ARUP LABORATORIES | LABORATORY TEST DIRECTORY

Idiopathic and Hereditary Pancreatitis Testing

Pancreatitis is a relatively common disorder with multiple etiologies that causes inflammation in the pancreas. Acute pancreatitis (AP) is a result of sudden inflammation, and patients may 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 determine 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]

	Symptoms/Presentation	Etiologies
Acute pancreatitis	Sudden onset of pain in the upper abdomen, fever, nausea and vomiting, rapid pulse Increased concentrations of pancreatic enzymes: lipase, amylase	Common • Gallstone passage or obstruction; chronic, heavy alcohol use Other • Abdominal trauma, medications, infections, tumors, genetic abnormalities, vascular abnormalities
Chronic pancreatitis	Abdominal pain, nausea, vomiting, weight loss, diarrhea, oily stools At advanced stages, pain often decreases, and malabsorption and diabetes may occur Patients with CP have up to a 40% lifetime risk for pancreatic cancer[3]	Alcohol related • 44-65% of cases[1] • Alcohol use and smoking are independent risk factors but together have a multiplicative effect on risk[1] Other • Autoimmune response, hereditary disorders of the pancreas, cystic fibrosis, hypercalcemia, hyperlipidemia, hyperparathyroidism, medications

Genetics

Tests to Consider

Pancreatitis, Panel (CFTR, CTRC, PRSS1, SPINK1) Sequencing (Temporary Referral as of 12/7/20) 2010876

Method: Polymerase Chain Reaction/Sequencing

Preferred test for individuals with history of idiopathic pancreatitis

Pancreatitis (CTRC) Sequencing 2010703

Method: Polymerase Chain Reaction/Sequencing

For adults with idiopathic pancreatitis if other components of panel (*CFTR*, *PRSS1*, *SPINK1*) have been sequenced without providing a complete explanation for the pancreatitis

Pancreatitis (PRSS1) Sequencing and Deletion/Duplication (Temporary Referral as of 01/14/21) 3001768

Method: Polymerase Chain Reaction/Sequencing and Multiplex Ligation Dependent Probe Amplification

Preferred test for individuals with idiopathic pancreatitis who:

- Are <20 years of age **OR**
- Have two affected first-degree relatives

Pancreatitis (SPINK1) Sequencing (Temporary Referral as of 12/07/20) 2002012

Method: Polymerase Chain Reaction/Sequencing

For adults with idiopathic pancreatitis if other components of panel (*CFTR*, *CTRC*, *PRSS1*) have been sequenced without providing a complete explanation for the pancreatitis

Cystic Fibrosis (CFTR) Sequencing (Temporary Referral as of 12/07/20) 0051110

Method: Polymerase Chain Reaction/Sequencing

May be used to test for variants causative for mild cystic fibrosis in individuals with idiopathic pancreatitis

Related Tests

Familial Mutation, Targeted Sequencing 2001961

Method: Polymerase Chain Reaction/Sequencing

Useful when a pathogenic familial variant identifiable by sequencing is known

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
  - 80% in the U.S. for *PRSS1* variants R122H (p.Arg122His) and N29I (p.Asn29Ile)[4]
- *CFTR*, *CTRC*, *SPINK1* are autosomal recessive/digenic

Deletion/Duplication Analysis by MLPA 3003144

Method: Multiplex Ligation-dependent Probe Amplification

Use to asses for large deletion/duplication in *CFTR*, *PRSS1*, or *SPINK1* previously identified in a family member

Test Interpretation

Sensitivity/Specificity in Idiopathic Pancreatitis

- Clinical sensitivity for contributory or causative variants
  - Pancreatitis panel (*CFTR*, *CTRC*, *PRSS1*, *SPINK1*) sequencing: ~48%[5]
  - Pancreatitis (*CFTR*) sequencing: ~28%
  - Pancreatitis (*SPINK1*) sequencing: ~16%
  - Pancreatitis (*PRSS1*) sequencing: ~ 9%
  - Pancreatitis (*CTRC*) sequencing: ~4%
  - Pancreatitis (*PRSS1*) deletion/duplication analysis: ~6%
- Analytical sensitivity/specificity: 99%

Results

Result	Interpretation
Positive	One of the following: • One *PRSS1* pathogenic variant or copy number variant detected • Two pathogenic *CFTR*, *SPINK1*, or *CTRC* gene variants detected • One pathogenic variant detected in two different genes (digenic inheritance) • One pathogenic variant detected in *CFTR*, *CTRC*, or *SPINK1* genes (may increase the risk for pancreatitis but is not causative)
Negative	No pathogenic variants detected in any of the genes; reduces the risk for hereditary pancreatitis but genetic etiology is not excluded
Uncertain	Variant(s) of uncertain clinical significance detected; may be disease-causing or benign

Limitations

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

References

1. Conwell DL, Lee LS, Yadav D, et al. American Pancreatic Association practice guidelines in chronic pancreatitis: evidence-based report on diagnostic guidelines. Pancreas. 2014;43(8):1143-1162. PubMed
2. Gupte A, Goede D, Tuite R, et al. Chronic pancreatitis. BMJ. 2018;361:k2126. PubMed
3. Shelton C, Solomon S, LaRusch J, et al. *PRSS1*-related hereditary pancreatitis. In: Adam MP, Ardinger HH, Pagon RA, et al, editors. GeneReviews, University of Washington; 1993-2020. [Last Update: Apr 2019; Accessed: Feb 2020]
4. Sossenheimer MJ, Aston CE, Preston RA, et al. Clinical characteristics of hereditary pancreatitis in a large family, based on high-risk haplotype. The Midwest Multicenter Pancreatic Study Group (MMPSG). Am J Gastroenterol. 1997;92(7):1113-1116. PubMed
5. Masson E, Chen JM, Audrézet MP, et al. A conservative assessment of the major genetic causes of idiopathic chronic pancreatitis: data from a comprehensive analysis of PRSS1, SPINK1, CTRC and CFTR genes in 253 young French patients. PLoS One. 2013;8(8):e73522. PubMed

Additional Resources

LaRusch J, Whitcomb DC. Genetics of pancreatitis. Curr Opin Gastroenterol. 2011;27(5):467-474. PubMed

Yadav D, Lowenfels AB. The epidemiology of pancreatitis and pancreatic cancer. Gastroenterology. 2013;144(6):1252-1261. PubMed

Related Information

Chronic Pancreatitis

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