Vol. 5 No. 1 January 2001

Pediatric Pain Letter

Abstracts and Commentaries on Pain in Infants, Children and Adolescents

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Editorial note

This edition of the Pediatric Pain Letter has commentaries on two related issues, intubation of newborns by non-anesthetists and management of painful procedures. These might be regarded as merely different points on the same continuum, but poorly managed intubation can have immediate and dramatic effects on oxygenation, and consequently on cardiovascular parameters and intracranial pressure. Management of neonatal intubation must thus involve more complex techniques and skills, and requires attention beyond the level of pain control. Other painful procedures can benefit from a combined approach that emphasizes non-pharmacological as well as pharmacological techniques. As one might expect, the outstanding issues are those of education and training, rather than pharmacology.

Commentary

On intubation

The need to avoid and treat pain in neonates has become widely accepted in the past decade. However, surgical procedures such as circumcision are still performed with inadequate analgesia or anesthesia. The question of circumcision has frequently been debated in the international forum. Endotracheal intubation in the neonate is another painful and traumatic experience but it has received only minor attention.

"There is every reason to focus on establishing an effective and safe regime for intubation in neonates..."

When intubating adults, the use of analgesics and anesthetics, and often muscle relaxants, is standard clinical practice. When intubating neonates there does not seem to be an established clinical standard. Intubation while awake could be considered a major trauma, not only in the adult but also in the neonate. Apart from the obvious short-term consequences, recent studies have shown that early painful experiences can have long-term consequences (Taddio et al., 1997; Taylor et al., 2000).

In 1984, Kelly and co-workers concluded that infants receiving no drugs, or anticholinergics with or without muscle relaxants, all reacted with a significant decrease in transcutaneous PO_2 as well as a significant increase in blood pressure and intracranial pressure. In a more recent paper, Pokela and Koivisto (1994) compared the physiological changes during nasotracheal intubation. Twenty neonates were allocated to two groups, one group receiving pethidine (meperidine) (1 mg/kg) and the other alfentanil (20 mg/kg) and suxamethonium (1.5 mg/kg). Both groups were given glycopyrrolate. Results indicated that hypoxemia occurred in all infants in the pethidine

group and in 7 of 10 in the alfentanil group. In the former group, the hypoxic period was significantly longer. It is also noteworthy that successful intubation at the first attempt was documented in only 3 of 10 cases in the pethidine group and that it took twice as long to complete intubation. Moreover, 8 of 10 infants struggled violently during intubation in the pethidine group. Pokela and Koivisto (1994) concluded that:

1. Newborns suffer from hypoxemia during awake intubation.
2. Newborns need adequate medication before elective intubation.
3. The ideal medication and dosage remain to be defined.

"...placebo-controlled studies will be considered an ethical impossibility in the near future."

To determine the effects of premedication before intubation, Bhutada et al. (2000) allocated 30 neonates to receive thiopental or placebo. They found that heart rate and blood pressure were maintained nearer baseline in the thiopental group. The total time needed to complete the intubation was significantly longer in the placebo group. The authors concluded that intubation, following an induction dose of an anesthetic agent, seems to be not only easier but also a more humane strategy which saves the neonate needless distress. This reviewer agrees wholeheartedly with this statement and hopes that placebo-controlled studies will be considered an ethical impossibility in the near future.

In a national survey, Whyte et al. (2000) aimed to determine the use of medication before intubation in neonatal units in the UK. They found that most units did not sedate the infants before intubation and that only a few had written guidelines. This survey could very well be representative of a global perspective.

Not only is the necessity of an adequate intubation strategy essential from a humane viewpoint but probably also vital in order to avoid short- and long-term consequences for the neonate. There is every reason to focus on establishing an effective and safe regime for intubation in neonates and no reason not to.

Björn Larsson, M.D., Ph.D.
Department of Surgical Sciences
Section for Anesthesiology and Intensive Care
Karolinska Institutet
Stockholm, Sweden

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Taylor A, Fisk NM, Glover V. Mode of delivery and subsequent stress response. *Lancet* 2000;355(9198):120.

Abstracts

Bhutada A, Sahni R, Rastogi S, Wung JT. Randomised controlled trial of thiopental for intubation in neonates. *Archives of Diseases in Childhood Fetal and Neonatal Edition* 2000;82(1):F34-F37.

Previously abstracted in the *Pediatric Pain Letter*, Vol. 4, No. 3; p. 32. **www.dal.ca/~pedpain/pplet/v4n3c.PDF**

Kelly MA, Finer NN. Nasotracheal intubation in the neonate: physiologic responses and effects of atropine and pancuronium. *Journal of Pediatrics* 1984; 105(2):303-309.

