Cefepime is a semisynthetic broad spectrum cephalosporin antibiotic for parental administration. It is indicated for treatment of pneumonia, neutropenia, urinary tract infection, skin and skin structure infections, and complicated intra-abdominal infections caused by Streptococcus pneumonia, Pseudomonas aeruginosa, Klebsiella pneumoniae, Enterobacter species, Escherichia coli, Proteus mirabilis, Staphylococcus aureus, Streptococcus pyogenes, or Bacteroides fragilis.

Cefepime is approximately 20% protein bound and has a small volume of distribution (0.2-0.4 L/kg) indicating that it does not distribute into deep tissues. Cefepime is metabolized by N-oxidation, but decreased hepatic function has little impact on excretion. Approximately 85% of administered cefepime is excreted in the urine as either parent drug or metabolites. The apparent elimination half-life is 1.5 hours. Compromised renal function significantly decreases the rate of elimination causing cefepime to accumulate. Distribution and elimination are similar in adults, children as young as 2 months, and geriatric patients.

Severe encephalopathy has been observed in renally impaired patients treated with high-dose cefepime. Patients present with prolonged confusion states: diffuse, rhythmic, nonreactive, triphasic, sharp waves on electroencephalogram (EEG). Symptoms disappear 1-2 days after discontinuation of the drug.

- Managing cefepime therapy in patients who have severely compromised renal function or are undergoing dialysis
- Guiding dose adjustment to ensure adequate coverage while avoiding high concentrations associated with toxicity
- Routine drug monitoring is not indicated for all patients because cefepime has a wide therapeutic index and demonstrates dose-dependent toxicity.

Blood serum concentration of cefepime correlates with dose (typically 0.5, 1.0, or 2.0 g administered intravenously every 12 hours).

- Expected peak serum concentrations (drawn 30 minutes after completion of infusion of an intravenous dose or 60 minutes after an intramuscular or oral dose) in adults:
  - After receiving a 0.5 g dose: 30-40 ug/mL
  - After receiving a 1.0 g dose: 70-90 ug/mL
  - After receiving a 2.0 g dose: 120-180 ug/mL

- Peak serum concentrations <30 ug/mL are likely to be ineffective and peak concentrations >180 ug/mL do not provide increased efficacy but may predispose the patient to toxicity
- Because cefepime’s half-life is short, trough concentrations are <10 ug/mL.

No significant cautionary statements

Cefepime, Serum

Method

Specimen Required: Draw blood in a plain, red-top tube(s). Spin down and send 1.0 mL of serum frozen in plastic vial. Serum for a peak level should be drawn 30 minutes after completion of infusion of an intravenous dose or 60 minutes after an intramuscular or oral dose of the antimicrobial to be assayed.

Reference Values: 30-180 ug/mL (Peak)

Analytic Time: Same day/1 day
Days Set Up: Monday through Saturday
Fee: $104.40
CPT Code: 82491
Pheochromocytoma is a rare, though potentially lethal, tumor of chromaffin cells of the adrenal medulla that produces episodes of hypertension with palpitations, severe headaches, and sweating (“spells”). Pheochromocytomas and other tumors derived from neural crest cells (eg, paragangliomas and neuroblastomas) secrete catecholamines (epinephrine and norepinephrine). Metanephrine and normetanephrine are the 3-methoxy metabolites of epinephrine and norepinephrine, respectively. Metanephrine and normetanephrine are both further metabolized to vanillylmandelic acid (VMA). Pheochromocytoma cells also have the ability to oxy-methylate catecholamines into metanephrines that are secreted into circulation. While screening for pheochromocytoma is best accomplished by measuring plasma free fractionated metanephrines (a more sensitive assay), follow-up testing with urinary fractionated metanephrines (a more specific assay) may identify false positives. Twenty-four hour urine collections are preferred, especially for patients with episodic hypertension; ideally the collection should begin at the onset of a “spell”.

