From the review article:

Complex Regional Pain Syndrome-
Reflex Sympathetic Dystrophy Syndrome: Diagnosis and Therapy - A Review of 824 Patients
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STAGES OF CRPS/RSD

CRPS/RSD has been divided into different stages. Depending on nature of injury, the stages vary in their duration. In the 17 patients suffering from venipuncture CRPS in our series, deterioration from stage I to stage III was measured in a few weeks up to less than 9 months. This is in contrast with CRPS in children in whom stages would stagnate, reverse or improve slowly.

In STAGE I, is a sympathetic dysfunction with typical thermatomal distribution of the pain. The pain may spread in a mirror fashion to contralateral extremity or to adjacent regions on the same side of the body. In stage one; the pain is usually SMP in nature.

In STAGE II, the dysfunction changes to dystrophy manifested by edema, hyperhidrosis, neurovascular instability with fluctuation of livedo reticularis and cyanosis - causing change of temperature and color of the skin in matter of minutes. The dystrophic changes also include bouts of hair loss, ridging, dystrophic, brittle and discolored nails, skin rash, subcutaneous bleeding, neurodermatitis, and ulcerative lesions. Due to the confusing clinical manifestations, the patient may be accused of factitious self-mutilation and "Münchausen syndrome." All these dystrophic changes may not be present at the same time nor in the same patient. Careful history taking is important in this regard.

In STAGE III, the pain is usually no longer SMP and is more likely a sympathetically independent pain (SIP). Atrophy in different degrees is seen. Frequently, the atrophy is overshadowed by subcutaneous edema. The complex regional pain and inflammation spread to other extremities in approximately 1/3 of CRPS patients. At stage II or III it is not at all uncommon for CRPS to spread to other extremities. At times, it may become generalized. The generalized CRPS is an infrequent late stage complication. It is accompanied by sympathetic dysfunction in all four extremities as well as attacks of headache, vertigo, poor memory, and poor concentration. The spread through paravertebral and midline
sympathetic nerves may be vertical, horizontal, or both. The original source of CRPS may sensitize the patient to later develop CRPS in another remote part of the body triggered by a trivial injury. The ubiquitous phenomenon of referred pain to remote areas (e.g., from foot or hand to spine) should not be mistaken for the spread of CRPS.

At STAGE III, inflammation becomes more problematic and release of neuropeptides from c-fiber terminals results in multiple inflammatory and immune dysfunctions. The secondary release of substance P may damage mast cells and destroy muscle cells and fibroblasts.

**STAGE IV:**

1. Failure of the immune system, reduction of helper T-cell lymphocytes and elevation of killer T-cell lymphocytes.

2. Intractable hypertension changes to orthostatic hypotension.

3. Intractable generalized edema involving the abdomen, pelvis, lungs, and extremities.

4. Ulcerative skin lesions which may respond to treatment with I.V. Mannitol, I.V. Immunoglobulin, and ACTH treatments. Calcium channel blockers such as Nifedipine may be effective in treatment.

5. High risks of cancer and suicide are increased.

6. Multiple surgical procedures seem to be precipitating factors for development of stage IV.

Stage IV is almost the flip side of earlier stages, and points to exhaustion of autonomic and immune systems. Ganglion blocks in this stage are useless and treatment should be aimed at improving the edema and the failing immune system. Sympathetic ganglion blocks, alpha blockers, including Clonidine, are contraindicated in stage IV due to hypotension. Instead, medications such as Proamantin (midodrin) are helpful to correct the orthostatic hypotension.