TABLE 129-5 DRUGS THAT CARRY RISK OF CLINICAL HEMOLYSIS IN PERSONS WITH GLUCOSE 6-PHOSPHATE DEHYDROGENASE DEFICIENCY

	Definite Risk	Possible Risk	Doubtful Risk
Antimalarials	Primaquine Dapsone/chlorproguanil[a]	Chloroquine	Quinine
Sulphonamides/sulphones	Sulfamethoxazole Others Dapsone	Sulfasalazine Sulfadimidine	Sulfisoxazole Sulfadiazine
Antibacterial/antibiotics	Cotrimoxazole Nalidixic acid Nitrofurantoin Niridazole	Ciprofloxacin Norfloxacin	Chloramphenicol *p*-Aminosalicylic acid
Antipyretic/analgesics	Acetanilide Phenazopyridine	Acetylsalicylic acid high dose (>3 g/d)	Acetylsalicylic acid (<3 g/d) Acetaminophen Phenacetin
Other	Naphthalene Methylene blue Rasburicase	Vitamin K analogues Ascorbic acid (>1 g)	Doxorubicin Probenecid

[a]Marketed as Lapdap from 2003 to 2008.

bilirubin, indicating that there is also extravascular hemolysis. The most serious threat from AHA in adults is the development of acute renal failure (this is exceedingly rare in children). Once the threat of acute anemia is over and in the absence of comorbidity, full recovery from AHA associated with G6PD deficiency is the rule.

Although it was primaquine (PQ) that led to the discovery of G6PD deficiency, this drug has not been very prominent subsequently, because it is not necessary for the treatment of life-threatening *P. falciparum* malaria. Today there is a revival of interest in PQ because it is the only effective agent for eliminating the gametocytes of *P. falciparum* (thus preventing further transmission) and eliminating the hypnozoites of *Plasmodium vivax* (thus preventing endogenous relapse). In countries aiming to eliminate malaria, there may be a call for mass administration of PQ; this ought to be associated with G6PD testing. At the other end of the historic spectrum, the latest addition to the list of potentially hemolytic drugs (Table 129-5) is rasburicase; again G6PD testing ought to be made mandatory before giving this drug because fatal cases have been reported in newborns with kidney injury and in adults with tumor lysis syndrome.

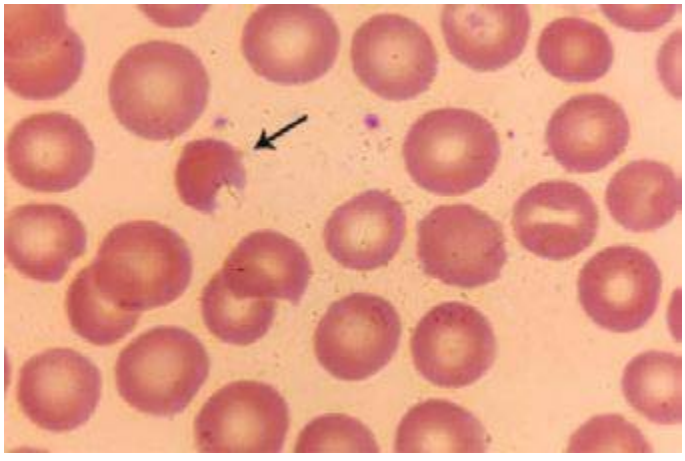

FIGURE 129-7 Peripheral blood smear from a glucose 6-phosphate dehydrogenase (G6PD)-deficient boy experiencing hemolysis. Note the red cells that are misshapen and called "bite" cells. *(From MA Lichtman et al: Lichtman's Atlas of Hematology: http://www.accessmedicine.com. Copyright © The McGraw-Hill Companies, Inc. All rights reserved.)*

A very small minority of subjects with G6PD deficiency have *chronic nonspherocytic hemolytic anemia* (CNSHA) of variable severity. The patient is nearly always a male, usually with a history of NNJ, who may present with anemia, unexplained jaundice, or gallstones later in life. The spleen may be enlarged. The severity of anemia ranges in different patients from borderline to transfusion dependent. The anemia is usually normomacrocytic, with reticulocytosis. Bilirubin and LDH are increased. Although hemolysis is, by definition, chronic in these patients, they are also vulnerable to acute oxidative damage, and therefore the same agents that can cause AHA in people with the ordinary type of G6PD deficiency will cause severe exacerbations in people with CNSHA associated with G6PD deficiency. In some cases of CNSHA, the deficiency of G6PD is so severe in granulocytes that it becomes rate-limiting for their oxidative burst, with consequent increased susceptibility to some bacterial infections.

Laboratory diagnosis The suspicion of G6PD deficiency can be confirmed by semiquantitative methods often referred to as screening tests, which are suitable for population studies and can correctly classify male subjects, in the steady state, as G6PD normal or G6PD deficient. However, in clinical practice, a diagnostic test is usually needed when the patient has had a hemolytic attack; this implies that the oldest, most G6PD-deficient red cells have been selectively destroyed, and young red cells, having higher G6PD activity, are being released into the circulation. Under these conditions, only a quantitative test can give a definitive result. In males, this test will identify normal hemizygotes and G6PD-deficient hemizygotes; among females, some heterozygotes will be missed, but those who are at most risk of hemolysis will be identified. Of course, G6PD deficiency also can be diagnosed by DNA testing.

TREATMENT G6PD DEFICIENCY

The AHA of G6PD deficiency is largely preventable by avoiding exposure to triggering factors of previously screened subjects. Of course, the practicability and cost-effectiveness of screening depend on the prevalence of G6PD deficiency in each individual community. Favism is entirely preventable in G6PD-deficient subjects by not eating fava beans. Drug-induced hemolysis can be prevented by testing for G6PD deficiency before prescribing; in most cases, one can use alternative drugs. When AHA develops and once its cause