Objective. To determine the physiological responses of neonates to intubation and the mitigating effects of atropine alone or atropine and pancuronium on these responses when administered prior to intubation.
Design. Non-blinded, prospective, randomized trial
Setting. Neonatal intensive care unit, Canada.
Participants. Neonates (n=30; weight range 580-3450 g; gestational age range 25-40 weeks) requiring nasotracheal intubation, due to immaturity, apnea, progressive respiratory distress or intractable hypoxia, were randomized into 1 of 3 groups (n=10 for each group; no differences between groups for gestational age, weight, Apgar scores, age at time of study and baseline arterial blood gas levels).
Intervention. Group 1 (control) received no pre-treatment, group 2 received atropine 3 minutes prior to intubation and group 3 received atropine 3 minutes prior to intubation followed by pancuronium 2 minutes prior to intubation.
Main Outcome Measures. Baseline levels for blood pressure (BP), transcutaneous PO_2 and intracranial pressure (ICP) were compared with post-intubation levels for all 3 groups. For heart rate (HR), levels immediately prior to intubation were compared with post-intubation levels.
Results. Decrease in mean transcutaneous PO_2 ($p<0.02$) was associated with increase in mean BP ($p<0.01$) and ICP ($p<0.01$) in all 3 groups. Decreases in HR were found only in group 2 and group 1 (p's<0.01). Group 1 experienced the greatest decrease in HR ($p=0.035$) of the 3 groups. Group 3 infants experienced smaller increases

in ICP ($p<0.05$).
Conclusions. Nasotracheal intubation in neonates is associated with increases in BP and ICP as well as decreases in HR and transcutaneous PO_2. These physiological responses are likely associated with reflex cardiovascular responses (bradycardia, hypertension) and nonreflex responses (struggling, mechanical effects). Further studies are recommended.

Pokela ML, Koivisto M. Physiological changes, plasma beta-endorphin and cortisol responses to tracheal intubation in neonates. *Acta Paediatrica* 1994;83(2):151-156.

Objective. To assess physiological changes, plasma beta-endorphin levels, serum cortisol, blood glucose and clinical responses associated with elective endotracheal intubation in neonates.
Design. Non-blinded, randomized trial.
Setting. Neonatal intensive care unit, Finland.
Participants. Newborn infants requiring elective tracheal intubation, randomized to receive either pethedine (PET group; n=10; mean gestational age=33 weeks; mean birth weight=1955 g) or alfentanil plus suxamethonium (ALF group; n=10, mean gestational age=33 weeks; mean birth weight=1715 g) prior to nasotracheal intubation.
Main Outcome Measures. Heart rate, respiratory rate, transcutaneous PO_2 and/or O_2 saturation, mean blood pressure (BP) and general activity were continuously monitored from 10 minutes pre-intubation to 1 hour post-intubation. Arterial blood was sampled for serum cortisol, blood glucose, blood-gas analysis and plasma beta-endorphin prior to and at least 1 hour following intubation.
Results. There was a clinically significant decrease in oxygenation during intubation in all PET group patients and 7 ALF group patients, with the duration of hypoxemia lasting longer in the PET group ($p=0.036$). Mean duration of intubation was shorter for the ALF group (60 vs. 120 seconds; $p=0.012$). Plasma beta-endorphin, cortisol and blood glucose did not differ between groups either prior to or following intubation, however plasma beta-endorphin were significantly higher in those patients undergoing initial intubation (as opposed to re-intubation) ($p=0.018$). Bradycardia occurred in 1 infant in each group and was associated with simultaneous decreases in oxygenation. Differences in BP between the 2 groups were not significant.
Conclusions. Physiological stress is associated with endotracheal intubation in newborn infants, particularly in the form of hypoxemia. Adequate premedication is a necessity. Although the combination of glycopyrrolate, alfentanil and suxamethonium used in the present study appears to work well, other combinations should be investigated.

Taddio A, Katz J, IIersich AL, Koren G. Effect of neonatal circumcision on pain response during subsequent routine vaccination. *Lancet* 1997;349:599-603.

Previously abstracted in the Pediatric Pain Letter, Vol. 2, No. 1; p. 5. **www.dal.ca/~pedpain/pplet/v2n1c.PDF**

Whyte S, Birrell G, Wyllie J. Premedication before intubation in UK neonatal units. *Archives of Diseases in Childhood Fetal and Neonatal Edition* 2000;82(1): F38-F41.

Objective. To determine what type and to what extent premedication is used before intubation in neonatal units in the United Kingdom.
Design. Telephone survey.
Setting. Neonatal units, United Kingdom.
Participants. Neonatal units (98% of those known) were subdivided into those that routinely intubated and ventilated neonates (routine group – 190 units) and those who transferred intubated and ventilated neonates (transfer group – 49 units).
Main Outcome Measures. A structured telephone survey was used to determine: whether the unit routinely used sedation in elective and/or emergency intubation; if so, whether the unit had a written policy regarding intubation and sedation; what sedatives and dosages were used by the units.
Results. Of the units surveyed, 88 (37%) reported using some form of sedation before intubation and 34 (14%) had written policies addressing this issue. More units in the routine group used sedation (41%) than in the transfer group (22%). Morphine was the most commonly reported sedative (58/88 units using sedation), although reported dosages varied greatly (5-1000 mcg/kg). Other opioids and benzodiazepines were reported less frequently. Muscle relaxants were also used by 19 of the 88 units reporting sedation.
Conclusions. Despite evidence of physiological and practical benefits of sedation for neonatal intubation, this procedure in not routinely practiced in most United Kingdom neonatal units. Moreover, when sedation is used, the drug choice and dosage vary greatly and few units have written policies addressing this issue.

Commentary

Repeated Invasive Medical Procedures

Children who undergo treatment for childhood cancer must endure repeated invasive medical procedures to monitor and treat their disease. The experience of such procedures is distressing to children and their parents and many empirical efforts have been dedicated to the accurate assessment and alleviation of this distress.

