Meaning and interpretation of the CD57+ test

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CD57+ Natural Killer cells (NK cells): CD57 flow cytometry
CD3-/CD57+ T-Lymphocytes (CD = cluster of differentiation)

1. Subpopulation of the CD56+ NK cells
2. Reduction may be an indication of **chronic activity** of Lyme disease (symptoms > 1 year)
3. Reduction in untreated and inadequately treated Lyme disease
4. After the end of therapy for chronic Lyme disease: their normalization > 130 /ul represents therapeutic success
5. Not highly specific: Also low in other bacterial infections, esp. Chlamydia pneumonia and Mycoplasma pneumoniae

**Reference range**
- Lyme patient: < 130 /ul
- Healthy: > 130 /ul
Understanding the different markers and figures in the calculation

There are B lymphocytes and T lymphocytes; CD3 is the main marker for all T lymphocytes. The lower the overall CD3 figure, the fewer T helper cells you have; the higher, the better your T cell immune population.

Natural killer cells are T cells, not B cells. CD3+ are the mature T lymphocytes; CD56 are all the mature NK cells. CD57 is a subset of the CD56 cells: CD57 are also mature NK cells.

We always want to know the absolute number, the percentage is just for the calculation: clinical interpretation has to be done on the absolute number.

In order for a lab to measure the CD57+ NK level, it first measures the percentage of lymphocytes that are CD57+ NK cells. Then an absolute count is calculated by multiplying that percentage by the patient’s total lymphocyte count.

The minimum range is 100, but between 100 and 130 is considered borderline. CD57+ provides an indirect measure of bacterial load and severity of illness.

Source (partly, rest Dr. Schwarzbach): Ginger Saveley PhD, http://www.publichealthalert.org/everything-you-always-wanted-to-know-about-the-cd-57-test-but-were-too-sick-to-ask.html
CD57 is a stable marker of human natural killer (NK) cell subsets

Low CD57 count: Laboratory test report

### CD3-/CD57+ Cells

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>Reference Range</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>5 CD3-/CD56+ Flow Cytometry</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 T cells CD3+ (%)</td>
<td>82.18 %</td>
<td>62.00 - 80.00</td>
<td>[ ........... *]</td>
</tr>
<tr>
<td>5 T cells CD3+ (absolute)</td>
<td>1225 /ul</td>
<td>900 - 1900</td>
<td>[ ........... ]</td>
</tr>
<tr>
<td>5 NK cells CD56+ CD3- (%)</td>
<td>4.75 %</td>
<td>6.00 - 29.00</td>
<td>&lt;*&gt; ..........</td>
</tr>
<tr>
<td>5 NK cells CD56+ CD3- (absolute)</td>
<td>71 /ul</td>
<td>60 - 700</td>
<td>[ .......... ]</td>
</tr>
<tr>
<td>5 CD57+ NK-cells (%)</td>
<td>18.27 %</td>
<td>2.00 - 77.00</td>
<td>[ .......... ]</td>
</tr>
<tr>
<td>5 CD57+ NK-cells (absolute)</td>
<td>13 /ul</td>
<td>100 - 360</td>
<td>&lt;*&gt; ..........</td>
</tr>
</tbody>
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The result of the CD57-cell count indicates chronic immune-suppression, which can be caused by *Borrelia burgdorferi* or other bacteria like *Chlamydia pneumoniae* or *Mycoplasma pneumoniae*. 
Decreased CD57+ subset in chronic Lyme Disease

“All 31 chronic LD patients who were tested prior to antibiotic treatment had significantly decreased CD57 lymphocyte counts (mean, 30±16 cells per μl; normal, 60–360 cells per μl, P<0.001).”
Changes in the CD57+ count have particularly been observed in patients with neurological symptoms.

Patients with chronic LD and predominant neurologic symptoms had significantly lower mean CD57 levels than patients with predominant musculoskeletal symptoms (30±21 vs. 58±37 cells per μl, P=0.002). CD57 levels increased in chronic LD patients whose symptoms improved, while patients with refractory disease had persistently low CD57 counts.

Conclusions: A decrease in the CD57 lymphocyte subset may be an important marker of chronic LD. Changes in the CD57 subset may be useful to monitor the response to therapy in this disease.

The CD57 lymphocyte subset appears to be a useful marker of long-term infection with the Lyme disease spirochete.

(Stricker, Burrascano, 2002)
CD57+ numbers tend to rise in patients with viral burdens ...

“Chronic viral infections such as HCMV (104), human immunodeficiency virus (HIV) (105), hepatitis C virus (106), and Epstein–Barr virus (EBV) (107) infections offer some of the clearest examples of expansion of CD57+CD8+ T cells, presumably as a result of persistent antigenic stimulation”

“Similar skewing of NK cells toward the CD57+ phenotype is now reported in a variety of viral infections”

Historically, human NK cells have been identified as CD3−CD56+CD16− lymphocytes. More recently it has been established that CD57 expression defines functionally discrete sub-populations of NK cells. CD57 expression has been regarded as a marker of terminal differentiation and (perhaps) senescence. Similarly, CD57 expression seems to identify the final stages of peripheral maturation; its expression increases with age and is associated with chronic infections, particularly cytomegalovirus infection. However, CD57+ NK cells are highly cytotoxic and their presence seems beneficial in a number of non-communicable diseases. The purpose of this article is to review our understanding of CD57 expression as a marker of NK cell function and disease prognosis, as well as to outline areas for further research.

Keywords: CD57, NK cells, HCMV infection, ageing, chronic infection, cancer, autoimmune diseases, T cells

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3856678/
... whereas the CD3+ count tends to be low

There is also one sign for a viral infection, this can be seen with the low CD3+ cells, which should be looked at with CMV-Elispot, EBV-Elispot, HSV 1/2-Elispot, VZV-antibodies, Coxsackie Virus antibodies.
A high absolute CD3+ count can mean general T-cell stimulation

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3856678/table/T2/

High absolute CD3+ T cells can be sign of general T-cell stimulation – herbs such as teasel root can do this. T cells can also be higher in autoimmune disorders; allergies and parasites can also stimulate them.
Joe Burrascano: CD57+ a “breakthrough in Lyme Borreliosis diagnosis”

"Our ability to measure CD-57 represents a breakthrough in LB diagnosis and treatment. Chronic LB infections are known to suppress the immune system and decrease the quantity of the CD-57 subset of natural killer cells. As in HIV infection, where abnormally low T-cell counts are routinely used as a marker of how active that infection is, in LB we can use the degree of decrease of the CD-57 count to indicate how active the Lyme infection is and whether, after treatment ends, a relapse is likely to occur. It can even be used as a simple inexpensive screening test, because at this point we believe that only Borrelia (Lyme bacteria) will depress the CD-57. Thus a sick patient with a high CD-57 is probably ill with something other than Lyme, such as co-infections.”

Literature

- Nielsen et al. Functional significance of CD57 expression on human NK cells and relevance to disease; Front Immunol. 2013 Dec 9;4:422