accumulation of focal pseudoexfoliation material in the adventitial and subendothelial connective tissue, pronounced fibrosis, and elastosis of the tunica intima (figure). These alterations were not seen in normal age-matched control samples obtained at necropsy.

These findings suggest an association between aneurysms of the abdominal aorta and pseudoexfoliation syndrome, which is also associated with a history of cardiovascular events.[5] Histopathological alterations of the abdominal-aorta wall in pseudoexfoliation syndrome might predispose patients to the development of aortic aneuryms. Pseudoexfoliation syndrome might, therefore, be an important marker for the risk of systemic vascular disease.


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# Genetic resistance factor for HIV-1 and immune response to varicella zoster virus


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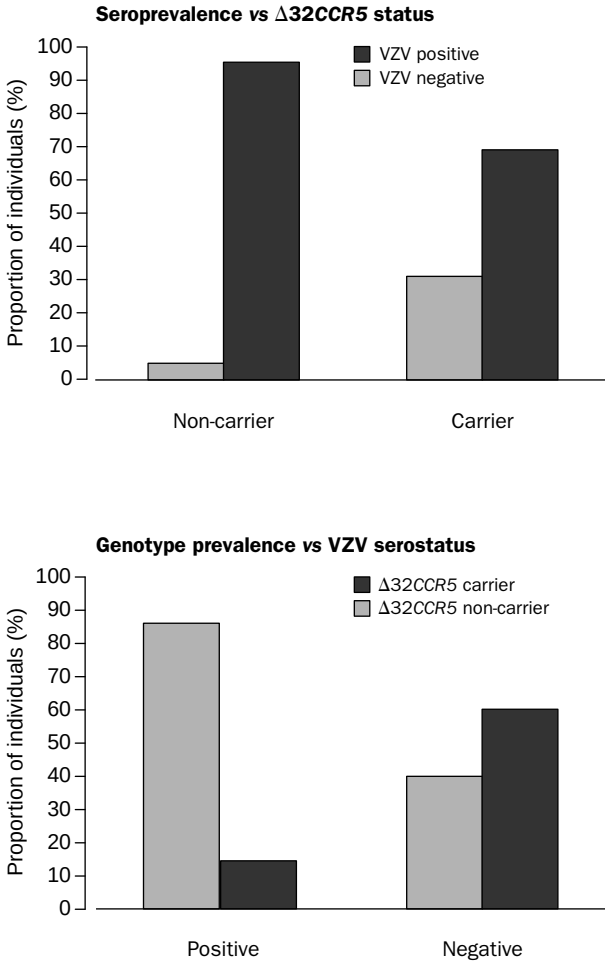
**A 32 bp deletion in the chemokine receptor *CCR5* gene modulates HIV-1 infection. However, whether this *CCR5* gene variation modifies immunity to common herpesvirus infections is unknown. We investigated whole blood IgG concentrations of 157 normal adult blood donors. Also we assessed whether the 32 bp deletion of *CCR5* (Δ32*CCR5*) was associated with circulating IgG to four herpesviruses: varicella zoster virus, Epstein-Barr virus, cytomegalovirus, and herpes simplex virus type 1 and type 2. Individuals who carried Δ32*CCR5* were 9·2 times more likely to be seronegative for varicella zoster virus than non-carriers (95% CI 2·9–29·1), but no differences were seen for the other herpesviruses studied. Variation in *CCR5* may modulate humoral immunity to varicella zoster virus.**


Varicella zoster virus, which causes chickenpox (varicella) and shingles (herpes zoster), initially infects T cells and subsequently establishes a life-long latency in sensory ganglia of the host. Some naturally exposed and vaccinated individuals are seronegative to varicella zoster virus despite having cell-mediated immunity to the virus.[1,2] Chemotactic peptides and their receptors are expressed in the central nervous system and have been implicated in various antiviral and neuropathogenic processes.[3] We did a study to assess the potential role of a genetic variant in the CCR5 chemokine receptor with humoral immunity to varicella zoster virus in healthy adults.[4]

The *CCR5* gene encodes a cell-surface chemokine receptor that serves as a co-receptor for HIV-1. A common polymorphism involving a 32 bp deletion in the *CCR5* gene (Δ32*CCR5*) modifies HIV-1 infection and progression.[3] We investigated whole blood IgG concentrations in 157 normal adult blood donors and assessed the potential relation between Δ32*CCR5* and the presence of IgG in heparinised whole blood to varicella zoster virus, Epstein-Barr virus, cytomegalovirus, and herpes simplex virus type 1 and type 2. Varicella zoster virus IgG was measured by ELISA (BioWhittaker, Walkersville, MD).

Of the 157 individuals studied, 96% were non-Hispanic whites, 53% were male, and mean age was 53 years (SD 15). 15 (10%) were seronegative for varicella zoster virus and 29 (18%) were Δ32*CCR5* carriers (allele frequency 31 [10%] of 314). Of the carriers, two were homozygous and




**Relation between Δ32*CCR5* and varicella zoster virus serological status in healthy adults**
VZV=varicella zoster virus.