Over the past several years, increasing attention has been paid to the pharmacologic management of procedural pain. The goals of sedation in the pediatric patient are to guard the patient's safety and welfare, to minimize physical discomfort or pain, to minimize negative psychologic responses to treatment by providing analgesia and to maximize the potential for amnesia, to control behaviour, and to return the patient to a state in which safe discharge is possible (American Academy of Pediatrics Committee on Drugs, 1992).

Propofol is a very short-acting hypnotic that has become the preferred agent for induction and maintenance of general anesthesia. Research efforts examining the use of propofol have provided evidence for its safe and effective use for children undergoing invasive medical procedures (e.g., Hannallah et al., 1991). Other commonly used agents include opioids (morphine, fentanyl), benzodiazepines (diazepam, lorazepam, midazolam), anesthetic interventions (ketamine) and local anesthetics (lidocaine, EMLA). The efficacy of these pharmacologic interventions, as well as combinations of these agents, such as midazolam and opioid, has also been established (Parker et al., 1997; Schechter et al., 1995; Sievers et al., 1991).

"...staff, as well as parents, may be taught cognitive behaviour therapy..."

Over the last two decades numerous studies have demonstrated the efficacy of cognitive behavioural therapy (CBT) interventions for decreasing anxiety and distress related to procedural pain in children with cancer (e.g., Blount et al., 1994; Jay et al., 1995). Techniques such as systematic desensitization, psychoeducation, positive incentive techniques, distraction (including hypnosis) and relaxation strategies are used to provide children with a specific set of responses and behaviours that facilitate mastery over a stressful situation, ideally in a manner consistent with their basic coping strategies. A variety of staff, as well as parents, may be taught these techniques in a systematic way and then use them successfully in clinical settings.

Studies that examined the effectiveness of CBT versus pharmacologic interventions in reducing distress have not identified significant differences between the two approaches (Jay et al., 1995). Such findings provide evidence that both pharmacologic and psychologic interventions are viable treatment approaches in the pediatric oncology setting.

Clearly one does not need to choose pharmacologic versus psychologic strategies. Instead, the goal is to examine the relationship among self-report, behavioural indicators and physiologic responses to pain in an attempt to match individual patients to specific pain treatment protocols that involve an optimal combination of pharmacologic and psychological interventions. The result would be an intervention tailored to the needs and interests of the individual patient that will maximally reduce pain and distress while minimally introducing risk.

"...research is aimed at developing clinical algorithms..."

While it would be ideal to identify the optimal combination of psychologic and pharmacologic strategies for each individual child, the reality is that this combination cannot be identified with absolute certainty. Ongoing research is aimed at developing clinical algorithms that will more specifically guide the clinician in choices of pain treatment regimens that are clinically efficacious and cost effective.

In the interim, professionals conducting invasive procedures in pediatric cancer patients must rely on clinical judgement to identify the interventions that are most appropriate for an individual child. This entails an assessment of the array of developmental, individual and environmental factors that might influence pain or distress associated with a painful procedure. Data obtained from such assessments should be used initially to choose the optimal technique to alleviate distress and subsequently to assess the effectiveness of the intervention. Eventually, through empirical efforts aimed at matching specific patient needs to defined treatment protocols, it is hoped that procedural distress will be at absolutely minimal levels with as little risk of complications as possible.

Larissa Labay, M.A., Psy.M.
Tomorrows Children's Institute
Hackensack University Medical Centre
Hackensack, NJ

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Jay S, Elliott CH, Fitzgibbons I, Woody P, Siegel S. A comparative study of cognitive behaviour therapy versus general anesthesia for painful medical procedures in children. *Pain* 1995;62:3-9.

Abstracts

Blount RL, Powers SW, Cotter MW, Swan S, Free K. Making the system work: training pediatric oncology patients to cope and their parents to coach them during BMA/LP procedures. *Behavior Modification* 1994; 18(1):6-31.

Previously abstracted in the *Pediatric Pain Letter*, Vol. 1, No. 5; p. 58. **www.dal.ca/~pedpain/pplet/v1n5c.PDF**

Parker RI, Mahan RA, Guigliano D, Parker MM. Efficacy and safety of intravenous midazolam and ketamine as sedation for therapeutic and diagnostic procedures in children. *Pediatrics* 1997;99(3):427-431.

Previously abstracted in the *Pediatric Pain Letter*, Vol. 1, No. 3; p. 34. **www.dal.ca/~pedpain/pplet/v1n3c.PDF**

Sandler ES, Weyman C, Conner K, Reilly K, Dickson N, Luzins J, McGorray S. Midazolam versus fentanyl as premedication for painful procedures in children with cancer. *Pediatrics* 1992;89:631-634.

