Correspondence

Accepted: August 1, 1984

Acta haemat. 1984;72:211-212

Acetaminophen and G-6-PD Deficiency

E.

Ernest

Beutler

La Jolla, Calif.

Dr. Ernest Beutler, Department of Basic and Clinical Research, Scripps Clinic and Research Foundation, 10666 N. Torrey Pines Road, La Jolla, CA 92037 (USA)

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].

1 This publication is manuscript No. 3569 BCR from the Research Institute of Scripps Clinic. This work has been supported in part by grant HL25552 from the National Institutes of Health, Division of Heart, Lung and Blood.

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 ⁵¹Cr-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 ⁵¹Cr-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 ⁵¹Cr 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

Correspondence

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

Bartsocas, C.S.; Schulman, J.D.; Corash, L.: Can acetaminophen cause hemolysis in G6PD deficiency? *Acta haemat.* 67: 228 (1982).

Pootrakul, P.; Panich, V.: Effect of acetaminophen on glucose-6-phosphate dehydrogenase, Mahidol variant. *Acta haemat.* 69: 358–359 (1983).

Beutler, E.: Hemolytic anemia in disorders of red cell metabolism (Plenum Publishing Company, New York 1978).

Beutler, E.: The hemolytic effect of primaquine and related compounds. A review. *Blood* 14: 103–139(1959).

Chan, T.K.; Todd, D.; Tso, S.C: Red cell survival studies in glucose-6-phosphate dehydrogenase deficiency. *Bull. Hong Kong Med. Ass.* 26: 41–48(1974).

Cayanis, E.; Gomperts, E.D.; Balinsky, D.; Disler, P.; Myers, A.: G6PD Hillbrow: a new variant of glucose-6-phosphate dehydrogenase associated with drug-induced haemolytic anaemia. *Br. J. Haemat.* 30: 343–350(1975).

Dern, R.J.; Beutler, E.; Alving, A.S.: The hemolytic effect of primaquine. II. The natural course of the hemolytic anemia and the mechanism of its self-limited character. *J. Lab. clin. Med.* 44: 171 – 175(1954).

Dern, R.J.; Beutler, E.; Alving, A.S.: The hemolytic effect of primaquine. V. Primaquine sensitivity as a manifestation of a multiple drug sensitivity. *J. Lab. clin. Med.* 45: 40–50 (1955).