General Discussion

Stiff-person syndrome (SPS) is a rare acquired neurological disorder characterized by progressive muscle stiffness (rigidity) and repeated episodes of painful muscle spasms. Muscular rigidity often fluctuates (i.e., grows worse and then improves) and usually occurs along with the muscle spasms. Spasms may occur randomly or be triggered by a variety of different events including a sudden noise or light physical contact. In most cases, other neurological signs or symptoms do not occur. The severity and progression of SPS varies from one person to another. If left untreated, SPS can potentially progress to cause difficulty walking and significantly impact a person's ability to perform routine, daily tasks. Although the exact cause of SPS is unknown, it is believed to be an autoimmune disorder and sometimes occurs along with other autoimmune disorders.

Stiff-person syndrome has been described in the medical literature under many different, confusing names. Originally described as stiff-man syndrome, the name was changed to reflect that the disorder can affect individuals of any age and of either gender. In fact, most individuals with the condition are women. Stiff-person syndrome is considered by many researchers to be a spectrum of disease ranging from the involvement of just one area of the body to a widespread, rapidly progressive form that also includes involvement of the brain stem and spinal cord (PERM).
NORD Video: Ehlers-Danlos Syndrome/Stiff Person Syndrome, Sarah's Story
Signs & Symptoms

The characteristic findings associated with SPS are progressive, fluctuating muscular rigidity that occurs along with muscle spasms. The severity and progression of SPS can vary from one person to another. The symptoms usually develop over a period of months and may remain stable for many years or slowly worsen. In some people, symptoms can be stabilized through medication. Affected individuals should talk to their physician and medical team about their specific case, associated symptoms and overall prognosis.

In many cases, SPS begins slowly over several months or a few years. Affected individuals may initially experience aching discomfort, stiffness, or pain, especially in the lower back or legs (predominantly classic type). Early on, stiffness may come and go, but it gradually becomes fixed. The shoulders, neck, and hips may also be affected. As the disease progresses, stiffness of the leg muscles develops, and is often more pronounced on one side than the other (asymmetrical). This leads to a slow, stiff manner of walking. As stiffness increases, affected individuals may develop a hunched or slouched posture due to outward curving of the upper spine (kyphosis) or an arched back due to inward curving of the lower spine (hyperlordosis). In some individuals, stiffness may progress to involve the arms or face.

In addition to muscular rigidity/stiffness, individuals with SPS also develop muscle spasms, which may occur for no apparent reason (spontaneously) or in response to various triggering events (i.e., stimuli). Spasms can be triggered by unexpected or loud noises, minor physical contact, cold environments, stress or situations that cause a heightened emotional response. Muscle spasms are often very painful and usually worsen existing stiffness. The spasms may involve the entire body or only a specific region. The legs are often involved, which may lead to falls. Spasms of abdominal muscles may lead to individuals feeling full faster than normal (early satiety) leading to unintended weight loss. Spasms involving the chest and respiratory muscles can be serious, potentially requiring emergency medical treatment with ventilatory support. Spasms may last several minutes, but occasionally last for hours. Sudden withdrawal of medication in individuals with SPS may result in a life-threatening situation with overwhelmingly severe muscle spasms. Sleep usually suppresses the frequency of contractions.

In some cases, SPS becomes severe enough to affect an individual's ability to perform daily activities and routines. Some individuals may need to use an assist device such as a cane, walker or wheelchair. Some affected individuals experience uncontrollable anxiety when they need to cross large, open areas unassisted (agoraphobia) and become reluctant to go outside. If left untreated, SPS can potentially progress to cause significant disability or life-threatening complications such as respiratory compromise.

SPS may be associated with other autoimmune disorders more frequently than would be regularly expected to occur in the general population. The most common associated condition is diabetes. Less commonly, affected individuals may also develop inflammation of the thyroid (thyroiditis), pernicious anemia and vitiligo. Pernicious anemia is characterized by low levels of red bloods cells due to the body's inability to absorb vitamin B12 from the gastrointestinal tract. Vitiligo is a skin condition in which loss of color (pigmentation) of areas of skin results in the development of abnormal white patches. Clinical reports indicate that individuals with SPS also have an increased incidence of epilepsy.

Several variants of SPS have been reported in the medical literature suggesting that SPS represents a spectrum of disease ranging from the involvement of one specific, localized area to widespread involvement. These variants include stiff-limb syndrome, jerking stiff-person syndrome, progressive encephalomyelitis with rigidity and myoclonus, and paraneoplastic-related SPS. These variants are sometimes collectively referred to as "stiff-person plus syndromes".

Stiff-limb syndrome is characterized by the localized involvement of one limb, usually a leg. The stiffness and muscle spasms are extremely similar to those found in classic stiff-person syndrome. Stiff-limb syndrome may progress to eventually affect both legs and may cause difficulty walking. Some individuals may eventually develop classic stiff-person syndrome or variant SPS. When SPS affects only one specific area of the body, it may also be referred to as focal or partial stiff-person syndrome.

Jerking stiff-person syndrome is characterized by muscles stiffness and spasms usually affecting the legs. Affected individuals also develop involvement of the brainstem, which can cause myoclonus. Myoclonus is a general term used to describe the sudden, involuntary jerking of a muscle or group of muscles caused by muscle contractions (positive myoclonus) or muscle relaxation (negative myoclonus). The twitching or jerking of muscles cannot be controlled by the person experiencing it. Only a handful of cases of jerking stiff-person syndrome have been described in the medical literature.

Progressive encephalomyelitis with rigidity and myoclonus (PERM) is characterized by stiffness and painful muscles that are similar to those seen in individuals with classic stiff-person syndrome. PERM is more rapidly progressive than other forms of SPS; onset of symptoms usually occurs over several weeks. Stiffness and spasms may occur along with, before or after the development of other symptoms including vertigo, a lack of coordination of voluntary muscles (ataxia), and difficulty speaking (dysarthria). In some cases, the cranial nerves may also become involved causing paralysis of certain eye muscles (ophthalmoplegia), rapid, involuntary eye movements (nystagmus), difficulty swallowing (dysphagia), and hearing loss. PERM is considered a distinct disorder from classic SPS and some feel that it is a distinct condition all together. There is no evidence that SPS will inevitably evolve into PERM.

