BARE YOUR RARE
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PATIENT & CAREGIVER GUIDE

Stiff Person Syndrome
(SPS / SPSD)

A rare immune-mediated disorder — real, treatable, and on the verge of genuinely transformative therapy.

Built from peer-reviewed literature, registry data, and patient-advocate consensus. Includes the December 2025 KYSA-8 CAR-T results in context. Designed to be printed, marked up, and brought to every appointment.

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1.36–2.11
per 100,000 (revised from 1 per million)

Anti-GAD65
most common biomarker

Dec 2025
KYSA-8 CAR-T Phase 2
first transformative results in SPS

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A NOTE BEFORE YOU READ

Stiff Person Syndrome (SPS) — now more accurately described as Stiff Person Spectrum Disorder (SPSD) — is a real, immune-mediated neurological condition. It is not psychological. It is not "all in your head." Muscles that should relax stay contracted because inhibitory signaling in the nervous system has been disrupted by the immune system itself. This matters because far too many patients have spent years being told their symptoms weren't real. They are.

This guide opens with a genuinely hopeful development: the December 2025 Phase 2 results of the KYSA-8 CAR-T trial. For the first time, a therapy has shown outcomes in SPS that clinicians describe as unprecedented. Approval is not guaranteed — but the trajectory of care for this condition has begun to change.

BREAKINGNEWS·DECEMBER2025

Phase 2 CAR-T Trial Delivers "Unprecedented" Results

The KYSA-8 trial reported Phase 2 outcomes that investigators called "truly remarkable" — results not previously seen with existing therapies. If approved, this would become the first FDA-approved therapy specifically for Stiff Person Syndrome. Regulatory review is expected in the first half of 2026.

81%
clinically meaningful improvement

46%
median improvement in walking ability

67%
wheelchair/walker users regained independent walking

100%
remained free of chronic immunotherapies

SECTION 01

What SPS Is — and What It Isn't

Stiff Person Syndrome is a rare immune-mediated neurological condition in which inhibitory signaling in the nervous system becomes impaired. Most patients have antibodies such as anti-GAD65 that act as biomarkers of the autoimmune process. Some variants involve antibodies that may directly disrupt synaptic targets — glycine receptors, amphiphysin, or GABARAP.

When inhibitory signaling is disrupted, muscles stay continuously active and can spasm suddenly. Patients describe feeling trapped in a rigid body. Many develop startle sensitivity — unexpected sounds, touch, or emotional stress trigger severe spasms — and significant pain and fatigue follow. Falls and fractures are real risks.

Prevalence	~1.36–2.11 per 100,000 (Colorado health-system study — higher than earlier "1 in a million" estimates)
Diagnostic Delay	Average 7 years from first symptoms to diagnosis
Most Common Antibody	Anti-GAD65 — but low titers alone are NOT diagnostic
Nature of Condition	Real immune-mediated neurological disorder — not psychological, not functional
Treatment Landscape	No cure. Symptomatic therapy + immune therapy helps most patients. CAR-T may change long-term control.

> *"We know the suffering, the severe rigidity, the falls, the fractures, the spasms."*
>
> **— Lea Jabre Fayad, SPS advocate, founder of Bent Not Broken Autoimmune**

> *"Seventeen years just shows how long it takes for some people to get diagnosed, even the person who has the most resources available to her."*
>
> **— Joy Lwangu, diagnosed at 35, reflecting on Céline Dion's journey**

SECTION 02

The Biology — How SPS Affects the Body

Normal muscle control is a conversation. One muscle talks, the opposing muscle listens. In SPS, both sides shout at once. The brain loses the ability to tell opposing muscles to take turns. Muscles that should relax stay contracted — producing the rigidity, the spasms, the characteristic "tin-soldier" posture that Moersch and Woltman first described in 1956.

Normal movement requires a balance between excitatory signaling (telling muscles to fire) and inhibitory signaling (telling them to stand down). In SPS, inhibitory signaling is impaired. Two neurotransmitters are at the center of this: GABA and, in some variants, glycine. The immune system interferes with the machinery that produces or receives these calming signals.

