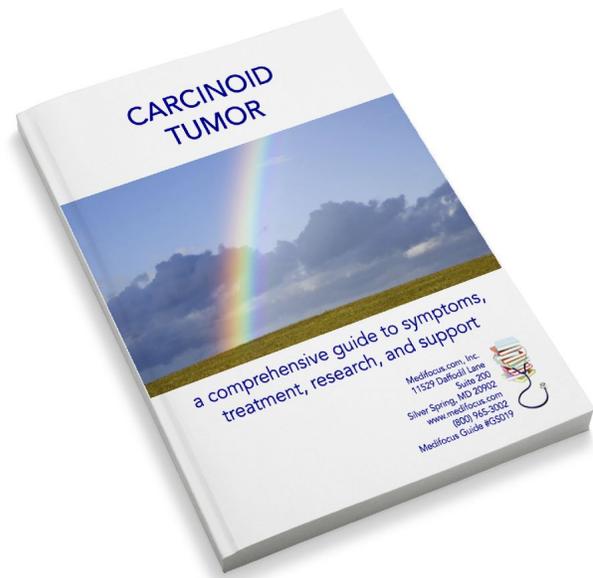


Preview of the Medifocus Guidebook on: Carcinoid Tumors

Updated January 2, 2022



This document is only a SHORT PREVIEW of the **Medifocus Guidebook on Carcinoid Tumors**. 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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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 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. 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

CARCINOID TUMORS

Introduction to Carcinoid Tumors

The *neuroendocrine system* is made up of cells that "connect" the nervous system and the endocrine system. Neuroendocrine cells release hormones (sometimes called *peptides*) into the circulatory system in response to a stimulus received from the nervous system. These specialized cells are scattered throughout the organs in the body and are the cells that give rise to neuroendocrine tumors.

Neuroendocrine tumors (NETs) include both *carcinoid tumors* and *pancreatic endocrine tumors* (PETs). Carcinoid tumors represent the largest number of neuroendocrine tumors and pose a significant challenge to the clinician because they produce a unique clinical syndrome. Consequently, their diagnosis is difficult and often delayed. The clinician requires a high index of suspicion and confirmation with biochemical tests in order to establish their diagnosis. Because the majority of neuroendocrine tumors of the pancreas and carcinoid tumors that involve the wall of the gut have similar biological characteristics, the approach to diagnosis and treatment can be applied broadly to all classes of NETs.

The origins of NETs are thought to occur in the enterchromaffin-like cells, which are present in the wall of the gastrointestinal tract, pancreas, and lung. Enterochromaffin-like cells are neuroendocrine cells in the gastric mucosa that control acid secretion by releasing histamine. In normal physiology these cells regulate *secretion* and *motility* (movement of food through the digestive tract).

There are many types of tumors that arise from the neuroendocrine system of which carcinoid tumors are the most common. Carcinoid tumors were initially identified in 1888 and were thought to clinically and histologically (cellular appearance under a microscope) resemble carcinoma cells (highly malignant cancer cells) but behave in a more benign fashion than true cancer cells. Over the years it became clear that carcinoid tumors can be quite aggressive, can metastasize, and can cause *carcinoid syndrome*. Most carcinoid tumors are now known to be slow growing malignant tumors that have their own specific biological and clinical characteristics.

Like many types of cells in the body, neuroendocrine cells can begin to reproduce out of control and cause cancer. This occurs more commonly as part of the Multiple Endocrine Neoplasia (MEN) Type I Syndrome which is characterized by a genetic mutation as described later. Carcinoid tumors share some properties with other cancer cells such as uncontrolled, overproduction of the cells that results in tumor formation and malignant potential. However, carcinoid tumor cells are distinguished from most other types of tumors in that they secrete various hormone-like substances (e.g., serotonin, noradrenalin, histamines) which may cause symptoms throughout the body rather

than symptoms localized to the organ where the tumor originates.

Carcinoid tumors can appear anywhere neuroendocrine cells are present including the gastrointestinal (GI) tract, lungs, ovaries, pancreas, appendix, small and large intestine, testes, and rectum. The location of origin of carcinoid tumors is divided into three categories:

- *Foregut Carcinoid Tumors* - These tumors originate in the lungs, thymic gland, pancreas, stomach, and duodenum (lung and stomach are most common locations)
- *Midgut Carcinoid Tumors* - These tumors originate in the small intestines, appendix, and right colon (small intestines and appendix are most common locations)
- *Hindgut Carcinoid Tumors* - These tumors originate in the large intestines, specifically in the transverse colon, descending colon, and rectum (rectum is most common location)

The largest number of neuroendocrine cells is found in the gastrointestinal tract, since it is the largest endocrine organ in the body. Indeed, according to the National Cancer Data Registry, approximately 70% of carcinoid tumors arise from locations within the gastrointestinal tract and up to 25% arise from the lungs.