Paraneoplastic-related stiff-person syndrome is a rare disorder that affects the nervous system in some individuals with cancer, especially individuals with cancer of the lungs or breast. The disorder is characterized by stiffness and rigidity, along with painful spasms. Symptoms usually begin in the muscles of the lower back and legs, although some individuals experience neck and upper torso symptoms first. The disorder may grow progressively worse eventually affecting the arms and other parts of the body. Painful muscle spasms can be worsened or triggered by a variety of events including anxiety, loud or unexpected noises or light physical contact. Paraneoplastic stiff-person syndrome is thought to be immune-mediated and is typically associated with a different auto-antibody (called anti-amphiphysin) than is found in individuals with classic stiff-person

syndrome. This antibody is usually found in the blood and spinal fluid of affected individuals. (For more information on this disorder, choose “paraneoplastic neurologic syndromes” as your search term in the Rare Disease Database.)

Causes

The exact cause of SPS is not known. Some studies in the medical literature indicate that it may be an autoimmune disorder. Autoimmune disorders are caused when the body’s natural defenses (e.g., antibodies) against “foreign” or invading organisms begin to attack healthy tissue for unknown reasons.

Most of those affected have antibodies to glutamic acid decarboxylase (GAD), a protein in inhibitory nerve cells that is involved in the creation (synthesis) of the main inhibitory neurotransmitter called gamma-aminobutyric acid (GABA). GABA helps control muscle movement and prevent hyperexcitibility within the brain and spine. The symptoms of SPS may develop when the immune system mistakenly attacks certain nerve cells (neurons) that produce GAD leading to a deficiency of GABA in the body.

Less commonly, individuals with SPS will have antibodies to amphiphysin, a protein involved in the transmission of signals from one nerve cell to another. In these individuals, breast cancer is quite prevalent.

The exact role that deficiency of GAD plays in the development of SPS is not fully understood. Antibodies to GAD-65 are associated with several other disorders including diabetes. In fact, GAD-65 is the most common antibody produced by people with autoimmune diabetes and many people have these antibodies in that context. In some individuals with SPS no antibodies to GAD are detectable. The cause of SPS in these individuals may ultimately be unknown (idiopathic), but testing for other causes (e.g. amphiphysin antibodies) is usually appropriate. More research is necessary to determine the exact, underlying mechanisms that ultimately cause SPS and the exact role that anti-GAD antibodies play in the development and progression of the disorder.

Affected Populations

SPS is an extremely rare disorder. The exact incidence and prevalence of SPS is unknown, although one estimate places the incidence at approximately 1 in 1,000,000 individuals in the general population. The distribution of SPS between men and women indicates a female predominance. SPS usually becomes apparent sometime between 30-60 years of age. However, SPS has been reported to occur in children and older adults as well.

SPS was first described in the medical literature by doctors Moersch and Woltman in 1956 as stiff-man syndrome. The disorder is now known as stiff-person syndrome to reflect that the disorder affects individuals of any age and both genders.

Related Disorders

Symptoms of the following disorders can be similar to those of SPS. Comparisons may be useful for a differential diagnosis.

Tetanus is an infectious disorder that affects the central nervous system. It is caused by the microorganism, Clostridius tetani, a type of bacterium. This microorganism usually enters the body through wounds, injections, or skin ulcers. The incubation period of tetanus is usually seven to twenty one days. Symptoms of this syndrome include muscle stiffness, especially of the jaw (lock jaw) and painful muscle spasms. Affected individuals may also experience low-grade fever, difficulty in swallowing (dysphagia), difficulty breathing, alteration in the rhythm of the heartbeat, and convulsions. Tetanus can also cause behavioral changes including anxiety and restlessness. The symptoms of tetanus usually last for three to four weeks. Although tetanus is a treatable disease, vaccination is recommended during infancy and every few years thereafter.

A wide variety of other disorders can also cause signs and symptoms that are similar to SPS. Usually, these

disorders have additional symptoms that can be used to distinguish them from SPS. Such disorders include hyperekplexia, multiple sclerosis, transverse myelitis, occult vascular malformations, neuromyotonia (Isaac's syndrome), Schwartz-Jampel syndrome, muscular dystrophies, and metabolic myopathies. (For more information, choose the specific disorder name as your search term in the Rare Disease Database).
Diagnosis

A diagnosis of SPS is made based upon identification of characteristic symptoms, a detailed patient history, and a thorough clinical evaluation. Additional tests can be used to support a diagnosis and to rule out other conditions. Such tests include screening tests to detect the presence of antibodies against GAD-65, antibodies against amphiphysin (which are associated with paraneoplastic SPS) and an electromyography (EMG), a test that records electrical activity in skeletal (voluntary) muscles at rest and during muscle contraction. An EMG can demonstrate continuous muscle motor unit firing in stiff muscles, which is characteristic of SPS. High doses of diazepam will suppress the characteristic EMG results.
Standard Therapies

Treatment
The treatment of SPS is directed toward the specific symptoms that are apparent in each individual which often requires a multifaceted approach including non-medication interventions (stretching, heat therapy, aqua therapy, massage therapy, acupuncture, etc). Drugs that are considered GABA-ergic agonists therapies such as benzodiazepines, specifically diazepam and clonazepam, are used to treat muscle stiffness and episodic spasms. Affected individuals may also benefit from baclofen, usually given in addition to benzodiazepines. Other medications reported to have benefit in a small number of individuals include anti-seizure (anticonvulsant) drugs including vigabatrin, valproate, pregabalin, and gabapentin.

Peer-reviewed clinical studies have shown that intravenous immunoglobulin (IVIG) is effective and well-tolerated in improving the symptoms commonly associated with SPS. IVIG is commonly used as a therapy for immune-mediated disorders as SPS is believed to be. IVIG, under certain conditions, has been associated with increased risks for stroke and heart attacks and can rarely cause kidney injury and meningitis. Treatment should be prescribed only after a discussion of the attendant risks and benefits. More research is necessary to determine the long-term safety and effectiveness of IVIG for the treatment of individuals with SPS.

There are classes of medications that should be avoided in SPS, including serotonin-norepinephrine reuptake inhibitors (SNRIs; i.e, tricyclic antidepressants and duloxetine) and opioids. SNRIs have previously been shown to worsen the EMG activity and clinical symptoms in SPS. Opioids are not recommended for pain control because most individuals with SPS are on benzodiazepines. Mixing these two classes of medications can lead to severe respiratory depression and death.
Investigational Therapies

Several different immune therapies have been used to treat individuals with SPS beyond IVIG including plasmapheresis, corticosteroids, rituximab, and oral immunosuppressive drugs. Other therapies are being evaluated including non-myeloablative and myeloablative stem cell therapies.

