigned to receive either long-term (28 months; $n=316$) or short-term (4 months; $n=270$) neoadjuvant, concurrent and adjuvant androgen deprivation therapy (ADT) plus external-beam radiation therapy. Tissue samples, obtained from either transurethral resection or needle-core biopsy, were analyzed for COX-2 staining intensity.

On univariate analysis, increased COX-2 staining intensity independently predicted distant metastasis (hazard ratio [HR] 1.181, $P=0.0004$), biochemical failure (for both the ASTRO definition [HR 1.073, $P=0.008$] and Phoenix definition [HR 1.073, $P=0.014$]), and any failure (defined as “a first event from ASTRO biochemical failure, local failure, distant metastasis, or cause-specific mortality”; HR 1.068, $P=0.011$). COX-2 overexpression seemed to be most predictive of outcomes in patients who underwent short-term ADT.

The authors conclude that COX-2 staining intensity could be used to select patients who might benefit from long-term ADT rather than short-term ADT. Furthermore, the authors suggest that COX-2 inhibitors might improve patient response to radiation therapy, with or without ADT.

Original article Khor LY *et al.* (2007) COX-2 expression predicts prostate-cancer outcome: analysis of data from the RTOG 92-02 trial. *Lancet Oncol* 8: 912–920

Cystectomy or conservative therapy for patients with high-risk, T1G3 bladder cancer?

The optimum treatment for high-risk T1G3 bladder cancer is controversial. Cystectomy might offer a better probability of cure than conservative therapy, but could also be associated with worse post-treatment quality-of-life (e.g. poor sexual function). Kulkarni *et al.* performed a validated decision analysis that compared the outcomes of both treatment approaches.

Published outcome probability data were used to estimate the life expectancy and quality-adjusted life expectancy (QALE; i.e. the number of years with good quality-of-life) of patients who undergo either immediate nerve-sparing cystectomy with orthotopic neobladder creation or initial conservative therapy with intravesical bacillus Calmette–Guérin. The base case was defined as a 60-year-old male with no comorbidity, good potency and newly diagnosed high-risk T1G3 transitional cell carcinoma of the bladder.

Compared with conservative management, immediate cystectomy yielded a higher mean life expectancy (14.3 years versus 13.6 years) and QALE (12.32 years versus 11.97 years) when the model was applied to the base case. Additional comorbidities and increased age reduced the benefit of immediate cystectomy: in terms of life-expectancy, conservative treatment was the preferred option above the age of 70 years; in terms of QALE, conservative treatment was preferred above the age of 65 years. In patients with significant concerns about post-cystectomy adverse effects (i.e. sexual and/or gastrointestinal dysfunction), conservative treatment yielded the best QALE.

The authors conclude that immediate cystectomy seems to result in a longer life expectancy and QALE than conservative management;