tor and infused 4 days later. Patients received nonmyeloablative treatment with busulfan.

Results. Both patients experienced immune reconstitution (although the infant showed a swifter and more complete response). Genetically corrected granulocytes, monocytes, megakaryocytes, and erythroid cells were detected, T cell responses normalized, antibody production was corrected, and specific responses to vaccination were documented. Infections also abated. Red blood cell toxic metabolites declined and liver enzyme abnormalities resolved. The less complete response of the older patient was attributed to a lower dose of transfected cells, less myeloablation, and possibly an effect of his older age.

Conclusions. A combined approach of using autologous genetically corrected stem cells and nonmyeloablative conditioning allowed more complete restoration of immune and metabolic functioning in ADA-SCID patients than has been previously achieved.

Reviewer's Comments. ADA leads to the accumulation of toxic metabolites that cause immune cell death and results in SCID. Previous studies of therapy using genetically corrected peripheral blood lymphocytes (PBLs) and exogenous ADA in the form of PEG-ADA to support immune function lead to poor engraftment of the corrected cells possibly because there was not a sufficient survival advantage for these cells in the presence of exogenous ADA. When PEG-ADA was not given, full correction was still not achieved, indicating that such correction may require a more global therapy, not just infusion of genetically corrected PBLs. This study shows that rather amazing immune reconstitution was possible with the successful engraftment of multipotent, genetically corrected stem cells, and provides hope for more definitive therapy for this and other disorders.

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PREVALENCE OF MONOCLONAL GAMMOPATHY IN PATIENTS PRESENTING WITH ACQUIRED ANGIOEDEMA TYPE 2

Fremeaux-Bacchi V, Guinnepain MT, Cacoub P, et al. *Am J Med.* 2002;113:194–199

Purpose of the Study. Acquired angioedema type 1 is characterized by a C1 inhibitor deficiency in patients with lymphoproliferative disorders, whereas acquired angioedema type 2 is characterized by anti-C1 inhibitor antibodies, and has not been thought to be associated with lymphoproliferative disease. We studied the clinical features, complement profiles, and associated diseases in 19 new patients with diagnosed acquired angioedema type 2.

Study Population and Methods. Plasma concentrations and functional activity of complement components were measured by conventional techniques. Functional C1 inhibitor activity was assessed by a chromogenic assay. Autoantibodies to C1 inhibitor were detected using an enzyme-linked immunosorbent assay.

Results. The 11 men and 8 women (median age: 60 years) presented with recurrent attacks of angioedema. All patients had detectable anti-C1 inhibitor antibodies in serum. A monoclonal gammopathy was detected in 12 patients (63%) at the time of diagnosis, 11 of whom had an immunoglobulin peak of the same heavy- and light-chain isotypes as the acquired anti-C1 inhibitor antibody. Three of these 12 patients developed a malignant lymphoproliferative disease.

Conclusions. As with type 1 disease, a large proportion of patients with acquired angioedema type 2 have a lymphoproliferative disorder.

Reviewer's Comments. These disorders present only rarely, so I'm always having to go back and refresh my memory. However, unlike the acquired chronic urticarias, the acquired C1 inhibitor deficiency syndromes are commonly associated with lymphoproliferative disorders, so we need to pursue things pretty aggressively. Don't be afraid to consult your friendly oncologist.

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HUMAN IMMUNODEFICIENCY VIRUS

CONTRIBUTION OF HUMAN α–DEFENSIN 1, 2, AND 3 TO THE ANTI-HIV-1 ACTIVITY OF CD8 ANTIVIRAL FACTOR

Zhang L, Yu W, He T, et al. *Science.* 2002;298:995–1000

Purpose of the Study. Since 1986, it has been known that CD8+ T-cells from human immunodeficiency virus (HIV)-infected, immunologic stable long-term survivors secrete a soluble factor that has been termed CD8 antiviral factor (CAF). The molecular identity of CAF has remained elusive. Some of the antiviral activity in CAF appears to be mediated by β−chemokines, MIP-1α, MIP-1 β and RANTES; however, these factors do not account for all of the anti-HIV activity in CAF. The purpose of this study was to describe the anti-HIV activity of human α-defensins.

Methods. Protein chip technology was used to identify a cluster of proteins that were secreted when CD8+ T-cells from long-term nonprogressors were stimulated in vitro. After identification of these proteins, HIV suppressive activity was measured and the source of these molecules was identified.

Results. The proteins were identified as α-defensins 1, 2, and 3 on the basis of specific antibody recognition and amino acid sequencing. A significant proportion of CAF activity was eliminated or neutralized by antibody specific for human α-defensins. Synthetic and purified preparation of α-defensins inhibited the replication of HIV isolates in vitro. Finally, a subset of CD8+ T-cells express and secrete α-defensins.

Conclusions. These results indicate that α-defensins 1, 2, and 3 collectively account for much of the anti HIV activity in CAF that is not attributable to β-chemokines. The potential usefulness of α-defensins as therapeutic agents in patients with HIV remains to be demonstrated.

Reviewer's Comments. Defensins are members of a family of antimicrobial peptides that are particularly abundant in neutrophils. The demonstration that defensins constitute a component of CAF has important implications. Perhaps these defensins are causally involved in the reduction of HIV progression. If so, the administration of extrinsic defensins or the stimulation of in vivo production of defensins would be appropriate therapeutic goals. Alternatively, the presence of a subset of T cells capable of generating α-defensins may simply reflect the preservation of selected immune functions in individuals in which other mechanisms are responsible for this preservation. Importantly the amount of α-defensins produced by CD8+ T cells is tiny relative to the amount routinely expressed in neutrophils, including those of progressing HIV-infected patients.

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PREVALENCE OF MONOCLONAL GAMMOPATHY IN PATIENTS PRESENTING WITH ACQUIRED ANGIOEDEMA TYPE 2

Allen Adinoff

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PREVALENCE OF MONOCLONAL GAMMOPATHY IN PATIENTS PRESENTING WITH ACQUIRED ANGIOEDEMA TYPE 2

Allen Adinoff

Pediatrics 2003;112;490