Plasmapheresis may be of benefit in individuals with SPS. This procedure is a method for removing unwanted substances (toxins, bad antibodies, metabolic substances, plasma parts) from the blood. Blood is removed from an affected individual and blood cells are separated from plasma. The plasma is then replaced with other human plasma or albumin.
This therapy remains under investigation to analyze side effects and effectiveness. More research is needed to determine what role plasmapheresis may play in the treatment of individuals with SPS.

Information on current clinical trials is posted on the Internet at www.clinicaltrials.gov. All studies receiving

U.S. Government funding, and some supported by private industry, are posted on this government web site.

For information about clinical trials being conducted at the NIH Clinical Center in Bethesda, MD, contact the

Some current clinical trials also are posted on the following page on the NORD website:
https://rarediseases.org/for-patients-and-families/information-resources/news-patient-recruitment/

For information about clinical trials sponsored by private sources, contact:
www.centerwatch.com

For information about clinical trials conducted in Europe, contact:
https://www.clinicaltrialsregister.eu/
Supporting Organizations

Autoimmune Association
19176 Hall Road, Suite 130
Clinton Township, MI 48038 USA
Phone: (586) 776-3900
Toll-free: (888) 852-3456
Email: hello@autoimmune.org
Website: https://autoimmune.org

Genetic and Rare Diseases (GARD) Information Center
PO Box 8126
Gaithersburg, MD 20898-8126
Phone: (301) 251-4925
Toll-free: (888) 205-2311
Website: http://rarediseases.info.nih.gov/GARD/

Living With Stiff Person Syndrome
Phone: (904) 375-9385
Email: debbie@livingwithsps.com
Website: https://www.livingwithsps.com/

Movement Disorder Society
555 E. Wells Street
Suite 1100
Milwaukee, WI 53202-3823
Phone: (414) 276-2145
Email: info@movementdisorders.org
Website: http://www.movementdisorders.org

NIH/National Institute of Neurological Disorders and Stroke
P.O. Box 5801
Bethesda, MD 20824
Phone: (301) 496-5751
Toll-free: (800) 352-9424
Website: http://www.ninds.nih.gov/

Stiff Man Syndrome Support group
75 Normandy Avenue
East Yorkshire, HU17 8PF United Kingdom
Phone: (148) 286-8881
Email: liz.blows@smssupportgroup.co.uk
Website: http://www.smssupportgroup.co.uk/

Stiff Person Syndrome.Net

5667 Swamp Fox Rd.
Jacksonville, FL 32210
Phone: (904) 771-9185
Email: john@stiffpersonsyndrome.net

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Cleveland Clinic

Stiff person syndrome is a rare autoimmune movement disorder that affects the central nervous system (the brain and spinal cord). People with this condition first experience a stiffening of the muscles of their trunk followed, over time, by the development of stiffness and rigidity in the legs and other muscles in the body.

Stiff person syndrome, also called Moersch-Woltman syndrome and formerly stiff man syndrome, can also cause painful muscle spasms. The muscle spasms occur randomly or can be triggered by noise, emotional distress and light physical touch.

Over time, stiff person syndrome can lead to an altered posture. Severe cases can limit your ability to walk or move. Some people with this disorder need ongoing treatment for years to manage symptoms and maintain quality of life.

Stiff person syndrome is thought to be part of a wide range of similar diseases that involve one area of the body and then spread throughout the body.
Who might get stiff person syndrome?

Stiff person syndrome is extremely rare. Only about one out of every one million people have been diagnosed this syndrome. Twice as many women have stiff person syndrome as men. Symptoms can occur at any age but usually develop between ages 30 and 60.

Stiff person syndrome is more likely seen in people with certain types of diseases including:

- Autoimmune disorders including diabetes, thyroiditis, vitiligo and pernicious anemia.
- Certain cancers including breast, lung, kidney, thyroid, colon and Hodgkin’s lymphoma.

Symptoms and Causes

What causes stiff person syndrome?

Researchers are not sure of the exact cause stiff person syndrome. However, they believe it to be an autoimmune disorder, a condition where your immune system attacks healthy cells. Many people with this disorder make antibodies that attack an enzyme called glutamic acid decarboxylase (GAD). GAD plays a role in making a neurotransmitter called gamma-aminobutyric acid (GABA), which helps control muscle movement. It is thought that the immune system in people with stiff person syndrome mistakenly attacks GAD enzyme, which decreases the amount of GABA in the body.

Antibodies to another protein called amphiphysin is a less common finding in people with this syndrome. This protein is found in nerve terminals and is involved in helping nerve cells communicate with each other.

The exact role that GAD plays in the development and worsening of stiff person syndrome is not totally understood. In fact, there are people with the syndrome that do not have detectable antibodies to GAD.
What are the symptoms of stiff person syndrome?

Symptoms of stiff person syndrome can take several months to a few years to develop. Some patients remain stable for years; other slowly worsen.

In most people with stiff person syndrome, the trunk and abdomen muscles are the first to become stiff and enlarged. Symptoms include pain, muscle stiffness and aching discomfort. Early on, stiffness may come and go but eventually the stiffness remains constant. Over time, leg muscles become stiff and more muscles throughout your body become stiff including the arms and even the face. As stiffness increases, some people developed a hunched posture. In severe cases, this stiffness can make it hard to walk or move.

Painful muscle spasms also occur. These spasms can last a few seconds, minutes or occasionally a few hours. Sometimes, the spasms can be severe enough to dislocate a limb, break a bone or cause uncontrolled falls. The spasms usually worsen the muscle stiffness. Spasms can occur for no reason or can be triggered when you're exposed to an unexpected or loud noise, physical touch, cold environment or stressful event that causes an emotional response. The muscle spasms can involve the entire body or only a specific area. Sleep usually reduces the number of spasms.
Diagnosis and Tests
How is stiff person syndrome diagnosed?

Symptoms of stiff person syndrome are similar to other conditions such as tetanus, multiple sclerosis and muscular dystrophies. Your healthcare provider may use several tests to rule out these conditions and look for signs of stiff person syndrome.

