Introduction

Chronic pain has a substantial adverse impact on the health-related quality of life of children and adolescents, resulting in significantly worse physical functioning, psychological functioning, social functioning, lower satisfaction with life, and poorer self-perceived health status (Merlijn et al. 2006; Palermo 2000; Palermo et al. 2008). The current Pediatric Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (PedIMMPACT) has accordingly recommended that investigators conducting pediatric clinical trials in chronic and recurrent pain consider assessing not only pain intensity but also physical function, emotional function, role function, other condition-related symptoms and adverse events, global judgment of satisfaction with treatment, sleep, and economic factors (www.immpact.org) (McGrath et al. 2008).

Chronic pain is very common in the pediatric population and therefore represents both an individual and a public health concern (Vetter 2008). It has been convincingly opined that the health of a nation is largely a reflection of the past and present health of its children, in large part because childhood is an incubation period for many disorders that affect the health of the whole population (Forrest and Riley 2004). This mandates that greater attention be paid to the promotion of pediatric biopsychosocial resilience and adaptability in addition to other approaches to prevent the precursors of future adult health disorders (Forrest and Riley 2004). This vital continuum of health versus disease between childhood, adolescence, and adulthood is intuitively very applicable to the chronic pain experience.

This chapter addresses the epidemiology, including the demographics, natural history, and financial impact of pediatric chronic pain. Attention will initially be focused on the overall prevalence and impact of chronic pain in children and adolescents. Regional differences, the effect of age and gender on the onset, and natural history of pediatric chronic pain will also be examined. Finally, given their predominance in the pediatric age group, the available specific epidemiologic data on headaches, recurrent abdominal pain, chest pain, musculoskeletal pain, and complex regional pain syndrome will be presented.
The Overall Prevalence and Impact of Chronic Pain in Children and Adolescents

An increasing amount of attention has been focused on the epidemiology of pediatric chronic pain (Huguet and Miro 2008). However, until as recently as 2000, very little was known in North America or Europe about the prevalence of pain in children and adolescents (McGrath et al. 2000; Perquin et al. 2000a). In an attempt to remedy this deficiency, tools such as the Pain Experience Interview have been devised, validated, and applied to provide estimates of the lifetime and point prevalence of various types of pain in children, as well as data on the intensity, effect, duration, and frequency of their pain experiences (McGrath et al. 2000).

A cross-sectional, population-based survey of 5,424 Dutch children and adolescents, 0–18 years of age, drawn randomly from census registries and the enrollment records of 27 primary schools and 14 secondary schools in the greater Rotterdam area revealed that 54% had experienced pain of some type and intensity within the previous 3 months, while 25% of the respondents reported chronic pain, defined as recurrent or continuous pain of more than 3 months duration (Perquin et al. 2000a). A subsequent cross-sectional German study observed a 46% point prevalence of chronic pain of at least 3 months duration in the 10–14-year-old age group (Roth-Isigkeit et al. 2004).

When an expanded-age cohort of 749 German children and adolescents were surveyed in their elementary and secondary school setting, using the Luebeck Pain-Screening Questionnaire, 83% had experienced pain during the preceding 3 months, and pain had been present for greater than 6 months in 31% of the respondents (Roth-Isigkeit et al. 2005). Headache (60%), abdominal pain (43%), limb pain (34%), and back pain (30%) were the rank-ordered most commonly reported types of pain (Roth-Isigkeit et al. 2005). This cross-sectional community sample of children and adolescents also reported a number of perceived chronic pain-related functional issues, including sleep problems (54%), inability to pursue hobbies (53%), eating problems (51%), school absence (49%), and inability to interact with friends (47%). Of note, the prevalence of these restrictions in daily living attributable to pain increased with participant age, and among the children and adolescents with chronic pain, the likelihood of physician visits and medication use also increased with age (Roth-Isigkeit et al. 2005).

