Pediatric clinical chemistry

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Introduction

The investigation of diseases in children is different from adults and is affected by several issues, including:

- **Different types of disease**
- **Different presentation of disease**
- **Different reference ranges.**

Chronic diseases are fortunately less common in this age group and generally healing processes are faster and there is a good functional organ reserve.

For children, a problem in the clinical biochemistry lab relates to the size of the blood sample. For the very young, it is essential to apply analytical methods that will use the smallest possible amount of plasma.

Small quantities of capillary blood can be conveniently collected by pricking the **baby's heel**, but this should be done by experienced personnel, as the results obtained may be affected by haemolysis or by contamination with tissue fluid.

Reasons for hemolysis

☒ contamination of the specimen with alcohol from the skin.

☒ milking the site.

☒ scraping the blood instead of allowing the blood to flow in the collection container.

☒ Strong mixing of the specimen tube will also cause hemolysis.

☒ In infant patients, there is an increase in red blood cell fragility and increased RBC volume, which can cause hemolysis.

To collect a urine sample from an infant:

1. Thoroughly wash the area around the urethra. Use the soap or cleansing wipes.
2. 2. Use a special bag to collect the urine, it will be a plastic bag with a sticky strip on one end, made to fit over your baby's genital area. Open this bag and place it on the infant.

For males, place the entire penis in the bag and attach the adhesive to the skin.

For females, place the bag over the two folds of skin on either side of the vagina (labia).

In the **immediate neonatal period**, the concentrations of metabolites in infants may still reflect maternal metabolism and may be affected by the function of organs that are relatively immature.

Reference ranges (Normal Range)

The reference ranges for certain analytes are different in the newborn from the adult (Table 22.1) and may vary through childhood.

Some even continue to change throughout adulthood, such as plasma low-density lipoprotein (LDL) cholesterol which continues to rise from birth and uric acid which, after a rapid reduction in the first year, continues to rise gradually with age.

A result should always be interpreted considering the reference range appropriate to the child's age.

Table 22.1 **Common analytes with different reference ranges in children**

Analyte	Difference
potassium	mean and upper limit higher in newborn
calcium	higher at birth; normal adult concentrations by 72 h
phosphate	higher at birth, then falls but remains higher than adult concentrations throughout childhood; rises at puberty, then falls to adult concentration
alkaline phosphatase	as phosphate but more marked rise and fall at puberty
creatinine	rapid decrease after birth; gradual increase to adult values, particularly after puberty
thyroid-stimulating hormone	rapid increase for a few days immediately after birth; slightly higher than adult values maintained throughout childhood
free thyroxine	higher for first month, slowly falling to reach values similar to adulthood by 1 year

Childhood disorders

Neonatal hypoglycemia

It is an important condition that is particularly likely to occur in:

low birth weight infants, both premature and ‘small-for-dates’ infants born to diabetic mother’s infants who are ill or who have feeding problems.

In such infants, blood glucose measurements should be made every 4 h for the first 48h and at appropriate intervals to monitor treatment if hypoglycaemia has occurred.

Persistent hypoglycaemia or requirement for a high-rate glucose infusion to prevent hypoglycaemia should prompt a search for metabolic and endocrine causes…

Neonatal hypocalcaemia and hypomagnesaemia

The clinical signs of hypoglycaemia include irritability, twitching and convulsions.

If the baby's plasma glucose concentration is not low, hypocalcaemia or hypomagnesaemia, which present with similar signs, should be suspected.

Plasma calcium concentration, which at birth is higher (up to 3.00 mmol/L) than in healthy adults, falls rapidly and then rises to reach adult values by the third or fourth day of life.

This transient physiological hypocalcaemia is rarely symptomatic but tends to be exaggerated, and may be symptomatic, in preterm infants, infants born to mothers with diabetes and following birth asphyxia.

Hypocalcaemia occurring after first 2–3 days of life is uncommon.

