Complete Blood Count (CBC) Interpretation

WBCs are involved in protection against infective organisms and foreign substances and are produced in the bone marrow along with red blood cells and platelets. There are five main types of WBCs, as illustrated in Figure 5.1: neutrophils, eosinophils, basophils, lymphocytes, and monocytes. **Neutrophils** are the WBCs primarily responsible for killing and digesting bacteria. In neonates, and especially in preterm neonates, neutrophil chemotaxis (movement) is immature; in the face of serious bacterial infection, the neutrophils may not be capable of mounting an adequate response. The following discussion focuses on the neutrophil and how to calculate its concentration in the blood.

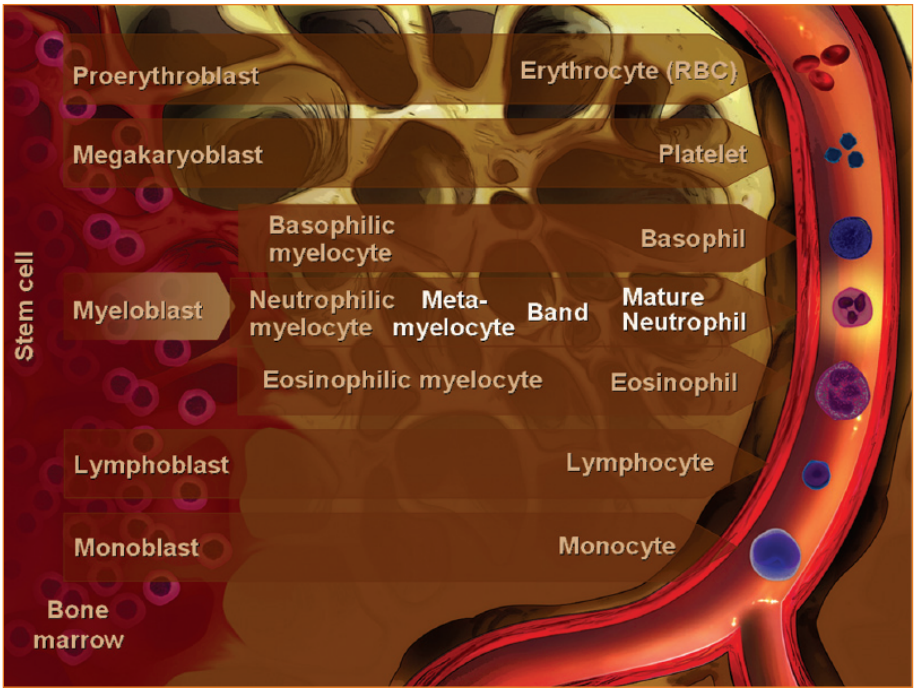


Figure 5.1. Blood cell development – from the bone marrow to the bloodstream. The stem cell differentiates into red blood cells, platelets, basophils, neutrophils, eosinophils, lymphocytes, and monocytes.

⚠ A neonate with sepsis may have a completely normal CBC and a normal CRP in the early phase of illness.[12,25] The time between the onset of the infection and the first change in the CBC may be as long as 4 to 6 hours. The time between the onset of the infection and elevation in the CRP may be as long as 8 to 12 hours. During this "latent" period, the neonate is infected, and needs antibiotic treatment, but has a normal CBC and a normal CRP.

Never withhold antibiotic treatment in an *ill* neonate on the sole basis that the CBC (or CRP) is normal.

Neutrophil Maturation

As shown in Figure 5.1, the neutrophil matures in the bone marrow, from the myeloblast, to the promyelocyte, to the myelocyte, to the metamyelocyte, to the band neutrophil, and finally to the mature **segmented neutrophil**. In the bone marrow, the metamyelocytes, band neutrophil, and segmented neutrophil comprise what is called the neutrophil storage pool (NSP). In neonates, the NSP is significantly smaller, per kilogram of body weight, than in adults; depletion of the NSP may occur with severe bacterial infection.[26,27] Under normal, non-infected, non-stressed, circumstances, mature segmented neutrophils are released from the NSP into the bloodstream where they circulate for a short period (6 to 8 hours) and then they migrate into the tissue where they live for approximately 24 hours.[28] In the presence of infection, immature forms of neutrophils – **bands and metamyelocytes** – are also released from the bone marrow into the blood stream as the body attempts to maximize the number of circulating neutrophils (illustrated in Figure 5.2). The term **left shift** refers to the appearance of immature neutrophils in the blood. The immature to total ratio (I/T ratio) calculation provides information about the proportion of immature to mature neutrophils in the blood. Interpretation of, and how to calculate the I/T ratio is discussed later in this module.