Carcinoid tumors of the lung can be divided into two types:

- *Typical carcinoids* which grow slowly and only rarely spread beyond the lungs. They are usually found along the major airways and, according to the American Cancer Society, are approximately nine times more common than atypical carcinoids.
- *Atypical carcinoids* are faster growing tumors and are more likely to spread to other organs. They are also more likely to be located in the peripheral areas of the lung.

Although estimates vary regarding the incidence of specific locations of origin for carcinoid tumors, the Carcinoid Cancer Foundation reports that approximately two-thirds of diagnosed cases arise from the GI tract. Within the GI tract, the incidence of tumor by location is:

- Small intestines - 39%
- Appendix -26%
- Rectum - 15%
- Colon - 5-7%
- Stomach - 2-4%

An updated population-based review of carcinoid tumor that was published in 2004 in *Annals of Surgery* (vol.240(1):117-122) reported that tumors of the GI tract accounted for approximately 55% of all carcinoids and that the breakdown of carcinoid tumor within the GI tract includes:

- Small intestines - 44%
- Rectum - 19%
- Appendix - 16%
- Colon - 10%
- Stomach - 7%

There are approximately 3,000 cases of carcinoid cancer arising from the lung diagnosed each year. They comprise one to two percent of all lung cancers.

Other locations for carcinoid tumors (e.g., testis, ovary, prostate, breast, bladder, larynx) are infrequent or rare and account for only about 3 to 5% of all carcinoid tumors. It is estimated that in up to 15% of patients with carcinoid tumors, distant metastases have developed by the time they are diagnosed with a carcinoid tumor.

The potential for malignant growth of carcinoid tumors appears to be related to several factors including:

- The site at which the tumor originates
- The depth of tumor invasion into adjacent tissue
- The size of the tumor

It is estimated that approximately 10% of patients with carcinoid tumors develop *carcinoid syndrome* that manifests itself with symptoms related to the various substances produced by the tumors. A more detailed description of carcinoid syndrome follows later in this section.

Carcinoid Tumor Statistics

According to the American Society of Clinical Oncology (ASCO), approximately 11,500 people in the United States are diagnosed each year with a carcinoid tumor. About 66% of all carcinoid tumors develop in the gastrointestinal tract. If the tumor can be surgically removed and has not spread outside of the organ where it started, the 5-year relative survival rate for gastrointestinal carcinoid tumors is in the range of 70% to 90%. The next most common site for the development of carcinoid tumors is in the lungs. Approximately 3,000 new cases of lung carcinoid tumors are diagnosed in the United States each year. There are two types of lung carcinoid tumors:

- Typical carcinoid lung tumors - grow slowly and rarely metastasize (spread) to other areas of the body. About 90% of all carcinoid lung tumors are classified as "typical".
- Atypical carcinoid lung tumors - more aggressive than typical carcinoid lung tumors and are more likely to spread to other organs. Approximately 10% of all carcinoid lung tumors are classified as "atypical".

According to ASCO, the 5-year relative survival rate for lung carcinoid tumors is as follows:

- Typical carcinoid lung tumors - 85% to 90%
- Atypical carcinoid lung tumors - 50% to 60%

Carcinoid tumors are in general quite rare and occur in approximately 2.5-5 per 100,000 people. It is probable that more people may actually have carcinoid tumors but because carcinoids are often asymptomatic, an individual may never know that a carcinoid has developed. Consequently, the majority of cases are discovered incidentally during a routine medical examination. The age at diagnosis varies somewhat among specific tumor locations but typically, most people diagnosed

with carcinoid tumor are in their 50s.

Carcinoid tumors are more prevalent among African-American males (approximately 4.5 per 100,000 people) than among Caucasian males (approximately 2.5 per 100,000 people). Estimates vary as to whether the incidence is equal among men and women or if it is slightly higher for men. The most common site of carcinoid tumor occurrence for men is in the small intestines and the appendix for women. Carcinoid lung cancer is more common in Caucasians than in African-American, Asian-Americans, or Hispanic/Latinos. It is more common in women than men and the average age at diagnosis is 60.

While the incidence of carcinoid tumors has increased over the past 30 years, it is not clear whether this is due to unknown factors or if it is due to the improvement of diagnostic testing so that more cases are being identified. With the recent ability to measure serum hormone levels combined with refined diagnostic imaging studies the increase in the incidence probably reflects a greater public awareness of these tumors. The majority of patients with carcinoid tumors present in the fifth decade of life. In general these patients are otherwise healthy and there are no pre-existing medical problems or environmental exposures. Some studies have suggested that patients with carcinoid tumors may have a higher risk of developing other malignancies.