If your healthcare provider suspects stiff person syndrome, tests to confirm the diagnosis may include:

Blood test: Your blood is checked for the presence of antibodies to GAD or amphiphysin and for other signs that might indicate or rule out other diseases. Between 60 and 80% of people with stiff person syndrome have antibodies against GAD.
Electromyography (EMG): A machine measures electrical activity in your muscles to look for continuous motor activity in the muscles.
Lumbar puncture (spinal tap): During a lumbar puncture, a doctor uses a needle to draw fluid from your spinal canal to check for the presence of antibodies to GAD and for other signs that might indicate or rule out other diseases.

Management and Treatment
How is stiff person syndrome managed or treated?

Treatment for stiff person syndrome is based on your symptoms. The goal of treatment is to manage symptoms and improve your mobility and comfort.

Therapies your healthcare provider may try include benzodiazepines (such as diazepam and clonazepam) or baclofen to treat muscle stiffness and spasms. Anti-seizure drugs may lessen pain. Occasional use of anti-inflammatories and corticosteroids may be useful in some cases for pain flares.

Other treatment options include intravenous immunoglobulin (IVIG), plasmapheresis, rituximab and autologous stem cell transplant. Your healthcare provider will work with you to provide the best options and order of treatment options to manage your specific symptoms.

Effective non-medication options (given along with medication) include physical therapy, massage, water therapy, heat therapy, acupuncture and others.
What are the complications of stiff person syndrome or its treatment?

Stiff person syndrome causes limited movement and muscle spasms. These issues can lead to complications including:

- Anxiety and depression.
- Dislocated or broken bones from severe muscle spasms.
- Frequent falls.
- Excessive sweating (hyperhidrosis).

Prevention
How can I prevent stiff person syndrome?

Scientists do not know what causes stiff person syndrome. There is no known way to prevent it.
Outlook / Prognosis
What is the prognosis (outlook) for people with stiff person syndrome?

The prognosis for stiff person syndrome varies depending on a person's symptoms. The severity of the syndrome and speed of decline varies from person to person.

Over time, walking can become more and more difficult. In addition, a person's ability to perform daily, routine tasks may also decline over time. Various treatments may be helpful in reducing the symptoms in some patients. The increased risk of falls becomes a growing concern as the disorder worsens. Some people may need to use a cane, walker or wheelchair for assistance.
Living With
When should I call the doctor?

Contact your healthcare provider if you experience muscle spasms or stiffening of the muscles in your trunk, arms or legs. If you have any of the risk factors, especially an autoimmune condition, ask your doctor specifically about stiff person syndrome.
What questions should I ask my doctor?

If you have stiff person syndrome, you may want to ask your doctor:

- What drugs should may work best based on my symptoms?
- What signs of complications should I look out for?
- What should I expect to happen to my health in the future?

Resources

To look for clinical trials, go to Clinical Trials.gov .
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Last reviewed by a Cleveland Clinic medical professional on 03/12/2020.
References
Get useful, helpful and relevant health + wellness information
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Related Institutes & Services
Neurological Institute
The Neurological Institute is a leader in treating and researching the most complex neurological disorders and advancing innovations in neurology.
Orthopaedic & Rheumatologic Institute
Cleveland Clinic offers expert diagnosis, treatment and rehabilitation for bone, joint or connective tissue disorders and rheumatic and immunologic diseases.

MSD MANUAL
Professional Version

Stiff-Person Syndrome

By Michael Rubin , MDCM, New York Presbyterian Hospital-Cornell Medical Center
Last full review/revision Dec 2020| Content last modified Dec 2020
CLICK HERE FOR PATIENT EDUCATION
Stiff-person syndrome is a CNS disorder that causes progressive muscle stiffness and spasms.
(See also Overview of Peripheral Nervous System Disorders.)

Stiff-person syndrome (formerly called stiff-man syndrome) affects the central nervous system (CNS) but has neuromuscular manifestations.

Most patients with stiff-person syndrome have antibodies against glutamic acid decarboxylase (GAD), the enzyme involved in the production of the inhibitory neurotransmitter GABA (gamma-aminobutyric acid). However, stiff-person syndrome may be

Autoimmune
Paraneoplastic
Idiopathic
The autoimmune type often occurs with type 1 diabetes, as well as other autoimmune disorders including thyroiditis, vitiligo, and pernicious anemia. Autoantibodies against several proteins involved in GABA synapses are present in the autoimmune type, affecting primarily inhibitory neurons that originate in the anterior horn of the spinal cord.

Fewer than 1 to 2% have the paraneoplastic type. Antiamphiphysin antibodies are often present; anti-GAD are usually not. Paraneoplastic stiff-person syndrome is commonly associated with breast cancer but may also

occur in patients with lung, renal, thyroid, or colon cancer or Hodgkin lymphoma.

Clinical manifestations of stiff-person syndrome are similar in all types. Muscle stiffness, rigidity, and spasms progress insidiously in the trunk and abdomen and, to a lesser degree, in the legs and arms. Patients are otherwise normal, and examination detects only muscle hypertrophy and stiffness. Stiff-person syndrome typically progresses, leading to disability and stiffness throughout the body.

Diagnosis of stiff person syndrome is based on recognizing the symptoms and is supported by antibody testing, response to diazepam, and results of electromyography (EMG) studies, which show the electrical activity of apparent normal contraction.

Treatment of Stiff-Person Syndrome
Diazepam or baclofen
IV immune globulin (IVIG)
Sometimes rituximab or plasma exchange.
Symptomatic therapy is available for stiff-person syndrome. Diazepam is the drug of choice; it most consistently relieves muscle stiffness. If diazepam is ineffective, baclofen, given orally or intrathecally, can be considered.

Corticosteroids are reportedly effective but have many long-term adverse effects.

IVIG can result in improvement lasting up to a year. If patients do not respond to IVIG, rituximab or plasma exchange may be suggested.

Key Points
There are 3 types of stiff-person syndrome: autoimmune, paraneoplastic, and idiopathic.
Stiff-person syndrome affects the CNS but causes progressive muscle stiffness, rigidity, and spasms, mainly in the trunk and abdomen.
Diagnose based on symptoms, response to diazepam, and results of antibody testing and EMG studies.
Treat with diazepam or, if it is ineffective, baclofen; other options include IVIG, rituximab, and plasma exchange.

