Preview of the Medifocus Guidebook on: Chronic Pancreatitis

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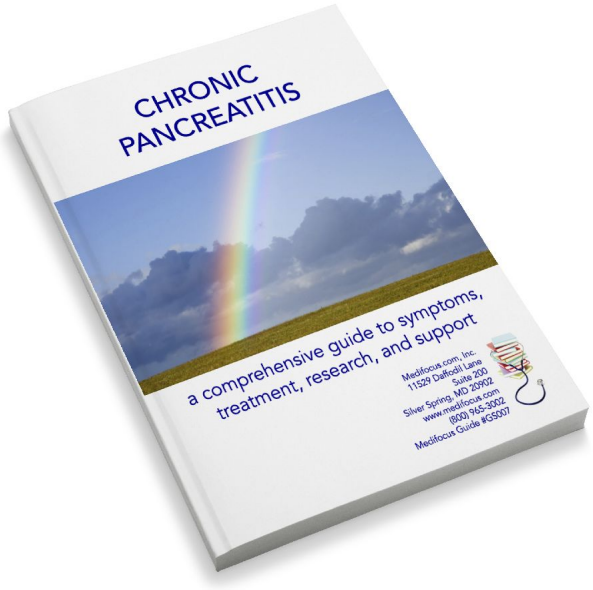

This document is only a SHORT PREVIEW of the **Medifocus Guidebook on Chronic Pancreatitis**. It is intended primarily to give you a general overview of the **format and structure** of the Guidebook as well as select pages from each major Guidebook section listed in the Table of Contents.

To purchase the **COMPLETE** Medifocus Guidebook on Chronic Pancreatitis (149 pages; Updated July 6, 2020), please:

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1 - Background Information

Introduction

Chronic or life-threatening illnesses can have a devastating impact on both the patient and the family. In today's new world of medicine, many consumers have come to realize that they are the ones who are primarily responsible for their own health care as well as for the health care of their loved ones.

When facing a chronic or life-threatening illness, you need to become an educated consumer in order to make an informed health care decision. Essentially that means finding out everything about the illness - the treatment options, the doctors, and the hospitals - so that you can become an educated health care consumer and make the tough decisions. In the past, consumers would go to a library and read everything available about a particular illness or medical condition. In today's world, many turn to the Internet for their medical information needs.

The first sites visited are usually the well known health "portals" or disease organizations and support groups which contain a general overview of the condition for the layperson. That's a good start but soon all of the basic information is exhausted and the need for more advanced information still exists. What are the latest "cutting-edge" treatment options? What are the results of the most up-to-date clinical trials? Who are the most notable experts? Where are the top-ranked medical institutions and hospitals?

The best source for authoritative medical information in the United States is the National Library of Medicine's medical database called PubMed®, that indexes citations and abstracts (brief summaries) of over 7 million articles from more than 3,800 medical journals published worldwide. PubMed® was developed for medical professionals and is the primary source utilized by health care providers for keeping up with the latest advances in clinical medicine.

A typical PubMed® search for a specific disease or condition, however, usually retrieves hundreds or even thousands of "hits" of journal article citations. That's an avalanche of information that needs to be evaluated and transformed into truly useful knowledge. What are the most relevant journal articles? Which ones apply to your specific situation? Which articles are considered to be the most authoritative - the ones your physician would rely on in making clinical decisions? This is where *Medifocus.com* provides an effective solution.

Medifocus.com has developed an extensive library of *MediFocus Guidebooks* covering a wide spectrum of chronic and life threatening diseases. Each *MediFocus Guidebook* is a

high quality, up- to-date digest of "professional-level" medical information consisting of the most relevant citations and abstracts of journal articles published in authoritative, trustworthy medical journals. This information represents the latest advances known to modern medicine for the treatment and management of the condition, including published results from clinical trials. Each *Guidebook* also includes a valuable index of leading authors and medical institutions as well as a directory of disease organizations and support groups. *MediFocus Guidebooks* are reviewed, revised and updated every 4-months to ensure that you receive the latest and most up-to-date information about the specific condition.

About Your MediFocus Guidebook

Introduction

Your *MediFocus Guidebook* is a valuable resource that represents a comprehensive synthesis of the most up-to-date, advanced medical information published about the condition in well-respected, trustworthy medical journals. It is the same type of professional-level information used by physicians and other health-care professionals to keep abreast of the latest developments in biomedical research and clinical medicine. The *Guidebook* is intended for patients who have a need for more advanced, in-depth medical information than is generally available to consumers from a variety of other resources. The primary goal of a *MediFocus Guidebook* is to educate patients and their families about their treatment options so that they can make informed health-care decisions and become active participants in the medical decision making process.

The *Guidebook* production process involves a team of experienced medical research professionals with vast experience in researching the published medical literature. This team approach to the development and production of the *MediFocus Guidebooks* is designed to ensure the accuracy, completeness, and clinical relevance of the information. The *Guidebook* is intended to serve as a basis for a more meaningful discussion between patients and their health-care providers in a joint effort to seek the most appropriate course of treatment for the disease.

Guidebook Organization and Content

Section 1 - Background Information

This section provides detailed information about the organization and content of the *Guidebook* including tips and suggestions for conducting additional research about the condition.

Section 2 - The Intelligent Patient Overview

This section of your *MediFocus Guidebook* represents a detailed overview of the disease or condition specifically written from the patient's perspective. It is designed to satisfy the basic informational needs of consumers and their families who are confronted with the illness and are facing difficult choices. Important aspects which are addressed in "The Intelligent Patient" section include:

- The etiology or cause of the disease
- Signs and symptoms
- How the condition is diagnosed
- The current standard of care for the disease
- Treatment options

- New developments
- Important questions to ask your health care provider

Section 3 - Guide to the Medical Literature

This is a roadmap to important and up-to-date medical literature published about the condition from authoritative, trustworthy medical journals. This is the same information that is used by physicians and researchers to keep up with the latest developments and breakthroughs in clinical medicine and biomedical research. A broad spectrum of articles is included in each *MediFocus Guidebook* to provide information about standard treatments, treatment options, new clinical developments, and advances in research. To facilitate your review and analysis of this information, the articles are grouped by specific categories. A typical *MediFocus Guidebook* usually contains one or more of the following article groupings:

- *Review Articles:* Articles included in this category are broad in scope and are intended to provide the reader with a detailed overview of the condition including such important aspects as its cause, diagnosis, treatment, and new advances.

- *General Interest Articles:* These articles are broad in scope and contain supplementary information about the condition that may be of interest to select groups of patients.

- *Drug Therapy:* Articles that provide information about the effectiveness of specific drugs or other biological agents for the treatment of the condition.