What goes wrong, mechanistically

G GAD65 — The Enzyme That Makes GABA

Glutamic acid decarboxylase (GAD65) is the enzyme that converts glutamate into GABA, the brain's main inhibitory neurotransmitter. Most SPS patients have antibodies against GAD65. These antibodies are strongly associated with the disease, but their precise pathogenic role remains under investigation — they may be biomarkers, direct drivers, or both.

R Glycine Receptor — The Other Pathway

In severe variants like PERM (progressive encephalomyelitis with rigidity and myoclonus), antibodies target the glycine receptor directly. Glycine is the dominant inhibitory neurotransmitter in the brainstem and spinal cord. When its receptors are blocked, the loss of inhibition is more abrupt and more dangerous.

C Loss of Reciprocal Inhibition

When inhibition fails, opposing muscle groups contract at the same time. Flexors and extensors pull against each other continuously. This is what produces the characteristic stiffness — and why spasms, once triggered, can be so severe.

A note on antibody interpretation

Anti-GAD65 antibodies are widely considered markers of autoimmune dysfunction, and their exact pathogenic role remains an active research question. This distinction matters for patients — a positive test supports the diagnosis in context, but on its own does not prove it.

SECTION 03

How the Understanding of SPS Evolved

For most of its history, SPS was considered so rare — and so strange — that many clinicians had never seen a case. The path from first description to first targeted therapy has taken nearly seventy years.

Year	Development
1956	Moersch & Woltman at Mayo Clinic describe 14 patients with rigid "tin soldier" posture. Call it Stiff Man Syndrome.
1960s	Benzodiazepines recognized as effective symptomatic therapy. Remain a mainstay today.
1970s	Paraneoplastic cases identified — some SPS presentations are triggered by an underlying cancer.
Late 1980s–1990s	Autoimmune basis established. Anti-GAD65 antibodies described as the first biomarker.
1990s	Term "Stiff Person Syndrome" formally adopted, reflecting recognition that both sexes are affected.
2001	Randomized controlled trial (Dalakas et al.) shows IVIg reduces symptoms. First evidence-based immune therapy.
2000s	Additional autoantigens identified: amphiphysin, glycine receptor, GABARAP. The spectrum framework emerges.
2020s	Shift toward Stiff Person Spectrum Disorder (SPSD) framing. Classic SPS is one phenotype among many.
2022	Public awareness rises sharply after Céline Dion's disclosure. Patient community grows significantly.
Dec 2025	KYSA-8 Phase 2 CAR-T topline results — the first therapy to show transformative outcomes in SPS.
2026 →	BLA submission for miv-cel planned. FcRn inhibitors and neuromodulation strategies in development.

SECTION 04

How Rare Is SPS, Really?

For decades, textbooks described SPS as occurring in roughly one person per million. Recent population-based data tell a different story.

Old estimate	Revised estimate
~1 per 1,000,000	1.36–2.11 per 100,000
legacy figure	Colorado health-system study — incidence ~0.35 per 100,000 person-years

The newer estimates almost certainly reflect better recognition, wider availability of antibody testing, and the broader spectrum framework — not a genuine increase in disease frequency. The condition has not become more common. It has become more visible. Many patients who would previously have been diagnosed with a functional disorder, fibromyalgia, or "medically unexplained" stiffness are now correctly identified.

SECTION 05

The Spectrum — Six Variants, One Disease

SPS is not one uniform disease. The Stiff Person Spectrum Disorder (SPSD) framework recognizes distinct clinical presentations that share underlying autoimmune biology but differ in what muscles are affected, how severe the course is, and which antibodies drive them.

C Classic SPS

The most common presentation. Truncal and limb stiffness with startle sensitivity. Progresses over months to years. Anti-GAD65 antibodies are typical. Responds reasonably well to standard immune therapy.

L Stiff-Limb Syndrome

Stiffness localized to one or more specific limbs rather than the trunk. Can be a distinct presentation or a precursor to more widespread disease. Diagnostic delay is common because the pattern is atypical.

T Stiff-Trunk Syndrome

Primarily affects the torso and back. Lordosis (exaggerated inward curve of the lower spine) is a classic finding. Falls from sudden spasms are a major risk.

