10 11/12 years the bone age was 9 years. There was a
simian line in the palm of the right hand. The
chromosomes showed a normal pattern, after examining
a total of 100 cells and 6 karyotypes.

Case 3. He was born in April 1964 after a normal
40 weeks' gestation and spontaneous delivery. When
4 months old it was noticed that growth and development
were retarded, and that chest deformities and contract-
tures of the lower extremities were appearing. The
clinical picture was identical to that of Case 2 (see
Table and Fig. 2). At 4½ years he was admitted to
hospital with pneumonia; at that time his weight was
only 9 kg., head circumference 53 cm. He died
suddenly a few hours after admission.

Necropsy. External findings are summarized in
the Table. There was hardly any subcutaneous fatty
tissue. The entire musculature was pale and atrophic.
The wall of the left main bronchus was thinner than that
of the right main bronchus. On microscopical examina-
tion the cartilagenous rings were not continuous. There
were no cardiovascular abnormalities. The penis was
normal, but the scrotum 'empty'; examination of the
abdominal cavity failed to show testes; it was concluded
that there was testicular agenesis. The prostate and
the ejaculatory ducts were normal. Examination of the
brain was not allowed. Bronchiolitis was the probable
cause of death.

Discussion
The main characteristics of the clinical picture in
the three brothers were: serious chest deformities
with pulmonary disorders; agenesis of the testes;
grossly depressed weight gain; hypoplasia of the
musculature and absence of subcutaneous fatty
tissue; severe mental retardation; and dolicho-
cephaly.

Since three sibs were affected, the condition is
probably inherited either as an autosomal or a
sex-linked recessive. The cause of death in the
twin sister is uncertain, so we cannot distinguish
between these two possibilities. As far as we know
this complex of symptoms has not been described.
In 1912 Benjamin described a syndrome with
clinical features of anaemia, skeletal and muscular
underdevelopment, anomalies of the ear, hypoplasia
of the genitals, and cardiac disorders. As none of
our patients were anaemic and as chest deformities,
so outstanding in our patients, were not mentioned
by Benjamin, we do not think our patients had the
same syndrome.

Summary
A family is described in which all male offspring
(3 brothers) displayed the same multiple congenital
anomalies. The syndrome consisted of severe
chest deformities with pulmonary anomalies; agene-
sis of the testes; hypoplasia of the musculature and
absence of subcutaneous fatty tissue; and dolicho-
cephaly with severe mental retardation. No
chromosomal abnormality was found.

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L. H. B. M. van Benthem, O. Driessen, G. T.
Haneveld, and H. P. Rietema
Departments of Paediatrics and Pathology, State
University of Utrecht, and the Departments of
Paediatrics, St. Joseph Hospital Heemskerk,
Rehabilitation Centre 'de Hoogstraat', Leersum,
The Netherlands.

Plasma Cortisol Levels in the
Neonatal Period
At birth the concentrations of 17-hydroxycortico-
steroids (17-OHCS) in the cord blood reflect the
maternal levels and are also related to the degree
of stress occurring at birth (Migeon, 1959). Babies
born by caesarian section usually have low levels
less than 10 μg./100 ml., whereas in these born
vaginally the level is usually greater than 10 μg./
100 ml. (Gemzell, 1954; Migeon, Keller, and
Holmstrom, 1955). The cord plasma values are in
most cases lower than the corresponding maternal
values. It has been shown that there is a gradual
fall in the plasma 17-OHCS level after birth
(Bayliss et al., 1955; Klein, Fortunato, and Papada-
tos, 1954), and at the end of the first week of life
the plasma levels in normal full-term babies are similar
to those of the normal adult (Gray, Greenaway, and
Holness, 1961).

