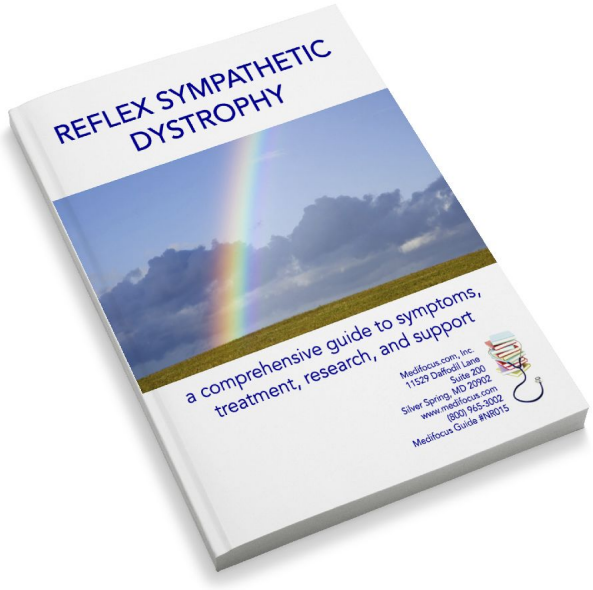
Preview of the Medifocus Guidebook on: Reflex Sympathetic Dystrophy

Updated January 11, 2024



This document is only a SHORT PREVIEW of the **Medifocus Guidebook on Reflex Sympathetic Dystrophy**. 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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Table of Contents

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

REFLEX SYMPATHETIC DYSTROPHY

Introduction to Reflex Sympathetic Dystrophy

What is Reflex Sympathetic Dystrophy?

Reflex sympathetic dystrophy (RSD), also known as *complex regional pain syndrome* (CRPS) *Type I*, is a chronic pain syndrome that can affect any part of the body; however, it occurs most frequently in the extremities - hands, feet, arms, legs, shoulders or knees. It has been recognized by many clinicians as a distinct clinical condition for over 100 years and has been known by various names including *algodystrophy*, *Sudeck's atrophy*, *causalgia* (now known as CRPS II), and *sympathetically-maintained pain*.

Reflex sympathetic dystrophy is characterized by:

- Severe, chronic pain often described as stinging or burning
- Sensory abnormalities such as *allodynia* (pain due to a stimulus which does not normally provoke pain) or *hyperesthesia* (increased sensitivity to stimuli)
- Motor impairment such as weakness, tremor, stiffness, or decreased range of motion
- *Edema* (tissue swelling) and *hyperhydrosis* (excessive sweating)
- Progressive *trophic* changes to skin, hair, nails, muscle, and bone (such as thinning of bones or changes in how hair and nails grow)
- Increasing dysfunction of the affected limb

Reflex sympathetic dystrophy causes great suffering and distress in most patients. In addition to severe pain, which in some people remains chronic and unremitting, patients may also experience serious physical disabilities and reduction in their quality of life leading to:

- Depression
- Fear
- Anxiety
- Anger

The syndrome of RSD is not well understood but it occurs most often after trauma such as a bone fracture or surgery to an extremity. The trauma can also be very minor such as a splinter, sprained ankle, or following intravenous needle insertion. RSD can also occur following a serious medical condition such as a heart attack or stroke. In up to 25% of RSD patients, however, no apparent cause can be established with certainty. Although the symptoms and clinical features of RSD can vary from patient to patient, the one common cardinal feature that is shared by all patients is severe pain that is disproportionate to the original injury. Reflex sympathetic dystrophy does not

exist in the absence of pain.

The perception of pain is a complex event and relates to physiological as well as psychological components. Usually pain is perceived immediately following a precipitating event such as trauma and, after the pain stimulus has been eliminated, the body returns to the previous state of being pain-free. When pain continues beyond an acceptable time period and/or appears to intensify, the pain is said to become *pathologic*. This is the essence of RSD. As the body responds for a prolonged time period to pathologic pain, it can cause permanent structural or functional changes within the affected extremity and, ultimately, in the central nervous system. Even within the variability of individual perception, tolerance, and response to pain, the pain of RSD is totally out of proportion to the precipitating event.