- *Surgical Therapy:* Articles that provide information about specific surgical treatments for the condition.

- *Clinical Trials:* Articles in this category summarize studies which compare the safety and efficacy of a new, experimental treatment modality to currently available standard treatments for the condition. In many cases, clinical trials represent the latest advances in the field and may be considered as being on the "cutting edge" of medicine. Some of these experimental treatments may have already been incorporated into clinical practice.

The following information is provided for each of the articles referenced in this section of your *MediFocus Guidebook:*

- Article title
- Author Name(s)
- Institution where the study was done
- Journal reference (Volume, page numbers, year of publication)

- Link to Abstract (brief summary of the actual article)

Linking to Abstracts: Most of the medical journal articles referenced in this section of your *MediFocus Guidebook* include an abstract (brief summary of the actual article) that can be accessed online via the National Library of Medicine's PubMed® database. You can easily access the individual abstracts online via PubMed® from the "electronic" format of your *MediFocus Guidebook* by clicking on the corresponding URL address that is provided for each cited article. If you purchased a printed copy of a *MediFocus Guidebook*, you can still access the article abstracts online by entering the individual URL address for a particular article into your web browser.

Section 4 - Centers of Research

We've compiled a unique directory of doctors, researchers, medical centers, and research institutions with specialized research interest, and in many cases, clinical expertise in the management of the specific medical condition. The "Centers of Research" directory is a valuable resource for quickly identifying and locating leading medical authorities and medical institutions within the United States and other countries that are considered to be at the forefront in clinical research and treatment of the condition.

Inclusion of the names of specific doctors, researchers, hospitals, medical centers, or research institutions in this *Guidebook* does not imply endorsement by Medifocus.com, Inc. or any of its affiliates. Consumers are encouraged to conduct additional research to identify health-care professionals, hospitals, and medical institutions with expertise in providing specific medical advice, guidance, and treatment for this condition.

Section 5 - Tips on Finding and Choosing a Doctor

One of the most important decisions confronting patients who have been diagnosed with a serious medical condition is finding and choosing a qualified physician who will deliver high-level, quality medical care in accordance with curently accepted guidelines and standards of care. Finding the "best" doctor to manage your condition, however, can be a frustrating and time-consuming experience unless you know what you are looking for and how to go about finding it. This section of your Guidebook offers important tips for how to find physicians as well as suggestions for how to make informed choices about choosing a doctor who is right for you.

Section 6 - Directory of Organizations

This section of your *Guidebook* is a directory of select disease organizations and support groups that are in the business of helping patients and their families by providing access to information, resources, and services. Many of these organizations can answer your questions, enable you to network with other patients, and help you find a doctor in your geographical area who specializes in managing your condition.

2 - The Intelligent Patient Overview

CHRONIC PANCREATITIS

Introduction to Chronic Pancreatitis

Chronic Pancreatitis is a chronic, progressive, inflammatory condition that leads to permanent damage of pancreatic structure and function.

What is the Pancreas?

The pancreas is a long slender gland (12-20 centimeters, 6-8 inches), that is located in the upper part of the abdomen and is attached to the back wall of the abdominal cavity. Shaped like a fish, the pancreas has five parts: head, *uncinate process* (a prolongation of the head), a short neck, body, and tail. The "head" of the pancreas (approximately aligned with the spinal cord), is surrounded by the upper portion of the small intestine, called the *duodenum*; the "body" is located behind the stomach; and the "tail" is located at the left upper portion of the abdomen, below the rib cage and touching the spleen. Many major nerve trunks and blood vessels, such as the aorta and the vena cava, pass through or very close to the pancreas.

The pancreas is a very complex gland with two major functions: *exocrine* and *endocrine*.

- Exocrine Function - The exocrine function of the pancreas is to produce enzymes that are essential for the digestion of food. An *enzyme* is a protein made by the body that facilitates a chemical reaction. The pancreas produces three enzymes: *amylase*, *lipase*, and *trypsin*. They are produced by specialized pyramid-shaped cells called *acinar cells*, and are capable of breaking down fats, carbohydrates, and proteins during the digestion process. The enzymes empty into many small collecting ducts that are spread throughout the pancreatic tissue, and finally empty into the large *pancreatic duct* which runs the length of the pancreas. The pancreatic duct joins the *common bile duct* that brings bile (a mixture of water and salts and other components) from the gall bladder to the pancreatic head where they empty together into the duodenum through the *sphincter of Oddi* (a muscle that surrounds both ducts). The stomach empties partially digested food and liquid into the duodenum where it mixes with the secretions from the ducts and then progresses into the small intestine. A normally functioning pancreas releases up to 2.5 liters (2.6 quarts) of exocrine secretions per day.

- Endocrine Function - The endocrine function of the pancreas is to produce hormones that travel through the blood and directly affect the operations of other cells and organs. The hormones produced by the pancreas are *insulin*, *glucagon*, and *somatostatin*, and they are secreted directly into the blood. The specialized cells that produce these hormones are often referred to as *islet cells* because they are found in small clusters called *islets of Langerhans*. These hormones play a major role in controlling and regulating the levels of glucose (sugar)

in the blood.

What is Pancreatitis?

Pancreatitis is an inflammation of the pancreas. Under normal circumstances, digestive enzymes produced in the pancreas do not become active until they reach the small intestine. Pancreatitis develops when pancreatic enzymes cannot pass into the duodenum, and as a result of the blockage, the enzymes become active while still in the pancreas where they begin to "digest" surrounding tissue in the pancreas, resulting in inflammation of the pancreas.

There are two types of pancreatitis: *acute* and *chronic*.

Acute Pancreatitis

Acute pancreatitis is characterized by moderate to severe inflammation of the pancreas with minimal organ dysfunction. It ranges in severity from mild, in which patients recover on their own in a few days, to severe, in which there may be necrosis, hemorrhage, or multiorgan failure (such as pulmonary insufficiency, renal failure, or shock) that may result in death. For mild cases, there may be a short period of hospitalization during which supportive care may include pain management, restoration of fluid balance, and nutritional management. Severe cases of acute pancreatitis may involve a prolonged hospitalization to manage organ failure or sepsis (generalized infection). Acute pancreatitis requires immediate medical attention.

Usually patients with acute pancreatitis experience upper abdominal pain which may radiate to the back. The pain may be mild, or sudden and intense, and may be exacerbated by eating. Pain usually lasts for several days and is usually accompanied by fever, nausea or vomiting, rapid pulse, and a tender abdomen. Severe cases may cause dehydration and low blood pressure.