Clinical Tip

Mature and immature neutrophil terminology are as follows:

- Segmented (mature) neutrophils may also be referred to as polymorphonuclear neutrophil, polys, PMNs, segs, and neuts.
- Band neutrophils are also called bands, juveniles, or stabs.

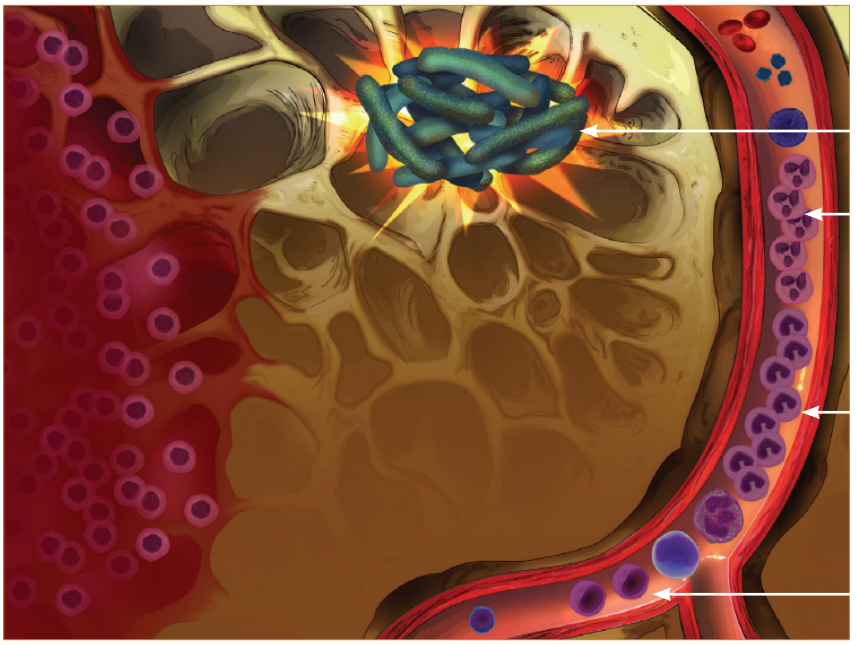


Figure 5.2. Bone marrow response to bacterial infection. In response to bacterial infection, the NSP released immature and mature neutrophils into the blood. Notice the increased numbers of band neutrophils and metamyelocytes with the appearance of a bacterial infection (Escherica coli bacteria is shown).

The Absolute Neutrophil Count (ANC)

When evaluating the CBC for possible sepsis, it is useful to know the concentration of neutrophils in the blood. The ANC calculation will provide this information. Repeating the CBC at 12 to 24 hour intervals may be useful since the initial CBC may be normal and subsequent CBC results abnormal. However, the decision to treat with antibiotics should be made quickly and must be based upon clinical history, patient condition and signs, and not solely on CBC results!

> ⚠ Remember, infection may still be present even if CBC results are normal. Conversely, abnormal CBC results do not always mean that an infant has an infection.[12,15,]

Why is it helpful to calculate the ANC?

The ANC may be helpful when evaluating an infant for potential bacterial infection. Normally, the WBC count and neutrophil count rise for the first day after birth. In term infants, the neutrophil count peaks at about 8 hours after birth. Therefore, a declining neutrophil count, rather than the expected physiologic rise in count, should raise concern that the infant may be infected.[21]

Most concerning are infants who have a **low ANC** for their postnatal age, because this can indicate depletion of the NSP, or that the infant is not going to be able to mobilize enough neutrophils necessary to fight a bacterial infection.[13,21] Exhaustion of the NSP is very serious for the newborn.