P SPS-Plus

Classic SPS features plus cerebellar or brainstem symptoms — coordination problems, eye movement abnormalities, difficulty with balance beyond what stiffness alone would explain.

E PERM — Progressive Encephalomyelitis with Rigidity and Myoclonus

The most severe variant. Often driven by glycine receptor antibodies rather than anti-GAD65. Can affect breathing and autonomic function. Requires aggressive immune therapy and careful monitoring.

N Paraneoplastic SPSD

Triggered by an underlying cancer — typically breast, lung, or thymoma. Anti-amphiphysin antibodies are characteristic. Treating the cancer is central to treating the SPS.

SECTION 06

Diagnosis — What Should Be Tested

SPS is diagnosed clinically. There is no single definitive test. The combination of characteristic symptoms, supporting electromyography findings, and antibody results — interpreted together — is what establishes the diagnosis.

1 Characteristic Stiffness/Spasm Pattern

Truncal or limb stiffness with exaggerated startle, triggered spasms, and fear of movement. History and examination remain the first step. A neurologist familiar with SPS is the most important single resource.

2 EMG — Continuous Motor Unit Activity

Electromyography in SPS shows continuous motor unit activity even at rest — muscles that should be quiet are firing constantly. This is a supportive finding when present but is not invariable.

3 Antibody Testing

Serum and CSF anti-GAD65, glycine receptor, amphiphysin, and GABARAP antibodies. High titers in both serum AND CSF support the diagnosis when clinical features are consistent. Low titers are not diagnostic on their own.

4 Exclusion of Mimics

Functional neurological disorder, parkinsonism, multiple sclerosis, dystonia, hereditary spastic disorders, and fibromyalgia can all overlap. Response to GABA-enhancing medication (benzodiazepines, baclofen) supports the diagnosis but is not definitive.

SECTION 07

What Antibody Results Mean — and Don't

This is the single most important thing to understand about SPS diagnosis. Anti-GAD65 is a useful biomarker but a poor yes/no test. Both false reassurance and false diagnosis are common.

H High Titers — Especially in Serum AND CSF

Support the diagnosis of SPS **when combined with clinical features**. The presence of antibodies in the cerebrospinal fluid is particularly supportive. High titer alone without symptoms is not a diagnosis.

L Low Titers Are Common in Other Conditions

Type 1 diabetes, autoimmune thyroid disease, and other autoimmune disorders can produce low-titer anti-GAD65. A low titer alone **does not** mean you have SPS. Many people are diagnosed incorrectly because of this.

N Negative Antibodies Do Not Rule Out SPS

Some variants involve glycine receptor, amphiphysin, or GABARAP antibodies instead. A subset of patients are seronegative — they have the clinical syndrome but no detectable antibodies. Clinical judgment and EMG matter.

P Positive Antibodies Without Symptoms Are Not a Diagnosis

Asymptomatic antibody positivity is not SPS. Screening people without neurological symptoms is not recommended. The diagnosis requires the clinical picture, not just a lab value.

Bottom line — the lab value alone is not the answer.

Diagnosis requires the complete clinical picture. This prevents both missed diagnoses and wrongful diagnoses — either of which can cause years of harm.

SECTION 08

Genetics, Comorbidities & The Patient Journey

SPS is not caused by a single gene. There is no genetic test that confirms or excludes it. But immune-related genetic susceptibility contributes to risk, and certain comorbidities run alongside it consistently enough to be worth monitoring.

Genetic associations

HLA-DQB1 variants are the most robustly replicated genetic association. A reported KLK10 association exists but requires independent replication before it can be considered established.

Common comorbidities

Type 1 diabetes is the most common associated condition — shared GAD65 target. Autoimmune thyroid disease, vitiligo, and pernicious anemia occur at higher rates than in the general population. Anxiety and trauma-related symptoms are frequent, typically secondary to living with the unpredictability of the condition.

The typical path to diagnosis

#	Stage
1	Early stiffness often dismissed as muscle tension, stress, or anxiety
2	Worsening spasms — episodes become more frequent and severe
3	Specialist referral (neurology, rheumatology) — often after years of seeking answers
4	Antibody and EMG testing — diagnostic workup begins
5	Diagnosis — a name is finally given to the experience
6	Symptomatic therapy — benzodiazepines, baclofen, physical therapy
7	Immune therapy — IVIg, rituximab, other agents
8	Rehabilitation and long-term management — ongoing adaptation

Delays of 7+ years are common.

