
Meaning and interpretation of the CD57+ test

Armin Schwarzbach PhD

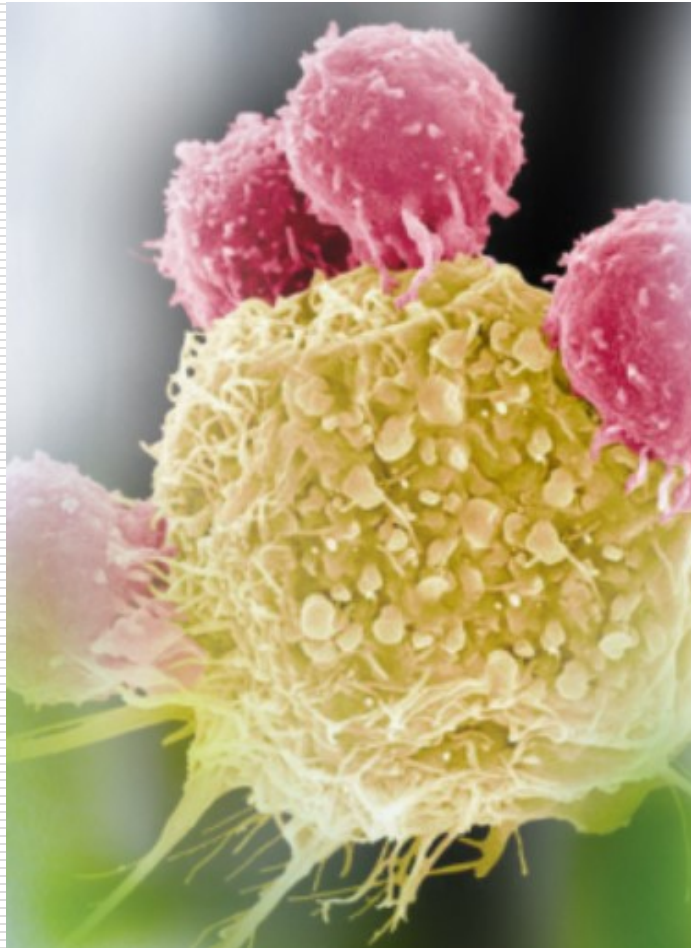
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CD57+ Natural Killer cells (NK cells): CD57 flow cytometry



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

6 CD3-/CD56+ Flow Cytometry				
6 T cells CD3+ (%)	76,09 %	62,00 - 80,00	[.....*]	
6 T cells CD3+ (absolute)	1292 /ul	900 - 1900	[...*....]	
6 NK cells CD56+ CD3- (%)	11,20 %	6,00 - 29,00	[.*.....]	
6 NK cells CD56+ CD3- (absolute)	190 /ul	60 - 700	[.*.....]	
6 CD57+ NK-cells (%)	14,83 %	2,00 - 77,00	[.*.....]	
6 CD57+ NK-cells (absolute)	- 28 /ul	100 - 360	<*	

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*.

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.