Diagnosis is difficult because there are many other conditions that present with similar symptoms. Final diagnosis is usually based on:

- Elevated levels of amylase and lipase (typically at least three times higher than normal)
- Inflamed tissue or pseudocyst visualized on an abdominal CT scan
- Biliary and pancreatic stones visualized on an abdominal CT scan

In most cases, elevated serum amylase in conjunction with either a positive CT scan or positive ultrasound image provides sufficient diagnostic information to accurately identify acute pancreatitis in approximately 80-95% of patients. If there is obstruction of the biliary tract (of ducts coming from the liver) there may be jaundice or elevated bilirubin as well.

Treatment for acute pancreatitis focuses on preventing complications, pain management, nutrition, and antibiotic therapy if infection is present. Most patients recover after a few days. Some patients may require surgical intervention if there is evidence of gallstones blocking the bile duct, if pseudocysts develop, or if there is evidence of multiorgan involvement.

The majority of cases of acute pancreatitis are caused by two factors: the presence of gallstones

(typically small gallstones) which prevent bile from the gallbladder and enzymes from the pancreas from entering the duodenum, and alcohol abuse. Together, they are thought to be the cause of approximately 80% of cases of acute pancreatitis worldwide, even though only a small percentage of people who have gallstones and who abuse alcohol develop acute pancreatitis. Some cases of acute pancreatitis are *idiopathic*, meaning that no cause can be found. Other causes, which are rare, include:

- Hypercalcemia - elevated levels of calcium in the blood
- Hypertriglyceridemia - elevated levels of triglycerides in the blood
- Hypothermia - low core body temperature
- Pancreas divisum (congenital anomaly in which internal pancreatic ducts fail to fuse)
- Vascular disorders such as ischemia (restricted blood flow to an area of the body)
- Metabolic disorders
- Pancreatic tumor
- Trauma to the abdominal region
- Drug reaction

It is estimated that acute pancreatitis affects 80,000 people a year in the U.S. Approximately 80% of cases are mild and 15-20% are severe, with multiple complications that can include:

- Pseudocyst - collection of pancreatic fluid enclosed in a sac of fibrous tissue
- Abscess - intra-abdominal collection of pus
- Pseudoaneurysm formation - malformation of blood vessel walls adjacent to the pancreas due to exposure of tissue to pancreatic enzymes, often associated with presence of pseudocyst (rare)
- Sepsis - presence of toxins in the blood or tissue
- Necrosis - death of pancreatic tissue

Other facts about acute pancreatitis:

- Incidence and hospitalizations for first attacks of acute pancreatitis are rising worldwide. The incidence in the U.S. is believed to be one of the highest in the world, with up to 44 cases per 100,000 people. This may be partially due to increasing numbers of gallstone-related pancreatitis. It is not clear whether the increasing rate of obesity, which is a risk factor for gallstones, is related.
- Incidence of acute pancreatitis increases with age.
- Mortality following the first attack in acute pancreatitis is believed to be between 3% - 10% of cases.
- Recurrence rate of attacks of acute pancreatitis is believed to be primarily due to alcohol use (approximately 27%), followed by gallstones (25%).
- In some patients it may be difficult to distinguish between repeated attacks of acute pancreatitis and early stages of chronic pancreatitis.
- It is thought that up to 6% of patients with acute pancreatitis develop chronic pancreatitis.

Chronic Pancreatitis

Chronic pancreatitis (CP) is an inflammatory condition that involves progressive and irreversible scarring, structural changes, and damage to the pancreatic tissue as well as permanent impairment

of pancreatic function. Early chronic pancreatitis may begin with recurrent bouts of chronic abdominal pain with normal or mildly elevated pancreatic enzymes. Over time, patients experience permanent structural and functional pancreatic impairment which results in:

- *Exocrine* insufficiency - dysfunction of pancreatic enzyme and reduced production that result in impairment of digestion
- *Endocrine* insufficiency - dysfunction of insulin production that results in elevated levels of blood sugar

Additional characteristics of chronic pancreatitis may include:

- Inflammation
- Fibrotic tissue replacing normal tissue
- Destruction of pancreatic tissue (necrosis)
- Infiltration of inflammatory cells, especially into the head of the pancreas
- Acinar cell destruction
- Injury or changes to the pancreatic duct, such as dilatation (widening)
- Development of intraductal stones (calcifications in the pancreatic or bile ducts)

The primary and most common symptom associated with chronic pancreatitis is severe pain (experienced by at least 75% of patients), either episodic or intractable (unceasing), which significantly impacts quality of life. The pain may actually abate as the condition worsens and the pancreas ceases to function. Progressive chronic pancreatitis may also be associated with the development of complications (outlined below), such as, progressive fibrosis which may entrap nerves and contribute to pain levels and calcification of pancreatic tissue. In general, the degree of exocrine dysfunction typically reflects disease severity.

The predominant structural change of the pancreas in chronic pancreatitis consists of the replacement of healthy pancreatic glandular tissue with scar tissue that affects both exocrine and endocrine function. The glandular cells responsible for producing pancreatic enzymes that are excreted into the pancreatic duct and then into the digestive tract are destroyed, leading to pancreatic insufficiency and impaired digestion. As a result, patients may lose weight. The undigested food containing fat is evacuated through bowel movements. The stool is rich in undigested fat, and often bulky, oily, foul smelling, and difficult to be flushed away. This condition is referred to as *steatorrhea*. Patients may also experience diarrhea.

Patients often develop glucose intolerance as endocrine function begins to decrease. As chronic pancreatitis progresses and insulin producing islet cells are destroyed, endocrine function is severely reduced and patients develop Type I (insulin dependent) diabetes mellitus. Onset of diabetes generally occurs approximately 20 years after the disease develops.

In 2001, a classification system called TIGAR-O was published in the journal *Gastroenterology* (Vol.120(3):pp.682-707) to organize the various types of chronic pancreatitis by prevalence as well as by etiology and mechanism of injury to pancreatic tissue. TIGAR-O is an abbreviation of the following:

- T - toxic or metabolic etiology such as alcohol consumption and smoking

- I - idiopathic pancreatitis where a cause cannot be identified
- G - genetic etiology, also known as hereditary pancreatitis
- A - autoimmune etiology of pancreatitis
- R - recurrent severe acute pancreatitis
- O - obstructive mechanisms that cause chronic pancreatitis

Toxic/Metabolic Pancreatitis

Although only a small percentage of people who consume large quantities of alcohol develop chronic pancreatitis (approximately 5%), a large percentage (70-80%) of patients with chronic pancreatitis have a history of consuming large quantities of alcohol over a long period of time. Estimates vary regarding the quantity of alcohol and duration that raise the risk of CP, and they range from intake exceeding approximately three ounces per day for at least ten years, to exceeding five ounces per day for at least 10-15 years or more. Other causes included in this category include:

- Tobacco
- Toxins from kidney failure
- Metabolic disorders such as hypercalcemia and hyperlipidemia
- Certain medications

Exocrine insufficiency may develop as early as six years after diagnosis of alcoholic chronic pancreatitis, and endocrine insufficiency can appear as soon as eight years following a diagnosis. Approximately 95% of patients with alcoholic pancreatitis achieve pain relief about 10 years after diagnosis - a time which generally coincides with significant tissue damage and the onset of endocrine and exocrine insufficiency. However, the correlation between these two events is not clearly understood and is under investigation.