Metanephrines, Fractionated, Random, Urine

#83005

Profile

- Pheochromocytoma is a rare, though potentially lethal, tumor of chromaffin cells of the adrenal medulla that produces episodes of hypertension with palpitations, severe headaches, and sweating (“spells”).
- Pheochromocytomas and other tumors derived from neural crest cells (eg, paragangliomas and neuroblastomas) secrete catecholamines (epinephrine and norepinephrine).
- Metanephrine and normetanephrine are the 3-methoxy metabolites of epinephrine and norepinephrine, respectively. Metanephrine and normetanephrine are both further metabolized to vanillylmandelic acid (VMA).
- Pheochromocytoma cells also have the ability to oxy-methylate catecholamines into metanephrines that are secreted into circulation.

Useful For

- A second-order screening test for the presumptive diagnosis of pheochromocytoma in patients with nonepisodic hypertension
- Confirming positive plasma metanephrine results in patients with nonepisodic hypertension

Interpretation

- Increased metanephrine/normetanephrine levels are found in patients with pheochromocytoma and other tumors derived from neural crest cells.
- Increased urine metanephrines can be detected in nonpheochromocytoma hypertensive patients; quantification may help distinguish these patients from those with tumor-induced symptoms.

Cautions

- Tricyclic antidepressants (TCA) and labetalol and sotalol (beta blockers) may elevate levels of metanephrines. If clinically feasible, these medications should be discontinued at least 1 week before collection.
- This test utilizes a high-performance liquid chromatography/tandem mass spectrometry (LC-MS/MS) method and is not affected by the interfering substances that affected the previously utilized spectrophotometric (Pisano reaction) method (ie, diatrizoate, chlorpromazine, hydrazine derivatives, imipramine, MAO inhibitors, methyldopa, phenacetin, ephedrine, or epinephrine).
- This method is also not subject to the known interference of acetaminophen (seen with the plasma metanephrine HPLC-EC method).

References

Method

Urinary metanephrines are determined by reverse phase LC-MS/MS stable isotope dilution analysis. Urinary metanephrines occur largely in conjugated form. After urine specimens are acidified and hydrolyzed for 20 minutes in a boiling water bath, metanephrine and normetanephrine are extracted from the specimens utilizing extraction cartridges. The metanephrine and normetanephrine are eluted from the cartridge using 20% methanol (MeOH) and analyzed by LC-MS/MS using multiple reaction monitoring in positive mode. Deuterated metanephrine (d[3]-metanephrine, 200 ng) and deuterated normetanephrine (d[3]-normetanephrine, 500 ng) are added prior to the hydrolysis as an internal standard. The following ion pairs are used for analysis: metanephrine, (180/148); normetanephrine, (166/134); d[3]-metanephrine, (183/151); d[3]-normetanephrine, (169/137). The metanephrine and normetanephrine concentrations are quantified using ratios of the peak areas to deuterium-labeled internal standards by LC-MS/MS. A calibration curve, generated from 20% MeOH spiked standards, is included with each batch of patient specimens. (Chan EC, Ho PC: High-performance liquid chromatography/atmospheric pressure chemical ionization mass spectrometric method for the analysis of catecholamines and metanephrines in human urine. Rapid Commun Mass Spectrom 2000;14:1959-1964; Sawka AM, Singh RJ, Young WF Jr.: False positive biochemical testing for pheochromocytoma caused by surreptitious catecholamine addition to urine. Endocrinologist 2001;11:421-423; Roden M, Raffesberg W, Raber W, et al: Quantification of unconjugated metanephrine in human plasma without interference by acetaminophen. Clin Chem 2001;47:1061-1067)

Specimen Required:
5.0 mL (pediatric: 2.0 mL) from a random urine collection. No preservative. Send specimen refrigerated in a plastic, 13-mL urine tube.

