Serum tri-iodothyronine, thyroxine, and thyrotrophin concentrations in newborns during the first 2 days of life* 

Previous experimental data indicate that the fetal pituitary-thyroid axis functions autonomously and no or only minimal placental transfer of thyroxine (T₄), tri-iodothyronine (T₃), or thyrotrophin (TSH) occurs. Human fetal T₄ and TSH secretions increase after 18–22 weeks of gestation. Serum T₃ concentrations are low before the 24th gestational week, but increase progressively thereafter to term (Fisher et al., 1973).

The earlier data on T₃ concentrations in cord blood differ. Dussault et al. (1969) found similar T₃ values in maternal and cord blood. In later studies, however, low cord T₃ values have been found (Hotelling and Sherwood, 1971; Larsen, 1972; Lieblich and Utiger, 1973). On the other hand, the plasma TSH, T₄, and T₃ concentrations are known to rise after birth (Fisher and Odell, 1969; Hüfner et al., 1973). It therefore seemed to be reasonable to measure the T₃ concentrations repeatedly after birth to compare with the serum T₄ and TSH concentrations.

Subjects and methods

Blood samples were taken immediately after delivery from 10 mothers, from cord blood, and from the newborns at 1, 2, 6, 12, 24, and 48 hours. Blood samples were obtained by venepuncture with permission of the mothers, were allowed to clot, and the serum was then separated and stored at −20°C until assayed. The mothers tested had no previous history of thyroid disease, and none was on medication in addition to taking vitamins and iron. Gestational age of their newborns ranged from 37 to 41 weeks (mean 39.7 weeks), birthweight from 3150 to 4180 g (mean 3753 g), and the Apgar scores at one minute from 7 to 10 (mean 8.4). T₃ was assayed by the direct immunooassay method (RIA-mat—T₃-test*), and the results are expressed as µg/l. The normal values of non-pregnant women are 0.75–1.65 µg/l. T₄ was assayed by the RES-O-mat—T₄-test,* and the results are expressed as µg/l. The normal values of non-pregnant women are 65–175 µg/l. TSH in 200 µl serum samples was estimated by the NIAMD human TIA method. Human TSH 63/68 from the Medical Research Council (England) was used as the standard, and expressed as mU/l. The binding of the label was significantly inhibited by 0.2 µg/l. The normal values of non-pregnant women are 2–10 mU/l in our laboratory.

Results

Maternal serum T₃ and T₄ levels immediately after delivery were higher than those in healthy nonpregnant women, but serum TSH remained in the normal range (see Fig., left-hand columns). In the cord blood TSH was 5.7±2.2 mU/l (mean±SD), increasing to 20.6±6.5 mU/l at 2 hours and then decreasing to the normal range within 12 hours. At age 48 hours TSH was already at a lower level (2.7±0.7 mU/l) than at birth (P<0.001).

T₃ concentration in cord blood was about one-third of the corresponding maternal blood value (0.63±0.21 µg/l against 1.62±0.44 µg/l; P<0.001; Fig.). Soon after birth the T₃ level of the neonates rose to the maternal level, reaching its maximum as early as at the age of 2 hours (1.76 ±0.34 µg/l). Thereafter the T₃ level dropped rapidly to the normal range (see Fig.).

Serum T₄ concentration increased more slowly than that of the T₃ and was at its maximum at 24 hours (205±15 µg/l against 145±27 µg/l at birth). At 48 hours serum T₄ level (202±17 µg/l) was still significantly higher than that at birth.

Discussion

When the concentrations of thyroid hormones and TSH in the cord blood and newborn serum samples were compared with those of the mother, a biphasic change as a function of time could be shown. The hormone levels were low in the cord samples but high in the subsequent newborn

*In the Editorial we wrote on 'The ethics of research involving children as controls', Archives, 1973, 48, 751, we mentioned that, 'we have sometimes invited an author to agree to our adding an editorial note to his paper, pointing out that there has been a difference of opinion on the ethical propriety of the publication', but that the authors have usually declined the invitation and withdrawn the paper. The authors of this study have availed themselves of such an invitation, and their letter on the subject is to be found on p. 575 of this issue. We are thus pleased to be able to publish both the results of their study and their, to us convincing, defence of its ethical propriety. Editors.

*Malinckrodt Chemical Works, St. Louis, Missouri, USA.
samples. These results generally agree with previous findings (Hotelling and Sherwood, 1971; Larsen, 1972; Lieblich and Utiger, 1973; Hufner et al., 1973).

The very low cord T₃ levels found in this study agree with most previous reports (Hotelling and Sherwood 1971; Larsen, 1972; Lieblich and Utiger, 1973; Hufner et al., 1973). The present results offer no explanation for the finding, but the following assumptions are feasible. (1) Extrathyroidal conversion from T₄ to T₃ is decreased. (2) The amount of specific T₃-binding proteins in the cord serum is reduced. (3) The distribution volume to T₃ is increased. (4) The formation of T₃ by the fetal thyroid is decreased. The T₃ level of fetal serum has recently been shown to be low in the human fetus (Fisher et al., 1973), which favours the first or the last alternative. Fisher et al. (1973) found the ratio of T₄/T₃ content of 14 human fetal thyroid glands to be similar to that of adult glands, concluding either that the fetus cannot convert T₄ to T₃ at a rate comparable to the adults, or that T₄ is unavailable for such conversion.

Fisher and Odell (1969) showed that the umbilical cord plasma TSH concentration is more than twice as high as that found in the mother at term. However, we could not find any statistically significant difference in these samples, and the cord TSH values tended to be even lower than the maternal ones. In our subsequent samples the serum TSH level increased markedly (over 300%), reaching a maximum at 2 hours and declining to subnormal values at 48 hours, evidently due to the raised secretion of thyroid hormones.

After birth serum TSH and T₃ concentrations rose sharply and concurrently, reaching maximum at 2 hours. It is believed that the increase of TSH secretion is due to the decrease of environmental temperature (Fisher and Odell, 1969). The cause of the simultaneous increase of T₃ secretion remains unknown. It is, however, generally known that TSH-dependent secretion of thyroid hormones occurs clearly after the TSH release.

The measurement of TSH (and possibly T₃ and T₄) in cord serum or immediately after birth has proved to be a reliable technique of screening for congenital hypothyroidism (Klein, Agustin, and Foley, 1974). Because there are great, rapid physiological changes in the serum concentrations of T₃, TSH, and T₄ during the first 12 hours of life, we recommend that screening should be carried out at the age of 24 hours or after.
Summary

The serum concentrations of tri-iodothyronine (T₃), thyroxine (T₄), and thyrotrophin (TSH) were measured in 10 term newborn infants between birth and the age of 2 days by radioimmunoassay. The mean concentration of T₃ in maternal serum was 1·62 μg/l, and it increased from the low cord blood level of 0·63 μg/l to the peak value of 1·76 μg/l within the first 2 hours of life. Mean serum T₄ concentrations increased from the cord blood level of 145 μg/l to the peak value of 205 μg/l within the first 24 hours of life. The postnatal increase of the mean serum TSH concentrations from the cord blood level of 5·7 mU/l to the peak value of 20·6 mU/l within 2 hours was similar to the increase of T₃.

These data confirm earlier reports which show that T₃ secretion is low at birth and TSH secretion is stimulated strongly but transiently after birth, and that the low T₃ secretion is rapidly normalized in 2 hours along with the TSH release. Because of these strong and rapid changes, we recommend screening of the function of the pituitary-thyroid axis in neonates after the age of 24 hours.

REFERENCES


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