Spotlight on hematology

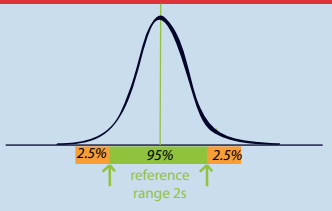
Reference Ranges in Hematology MQZH 2018-01

Introduction

For purposes of interpretation, patient lab results are compared with the respective reference ranges for the selected parameters. In everyday laboratory work, users often have little understanding as to where the utilized reference ranges originated because there are so many different sources for them (e.g. professional literature, values from external laboratories or companies). But how are these reference ranges determined and what are they hinged upon? Our current viewpoint 2018-01 is devoted to this topic in general and to the various, age-related changes in hematological reference ranges in particular.

What does the reference range represent??

A reference range (previously also called normal value) is determined by means of studies in a larger number of healthy people. For this, the respective parameter is determined for all persons of the reference group with the same method of measurement under the same, defined measurement conditions. The majority (95%) of those studied will obtain values around a central value. Each 2.5% of the studied values will receive slightly below or above this reference range. This can be depicted graphically with the Gaussian bell-shaped curve. From a statistical viewpoint, we find a value in laboratory analyses, which is slightly beyond the reference range, in approximately every 20th «healthy person».



The well-selected reference range

Well-selected reference ranges enable a proper assessment of the patient findings, thus improving the significance and reducing potential misinterpretations.

Among other things, they take the utilized test method as well as important patient-related influencing factors into account, which have an effect for a longer period or cannot be changed (e.g. age, sex, and ethnicity).

While the use of highly distinct, age-dependent, and sex-specific reference ranges are most often taken into account, we rarely take others, e.g. the ethnicity of the patient, into consideration. Going forward, however, it is likely that they will also gain in importance in our multi-ethnic society.

Contributing Factors

A number of factors influence patient lab results, including both technical and patient-related influencing variables:

Method-related	Which method of measurement is used? Be careful, e.g. when changing devices or tests.
Constant influencing variables	Sex, ethnicity («race»)
Long-term influencing variables	Age, pregnancy, eating habits, environmental influences, drugs, tobacco, and alcohol, geographic elevation.
Short-term influencing variables	Meals, circadian rhythms (daily fluctuations), body position, physical strain, stress.

Hematological Reference Ranges in Relation to Age

Physiological processes affect the variation of hematological parameters throughout life. Thus, partially substantial differences arise between newborns, children and youth, adults, and older persons over the age of 65.

Erythrocytes, Hemoglobin, and Hematocrit

The erythrocyte count increases within the first 24 hours of life («polycythemia of the newborn») and slowly decreases after two weeks. Improved oxygen saturation leads to sharply declining erythropoietin values (negative feedback). Together with the decreased erythrocyte lifespan of ECs in children (60-70 days), «physiological anemia» of the newborn occurs in the 8th – 12th week of life. Moreover, erythroblasts may be detectable in the periphery during the first days of life. During infancy and childhood, erythrocyte and hemoglobin counts still remain in part well below adulthood values, to which they only slowly begin to adapt during adolescence.

Slight shifts occur once again in older persons. Thus, the number of erythrocytes and the concentration of hemoglobin decrease slightly in men over the age of 65, while they normally remain constant or increase slightly in women. These effects are primarily due to hormonal changes (reduced androgen levels of men or reduced estrogen levels of women).

The hemocrit in newborns is likewise still well below the adult level. The EC mass percentage of the overall blood volume also depends on how much blood passes from the placenta to the child after birth (a delayed cutting of the child's cord increases, e.g. the blood volume). The hemocrit increases once again slightly during the first two days after birth to then continually decrease until the 4th month of life. Adult values are only reached in youth beginning at 12 years of age.

Erythrocytes and hemoglobin

green= reference range adults *pink= average values of the respective age group*

Hematocrit

green = reference range adults *pink= tendency of the values of the respective age group*

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Deviations of hematological parameters in various ethnicities

Tendency of value deviation with respect to the reference ranges of whites (Caucasians) from American studies:

African-Americans

↓ Hematocrit, hemoglobin, MCH, MCHC and leukocytes

Asians

↓ Hematocrit, hemoglobin, MCV, MCH, MCHC and mean platelet volume (MPV) and monocytes %.

↑ Eosinophils %, lymphocytes %, RDW

Here, it is also necessary to consider that differences must be expected due to various living conditions even when belonging to the same ethnicity.

This means, the more specific a reference group is analyzed for a country/region, the more reliable the reference ranges will be for the local populations.

Literature

The data from the graphics came from the following publication, in which the reference ranges of 7 Swiss central hospitals are compared:

Herklotz R, Lüthi U, Ottiger C, Huber AR. Ther Umsch. 2006 Jan;63(1):5-24

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Hematological Reference Ranges in Relation to Age

Erythrocyte Indices

The MCV of newborns is considerably increased compared to adults. Macrocytosis is due to fetal hemoglobin (HbF). After birth, the MCV begins to decrease within the first weeks of life and reaches the range for adults in approximately the ninth week of life. The MCV decreases once again between the third and fourth month of life and is then below the adult range, which it only reaches again during adolescence (> 15 years of age). Compared with adults, the RDW in newborns is likewise still considerably elevated, although it then continually decreases and reaches the reference range for adults in approximately the 6th month of life. From a morphological perspective, signs of hyposplenism, e.g. Howell-Jolly bodies, acanthocytes or spherocytes, appear in newborns.

MCV

green= reference range adults *pink= tendency of the values of the respective age group*

Leukocytes

Newborns typically demonstrate substantially higher leukocyte counts than adults. In the differentiation of the leukocytes, the percentage of banded neutrophils appears increased. Metamyelocytes and myelocytes may also be found. The leukocyte counts decrease until the end of the first year of life, although they remain above the reference range for adults throughout all of childhood and adolescence.
Neither the overall leukocyte count nor the proportions between neutrophils and lymphocytes change substantially in older persons. However, changes can be determined in the functionality of the neutrophils and lymphocytes. Thus, older people respond less severely to bacterial infections with neutrophilia, or leukocytosis, than younger adults.

Leukocytes total

green= reference range adults *pink= tendency of the values of the respective age group*

Lymphocytes

The absolute lymphocyte count is highest in newborns and steadily decreases in the course of development until adulthood. Youth - like our example H3A - still have high lymphocyte values. Furthermore, the lymphocytes demonstrate a great variability in pediatric patients, such that it is sometimes difficult to distinguish between normal and pathological forms.
Increasingly age-related defects are found in the lymphocytopoiesis of older persons, which cause changes in humoral and cellular immunity.

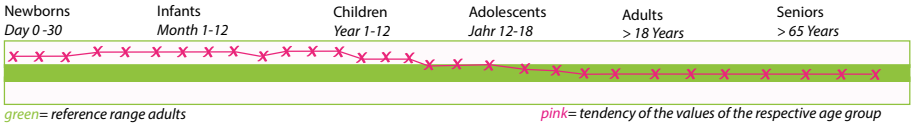
Neutrophils and lymphocytes

Neutrophils: blue= reference range adults/ dark blue = neutrophil counts age group
Lymphocytes: rose= reference range adults/ pink = neutrophil counts age group

Thrombocytes

The thrombocytes of newborns and infants are higher than those of adults. In addition, thrombocytes of newborns demonstrate a higher variability in size and shape. Slightly higher thrombocyte counts appear until adolescence. After this, the values adjust to adult levels.

Thrombocytes



green= reference range adults *pink= tendency of the values of the respective age group*