Reference Values:

**METANEPHRINE/CREATININE**
- Normotensives
  - 0-2 years: 82-418 μg/g creatinine
  - 3-8 years: 65-332 μg/g creatinine
  - 9-12 years: 41-209 μg/g creatinine
  - 13-17 years: 30-154 μg/g creatinine
  - ≥18 years: 29-158 μg/g creatinine

**NORMETANEPHRINE/CREATININE**
- Males: Normotensives
  - 0-2 years: 121-946 μg/g creatinine
  - 3-8 years: 92-718 μg/g creatinine
  - 9-12 years: 53-413 μg/g creatinine
  - 13-17 years: 37-286 μg/g creatinine
  - 18-29 years: 53-190 μg/g creatinine
  - 30-39 years: 60-216 μg/g creatinine
  - 40-49 years: 69-247 μg/g creatinine
  - 50-59 years: 78-282 μg/g creatinine
  - 60-69 years: 89-322 μg/g creatinine
  - ≥70 years: 102-367 μg/g creatinine
- Females: Normotensives
  - 0-2 years: 121-946 μg/g creatinine
  - 3-8 years: 92-718 μg/g creatinine
  - 9-12 years: 53-413 μg/g creatinine
  - 13-17 years: 37-286 μg/g creatinine
  - 18-29 years: 81-330 μg/g creatinine
  - 30-39 years: 93-379 μg/g creatinine
  - 40-49 years: 107-436 μg/g creatinine
  - 50-59 years: 122-500 μg/g creatinine
  - 60-69 years: 141-574 μg/g creatinine
  - ≥70 years: 161-659 μg/g creatinine

**TOTAL METANEPHRINE/CREATININE**
- Males: Normotensives
  - 0-2 years: 241-1272 μg/g creatinine
  - 3-8 years: 186-980 μg/g creatinine
  - 9-12 years: 110-582 μg/g creatinine
  - 13-17 years: 78-412 μg/g creatinine
  - 18-29 years: 96-286 μg/g creatinine
  - 30-39 years: 106-316 μg/g creatinine
  - 40-49 years: 117-349 μg/g creatinine
  - 50-59 years: 130-386 μg/g creatinine
  - 60-69 years: 143-427 μg/g creatinine
  - ≥70 years: 159-472 μg/g creatinine
- Females: Normotensives
  - 0-2 years: 241-1272 μg/g creatinine
  - 3-8 years: 186-980 μg/g creatinine
  - 9-12 years: 110-582 μg/g creatinine
  - 13-17 years: 78-412 μg/g creatinine
  - 18-29 years: 131-467 μg/g creatinine
  - 30-39 years: 147-523 μg/g creatinine
  - 40-49 years: 164-585 μg/g creatinine
  - 50-59 years: 184-655 μg/g creatinine
  - 60-69 years: 206-733 μg/g creatinine
  - ≥70 years: 230-821 μg/g creatinine
Metanephrines, Fractionated, 24-Hour, Urine

#83006

Clinical

- Pheochromocytoma is a rare, though potentially lethal, tumor of chromaffin cells of the adrenal medulla that produces episodes of hypertension with palpitations, severe headaches, and sweating ("spells").
- Pheochromocytomas and other tumors derived from neural crest cells (eg, paragangliomas and neuroblastomas) secrete catecholamines (epinephrine and norepinephrine).
- Metanephrine and normetanephrine are the 3-methoxy metabolites of epinephrine and norepinephrine, respectively. Metanephrine and normetanephrine are both further metabolized to vanillylmandelic acid (VMA).
- Pheochromocytoma cells also have the ability to oxy-methylate catecholamines into metanephrines that are secreted into circulation.
- While screening for pheochromocytoma is best accomplished by measuring plasma free fractionated metanephrines (a more sensitive assay), follow-up testing with urinary fractionated metanephrines (a more specific assay) may identify false positives. Twenty-four hour urine collections are preferred, especially for patients with episodic hypertension; ideally the collection should begin at the onset of a "spell".

Useful For

- A second-order screening test for the presumptive diagnosis of pheochromocytoma
- Confirming positive plasma metanephrine results

Interpretation

- Increased metanephrine/normetanephrine levels are found in patients with pheochromocytoma and tumors derived from neural crest cells.
- Total urine metanephrines up to 1,300 ug/24 hours can be detected in nonpheochromocytoma hypertensive patients.
- Further clinical investigation (eg, radiographic studies) are warranted in patients whose urinary fractionated metanephrine levels are >1,300 ug/24 hours (approximately 2 times the upper limit of normal). Radiographic studies are also indicated for patients in which there is a high index of suspicion, even if lower or normal urine metanephrine levels are found.

