GLOSSARY

ERYTHROCYTE SEDIMENTATION RATE

The rate at which red blood cells settle in anticoagulant-treated blood

HYPOSPADIAS

Congenital defect in males where the urethral opening is on the underside of the penis or the perineum, rather than on the glans

ANTIANDROGENS

Drugs that interfere with the function of androgens by binding to the androgen receptor

Interstitial cystitis therapy improved by adding galactose

The cause of interstitial cystitis is unknown, but one hypothesis is that it results from a defective bladder mucosa, which enables urine to penetrate the epithelium, resulting in irritation and bladder pain. The anionic polysaccharides pentosan polysulfate and heparin, used as therapy for interstitial cystitis, are thought to act by sealing the bladder mucosa, but have been found to have weak binding affinity for bladder epithelium. Galactose-containing mucin glycoproteins have been shown to bind strongly to bladder epithelium, which contains proteins called galectins that bind to lactose and galactose residues. Researchers in the US have assessed the feasibility of improving the binding affinity of pentosan polysulfate and heparin for bladder epithelium by attaching lactose to the drugs.

As measured by histochemical staining, the lactose-carrying pentosan polysulfate and heparin bound strongly to human and rabbit bladders, while the unmodified compounds bound weakly, or not at all. The authors suggest that the moderate effectiveness of pentosan polysulfate observed in clinical trials for interstitial cystitis might be caused by its weak affinity for bladder mucosa, which could be influenced by fluctuating ion concentrations in urine. They believe that the enhanced epithelial binding achieved by modification with lactose might improve the effectiveness of the drugs in a way that is not affected by ion concentrations in urine. They also suggest that the technique could potentially be extended to improve the efficacy of other intravesical agents for urinary tract infections or bladder cancer.

Jim Casey

Original article Muthusamy A *et al.* (2006) Enhanced binding of modified pentosan polysulfate and heparin to bladder—a strategy for improved treatment of interstitial cystitis. *Urology* 67: 209–213

Prognostic variable for renal cell carcinoma

The preoperative ERYTHROCYTE SEDIMENTATION RATE (ESR) has been suggested as a prognostic factor for renal cell carcinoma (RCC). Previous studies, however, have been limited by small sample sizes and a lack of histologic stratification.

A team from the Mayo Clinic retrospectively identified 1,075 patients with a recorded preoperative ESR who had undergone surgery for RCC between 1970 and 2002. Analysis showed that an elevated ESR (i.e. >22 mm/h in males and >29 mm/h in females) was common in the three main subtypes of RCC—clear-cell, papillary and chromophobe RCC. Patients with clear-cell ($n=889$) and papillary ($n=134$) RCC were almost four times more likely to die from their disease if they had an elevated ESR (relative risk 3.60 and 3.84, respectively). Although the death rate was statistically significantly higher for chromophobe RCC patients with an elevated ESR, the small number of patients ($n=48$) meant that the confidence interval was extremely wide (relative risk 10.33, 95% CI 1.19–89.53). The authors found that elevated ESR particularly influenced the risk of death for patients with low-risk or intermediate-risk pathology.

Elevated ESR was associated with almost every adverse clinical symptom and pathologic feature of RCC; moreover, in clear-cell RCC, elevated ESR was an independent predictor of death even after adjustment for such confounding variables.

The Mayo Clinic now routinely records preoperative ESR and uses it to help counsel patients before surgery. Studies are currently underway to identify the mechanism of ESR elevation, especially in localized RCC.

Katherine Sole

Original article Sengupta S *et al.* (2006) The preoperative erythrocyte sedimentation rate is an independent prognostic factor in renal cell carcinoma. *Cancer* 106: 304–312

Loratadine disrupts penile development in mice

Investigators at the University of California have shown that *in utero* exposure to loratadine, a common antihistamine, can lead to HYPOSPADIAS in mice. Hypospadias results from the disruption of normal penile development and can be elicited by exposure to ANTIANDROGENS or estrogens. Previous studies investigating the link between loratadine and hypospadias have yielded mixed results.

The team developed a mouse model to investigate the effect of loratadine on urethral development at the morphologic and molecular levels. Pregnant mice were fed a typical daily