Yale

the main symptoms of Stiff Person Syndrome are muscle stiffening in the torso and limbs, along with episodes of violent muscle spasms. These can be triggered by environmental stimuli (like loud noises) or emotional stress. The muscle spasms can be so severe that they cause the person to fall down. The muscles gradually relax after the stimulus is gone.

The Stiff Person Research Foundation

Stiff person syndrome (SPS) is a neurological disease with autoimmune features. Symptoms include muscle spasms, hyper-rigidity, debilitating pain, and chronic anxiety. Muscle spasms can be so violent they can dislocate joints and even break bones.

SPS is labeled as a rare disease. But more people are affected than reported due to misdiagnoses. It takes on average seven years to identify. It is often mistaken as Multiple Sclerosis, Parkinson’s, Fibromyalgia, Psychosomatic Illness, Anxiety, Phobia, and other autoimmune diseases.

Patients can be disabled, wheelchair bound or bed-ridden, unable to work and care for themselves.

IVIG INFUSION CENTERS- New Paltz

https://specialtyinfusion.com/gammagard/ is a human immune globulin used to treat Primary Immunodeficiency and Multifocal Motor Neuropathy **S/E** The more common side effects of GAMMAGARD® include fatigue, fever, nausea, chills/shaking chills, pain in hands or feet, diarrhea, migraine, dizziness, vomiting, cough, hives, asthma, sore throat, rash, joint pain, muscle pain, swelling in the arms or legs, itching, and heart murmur.

GAMUNEX-C® is a human immune globulin used to treat Primary Humoral Immunodeficiency, Idiopathic Thrombocytic Purpura, and Chronic Inflammatory Demyelinating Polyneuropathy. **S/E**
The more common side effects of GAMUNEX-C® include raised body temperature or fever; abnormally high blood pressure; feelings of coldness; noticeable skin texture or color change such as your skin becoming scaly, bumpy, itchy, or otherwise irritated; sensation of unease and discomfort in the upper stomach; joint pain; abnormal physical weakness or lack of energy; and blood clots in the lungs (pulmonary embolism).

HIZENTRA® is a subcutaneous immune globulin used to treat Chronic Inflammatory Demyelinating Polyneuropathy and Primary Immunodeficiency **S/E** The more common side effects of HIZENTRA® include thrombosis, kidney problems, blood clots, meningitis, brown or red urine, rapid heart rate, yellowing of the skin or eyes, chest pains or breathing trouble, and fever over 100°F.

RITUXAN® (Rituximab) is a prescription medicine used to treat adults with various forms of immunodeficient diseases. S/E The more common side effects of RITUXAN® include infusion-related reactions, infections (may include fever, chills), body aches, tiredness, and nausea. In patients with GPA or MPA, common side effects of Rituxan are low white and red blood cells, swelling, diarrhea, and muscle spasms. Other side effects include aching joints during or within hours of receiving an infusion, and more frequent upper respiratory tract infections.

https://www.aaaai.org/Utility/Global-Site-Search?cx=010195695855076926430%3A3j7wmn664zg&cof=FORID%3A11&q=New+York
ask locations, IV IG and price

https://specialtyinfusion.com/ambulatory-vs-hospital-infusion/ 5* (1) New Paltz

https://www.garnethealth.org/patients-visitors/billing-insurance 4* Middletown good f.aid

https://infusioncenterofnj.com/infusions Cliffton,NJ may need insurance 4.7*

https://www.rwjbh.org/ 5*

https://kabafusion.com/contact/ 1 hr 45 min Edison, NJ 5* (2)

https://www.mountsinai.org/locations/mount-sinai/care/infusion-center/conditions unknown everything

Mayo clinic

Diagnosed with stiff-person syndrome — an extremely rare autoimmune neurologic condition — Tara Zier looked to Mayo Clinic for help. There she found valuable guidance and gained a new outlook on how to manage her condition.

For three years, Dr. Tara Zier went from specialist to specialist in the Washington, D.C. area trying to find out what was causing the unexplained symptoms she had been experiencing: shortness of breath, fatigue, difficulty walking and excruciating back pain.

On her fourth visit to a local emergency department, the dentist from Bethesda, Maryland, remembers lying on a hospital bed crying. "My hips were stiff, and I was having a hard time walking," Tara says. "I had no idea what was going to happen. I was really scared."

Her symptoms began in January 2015 after a weeklong bout of pneumonia and three months after her former husband died. "I was devastated," she says. "The level of stress was way off the charts. It was nothing I could even describe."

Grief-stricken and trying hard to help her two children through their grief, the active 45-year-old started having difficulty exercising, and she experienced extreme fatigue. Despite taking kickboxing for years, she was getting short of breath during classes. She also experienced panic attacks regularly, which landed her in the emergency department several times.

"My kids were 12 and 14 at the time," she says. "I was worried they would lose me, too."

An anxious quest for answers

Tara's symptoms persisted, and the following year she started battling severe neck pain. "It felt like a deep spinal pain," Tara says. "I backed off from kickboxing and martial arts, but I was still short of breath and just didn't feel great."

Multiple MRIs and consults with several neurologists revealed Tara had spondylosis in her neck. She decided against surgery and instead sought relief through physical therapy and chiropractic visits. But her condition continued to deteriorate.

"I was pale. I couldn't eat. I was down to 107 pounds. My body was in crisis."
Tara Zier

After two years of searching for answers, Tara says things came to a head one night in March 2017 when she took her children out for a family dinner. "I was pale. I couldn't eat. I was down to 107 pounds," she says. "My body was in crisis."

She went to her primary care doctor who suggested Tara take the antidepressant Cymbalta, which can be used to treat certain forms of pain. She then went on to seek the opinion of an endocrinologist, psychiatrist, rheumatologist, a general cardiologist and an electrophysiology cardiologist. But her symptoms persisted, disrupting daily life.

"My in-laws moved in with me for three weeks during the time I couldn't function," Tara says. "I hired a woman to cook and help around the house, and had to hire someone to drive my daughter to soccer practice."

When a friend who has postural tachycardia syndrome described symptoms similar to hers, Tara asked her primary care doctor for a referral to a local neurologist who specialized in dysautonomia — disorders of autonomic nervous system, such as postural tachycardia syndrome.

"He told me that stress can throw your nervous system into fight-or-flight mode," Tara recalls. "He thought that all of the stress I had been through had caused the dysautonomia, and in a year and a half I would recover. I thought, 'OK, maybe there's a light at the end of the tunnel.'"