Pathology of Carcinoid Tumors

The term "carcinoid" tumor was originally used to describe a group of tumors that were thought to be benign (non-malignant). It is now clear that while carcinoid tumors are slow growing, depending on certain factors, they do carry a significant metastatic potential. Morphologically (by cellular appearance) there are approximately five different types of carcinoid tumor cells ranging from very well defined types, which carry the best prognosis, to undifferentiated types, which are associated with a poorer prognosis. There is also increased vascularity (blood supply) within the tumor.

Histologically, carcinoid tumors are characterized by monotonous sheets of cells containing small compact nuclei that are uniform in appearance and contain electron dense granules that contain biologically active amines and/or neuropeptides. These granules contain chromogranins (A and C), neuron specific enolase and synaptophysins in varying concentrations that can be measured to assess the biological function of the tumors.

Carcinoid tumors are unique from other cancer cell in that they produce numerous hormone-like substances including:

- Amines
 - serotonin
 - noradrenalin
- Polypeptides
 - ACTH (adrenocorticotrophic hormones)

- gastrin
 - insulin
 - growth hormone
-
- Prostaglandins

Each of these hormone-like substances can cause varying types of symptoms.

In many cases, the location of the primary tumor can be identified based on the bioactive hormone-like substances that it produces. These include:

- *Foregut tumors* - produce low amounts of serotonin but higher levels of other substances such as gastrin, 5-HTP, and corticotropins.
- *Midgut tumors* - tend to produce serotonin and tachykinins which are responsible for the symptoms of carcinoid syndrome when the tumor spreads to the liver
- *Hindgut tumors* - do not produce serotonin but may produce other hormones (e.g., low levels of gastrin)

Studies have shown that serum (blood) levels of a particular hormone have little predictive value for assessing the malignant potential of carcinoid tumors. Furthermore, the size of a particular tumor does not necessarily correlate with the level of hormone production or the severity of the clinical syndrome.

Risk Factors for Carcinoid Tumors

Though risk factors for the development of carcinoid tumors have not been clearly established, there appear to be some patterns that have emerged including:

- Age - most cases of carcinoid tumors appear in the 4th to 5th decade of life
- Race - incidence of carcinoid tumors is higher among African American men than Caucasian men
- Gender - some studies have shown that there may be a higher incidence of carcinoid tumors among men than women
- Family history - there appears to be a familial component since first degree relatives of patients have a higher risk of developing carcinoid tumors.
- Social history- there does not appear to be an association with environmental toxins, alcohol or tobacco products.
- Preexisting stomach conditions that relate to the production of stomach acid may increase the risk of developing carcinoid tumors of the GI tract.
- Smoking - the American Cancer Society estimates that smoking may double the risk of developing carcinoid tumors in the small intestines but seems to be unrelated to carcinoid tumors of the lung.

- Genetic component - there are three hereditary syndromes where genetic mutations may predispose individuals towards developing carcinoid tumors:
 - Multiple Endocrine Neoplasm Syndrome type 1 (MEN1) -mutation appears on chromosome 11. This is thought to elevate the risk of carcinoid tumors in the stomach.
 - Von Hippel-Landau Disease (VHL) - mutation is found on chromosome 3
 - Neurofibromatosis type 1 (NF-1) - the mutation for this disorder appears on chromosome 17

Better ways of identifying genetic aspects related to carcinoid tumors are being investigated on an ongoing basis and progress is being made such as relating midgut carcinoid tumors with abnormalities on chromosomes 11 and 18. This knowledge will eventually be helpful regarding screening, identification of those people at high risk, and treatment.

Multiple Endocrine Neoplasm Syndrome (MEN)

There are three major patterns of disease that comprise the MEN syndrome: type I and type II, which has been subdivided into MEN IIA and IIB. With the cloning of the genes for MEN we have a better understanding of the pattern of gene mutations occurring among affected families. Tumors involved in the MEN syndromes occur within endocrine, gastrointestinal, or neural (nervous system) tissues. MEN syndromes are inherited as autosomal dominant genes with varying degrees of penetrance. Therefore, the same mutation may manifest itself clinically in affected individuals at differing ages. There may also be variability in the malignant potential of neuroendocrine tumors within a given family.

MEN I Tumor Genetics

MEN-1 is an inherited syndrome characterized by the occurrence of neoplastic tumors involving the parathyroid, pancreas, gastrointestinal tract and lung. The MEN I gene locus (MENIN gene) is assigned to 11q13 and inactivating mutations of this gene result in the syndrome. Patients with this disorder have been demonstrated to have losses of heterozygosity (LOH) of this gene. Now that the gene locus has been discovered, it is possible to determine the patterns of inheritance observed in MEN I.