The exact mechanism regarding the relationship between smoking and the development of CP is unknown but the relationship has been confirmed. Smoking has recently been identified as an independent risk factor for various aspects of CP including:

- Progression of CP
- Development of calcifications and diabetes in people with alcoholic pancreatitis
- More rapid appearance of calcifications and diabetes in patients with non-alcoholic CP
- Development of pancreatic cancer

Idiopathic Chronic Pancreatitis

Idiopathic chronic pancreatitis, where no underlying cause can be identified, is said to account for up to 30% of all cases of chronic pancreatitis. There are two types of idiopathic chronic pancreatitis:

- Early onset - Average age at onset is 20 years old. Pain is a prominent symptom in up to 90% of patients. Other pancreatic features, such as endocrine and exocrine insufficiency and calcifications, are rare. Endocrine and exocrine insufficiency may develop in some individuals as long as 27 years after diagnosis.
- Late onset - Average age at onset is 56 and features are primarily the opposite of early-onset disease, i.e., frequent presence of calcifications and endocrine and exocrine insufficiency,

but little pain.

Genetic (Hereditary) Pancreatitis

Hereditary pancreatitis is transmitted via mutations on an autosomal dominant gene (PRSS1). Mutations of other genes (SPINK 1, PRSS2, and CFTR) have also been associated with hereditary pancreatitis. Incidence is equal among males and females. Pancreatitis is determined to be hereditary if two or more family members have or had pancreatitis in more than one generation.

Hereditary pancreatitis usually begins in childhood before the age of ten, although it can occur later in adolescence as well. The main symptoms are pancreatic pain and acute pancreatitis. The usual pattern of symptoms is recurrent episodes of upper abdominal pain lasting from two days to two weeks. Treatment for hereditary pancreatitis is usually similar to that of symptom relief for other types of chronic pancreatitis. Additional facts about hereditary pancreatitis include:

- Structural changes and calcifications occur typically between the ages of 22-25 years.
- Exocrine insufficiency occurs in up to 34% of people at a median age of 29 and endocrine insufficiency occurs in up to 26% at a median age of 38 years.
- Hereditary pancreatitis accounts for approximately 1% of cases of chronic pancreatitis.
- Approximately 20% of people with hereditary pancreatitis develop diabetes eight to ten years after the onset of pain.
- The risk of developing pancreatic cancer is approximately 10% at the age of 50, 18% at the age of 60, and 53% at the age of 75. Despite the elevated risk of pancreatic cancer, there does not appear to be a higher mortality rate among people with hereditary pancreatitis than among the general population. For patients with hereditary pancreatitis who smoke, there is a 50-fold increase of risk for developing pancreatic cancer.

For more information about hereditary pancreatitis, please click on the following link:
http://www.ncbi.nlm.nih.gov/pubmed/21907651

Autoimmune Pancreatitis

Autoimmune pancreatitis (AIP) is a T-cell mediated disease and is a rare form of chronic pancreatitis. There are more cases of AIP in Japan than in other countries, for unknown reasons. Attacks of acute pancreatitis, pancreatic calcifications, and/or cysts are rare. AIP is thought to account for 1-6% of cases of chronic pancreatitis, and onset is typically in late adulthood. Clinical features of AIP include:

- Abdominal pain (typically mild)
- Jaundice
- Weight loss
- Presence of a pancreatic mass

In 60% of cases, AIP is associated with other autoimmune diseases such as:

- Primary sclerosing cholangitis - a condition in which the bile ducts inside and outside the liver become inflamed, and scarring causes progressive blockage of ducts
- Primary biliary cirrhosis - an autoimmune disease of the liver marked by slow progressive destruction of the small bile ducts

- Sjogren's syndrome - an autoimmune disease that can affect many different parts of the body, but most often affects the tear and saliva glands, resulting in dry eyes and dry mouth
- Autoimmune hepatitis - an autoimmune disease in which the body's immune system attacks the liver

Autoimmune pancreatitis and pancreatic cancer share several features in common, making the differential diagnosis challenging. A distinguishing feature between them is that AIP will respond to steroid therapy, whereas pancreatic cancer will not. For more information about autoimmune pancreatitis, please click on the following link: http://www.ncbi.nlm.nih.gov/pubmed/21884246

Recurrent and Severe Acute Pancreatitis

Recurrent attacks of acute pancreatitis can eventually develop into chronic pancreatitis, with extensive tissue damage as well as endocrine and exocrine insufficiency.

Obstructive Chronic Pancreatitis

This condition is rare and is usually caused by a narrowing of the pancreatic duct which results in pancreatic tissue ischemia, fibrosis, acinar cell atrophy, and dilatation of the pancreatic duct before the blockage. This can be caused by factors such as trauma to the pancreas, pancreatic stones, pancreatic inflammation, or tumors.

There is another type of pancreatitis called *tropical pancreatitis* which is found throughout Asia, Africa, and other tropical regions. Tropical pancreatitis usually occurs between the ages of 12 and 15 and is characterized by recurrent episodes of abdominal pain. Diabetes usually develops later in life. Many patients also experience pancreatic stone formation.

Incidence of Chronic Pancreatitis

Most cases of chronic pancreatitis (CP) are diagnosed between the ages of 40-60. According to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the worldwide incidence of chronic pancreatitis is thought to be approximately 1.6 - 23 cases per 100,000 people, and it is thought to be rising, in part due to increasing alcohol consumption. The incidence of CP in all Western countries is approximately 6 per 100,000 people. It affects men four times as often as women. although the rate of chronic pancreatitis in women is rising. The average age of onset of CP is between 40 and 60 years. Among some of the various types of CP, the ages of onset include:

- 36 years old for alcoholic pancreatitis
- 10 years old for hereditary pancreatitis
- 23 years old for idiopathic early-onset pancreatitis
- 62 years old for idiopathic late-onset pancreatitis

Chronic pancreatitis is not reported as often as acute pancreatitis, possibly because it does not occur as frequently and is also not associated with as high a morbidity and mortality rate as acute pancreatitis. Also, CP is more difficult than acute pancreatitis to identify and diagnose due to the overlap of many symptoms with acute pancreatitis. As a result, acute pancreatitis and CP are often misdiagnosed by physicians.

