Idiopathic and Hereditary Pancreatitis Testing

Pancreatitis is a relatively common disorder with many etiologies that causes inflammation in the pancreas. Acute pancreatitis (AP) is a result of acute inflammation, and patients present with increased pancreatic enzyme concentrations. Chronic pancreatitis (CP) is a syndrome of progressive inflammation that may lead to permanent damage to pancreatic structure and function. Genetic testing can be utilized to uncover a genetic cause of idiopathic or hereditary AP or CP and/or to assess risk of disease in family members.

Disease Overview

Incidence/Prevalence

- Chronic pancreatitis
  - Incidence: ~4-12/100,000 per year\(^1\)
  - Prevalence: ~37-42/100,000\(^1\)
- Idiopathic chronic pancreatitis is more common than previously thought\(^2\)

<table>
<thead>
<tr>
<th>Symptoms/Presentation</th>
<th>Etiologies</th>
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<tbody>
<tr>
<td>Acute pancreatitis</td>
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<tr>
<td>Sudden onset of pain in the upper abdomen, fever, nausea and vomiting, rapid pulse</td>
<td>Common</td>
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<tr>
<td>Increased concentrations of pancreatic enzymes: lipase, amylase</td>
<td>Other</td>
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<td>- Gallstone passage or obstruction; chronic, heavy alcohol use</td>
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<td>- Abdominal trauma, medications, infections, tumors, genetic abnormalities, vascular abnormalities</td>
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Tests to Consider

<table>
<thead>
<tr>
<th>Test Description</th>
<th>Method</th>
<th>Details</th>
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<tbody>
<tr>
<td>Pancreatitis, Panel (CFTR, CTRC, PRSS1, SPINK1) Sequencing 2010876</td>
<td>Polymerase Chain Reaction/Sequencing</td>
<td>Preferred test for individuals with history of idiopathic pancreatitis</td>
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<tr>
<td>Pancreatitis (CTRC) Sequencing 2010703</td>
<td>Polymerase Chain Reaction/Sequencing</td>
<td>For adults with idiopathic pancreatitis if other components of panel (CFTR, PRSS1, SPINK1) have been sequenced without providing a complete explanation for the pancreatitis</td>
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<tr>
<td>Pancreatitis (PRSS1) Sequencing and Deletion/Duplication 3001768</td>
<td>Polymerase Chain Reaction/Sequencing and Multiplex Ligation Dependent Probe Amplification</td>
<td>Preferred test for individuals with idiopathic pancreatitis who</td>
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<tr>
<td>Pancreatitis (SPINK1) Sequencing 2002012</td>
<td>Polymerase Chain Reaction/Sequencing</td>
<td>For adults with idiopathic pancreatitis if other components of panel (CFTR, CTRC, PRSS1) have been sequenced without providing a complete explanation for the pancreatitis</td>
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<tr>
<td>Cystic Fibrosis (CFTR) Sequencing 0051110</td>
<td>Polymerase Chain Reaction/Sequencing</td>
<td>May be used to test for variants causative for mild cystic fibrosis in individuals with idiopathic pancreatitis</td>
</tr>
<tr>
<td>Familial Mutation, Targeted Sequencing 2001961</td>
<td>Polymerase Chain Reaction/Sequencing</td>
<td>Useful when a pathogenic familial variant identifiable by sequencing is known</td>
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</table>
### Genetics

#### Genes

- *CFTR, CTRC, PRSS1, SPINK1*
- Other genes have been reported to be associated with CP but are not currently included in the ARUP test menu

#### Inheritance

- *PRSS1* is autosomal dominant with gain-of-function variants
- *CFTR, CTRC, SPINK1* are autosomal recessive/digenic

#### Penetration

80% in the U.S. for *PRSS1* variants R122H (p.Arg122His) and N29I (p.Asn29Ile)\(^4\)

### Test Interpretation

#### Sensitivity/Specificity in Idiopathic Pancreatitis

- Clinical sensitivity for contributory or causative variants
  - Pancreatitis panel (*CFTR, CTRC, PRSS1, SPINK1*) sequencing: ~48%\(^5\)
  - *PRSS1* sequencing: ~28%
  - *PRSS1* deletion/duplication analysis: ~6%
- Pancreatitis (*SPINK1*) deletion/duplication analysis: unknown
- Analytical sensitivity/specificity: 99%

### Results
### Positive

- Single gain-of-function *PRSS1* gene variant detected, or copy number variant in *PRSS1* detected
- 2 pathogenic *CFTR*, *SPINK1*, or *CTRC* gene variants detected, or 1 pathogenic variant detected in 2 different genes (digenic inheritance) is causative for pancreatitis
- Single pathogenic *CFTR*, *SPINK1*, or *CTRC* gene variant detected (increases risk for pancreatitis, but is not causative)

### Negative

- No pathogenic variants detected in *CFTR*, *CTRC*, *PRSS1*, or *SPINK1* genes
- No genetic etiology for pancreatitis determined, but genetic etiology is not excluded

### Inconclusive

- Gene variant detected, but whether variant is pathogenic or benign is unknown
- Consider additional testing if suspicions remain

## Limitations

- Large deletions/duplications, regulatory region variants, and deep intronic variants will not be detected
- Diagnostic errors can occur due to rare sequence variations
- Variants in currently unknown genes may be associated with pancreatitis

## References


## Additional Resources


## Related Information

**Chronic Pancreatitis**

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