Neonates who deplete their neutrophil reserves while fighting infection are at highest risk of dying from sepsis.[29] It should be noted that infants born to mothers with hypertension may have a low ANC compared with infants whose mothers are not hypertensive.[26] This maternal history is important to consider when evaluating ANC results. Other infants with abnormal WBC counts include infants with Trisomy 13, 18, and 21.[30,31]

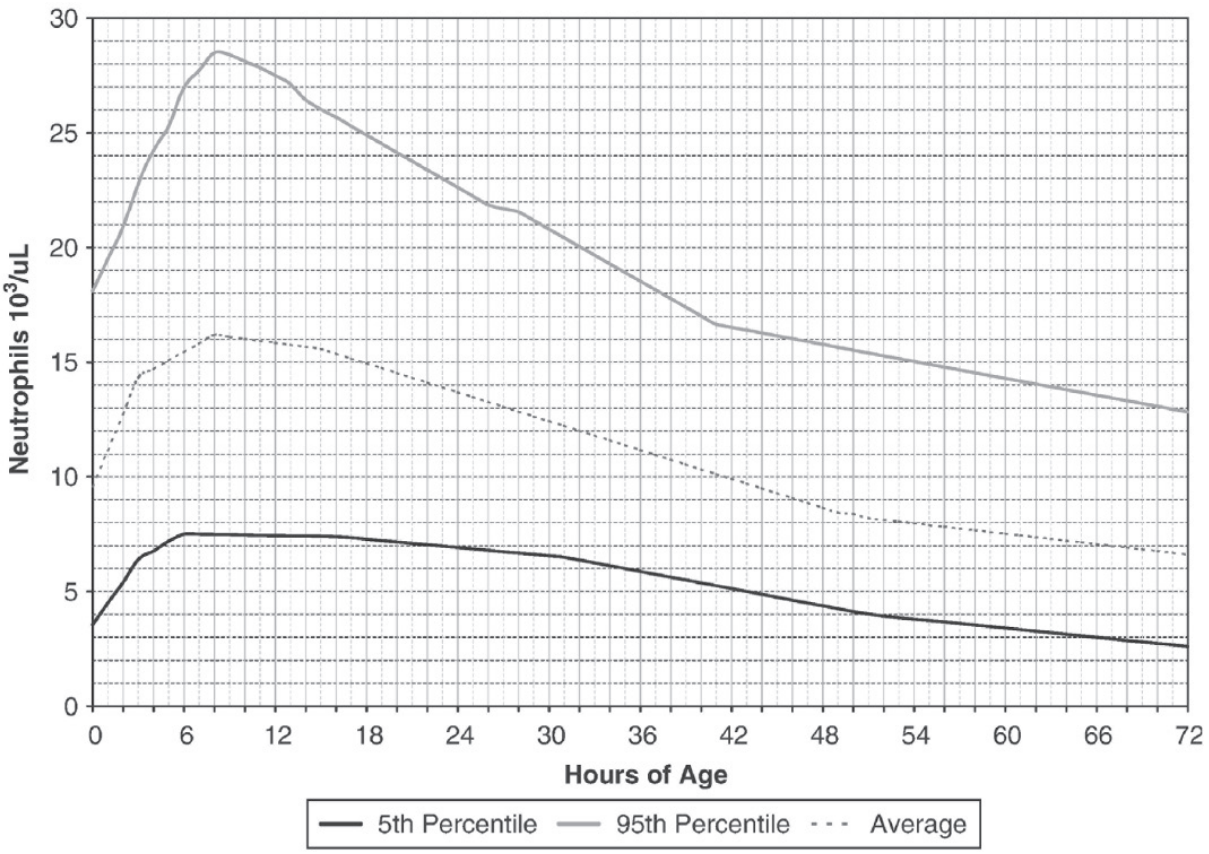
Neutrophil counts vary with age; preterm infants have a lower ANC than term infants because their circulating neutrophil concentration is lower prior to term gestation.[26,30,32] Figures 5.3, 5.4 and 5.5 are graphs that demonstrate the ANC (i.e., the blood neutrophil concentration) for infants > 36-weeks gestation, 28- to 36-weeks gestation and < 28 weeks gestation.[30]

Notes:

1. The peak ANCs reported in the study by Schmutz[30] are higher than the peak ANCs reported by Manroe.[33] This is attributed to either different methodology used to count the neutrophils, versus the effect of the higher altitude of the Intermountain region study hospitals (average 4800 feet above sea level), compared to Manroe's study, which was conducted in Dallas, Texas (500 feet above sea level).
2. A recent study by Hornik[13] of infants admitted to 293 neonatal intensive care units in the U.S. evaluated the association between the WBC count, ANC and immature-to-total (I/T) ratio to blood culture results and the likelihood that early-onset infection was present. A low WBC count, low ANC and elevated I/T ratio were associated with increased odds that an infection was present, whereas an elevated WBC count was not associated with increased odds of an infection being present. **For this reason, the S.T.A.B.L.E. Program recommends use of the ANC charts published by Schmutz.**[30]
3. It should be noted that in the Hornik study,[13] the CBC was not useful for predicting that infection was ***not*** present, which underscores the recommendation that antibiotics be started based on clinical history, patient presentation, signs, and not solely on CBC results.

⚠ When an infant's ANC falls into the neutropenic range for gestational age and postnatal age, the medical staff provider should be notified. Evaluation of risk factors, maternal pregnancy complications (i.e., pregnancy induced hypertension), clinical history, infant's presentation (current medical condition) and possibly follow up CBC (or additional) testing are recommended.

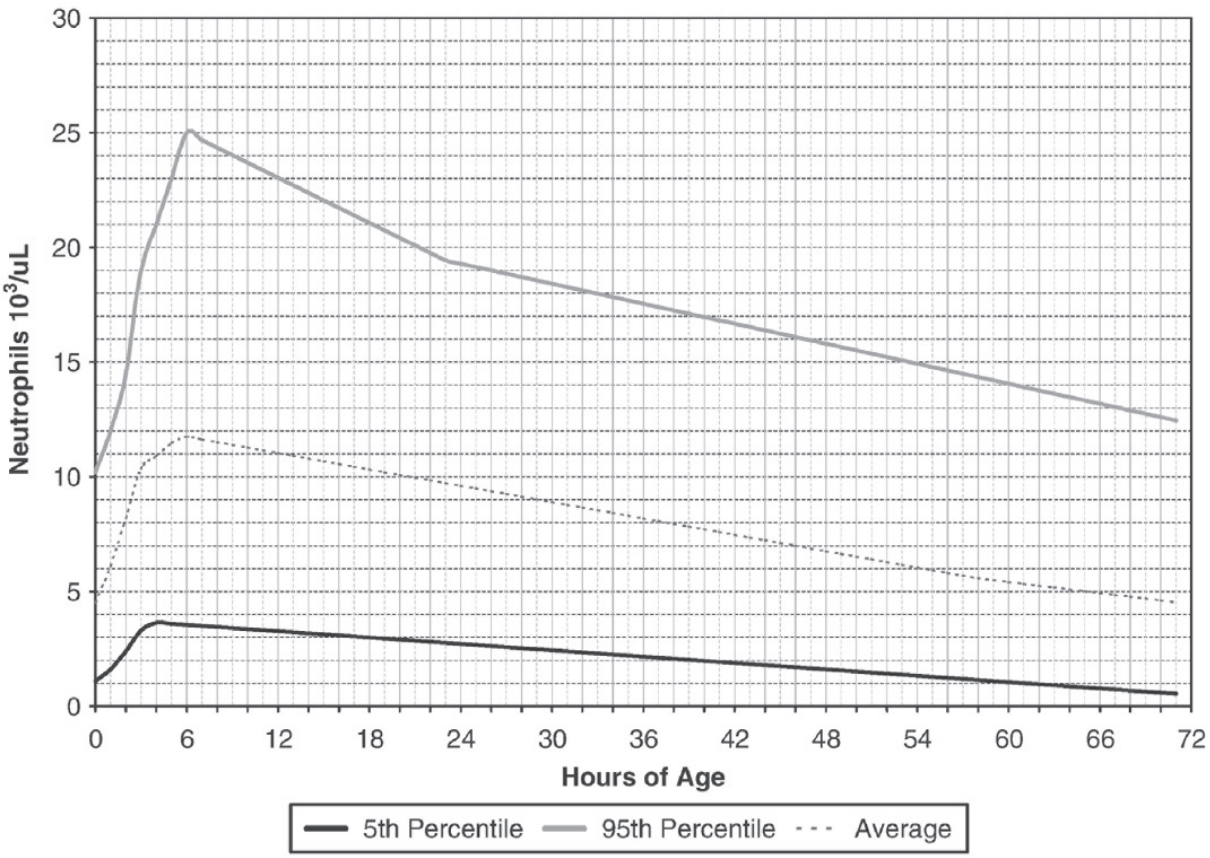
Figure 5.3. Graph represents the normal range for the ANC in infants > 36-weeks gestation in the first 72 hours of life.[30]