This is why awareness and early recognition matter so much. Every year of delay is a year of worsening rigidity and untreated autoimmune activity.

SECTION 09

Living With SPS — Including Pediatric Presentations

The daily reality of SPS is more than the list of symptoms. People describe the fear of sudden spasms in public, the loss of independence when mobility becomes unpredictable, the social isolation, and the hypervigilance of waiting for the next trigger. These are normal responses to an abnormal situation — not separate psychiatric conditions.

What patients consistently describe

Fear of sudden spasms in places where falling could be dangerous — stairs, crowds, traffic. **Loss of independence** as mobility becomes less predictable. **Social isolation** from activities that involve startling stimuli. **Hypervigilance** of environment and body state. All of these are rational. None of them are personality flaws.

Individual outcomes vary — widely.

Patient stories illustrate possibilities, not guarantees. Some patients stabilize on initial treatment. Others require years of escalating therapy to control the disease. Each person's course is unique.

Pediatric SPS

Pediatric SPS accounts for roughly 5% of cases. It often presents differently from adult SPS — gait abnormalities and spasms tend to appear before the classic truncal stiffness. Diagnostic delay can be even longer because specialists rarely consider SPS in children. Early immune therapy is important to prevent secondary complications like fixed contractures and developmental disruption.

SECTION 10

Treatment — Symptomatic and Immune

Treatment in SPS is hierarchical. Symptomatic therapy manages the stiffness and spasms. Immune therapy targets the underlying autoimmune process. Most patients need both. Individualization is essential because response varies significantly between patients and variants.

Core symptomatic therapy

B Benzodiazepines (diazepam, clonazepam)

Enhance GABA activity at the receptor level, directly counteracting the lost inhibitory signaling. Often the most effective single medication for spasm control. Sedation and dependency risk require careful dose titration.

M Baclofen (oral or intrathecal)

Another GABA-enhancing agent. Oral baclofen is first-line. For severe cases unresponsive to oral therapy, intrathecal baclofen delivered via implanted pump can dramatically reduce rigidity.

P Physical Therapy

Range-of-motion work, graded exposure to feared movements, and trigger management. A physical therapist familiar with SPS is the ideal resource; one who is not can make symptoms worse by pushing through spasm triggers.

T Trigger Management

Noise, stress, temperature changes, and emotional stimuli all trigger spasms. Systematic identification and modification of triggers is genuine treatment, not "just coping."

Evidence-based immune therapy

I IVIg — The Strongest Evidence Base

The 2001 Dalakas randomized controlled trial established IVIg as an effective immune therapy in classic SPS. It remains first-line immune therapy for most patients. Response is typically seen within weeks; infusions are usually repeated periodically.

R Rituximab

B-cell depletion therapy. Evidence is variable — some patients respond well, others do not. Often tried when IVIg is inadequate or in patients with higher autoantibody burden.

S Steroids and Plasma Exchange

Corticosteroids are used depending on presentation. Plasma exchange is reserved for severe or refractory cases, especially PERM.

SECTION 11

Emerging Therapies & The 2026 Horizon

For the first time, SPS treatment is moving beyond symptom management and broad immunosuppression toward targeted therapies that reset the immune system itself. The December 2025 KYSA-8 Phase 2 CAR-T results represent a potential inflection point.

C CAR-T Therapy (miv-cel) — The Breakthrough

81% of treated patients achieved clinically meaningful improvement; 67% of wheelchair or walker users regained independent walking; 100% remained free of chronic immunotherapies at the reporting interval. BLA submission planned for the first half of 2026. Approval is not yet final — but the signal is unusually strong.

F FcRn Inhibitors

A newer class of drugs that accelerate the clearance of pathogenic antibodies from circulation. Active trials in several antibody-mediated neurological conditions. Specific SPS trial data is in development.

N Neuromodulation Approaches

Including deep brain stimulation and peripheral nerve approaches. Still early-stage. Most useful so far in specific refractory presentations.