Hospitalization for Chronic Pancreatitis

A patient with chronic pancreatitis (CP) may require hospitalization under certain circumstances, including:

- Acute flare-ups
- Management of severe pain
- Weight loss
- Treatment of complications such as pseudocyst

Hospitalizations for CP are increasing yearly, perhaps because of increased identification of CP, or because it is being diagnosed earlier because of improved imaging techniques and better informed physicians, or perhaps related to the statistics of alcohol consumption of any given country or population.

Causes of Chronic Pancreatitis

A number of causes for chronic pancreatitis (CP) have been identified:

- Gallstones
- Tobacco
- Alcoholism (quantity and duration of alcohol intake)
- Pancreatic duct obstruction (caused by strictures or stones)
- Hyperparathyroidism (overproduction of the parathyroid hormone that causes elevated levels of calcium and an increase in calcium secretion by the pancreas)
- Hyperlipidemia (increased levels of lipids or fats in the blood)
- Trauma to the abdominal area that result in inflammation, pseudocysts, or strictures that impact pancreatic function
- Congenital disorders (occur in approximately 10% of the population; structural change affects the drainage of specific ducts)
- *Alpha 1-antitrypsin deficiency* (an enzyme deficiency that causes liver disease in adults and children)

Traditionally, alcohol has been considered to be the primary cause of chronic pancreatitis in industrialized countries. However, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) notes that the presence of gallstones is increasing rapidly as a major cause of chronic pancreatitis and that alcohol use and gallstones cause 80% of cases of chronic pancreatitis. There is a known link between obesity and the formation of gallstones; however, it is not clear if the increase in incidence of gallstone-related pancreatitis is connected to the increasing rate of obesity in the general population.

Smoking has been identified as an independent risk factor for both acute and chronic pancreatitis. It is associated with earlier onset of chronic pancreatitis and faster progression of alcoholic CP and late-onset idiopathic CP. Heavy smoking is also associated with recurrent acute pancreatitis. The association between smoking and pancreatitis appears to be related to cumulative exposure to

cigarettes (dose-dependent). The effect of smoking is independent of alcohol use but may be augmented by alcohol use. For further information about smoking, alcohol, and pancreatitis, please click on the following link: http://www.ncbi.nlm.nih.gov/pubmed/19506173

Genetics and Chronic Pancreatitis

There is growing evidence of a genetic component in the development of CP. Recent findings include:

- Chronic pancreatitis has been associated with the mutation of a gene identified as CFTR. In young patients who develop CP, there are two CFTR mutations, in addition to a mutation in a gene identified at SPINK1.
- Hereditary pancreatitis has been traced to mutations of Gene 7.
- Cystic fibrosis (CF) is a genetic abnormality and, depending on the types of mutations, some CF patients develop chronic pancreatitis of varying intensities.
- Although 70-80% of the cases of chronic pancreatitis are caused by alcoholism, only approximately 10% of alcoholics develop chronic pancreatitis. This suggests that in the 10% who develop CP, there may be a genetic predisposition which is necessary in order for the condition to occur when combined with alcohol.
- A genetic mutation in tropical calcific pancreatitis has been identified on the SPINK I gene or Pancreatic Secretory Trypsin Inhibitor (PSTI).
- Idiopathic chronic pancreatitis also has been shown to be associated with CFTR and PSTI mutations.

Pain in Chronic Pancreatitis

Pain is a predominant feature in up to 90% of patients with alcohol-induced pancreatitis and in up to 50% of patients with other types of CP. Chronic pancreatitis-related pain is responsible for up to 90,000 admissions to hospitals in the U.S. per year, as well as for narcotic dependency, and the pain has a strong impact on quality of life. Pain associated with acute pancreatitis initially is typically limited to the duration of the individual episode. Some people though, may experience chronic abdominal pain following recurrent episodes of acute pancreatitis with the progression to chronic pancreatitis. The pain of chronic pancreatitis is characterized in several ways, including:

- Worsens with eating or drinking
- May be relieved by sitting upright or leaning forward
- Described as "penetrating" and radiating to the back, or as a continuous dull abdominal pain

What causes the intense pain in chronic pancreatitis? For each individual, there may be a variety of factors leading to the intensity and duration of pain. Pain may result from various sources including:

- Increased pressure in the pancreatic duct (hypertension) due to the continued secretion of pancreatic enzymes, despite the presence of an obstruction in the duct
- Pressure on tissue around the distended or hypertensive duct and its branches
- Single or multiple strictures or calculi (stones)
- Pancreatic fibrosis and inflammation that causes bile duct or duodenal stenosis

- Scar tissue from pancreatic fibrosis that leads to increased pressure
- Pancreatic ischemia (decreased blood flow due to increased tissue pressure)
- Changes that occur to the nerves innervating the pancreas, including:

    - nerve growth - demonstration of increased number and diameter of pancreatic nerves
    - damage to the pancreatic nerves
    - large axonal trunks (the long part of a nerve cell that transmits impulses) in the pancreatic head and possible axonal degeneration in other areas
    - an increase in *eosinophils,* a type of white blood cell that increases with infection and allergy
    - infiltration of immune cells into the nerves in the pancreas correlates positively with the intensity of pain (known as *neuroimmune interaction* theory)

The investigation of neuropathy (nerve damage) in the pancreas and the relationship between nerve cells and inflammatory or immune cells may provide additional insight regarding the source of pain in chronic pancreatitis.

For further information about the relationship between pain and pancreatitis, please click on the following link: http://www.ncbi.nlm.nih.gov/pubmed/21676159

In addition to the intense physical discomfort caused by pain in patients with chronic pancreatitis, pain has a significant impact on the emotional and mental status of patients. Intense pain of CP strongly impacts the quality of life of patients as it leads to problems with:

- Depression
- Addiction to pain relievers (opiates)
- Unemployment (patients may not be able maintain jobs)
- Social isolation

This aspect of chronic pancreatitis must be seriously considered in the diagnostic workup and treatment protocol for all CP patients experiencing pain.

Nutrition and Chronic Pancreatitis

As noted above, the pancreas plays a crucial role in digestion via the endocrine and exocrine systems, and the hallmark of CP is permanent damage to both of these functions. As a result, malnutrition and diabetes are significant complications associated with CP. In addition, because eating provokes pain in many patients, in response they eat less to avoid the pain. Many clinicians recommend that CP patients at risk be screened for these two conditions.