Notes (infants > 36 weeks):

1. Based on this data, at the time of birth, neutropenia would be defined as an ANC (or blood neutrophil concentration) less than 3500.
2. At 8 hours of life, in infants > 36 weeks' gestation, when the peak ANC occurs, neutropenia would be defined as an ANC less than 7500.
3. Data are based on 12,149 values that were analyzed using modern automated blood cell counting instrumentation.
4. Infants were excluded from the study if they had early-onset bacterial sepsis, congenital neutropenia, abnormally low or high neutrophil concentrations, trisomy 13, 18, or 21, or the mother had pregnancy induced hypertension.

Figure 5.4. Graph represents the normal range for the ANC in infants 28- to 36-weeks gestation in the first 72 hours of life.[30]

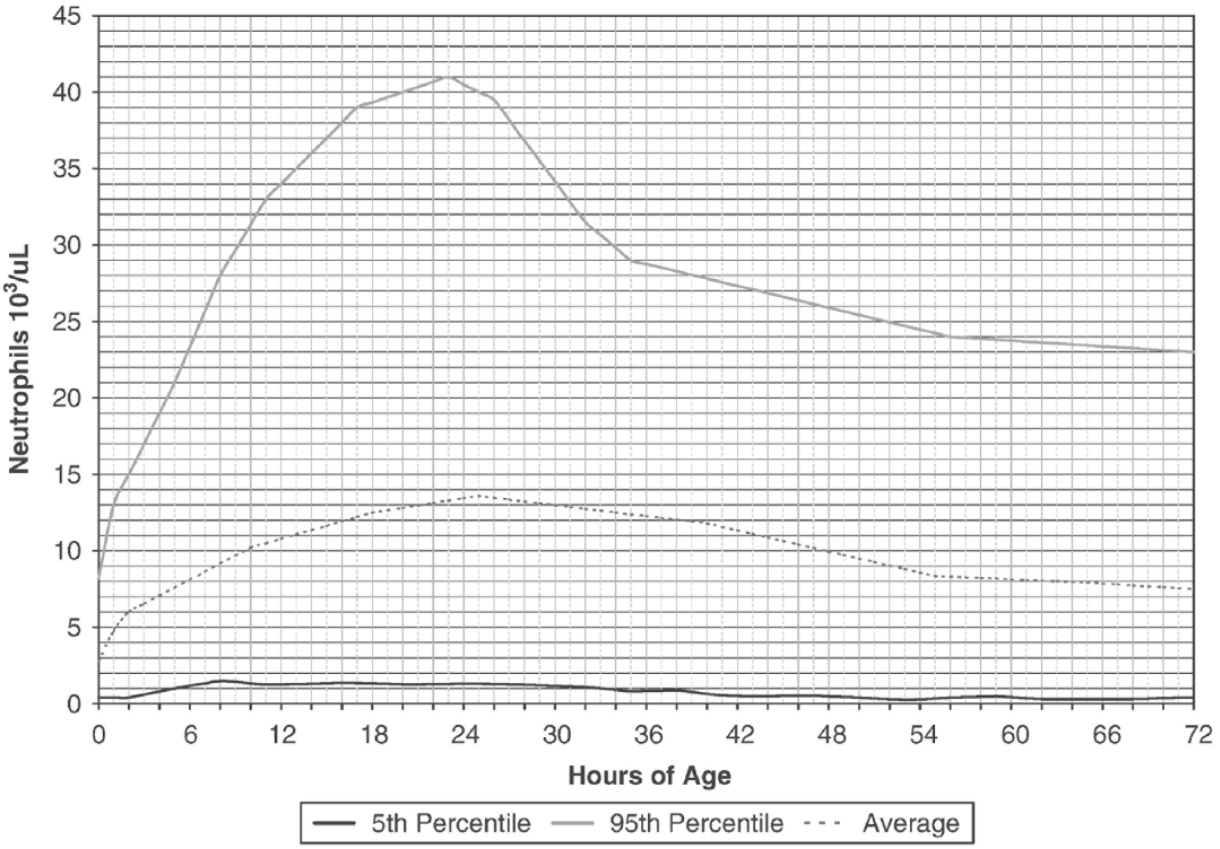


Notes (infants 28- to 36-weeks gestation):

