



Complex regional pain syndrome in Canadian children and youth

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Background

Complex regional pain syndrome (CRPS) is a chronic severe pain condition that involves peripheral, central, and autonomic nervous system and immune system mechanisms, previously referred to as *regional sympathetic dystrophy* (Harden et al., 2013). CRPS describes an array of painful conditions that are characterized by a continuing (spontaneous and/or evoked) regional pain that is seemingly disproportionate in time or degree to the usual course of any known trauma or other lesion. The pain is regional (not in a specific nerve territory or dermatome) and usually has a distal predominance of abnormal sensory, motor, sudomotor, vasomotor, and/or trophic findings. The syndrome shows variable progression over time and over the past 20 years has attracted increasing attention in paediatrics (Goldschneider 2012).

In adults, CRPS has incident rates ranging from 5.5 to 26.2 new cases per 100,000 annually (Sandroni et al., 2003 and de Mos et al., 2007). Prospective studies indicate that approximately 11 to 18% of adults will develop CRPS type 1 following fracture or total knee arthroplasty (Harden et al., 2003 and Puchalski, 2005). In children and

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adolescents, incidence rates and typical disease trajectory are unknown (Goldschneider 2012). Two recent retrospective chart reviews reported complex diagnostic and interventional histories of children with CRPS, with poor outcomes and rates of recurrence ranging from 10 to 55% (Bayle-Iniguez et al., 2015; Dietz et al., 2015).

When pain is persistent and severe, it results in psychological, physical, and neurological structural and functional changes (Davis et al., 2013). Pain-related disability affects participation in school, work, physical activity, and peer and family interactions (Bursch et al., 1998), placing children with complex pain at greater risk of poor long-term health and behavioural outcomes. Children with CRPS, due to the complexity of making the diagnosis and frequent treatment failure, are particularly vulnerable. CRPS is a devastating chronic pain condition that results in greater functional impairment and symptoms than other chronic pain conditions (Logan et al., 2013).

A diagnosis of CRPS relies on history and clinical examination. There is no diagnostic test or pathognomonic finding for CRPS. Patients present with unusual features such as spontaneous pain, altered sensation resulting in pain (e.g., allodynia and hyperalgesia), and pain outside the distribution of a peripheral nerve. These features do not correspond with well-understood mechanisms of injury or pathophysiology and may result in delayed diagnosis. Prolonged CRPS results in trophic changes. Radiographic evidence of osteoporosis can be seen as early as two weeks into the disorder (Rho et al., 2002). Importantly, pain is often not responsive to opioids or NSAID medications. Physiotherapy is the cornerstone of treatment for CRPS. Prompt referral to physiotherapy and initiation of a multidisciplinary approach to treatment relies upon a high index of suspicion (Clinch, 2009).

The International Association for the Study of Pain has adopted the Budapest diagnostic criteria (Harden et al., 2013) that include both clinical and research criteria used for diagnosis of CRPS in adults. For research purposes, with adults, the diagnostic decision rule is more rigorous than the clinical. The *research criteria* include at least *one symptom in all four symptom categories* whereas the *clinical criteria* include at least *one symptom in only three symptom categories*. Both research and clinical criteria require continuing pain disproportionate to the inciting event and at least one sign observed at evaluation in two or more sign categories. Although the clinical criteria are not validated in children, they are used for diagnosis.

Although CRPS is a relatively rare condition in the general population, the developing nervous and immune systems of children may present unique risk or protective factors, influencing susceptibility and disease course. Few interventions have been formally evaluated in the paediatric population. Canadian surveillance for CRPS in children and adolescents across Canada will provide important foundational data to determine the minimum incidence of the condition, highlight current resource needs, and promote early recognition and treatment. In addition, further exploration is needed to determine whether the disease trajectory in children differs from that of adults, and whether risk factors differ between paediatric and adult populations.

