MAYO CLINIC LABORATORIES

# Test Definition: CD4RT

CD4 T-Cell Recent Thymic Emigrants, Blood

## Overview

### Useful For

Evaluating thymic reconstitution in patients following hematopoietic cell transplantation, chemotherapy, immunomodulatory therapy, and immunosuppression

Evaluating thymic recovery in patients who are HIV-positive and on highly active antiretroviral therapy

Evaluating thymic output in patients with DiGeorge syndrome or other cellular immunodeficiencies

Assessing the naive T-cell compartment in a variety of immunological contexts (autoimmunity, cancer, immunodeficiency, and transplantation)

Identification of thymic remnants post-thymectomy for malignant thymoma or as an indicator of relapse of disease (malignant thymoma) or other contexts of thymectomy

### Testing Algorithm

For information see Newborn Screen Follow-up for Severe Combined Immunodeficiency Syndrome (SCID).

### Special Instructions

- Newborn Screen Follow-up for Severe Combined Immunodeficiency Syndrome (SCID)

### Method Name

Flow Cytometry

### NY State Available

Yes

## Specimen

### Specimen Type

Whole Blood EDTA

### Shipping Instructions

**Testing is performed Monday through Friday. Specimens not received by 4 p.m. (CST) on Friday may be canceled.**

**Samples arriving on the weekend and observed holidays may be canceled.**

Collect and package specimen as close to shipping time as possible. Ship specimen overnight in an Ambient Shipping Box-Critical Specimens Only (T668) following the instructions in the box.

It is recommended that specimens arrive within 24 hours of collection.

### Necessary Information

**Ordering healthcare professional name and phone number are required.**

### Specimen Required

**Supplies:** Ambient Shipping Box-Critical Specimens Only (T668)
**Container/Tube:** Lavender top (EDTA)
**Specimen Volume:** 3 mL
**Collection Instructions:** Send whole blood specimen in original tube. **Do not aliquot.**

### Specimen Minimum Volume

1.5 mL

### Reject Due To

| | |
|---|---|
| Gross hemolysis | Reject |
| Gross lipemia | Reject |

### Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| Whole Blood EDTA | Ambient | 48 hours | PURPLE OR PINK TOP/EDTA |

## Clinical & Interpretive

### Clinical Information

Naive T cells are generated in the thymus and exported to peripheral blood to form the peripheral T-cell repertoire. There is a decrease in naive T cells derived from the thymus with age due to age-related decline in thymic output. Recent thymic emigrants (RTE) typically refers to those populations of naive T cells that have not diluted their TREC (T-cell receptor excision circles) copies by homeostatic or antigen-driven cell division. Naive T cells can be long-lived in the periphery and postpuberty, and in adults, peripheral T-cell homeostasis is maintained by a balance of thymic output and peripheral T-cell expansion, this proportion changes with age. In infants and prepubertal children, the T-cell repertoire is largely maintained by thymic-derived naive T cells. RTE express TREC indicative of naive T cells derived from the thymus.(1) In the CD4 T-cell compartment, it has been shown that naive CD45RA+ T cells coexpressing CD31 had a higher frequency of TREC compared to T cells lacking CD31.(2) The higher proportion of TREC+ naive T cells indicate a more recent thymic ontogeny since TREC can be diluted by cell division (since they are extrachromosomal).

It has been shown that CD31+CD4+ T cells continue to possess a relatively higher proportion of TREC despite an age-related 10-fold reduction after the neonatal period.(3) CD4 RTE (CD31+CD4+CD45RA+) have longer telomeres and higher telomerase activity, which, along with the increased frequency of TREC positivity, suggests a population of T cells with low replicative history.(3) The same study has also shown that CD31+ CD4+ T cells are an appropriate cell population to evaluate thymic reconstitution in lymphopenic children post-hematopoietic cell transplant.(3) A Mayo study (unpublished) shows that the CD31 marker correlates with TREC-enriched T cells across the spectrum of age and

correlates with thymic recovery in adults after autologous hematopoietic cell transplantation.(4) CD31+ CD4 RTE have also been used to evaluate T-cell homeostatic anomalies in patients with relapsing-remitting multiple sclerosis.(5)

For patients with DiGeorge syndrome (DGS)-a cellular immunodeficiency associated with other congenital problems including cardiac defects, facial dysmorphism, hypoparathyroidism, and secondary hypocalcemia, and chromosome 22q11.2 deletion (in a significant proportion of patients)-measurement of thymic function provides valuable information on the functional phenotype, ie, complete DGS (associated with thymic aplasia in a minority of patients) or partial DGS (generally well-preserved thymic function seen the in the majority of patients). Thymus transplants have been performed in patients with complete DGS but are typically not required in partial DGS. There can be change in peripheral T-cell counts in DGS patients with age.(6)

### Reference Values

CD4 Absolute
Males
1 month-17 years: 153-1745 cells/mcL
18-70 years: 290-1,175 cells/mcL
Reference values have not been established for patients that are younger than 30 days of age.
Reference values have not been established for patients that are older than 70 years of age.

Females
1 month-17 years: 582-1630 cells/mcL
18-70 years: 457-1,766 cells/mcL
Reference values have not been established for patients that are younger than 30 days of age.
Reference values have not been established for patients that are older than 70 years of age.

