

CAD associated with lymphoproliferative disorders. Therefore, even in the absence of a formal trial, rituximab has become de facto first-line treatment: especially since previously used immunosuppressive/cytotoxic agents, although they can reduce the antibody titer, have limited clinical efficacy and, in view of the chronic nature of CAD, their side effects may prove unacceptable. Unlike in AIHA, prednisone and splenectomy are ineffective. In the management of CAD in relapse, there is an emerging role for the B-cell receptor inhibitors venetoclax and ibrutinib, as well as for the proteasome inhibitor bortezomib. A different approach targeting complement inhibitors has been also explored by using eculizumab (anti-C5) or sutimlimab (anti-C1s): a limitation of this approach is that hemolysis will be curbed only for as long as these agents are administered.

In terms of supportive treatment, blood transfusion may be helpful—in spite of the fact that red cells from the donor, being I-positive, will survive no longer than those of the patient: both the blood bag and the patient's extremities must be kept warm during transfusion.

Hemolytic Anemia from Toxic Agents and Drugs A number of chemicals with oxidative potential, whether medicinal or not, can cause hemolysis even in people who are not G6PD deficient (for which, see above). Examples are hyperbaric oxygen (or 100% oxygen), nitrates, chlorates, methylene blue, dapsone, cisplatin, and numerous aromatic (cyclic) compounds. Other chemicals may be hemolytic through nonoxidative, largely unknown mechanisms; examples include arsine, stibine, copper, and lead. The HA caused by lead poisoning is characterized by basophilic stippling; it is in fact a phenocopy of that seen in P5N deficiency (see above), suggesting it is mediated at least in part by lead inhibiting this enzyme.

In these cases, hemolysis appears to be mediated by a direct chemical action on red cells. But drugs can cause hemolysis through at least two other mechanisms. (1) A drug can behave as a hapten and induce antibody production; in rare subjects, this happens, for instance, with penicillin. Upon a subsequent exposure, red cells are caught, as innocent bystanders, in the reaction between penicillin