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Dehydroepiandrosterone* and Similar Substances in Urine of Premature Infants.† (19943)

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Dirscherl and Zilliken(2), using a modification of the Kober test for estrogens(3), de-

* Also known as dehydroisoandrosterone. The nomenclature will conform with that proposed by Feiser and Feiser(1).

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scribed a simple color test (the "blue test") for dehydroepiandrosterone (DHA) and other closely related compounds. Patterson(4), Allen, Hayward, and Pinto(5), and Gardner and Migeon(6) have utilized this colorimetric procedure on urinary steroids to distinguish between patients with adrenal tumors and

those with congenital adrenal hyperplasia. Among the 11 patients with adrenal tumor reported by the above authors, the test was positive 10 times. In the instance in which it was negative an abnormally large amount of DHA was found and it was stated that the typical blue color was obscured by contaminating yellow colors. Among the 15 patients with congenital adrenal hyperplasia, the test was always negative. The authors concluded that this is a valuable test to aid in differentiating between these conditions, particularly when it is positive.

It is the purpose of this communication to point out that the test is frequently positive in premature infants and in children under one year of age who have no evidence of an adrenal tumor.

Methods and material. 17-ketosteroids were determined by the method of Bongiovanni (7). For the Zimmerman reaction, DHA was used for the standard.† The "blue test" for DHA was performed according to the method of Gardner and Migeon (6) on part of the urinary extract obtained for the Zimmerman reaction. Absorption curves were done on the Beckman spectrophotometer using a 1 cm light path. Allen (8) states that this color reaction can be used quantitatively, but for the purposes of this communication a qualitative "yes" or "no" answer was all that was necessary. Urine was collected from premature infants of various ages and weights, and receiving various diets, who were hospitalized because of prematurity. Male infants had a rubber tube taped to the penis. Females were catheterized. Urine was collected in bottles containing 5 ml of concentrated hydrochloric acid. Occasionally 24-hour collections were made, but usually random samples were collected. The urine of the infants under one year of age who were not premature was collected without preservative. These patients were hospitalized for a variety of conditions.

Results. The urine of 9 out of 18 premature infants yielded a positive "blue test" at least once. Of the urines of those infants with negative tests, 5 were tested only once; the

remaining 4 were tested at least 3 times. Except for 2 infants who had positive tests on their only examination, the remaining infants had both positive and negative tests. Out of 66 examinations of the urine of these 18 infants, the "blue test" was positive 24 times. The test, when positive, seemed to be so in a random manner. Specimens of urine from the same child on different days, and at different times during the same day, would be either positive or negative. We could note no correlation between age, weight, diet, medication, time of day, or any stress factors, and the presence of a positive test. Nor was there any correlation between a positive "blue test" and the total amount of 17-ketosteroids. A 20 ml aliquot of urine containing as little as 0.05 mg of 17-ketosteroid was positive, and a sample containing 0.76 mg per 20 ml urine was negative. Conversely, a sample containing 0.58 mg was positive, and one containing 0.02 mg was negative. It has not yet been determined whether a negative test in the presence of relatively large amounts of 17-ketosteroids is due to interference with the production of the typical color by these steroids or contaminants, or whether there is an absolute decrease in the amount of DHA or DHA-like substances.

In 18 examinations of the urine of 15 patients under one year of age who were not prematures, but who were in the hospital for a variety of conditions, the test was positive once in 2 patients. One of these patients was recuperating from meningococcus meningitis, and the other had idiopathic hypoproteinemia.

The spectral transmission curves of many of these positive tests were studied. Fig. 1 shows a representative curve of a positive test with peaks at 375 m μ , 475 m μ , and a maximum at 605 m μ . On the same graph is a representative curve of a negative test, with peaks at 375 m μ and 475 m μ followed by a gentle slope without any peak at 605 m μ . The transmission curve of pure DHA has a peak at about 385, and a maximum peak at 605.

When urine giving a negative test was mixed with urine giving a positive test, the blue color appeared. When pure DHA was added to urine giving a negative test, an

† Kindly supplied by the Schering Corp., Bloomfield, N. J.

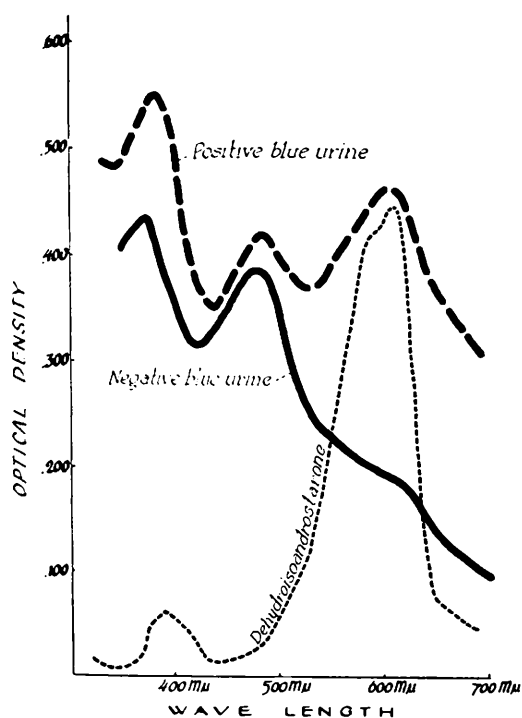


FIG. 1.

absorption curve was obtained which appeared to be virtually identical with that of a positive test. Therefore, it seems probable that the main compound giving the blue color is DHA.

Discussion. These observations oblige us to conclude that the test cannot be used to differentiate between an adrenal tumor and benign hyperplasia in premature infants; furthermore, it must be interpreted with caution in children under a year of age. The observations do not, of course, invalidate the conclusions of other authors concerning patients in the older age groups, and it may also be true, that the test will never be positive in children with the adrenogenital syndrome, even when they are very young. On two occasions the test was negative in a pseudo-

hermaphrodite who was less than two months old.

The obvious morphological differences between the adrenal gland of the newborn and the older child or adult suggest that functional differences also may be present. This has been demonstrated by Klein(9) who showed that when ACTH is given to a premature infant, a sodium diuresis and potassium retention occurs. The opposite effect of ACTH administration occurs in older children or adults(9).

To our knowledge, our observation is the first evidence that steroid excretion in the premature infant may be qualitatively different from that of more mature individuals.

Summary. Examination of the urine of premature infants and children less than a year of age for DHA or DHA-like substances by means of a colorimetric test disclosed that in the absence of an adrenal tumor the test was positive at least once in half of the patients. Of all the urine samples collected from patients in this age group, the test was positive 30% of the time.

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