Although the term *reflex sympathetic dystrophy* has been used to describe the condition since the 1940s, it has recently come under scrutiny since it is misleading for several reasons, including:

- There is little evidence of involvement of a reflex mechanism
- Symptoms of RSD reflect a complicated interplay of several neurological systems, such as the peripheral and central nervous systems, not only the sympathetic nervous system
- Only a subset of patients respond to a treatment to reduce pain called a *sympathetic block* which interrupts the activity of the sympathetic nervous system, indicating that not all RSD pain is sympathetically mediated
- *Dystrophy* (degeneration of muscle or tissue) is present only in a subset of RSD patients (approximately 10%)

In response to these inconsistencies, the International Association for the Study of Pain (IASP) adopted the term *complex regional pain syndrome* (CRPS) in 1994 to describe a debilitating pain syndrome that develops after a relatively minor injury to an extremity (arm or leg) but lasts longer than the actual injury and is more severe than would otherwise be expected from such an injury. There are two types of CRPS:

- *CRPS Type I*- also known as *reflex sympathetic dystrophy* where the pain is not associated with any identifiable nerve injury
- *CRPS Type II* - also known as *causalgia* where the pain can be traced to a nerve injury

Despite extensive research over the past several decades, researchers still do not understand clearly the underlying pathological mechanisms involved in the initiation and progression of RSD including:

- Why RSD develops in some people and not others
- Why RSD goes into remission for some people and not others
- Why some people experience recurrence of RSD
- What are the most effective treatments for RSD
- How to prevent RSD from occurring

What Causes Pain in Reflex Sympathetic Dystrophy?

The mechanism of action in reflex sympathetic dystrophy (RSD) is not well understood and is the subject of extensive debate. Much of the confusion is due to the fact that RSD is clearly not a condition caused exclusively by the sympathetic nervous system and many experts believe that there must be a more complex reaction occurring in response to precipitating events that cause RSD.

There are at least two possible origins of pain in RSD: *sympathetically-maintained pain* which is pain caused by some "malfunction" in the sympathetic nervous system, and *sympathetically-independent pain*.

Sympathetically-Maintained Pain

The sympathetic nervous system (SNS) regulates involuntary responses to stress such as increased heart rate and constriction of peripheral blood vessels as well as some of the body's initial response to any injury. Research indicates that the sympathetic nervous system also plays a role in neuropathic and inflammatory pain. In patients with RSD, there may be evidence of more widespread impairment of sympathetic nervous system function which is not necessarily limited to the affected extremity.

Until recently, it was thought that RSD was characterized by sympathetically-maintained pain where the SNS basically overreacted to an injury. Typically, after an injury occurs, the sympathetic nervous system is activated. It mobilizes the body's inflammatory response with the release of certain substances in order begin the process of healing the wound. The sympathetic response typically decreases within minutes or hours after the initial injury. When the inflammatory response continues unchecked, even when the stimulus is no longer present, the pain becomes sympathetically driven and the condition known as RSD develops. When treatment is directed towards interrupting the sympathetically-maintained pain, the patient experiences relief from pain.

Sympathetically-Independent Pain

With *sympathetically-independent pain*, the pain is caused by a combination of factors that interact with the SNS, such as the peripheral and central nervous systems. Treatments directed towards the SNS do not bring relief to people experiencing this type of pain.

Reflex sympathetic dystrophy appears to be disorder involving a combination of the sympathetic nervous system in addition to peripheral, central, immune, or vascular systems. In effect, what may be happening with RSD is that a vicious cycle is created: the sympathetic response leads to chemical changes which then activate the response of other systems (e.g., central nervous system) which leads to more pain, which leads to more chemical changes, and so on.

Some evidence indicating the RSD is not exclusively related to the sympathetic nervous system includes:

- While some symptoms of RSD can be traced to the sympathetic nervous system, such as pain, or changes in sweating of the affected limb, other symptoms, such as warming of the limb, or swelling, are caused by substances released from other sources such as damaged blood vessels and not the sympathetic nervous system.

- Sympathectomy, a procedure which interrupts the flow of the sympathetic nervous system, is effective for individual patients; however larger clinical studies have shown the procedure to be no more effective than a placebo.

- The symptoms of RSD do not include those typically seen by an overactive sympathetic nervous system, such as an overactive thyroid and increased heart rate, or by an underactive sympathetic nervous system, such as decreased sweating, orthostatic hypertension (drop in blood pressure when changing positions), or ejaculation problems.