Exocrine insufficiency, namely reduced production and secretion of digestive enzymes, causes impaired digestion of fats, carbohydrates, and protein. When lipase secretion is reduced more than 90%, stool becomes fatty, oily, and foul-smelling, a condition called *steatorrhea*. Fat content of stool is measured and, if there is more than 15g of fat per day excreted with the stool, the condition is considered severe. Impairment of fat absorption is more clinically significant than of other

nutrients.

Endocrine insufficiency leads to diabetes in up to 50% of patients with CP. The diabetes is caused by a loss of islet cell function that results in lack of insulin production. Managing CP-related diabetes is complicated by poor nutrient absorption caused by exocrine dysfunction, poor eating habits, and in many cases, alcohol abuse. As a result of these difficulties, CP-related diabetes elevates the risk of *hypoglycemia* (low blood sugar levels), not only *hyperglycemia* (elevated blood sugar), which is more commonly associated with non-CP-related diabetes.

Weight loss is a common concern for patients with CP and occurs because of malabsorption of nutrients and because many people limit food intake because of pain. In addition, weight gain and maintenance are challenges for many patients with CP, particularly if they are experiencing steatorrhea. If excessive alcohol intake is a factor in their CP, weight gain is even more difficult to achieve because of the effects of alcohol, which include:

- Poor choices for dietary intake
- Poor appetite
- Impaired absorption of nutrients, possibly because of the effect of alcohol on the pancreatic and gastrointestinal function

Approximately 40% of patients with severe exocrine insufficiency experience vitamin B12 malabsorption. Malabsorption of vitamins A, D, E, and K, calcium, and iron is less common in patients with CP.

Complications of Chronic Pancreatitis

In addition to pain, there are several complications that may occur in patients with chronic pancreatitis (CP), including:

- Diabetes
- Nutrient malabsorption - If pancreatic enzyme secretions are reduced more than 90%, absorption of nutrients is affected which can lead to weight loss and steatorrhea
- Deficiency of Vitamins A, D, E, K, and/or B12
- Calcifications - small deposits of mineral salts collect in the pancreas and can lead to destruction and hardening of the tissue; can develop up to ten years after the first attack of pancreatitis and are removed surgically, if needed
- Pseudocyst - fluid collection within a well-defined capsule that may develop with acute or chronic pancreatitis; may or may not be symptomatic; common in up to 30% of patients, especially those with alcoholic pancreatitis; complications include infection, rupture, obstruction of ducts, or intracystic bleeding
    - if asymptomatic, pseudocysts may resolve spontaneously
    - if symptomatic and connected to the pancreatic ductal system, pseudocysts usually require surgical intervention (e.g., drainage)
- Pancreatic duct dilatation or stricture

- Bile duct obstruction - stones or hard and fibrous pancreatic tissue can lead to stenosis or obstruction as duct passes through the head of the pancreas; duct may develop strictures or may be compressed due to inflammation; occurs in up to 9% of patients with CP
- Duodenal stenosis - narrowing of the duodenum
- Portal hypertension - increased pressure in the portal vein that carries blood into the liver
- Sphincter of Oddi Dysfunction (SOD) - rare but can occur in acute or chronic pancreatitis
- Ascites - collection of fluid in the peritoneal cavity that can occur if a cyst ruptures
- Pancreatic fistula - an opening in the pancreatic tissue that may allow pancreatic fluid out of the pancreas; most fistulae close spontaneously but some require surgical intervention
- Blood clots in the splenic vein (very rare)
- Sepsis
- Pancreatic abscess
- Pancreatic cancer

Risk of Pancreatic Cancer and Chronic Pancreatitis

Long-standing, pre-existing chronic pancreatitis (CP) in general, and hereditary pancreatitis in particular, are considered high risk factors for developing pancreatic cancer. There is a 15-fold increase in the risk of pancreatic cancer for people with chronic pancreatitis, especially for those with alcoholic pancreatitis; and a 40-50-fold increase for patients with hereditary pancreatitis. Presently, pancreatic cancer occurs in approximately 5% of all patients with CP but researchers expect that as the genetics of pancreatitis and pancreatic cancer are better understood, recognition of the relationship between these two pancreatic conditions will account for a higher percentage of cases.

There is a pancreatic lesion classification system which has been proposed, called *PanIN* (pancreatic intraepithelial neoplasia) which describes three stages of lesions with abnormal-appearing pancreatic ductal tissue that are linked to genetic alterations present in certain types of pancreatitis. These stages are considered to be precursors for cancer and all have been found in most patients with chronic pancreatitis who develop pancreatic cancer.

Doctors recommend that patients with chronic pancreatitis who develop a mass in the pancreatic duct wall undergo ultrasound with aspiration or biopsy once a year to monitor any changes. Some experts recommend screening all patients above the age of 40 who have hereditary pancreatitis. Any change in symptoms, such as pain, weight loss, or jaundice should be sufficient reason for these patients to be evaluated for pancreatic cancer. Patients with positive outcomes may need to consider prophylactic surgical resection in an effort to avoid what may be an increased probability of developing cancer.

For further information about pancreatitis-related pancreatic cancer, please click on the following link: http://www.ncbi.nlm.nih.gov/pubmed/20510834

Relationship between Acute Pancreatitis and Chronic Pancreatitis

Whereas in the past, the tendency was to view acute and chronic pancreatitis as two separate conditions, currently, the distinction between the two conditions is not so clear. Acute pancreatitis is characterized as discrete symptomatic events followed by pain-free intervals between episodes. As time goes on, patients may begin to experience pain even between episodes with eventual progression to chronic pancreatitis, characterized by injury to the pancreatic tissue, as well as endocrine and exocrine impairment. For some patients, the pain abates as the tissue damage progresses. Others may develop chronic pancreatitis after only one episode of acute pancreatitis, while yet others may develop chronic pancreatitis without ever having had an episode of acute pancreatitis.

In one study published in 2011 in *Pancreas* (Vol.40(8):pp.1195-200), the progression of acute pancreatitis to chronic pancreatitis was analyzed in 352 patients who were hospitalized because of AP or CP. Results indicated that in 85 patients (24%), AP progressed to CP; 48% of those patients had alcoholic CP, 47% had idiopathic CP, and 4.8% had CP from other causes. The mortality rate for patients whose conditions progressed from acute to chronic pancreatitis was 2.7 times higher than in patients with AP that did not progress to CP. Smoking was identified as the strongest risk factor associated with progression.