Cautions

- Tricyclic antidepressants (TCA) and labetalol and sotalol (beta blockers) may elevate levels of metanephrines. If clinically feasible, these medications should be discontinued at least 1 week before collection.
- This test utilizes a high-performance liquid chromatography/tandem mass spectrometry (LC-MS/MS) method and is not affected by the interfering substances that affected the previously utilized spectrophotometric (Pisano reaction) method (ie, diatrizoate, chlorpromazine, hydrazine derivatives, imipramine, MAO inhibitors, methyldopa, phenacetin, ephedrine, or epinephrine).
- This method is also not subject to the known interference of acetaminophen (seen with the plasma metanephrine HPLC-EC method).

References

Test Title: Metanephrines, Fractionated, Random, Urine #83005

Method

Urinary metanephrines are determined by reverse phase LC-MS/MS stable isotope dilution analysis. Urinary metanephrines occur largely in conjugated form. After urine specimens are acidified and hydrolyzed for 20 minutes in a boiling water bath, metanephrine and normetanephrine are extracted from the specimens utilizing extraction cartridges. The metanephrine and normetanephrine are eluted from the cartridge using 20% methanol (MeOH) and analyzed by LC-MS/MS using multiple reaction monitoring in positive mode. Deuterated metanephrine (d[3]-metanephrine, 200 ng) and deuterated normetanephrine (d[3]-normetanephrine, 500 ng) are added prior to the hydrolysis as an internal standard. The following ion pairs are used for analysis: metanephrine, (180/148); normetanephrine, (166/134); d[3]-metanephrine, (183/151); d[3]-normetanephrine, (169/137). The metanephrine and normetanephrine concentrations are quantified using ratios of the peak areas to deuterium-labeled internal standards by LC-MS/MS. A calibration curve, generated from 20% MeOH spiked standards, is included with each batch of patient specimens. (Chan EC, Ho PC: High-performance liquid chromatography/atmospheric pressure chemical ionization mass spectrometric method for the analysis of catecholamines and metanephrines in human urine. Rapid Commun Mass Spectrom 2000;14:1959-1964; Sawka AM, Singh RJ, Young WF Jr.: False positive biochemical testing for pheochromocytoma caused by surreptitious catecholamine addition to urine. Endocrinologist 2001;11:421-423; Roden M, Raffesberg W, Raber W, et al: Quantification of unconjugated metanephrine in human plasma without interference by acetaminophen. Clin Chem 2001;47:1061-1067)

Specimen Required:

10 mL (pediatric: 5.0 mL) from a 24-hour urine collection. Add 10 g (pediatric 3 g) of boric acid OR 25 mL (pediatric 15 mL) of 50% acetic acid as preservative at start of collection. See “Urine Preservatives” in Special Instructions in the 2002 Test Catalog for multiple collections. Measure and record the volume of the 24-hour collection. Send specimen refrigerated in a plastic, 13-mL urine tube.

NOTE: 24-HOUR VOLUME IS REQUIRED ON REQUEST FORM FOR PROCESSING.

Urine Preservative Collection Options

IMPORTANT NOTE: The addition of preservative or application of temperature controls must occur within 4 hours of completion of the collection OR an acceptable preservative must be added at the START of the collection. Urine tests which require that the preservative be added at the START of the collection are noted by an *(asterisk).

Ambient: Yes
Refrigerate: Yes
Frozen: Yes
6N HCl: Yes
Acetic Acid 50%: Preferred
Na2CO3: Yes
Toluene: Yes
HNO3: Yes
Boric: Preferred
Thymol: Yes

Tricyclic antidepressants (TCA), labetalol and sotalol medications (beta blockers) may elevate levels of metanephrines producing results which cannot be interpreted. If clinically feasible, it is optimal to discontinue these medications at least 1 week before collection. For advice on assessing the risk of removing patients from these medications and alternatives, you may consider consultation with a specialist in Endocrinology or Hypertension.
### METANEPHRINE