Objective. To compare the safety and efficacy of midazolam with fentanyl in premedicating pediatric oncology patients for painful procedures.
Design. Randomized, double-blind, crossover study.
Setting. Pediatric oncology clinic, USA.
Participants. Pediatric oncology patients diagnosed with either leukemia or lymphoma requiring lumbar puncture (LP) or bone marrow aspiration (BMA) were eligible for participation (n=25; 13 female; mean age=10.04 years, SD=5.01).
Intervention. Patients were randomly assigned to initially receive midazolam (n=12; dose=0.2 mg/kg) or fentanyl (n=13; dose=4 g/kg) diluted in 10 ml of saline. Drug was administered intravenously over a 10 minute period and titrated to produce sedation or slurring of speech. For the second procedure the child received the alternate drug. Local anesthetic was used for all procedures.
Main Outcome Measures. Parent questionnaires assessed previous experiences with, and adverse behaviours prior to procedures as well as concerns about the procedure or sedation. Parents and patients completed a visual analogue scale (VAS) prior to and following procedures. Behaviours were monitored using the Observational Scale of Behavioural Distress (OSBD). Telephone interviews were conducted 24 hours following the procedure to determine drug effectiveness and side effects.
Results. All parents and patients preferred study drugs to previous sedation ($p<.001$) and their drug of choice was predominantly midazolam (72% vs. 28% for fentanyl; $p<0.03$); preference was not a function of order in which drugs were given, procedure type or other demographic variables. More procedures using midazolam were followed by complete amnesia (91% vs. 31%; $p<0.03$). Behavioural variables and VAS improved from previous experiences, but not significantly. Follow-up questionnaires with parents indicated that the drug of choice was helpful, improved their child's tolerance and ought to be recommended.
Conclusions. Premedication can be used in an outpatient setting and should be routinely administered for painful pediatric oncology procedures. Midazolam was preferred due to its amnesic effect.

Schechter NL, Weisman SJ, Rosenblum M, Bernstein B, Conard P-L. The use of oral transmucosal fentanyl citrate for painful procedures in children. *Pediatrics* 1995;95(3):335-339.

Objective. To investigate the safety and efficacy of oral transmucosal fentanyl (OTF) in providing sedation and analgesia for painful diagnostic procedures.
Design. Randomized, placebo-controlled, clinical trial.
Setting. University hospital pediatric hematology/ oncology division, USA.
Participants. Children (n=48) referred for BMA or LP were sorted into younger (YC) and older (OC) groups and randomly assigned to receive OTF (YC: n=14; mean age=5.6 years, SD=1.5; 11 males; 11 underwent BMA, 2 had an LP and 1 had both, OC: n=10; mean age=11.2 years, SD=2.2; 5 males; 7 underwent BMA, 1 had an LP and 2 had both) or placebo (YC: n=15; mean age=4.8 years, SD=1.4; 9 males; 7 underwent BMA, 7 had an LP and 1 had both, OC: n=9; mean age=10.8 years, SD=2.5; 6 males; 4 underwent BMA, 3 had an LP and 2 had both). For YC 21/29 children suffered from acutelymphoblastic

leukemia. For OC 13/19 children suffered from either acutelymphoblastic leukemia or thrombocytopenia.
Intervention. Children were given an OTF (15-20 µg/kg) or placebo lollipop and instructed to place it between their gum and cheek until it dissolved (left in the mouth 20 minutes or less).
Main Outcome Measures. Vital signs and oxygen saturation were evaluated every 10 minutes during intervention and until the procedure was completed. VAS (10 point) pain ratings for the children's pain during the procedure were recorded immediately after the procedure by an oncology nurse and 30 minutes later by the parents and children 8-18 years old. Children 3-7 years old completed the Oucher.
Results. Children who received OTF reported less pain than placebo in both the YC and OC groups (p's≤0.013) and parental and nurse reported pain level was also lower (p's≤0.005). Treatment with OTF reduced pain, independent of procedure, when nurse (p=0.002) or parent (p=0.014) rated pain was the outcome assessed. Procedure had a independent effect associated with nurse ratings (p=0.031). The OTF group were more likely to experience itching and vomiting than the placebo group (p's≤0.003). Mean respiratory rate compared to baseline (p<0.001; none required intervention), mean oxygen saturation (98% vs. 99%; p<0.002) and mean systolic (at 10, 40, 50 and 60 minutes) and diastolic (at 40 minutes) blood pressure (p's<0.05) were lower for the OTF group, however, none of these differences were clinically significant. On follow-up one child required antiemetic therapy at home.
Conclusions. These results indicate that OTF is effective for relieving procedural pain in children, however, the frequency of vomiting may limit its usefulness in a clinical setting.

Sievers TD, Yee JD, Foley ME, Blanding PJ, Berde CB. Midazolam for conscious sedation during pediatric oncology procedures: safety and recovery parameters. *Pediatrics* 1991;88:1172-1179.