The mechanism that causes some cases of acute pancreatitis to progress into chronic pancreatitis is not clearly understood. One of the theories that explains this progression is called the *sentinel acute pancreatitis event* (SAPE), which posits that the first event or episode of acute pancreatitis causes pancreatic injury that makes the pancreas vulnerable to other exposures such as alcohol and tobacco. In response to recurrent injury, macrophages (white blood cells) release large amounts of an inflammatory suppressant called transforming growth factor (TGF)-b, and sustained high levels of TGF-b cause an accumulation of collagen, leading to fibrosis and scarring of pancreatic tissue, as well as loss of pancreatic function.

Another theory regarding the development of pancreatitis in general is that when a person with a predisposition for pancreatitis is exposed to certain toxins, such as alcohol, inflammation follows. If the exposure to the toxin continues and the inflammation is ongoing, certain types of cells are produced that result in fibrosis and chronic pancreatitis.

For more information about the development of chronic pancreatitis, please click on the following link: http://www.ncbi.nlm.nih.gov/pubmed/18092710

The **Intelligent Patient Overview** in the complete **Medifocus Guidebook on Chronic Pancreatitis** also includes the following additional sections:

- **Diagnosis of Chronic Pancreatitis**
- **Treatment Options for Chronic Pancreatitis**
- **The Role of Complementary Medicine in Chronic Pancreatitis**
- **Psychosocial Considerations for Chronic Pancreatitis**
- **New Developments in Chronic Pancreatitis**
- **Questions to Ask Your Health Care Provider about Chronic Pancreatitis**

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3 - Guide to the Medical Literature

Introduction

This section of your *MediFocus Guidebook* is a comprehensive bibliography of important recent medical literature published about the condition from authoritative, trustworthy medical journals. This is the same information that is used by physicians and researchers to keep up with the latest advances in clinical medicine and biomedical research. A broad spectrum of articles is included in each *MediFocus Guidebook* to provide information about standard treatments, treatment options, new developments, and advances in research.

To facilitate your review and analysis of this information, the articles in this *MediFocus Guidebook* are grouped in the following categories:

- Review Articles - 45 Articles
- General Interest Articles - 71 Articles
- Surgical Therapy Articles - 30 Articles
- Clinical Trials Articles - 13 Articles

The following information is provided for each of the articles referenced in this section of your *MediFocus Guidebook:*

- Title of the article
- Name of the authors
- Institution where the study was done
- Journal reference (Volume, page numbers, year of publication)
- Link to Abstract (brief summary of the actual article)

Linking to Abstracts: Most of the medical journal articles referenced in this section of your *MediFocus Guidebook* include an abstract (brief summary of the actual article) that can be accessed online via the National Library of Medicine's PubMed® database. You can easily access the individual abstracts online via PubMed® from the "electronic" format of your *MediFocus Guidebook* by clicking on the URI that is provided for each cited article. If you purchased a printed copy of the *MediFocus Guidebook*, you can still access the abstracts online by entering the individual URI for a particular abstract into your computer's web browser.

Recent Literature: What Your Doctor Reads

Database: PubMed <January 2016 to July 2020>

Review Articles

1.

Chronic Pancreatitis: Managing a Difficult Disease.

Authors: Hart PA; Conwell DL
Institution: Section of Pancreatic Disorders, Division of Gastroenterology, Hepatology, and Nutrition, The Ohio State University Wexner Medical Center, Columbus, Ohio, USA.
Journal: Am J Gastroenterol. 2020 Jan;115(1):49-55. doi: 10.14309/ajg.0000000000000421.
Abstract Link: http://www.medifocus.com/abstracts.php?gid=GS007&ID=31764092

2.

CT and MR features that can help to differentiate between focal chronic pancreatitis and pancreatic cancer.

Authors: Srisajjakul S; Prapaisilp P; Bangchokdee S
Institution: Division of Diagnostic Radiology, Department of Radiology, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wanglang Road, Bangkoknoi, Bangkok, 10700, Thailand. tiam.mahidol@gmail.com. Department of Internal Medicine, Pathum Thani Hospital, 7 Ladlumkaew-Patumthani Road, Muang District, Pathum Thani, 12000, Thailand.
Journal: Radiol Med. 2020 Apr;125(4):356-364. doi: 10.1007/s11547-019-01132-7. Epub 2020 Jan 13.
Abstract Link: http://www.medifocus.com/abstracts.php?gid=GS007&ID=31933064

3.

Geographical variance in reporting of elective surgery for chronic pancreatitis.

Authors: Baltatzis M; Jegatheeswaran S; Siriwardena AK
Institution: Regional Hepato-Pancreato-Biliary Surgery Unit.
Journal: Eur J Gastroenterol Hepatol. 2019 Mar;31(3):303-311. doi: 10.1097/MEG.0000000000001321.

Abstract Link: http://www.medifocus.com/abstracts.php?gid=GS007&ID=30489446

4.

Ductal Cell Reprogramming to Insulin-Producing Beta-Like Cells as a Potential Beta Cell Replacement Source for Chronic Pancreatitis.

Authors: Jawahar AP; Narayanan S; Loganathan G; Pradeep J; Vitale GC; Jones CM; Hughes MG; Williams SK; Balamurugan AN
Institution: Clinical Islet Cell Laboratory, Center for Cellular Transplantation, Cardiovascular Innovation Institute, Department of Surgery, University of Louisville, Louisville, KY 40202, United States.
Journal: Curr Stem Cell Res Ther. 2019;14(1):65-74. doi: 10.2174/1574888X13666180918092729.
Abstract Link: http://www.medifocus.com/abstracts.php?gid=GS007&ID=30227823

5.

Mechanism-based pain management in chronic pancreatitis - is it time for a paradigm shift?

Authors: Kuhlmann L; Olesen SS; Olesen AE; Arendt-Nielsen L; Drewes AM
Institution: a Centre for Pancreatic Diseases and Mech-Sense, Department of Gastroenterology and Hepatology , Aalborg University Hospital , Aalborg , Denmark.
Journal: Expert Rev Clin Pharmacol. 2019 Mar;12(3):249-258. doi: 10.1080/17512433.2019.1571409. Epub 2019 Feb 5.
Abstract Link: http://www.medifocus.com/abstracts.php?gid=GS007&ID=30664364

6.

Emerging Role of Chinese Herbal Medicines in the Treatment of Pancreatic Fibrosis.

