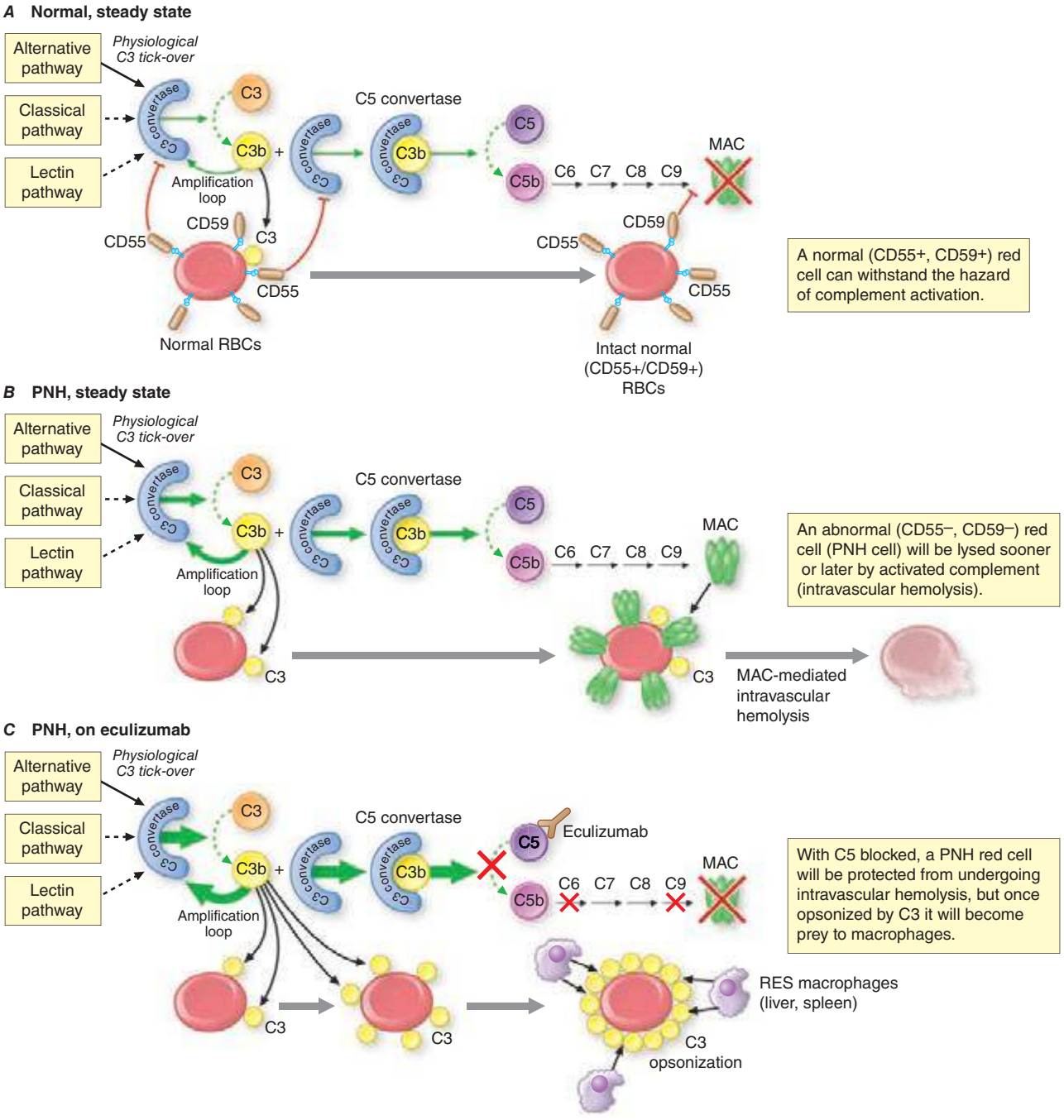

FIGURE 129-10 **The complement cascade and the fate of red cells.** ***A.*** Normal red cells are protected from complement activation and subsequent hemolysis by CD55 and CD59. These two proteins, being GPI-linked, are missing from the surface of PNH red cells as a result of a somatic mutation of the X-linked *PIG-A* gene that encodes a protein required for an early step of the GPI molecule biosynthesis. ***B.*** In the steady state, PNH erythrocytes suffer from spontaneous (tick-over) complement activation, with consequent intravascular hemolysis through formation of the membrane attack complex (MAC); when extra complement is activated through the classical pathway, an exacerbation of hemolysis will result. ***C.*** On eculizumab, PNH erythrocytes are protected from hemolysis from the inhibition of C5 cleavage; however, upstream complement activation may lead to C3 opsonization and possible extravascular hemolysis. GPI, glycosylphosphatidylinositol; PNH, paroxysmal nocturnal hemoglobinuria. *(From L Luzzatto et al: Haematologica 95:523, 2010.)*

TREATMENT PAROXYSMAL NOCTURNAL HEMOGLOBINURIA

Unlike other acquired hemolytic anemias, PNH may be a lifelong condition, and most patients receive supportive treatment only, including transfusion of filtered red cells[1] whenever necessary, which, for some patients, means quite frequently. Folic acid supplements (at least 3 mg/d) are mandatory; the serum iron should be checked periodically, and iron supplements should be administered as appropriate. Long-term glucocorticoids are not indicated because there is no evidence that they have any effect on chronic hemolysis; in fact, they are contraindicated because their side effects are considerable and potentially dangerous. A major advance in the management of PNH has been the development of a humanized monoclonal antibody, eculizumab, which binds to the complement component C5 near the site that, when cleaved, will trigger the distal part of the complement cascade leading to

[1]Now that filters with excellent retention of white cells are routinely used, the traditional washing of red cells, aiming to avoid white cell reactions triggering hemolysis, is no longer necessary and is wasteful.