#### Males

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Reference Value</th>
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<tbody>
<tr>
<td>0-2 years</td>
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<tr>
<td>3-8 years</td>
<td>29-92 ug/24 h</td>
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#### Females

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<td>3-8 years</td>
<td>18-144 ug/24 h</td>
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<td>9-12 years</td>
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<td>33-185 ug/24 h</td>
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<tr>
<td>≥18 years</td>
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### NORMETANEPHRINE

#### Males

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<td>0-2 years</td>
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<tr>
<td>3-8 years</td>
<td>34-169 ug/24 h</td>
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<td>9-12 years</td>
<td>84-422 ug/24 h</td>
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<td>13-17 years</td>
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<td>18-29 years</td>
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<tr>
<td>30-39 years</td>
<td>111-419 ug/24 h</td>
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<tr>
<td>40-49 years</td>
<td>119-451 ug/24 h</td>
</tr>
<tr>
<td>50-59 years</td>
<td>128-484 ug/24 h</td>
</tr>
<tr>
<td>60-69 years</td>
<td>138-521 ug/24 h</td>
</tr>
<tr>
<td>≥70 years</td>
<td>148-560 ug/24 h</td>
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#### Females

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<td>138-521 ug/24 h</td>
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<td>≥70 years</td>
<td>148-560 ug/24 h</td>
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### TOTAL METANEPHRINE

#### Males

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<td>3-8 years</td>
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<td>50-59 years</td>
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<td>246-753 ug/24 h</td>
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#### Females

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<tbody>
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<td>0-2 years</td>
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<td>3-8 years</td>
<td>57-210 ug/24 h</td>
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<td>≥70 years</td>
<td>180-646 ug/24 h</td>
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#### Hypertensives

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</tr>
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<tbody>
<tr>
<td>&lt;1300 ug/24 h</td>
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**Analytic Time:**
- 2 days

**Days Set Up:**
- Monday through Saturday

**Fee:**
- $102.00

**CPT Code:**
- 83835
A frequently encountered problem in hematopathology is distinguishing between reactive and neoplastic lymphoid processes. The demonstration of clonality can help make this distinction as clonality suggests the presence of a neoplastic process in the appropriate pathologic setting.

The T-cell antigen receptor (TCR) alpha-, beta-, gamma-, and delta-chain genes consist of noncontiguous variable, diversity, joining, and constant region segments. Rearrangement of these segments occurs randomly early in T-cell ontogeny.

Reactive T-cell processes consist of polyclonal populations of T cells in which each clone harbors a unique TCR gene rearrangement without clear predominance of one rearrangement. In contrast, T-cell neoplasms are clonal disorders in which all of the neoplastic cells have identical TCR gene rearrangements.

- Distinguishing reactive T-cell processes from T-cell neoplasms
- Detecting the presence of persistent clonal T-cell populations
- The finding of a discrete TCR gene rearrangement suggests that a clonal T-cell population is present.
- In the appropriate clinical and pathologic setting, T-cell clonality can be indicative of malignancy.

Some clonal TCR rearrangements may not be detected by these methods. Possible causes for false-negative results include failure of polymerase chain reaction (PCR) primer binding or rearrangements in the Southern blot assay that either occurred in regions not detected by the utilized probes or that were similar in size to germline fragments. A clonal cell population must comprise at least 1% of the analyzed cells to be detectable by these methods.

Identification of a TCR rearrangement does not establish T-cell lineage as these rearrangements can occur in other hematolymphoid neoplasms. Correlation with immunophenotyping analysis is necessary for accurate determination of cell lineage.

References

Method
To assure that necessary and appropriate studies are performed, each specimen is reviewed by a Mayo specialist before any testing is performed.

Polymerase chain reaction (PCR) analysis will be performed initially on all specimens. Confirmatory Southern blot analysis will be performed on PCR negative cases in which there is clinicopathologic evidence to suggest T-cell malignancy. If there is no such evidence, Southern blot testing will not be performed on PCR negative cases. All PCR positive cases will be confirmed either by Southern blot testing or correlation with other pathologic data.

