Test Definition: CD4RT
CD4 RTE, Flow Cytometry

Overview

Useful For
Evaluating thymic reconstitution in patients following hematopoietic cell transplantation, chemotherapy, immunomodulatory therapy, and immunosuppression
Evaluating thymic recovery in HIV-positive patients 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 postthymectomy for malignant thymoma or as an indicator of relapse of disease (malignant thymoma) or other contexts of thymectomy

Testing Algorithm
See Newborn Screen Follow-up for Severe Combined Immunodeficiency Syndrome (SCID) in Special Instructions.

Special Instructions

Method Name
FlowCytometry

NY State Available
Yes

Specimen

Specimen Type
Whole Blood EDTA

Shipping Instructions
Specimens are required to be received in the laboratory weekdays and by 4 p.m. on Friday. Draw 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 draw.

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

Necessary Information
Ordering physician name and phone number are required.

Specimen Required
Supplies: Ambient Shipping Box-Critical Specimens Only (T668)

Container/Tube: Lavender top (EDTA)
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Specimen Volume 3 mL

Collection Instructions: Send specimen in original tube. Do not aliquot.

Specimen Minimum Volume
1.5 mL

Reject Due To

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<th>Condition</th>
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<tr>
<td>Gross hemolysis</td>
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<tr>
<td>Gross lipemia</td>
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Specimen Stability Information

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<tr>
<td>Whole Blood EDTA</td>
<td>Ambient</td>
<td>48 hours</td>
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Clinical and 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 (RTEs) typically refers to those populations of naive T cells that have not diluted their TREC copies (T-cell receptor excision circles) 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 and this proportion changes with age. In infants and prepubertal children, the T-cell repertoire is largely maintained by thymic-derived naive T cells. RTEs 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 RTEs (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 posthematopoietic 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 RTEs 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.

**Reference Values**

**CD4 ABSOLUTE**

**Males**

1 month-17 years: 153-1,745 cells/mcL

18-70 years: 290-1,175 cells/mcL

Reference values have not been established for patients that are <30 days of age.

Reference values have not been established for patients that are >70 years of age.

**Females**

1 month-17 years: 582-1,630 cells/mcL

18-70 years: 457-1,766 cells/mcL

Reference values have not been established for patients that are <30 days of age.

Reference values have not been established for patients that are >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 <30 days of age.

Reference values have not been established for patients that are >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 <30 days of age.
Reference values have not been established for patients that are >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 <30 days of age.
Reference values have not been established for patients that are >70 years of age.

Females

1 month-17 years: 170.0-1,007.0 cells/mcL
18-70 years: 42.0-832.0 cells/mcL

Reference values have not been established for patients that are <30 days of age.
Reference values have not been established for patients that are >70 years of age.

**Interpretation**

The absence or reduction of CD31+CD4 recent thymic emigrants (RTEs) 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 has to 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 RTEs measured along with TREC (TREC / T-Cell Receptor Excision Circles [TREC] 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 posthematopoietic 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 (TREC / T-Cell Receptor Excision Circles [TREC] Analysis, Blood) for appropriate correlation of thymic output, especially in context of T cell lymphopenia, posthematopoietic 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, ages 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, ages 18 to 70 years. There were significant age relationships for CD4 RTE as % CD4 T-cells.
Clinical Reference


Performance

Method Description
CD4 recent thymic emigrants are assessed in peripheral blood drawn in EDTA tubes and the test is performed as a single-tube assay. 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 RBC lysis. Absolute counts are obtained using BD TruCount tubes. The sample is then centrifuged and resuspended in a paraformaldehyde solution for analysis on a BD FACS Canto A or Canto II flow cytometer. The data analysis is performed using BD FACS Diva software.(Unpublished Mayo method)

PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Friday

Do not send specimen after Thursday. Specimen must be received by 10 a.m. on Friday.

Analytic Time
3 days

Maximum Laboratory Time
4 days

Specimen Retention Time
4 days

Performing Laboratory Location
Rochester

Fees and 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 Regional Manager. 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 U.S. Food and Drug Administration.

CPT Code Information
86356

LOINC® Information

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