Objective. Evaluate the effectiveness of midazolam in conscious sedation, without the presence of an anesthesiologist, during bone marrow aspiration and/or lumbar puncture (BMA/LP) in a pediatric oncology patients.
Design. Non-blinded, non-placebo controlled trial.
Setting. Outpatient oncology clinic, USA.
Participants. Pediatric oncology patients (n=24; 14 male; age range 1.5 – 15.5 years) undergoing BMA/LP were studied. Selection of participants was at the discretion of the oncologist. Over 2 years 70 procedures were examined.
Intervention. At the discretion of the oncologist 1 of 2 protocols was used. One involved doses of midazolam (0.05 mg/kg, iv) prior to the BMA/LP and the other used an opioid (morphine sulfate 0.06 mg/kg or fentanyl 0.6 g/kg) in addition to midazolam. Additional doses (midazolam or opioid) were administered as required to a maximum of 3.
Main Outcome Measures. Vital signs were monitored (pulse, blood pressure, respiratory rate and oxygen saturation). Behavioural assessment was conducted using the Observational Scale of Behavioural Distress (OBSD) upon arrival at the clinic and upon entry to the treatment area. Both vital signs and OSBD were assessed at 15, 30, 45 and 60 minutes after the last administration of midazolam. The need for restraint during the procedure was recorded. Recall of events was assessed by means of a series of questions about events during the procedure. Recovery scores were calculated by assessment of activity, respiration, circulation, consciousness, colour and ambulation. After discharge parents kept track of drowsiness, lethargy, headache, nausea, vomiting, coughing, hiccoughing or swelling/redness at the injection site.
Results. Of the 70 procedures, 29 used midazolam only and 41 had an additional opioid. Total midazolam administration did not differ among procedures with and without opioid. Lowest respiratory rate was not correlated with total midazolam dose. Desaturation was noted in 9 procedures (4 with opioid) and 10 were asked to take deeper breaths. In the latter group midazolam dose was higher than those not asked to breath deeper (p=0.0011). Heart rate and blood pressure were stable throughout the procedure (systolic pressure dropped after midazolam (p=0.001)). OSBD scores were elevated upon entry into the treatment room. More restraint was required for younger than older participants (p<0.0001) but was not related to midazolam dose (45% of patients required restraint). Recovery scores were positively related to midazolam dose at 15 and 30 minutes (p's<0.05). The level of memory for events during surgery was not related to midazolam dose.
Conclusions. Midazolam may be an effective agent to produce conscious sedation although more than half of patients required restraint. Use of midazolam requires constant observation and monitoring of pulse oximetry is essential. Using midazolam may help reduce recovery time.

Recent Articles

Bener A, Uduman SA, Qassimi EM, Khalaily G, Sztriha L, Kilpelainen H, Obineche E. Genetic and environmental factors associated with migraine in schoolchildren. *Headache* 2000;40(2):152-157.

Objective. To determine the prevalence of migraine among schoolchildren and to investigate its association with sociodemographic, genetic and environmental factors.
Design. Cross-sectional, population survey.
Setting. Twelve primary schools in 3 cities of the United Arab Emirates.
Participants. Using a multistage stratified cluster sampling design, 1400 schoolchildren were recruited and usable data was collected from 1159 (594 males; age range 6-14 years).
Main Outcome Measures. Screening questionnaire based on the IHS diagnostic criteria (Arabic translation that was reverse-translated to English to insure accuracy and validated by the interview). A comprehensive standardised clinical interview of children and parents and physical and neurological examinations of children were conducted by a pediatrician, general practitioner and nurse.
Results. Prevalence rates were 36.9% for headache and 13.7% (76 male; mean age=10.3 years, SD=2.8; 83 female; mean age=9.9 years, SD=2.5) for migraine. Prevalence of headache was highest among 13 year olds (58%). Of children with migraine, 12.6% were without aura and 8.2% were with aura (***editorial note:*** there is no information on the other 126 (79.2%) children with migraine). For those with migraine: the most commonly reported migraine symptoms were aggravation by physical activity (39.5% of boys; 54.2% of girls) and positive family history of migraine (40.8% of boys; 51.8% of girls); the most commonly reported factors related to academic schedule were examination time (46.5%) and too much homework (40.3%); and the most commonly reported environmental factors were playing at the computer (45.9%), loud noise (41.6%) and hot climate (37.1%). Relatives with migraine were mother (17.6%), father (6.9%), maternal aunt (3.8%), paternal uncle (3.1%) and sister (3.1%). The most commonly reported illnesses associated with headaches were infectious (41.6% of children with migraine, 30.1% of those without) and abnormal refractive status of the eye (25.8% of children with migraine, 23.8% of those without). Logistic regression analysis showed that being unhappy at school or home, beginning the academic year, family history of migraine, more than 4 hours/day watching television, strong light, playing the computer and eating citrus fruit were the only predictors of migraine after adjusting for age and sex (p's<0.05).
Conclusions. Prevalence rates for headache and migraine are similar to those reported for other countries. Headache and migraine may be influenced by social, familial, environmental and psychological factors. Further research is required to determine the role of cultural factors specific to the United Arab Emirates such as attitudes towards education, gender differences in personal freedom and high incidence of consanguineous marriage.

Coté CJ, Notterman DA, Karl HW, Weinberg JA, McCloskey C. Adverse sedation events in pediatrics: a critical incident analysis of contributing factors. *Pediatrics* 2000;105(4):805-814.

***Objective*.** To investigate factors contributing to adverse sedation events in children undergoing medical procedures in hospital and non-hospital-based settings.
***Design*.** Chart audit, critical incident analysis.
Setting. Food and Drug Administration (FDA) Spontaneous Reporting System, USA.
***Participants*.** Adverse drug reports (n=629) from 1969 to 1996, collected from patients ≤20 years of age. Exclusion criteria were insufficient detail, non-US reports, alphaprodine cases, duplicate cases and general anesthesia cases; 118 cases were eligible for analysis.
***Main Outcome Measures*.** Four reviewers from different specialties assessed each incident across several variables (e.g. demographics, procedure, venue of sedation administration and adverse reaction, specialty of individual administering sedation, monitoring used, underlying medical conditions) and reached consensus on one of four outcomes (no harm, prolonged hospitalization without injury, permanent neurological injury or death).
***Results*.** Reviewers reached consensus on 95 cases (37 male, 33 female and 25 had no gender description; mean age=5.7 years, SD=5.5; mean weight=21.9 kg, SD=17.3; outcomes were 51 deaths, 9 permanent neurological injury, 21 prolonged hospitalization without injury, 14 no harm). Patients who received care in non-hospital-based settings were older (p=0.015), weighed more (p=0.021) and were healthier (p=0.001), but were still more likely to have a cardiac arrest as a result of sedation (p=0.001). Common causes of adverse events were: drug-related events, inadequate monitoring, inadequate resuscitation and inadequate medical evaluation. Inadequate resuscitation and the outcomes of death and permanent neurological injury occurred more frequently in non-hospital-based settings than in hospitals (p's=0.001).

