

### **Mast cell proteases as novel markers for the diagnosis of drug-induced allergic reactions and for predicting susceptibility to severe reactions**

Drug-induced anaphylaxis is being encountered with increasing frequency, but there are few reliable laboratory aids for confirming the allergic nature of such reactions, or for evaluating which patients who are allergic may be susceptible to a serious reaction. Patients may thus be put at risk by those treating them, or the drug of choice may needlessly be withheld. As the activation of mast cells and the explosive release of a range of inflammatory mediators is a pivotal process, we have investigated unique markers of mast cell activation in the circulation and in saliva following provocation of drug-induced reactions.

Sensitive enzyme-linked immunosorbent assays (ELISA) were developed using new specific monoclonal antibodies for the mast cell proteases tryptase, chymase, carboxypeptidase A3 (CPA3) and dipeptidyl peptidase I (DPPI). Blood and saliva samples were collected from patients attending the allergy clinic for diagnostic drug allergy testing before and following skin prick testing and/or intradermal injection of the drug implicated (including antibiotics, non-opioid analgesics and opioids). Demographic and clinical information were noted, and the nature and severity of the reactions provoked recorded. Serum and salivary concentrations of tryptase, chymase, CPA3, and DPPI were determined.

Levels of CPA3 and DPPI were increased in saliva following a reaction on drug challenge ( $p=0.025$ ), and in serum an increase in chymase ( $p=0.025$ ). There was little association between concentrations of mast cell products suggesting differences in rates of migration into these fluids and clearance. High baseline levels of CPA3 in both serum and saliva (ie before injection of drug) were observed in the drug allergic patients who experienced symptoms on drug challenge. Baseline CPA3 concentrations in serum were also higher in patients who historically had suffered severe reactions (involving cardiovascular or respiratory compromise) than in those with mild ( $p=0.0012$ ) or moderate reactions ( $p=0.004$ ).

Raised serum or salivary levels of mast cell proteases may be helpful in confirming that an allergic reaction to drugs has occurred, and baseline levels may be predictive of the potential for a severe allergic reaction in the future.