Various methods have been used in the past to
measure plasma 17-OHCS but the majority of these
methods are not specific for cortisol. Interference
from cortisone, corticosterone, and inactive break-
down products such as tetrahydrocortisone may
occur using methods based on the 'Porter Silber'
reaction (Porter and Silber, 1950) or a fluorimetric
technique (Mattingly et al., 1964). In 1963, a
complicated technique was described which utilized
the steroid-binding properties of a specific protein,
transcortin, the cortisol binding globulin (CBG) in
a competitive protein-binding 'radio-assay' using
C14-cortisol (Murphy, Engelberg, and Pattee, 1963).
Subsequently the method was modified by the use of
tritiated cortisol (Murphy, 1967) which greatly
increased the sensitivity of the method and allowed
a simplified procedure to be used. The increase in sensitivity allowed a cortisol assay to be performed on as little as 10 µl. plasma and makes this the method of choice for an investigation of cortisol levels in newborn infants.

Methods

The method of Murphy (1967) was used though the technique was modified slightly so that it could be performed using the apparatus already available. Tritiated cortisol 1, 2-T was supplied by the Radiochemical Centre at Amersham, and the final activity was measured on a Packard ‘Tri Carb’ scintillation counter. At a cortisol concentration of 10-8 µg./100 ml., the precision of the method (standard deviation) as measured from 10 analyses on a pooled plasma was ±1.5 µg. The recovery of added cortisol varied from assay to assay depending on the operating conditions and therefore a series of recovery samples was included with each batch so that the appropriate correction could be made. Wherever possible the analyses were performed in quadruplicate.

Samples

Cord blood was collected from 15 vaginally delivered full-term babies at birth and then by heel-prick from 131 full-term babies during the first week of life. The mothers' permission was obtained in all cases. The plasma was separated and frozen until assayed. Samples were collected at 9.00 a.m. each morning immediately before a feed in order to minimize the effect of any possible circadian variation. Serial samples were not collected.

Results

A scattergram of the individual results is shown in Fig. 1. It can be seen that cord levels (i.e. at age zero) are generally higher and have a wider range than at any subsequent period, though there is an occasional unexplained high value later in the week. Statistical evaluation of the results (excluding the cord blood values because the factors affecting the plasma cortisol level at birth are different from those subsequent periods) indicates that cortisol levels are logarithmically distributed. The mean and standard deviation for each day has been calculated using the logarithm of the cortisol level and then re converting to an arithmetic value. The mean value ± 2 SD for cord blood and each subsequent 24-hour period is shown in Fig. 2. It can be seen that the level drops during the first day of life but that for the rest of the period studied there is no further significant change.

Discussion

Bayliss et al. (1955) using a ‘Porter Silber’ technique measured the 17-OHCS in the plasma of pregnant women, and showed that the levels rose steadily throughout pregnancy from the normal adult level of 10 µg./100 ml. to 23 µg./100 ml. at delivery. The rise in plasma corticosteroids during pregnancy is due to the presence of increased quantities of cortisol and the specific binding protein transcortin. Radioisotope studies indicate that free cortisol can cross the placenta (Migeon, Bertrand, and Wall, 1957), so that the high cord blood level may merely reflect the high maternal cortisol level present at delivery, though the increased fetal adrenal cortisol activity in response to the stress of normal delivery may also contribute. Sandberg and Slaunwhite (1959) have shown that the cord blood level is always lower than the maternal level, and that the cortisol present is mainly of maternal origin. They have suggested that the gradient occurs because of the lower concentration of trans-
cortisol in the cord blood compared with maternal level. This seems unlikely to be the sole cause, since after birth the level falls rapidly and, in this study, remains stable during the first week of life. This is not in complete agreement with the changes observed by Bayliss et al. (1955) who showed a gradual decrease of 17-OHCS over the same period. The mean values obtained by them have been superimposed on Fig. 2. It can be seen that by the 7th day of life, the levels for both studies are comparable, and it may be that the ‘Porter Silber’ technique is measuring an interfering chromogen which has crossed the placenta and is gradually being broken down or excreted during the first week.

Summary

The normal range of plasma cortisol has been measured in 146 healthy full-term babies during the first week of life, using a ‘radio assay’ technique. After birth, the levels fall rapidly and then remain constant over the period studied.

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John F. Stevens*

Institute of Child Health, Hammersmith Hospital, Du Cane Road, London W.12.

*Correspondence to: Department of Chemical Pathology, King’s College Hospital, Denmark Hill London S.E.5.