MEN I-Associated Tumors

The MEN-1 Syndrome is associated with the development of gastroenteropancreatic (GEP) tumors, including carcinoid tumors. This association appears to be genetically linked and hyperparathyroidism (a condition marked by over production of the hormone parathormone by the parathyroid glands) occurs in 60% of the affected patients by age 20 and virtually 100% of patients by age 30. Pancreatic endocrine tumors (gastrinomas, glucagonomas, VIPomas, Ppomas and somatostatinomas) occur in 50% of patients.

MEN I, or Wermer's syndrome, usually present with hypercalcemia (the presence of an abnormally high concentration of calcium in the blood) or complications of hypercalcemia such as kidney stones. The clinical findings that are generally seen in descending order of frequency include:

- nephrolithiasis - the presence of kidney stones (calculi) in the kidneys
- peptic ulcer disease
- hypoglycemia - low blood sugar
- headache
- visual-field loss
- hypopituitarism - underactive pituitary gland resulting in low levels of pituitary hormones
- acromegaly - excessive growth due to overproduction of growth hormone by the pituitary gland
- galactorrhea - excessive or spontaneous flow of breast milk usually in a woman who is not breastfeeding
- amenorrhea - absence of menstruation
- Cushing's syndrome - a disease caused by the overproduction of the hormone cortisol by the adrenal glands
- complications related to the development of islet cell tumors of the pancreas.
- nephrocalcinosis - a kidney disorder involving the deposition of calcium and oxalate in the renal tubules of the kidneys.

The *Zollinger-Ellison Syndrome (ZES)*, a rare disorder that causes tumors in the pancreas and duodenum and ulcers in the stomach and duodenum, occurs in approximately one-third of patients with MEN I. As a corollary, approximately 25% of patients with the Zollinger-Ellison Syndrome also have MEN-1; therefore MEN I screening is recommended in all patients with ZES.

Carcinoid tumors particularly involving the duodenum are seen in a significant number of patients with MEN-1 and occur more frequently when both ZES and MEN I are present. Generally carcinoid tumors are identified in the gastric and duodenum. In general these carcinoids appear to be less metastatic than in sporadic carcinoid tumor (i.e., carcinoid tumors in patients who do not have the MEN I syndrome).

Specific skin abnormalities have been recently identified in MEN-1 patients. These skin abnormalities include multiple angiofibromas, collagenomas, and lipomas.

The prognosis of NETs associated with the MEN-I syndrome has been controversial. In one study approximately half of the patients died as a direct result of a MEN I-specific illness that included islet cell tumors, peptic ulcer disease, hypercalcemia/uremia and carcinoid syndrome.

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

- **Diagnosis of Carcinoid Tumors**
- **Treatment Options for Carcinoid Tumors**
- **The Role of Complementary and Alternative Therapies in Cancer**
- **Quality of Life Issues in Cancer**
- **New Developments in Carcinoid Tumors**
- **Questions to Ask Your Health Care Provider about Carcinoid Tumors**

To Order the Complete **Guidebook on Carcinoid Tumors** [Click Here](#)
Or Call 800-965-3002 (USA) or 301-649-9300 (Outside USA)

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 - 47 Articles
- General Interest Articles - 76 Articles
- Drug Therapy Articles - 18 Articles
- Surgical Therapy Articles - 34 Articles
- Clinical Trials Articles - 15 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.

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**

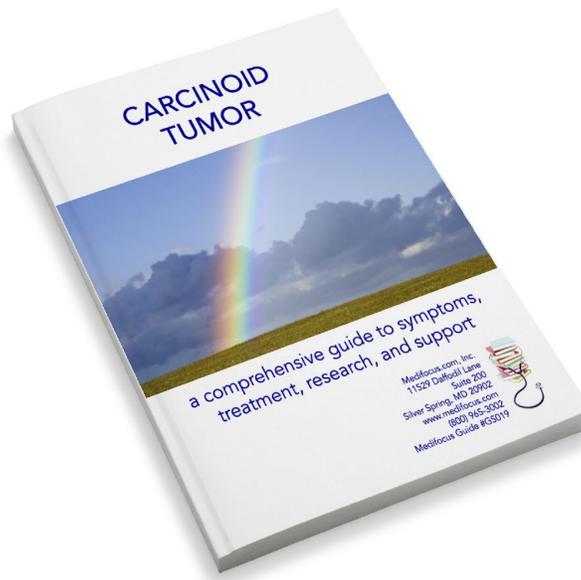
- United States: the information is divided by individual states listed in alphabetical order. Not all states may be included.
- Other Countries: information is presented for select countries worldwide listed in alphabetical order. Not all countries may be included.

- **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.



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