A comparable cross-sectional population study of 561 Spanish schoolchildren between the ages of 8 and 16 years revealed a 37% prevalence of chronic pain problems during the previous 3 months; however, only 5.1% of the respondents had experienced moderate or severe chronic pain (Huguet and Miro 2008). The most frequently reported pain locations were the lower limb (47%), the head (43%), and the abdomen (34%), with less common pain locations being the back (11%), the neck (5%), the pelvis (3%), and the chest (2%). Of note, headache and abdominal pain were more frequently reported by girls, whereas lower limb pain was more frequently reported by boys (Huguet and Miro 2008). The children with a chronic pain condition overall reported a worse quality of life, missed more days from school, and were more likely to use pain medicine and to seek medical care for pain relief (Huguet and Miro 2008). This concurs with previous findings that children in the USA who complained often of aches and pains used more health-care services, had more psychosocial problems, missed more days of school, and did worse academically (Campo et al. 2002).

However, the above-quoted European studies contrast sharply with a reported 6% lifetime prevalence of chronic pain in a community cohort of 495 Canadian school children, 9–13 years of age (van Dijk et al. 2006).

While a greater understanding thus presently exists regarding the prevalence of pediatric chronic pain, far less is known about its financial impact. Not surprisingly, children and adolescents suffering from chronic pain utilize various health-care services and require prescription analgesic...
medications at a significantly greater rate than their healthy peers (Perquin et al. 2000b). The utilization of various health-care services was studied in detail in a subset of 254 Dutch children and adolescents 0–18 years of age, with chronic non-cancer pain (Perquin et al. 2001). During a 3-month period, general practitioners and specialists were consulted for pain symptoms by 31% and 14% of subjects, respectively, and in 53% of the cases a medication was used for pain. Of note, in the preceding year, 6.4% of the sample had been hospitalized due to their pain (Perquin et al. 2001).

Parents and other care providers make significant adjustments to their lives in an attempt to cope with a child or adolescent with chronic pain. These efforts have micro and macro economic consequences. Although more is becoming known about the psychological and social burden of pediatric chronic pain – and despite its considerable prevalence – there are still very few data on the costs of living with, or caring for, a child or adolescent with chronic pain (Sleed et al. 2005). A preliminary retrospective study thus examined the financial burden or cost of illness in 52 families of adolescents with chronic pain (Sleed et al. 2005). Participants were recruited from pediatric rheumatology outpatient clinics and a multidisciplinary outpatient pain management clinic in the UK. The authors used the client service receipt inventory (CSRI), a comprehensive, retrospective, parent self-report inventory of direct and indirect costs, to capture all utilized health services, lost employment, out-of-pocket expenses, and informal care given as a result of the adolescent’s pain. Based upon the CSRI, a mean total cost of £8,027/year/adolescent was reported, with a stratified £4,495/year cost for the rheumatology subgroup versus £14,160/year cost for the pain management sub-group. Extrapolating from the prevalence data reported by Perquin et al. (2000a) from the Netherlands, these authors estimated a UK prevalence of 480,000 adolescents/year with severe chronic pain. This equated to a UK societal economic burden of £3,840 million/year due to adolescent pain (Sleed et al. 2005).

### The Effect of Age and Gender on the Onset and Natural History of Pediatric Chronic Pain

The British national child development study, a prospective population-based birth cohort study, initially enrolled 17,414 infants, born between March 3 and March 9, 1958 to parents residing in Great Britain (98% of all such births). The study undertook follow-up data collection at the ages of 7, 11, 16, 23, and 33 years. As part of this longitudinal cohort study, parents were interviewed when the subjects were 7 years of age (1965) and 11 years of age (1969), at which time they were asked if their child suffered from frequent headache or migraine (then as now the most common pediatric somatic pain complaint). At 33 years of age (1991), the participants were asked about a variety of specific somatic symptoms, including severe headaches. Children with frequent headache had an increased risk in adulthood of experiencing not only headache (odds ratio of 1.87, 95% CI: 1.58–2.20) but also multiple other physical symptoms (odds ratio of 1.75, 95% CI: 1.46–2.10) and psychiatric morbidity (odds ratio of 1.41, 95% CI: 1.20–1.66) (Fearon and Hotopf 2001). A similar longitudinal British birth cohort study was undertaken from 1946 to 1989 and examined in part the natural history of abdominal pain (Hotopf et al. 1998). While children with persistent and hence chronic abdominal pain on three occasions in childhood (at ages 7, 11, and 15 years) were considerably more likely to suffer from a psychiatric disorder in adulthood (odds ratio of 2.72, 95% CI: 1.65–4.49), they were not more likely to experience recurrent abdominal pain in adulthood (odds ratio of 1.39, 95% CI: 0.83–2.36) (Hotopf et al. 1998).

