Letters

Glucuronic Acid and Hyperbilirubinemia

The observation by Danoff *et al.* [*Science* **127**, 795 (1958); *Lancet* (8 Feb. 1958)] that administration of glucuronic acid and its sodium salt to infants with hyperbilirubinemia resulted in a striking but transient fall in unconjugated bilirubin is of extreme interest to all pediatricians. In our work with glucuronic acid we have been unable as yet to demonstrate a significant fall in bilirubin level. However, we wish to call attention to the potential hazard in the use of these preparations in view of the fact that physicians may be tempted to substitute glucuronic acid therapy for replacement transfusions in newborn infants with dangerously high serum bilirubin levels. Should the reported findings be confirmed, there is no indication regarding the fate of the declining serum bilirubin. The possibility has not been excluded that bilirubin is driven from the blood into the tissues, thus increasing the risk of brain damage.

Until further investigative work determines the exact pharmacodynamic action of these compounds, we feel strongly that physicians should refrain from using them in the newborn.

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Schmid, Jeliu, and Gellis comment as follows on our recent report dealing with the reduction of indirect bilirubinemia: (i) They state that they have not been able to duplicate our results. (ii) They suggest that we may be doing harm by driving bilirubin from the blood to the tissues, increasing the risk of brain damage. (iii) They urge all to desist from this therapy until further pharmacodynamic studies of glucuronic acid are carried out.

It would seem that the discrepancy between the results of the Boston workers and our own may be explained by differences in technique. This matter is now being explored. It would seem to us unfortunate if the concern of our Boston colleagues were to result in discontinuance of studies with this promising therapeutic approach.

It goes without saying that all new drugs should be thoroughly tested prior to clinical use and that they should not be used without due information in regard to their pharmacodynamic action. We might point out, however, that glucuronic acid, although not previously used for this particular purpose, is by no means a new drug. It has been known

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for two generations, and its safe and toxic levels have been documented [N. E. Artz and E. M. Osman, *Biochemistry of Glucuronic Acid* (Academic Press, New York, 1950)]. There are numerous references dealing with its administration to experimental animals and to man.

Our critics do not document the basis of their expressed fear that by lowering the level of bilirubin in the blood we are driving it into the tissues. It was presumably based on two observations that have been recently reported—the finding of Silverman *et al.* [*Pediatrics* **18**, 614 (1956)] that certain sulfa drugs, notably sulfasoxazole, would facilitate the passage of bilirubin from the blood stream into the brain and the finding by Johnson, Sarmiento, and Day [*Trans. Soc. Pediatric Research* (1958), p. 63] that kernicterus occurred in five rats of the Gunn strain whose bilirubin was lowered by the administration of glucuronic acid.

We should like to point to evidence that glucuronic acid and sulfa drugs do not act similarly on bilirubin. Odell [*Trans. Soc. Pediatric Research* (1958), p. 147] has made in vitro studies of sera with a high bilirubin content. When sulfa drugs were added to such sera and the sera were ultrafiltered, the bilirubin passed out into the ultrafiltrate, presumably because the sulfonamide displaced bilirubin from combination with serum proteins. The addition of glucuronic acid to serum had no such effect. Regarding the Gunn rats, we do not question the observation that increased bilirubin concentrations of the tissues may have occurred. These rats, however, differ from newborn infants in several respects. Their skin was noted to become increasingly icteric after administration of glucuronic acid, whereas in our infants not only was a decrease in skin icterus observed but this was confirmed by measurements of the bilirubin specimens of subcutaneous fat obtained at biopsy before and after therapy. For these reasons and because of our favorable clinical experiences we do not share the fears that have been expressed.

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Human Values

H. J. Muller's recent article [*Science*, **127**, 625 (1958)] on the evolutionary basis of human values was most interesting and informative. As one not trained in biological science, I certainly accept his interpretation of the evidence as authoritative. However, since he follows his scientific discussion by proposing a system of ethics, I think that I am no further afield in commenting on his ideas than he is in presenting them.

As a result of natural selection, Muller points out, species for which social living is helpful for survival develop natural tendencies and desires which promote the success of cooperative enterprises. Thus, such ideas as "brotherly love" have a basis in natural evolution. In human beings, then, these inherited tendencies mean that actions which advance the welfare of one's fellows—thus aiding the survival of the species—satisfy basic natural desires and are therefore emotionally rewarding. In addition, the culture based upon this natural heritage recognizes the need for cooperative actions and adds its own rewards and punishments. On the other hand, as a society grows large, individuals who do not have these genetic traits are no longer discriminated against but are helped by the society to adopt the necessary cooperative attitudes. This leads to a gradual dilution of the genetic basis of the cooperative society.

From these considerations, Muller proposes that a new system of ethics be adopted, based upon the idea that those actions which contribute to the survival and advancement of the species be regarded as good and praiseworthy and that opposing actions be condemned. Clearly, from the biological discussion it is necessary that any successful system of