1. Based on this data, at the time of birth, neutropenia would be defined as an ANC (or blood neutrophil concentration) less than 1000.
2. At 6 hours of life, when the peak ANC occurs, neutropenia would be defined as an ANC less than 3500.
3. Data are based on 8,896 values that were analyzed using modern automated blood cell counting instrumentation.
4. Infants were excluded from the study if they had early-onset bacterial sepsis, congenital neutropenia, abnormally low or high neutrophil concentrations, trisomy 13, 18, or 21, or the mother had pregnancy induced hypertension.

Reprinted by permission from Macmillan Publishers Ltd: Journal of Perinatology, Schmutz N, Henry E, Jopling J, Christensen RD. Expected ranges for blood neutrophil concentrations of neonates: the Manroe and Mouzinho charts revisited; Figure 2. 28:275-81, © 2008.

Figure 5.5. Graph represents the normal range for the absolute neutrophil count (ANC) in infants <28-weeks gestation in the first 72 hours of life.[30]



Notes (infants <28-weeks gestation):

1. Based on this data, at the time of birth, neutropenia would be defined as an ANC (or blood neutrophil concentration) less than 500.
2. At 24 hours of life, when the peak ANC occurs, neutropenia would be defined as an ANC less than 1500.
3. Data are based on 852 values that were analyzed using modern automated blood cell counting instrumentation.
4. Infants were excluded from the study if they had early-onset bacterial sepsis, congenital neutropenia, abnormally low or high neutrophil concentrations, trisomy 13, 18, or 21,[31] or the mother had pregnancy induced hypertension.

Which cells are included in the ANC calculation?

As mentioned earlier, the total white blood cell (WBC) count is comprised of neutrophils, eosinophils, basophils, lymphocytes, and monocytes. When calculating the ANC, only the total white blood cell count and the mature and immature neutrophils are included in the calculation. The non-neutrophil cell types (eosinophils, basophils, lymphocytes, and monocytes) are not included.

Understanding the calculation.

The neutrophils are a portion of the whole number of white blood cells. For example, a neutrophil count of "35" means 35 percent of the white blood cells are segmented neutrophils. A band count of "15" means 15 percent of the white blood cells are band neutrophils. Thus, 50% of the white blood cells in this scenario (35% segmented neutrophils plus 15% band neutrophils) are those primarily responsible for phagocytizing and killing bacteria. The remaining 50% of the white blood cells are a combination of eosinophils, basophils, lymphocytes, and monocytes, and are involved with other functions in the hematologic system.

Example ANC calculation.

To obtain the ANC, multiply the white blood cell count by the neutrophil count as shown in the following example.

History: a **term** infant was delivered to a mother with poor prenatal care and foul smelling amniotic fluid. At four hours of life, the infant developed respiratory distress (cyanosis, tachypnea and retractions) and hypothermia. A CBC, blood culture and blood gas were ordered and obtained when the infant was five hours old.