The aims of a similar but more contemporary longitudinal Swedish study were to determine if headache and back pain were transitory in nature or had become chronic and to identify the predictors of such long-term pain in young adults (Brattberg 2004). A total of 335 children, 8, 11, and 14 years old, were first studied in 1989 and then followed up in 1991 and 2002. The subjects
completed questionnaires on pain, the first two times in school, the last via a postal survey. Among those subjects suffering from chronic headache or chronic back pain, 59% of the females and 39% of the males reported similar pain at 21, 24, and 27 years of age. A total of 68 (20%) of the subjects reported pain symptoms at all three study time points. Based upon a multiple logistic regression model, three significant predictors of long-term pain were identified: reported back pain in 8–14-year-olds; reported headaches once a week or more in 8–14-year-olds; and a positive response in the 10–16 year olds to the question: “Do you often feel nervous?” (odds ratio of 2.1, 95% CI: 1.3–3.4). Participants also completed the SF-36 Health Survey, a generic health-related quality-of-life instrument, at the 13-year follow-up point. When compared to normative age-group values, the SF-36 scores of those with pain symptoms were significantly lower scores across all eight physical, social, emotional, and general well-being dimensions, including pain (Brattberg 2004). A similar frequent persistence into adulthood of tension headache (33%), migraine headache (17%), and tension plus migraine headache (23%) was observed in a 20-year follow-up study of an Atlantic Canadian cohort of children (Brna et al. 2005). These collective findings support the applicability of the above-noted continuum of health versus disease between childhood, adolescence, and adulthood with chronic pain.

Gender and chronological differences in headache have been extensively reported. Pediatric migraine occurs in approximately 11% of children between the ages of 5 and 15 years and in approximately 28% of adolescents between the ages of 15 and 19 years (Hershey 2005). The incidence of migraine with aura in males is 6.6/1,000 and peaks at 5–6 years of age; in females, it is 14/1,000 and peaks at 12–13 years of age. The incidence of migraine without aura in males is 10/1,000 and peaks at 10–11 years of age; in females, it is 18/1,000 and peaks at 14–17 years of age (Stewart et al. 1991). In a population-based study of 10,169 community residents, 12–29-year olds living outside Baltimore, Maryland, 6.1% of males and 14.0% of females, when interviewed by telephone, reported four or more headaches in the preceding month. The average duration of the subjects’ most recent headache was 5.9 h for males and 8.2 h for females; 7.9% of males and 13.9% of the females missed part of a day or more of school or work because of that headache. During the month before the interview, 3.0% of males and 7.4% of females had suffered from a migraine headache (Linet et al. 1989). The majority of patients with so-called chronic daily headache or chronic nonprogressive headache appear to be female adolescents (Gladstein 2004; Koenig et al. 2002; Moore and Shevell 2004; Rothner et al. 2001; Seshia 2004).

As discussed further below, pediatric chest pain is common; however, the preponderance of published data, derived mainly from emergency department visits and cardiology clinic evaluations, have indicated a low incidence of identifiable cardiac pathology in children and adolescents with chest pain (Danduran et al. 2008). However, a recently published report examined not only the role of patient gender, race, and age, but also the association between obesity and physical capacity and chest pain in this age group (Danduran et al. 2008). This is particularly relevant given that the prevalence of children who are overweight or at risk of becoming overweight has reached epidemic proportions in the USA (Danduran et al. 2008). In a cohort of 263 patients (141 males and 122 females, mean age of 13.4 years) with a primary complaint of chest pain, who underwent an extensive cardiopulmonary evaluation at a children’s hospital in Milwaukee, Wisconsin, 28% were at risk of overweight (BMI > 85th percentile) and 16% were overweight (BMI > 95th percentile). Preteens and Hispanics in the study cohort were more likely to be overweight. While true cardiac pathology was rare in this study group, reactive airways disease was significantly more prevalent in African American patients, while a significantly decreased exercise tolerance (endurance time) was observed in Hispanics (Danduran et al. 2008).