The TCR PCR assay utilizes multiplex primer sets to TCR-gamma gene V and J segments. The V-region primers are fluorescently labeled and the reaction products are separated by capillary electrophoresis with a fluorescence detection system on an ABI instrument. For the Southern blot assay, DNA is completely digested with the restriction enzyme EcoR1, electrophoresed on an agarose gel, and transferred to nylon membrane. Individual membranes are then hybridized with radiolabeled probes to either the TCR beta-gene first (Jbeta1) or (Jbeta2) joining regions. Rearranged fragments are detected by autoradiography. (Greiner TC, Raffeld M, Lutz C, et al: Analysis of T cell receptor-gamma gene rearrangements by denaturing gradient gel electrophoresis of GC-clamped polymerase chain reaction products; Correlation with tumor-specific sequences. Am J Path 1995;146:46-55; McCarthy KP, Sloane JP,
Test Title: T Cell Gene Replacement  
#83122

Method (continued)

Specimen Required: Specimen should include a “Hematopathology/Molecular Oncology Request Form” (Supply T241) or a “MayoConnect Additional Test Information Form” (Supply T357) with relevant clinical information and cytogenetic results, if available. Specimen must arrive within 72 hours of draw.

SUBMIT 1 OF THE FOLLOWING SPECIMENS:

Blood
Draw 2 lavender-top (EDTA) tube(s) of whole blood (5.0 mL) and send in the original VACUTAINER(S). Invert several times to mix blood. Forward unprocessed whole blood promptly at ambient temperature only.

Bone Marrow: Place 2.0 mL of bone marrow in a lavender-top (EDTA) tube(s) and send in the original VACUTAINER. Invert several times to mix bone marrow. Forward unprocessed bone marrow promptly at ambient temperature only.

Spinal Fluid: Obtain 5.0-10 mL of spinal fluid. Forward promptly in a screw-capped, sterile vial at ambient temperature only.

Tissue: Obtain 200 mg of tissue. Specimen must be frozen within 1 hour of collection. Send specimen frozen in plastic container.

Reference Values: An interpretive report will be provided

Analytic Time: 5 days if PCR only performed; 14 days if both PCR and Southern performed

Days Set Up: Monday through Thursday
$60.00 for 8874

Fee: Path Consult, Limited w/o review of patients medical record

An additional fee will be charged if one or more of the following are ordered:

$327.90 for 19024 T-Cell Rearrangement By PCR
$180.70 for 19023 Gene Rearrangement Extract/Interp
$384.10 for 19026 T-Cell Gene Rearrangement, Southern Blot

CPT Code: #83894x2/ Electrophoresis  
83891/ Each multiplex PCR  
83912/ Interpretation and report  

#19024  
T-Cell Rearrangement By PCR  
83894x3/ Enzyme digestion  
83894x3/ Electrophoresis  
83896x3/ Nucleic acid probe, each  
83897x3/ Nucleic acid transfer  
83912/ Interpretation and report  

#8874  
Path Consult, Limited w/o review of patients medical record  
80500  

#19026  
T-Cell Gene Rearrangement, Southern Blot  
83892x3/ Enzyme digestion  
83894x3/ Electrophoresis  
83896x3/ Nucleic acid probe, each  
83897x3/ Nucleic acid transfer  
83912/ Interpretation and report
A frequently encountered problem in hematopathology is distinguishing between reactive and neoplastic lymphoid processes. The demonstration of clonality can help make this distinction as clonality suggests the presence of a neoplastic process in the appropriate pathologic setting.

The immunoglobulin heavy- and light-chain (kappa and lambda) genes consist of noncontiguous variable, diversity, joining, and constant region segments. Rearrangement of these segments occurs randomly early in B-cell ontogeny.

Reactive B-cell processes consist of polyclonal populations of B cells in which each clone harbors unique immunoglobulin gene rearrangements without clear predominance of one rearrangement. In contrast, B-cell neoplasms are clonal disorders in which all of the neoplastic cells have the identical immunoglobulin heavy-and light-chain gene rearrangements.

