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Medical Education

Developmental Milestones in Newborns: Adaptation to Extrauterine Life

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In the early phases of extrauterine life, the human body goes through various circulatory, thermoregulatory, renal, pulmonary, immune and metabolic adaptations to achieve proper function outside the protective environment of the womb. The process of birth lays significant challenges for the newborn.

Metabolic Changes

As soon as the **placental circulation** stops as a result of severed umbilical cord, the **glucose supply** to the infant through maternal blood ends. This leads to a fall in blood glucose levels immediately after birth. An infant has a low store of glycogen and insulin and increased glucagon.

Gluconeogenesis, **glycogenolysis**, **lipolysis,** and **ketogenesis** replace the processes of glycogenesis and lipogenesis right after birth. This results in a **metabolic switch from glucose to fat**. The newborn therefore has a diet initially higher in fats and lower in carbohydrates.

- **Mitochondrial** density increases as the **metabolic rate** increases, which occurs after birth.
- A surge in **catecholamine** and **glucagon** is observed in infants at birth which aims to maintain blood glucose levels after birth.

- Insulin levels are decreased to prevent hypoglycemia.
- Serum **cortisol** levels also peak at the time of delivery.
- **Renin-angiotensin** and **vasopressin** levels are also elevated after birth.
- There is **increased ketone body formation** in newborns.
- Increased chances of **hypothermia**, **hypoglycemia**, **hypoxia,** and **acidosis**
- **Relative hepatic maturity** is seen near six months after birth.
- **Thyroid hormones** also show a surge after birth in response to hypothermia and the cold extra-uterine environment.

Neurological Changes

Brain growth

- The brain of a newborn has a weight of 400 grams.
- By one year of age the weight increases to 1,000 grams.
- By two years, it is 80 percent of the size of the brain of an adult.
- By 18 years of life, an adult brain weighs 1,400 grams.

Myelination

The process of myelination begins in the **7th month of intrauterine life**. Myelination occurs most rapidly in the first two years after birth. The structures that are necessary for reflex behavior are myelinated first. These include:

- Motor-sensory roots
- Special senses
- The brainstem

The pattern for **axon myelination** also follows the cephalocaudal gradient of growth. The shortest axons of the corticospinal tract are myelinated first. Upper extremities and trunk axons myelinate next. The longest axons that are present in the lower extremities are the last to myelinate. The whole process **completes by 24 months** of age.

Cerebral hemisphere myelination

The areas that myelinate first in the cerebral hemisphere are:

- Posterior portion of the frontal lobes
- The parietal lobes
- Areas of the occipital lobes

The **frontal and temporal lobes** myelinate next. The **cerebrum** is mostly completed regarding myelination by the end of the second year of life. However, certain interconnections of associated cortex continue to myelinate until the second and third decades of life.

The right and the left cerebral hemispheres are myelinated at different rates, the left one is almost entirely developed in early childhood, while the right one continues to grow until 11 years of age. The left hemisphere is the predominant one in earlier stages of life. This explains why children can learn languages with ease.

Thermoregulation

A newborn comes from a warm intrauterine environment to the cold outer world. Right after birth, infants are wet and naked. They have a large surface area–to–mass ratio which results in **radiant heat loss**.

Neonates lack the ability to shiver and hence rely upon **non-shivering thermogenesis** that occurs in brown fat, the adipose tissue. It has a higher concentration of mitochondria that is designed to oxidize fatty acids and generate heat rapidly. Moreover, it has high vascularity, four-to-six times that of white adipose tissue, and high innervation. **Norepinephrine release** stimulates metabolism for adipose tissue. The subcutaneous adipose tissue decreases with age.

Thermoregulation is a critical physiologic phenomenon **influenced by prematurity, illness and environmental conditions**. The temperature in newborns increases during the day reaches its maximum by the evening and is low during night time. With growth and development, surface area–to–mass ratio decreases and therefore there is a decreased heat loss in cold environment and vice versa.