Musculoskeletal pain in preadolescents does not appear to be a self-limiting phenomenon, and more studies appear warranted to explore its
determinants with the goal of improving the long-term outcome of such often widespread symptoms. This conclusion was based on the findings of a rigorous longitudinal study of 1,756 Finnish schoolchildren (El-Metwally et al. 2004). A baseline cross-sectional survey of the study cohort (mean age 10.8 years) identified a 32% prevalence of musculoskeletal pain. Using the same pain questionnaire, the children were reevaluated after 1 year and 4 years (at adolescence). At 1-year follow-up, 54% of the children reported persistent preadolescent musculoskeletal pain and at 4-year follow-up, 64% had musculoskeletal pain. Neck pain was the most persistent/recurrent type of musculoskeletal pain. Those with persistent preadolescent musculoskeletal pain had an approximately three times higher risk of pain recurrence (OR of 2.90 with 95% CI: 1.9–4.4). Female gender, older age (greater than 11 years), hypermobility, coexistence of psychosomatic symptoms (headache, abdominal pain, and depressive feelings), having a high disability index, and reporting multiple types of musculoskeletal pain at baseline were significant predictors of pain recurrence at adolescence (El-Metwally et al. 2004). Subsequent analyses of the Finnish cohort subgroups with neck pain and widespread pain (fibromyalgia) revealed that the co-occurrence of frequent other somatic pain symptoms and markers of psychological stress were predictive risk factors for more persistent pain (Mikkelsson et al. 2008; Stahl et al. 2008). Given that chronic neck pain and fibromyalgia in adulthood may thus originate in childhood, further studies, including preventive interventions, appear indicated (Mikkelsson et al. 2008; Stahl et al. 2008).

There are limited population-based data on the demographics and natural history of pediatric complex regional pain syndrome (CRPS). Nevertheless, valid inferences can be drawn from the published randomized controlled trials of treatment of pediatric CRPS (Berde and Lebel 2005; Dadure et al. 2005; Finniss et al. 2006; Lee et al. 2002; Low et al. 2007; Meier et al. 2006; Sherry et al. 1999), which collectively indicate that the condition tends to afflict disproportionately early adolescent females, with a strong predilection for the lower extremity, particularly the foot. Interestingly, whereas pediatric CRPS predominantly involves the lower extremity, the upper extremity is the more common location in adults (de Mos et al. 2007; Sandroni et al. 2003).

The Types and Characteristics of Patients Referred to a Pediatric Pain Medicine Program

Patients are typically referred to a dedicated, multidisciplinary pediatric pain medicine program when they fail to achieve adequate pain and symptoms relief under the care of their primary care physician or subspecialist(s). Thus any cohort of such patients is innately fraught with selection bias and has limited external generalizability. This notwithstanding, this subset of chronic pain patients is the result of a naturalistic process and worthy of discussion.

The clinical characteristics of a sequential sample of 100 pediatric chronic pain patients, who were previously under the care of another subspecialist and subsequently referred to an anesthesiology-based pediatric chronic pain medicine program have been reported (Vetter 2008). These patients presented with a variety of primary chronic pain-related disorders: abdominal pain (18%), lumbago (14%), fibromyalgia (14%), headache (12%), complex regional pain syndrome (11%), other musculoskeletal pain (11%), and chest and rib pain (6%). These patients were predominantly adolescent females (73%) with frequent coexisting clinically significant anxiety (63%) and depression (84%). The patients in this study reported significantly lower overall health-related quality-of-life scores than those previously reported by pediatric rheumatology, pediatric migraine, and pediatric cancer patients receiving care in a rheumatology, neurology, and oncology subspecialty setting, respectively (Powers et al. 2004; Varri et al. 2002a, b; Vetter 2008).