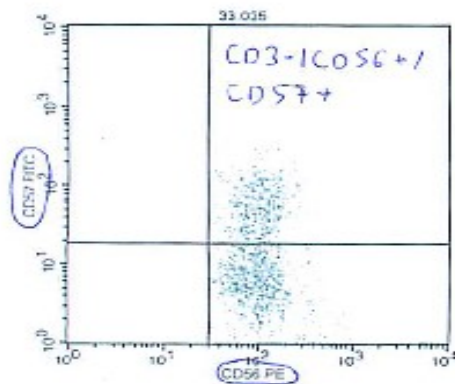
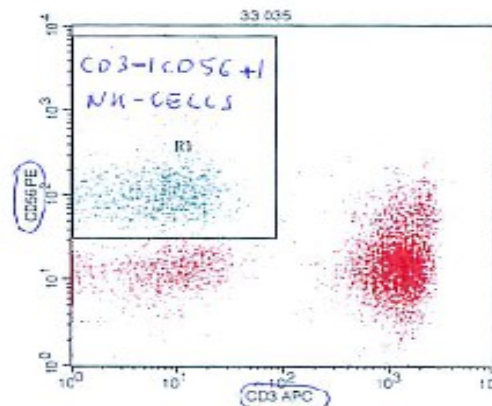
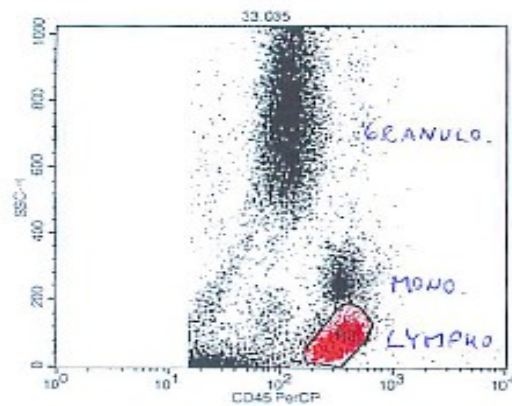
Source (partly, rest Dr. Schwarzbach): Ginger Saveley PhD, <http://www.publichealthalert.org/everything-you-always-wanted-to-know-about-the-cd-57-test-but-were-too-sick-to-ask.html>

CD57 is a stable marker of human natural killer (NK) cell subsets

Messung der CD57+ NK Zellen

Sample ID: 33
Acquisition Date: 09-Feb-11

Patient ID: 12171428



Gate: Lymphos

Gate	Events	% Gated
Lymphos	6720	100.00
NK Zellen	1208	17.98

NK-Zellen % = 17.98 %LY

CD57+ NK-Zellen %NK = 33.69 %NK Zellen

CD57+ NK Zellen %LY = 6.06 %LY

Source: Differential activation of CD57-defined natural killer cell subsets during recall responses to vaccine antigens. White MJ, Nielsen CM, McGregor RH, Riley EH, Goodier MR - Immunology (2014)

Low CD57 count: Laboratory test report

CD3-/CD57+ Cells

5 CD3-/CD56+ Flow Cytometry

5 T cells CD3+ (%)	+	82,18 %	62,00 - 80,00	[..... *>
5 T cells CD3+ (absolute)		1225 /ul	900 - 1900	[..*.....]
5 NK cells CD56+ CD3- (%)	-	4,75 %	6,00 - 29,00	<*]
5 NK cells CD56+ CD3- (absolute)		71 /ul	60 - 700	[*.....]
5 CD57+ NK-cells (%)		18,27 %	2,00 - 77,00	[.*.....]
5 CD57+ NK-cells (absolute)	-	13 /ul	100 - 360	<*]

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



Immunology Letters

Volume 76, Issue 1, 1 February 2001, Pages 43-48



Decreased CD57 lymphocyte subset in patients with chronic Lyme disease

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Abstract

Background: Chronic Lyme disease (LD) is a debilitating illness caused by tickborne infection with the spirochete *Borrelia burgdorferi*. Although immunologic abnormalities appear to play a role in this disease, specific immunologic markers of chronic LD have not been identified. **Methods:** We evaluated 73 patients with chronic LD for lymphocyte subset abnormalities using flow cytometry. Of these, 53 patients had predominant musculoskeletal symptoms, while 20 patients had predominant neurologic symptoms. The estimated duration of infection ranged from 3 months to 15 years, and all patients had positive serologic tests for *B. burgdorferi*. Ten patients with acute LD (infection less than 1 month) and 22 patients with acquired immunodeficiency syndrome (AIDS) served as disease controls. **Results:** 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 , $P < 0.001$). Nineteen of 37 patients (51%) who were tested after initiating antibiotic therapy had decreased CD57 levels (mean, 66 ± 39 cells per μl), and all five patients tested after completing antibiotic treatment had normal CD57 counts (mean, 173 ± 98 cells per μl). In contrast, all 10 patients with acute LD and 82% of AIDS patients had normal CD57 levels, and the difference between these groups and the pre-treatment patients with chronic LD was

