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 contractures 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 examination the cartilaginous 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 dolichocephaly.

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-

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 Papadatos, 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 breakdown 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. Tritated 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 the 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 reconverting 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 cortical 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-
cortin 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.

I am indebted to Miss L. Cooper who collected the samples of plasma, and to the Sir William Coxen Trust Fund and the Medical Research Council for providing the facilities for this study.

**References**


—. *Bulletin of the Johns Hopkins Hospital*, 87, 415.

Murphy, B. E. P. (1967). Some studies of the protein-binding of steroids and their application to the routine micro and ultramicro measurement of various steroids in body fluids by competitive protein-binding radioassay. *Journal of Clinical Endocrinology*, 27, 973.


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.
Plasma cortisol levels in the neonatal period.

J F Stevens

Arch Dis Child 1970 45: 592-594
doi: 10.1136/adc.45.242.592

Updated information and services can be found at:
http://adc.bmj.com/content/45/242/592.citation

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/