There are the following **circadian temperature variations**:

- Low nightly temperature for 1 to 3 months
- Rhythm with a lower degree of magnitude for 3 to 6 months
- Adult rhythm is achieved in 2-to-5 years of life

Sleep Changes

The average sleeping time decreases with age. Neonates spend **16-17 hours per day** sleeping. They can enter the **REM stage** of sleep cycle immediately upon falling asleep, and more than 50 percent of the sleep is REM contrary to less than 25 percent in adults. They can sleep for a duration of 4 hours at one time. Four- to five-month infants can sleep 8-to-10 hours at a time. By the age of 1 year, REM sleep drops to 40 percent.

For a child who is **2-to-5 years** of age, average sleep during the day drops to **10-12 hours**. It is at this age that the child begins to acquire **adult sleeping patterns** though they face **higher arousal rates** when compared to adults. REM sleep drops to 25 percent, as seen in adults. By this age, they have gained a **sleep cycle of 90 to 110 minutes**.

Hematological Changes

After birth, the newborn goes through various **circulatory changes** and **changes in oxygenation**. The increased oxygenation of the extra-uterine environment results in decreased **erythropoietin** production and subsequent decrease in **erythropoiesis** in the first month of life. This influences the **hematopoiesis**. Given below are the normal hemoglobin and hematocrit values:

- Newborn: 16.5 g/dl, Hct 50 %
- Early childhood: 12g/dl, Hct 36 %
- Late childhood: 13 g/dl, Hct 37—38 %
- Adult:
    - Males: 14—18 g/dl, Hct 40—54 %
    - Females: 12—16 g/dl Hct 37—47 %

Fetal hemoglobin is the main protein for oxygen transportation until 6 months of life. It has a greater affinity for oxygen binding, hence different from adult hemoglobin, giving the newborn an adequate supply of oxygen. The amount of fetal hemoglobin decreases with age. It is up to 85% of the total hemoglobin at birth and reduces to 2% of the total hemoglobin after 2 years of age.

Iron values:

- Newborns: 20—157 g/dl
- 6 weeks–3 years: 20—115g/dl
- 3–9 years: 20—141 g/dl
- 9–14 years: 21—151 g/dl
- 14–16 years: 20—181 g/dl
- Adults: 44—196 g/dl

Immunoglobulins:

The newborn acquires **passive immunity** from the mother. Immune factors produce IgG early and IgA, IgD, and IgE later in life. IgM is produced at birth. The table below shows the different values of immunoglobulins at various ages.

Age	IgG mg/dl	IgA mg/dl	IgM mg/dl
1–30 days	221-1031	1–19	12–117
1–6 months	195-794	1–59	9–212
1–3 years	507-1407	18–171	63–298
4–6 years	571–1550	47–231	64–298
18 years	632–2108	89–322	59–360

Cardiovascular Changes

There is a **redistribution of workload** between the right ventricle and the left ventricle after birth. These changes produce a **change in cardiac output**. The right ventricle ejects blood against a lower afterload, while the left ventricle has to eject blood against a high afterload. This results in **left ventricular hypertrophy**, mainly because of a faster rate of cell replication in the left myocardium.

Left ventricular dominance can be seen in the first 3—6 months of life. Both left and right ventricles, however, are equal in size by the age of 6—10 months. By 7 years, the left ventricle is once again larger than the right one. This is the adult relation. There is **increased P wave duration, RR interval and QRS duration** on an ECG. These changes disappear by the age of 6 and after that, the ECG is similar to that of an adult.

Heart size doubles by the age of 1 year. There is a 4-fold increase by the age of 5 and a 6-fold increase by 9 years of age. This rapid change in size is associated with **changes in height and weight**. **Pulse rate** decreases and the range becomes narrower with age. **Blood pressure** increases with age. It reaches the plateau by 17 years in females and 20 years in males.