The neurologist put Tara on a medication to treat nerve and muscle pain, a beta blocker and a skin patch for chronic pain. But instead of improving, her symptoms got worse. She started feeling numbness on the left side of her face, and she noticed itching in her abdomen and between her shoulder blades.

A one-in-a-million diagnosis

Tara found a new primary care doctor in summer 2017 who did a full body CT scan and referred her to another neurologist who ordered several blood tests. The results revealed a rare disorder: stiff-person syndrome. Tara's primary care doctor recommended she consider going to Mayo Clinic.

Tara made an appointment with Andrew McKeon, M.B., B.Ch., M.D., a neurologist who is part of the Mayo Clinic Center for Multiple Sclerosis and Autoimmune Neurology and co-director of the Neuroimmunology Laboratory.

"Stiff-person syndrome is a very rare autoimmune disease of the central nervous system that was discovered at Mayo in 1954. It has a one-in-a-million diagnosis," Dr. McKeon says. "We only saw 100 patients with this condition between 1984 and 2008 as part of a large cohort study Mayo conducted on our Rochester campus, where we have a specialized clinic for people with rare central nervous system autoimmune diseases."

People who experience stiff-person syndrome typically have other autoimmune diseases, such as Type 1 diabetes or autoimmune thyroid disease. There are three presentations of the disorder: stiff limb, which only involves the legs; stiff trunk, which affects the back; and classical stiff-person syndrome, which involves both the back and the legs.

"Dr. Zier has a more limited type of the disorder affecting her neck and back, where she experiences a lot of spasms which cause her a great deal of pain and trouble breathing," Dr. McKeon says.

A way to regain control

Prior to her first consult with Dr. McKeon in December 2017, Tara underwent six days of immunotherapy infusions recommended by her local neurologist. Unfortunately, the therapy didn't relieve her pain, and it made her feel worse. On Dec. 10, Tara was transported to Mayo Clinic's Rochester campus by air ambulance. "I hadn't been driving in months and wasn't well enough to fly commercially, so this was the safest way to travel," she says.

When she arrived at Mayo, Tara spent a week undergoing a battery of tests. "No stone was left unturned," she says. "Every part of me was evaluated from my brain all the way down."

"Dr. McKeon is a great listener. I think of him as top-notch. He's very committed to helping me get better."
Tara Zier

"When I first saw her, she was on several medications that weren't helping. Very often the conversation is really about trying to think outside the box to provide pain relief," Dr. McKeon says. "We treated her spasms and pain with Valium and continued our efforts to find individualized approaches that could improve her quality of life."

"Dr. McKeon is a great listener. I think of him as top-notch," Tara says. "He's very committed to helping me get better."

In an effort to help Tara live a full life despite her pain, Dr. McKeon referred her to Mayo Clinic's Pain

Rehabilitation Center.

Staffed with an integrated team of health care professionals, including those who specialize in pain medicine, physical therapy, psychology, occupational therapy, biofeedback and nursing, the Pain Rehabilitation Center offers a three-week program for adults. It helps patients like Tara regain strength and stamina, and shift their focus away from pain.

"A lot of patients come in and are afraid of movement. So, they lose faith," says Ross Pollert, a physical therapist assistant in the center. "Dr. Zier came in here afraid of moving. By the time she left the program, she was independent. She was a different person. It was nice to see her having faith in her own ability."

"The center taught me to incorporate more physical activity into my day despite my pain and to do things in moderation. Now I do tai chi instead of kickboxing," Tara says. "The program also taught me the importance of following a regular schedule to help gain control of my life."

After she successfully completed the three-week program, Tara returned to the center's six-month aftercare program in December 2018. She plans to come back to Rochester for the one-day class every six months.

"It keeps me in check," Tara says. "The nicest part is I get to see Dr. McKeon and reconnect with some of the people I've met who have become friends."

An effort to inspire

Dr. McKeon last saw Tara during a video consult in February. "Ultimately, she's been doing better. The fluidity of her walking has improved," Dr. McKeon says. "I think she'll likely have some symptoms going forward. But the more active she becomes, the better her quality of life will be."

Daily life for Tara is easier now, and she's been able to start driving again. She's also working to manage her health by exploring holistic therapies that include a restricted diet and light therapy.

In an effort to raise awareness about stiff-person syndrome that will lead to more research into the rare and often misdiagnosed condition, Tara's in the early stages of writing a book about her journey. "It's an effort to take this crappy thing and hopefully end up inspiring and helping people," she says. "Instead of waking up angry about your illness, how do you befriend it and live with it?"

"If something is not right, and you're not getting better, you need to keep going to other doctors until you get the answers you need."

Tara Zier

As she reflects on what she's been through, Tara says one of the most significant lessons she's learned is the importance of taking control of your own health. "If something is not right, and you're not getting better, you need to keep going to other doctors until you get the answers you need," she says.

That's what brought her to Mayo Clinic, and she's glad it did. "I would recommend Mayo to anyone. It's fantastic," Tara says. "It's so true that your environment does make a difference in your healing and overall well-being. If you're at Mayo for a week, and you're in a happy and positive environment, you can actually feel better. It's about people being human and caring."

NIH-Genetic and Rare Disease GARD

Stiff person syndrome (SPS) is a rare, progressive syndrome that affects the nervous system, specifically the brain and spinal cord. Symptoms may include extreme muscle stiffness, rigidity and painful spasms in the trunk and limbs, severely impairing mobility. Spasms can generate enough force to fracture bone. People with SPS often have heightened sensitivity to noise, sudden movements, and emotional distress, which can set off muscle spasms. Persistent symptoms can lead to abnormal posturing of the spine, such as being hunched over. The syndrome affects twice as many women as men.[1][2]