CAR-T remains experimental for SPS.

The December 2025 Phase 2 results are extraordinary, but regulatory approval has not yet happened. Patients and families considering CAR-T should work with a center participating in the trial program, and should weigh the well-known risks of CAR-T therapy (cytokine release syndrome, neurotoxicity, prolonged cytopenias) against the potential benefit.

SECTION 12

Safety, Prognosis & Current Research

Key safety risks to manage

Falls and fractures are the most consequential short-term risks. **Medication sedation** from benzodiazepines and baclofen affects daily function. **Startle triggers** (sound, touch, temperature, stress) need active management. **Reduced mobility** affects long-term bone health, cardiovascular conditioning, and mental health. Bone density monitoring is appropriate for patients with reduced mobility and benzodiazepine exposure.

Prognosis

The course varies significantly. Some patients stabilize with treatment and maintain good function for years. Others experience fluctuating symptoms with intermittent flares. A subset progresses despite therapy and faces increasing disability. Early immune therapy is consistently associated with better functional outcomes — which is the strongest argument for prompt diagnosis.

Current research directions

B-cell-targeted therapies (beyond rituximab) continue to advance. Cellular immune reset strategies (CAR-T, stem cell) now have Phase 2 data. Biomarker refinement aims to better distinguish active from quiescent disease. Earlier diagnosis strategies focus on primary-care recognition of SPS red flags. Spectrum classification work is ongoing to better match patients to therapy based on their specific phenotype.

Early immune therapy is associated with better outcomes.

This is the strongest argument for prompt, accurate diagnosis. Every year of untreated autoimmune activity increases the burden on the nervous system and the probability of long-term disability.

SECTION 13

Community & Support Resources

SPS is isolating. Peer support is not optional — it changes outcomes. What follows are the resources most consistently recommended by active patient advocates.

S Stiff Person Syndrome Research Foundation (SPSRF)

The main global hub for SPS resources, research, and community. Offers support groups, a patient registry, educational webinars, and strong connections to SPS-specialist clinicians. Typically the first destination for newly diagnosed patients.

R RareConnect (EURORDIS)

International moderated rare disease community with SPS-specific discussion groups. Well-moderated, cross-language. Good for finding patients in other countries with similar experiences.

N NORD IAMRARE Registry

Research-focused patient registry that also connects community members. Contributes to research data while providing a community link.

F Facebook Support Groups

Large, active communities where practical knowledge lives — medication experiences, trigger identification, disability navigation, appeals, daily workarounds. "Stiff Person Syndrome Support Group" is the largest. "Stiff Person Syndrome Awareness" is also active. Several smaller patient-only private groups exist for specific variants or demographics.

Peer groups share lived experience — not medical guidance.

Community wisdom is real and valuable. But treatment decisions belong with your clinical team. Use community knowledge to ask better questions of your specialist, not to bypass them.

SECTION 14

Moving Forward

Stiff Person Syndrome is rare, complex, and often misunderstood. It is also real, treatable, and — for the first time in nearly seventy years — on the edge of genuinely transformative therapy. The December 2025 CAR-T results will take time to translate into widely available treatment, but the trajectory has shifted. The research community, clinical teams, and patient advocates continue to push for earlier diagnosis, better treatments, and improved quality of life.

If you or someone you know is navigating SPS

- ✓ You are not alone — community matters.
- ✓ Diagnosis takes time, but persistence pays off.
- ✓ Treatment options exist and are expanding.
- ✓ Early intervention improves outcomes.
- ✓ Your experience is valid. SPS is not psychological.
- ✓ There is hope on the horizon.

Your story can help someone diagnosed last week.

If you live with SPS, your experience — treatment notes, trigger patterns, IVIg or rituximab responses, CAR-T considerations — matters to the next person starting this journey. Bare Your Rare is a living resource, and your voice belongs on it.

Share your story: **bareyourrare.org/contact/**

You Found This Place.

Bare Your Rare exists because patient experience is expertise.
This guide was built to make what took years of lived experience
and thousands of pages of literature to understand,
findable in one evening — for the person who needs it tonight.

Share it freely with your neurologist, your family,
or anyone navigating this diagnosis.

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