	Infant	Adult
Heart rate	145 bpm	72 bpm
Stroke volume	9 ml/beat	70 ml/beat
Cardiac output	1.3 L/min	5.0 L/min

Pulmonary Changes

Potential obstructive issues and potential restrictive issues

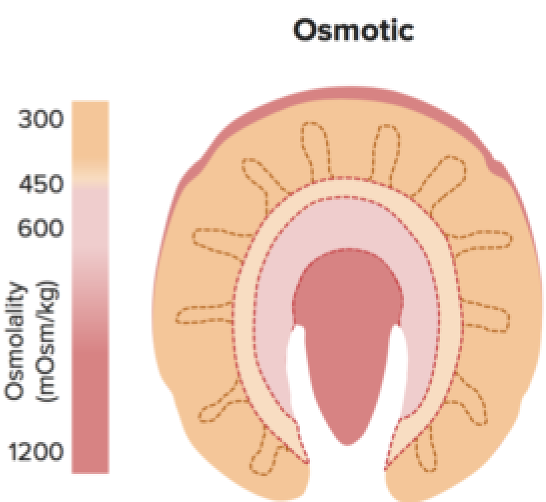
Lung volume values in infants are usually lower than in adults.

	Infants	Adults
Tidal volume	6 ml/kg	6 ml/kg
Residual volume	23 ml/kg	16 ml/kg
Total lung capacity	63 ml/kg	86 ml/kg
Functional residual capacity	30 ml/kg	34 ml/kg
Vital capacity	35 ml/kg	70 ml/kg

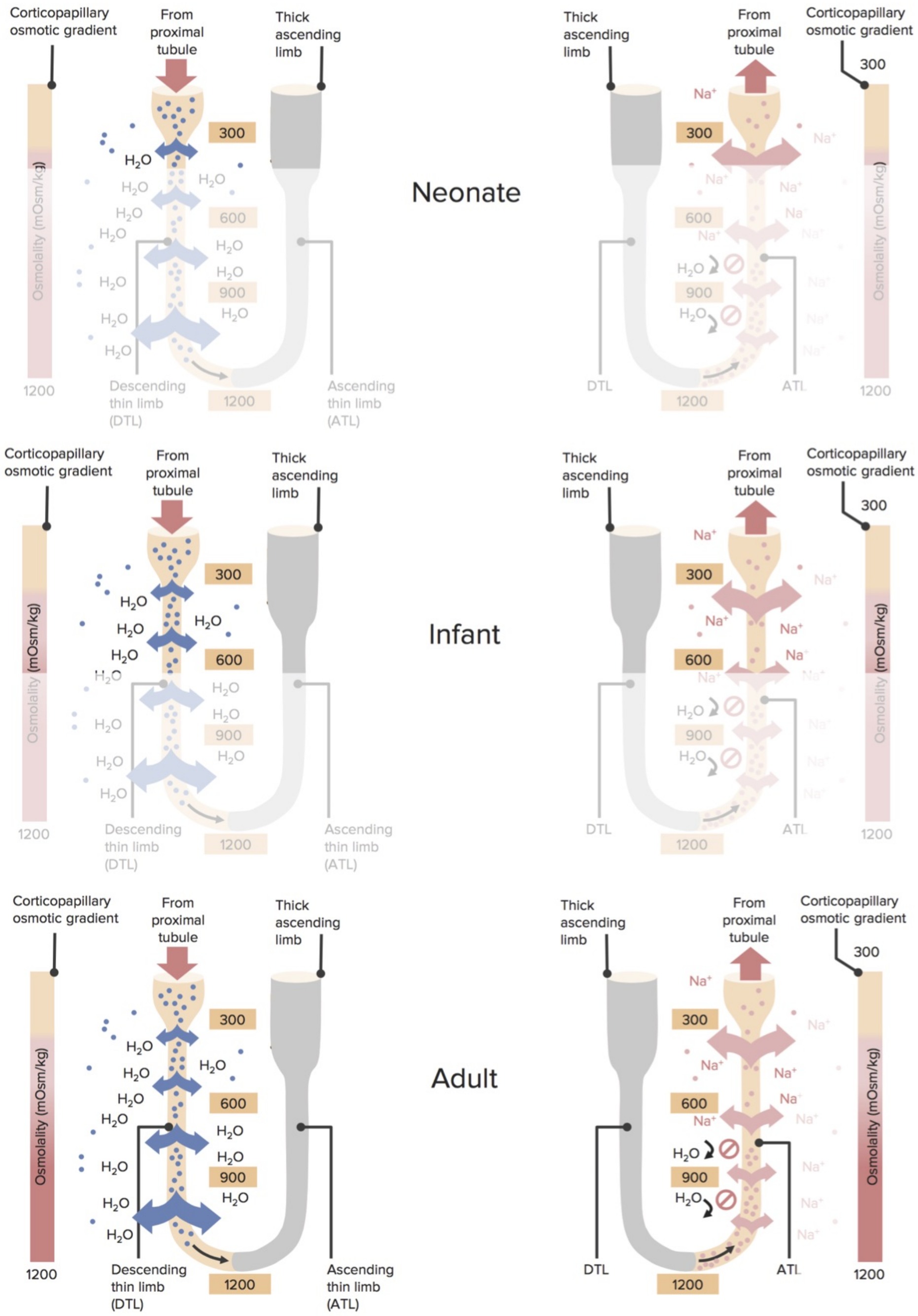
- **Oxygen consumption** in infants is 6—8 ml/kg/min which is higher than the 3—4 ml/kg/min in adults.
- **Respiratory rate** in infants is 35 bpm, and in adults, it is 15 bpm.
- **Closing volume** is higher in infants and decreases with age.
- Lower **diffusing capacity** of the lungs for carbon monoxide (DLCO)
- **Pulmonary function test** cannot be performed before 4 years of age. **Asthma** and other obstructive disorders are therefore difficult to diagnose.
- **Alveoli number** increases rapidly in the first 18 months, and the functional development continues until the first decade of life.
- There are potential obstructive and restrictive issues in newborns.
- There is a low amount of collagen in the lung matrix of a neonate. The **elastin-to-collagen ratio** increases with age. Over 6 years of age, lung recoil increases.
- **Compliance of lungs** increases to 150 % during the first year of life.
- **Chest wall compliance** decreases with age.
- **Rib's orientation** in infants is horizontal and changes to a downward direction by the age of 10.