- Distinguishing reactive B-cell processes from B-cell neoplasms
- Detecting the presence of persistent clonal B-cell populations
- The finding of a discrete immunoglobulin gene rearrangement suggests that a clonal B-cell population is present.
- In the appropriate clinical and pathologic setting, B-cell clonality can be indicative of malignancy.

Some clonal immunoglobulin gene rearrangements may not be detected by these methods. Possible causes for false-negative results include failure of polymerase chain reaction (PCR) primer binding or rearrangements in the Southern blot assay that either occurred in regions not detected by the utilized probes or that were similar in size to germline fragments. A clonal cell population must comprise at least 1% of the analyzed cells to be detectable by these methods.

References


Method

To assure that necessary and appropriate studies are performed, each specimen is reviewed by a Mayo specialist before any testing is performed.

Polymerase chain reaction (PCR) analysis will be performed on all specimens. Confirmatory Southern blot analysis will be performed on PCR negative cases unless such testing is not deemed necessary after correlation with other pathologic information.

The immunoglobulin gene PCR assay utilizes consensus primer sets to the immunoglobulin heavy-chain and kappa-light chain gene V and J regions. The V-region primers are fluorescently labeled and the reaction products are separated by capillary electrophoresis with a fluorescence detection system on an ABI instrument. For the Southern blot assay DNA is completely digested with either BgIII or BamHI, electrophoresed on an agarose gel, and transferred to a nylon membrane. Individual membranes are then hybridized with radiolabeled probes to either the heavy-chain gene joining region (BgIII digest) or the kappa-chain gene constant region (Bam-HI digest) joining regions. Rearranged fragments are detected by autoradiography. (Achille A, Scarpa A, Montresor M, et al: Routine application of polymerase chain reaction in the diagnosis of monoclonality of B-cell lymphoid proliferations. Diag Molec Path 1985;4:14-24; Sioutos N, Bagg A, Michaud GY, et al: Polymerase chain reaction versus southern blot hybridization. Detection of immunoglobulin heavy-chain gene rearrangements. Diag Molec Path 1995;4:8-13; Trainor KJ, Brisco MJ, Wan JH, et al: Gene rearrangement in B-and T-lymphoproliferative disease detected by the polymerase chain reaction. Blood 1991;78:192-196)
Test Title: B Cell Gene Rearrangement  
#83123

Specimen Required: Specimen should include a “Hematopathology/Molecular Oncology Request Form” (Supply T241) or a “MayoConnect Additional Test Information Form” (Supply T357) with relevant clinical information and cytogenetic results, if available. Specimen must arrive within 72 hours of draw.

SUBMIT 1 OF THE FOLLOWING SPECIMENS:

Blood: Draw 2 lavender-top (EDTA) tube(s) of whole blood (5.0 mL) and send in the original VACUTAINER(S). Invert several times to mix blood. Forward unprocessed whole blood promptly at ambient temperature only.

Bone Marrow: Place 2.0 mL of bone marrow in a lavender-top (EDTA) tube(s) and send in the original VACUTAINER. Invert several times to mix bone marrow. Forward unprocessed bone marrow promptly at ambient temperature only.

Spinal Fluid: Obtain 5.0-10 mL of spinal fluid. Forward promptly in a screw-capped, sterile vial at ambient temperature only.

Tissue: Obtain 200 mg of tissue. Specimen must be frozen within 1 hour of collection. Send specimen frozen in plastic container.

Reference Values: An interpretive report will be provided.

Analytic Time: 5 days if PCR only performed; 14 days if both PCR and Southern performed
Days Set Up: Monday through Thursday
Fee: $60.00 for 8874
Path Consult, Limited w/o review of patients medical record
An additional fee will be charged if one or more of the following are ordered:
$344.90 for 19025
B-Cell Rearrangement By PCR
$180.70 for 19023
Gene Rearrangement Extract/Interp
$384.10 for 19027
B-Cell Gene Rearrangement, Southern Blot

CPT Code: 
#8874
Path Consult, Limited w/o review of patients medical record
80500
#19025
B-Cell Rearrangement By PCR
83901/Each multiplex PCR
83912/Interpretation and report
#19023
Gene Rearrangement Extract/Interp
83891/DNA extract/purify
83912/Interpretation and report
#19027
B-Cell Gene Rearrangement, Southern Blot
83892x 2/Enzyme digestion
83894x 2/Electrophoresis
83896x 2/Nucleic acid probe, each
83897x 2/Nucleic acid transfer
83912/Interpretation and report
Epstein-Barr virus (EBV) is present in various lymphoproliferative disorders, including those occurring in immunosuppressed patients, in some extranodal T-cell neoplasms, and nasal angiocentric T-Cell/natural killer cell (T/NK) lymphomas.

