myocardial infarction or coronary death, a 24% decrease in the need for coronary bypass surgery, and a 17% decrease in the rate of fatal or nonfatal stroke. The recently reported results of the Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) trial of rosuvastatin (20 mg per day) show that even patients with moderate risk can benefit very substantially from statin treatment. The study included only patients with initial LDL levels below 130 mg per deciliter (median, 108 mg per deciliter) and achieved on-treatment levels averaging 55 mg per deciliter. Statin treatment decreased all-cause mortality by 20%, the primary end point of combined cardiovascular events by 44%, myocardial infarction by 54%, and stroke by 48%. What do we have in our medical bag that can match that? Moreover, the statins are probably safer than aspirin, and they are cost effective. Finally, there is good reason to believe that even more striking results may be seen when we start treating hypercholesterolemia in patients at an earlier age.

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Eculizumab for Atypical Hemolytic–Uremic Syndrome

TO THE EDITOR: Atypical hemolytic–uremic syndrome is a disease of uncontrolled complement activation associated with a high mortality rate, and most cases progress to end-stage renal disease. About 50% of patients with this syndrome carry mutations in genes encoding complement proteins. Complement inhibition has been suggested for the treatment of atypical hemolytic–uremic syndrome, but currently no data on this treatment option are available. We report on a case of atypical hemolytic–uremic syndrome that was successfully treated with eculizumab, a humanized monoclonal antibody that blocks complement activity by cleavage of the complement protein C5, thereby preventing the generation of the inflammatory peptide C5a and the cytotoxic membrane-attack complex, C5b-9. Eculizumab has been approved for the treatment of paroxysmal nocturnal hemoglobinuria.

End-stage renal disease due to atypical hemolytic–uremic syndrome developed in a woman at 25 years of age. At 30 years of age, after 5 years of undergoing dialysis, she received a cadaveric renal transplant. Five weeks after transplantation, atypical hemolytic–uremic syndrome recurred and led to the loss of transplant function despite 18 plasma exchanges. The patient underwent dialysis for another 7 years until she received a second...
cadaveric transplant at 37 years of age. Six weeks after the second transplantation, atypical hemolytic–uremic syndrome again recurred. The onset of atypical hemolytic–uremic syndrome may have been associated with the additional use of tacrolimus, which the patient received after three episodes of cellular rejection developed.

Genetic analysis revealed a novel heterozygous missense mutation in exon 10, codon 475 (Y475S), of the gene encoding complement factor H. This missense mutation leads to a substitution of a serine by a tyrosine that belongs to the highly conserved residues of the factor H protein sequence; this sequence may be responsible for the
observed reduction in the plasma level of factor H to 180 μg per milliliter (normal range, 284 to 528). Furthermore, we detected a homozygous deletion comprising at least exon 2 within the CFHR1 gene. No mutation was found in the MCP or CFI genes. Transplant biopsy specimens showed thrombotic microangiopathy (Fig. 1A through 1C).

Since recurrent atypical hemolytic–uremic syndrome leads to graft loss in more than 90% of patients, we decided to administer a single dose of 600 mg of eculizumab after renal function worsened in this patient despite four plasma exchanges. After the administration of eculizumab, the total complement activity was completely blocked, the hemolysis resolved, and the transplant function recovered (Fig. 1D). The patient’s renal graft function has been stable for 8 months.

These findings show the positive effect of complement inhibition on the course of atypical hemolytic–uremic syndrome in our patient and, in our view, the use of eculizumab in atypical hemolytic–uremic syndrome warrants further investigation.

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Eculizumab for Atypical Hemolytic–Uremic Syndrome

Eculizumab for Atypical Hemolytic–Uremic Syndrome. Thomas Philipp, M.D., should be added as the second author of the letter. We regret the omission. The article has been corrected at NEJM.org.