These observed clinical characteristics are consistent with those previously reported in a diverse
group of 207 children and adolescents referred over a 2-year period to a similar multidisciplinary pediatric pain medicine clinic (Chalkiadis 2001). While no formal measurement of health-related quality of life was performed, a substantial majority of these patients exhibited practical evidence of chronic pain-related disability, including school absenteeism (94%), sleep disruption (71%), and an inability to participate in a previous sport (90%) (Chalkiadis 2001). While a different set of measurement instruments were applied, these findings are also consistent with a previous report on the clinical characteristics, effect of maladaptive coping strategies, prevalence of depression, and functional disability in a clinically similar cohort of 73 children and adolescents referred to a dedicated outpatient pediatric pain medicine clinic for further evaluation and treatment (Kashikar-Zuck et al. 2001). These previous authors observed that chronic pain had a substantial adverse impact on functional ability and that coexisting depression was strongly associated with functional disability (Kashikar-Zuck et al. 2001).

Headache

A substantial amount of health care and clinical research has been focused on pediatric headache (Bandell-Hoekstra et al. 2000; Hershey et al. 2007; Kondev and Minster 2003; Lewis et al. 2002; Lipton 1997). This is not surprising in light of the very high and reportedly increasing prevalence of headache in children and adolescents (Brna and Dooley 2006; Winner 2008b). However, pediatric headache disorders, especially migraine, are subject to retrospective patient recall bias (van den Brink et al. 2001). Migraine, the most common headache disorder for which patients see a physician, still remains frequently misdiagnosed, under-diagnosed, and undertreated – this despite standardized, widely published criteria (Winner 2008a; Winner and Hershey 2007). Chronic daily headache or chronic nonprogressive headache (i.e., transformed migraine or tension headache) is increasingly recognized as a problem not only in adults but also in adolescents and older children (Gladstein 2004; Hershey et al. 2006; Koenig et al. 2002; Moore and Shevell 2004; Rothner et al. 2001; Seshia 2004).

A landmark Scandinavian prevalence study of 9,000 subjects from the early 1960s observed that by 7 years of age, 1.4% of children had migraine headaches, 2.5% had frequent non-migraine headaches, and 35% had infrequent non-migraine headaches (Bille 1962). By 15 years of age, 5.3% of this cohort had migraine headaches, 15.7% had frequent non-migraine headaches, and 54% had infrequent non-migraine headaches (Bille 1962). More recent data from the late 1990s indicate a greater overall prevalence of pediatric headache (Kondev and Minster 2003). A 2002 meta-analysis of five retrospective pediatric headaches studies published between 1977 and 1991, involving a total of 27,606 children, found the prevalence of any type of headache to range from 37% to 51% in 7-year olds, and steadily increasing to 57–82% by age 15 years (Lewis et al. 2002). In a 2001 survey of 2,358 Dutch school children between the ages of 10 and 17 years, 21% of the boys and 26% of the girls in elementary school level, and 14% of boys and 28% of girls in high school reported weekly headaches (Bandell-Hoekstra et al. 2001).

Hunfeld and colleagues (2001) compared a group of adolescents suffering from chronic headaches with a similar group of adolescents suffering from either chronic abdominal pain, back pain, or limb pain. They observed that the adolescent headache patients reported the poorest quality of life, as measured by the Quality of Life Pain-Youth Questionnaire. The headache patients also exhibited the greatest amount of school absenteeism. A subsequent study of children with chronic headaches supported the previously proposed complex relationship between pediatric headache, patient quality of life, coping strategies, and both personal and situational factors (Frare et al. 2002). Affecting between 5% and 7% of adolescents, migraine headaches are especially problematic in the 12–17-year-old age group, due to an even greater reduction in quality of life and attendant patient disability (Hershey 2005; Tkachuk et al. 2003).
The Epidemiology of Pediatric Chronic Pain

Recurrent Abdominal Pain

Pediatric recurrent abdominal pain (RAP) has been clinically recognized for at least 50 years; it was originally defined as a pain syndrome consisting of at least three episodes of abdominal pain over a period of not less than 3 months and severe enough to affect activities (Apley and Naish 1958; Weydert et al. 2003). In the interim, RAP has been extensively studied (Di Lorenzo et al. 2005), with a number of proposed etiologies, including autonomic nervous system instability (Chelimsky et al. 2001), visceral hyperalgesia (Castilloux et al. 2008; Di Lorenzo et al. 2001), intestinal motility disorders (Youssef and Di Lorenzo 2001), and stressful life events and poor coping skills (Robinson et al. 1990).