The latently infected lymphoid cells contain episomal EBV DNA, and the circular EBV DNA configuration in each cell has a unique number of terminal repeat sequences.

In a polyclonal population of EBV-infected lymphoid cells, the number of EBV terminal repeat sequences varies from cell to cell. In contrast, monoclonal populations of EBV-infected lymphoid cells consist of lymphoid cells with the same episomal EBV DNA configuration.

Southern blot hybridization studies, using probes that assess the number of EBV terminal repeat sequences, assess clonality of EBV-infected lymphoid cells.

Assessing clonality of other EBV-infected lymphoid proliferations
- Absence of any bands indicates absence of EBV in the lymphoid population.
- One band indicates a monoclonal EBV-infected lymphoid population.
- Two bands indicate a biclonal population of EBV-infected cells.
- Polyclonal EBV-infected lymphoid cells show multiple bands.
- Results of the EBV Southern blot assay will be correlated with available pathologic data by a hematopathologist for the most accurate interpretation of these results.

Cautions
- This test may not detect rare (1% or less) EBV-infected lymphoid cells. In situ hybridization techniques are better for detecting the presence or absence of EBV-infected cells in these cases.
- Clonality of a lymphoproliferative disorder, as assessed by these techniques, does not always predict malignant clinical behavior.

References

Method
To assure that necessary and appropriate studies are performed, each specimen is reviewed by a Mayo specialist before any testing is performed.

Southern blot analysis will be used to detect EBV clonality. This method uses the restriction endonuclease BamHI and 2 DNA probes that are specific for the terminal repeat sequences of the EBV.
Specimen Required: Specimen should include a “Hematopathology/Molecular Oncology Request Form” (Supply T241) or a “MayoConnect Additional Test Information Form” (Supply T357) with relevant clinical information and cytogenetics results, if available. Specimen must arrive within 72 hours of draw.

SUBMIT 1 OF THE FOLLOWING SPECIMENS:
Blood: Draw a lavender-top (EDTA) tube(s) or a yellow-top (ACD) tube(s) of whole blood (5.0 mL) and send in the original VACUTAINER(S). Invert several times to mix blood. Forward unprocessed whole blood promptly at ambient temperature only.

Bone Marrow: Place 2.0 mL of bone marrow in a lavender-top (EDTA) tube(s) and send in the original VACUTAINER. Invert several times to mix bone marrow. Forward unprocessed bone marrow promptly at ambient temperature only.

Spinal Fluid: Obtain 5.0-10 mL of spinal fluid. Forward promptly in a screw-capped, sterile vial at ambient temperature only.

Tissue: Obtain 200 mg of tissue. Specimen must be frozen within 1 hour of collection. Send specimen frozen in plastic container.

Reference Values: An interpretive report will be provided.

Analytic Time: 14 days
Days Set Up: Friday
Fee: $60.00 for 8874
Path Consult, Limited w/o review of patients medical record

An additional fee will be charged if one or more of the following are ordered:

$383.30 for 19033
Epstein-Barr Virus, Southern Blot

$180.70 for 19023
Gene Rearrangement Extract/Interp

CPT Code:
#8874
Path Consult, Limited w/o review of patients medical record
80500

#19033
Epstein-Barr Virus, Southern Blot
83912/Interpretation and report
83894/Electrophoresis
83892/Enzymatic digestion
83896/Nucleic acid probe
83897/Nucleic acid transfer

#19023
Gene Rearrangement Extract/Interp
83891/DNA extract/purify
83912/Interpretation and report