Hypocalcaemia is a potential complication of exchange blood transfusion (clotting of donor blood is prevented by chelation of calcium ions) and can be prevented by giving calcium during transfusion.

Box 22.1 Causes of hypocalcaemia in infancy

high phosphate intake (unmodified cows' milk)
vitamin D deficiency
hypoparathyroidism including DiGeorge syndrome
pseudohypoparathyroidism
blood transfusion (exchange transfusion)
hypomagnesaemia
transient neonatal hypocalcaemia

Hypocalcaemia is often accompanied by hypomagnesaemia, and magnesium supplements should be given together with calcium in treating hypocalcaemia.

If magnesium is not given, hypocalcaemia is often resistant to treatment.

Isolated hypomagnesaemia is rare: it most frequently occurs in the infants of mothers with diabetes.

Jaundice

Most newborns become mildly jaundiced shortly after birth.

This 'physiological' jaundice is due to:

1. The immaturity of the hepatic conjugating enzymes
2. Normal postnatal haemolysis
3. Enterohepatic circulation of bilirubin (conversion of bilirubin to urobilinogen in the GUT cannot occur until the GUT becomes colonized with bacteria).

In **physiological jaundice**, the bilirubin is primarily unconjugated, and its plasma concentration rarely exceeds 100 μmol/L; the jaundice is never present at birth and does not persist beyond 14 days of life.

Physiological jaundice can be exacerbated by various factors that lead to bruising or a cephalohematoma:

- ⊗ Dehydration
- ⊗ Hypoxia
- ⊗ Prematurity
- ⊗ Breastfeeding
- ⊗ Birth trauma.

At high concentrations of unconjugated bilirubin (>340 μmol/L in a full-term newborn) there is a risk of **Brain damage (kernicterus) developing**

The risk is higher in premature infants. As unconjugated bilirubin is bound to albumin, the risk is greater if the plasma albumin concentration is decreased or bilirubin is displaced from albumin, **for example by hydrogen ions in acidosis, by certain drugs or by high concentrations of free fatty acids.**

Some conditions that should investigate neonatal jaundice!

☒ present at birth or appears during first 24 hours of life and persists beyond 14 days of life

☒ Total plasma bilirubin concentration >250 µmol/L

☒ conjugated hyperbilirubinaemia jaundice associated with other signs or symptoms of the disease.

Other causes of unconjugated hyperbilirubinaemia in the newborn:

Increased haemolysis

rhesus blood group incompatibility
ABO blood group incompatibility
red cell enzyme defects:
- glucose 6-phosphate dehydrogenase deficiency
- pyruvate kinase deficiency

Decreased conjugation

Crigler–Najjar syndrome
hypothyroidism
breast milk jaundice (a benign condition seen in some breast-fed infants and thought to be due to interference with bilirubin conjugation by free fatty acids and progesterone metabolites)

Inherited metabolic disorders

Conditions that may present, include disorders of amino acid, organic acid and carbohydrate metabolism, and urea cycle disorders.

Failure to thrive

Failure to thrive is a term used to describe the failure of infants to grow and develop normally.

It is a common paediatric problem and can be a consequence of any acute illness in neonates and more chronic conditions at any time in infancy:

- malnutrition
- malabsorption
- inherited metabolic diseases
- infection
- chronic diseases
  - renal
  - hepatic
  - pulmonary
  - cardiac
- psychosocial deprivation
- hypothyroidism
- hypopituitarism

Disorders of sex development and abnormal puberty

Precocious sex development, which may become apparent shortly afterbirth, is rare, Some causes:

Gonadotrophin dependent

idiopathic (particularly females)
pineal tumours, hypothalamic hamartomas
raised intracranial pressure (trauma, hydrocephalus)
cerebral palsy
cranial irradiation

Gonadotrophin independent[a]

congenital adrenal hyperplasia
adrenal tumours
ovarian and testicular tumours

[a]Also known as pseudoprecocious puberty.