Renal Changes

GFR at birth is low, rapidly rises over the first few weeks, and by the age of 2, it reaches adult levels. **Intravascular resistance** at birth is low along with **systemic blood pressure**. This reduces **kidney perfusion**. 15—20 % of the cardiac output goes to the infant's kidney, in contrast to 25 % in adults.



- GFR in neonates: 20 ml/min/1.73 m^2 with low urine concentration ability of 450 mOms
- GFR in infants: 35—45 ml/min/1.73 m^2 with low urine concentration ability of 600—700 mOms
- GFR in children 2 years of age: 90—110 ml/min/1.73 m^2



Acid-base balance and other substances

Up to 2 years, **potassium excretion**, **reabsorption of bicarbonate** and **H-ion buffer capacity** is low. This capability increases with age. **Bicarbonate levels** in neonates are 18—20 mEq/L while adults have 24—26 mEq/L bicarbonate. The adult level is reached within the first year of life. **Fractional excretion of sodium** (FENa) is as high as 5 % immediately after birth, contrary to 1 % in the adult.

Kidney maturation occurs rapidly in the first 6 months and is slower after that. Despite that it reaches adult maturation level in 2 years, children are more prone to injuries due to lower adaptation capacities.

Serum creatinine is an index of renal function in neonates and children. Its concentration is highest at birth with a rapid drop in the first 2 weeks. It stabilizes at 0.3—0.4 mg/dl in infancy. Little changes occur in the first 2 years of life, and after that, the serum creatinine level increases with increased muscle mass.

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Notes