SPS is caused by increased muscle activity due to decreased inhibition of the central nervous system. It is thought to have an autoimmune component and is often associated with diabetes, as well as other autoimmune diseases such as thyroiditis, vitiligo, and pernicious anemia.[1][2] It may be diagnosed after having various tests including blood tests (such as for glutamic acid decarboxylase (GAD) antibodies which is elevated in about 2 in 3 people with SPS), a lumbar puncture, and electromyography. Treatment aims to control symptoms and improve mobility. Examples of treatments that have been used for SPS, include benzodiazepines, muscle relaxants, intravenous immune globulin (IVIG) therapy, plasmapheresis (also called plasma exchange), and rituximab.[1][2] While some people with SPS may maintain reasonable levels of activity with treatment, the majority become disabled over time.[2]
Last updated: 4/9/2020
Symptoms
Stiff person syndrome (SPS) is a progressive syndrome characterized by recurrent episodes of severe muscle stiffness, rigidity, and painful spasms in the trunk and limbs. The age that symptoms begin can vary, but most people start experiencing symptoms between ages 30 and 60. Spasms can be prolonged and extremely forceful, with the ability to generate enough force to fracture bone. They may cause a person to fall when walking or standing. Spasms are especially likely or may worsen during times of emotional distress, when being touched, when there is sudden movement, or with noise.[2][3]

Over time, persistent symptoms can lead to abnormal posturing of the spine, such as being stiffened and hunched over.[1] Daily activities such as getting into or out of bed, getting up from a chair, or dressing may become increasingly difficult.[2] People with SPS also may become fearful and anxious about navigating daily life, which in turn may trigger additional spasms. Many people with SPS develop depression as the syndrome progresses and quality of life becomes severely impaired.[2][3]
Last updated: 3/13/2018

This table lists symptoms that people with this disease may have. For most diseases, symptoms will vary from person to person. People with the same disease may not have all the symptoms listed. This information comes from a database called the Human Phenotype Ontology (HPO) . The HPO collects information on symptoms that have been described in medical resources. The HPO is updated regularly. Use the HPO ID to access more in-depth information about a symptom.
Showing 1-5 of 31 |
Medical Terms Other Names
Learn More:
HPO ID
80%-99% of people have these symptoms
Anxiety
Excessive, persistent worry and fear
0000739
EMG abnormality 0003457
Falls 0002527
Hyperhidrosis

Excessive sweating
[more] 0000975
Intermittent painful muscle spasms 0011964
Showing 1-5 of 31 |
Do you have more information about symptoms of this disease? We want to hear from you.
Last updated: 2/1/2021
Do you have updated information on this disease? We want to hear from you.
Cause
Scientists don't yet understand the complete picture of what causes stiff person syndrome, but research indicates that it is the result of an abnormal autoimmune response in the brain and spinal cord.[1] Autoimmune responses occur when the immune system mistakenly attacks the body.

Most people with stiff person syndrome have antibodies that are made to attack glutamic acid decarboxylase (GAD). GAD is a protein in some neurons that are involved in making a substance called gamma-aminobutyric acid (GABA), which is responsible for controlling muscle movement. The symptoms of stiff person syndrome may develop when the immune system mistakenly attacks the neurons that produce GAD. When GAD is not working properly, there is not enough GABA to help control muscle movement. The exact role that deficiency of GAD plays in the development of stiff person syndrome is not fully understood.[3]

Some individuals with stiff person syndrome will have antibodies to amphiphysin, a protein involved in the transmission of signals from one neuron to another. Individuals with these antibodies have a higher risk for developing breast, lung, or colon cancer.[3][4][5][6]
Last updated: 7/23/2017
Inheritance
As is the case with most autoimmune diseases, genetic factors involved in causing stiff person syndrome have not been established. While most cases appear to occur in an isolated manner, there have been reported cases of multiple people in the same family being affected by SPS.[7] Although one specific genetic change (mutation) is not known to cause stiff person syndrome, it is thought that genetics in combination with other factors may play a role in causing SPS.[3]
Last updated: 7/23/2017
Diagnosis
A diagnosis of stiff person syndrome (SPS) is typically made based on symptoms, a detailed medical history, and various tests used to support the diagnosis or rule out other diseases with overlapping symptoms.[4][8] One commonly used test is a blood test to detect the presence of glutamic acid decarboxylase (GAD) antibodies. About 60-80% of people with SPS have antibodies against GAD that can be detected on a blood test.[8] The absence of GAD antibodies does not rule out SPS, but the presence of high levels of GAD antibodies strongly supports the diagnosis.[5] GAD antibodies may also be measured in the cerebral spinal fluid from a lumbar puncture.[9]

Additionally, a doctor may recommend electromyography (EMG), which records electrical activity in skeletal muscles.[4][8] The EMG of a person with SPS typically shows continuous motor activity in the skeletal muscles.[4][8]

Other testing that may be used to confirm or rule out the diagnosis includes:

A hemoglobin A1C test to rule out diabetes mellitus.
A complete blood count to rule out pernicious anemia.
A thyroid-stimulating hormone (TSH) test to rule out thyroiditis.
A lumbar puncture to look for oligoclonal bands which indicate that the central nervous system is inflamed (these bands can be seen in about two thirds of people who have GAD antibodies).[3]

Genetic testing currently is not available because the underlying genetic cause of stiff person syndrome has not been established.[5]
Last updated: 3/13/2018
Treatment
Treatment aims to control symptoms and improve mobility and function. While some people on treatment for SPS may maintain reasonable levels of activity, the majority become increasingly disabled over time. Treatment options depend on the symptoms and severity in each person and may include:[2][3]

Benzodiazepines - these are drugs that slow down the nervous system and may relieve muscle spasms and anxiety. They are generally considered the best initial therapy for SPS. Examples include diazepam and clonazepam.
Baclofen - this is a muscle relaxant that may be used for people in whom benzodiazepines are not effective or not well-tolerated. Some people benefit from using baclofen in addition to benzodiazepines.
Immune modulating therapies - these may be considered in people with severe symptoms who do not experience relief with benzodiazepines and baclofen. Options may include intravenous immune globulin (IVIG) therapy, **plasmapheresis** (also called plasma exchange), and **rituximab**. However studies supporting the effectiveness and safety of these therapies for SPS are limited.

Physical therapy and occupational therapy are also an important part of management for SPS and may help with side effects of medications (such as weakness) in addition to symptoms of the disease.[3]
Last updated: 3/14/2018
Management Guidelines

Project OrphanAnesthesia is a project whose aim is to create peer-reviewed, readily accessible guidelines for patients with rare diseases and for the anesthesiologists caring for them. The project is a collaborative effort of the German Society of Anesthesiology and Intensive Care, Orphanet, the European Society of Pediatric Anesthesia, anesthetists and rare disease experts with the aim to contribute to patient safety.