Pulse oximetry monitoring was associated with more successful outcomes in hospitals (p=0.001), but not in non-hospital settings where 4 out of 5 who were monitored still suffered adverse outcomes (p<0.01).
Conclusions. Successful outcomes were more common in hospital than non-hospital settings. Inadequate and inconsistent monitoring contributed to poorer outcomes. Authors recommend: (1) uniform, specialty-independent guidelines for monitoring children during sedation, (2) availability of age-appropriate equipment and medications for resuscitation regardless of venue, (3) training in airway assessment and monitoring and resuscitation of infants and children for all health care providers who sedate children.

McGrath PA, Speechley KN, Seifert CE, Biehn JT, Cairney AEL, Gorodzinsky FP, Dickie GL, McCusker PJ, Morrissy JR. A survey of children's acute, recurrent, and chronic pain: validation of the Pain Experience Interview. *Pain* 2000;87(1):59-73.

Objective. To validate the Pain Experience Interview using the discriminant validation procedure of group differences.
Design. Survey.
Setting. Outpatient health clinic, Canada.
Participants. Children (n=187) recruited consecutively from five different health groups (arthritis, cancer, enuresis, recurrent headaches, and healthy) stratified into four age groups (5-7, 8-10, 11-13 and 14-16 years old).
Main Outcome Measures. Children were administered the Pain Experience Interview by a trained research assistant. Parents also completed a brief survey about their child's experience with the pains listed in the child's interview.
Results. The Pain Experience Interview discriminated among children by health group as predicted. Children in the headache group reported more headaches within the previous month than children in the other health groups (p=0.004). Children in the cancer group experienced more treatment care items than the other health groups (p=0.0001). The headache group had the highest proportion of definite recurrent pain syndrome cases (95%), while the other health groups ranged from 16% for the enuresis group to 30% for the arthritis group. The arthritis group had the highest proportion of definite chronic pain cases (78%); the other health groups ranged from 2.2% for the enuresis group to 12.5% for the cancer group. In comparison with the other groups: children in the cancer group reported more treatment-related pain as their strongest pain (p<0.001); children in the healthy comparison group reported more types of trauma/injury as their strongest pain (p<0.001); children in the headache group reported more headaches as their strongest pain (p<0.001). The majority of children accurately identified their health condition. There was substantial agreement between parents and children (kappa coefficients for the three types of recurrent pain syndrome, for the presence of any chronic pain and for the 7 chronic health conditions ranged from 0.68 to 1.00).
Conclusion. The Pain Experience Interview is a valid screening instrument for acute, recurrent and chronic pain for children, at or above an approximate cognitive age of 5 years old. The Interview can also provide information about the lifetime and point prevalence of various pains, as well as the intensity, duration and frequency of children's pains.

Murray CS, Cohen A, Perkins T, Davidson JE, Sills JA. Morbidity in reflex sympathetic dystrophy. *Archives of Diseases in Children* 2000;82(3):231-233.

Objective. To report and characterize the clinical course of reflex sympathetic dystrophy in children, and determine their responses to treatment after correct diagnosis, with a view to stress the importance of early recognition of the disease in general pediatric practice.
Design. Longitudinal study with initial case review and 3-6 month follow-up.
Participants. Children (n=46; 35 female; age range 8-15 years, median=12.0 years) diagnosed with reflex sympathetic dystrophy and presenting with an affected upper and/or lower limb.
Setting. Paediatric rheumatology clinic, United Kingdom.
Main outcome measures. Descriptions and basic statistics of the patient's case history from the time of presentation in the clinic to diagnosis, including physical symptoms, history of onset, family history of disease and previous medical investigations and interventions (i.e., tests, treatments, surgery). The period of onset to diagnosis of the disease was calculated and averaged, as was the time to recovery after inception of treatment. Rates of relapse were recorded.
Results. More children suffered impairment in a lower limb (65%) and only two children showed simultaneous impairment in both upper and lower limbs. Twenty-five patients (54%) reported a possible precipitating traumatic event and 17 patients (39%) reported a history of joint problems. Prior to referral, professional consults from other specialties averaged 2.3 (range 1-5). All but 3 patients had undergone medical investigation (mean=2.2) and 41 children had undergone treatment such as physiotherapy (n=23) and NSAIDs (n=21). Two children had surgery. Period from symptom onset to diagnosis averaged 23.6 weeks (median=12 weeks, range 1-130

weeks). Post-diagnosis treatments included physiotherapy (n=28) and administration of analgesics (NSAIDs, n=19); 9 patients were referred for psychiatric consult. Time from treatment initiation to full recovery ranged from 1 to 140 weeks (median=7 weeks). During follow-up, 11 children (27.5%) relapsed from full recovery.
Conclusions. The study indicates that there are significant difficulties and potentially harmful delays in diagnosing RSD, a rare disease in children. Although the authors cannot confirm delayed diagnosis and treatment result in prolonged course of illness and protracted recovery, they suggest that high morbidity associated with the disease requires increased awareness and alertness of clinicians to avoid needless medical investigations and inappropriate or harmful treatments.