Methods

The CPSP will enable detection of CRPS cases that present in all settings, including paediatric primary care, subspecialty care, inpatient care, and paediatric pain clinics. Through the established methodology of the CPSP, paediatricians and paediatric subspecialists will be asked each month if they have seen cases of CRPS. Respondents who identify cases will subsequently be asked to complete a detailed questionnaire for each case.



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All of the paediatric pain clinics at tertiary hospitals across Canada have been engaged to participate in this study. The paediatric pain clinics will each have a local site champion who will coordinate the submission of all cases that are referred to the clinic. This is intended to minimize duplicate reporting from clinicians at the same institution.



Case definition

Report any new patient presenting between the ages of 2 and 18 years (up to the 18th birthday) with a new diagnosis of CRPS, meeting the following International Association for the Study of Pain clinical diagnostic criteria:

1. Continuing pain, which is disproportionate to any inciting event
2. Reports at least one symptom in at least three of the following four categories:
 - **Sensory:** hyperesthesia and/or allodynia
 - **Vasomotor:** temperature asymmetry and/or skin color changes and/or skin color asymmetry
 - **Sudomotor/Edema:** edema and/or sweating changes and/or sweating asymmetry
 - **Motor/Trophic:** decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
3. Displays at least one sign at time of evaluation in at least two of the following four categories:
 - **Sensory:** hyperalgesia (to pinprick) and/or allodynia (to light touch and/or temperature sensation and/or deep somatic pressure and/or joint movement)
 - **Vasomotor:** temperature asymmetry (>1°C) and/or skin color changes and/or asymmetry
 - **Sudomotor/Edema:** edema and/or sweating changes and/or sweating asymmetry
 - **Motor/Trophic:** decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)

Exclusion criteria

Presence of another diagnosis that better explains the signs and symptoms

Objectives

- 1) Determine the minimum incidence and geographic distribution of cases of CRPS in Canadian children and youth
- 2) Describe predisposing features or inciting factors and clinical presentation
- 3) Describe pathways of referral, duration of symptoms prior to diagnosis, and common diagnostic investigations
- 4) Document the pharmacologic, physical, and psychological interventions recommended by paediatricians and other pain specialists
- 5) Ascertain complementary and alternative treatments sought by patients
- 6) Examine possible adverse events related to delayed diagnosis or treatment alternatives

Duration

September 2017 to August 2019

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Expected number of cases

Based on adult incidence, we expect approximately 5 cases per 100,000 population. According to Statistics Canada, the Canadian population on July 1, 2015 was an estimated 35,851,774, with 7,848,844 individuals 0 to 19 years of age; therefore, the estimated number of cases is around 390 per year.

Ethical approval

University of Saskatchewan Research Ethics Board

Funding

The CPSP is a joint project of the Public Health Agency of Canada (PHAC) and the Canadian Paediatric Society (CPS), funded by PHAC and managed by the CPS. Funding for this specific surveillance project was provided through an unrestricted grant by the Chronic Pain Network, a Canadian Institutes for Health Research initiative.

Analysis and publication

Analysis will include estimation of the incidence of CRPS in Canadian children and youth as well as descriptive analysis of survey data from definite and probable cases. Analysis will be completed within six months of study closure and dissemination of study results will begin. Abstracts and manuscripts will be prepared and submitted within one year of study closure.

Reports will be disseminated through the CPSP. Final results will be published in peer-reviewed journals and will be presented at regional (e.g., Saskatchewan Pain Conference), national (e.g., Canadian Paediatric Society, Canadian Pain Society), and international conferences (e.g., World Congress on Pain, International Symposium on Pediatric Pain). A study summary will be published in the University of Saskatchewan Pediatric Research newsletter and displayed on the university webpage. A link to the study summary will be disseminated through professional social media routes, such as the Pediatric Chronic Pain Clinic Directors list-serv, the international Pediatric Pain list-serv, and Canadian pain educators.

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