27 heterozygous for Δ32*CCR5*. Only six individuals were non-white, all of whom were seropositive for varicella zoster virus. Among those seronegative for varicella zoster virus, nine (60%) of 15 were Δ32*CCR5* carriers, whereas among seropositive individuals, 20 (14%) of 142 were Δ32*CCR5* carriers (figure). 31% of Δ32*CCR5* carriers were seronegative compared with only 4·7% of Δ32*CCR5* non-carriers.

The Δ32*CCR5* carriers were more likely to be seronegative for varicella zoster virus than those who did not have the variation (odds ratio adjusted for age and sex 9·1 [95% CI 2·9–28·8], p=0·0002). If the analysis was restricted to white individuals, the result was nearly identical (9·2 [2·9–29·1], p=0·0002). *CCR5* genotype was not associated with IgG to Epstein-Barr virus, cytomegalovirus, or herpes simplex virus type 1 and type 2.

Although most research on Δ32*CCR5* in viral immunity has focused on the HIV-1 co-receptor, some researchers have speculated that the increasing frequency of Δ32*CCR5* in humans beings might be traced to its ability to confer higher resistance to variola virus (smallpox).[5] Moreover, investigators have indicated a broad role for chemokines in antiviral responses. The higher number of varicella zoster virus seronegative individuals among Δ32*CCR5* carriers than non-carriers could be associated with a low exposure to varicella zoster virus. However, low virus exposure is unlikely because there is near ubiquitous exposure of individuals in the USA: 90% of adults and 98% of health-care workers have circulating IgG to varicella zoster virus. Our investigations suggest that Δ32*CCR5* might modulate the immune response to varicella zoster virus and might help explain varicella zoster virus seronegativity in individuals immune to this virus. Because serology remains the most important method for identifying health-care workers and other individuals at risk of varicella zoster virus infection who might require vaccination, further research is warranted into the role of common cytokine gene polymorphisms and the immune response to viruses.

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# Constitutively raised serum concentrations of mast-cell tryptase and severe anaphylactic reactions to *Hymenoptera* stings

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**Anaphylactic IgE-mediated reactions to *Hymenoptera* stings vary in their severity for reasons that are not clear. We investigated patients with a history of systemic anaphylatic reactions to honeybee or wasp stings. Nine (75%) of 12 patients with raised tryptase concentrations but only 28 (28%) of 102 patients with lower tryptase concentrations, had a history of severe sting reactions (p=0·004). Raised baseline serum concentrations of mast-cell tryptase and mastocytosis are potential risk factors for severe allergic reactions to *Hymenoptera* venom.**

Anaphylactic reactions to honeybee or wasp stings are seen in up to 5% of the adult population in Europe and the USA.[1] For reasons that are not clear these reactions vary greatly in severity, with manifestations ranging from skin involvement (flushing, urticaria) to cardiovascular, respiratory, or gastrointestinal symptoms, to full shock. In a few patients, especially those with severe or fatal systemic anaphylactic reactions, an association with mastocytosis has been reported.[2]

The protease, tryptase, is expressed almost exclusively in mast cells. The baseline concentration of tryptase in the circulation is thought to reflect total mast-cell numbers, and is permanently raised in many patients with mastocytosis; systemic anaphylactic reactions are frequently accompanied by a temporary rise in tryptase concentrations for several hours.[3] We investigated the relation between the severity of systemic anaphylactic reactions to *Hymenoptera* stings and baseline serum tryptase concentrations.

Patients with a history of systemic anaphylactic reactions to honeybee or wasp stings were allocated to three groups, according to the severity of their reactions. We excluded several patients from the study because of incomplete data. 38 patients had only generalised skin reactions (group A), 39 had intermediate symptoms exceeding skin reactions, but no loss of consciousness (group B), and 37 had life-threatening symptoms, including loss of consciousness (group C). We confirmed honeybee or wasp venom allergy in all patients by immediate-type skin-test reactions, the presence of specific serum IgE antibodies to venom, or both. Tryptase was measured by a fluoroenzyme immunoassay (Unicap Tryptase, Pharmacia and Upjohn) in blood samples taken at least 2 weeks after the last honeybee or wasp sting.

Serum tryptase concentrations higher than 13·5 μg/L (95th percentile of normal) were considered to be raised. All patients had undergone at least one dermatological examination; those with raised tryptase concentrations were re-examined. Cutaneous mastocytosis was diagnosed if characteristic lesions were present; if possible, the diagnosis was corroborated by histological assessment of a skin biopsy sample.

The three groups did not differ significantly for age, sex, diagnosis of honeybee or wasp venom allergy, and skin test reactivity or concentrations of specific serum IgE antibodies to the venom. Serum tryptase concentrations were 1·3–22·6 μg/L in group A, 1·6–22·0