THE PROBLEM OF NEONATAL JAUNDICE IN GREECE

Role of G - 6 - PD Deficiency *

S. A. Doxiadis, M. D.,** T. Valaes, M. D. *** Ph. Fessas, M. D.****

We became interested in the problem of neonatal jaundice in Greece when we were faced with severely jaundiced full term newborns in whom there was no evidence of iso - immunization. After the first few disasters of kernicterus developing under our eyes, we realized that independently of the etiology, the risk to the central nervous system was the same as in jaundice due to hemolytic disease of the newborn. We started, therefore, treating these newborns by exchange transfusion relying for the indication of this treatment on the height of the serum bilirubin.

The problem of this type of severe neonatal jaundice in Greece is not negligible as Table 1 shows.

TABLE 1

ETIOLOGY OF SEVERE ICTERUS IN FULL TERM INFANTS WHO RECEIVED EXCHANGE TRANSFUSION OR HAD KERNICTERUS ON ADMISSION

	EXCHANGE TRANFUSION CASES	KERNICTERUS CASES
Hemolytic disease due to Rh. incompatibility	56	1
A.B.O. incompatibility	71	7
No incompatibility	78	34
TOTAL	205	42

* Paper presented at the Second Middle Eastern - Mediterranean Pediatric Congress, Ankara, 1961; based in part on material previously published in the Lancet.

** Consultant Pediatrician, Alexandra Maternity Hospital, Athens.
*** Senior Pediatric Registrar, Alexandra Maternity Hospital, Athens.
**** Consultant Hematologist, Alexandra Maternity Hospital, Athens.

As may be seen from this table, among the babies whose bilirubin was rising to levels necessitating an exchange transfusion, in more than one third there was no Rhesus or ABO incompatibility. The importance of this group without iso - immunization was more striking in the babies sent to us too late with established kernicterus. In about 80 per cent of these babies, there was no demonstrable incompatibility.

Now most of the babies of this group of severe neonatal jaundice had some ccmmon features. As two of these features were evidence of hemolysis and the presence in the same family of similar cases, we looked for a hereditary hemolytic mechanism operating in these babies and we were able to prove that in about three quarters of the cases of severe neonatal jaundice not due to incompatibility, there was a deficiency of a red cell enzyme, the glucose - 6 - phosphate dehydrogenase. It is the deficiency of this same enzyme which is the cause of favism and of many drug induced hemolytic anemias

The finding of this enzyme deficiency immediately poses another problem. Why is it that in only a very small number of the enzyme deficient babies do we see the development of severe jaundice? Thus we found the incidence of the G - 6 - PD defect in male newborns in Greece to be 3 per cent, but only a very small fraction of this number developed severe jaundice. In about half of these, the answer is easy because we found an extrinsic precipitating factor operating in the neonatal period, a factor known to increase hemolysis. This factor was in most instances the injection of a vitamin K analogue and, in a few, exposure to naphthalene inhalation. There remained, however, a significant number of babies with no known extrinsic precipitating factor and, at present, we can offer no satisfactory explanation. This aspect of the jaundice, as well as the problem of the etiology of the jaundice in those newborns in whom neither iso - immunization, nor G - 6 - PD deficiency is found, is under investigation.

From the practical point of view, the correct management of this type of jaundice is more difficult than that of the jaudice due to hemolytic disease. And the deficiency lies not in the treatment, which is the same as in any severe hyperbilirubinemia, but in the early recognition of such a type of jaundice. There is nothing in routine laboratory practice comparable to, and as specific as, the Coombs test in Rhesus hemolytic disease. There are methods to

detect the G - 6 - PD deficient individuals, but these are still done in very few laboratories. The suspicion, therefore, that a neonatal jaundice may not be an innocent manifestation, and may be one that needs careful watching, will have to be based on clinical criteria.

Family history. A family history of previous unexplained severe neonatal jaundice, of favism or of drug induced hemolytic anemia should warn the doctor that this baby may have an increased susceptibility to hemolysis.

Sex. G - 6 - PD deficiency being due to a gene in the chromosome X, a great preponderance of male newborns was found among our cases as was to be expected. We have had, however, cases of extreme severity in girls.

Time of appearance of jaundice. In most of our cases, the jaundice was evident before the end of the second day, but in a very few it appeared on the first. So the early appearance of jaundice is not a reliable warning sign. Neither does the late appearance exclude a severe course, since there were some babies whose jaundice was noticed after the third day and who either became so jaundiced as to need an exchange transfusion or were sent to us too late with kernicterus.

Taking into consideration all the above, the conclusion is inevitable that only very careful observation of the course of the bilirubinemia and timely exchange transfusion will prevent damage to the central nervous system. Our experience confirms this conclusion.

For the last four and a half years, in spite of the multiplicity of causes of severe neonatal jaundice in the Greek population and in spite of the still unknown etiology in a fair number of cases, we have been successful in eliminating entirely the risk of kernicterus in all babies either born in our hospital or sent to us early, by estimating the serum bilirubin every 12 hours and sometimes, if necessary, every six hours, and performing an exchange transfusion when the level of the serum bilirubin approached the critical, according to our method, level of 25 mg. per 100 ml.