Chronic abdominal pain is a common pediatric problem encountered by primary care physicians, medical subspecialists, and surgical specialists (American Academy of Pediatrics 2005). RAP has a consistently reported prevalence of 10–20% in school-aged children and adolescents (Duarte et al. 2006). Chronic abdominal pain in children is usually functional, that is, without objective evidence of an underlying organic disorder (American Academy of Pediatrics 2005). Only 5–10% of pediatric patients with RAP in the community setting have an identifiable, underlying organic cause (Weydert et al. 2003), versus approximately 50% who do in a pediatric gastroenterology clinic setting (Croffie et al. 2000). Despite the often functional and ostensibly benign nature of RAP, this often underappreciated disorder has been associated with significant morbidity, including increased school absenteeism, frequent doctor visits, family disruption, and significant anxiety and depression – all leading to a marked reduction in health-related quality of life (Garber et al. 1990; Varni et al. 2006; Weydert et al. 2003; Youssef et al. 2006, 2008).

Beginning in 1994, three evidence-based, international consensus statements on functional gastrointestinal disorders (Rome I, Rome II, and Rome III) have been developed and promulgated (Drossman 2007; Drossman and Dumitrascu 2006). The 2006 Rome III (www.romecriteria.org) standardized criteria for making a diagnosis of a functional abdominal pain syndrome are: (1) continuous or nearly continuous abdominal pain; (2) no or only occasional relationship of pain with physiological events (e.g., eating, defecation, or menses); (3) some loss of daily functioning; (4) the pain is not feigned (e.g., malingering); (5) insufficient symptoms to meet criteria for another functional gastrointestinal disorder that would explain the pain (Drossman et al. 2006). When applied in a cohort of 368 pediatric patients with no evidence of organic disease, as compared to the Rome II criteria, the Rome III criteria classified a greater percentage of the children as having the diagnosis of irritable bowel syndrome (45%), abdominal migraine (23%), or functional abdominal pain (11%) (Baber et al. 2008). Applying the more inclusive Rome III criteria allowed for the classification of 87% of the patients with medically unexplained chronic abdominal pain (Baber et al. 2008).

Chest Pain

Chest pain is another frequent complaint in the pediatric age group. Although chest pain in children rarely is the result of a serious, organic cardiac condition, it is perceived as “heart pain” by most children and their parents and thus can be physically and emotionally distressing (Evangelista et al. 2000). The typically noncardiac etiology of pediatric chest pain is supported by a prospective study of 50 patients, 5–21 years old, referred to a pediatric cardiology clinic in Boston with a chief complaint of chest pain. All 50 patients underwent a systematic evaluation, and none were found to have a cardiac condition but instead 76% had musculoskeletal or costochondral chest pain, 12% had exercise-induced asthma, 8% had chest pain resulting from gastrointestinal causes, and 4% had chest pain resulting from psychogenic causes (Evangelista et al. 2000). Of 100 consecutive patients, 2–16 years old (54 girls, 46 boys), referred to a pediatric cardiology department in Turkey with the primary complaint of chest pain, 92 cases were concluded to be idiopathic in origin. Interestingly, of the 74 patients who underwent a
psychiatric evaluation, 55 of them (74%) had psychiatric symptoms and five required psychiatric care. Anxiety, conversion disorder, and depression were the main psychiatric symptoms (Tunaoglu et al. 1995).

Of 336 consecutive patients presenting to an urban pediatric emergency department in Ottawa, Canada with chest pain, nonspecific chest-wall pain was the most common diagnosis (28%), followed by pain referred from the upper respiratory tract or the abdomen (21%), pulmonary (19%), minor traumatic (15%), idiopathic (12%), and psychogenic (5%) (Rowe et al. 1990). A prospective analysis of 168 pediatric patients, consecutively evaluated in an emergency department in Belgium with a chief complaint of chest pain, also revealed chest-wall pain to be the most common diagnosis (64%), followed by pulmonary (13%), psychological (9%), cardiac (5%), traumatic (5%), and gastrointestinal problems (4%) (Massin et al. 2004). Chest-wall pain was also the most common diagnosis (89%) in a concurrently obtained and reported sample of 69 consecutive pediatric patients referred to the cardiology clinic at the same institution because of chest pain (Massin et al. 2004).