Authors: Liu C; Li S; Zhang Q; Guo F; Tong M; Martinez MFYM; Wang HH; Zhao Y; Shang D
Institution: * Department of General Surgery, The First Affiliated Hospital of Dalian Medical University, Dalian, Liaoning, P. R. China.
Journal: Am J Chin Med. 2019;47(4):709-726. doi: 10.1142/S0192415X1950037X. Epub 2019 May 15.
Abstract Link: http://www.medifocus.com/abstracts.php?gid=GS007&ID=31091974

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- Review Articles - 45 Articles
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- Clinical Trials Articles - 13 Articles

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4 - Centers of Research

This section of your *MediFocus Guidebook* is a unique directory of doctors, researchers, medical centers, and research institutions with specialized research interest, and in many cases, clinical expertise in the management of this specific medical condition. The *Centers of Research* directory is a valuable resource for quickly identifying and locating leading medical authorities and medical institutions within the United States and other countries that are considered to be at the forefront in clinical research and treatment of this disorder.

Use the *Centers of Research* directory to contact, consult, or network with leading experts in the field and to locate a hospital or medical center that can help you.

The following information is provided in the *Centers of Research* directory:

- **Geographic Location**
    - United States: the information is divided by individual states listed in alphabetical order. Not all states may be included.
    - Other Countries: information is presented for select countries worldwide listed in alphabetical order. Not all countries may be included.
- **Names of Authors**
    - Select names of individual authors (doctors, researchers, or other health-care professionals) with specialized research interest, and in many cases, clinical expertise in the management of this specific medical condition, who have recently published articles in leading medical journals about the condition.
    - E-mail addresses for individual authors, if listed on their specific publications, is also provided.
- **Institutional Affiliations**
    - Next to each individual author's name is their **institutional affiliation** (hospital, medical center, or research institution) where the study was conducted as listed in their publication(s).
    - In many cases, information about the specific **department** within the medical institution where the individual author was located at the time the study was conducted is also provided.

Centers of Research

United States

CA - California

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Dua MM	Department of Surgery, Stanford University School of Medicine, Stanford, CA, USA. mdua@stanford.edu.
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Machicado JD	University of Colorado Anschutz Medical Center, Aurora, CO, United States. University of Pittsburgh Medical Center, Pittsburgh, PA, United States. Electronic address: yadavd@upmc.edu.

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- Centers of Research for relevant states in the United States
- Centers of Research listed for relevant countries outside the United States

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5 - Tips on Finding and Choosing a Doctor

Introduction

One of the most important decisions confronting patients who have been diagnosed with a serious medical condition is finding and choosing a qualified physician who will deliver a high level and quality of medical care in accordance with currently accepted guidelines and standards of care. Finding the "best" doctor to manage your condition, however, can be a frustrating and time-consuming experience unless you know what you are looking for and how to go about finding it.

The process of finding and choosing a physician to manage your specific illness or condition is, in some respects, analogous to the process of making a decision about whether or not to invest in a particular stock or mutual fund. After all, you wouldn't invest your hard eared money in a stock or mutual fund without first doing exhaustive research about the stock or fund's past performance, current financial status, and projected future earnings. More than likely you would spend a considerable amount of time and energy doing your own research and consulting with your stock broker before making an informed decision about investing. The same general principle applies to the process of finding and choosing a physician. Although the process requires a considerable investment in terms of both time and energy, the potential payoff can be well worth it--after all, what can be more important than your health and well-being?

This section of your Guidebook offers important tips for how to find physicians as well as suggestions for how to make informed choices about choosing a doctor who is right for you.

Tips for Finding Physicians

Finding a highly qualified, competent, and compassionate physician to manage your specific illness or condition takes a lot of hard work and energy but is an investment that is well-worth the effort. It is important to keep in mind that you are not looking for just any general physician but rather for a physician who has expertise in the treatment and management of your specific illness or condition. Here are some suggestions for where you can turn to identify and locate physicians who specialize in managing your disorder:

- **Your Doctor** - Your family physician (family medicine or internal medicine specialist) is a good starting point for finding a physician who specializes in your illness. Chances are that your doctor already knows several specialists in your geographic area who specialize in your illness and can recommend several names to you. Your doctor can also provide you with information about their qualifications, training, and hospital affiliations.

The **Tips on Finding and Choosing a Doctor** in the complete **Medifocus Guidebook on Chronic Pancreatitis** includes additional information that will assist you in locating a highly qualified and competent physician to manage your specific illness.

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6 - Directory of Organizations

American College of Gastroenterology
POB 342260; Bethesda, MD 20827
301.263.9000
www.acg.gi.org

American Gastroenterological Association
4930 Del Ray Avenue; Bethesda, MD 20814
301.654.2055
info@gastro.org
www.gastro.org

American Pancreatic Association
POB 14906 Minneapolis, MN 55414
612.625.7700
apa@umn.edu
www.american-pancreatic-association.org

Digestive Disease National Coalition
507 Capitol Court, NE, Suite 200; Washington, DC 20002
202.544.7497; 202.546.7105 (fax)
edberg@hmcw.org
www.ddnc.org

Digestive Disorders Foundation
CORE; 3 St. Andrews Place; London NW1 4LB UK
020.7486.0341; 020.7224.2012 (fax)
info@corecharity.org.uk
www.digestivedisorders.org.uk

International Foundation for Functional Gastrointestinal Diseases
POB 170864; Milwaukee, WI 53217
888.964.2001; 414.964.1799
iffgd@iffgd.org
www.iffgd.org

The **Directory of Organizations** in the complete **Medifocus Guidebook on Chronic Pancreatitis** includes a list of selected disease organizations and support groups that are helping people diagnosed with Chronic Pancreatitis.

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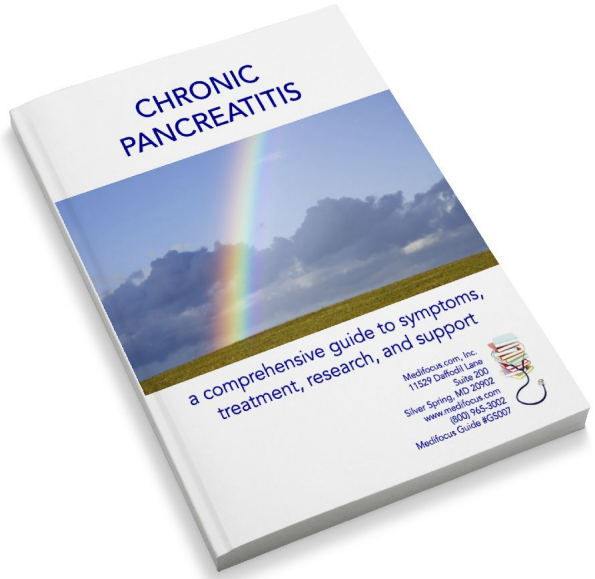

This document is only a SHORT PREVIEW of the **Medifocus Guidebook on Chronic Pancreatitis**. It is intended primarily to give you a general overview of the **format and structure** of the Guidebook as well as select pages from each major Guidebook section listed in the Table of Contents.

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