“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



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“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)**

decreased CD57 lymphocyte counts (mean, 66±19 cells per µl, normal, 60–100 cells per µl, P<0.001). Nineteen of 37 patients (51%) who were tested after initiating antibiotic therapy had decreased CD57 levels (mean, 66±39 cells per µl), and all five patients tested after completing antibiotic treatment had normal CD57 counts (mean, 173±98 cells per µl). In contrast, all 10 patients with acute LD and 82% of AIDS patients had normal CD57 levels, and the difference between these groups and the pre-treatment patients with chronic LD was

CD57+ numbers tend to rise in patients with viral burdens ...



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PMCID:

Functional Significance of CD57 Expression on Human NK Cells Relevance to Disease

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Abstract

Go to:

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 wrong) anergy and senescence. Similarly, CD57 expression seems to identify the final stages of peripheral T cell 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 current 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/>

“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”

... whereas the CD3+ count tends to be low

CD 57 Flow Cytometry

T cells CD3 + (%)	76.58	%	62-80
T cells CD3 + (absolute)	- 659	/ul	900-1900
NK cells CD56+CD3- (%)	16.91	%	6-29
NK cells CD56+CD3- (absolute)	146	/ul	60-700

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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

CD3-/CD57+ cells

5 CD3-/CD56+ Flow Cytometry				
5 T cells CD3+ (%)	+	79,00 %	69,00 - 74,00	[..... *>
5 T cells CD3+ (absolute)	+	2773 /ul	1000 - 2200	[..... *>
5 NK cells CD56+ CD3- (%)		8,52 %	6,00 - 29,00	[*......]
5 NK cells CD56+ CD3- (absolute)		299 /ul	60 - 700	[..*.....]
5 CD57+ NK-cells (%)		22,56 %	2,00 - 77,00	[..*.....]
5 CD57+ NK-cells (absolute)	-	67 /ul	100 - 360	<*]

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*.

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.

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

Joe Burrascano: CD57+ a “breakthrough in Lyme Borreliosis diagnosis”

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TICK BORNE ILLNESSES

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JOSEPH J. BURRASANO JR., M.D.

"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."

Source: Dr. Burrascano's Lyme Disease treatment guidelines <http://www.lymenet.org/BurrGuide200810.pdf>

Literature

- Stricker RB, Winger EE. Normalization of the CD57 natural killer cell subset associated with prolonged antibiotic therapy in patients with chronic Lyme disease. *Clin Immunol* (2002) 103, 117–8.
- Stricker RB, Winder EE. Decreased CD57 lymphocyte subset in patients with chronic Lyme disease. *Immunology Letters* 76 (2001) 43-48
- Stricker RB, Burrascano JJ, Winger EE. Longterm decrease in the CD57 lymphocyte subset in a patient with chronic Lyme disease. *Ann Agric Environ Med* 2002, 9, 111-113
- Sincovics JG, Horvarth JC., Human natural killer cells: A comprehensive review. *International Journal of Oncology* (2005) 27, 5-47
- Focosi D, Petrini M. CD57 Expression on Lymphoma Microenvironment As a New Prognostic Marker Related to Immune Dysfunction *Journal of Clinical Oncology*, (2007) 25, 10, 1289-1291 American Society of Clinical Oncology. DOI: 10.1200/JCO.2006.10.2251
- Focosi D., Bestagno M., Burrone O., Petrini M . (2010) CD57 T lymphocytes and functional immune deficiency . *Journal of Leukocyte Biology* Volume 87
- Nielsen et al. Functional significance of CD57 expression on human NK cells and relevance to disease; *Front Immunol*. 2013 Dec 9;4:422
- Alco et al Decreased Numbers of CD57+CD3- Cells Identify Potential Innate Immune Differences in Patients with Autism Spectrum Disorder; *in vivo* 30: 83-90 (2016)