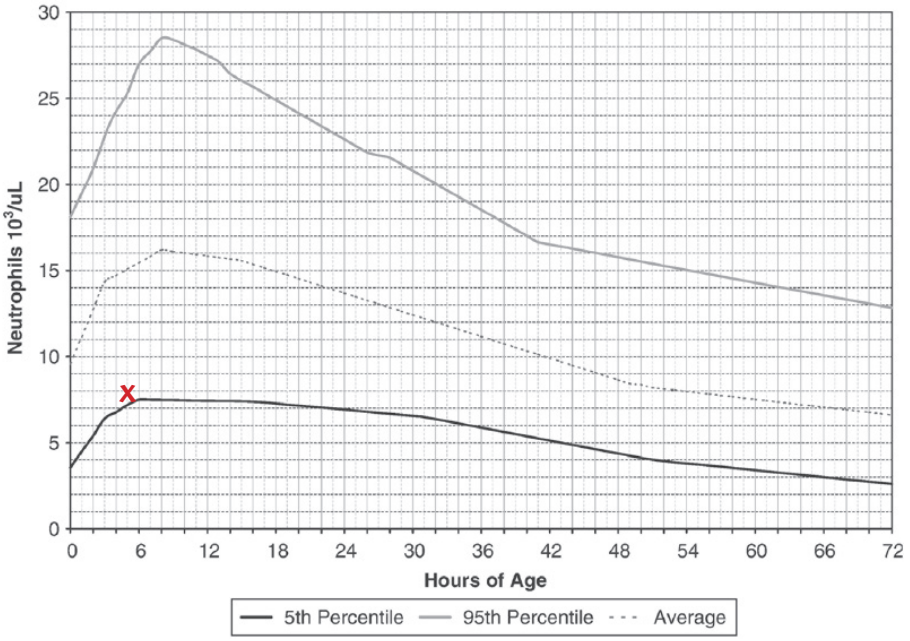
White Blood Cell Count (WBC)	**15,000 (15 x 10^3/µL)**
Segmented neutrophils (segs)	35 (%)
Band neutrophils (bands)	15 (%)
Metamyelocytes (metas)	3 (%)
Lymphocytes	42 (%)
Basophils	4 (%)
Eosinophils	1 (%)

Directions to calculate the ANC.

Identify the immature and mature neutrophils on the CBC (highlighted in blue). Add the segmented neutrophils, band neutrophils, and metamyelocytes together. Multiply this number by the total white blood cell count.

1) 35 segs + 15 bands + 3 Metas = 53 (percent)
   (i.e, 53% of the white blood cell types are neutrophils)
2) 15,000 multiplied by 0.53 = 7950
3) The ANC is 7950
4) Plot this number (7950) for a 5-hour-old infant on the chart appropriate for this gestational age.

This means that the total neutrophil concentration is 7950 which, when plotted on the Schmutz ANC chart, is within normal range for an infant of this gestation and age.



The Immature to Total (I/T) Ratio

Another calculation used to evaluate neutrophils is the immature-to-total ratio (I/T ratio). This calculation will reveal what proportion of the circulating neutrophils, released from the NSP in the bone marrow, are the immature forms. The I/T ratio is the most sensitive for estimating the risk that infection may be present.[13]

Why is it helpful to calculate the I/T ratio?

The majority of neutrophils that appear in the bloodstream should be mature cells, or segmented neutrophils. When more than 20 to 25% of the neutrophils in the blood are immature neutrophils, suspicion should increase that the infant is responding to a bacterial infection.[13,15]

Directions to calculate the I/T ratio.

Identify the immature neutrophil forms (metamyelocytes and band neutrophils), and add them together. Place this number as the numerator. Next, add the mature (segmented neutrophils) and immature neutrophils (metamyelocytes and band neutrophils) together and place this number as the denominator. Divide the immature by the total neutrophil count.

$$\frac{\text{Immature (I)}}{\text{Total (T)}} = \text{I/ T ratio}$$

Example I/T ratio calculation.

Using the previous CBC from the five-hour-old infant with respiratory distress and risk factors for sepsis, calculate the I/T ratio as follows:

White Blood Cell Count (WBC)	**15,000 (15 x 10^3/µL)**
Segmented neutrophils (segs)	35 (%)
Band neutrophils (bands)	15 (%)
Metamyelocytes (metas)	3 (%)
Lymphocytes	42 (%)
Basophils	4 (%)
Eosinophils	1 (%)

1) 15 bands + 3 metas = 18 (%) of the neutrophils are immature

2) 15 bands + 3 metas + 35 segs = 53 (%) of the WBCs

3) 18 divided by 53 = 0.34

18 / 53 = .34

4) The I/T ratio is 0.34

This means that **34 percent** of the neutrophil types are the **immature forms**. This should raise concern that the NSP in the bone marrow is responding to a bacterial infection by sending immature forms into the bloodstream before they have had time to fully mature.

I/T ratio > 0.20 raises index of suspicion for infection.[13]

I/T ratio > 0.8 correlated with a higher risk of death from sepsis.[29]