**Musculoskeletal Pain**

Chronic musculoskeletal pain, either idiopathic or disease-related, is also common in childhood, and the differential diagnosis of such is pain is extensive (Anthony and Schanberg 2005, 2007). The assessment and treatment of pediatric chronic musculoskeletal pain optimally involves a biopsychosocial, interdisciplinary approach, which integrates the biologic, environmental, and cognitive behavioral mechanisms underlying such chronic pain (Anthony and Schanberg 2007; Connelly and Schanberg 2006; Sen and Christie 2006). Of note, as many as 25% of new patients present to pediatric rheumatology clinics with idiopathic musculoskeletal chronic pain, including due to juvenile primary fibromyalgia syndrome – with its often markedly adverse functional and psychosocial impact (Anthony and Schanberg 2001; Connelly and Schanberg 2006; Sen and Christie 2006). From the 1950s through the early 1990s, the reported point prevalence of musculoskeletal pain in North American and European school-age children ranged from 7% to 15% (de Inocencio 1998; Goodman and McGrath 1991). However, figures as high as 32–40% have more recently been reported, indicating either an overall increasing prevalence or the recognition of juvenile primary fibromyalgia syndrome (or both).

Despite potential selection bias, the prevalence of musculoskeletal pain was determined in a prospective evaluation of 1,000 consecutive clinic visits to an urban general pediatric clinic in Madrid, Spain (de Inocencio 1998). In this convenience sample of 3–14-year olds (mean age of 9.7 years), 6.1% of clinic visits were related to musculoskeletal pain, in keeping with older reports. The presenting complaints included knee arthralgia (33%), other large peripheral joint arthralgias (28%), soft tissue pain (18%), heel pain (8%), hip pain (6%), and back pain (6%). The musculoskeletal pain symptoms were attributed to trauma in 30%, overuse syndromes (e.g., chondromalacia patellae, mechanical plantar fasciitis, overuse muscle pain) in 28%, and skeletal growth variants (e.g., Osgood–Schlatter syndrome, hypermobility, Sever’s disease) in 18% of patients (de Inocencio 1998).

The prevalence and persistence of self-reported musculoskeletal pain symptoms was determined using with a structured pain questionnaire in 1756 Finnish third-grade and fifth-grade schoolchildren. In this comprehensive, population-based survey, musculoskeletal pain occurring at least once a week was reported by 32% of the study subjects (Mikkelsson et al. 1997). A cross-sectional study was also performed on an entire private school population of adolescents in the city of São Paulo, Brazil (Zapata et al. 2006a). In this cohort with a male to female sex ratio of 1.1 to 1 and a mean age of 14.2 years, musculoskeletal pain was reported by 40% of the 833 surveyed students. Interestingly, despite frequent computer and video game use in this adolescent cohort, these activities were not associated with the presence of a musculoskeletal pain syndrome (Zapata et al. 2006b). Back pain was instead the
most frequently self-reported location (23%) in this Brazilian study (Zapata et al. 2006a). This is consistent with both a previous Icelandic study, in which 21% of a random national sample of 2,173 preteens and teenagers reported recurrent (weekly or more often) back pain (Kristjansdottir and Rhee 2002) and a Danish study, in which recurrent or continuous LBP of a moderate to severe nature was reported by 19% of 1,389 13–16-year-old schoolchildren (Harreby et al. 1999).

**Complex Regional Pain Syndrome**

CRPS is a neuropathic pain disorder that afflicts all ages (Grabow et al. 2004; Low et al. 2007; Rho et al. 2002; Wilder 2006). Despite over 20 years of focused research and a well-evolved treatment paradigm, the exact mechanism of CRPS remains elusive; however, peripheral sensitization of A-delta and C afferent fibers to noxious stimuli appears to be the basis for CRPS-associated hyperalgesia (Stanton-Hicks 2000, 2003). While it has been posited that enough is now known about its pathophysiology to recommend quantitative sensory and autonomic nervous system testing (Stanton-Hicks 2003), there is no specific diagnostic laboratory test for CRPS, requiring clinicians to rely predominantly upon signs and symptoms. Of note, the presentation, treatment, and prognosis of CRPS can be quite variable in and between pediatric and adult patients, likely related in part to differences in patient populations, referral patterns, and medical practice (Berde and Lebel 2005; Low et al. 2007; Matsui et al. 2000; Sherry et al. 1999).