Rhee H. Prevalence and predictors of headaches in US adolescents. *Headache* 2000;40(7):528-538.

Objective. To examine the prevalence of headache in US adolescents in relation to gender, age and race and to investigate the relationship between self-esteem, depression, insomnia and headache.
Design. Longitudinal, repeated measures study.
Setting. Participants' homes, USA.
Participants. A representative sample of adolescents from high schools and feeder schools (n=6072; age range 11-21 years old; 48% male; 71% Caucasian, 20% African American, 1% American Indian, 4% Asian and 5% were other minorities) who participated in the National Longitudinal Study of Adolescent Health. Mean age of participants was 16.1 years at time 1 and 15.6 years at time 2. Attrition rate was over 24% (4591 (75.6%) participated in the follow-up interview) and dropouts tended to be older than participants (17.4 vs. 15.6 years old; p<0.0001).
Main Outcome Measures. Interviews were conducted a year apart. Participants were asked to rate how frequently they suffered from headache and insomnia on a five-point scale (0 (never) to 4 (every day)). Depressive symptoms were measured using a modified version of the Center for Epidemiological Studies Depression Scale (CES-D). Questions relating to sleep problems and crying spells were excluded from the CES-D and the feeling of worthlessness was added. Self-esteem was measured using the relevant "Personality and Family" questionnaire items rated on a four-point scale (1 (most of the time or all of the time) to 4 (absent)).
Results. More than 90% of participants reported having at least 1 headache in the previous 12 months. Of these, 30% experienced recurrent or chronic headaches. Boys were more likely to experience episodic headaches (just a few times), while girls tended to experience more chronic or recurrent headaches (p<0.001). There were differences among races in prevalence (American Indian 36%, Caucasians 32%, African American 24.3% and other minorities 23.7%; p<0.001). All variables were stable over time (r's=0.43). Depression and low self-esteem at time 1 were found to predict headaches at time 2 in girls (p's<0.001), but not boys. No relationship was found between insomnia and headaches.
Conclusions. Headache prevalence is high among American adolescents with significant variation between genders and races. Recurrent and chronic headaches are most prevalent among girls and American Indians. Depression and low self-esteem are predictors of headaches in girls, but not boys, which suggests gender and racial specific headache etiology.

Runefors P, Arnbjornsson E, Elander G, Michelsson K. Newborn infants' cry after heel-prick: analysis with sound spectrogram. *Acta Paediatrica* 2000;89(1):68-72.

Objective. To determine if an infant cry can be used as part of a pain measurement instrument.
Design. Prospective, descriptive study.
Setting. Department of Obstetrics and Gynaecology, Sweden.
Participants. Healthy newborn infants (n=50; 30 male; mean age=3.6 days, SD=1; mean weight=3645g, SD=435; mean gestational age=39.7 weeks, SD=1.1; mean Apgar scores of 9, 10 and 10 at 1, 5 and 10 minutes respectively) undergoing standard heel-prick for phenylketonuria (PKU) screening who had been breast-fed within 30 minutes before the procedure.
Main Outcome Measures. The microphone of a tape recorder (frequency response 40-13000 Hz) was held 10 cm from infants' mouths to record their cries (individual cries were defined as the vocalisation during a single expiration) from before the heel-prick until sampling was completed and crying had stopped. The time between the heel-prick and the first cry (latency), cry duration after the heel-prick and the total crying time during the sample were recorded. Computer-assisted acoustical analysis was used to compare the fundamental frequency (FF; bottom-most curve on the spectrogram) and melody (variation in the FF) of the first 5 cries.
Results. The first cry after heel-prick had a longer mean duration (2.7 vs. 0.8 seconds), higher mean FF (598 vs. 495 Hz) and more shifts in melody (abrupt change in FF; 12 vs. 4) than cry 5 (p's<0.001). First cries tended to be flat (less than 10% change in FF during cry; n=23) and falling (decrease in FF of more than 10%; n=18) while

fifth cries were predominantly flat (n=32). There were large variations in the melody of individual cries from each infant, duration of each cry (range 0.1-10 seconds) total crying time (range 13-257 seconds) and FF's between infants (range 260-1269 Hz over all cries).
Conclusions. When compared to results from other studies the first cry resembled a cry of pain while the fifth cry was more similar to crying for a reason other than pain. Since other stimuli may elicit a similar reaction to that seen to heel-prick induced pain in this study, crying may only be useful as a measure of pain in newborn infants when the stimuli is known.

Winner P, Rothner AD, Saper J, Nett R, Asgharnejad M, Laurenza A, Austin R, Peykamian M. A randomized, double-blind, placebo-controlled study of sumatriptan nasal spray in the treatment of acute migraine in adolescents. *Pediatrics* 2000;106(5):989-997.