In short, it appears that the pain of RSD is not related to an overactive sympathetic nervous system, but rather, reflects a more global involvement including:

- Peripheral nervous system
- Sympathetic nervous system
- Central nervous system
- Vascular system
- Immune system
- Inflammatory responses

Risk Factors for Reflex Sympathetic Dystrophy

Several risk factors for the development of reflex sympathetic dystrophy (RSD) have been identified including:

- Trauma - Bone fracture, sprain, or other injury to the affected limb, often minor in nature, is considered the leading provocative event. Bone fractures account for up to 45-50% of cases of RSD.
- Surgery - RSD has been reported to occur following certain surgical procedures on the extremities such as carpal tunnel release surgery, knee arthroscopy, hip arthroplasty, amputation, or ankle arthrodesis (surgical fusion of the joint), and knee replacement surgery. It is estimated that up to 19% of patients with RSD have undergone knee replacement surgery.
- Cardiovascular events - Ischemic heart disease, heart attack, or stroke have been reported as risk factors for developing RSD. Estimates of RSD in stroke patients range from 12-60%.
- Neurological events - RSD may be seen as part of other neurological diseases such as carpal tunnel syndrome or pinched spinal nerves.
- Neoplasms - Certain types of cancers may produce a CRPS-like syndrome (e.g., lung cancer, breast cancer, and ovarian cancer).
- Age - Incidence of RSD is highest in people between the ages of 50-70 years old. The mean age of diagnosis reported in studies ranges between 46-52 years old.
- Gender - Adult females are affected at a rate three times higher than males.
- Genetic predisposition - It appears that people with RSD are more likely to have certain HLA tissue types than control groups, but the meaning of this finding is unclear. HLA stands for Human Leukocyte Antigens and they are proteins found on the surface of white blood cells.

- Incorrect immobilization of a limb - While immobilization may be necessary in certain situations, it could also become a precipitating factor in the development of RSD. Studies involving immobilization of limbs in healthy subjects resulted in symptoms identical with RSD, such as *trophic* changes, muscle stiffness or atrophy, changes in skin color and temperature, circulation problems to the affected limb, and pain when the casts were removed. Trophic changes are abnormalities of the skin, hair, nails, subcutaneous tissues and bone, caused by peripheral nerve injury.
- Poorly fitted casts or splints.

In approximately 10-25% of patients with reflex sympathetic dystrophy, no precipitating event can be identified. Sometimes because the trauma may have been so minor (e.g., a splinter), the patient does not recall the event or may not have been aware of it when it occurred.

There is continuing discussion regarding the prevention of RSD following situations involving immobilization of a fracture or stroke. Some clinicians have suggested that certain precautions may offset or at least minimize the development of RSD if performed before or after surgery takes place. These include:

- Attention to pain prevention
- Early mobilization of the limb
- Prophylactic physical therapy
- Attention to properly fitted cast or splint

Recent research has shown an advantage to prescribing 500 mg. of vitamin C daily from the time of the fracture or precipitating event (such as surgery).

Incidence of Reflex Sympathetic Dystrophy

The incidence of reflex sympathetic dystrophy (RSD) in the general population is a subject of extensive debate since only two population-based studies have been published and their results varied widely. A study conducted in 2003 in the U.S. reported that the incidence of RSD was approximately five per 100,000 people annually, while a study completed in the Netherlands in 2006 reported a rate of approximately 26 people per 100,000 annually. If those standards were applied in the U.S. population, it would translate into approximately 50,000 new cases of RSD annually. Part of the reason for this wide discrepancy in the two studies is the lack of standardized criteria for the diagnosis of RSD.

Additional information about the incidence of RSD includes:

- Female-to-male ratio is approximately 4:1
- Median age of onset is approximately 46 - 52, but RSD can occur at any age
- Upper limbs are affected approximately twice as often as lower limbs
- Fracture is the most common trigger for RSD (46% of cases)
- There is a higher incidence of RSD around puberty
- In children, the ratio of *lower* limb involvement to *upper* limb is approximately 5:1 (opposite of adults)

- Recurrence of RSD may be higher for childhood-onset RSD than for adult-onset

Reflex Sympathetic Dystrophy in Children

Reflex sympathetic dystrophy (RSD) in children and adolescents is similar to that in adults except that in children there is a preponderance of the lower extremity over the upper extremity (especially the foot) and RSD most often occurs following minor trauma. RSD affects girls more than boys and the incidence is greatest at and just before puberty. It is more common among Caucasian children that among non-Caucasians.

For more information about RSD in children, please click on the following link:
http://www.ncbi.nlm.nih.gov/pubmed/19143976

Reflex Sympathetic Dystrophy and Stroke

The incidence of reflex sympathetic dystrophy (RSD) in post-stroke patients is thought to be severely underdiagnosed. There are some reports that the incidence may be as high as 60% of patients. In this population, RSD is usually found in the upper extremity and is also known as *shoulder-hand syndrome*. It shares the same underlying problem encountered with most cases of RSD, namely immobilization of the limb.