There is a paucity of large-scale epidemiologic data on pediatric neuropathic pain, including CRPS. However, in recent years there has been an increased reporting of CRPS in children and adolescents (Finniss et al. 2006). Therefore, potentially valid inferences can be drawn from two adult population-based studies of CRPS (de Mos et al. 2007; Sandroni et al. 2003). Applying the International Association for the Study of Pain (IASP) criteria for CRPS, 74 cases of CRPS I were identified in a population of 106,470, resulting in an incidence rate of 5.46 per 100,000 person years at risk, and a low period prevalence of 20.57 per 100,000. Interestingly, 74% of these Minnesota patients experienced symptom resolution, often spontaneously, lending the authors to suggest that invasive treatment of CRPS may not be warranted in the majority of adult cases of CRPS I (Sandroni et al. 2003).

As part of the Integrated Primary Care Information project, using a comprehensive search term algorithm, potential CRPS cases were retrospectively identified from the electronic medical records of 600,000 adult patients who received health care throughout the Netherlands from 1996 to 2005 (de Mos et al. 2007). These potential cases were then validated by direct electronic medical record review, supplemented with original specialist letters and information from an inquiry of general practitioners. The estimated overall incidence rate of CRPS in this Dutch cohort was 26.2 per 100,000 person years (95% CI: 23.0–29.7). This observed incidence rate of CRPS in the Netherlands is more than four times higher than the incidence rate observed in the above population-based study, performed earlier in Olmsted County, Minnesota (de Mos et al. 2007).

**Conclusions and Health Policy Implications**

Chronic pain is a universal and thus multicultural experience that represents a major worldwide threat to health-related quality of life. A disease in its own right, the global burden of pain is substantial (Brennan 2007; Cousins et al. 2004; Lipman 2005). Despite the existence of cost-effective treatment options, pain control has been relatively neglected by national governmental agencies and international nongovernmental organizations (Brennan et al. 2007; Cousins et al. 2004; Lipman 2005). Despite all of the work to
date, more information is needed about the prevalence, manifestations, and long-term effects of chronic pain in children (Bhatia et al. 2008). There is likewise a need for increased training and resources for primary care physicians and pain clinicians who manage chronic pain in the pediatric age group (Bhatia et al. 2008).

A major gap presently exists between an increasingly sophisticated understanding of the pathophysiology of pain and the widespread inadequacy of its treatment (Brennan et al. 2007). This gap is most apparent and problematic in the poorest and most socially dysfunctional developing nations, which are contending with widespread poverty, oppression and violence, and war and its aftermath (Brennan et al. 2007). Consequently, in October 2004, the World Health Organization (WHO), the International Association for the Study of Pain (IASP), and the European Federation of the IASP Chapters (EFIC) jointly declared that such widespread, inadequately treated chronic pain must not be tolerated and furthermore that the relief of pain should be a universal human right (Brennan and Cousins 2004; Cousins et al. 2004; Lipman 2005). The two ultimate aims of this global pain initiative were to inform policy makers about the personal burden and the economic costs of chronic pain and to educate physicians and allied health-care professionals about pain assessment and management so as to promote higher standards of care worldwide (Lipman 2005). More recently, similar attention has been focused on effective palliative care being a universal, international human right (Brennan 2007).

Acute, chronic, and cancer pain collectively represent the often unreported and hence silent dimension of many of the worldwide causes of both adult and pediatric morbidity and mortality (Brennan et al. 2007). Specifically, it is generally under-recognized that the pain and other symptom burden experienced by adult and pediatric patients with HIV/AIDS are as complex and widespread as in patients with cancer (Lipman 2005). Greater attention therefore needs to be focused on the pain experience in the developing world, including in the pediatric population.

References


Time to Pain: The Impact and Prevalence of Chronic Pain in Children and Adolescents

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