CD4 RTE %
Males
1 month-17 years: 19.4-60.9%
18-25 years: 6.4-51.0%
26-55 years: 6.4-41.7%
> or =56 years: 6.4-27.7%
Reference values have not been established for patients that are younger than 30 days of age.
Reference values have not been established for patients that are older than 70 years of age.

Females
1 month-17 years: 25.8-68.0%
18-25 years: 6.4-51.0%
26-55 years: 6.4-41.7%
> or =56 years: 6.4-27.7%
Reference values have not been established for patients that are younger than 30 days of age.
Reference values have not been established for patients that are older than 70 years of age.

CD4 RTE Absolute
Males
1 month-17 years: 50.0-926.0 cells/mcL

18-70 years: 42.0-399.0 cells/mcL
Reference values have not been established for patients that are younger than 30 days of age.
Reference values have not been established for patients that are older than 70 years of age.

Females
1 month-17 years: 170.0-1007.0 cells/mcL
18-70 years: 42.0-832.0 cells/mcL
Reference values have not been established for patients that are younger than 30 days of age.
Reference values have not been established for patients that are older than 70 years of age.

## Interpretation

The absence or reduction of CD31+CD4 recent thymic emigrants (RTE) generally correlates with loss or reduced thymic output and changes in the naive CD4 T-cell compartment, especially in infancy and prepubertal children. The CD4RTE result must be interpreted more cautiously in adults due to age-related decline in thymic function and correlated with total CD4 T cell count and other relevant immunological data. CD4 RTE measured along with TREC (TRECS / T-Cell Receptor Excision Circles Analysis, Blood) provides a comprehensive assessment of thymopoiesis but should not be used in adults over the sixth decade of life as clinically meaningful information on thymic function is limited in the older population due to a physiological decline in thymic activity.

To evaluate immune reconstitution or recovery of thymopoiesis post-T-cell depletion due to post-hematopoietic cell transplant, immunotherapy, or other clinical conditions, it is helpful to systematically (serially) measure CD4RTE and TREC copies in the appropriate age groups.

## Cautions

The CD4 recent thymic emigrants (RTE) assay is likely to be most helpful when used along with measurement of T-cell receptor excision circles (TRECS / T-Cell Receptor Excision Circles Analysis, Blood) for appropriate correlation of thymic output, especially in context of T cell lymphopenia, post-hematopoietic cell transplant and other cellular or combined immunodeficiencies.

## Supportive Data

CD4 recent thymic emigrant (RTE) pediatric reference values (95% confidence intervals) were obtained by evaluating 90 healthy individuals, aged 1 month to 17 years. There was no significant age relationship for CD4 RTE. Gender relationships for CD4 RTE were significant at the 50th percentile (p< or =0.0001). Adult reference values (95% confidence intervals) were obtained by evaluating 168 healthy adults, aged 18 to 70 years. There were significant age relationships for CD4 RTE as % CD4 T-cells.

## Clinical Reference

1. Hassan J, Reen DJ. Human recent thymic emigrants-identification, expansion, and survival characteristics. J Immunol. 2001;167(4):1970-1976
2. Kimmig S, Przybylski GK, Schmidt CA, et al. Two subsets of naive T-helper cells with distinct T-cell receptor excision circle content in human adult peripheral blood. J Exp Med. 2002;195(6):789-794
3. Junge S, Kloeckener-Gruissem B, Zufferey R, et al. Correlation between recent thymic emigrants and CD31+ (PECAM-1) CD4 T-cells in normal individuals during aging and in lymphopenic children. Eur J Immunol. 2007;37(11):3270-3280
4. Dong X, Hoeltzle MV, Abraham RS. Evaluation of CD4 and CD8 recent thymic emigrants in healthy adults and children. Unpublished data 2008
5. Duszczyszyn DA, Beck JD, Antel J, et al. Altered naiveCD4 and CD8 T-cell homeostasis in patients with

relapsing-remitting multiple sclerosis: thymic versus peripheral (non-thymic) mechanisms. Clin Exp Immunol. 2006;143(2):305-313

6. Nain E, Kiykim A, Ogulur I, et al. Immune system defects in DiGeorge syndrome and association with clinical course. Scand J Immunol. 2019;90(5):e12809. doi:10.1111/sji.12809

## Performance

### Method Description

CD4 recent thymic emigrants are assessed in peripheral blood drawn in EDTA tubes. A panel of antibodies is used for the assay: CD3, CD4, CD31, CD45RA, and CD45RO, conjugated to various fluorochromes. The blood is incubated with the antibodies in the dark, followed by red blood cell lysis. Absolute counts are obtained using BD TruCount tubes. The sample is then centrifuged and resuspended in a paraformaldehyde solution for analysis on a flow cytometer.(Unpublished Mayo method)

### PDF Report

No

### Day(s) Performed

Monday through Friday

### Report Available

3 to 4 days

### Specimen Retention Time

4 days

### Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Superior Drive

## Fees & Codes

### Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

### Test Classification

This test was developed using an analyte specific reagent. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

### CPT Code Information

86356

## LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| CD4RT | CD4 RTE, Flow Cytometry | 65758-5 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 29535 | CD4 RTE Absolute | 24467-3 |
| 89504 | CD4 Absolute (cells/uL) | 24467-3 |
| 29536 | CD4 RTE % | 8123-2 |
| 29178 | Interpretation | 69052-9 |