Prognosis
The long-term outlook for people affected by stiff person syndrome (SPS) can vary widely depending on the symptoms of each person. For some people with this syndrome, symptoms resolve with treatment, or symptoms only affect a particular area of the body. For other people, symptoms may progress to include the muscles of the face, and some of the muscles in the body may be constantly rigid. Progression of the symptoms related to SPS can lead to frequent falls, which can become dangerous.[3][4]

Treatment may be helpful for some people with SPS, but for others current treatment options do not relieve the symptoms of the disorder.[1][3] For these people, daily living can become very difficult due to symptoms of muscle rigidity, anxiety, and depression.[3]
Last updated: 7/23/2017

Healthcare Resources

To find a medical professional who specializes in genetics, you can ask your doctor for a referral or you can search for one yourself. Online directories are provided by the American College of Medical Genetics and the National Society of Genetic Counselors. If you need additional help, contact a GARD Information Specialist. You can also learn more about genetic consultations from MedlinePlus Genetics.

Related Diseases

Related diseases are conditions that have similar signs and symptoms. A health care provider may consider these conditions in the table below when making a diagnosis. Please note that the table may not include all the

possible conditions related to this disease.
Conditions with similar signs and symptoms from Orphanet
Differential diagnosis includes an atypical manifestation of a spinal cord disease (e.g. multiple sclerosis; tumours), axial dystonia, neuromyotonia, acquired hyperekplexia (startle disease), and psychogenic movement disorders (see these terms).
Visit the Orphanet disease page for more information.
Research

Research helps us better understand diseases and can lead to advances in diagnosis and treatment. This section provides resources to help you learn about medical research and ways to get involved.
Clinical Research Resources

The Centers for Mendelian Genomics program is working to discover the causes of rare genetic disorders. For more information about applying to the research study, please visit their website.

ClinicalTrials.gov lists trials that are related to Stiff person syndrome. Click on the link to go to ClinicalTrials.gov to read descriptions of these studies.

Please note: Studies listed on the ClinicalTrials.gov website are listed for informational purposes only; being listed does not reflect an endorsement by GARD or the NIH. We strongly recommend that you talk with a trusted healthcare provider before choosing to participate in any clinical study.

Patient Registry

The Autoimmune Registry supports research for Stiff person syndrome by collecting information about patients with this and other autoimmune diseases. You can join the registry to share your information with researchers and receive updates about participating in new research studies. Learn more about registries.

Organizations

Support and advocacy groups can help you connect with other patients and families, and they can provide valuable services. Many develop patient-centered information and are the driving force behind research for better treatments and possible cures. They can direct you to research, resources, and services. Many organizations also have experts who serve as medical advisors or provide lists of doctors/clinics. Visit the group's website or contact them to learn about the services they offer. Inclusion on this list is not an endorsement by GARD.
Organizations Supporting this Disease

European Alliance of Neuromuscular Disorders Associations
MDG Malta 4
Gzira Road
Gzira, Intl GAR 04
Malta
Telephone: 003-56 -21 346688
E-mail: eamda@hotmail.com
Website: http://www.eamda.eu/
International Parkinson and Movement Disorder Society
555 East Wells Street, Suite 1100
Milwaukee, WI 53202-3823
Telephone: +1-414-276-2145
Fax: +1-414-276-3349
E-mail: info@movementdisorders.org

Website: https://www.movementdisorders.org/

Social Networking Websites

Stiff Person Syndrome Facebook Group
Website: https://www.facebook.com/groups/StiffPersonSyndrome/

Organizations Providing General Support

American Autoimmune Related Diseases Association (AARDA)
19176 Hall Road, Suite 130
Clinton Township, MI 48038
Toll-free: 800-598-4668
Telephone: 586-776-3900
Fax: 586-776-3903
E-mail: aarda@aarda.org
Website: https://www.aarda.org/

Do you know of an organization? We want to hear from you.
Living With

Living with a genetic or rare disease can impact the daily lives of patients and families. These resources can help families navigate various aspects of living with a rare disease.
Financial Resources

The Social Security Administration has included this condition in their Compassionate Allowances Initiative. This initiative speeds up the processing of disability claims for applicants with certain medical conditions that cause severe disability. More information about Compassionate Allowances and applying for Social Security disability is available online.

Learn More

These resources provide more information about this condition or associated symptoms. The in-depth resources contain medical and scientific language that may be hard to understand. You may want to review these resources with a medical professional.
Where to Start

The National Institute of Neurological Disorders and Stroke (NINDS) collects and disseminates research information related to neurological disorders. Click on the link to view information on this topic.

The National Organization for Rare Disorders (NORD) has a report for patients and families about this condition. NORD is a patient advocacy organization for individuals with rare diseases and the organizations that serve them.

In-Depth Information

Medscape Reference provides information on this topic. You may need to register to view the medical textbook, but registration is free.

The Monarch Initiative brings together data about this condition from humans and other species to help physicians and biomedical researchers. Monarch's tools are designed to make it easier to compare the signs and symptoms (phenotypes) of different diseases and discover common features. This initiative is a collaboration between several academic institutions across the world and is funded by the National Institutes of Health. Visit

the website to explore the biology of this condition.

Online Mendelian Inheritance in Man (OMIM) is a catalog of human genes and genetic disorders. Each entry has a summary of related medical articles. It is meant for health care professionals and researchers. OMIM is maintained by Johns Hopkins University School of Medicine.

Orphanet is a European reference portal for information on rare diseases and orphan drugs. Access to this database is free of charge.

PubMed is a searchable database of medical literature and lists journal articles that discuss Stiff person syndrome. Click on the link to view a sample search on this topic.

NINDS Stiff-Person Syndrome Information Page. National Institute of Neurological Disorders and Stroke. https://www.ninds.nih.gov/Disorders/All-Disorders/Stiff-Person-Syndrome-Information-Page#disorders-r1. Accessed 7/12/2017.

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Murinson BB. Stiff Person Syndrome. National Organization for Rare Disorders (NORD). 2010; http://rarediseases.org/rare-diseases/stiff-person-syndrome/.

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NORD National organization for rare diseases

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Synonyms of Stiff Person Syndrome

- Moersch-Woltman syndrome
- stiff-man syndrome
- SMS
- SPS

Subdivisions of Stiff Person Syndrome

- classic stiff person syndrome
- focal stiff person syndrome

jerking stiff person syndrome
progressive encephalomyelitis with rigidity and myoclonus (PERM)
paraneoplastic-related stiff person syndrome