Recent correspondence [1, 2] readdresses the issue of whether acetaminophen (Tylenol, paracetamol) is a safe medication for patients with glucose-6-phosphate dehydrogenase (G-6-PD) deficiency. When we reviewed the evidence concerning this drug in 1978 [3], we concluded, on the basis of its experimental administration to patients both with G-6-PD A [4] and G-6-PD Canton [5] that it did not produce significant hemolytic anemia. In addition, it has been shown that administration of 2,000 mg of acetaminophen daily failed to effect the survival of G-6-PD Hillbrow red cells [6].

In a research setting, our experience with drug administration and hemolysis was that the latter did not occur until the drug had been given for at least 2 days [7]. On the basis of the history provided, therefore, it seems very unlikely that acetaminophen was the cause of hemolysis in this patient.

Observing the in vivo effect of drug administration on $^{51}$Cr-labelled G-6-PD-deficient red cells is still the only reliable way of appraising a cause-and-effect relationship between drug and hemolysis. The subsequent letter from Pootrakul and Panich [2] is therefore particularly instructive. In contrast to the three earlier studies [3–5] evidence is presented that acetaminophen does, indeed, destroy G-6-PD-deficient red cells. But the critical consideration is that only about 10% of the cells were destroyed and a very large dose, 3,000 mg daily for 14 days was required to achieve this effect. Pootrakul and Panich [2] imply that in a G-6-PD-deficient individual such cell destruction would be greater. In point of fact it would, if anything, be less. All of the labelled cells were, after all, G-6-PD-deficient and the proportion of a G-6-PD-deficient subject’s red cells would be expected to be similar. Cell destruction is age-dependent and the $^{51}$Cr-labelled red cells were allowed to age in the recipient for some 6 days before exposing them to a course of drug. Therefore a correction which reduces the effect somewhat needs to be applied [8]. We consider it extremely unlikely that the magnitude of cell destruction revealed by the $^{51}$Cr studies would be attended by any clinical effect. Dosages of drugs which produce red cell destruction of this magnitude do not produce clinical hemolytic anemia. This should hardly be considered surprising, since red cell destruction takes place over a period of 212
several days. Thus, destruction of 10% of circulating red cells represents a mere 2- or 3-fold increase of the normal rate of red cell destruction, an event which one would hardly consider to be clinically perceptible.

Examination of the evidence presented, therefore, tends to confirm the correctness of our original conclusion, namely that acetaminophen should be considered harmless when given to G-6-PD-deficient individuals, even those with variants associated with severe enzyme deficiency.

References