In a study that appeared in the *International Journal of Rehabilitation and Research* in 2007, researchers reported that RSD developed in 48% of the 82 patients included in the study in the first 28 weeks following the stroke. They noted that the presence of RSD was significantly correlated with the presence of:

- Shoulder subluxation - a partial dislocation of the shoulder joint
- Spasticity of shoulder muscles
- Loss of range of motion in the shoulder joint
- Loss of muscle strength

To read more about the relationship between stroke and RSD, please click on the following link:
http://www.ncbi.nlm.nih.gov/pubmed/17293718

Recurrence of Reflex Sympathetic Dystrophy

It has been estimated that the recurrence rate of reflex sympathetic dystrophy (RSD) in the same or another limb is 4-10% and that it recurs between three and twenty years after the initial event. Most cases of recurrence develop after a subsequent trauma or surgery. This has led some researchers to conclude that susceptibility to RSD recurrence may be increased after initial development of the condition. The recurrence rate of childhood-onset RSD is thought to be approximately 33%.

Does Reflex Sympathetic Dystrophy Spread?

Many patients report that RSD spreads from the location of the initial injury. Spreading may occur in three patterns:

- *Contiguous spread* - This occurs in almost all patients and involves the gradual enlargement of the affected area.
- *Independent spread* - Signs and symptoms appear at distant sites not adjacent to the initial site of the injury. This pattern occurs in up to 70% of patients with RSD.
- *Mirror image spread* - Signs and symptoms appear in the same area on the opposite (contralateral) limb. This pattern occurs in up to 15% of patients.

The Reflex Sympathetic Dystrophy Syndrome Association (RSDSA) notes that spreading represents chronic changes that take place in the central nervous system or may represent overuse of the unaffected limb or may be related to some type of invasive procedure. The RSDSA notes that spreading of the pain in the same limb or region of the body is more likely to be related to a *myofascial pain syndrome*.

The *myofascia* is a layer of loose but strong connective tissue that covers all muscles. Myofascial pain is a soft tissue disorder that is typically localized to one area of the body. It is characterized by "trigger points" which are highly irritable spots in a particular area of muscle fiber that, when compressed, cause significant pain and tenderness in an area larger than the trigger point itself. When patients with RSD make adaptive adjustments to protect the painful limb, for example, by tightening or contracting the supporting muscles of the shoulder or neck to protect a painful hand, they cause changes at the myofascial level of the muscle as well. Or, when patients overuse the unaffected limb to compensate for the disability of the affected limb, the overworked or poorly conditioned muscles and myofascia are affected and can cause pain that affects not only that limb but can radiate to other parts of the body, such as the head, or chest. Thus, myofascial pain is complex in its pattern and not necessarily related to the original location. This may be interpreted by the patient as the sensation of "spreading".

The RSDSA estimates that between 60-80% of people suffering from RSD are affected by myofascial pain.

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 - 34 Articles
- General Interest Articles - 39 Articles
- Drug Therapy Articles - 4 Articles
- Clinical Trials Articles - 8 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.

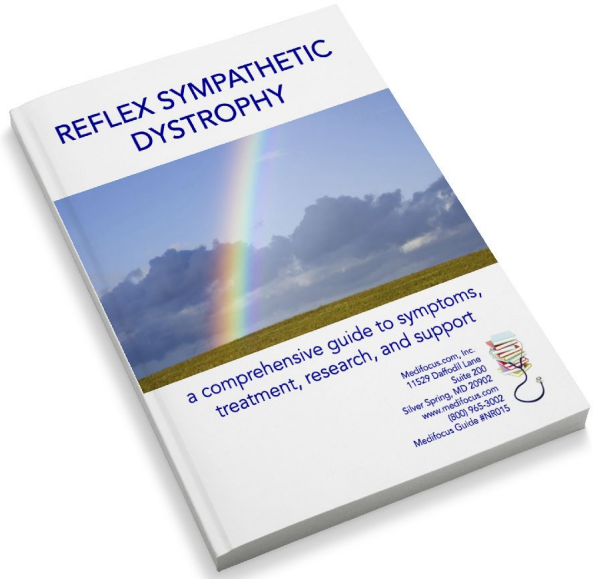
4 - Centers of Research

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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