Objective. To assess the efficacy and tolerability of sumatriptan nasal spray compared with placebo for the treatment of migraine in adolescents.
Design. Randomized, double-blind, placebo-controlled trial.
Setting. 46 outpatient sites, USA.
Participants. Adolescents (12-17 years old) were randomly assigned to either placebo (n=131, 65 male) or 1 of 3 treatment groups of varying doses of sumatriptan nasal spray (Group 1: n=128, 65 male;Group 2: n=133, 73 female; Group 3: n=118, 61 female). Inclusion criteria were: migraine with or without aura meeting the International Headache Society criteria; a history of 2-8 moderate to severe migraine attacks per month for the 2 previous months; ≤15 days of tension headaches per month; failure of at least 1 previously used over-the-counter or prescription migraine medication.
Intervention. Group 1 patients received 5 mg/dose of sumatriptan nasal spray, group 2 received 10 mg/dose and group 3 received 20 mg/dose. All doses were in single dose quantities in identical looking containers. Self-administration of individual doses took place in front of a guardian to treat moderate or severe migraine attacks.
Main Outcome Measures. Patients recorded the time of onset and time of medication administration (calculated as time to treatment). Patient-rated measures included headache relief using a 4-point scale, associated symptoms (baseline, 15, 30, 60 and 120 minutes following administration), headache recurrence (significant worsening) 2-24 hours post administration and use of second dose 2 to 24 hours after initial dose. Safety was determined through incidence of adverse events, abnormalities in physical examination, vital signs and clinical laboratory tests
Results. Migraine relief at 1 hour post-dose was greater for groups 2 and 3 versus placebo ($p<0.05$). At 2 hours post-dose, migraine relief was greater for group 1 versus placebo ($p<0.05$). More patients in group 3 reported complete migraine relief at 2 hours post-dose than placebo ($p<0.05$). Each dose of sumatriptan nasal spray was superior to placebo in terms of cumulative percentages of patients reporting headache relief in first 2 hours post-dose ($p<0.05$). Photophobia was lower at 2 hours post-dose in group 3 than placebo ($p<0.05$) and phonophobia was lower than placebo for groups 1 and 3 ($p<0.05$). There were no differences between groups in terms of headache recurrence or second dose administration. No drug-related adverse events were evident.
Conclusions. Sumatriptan nasal spray is effective, safe and well tolerated in adolescent patients experiencing migraine. All 3 doses investigated provided relief, however the 20mg/dose provided the most rapid and effective treatment.

Review Articles

The *Pediatric Pain Letter* briefly notes the following recent review article:

Garrison MM, Christakis DA. A systematic review of treatments for infant colic. *Pediatrics* 2000;106(1 Pt 2):184-190.

Colic is a common problem that has received too little attention. This systematic review evaluates the randomized trials in the area and found that most trials suffer methodologic flaws. Although dietary changes, herbal tea and reducing stimulation were found to be helpful, more studies are needed.

Announcements

Meetings

April 19-22, 2001: *20th Annual Scientific Meeting of the American Pain Society, Phoenix Civic Plaza Convention Centre, Phoenix, Arizona, USA.* Changing the Face of Pediatric Pain, a preconference event on the 19th, will present and explore challenging, contemporary issues in developmental pain research and pediatric pain management for physicians, nurses, pharmacists, psychologists and other healthcare professionals. For more information contact the American Pain Society, 4700 W. Lake Avenue, Glenview, IL, 60025, tel 847-375-4715, fax 847-375-6315, web-site **www.ampainsoc.org/meeting/**.

April 26-27, 2001: *Children in Pain: Effective Strategies for Pain Management, Crowne Plaza, Ann Arbor, Michigan, USA.* Sponsored by the C.S. Mott Children's Hospital (University of Michigan Medical System) and Children's Hospital of Michigan (Wayne State University). This third interdisciplinary conference will address issues relevant to the management of pain in children. For more information contact Carol Williams, tel 734-763-5283, email **cwms@umich.edu**, web-site **www.chmkids.org/chm/painconference.html**.

May 10-12, 2001: *Canadian Pain Society Annual Conference: An Odyssey of Discoveries, DELTA Montreal Hotel, Montreal, Quebec, Canada.* A Pain Education Day with pediatric pain, cancer pain, impact of pain and evidenced-based practice as tentative topics. Keynote speaker for the scientific program will be Jean-Marie Besson. Topics to be covered in the plenary sessions include: pain and brain imaging; update on opioid therapy; update on pediatric pain; basic research on ion channels; clinical research on evidenced-based decision making for pain treatment; update on cancer pain/ palliative care. For more information contact Marie-Christine Bournaki, Ph.D., Chair, Local Arrangements Committee, tel 514-343-7181, fax 514-343-2306, email **Marie.Christine.Bournaki@umontreal.ca**, web-site **www.medicine.dal.ca/cps/montreal2001/**.

May 19-24, 2001: *2nd European Course on Palliative Care for Children, Warsaw, Poland*. For more information contact Marek Karwacki, Warsaw Hospice for Children, 03-680 Warsaw, ul.Agatowa 10, tel +48-22- 678-16-11, fax +48-22-678-99-32, email **marekwk@ astercity.net**, web-site **www.hospicjum.waw.pl/kurs/ kurs.htm**.

June 8-12, 2001: *Canadian Anesthesiologist's Society Annual Meeting, Halifax, Nova Scotia, Canada.* For more information contact CAS Meeting Coordinator, 1 Eglinton Avenue East, Suite 208, Toronto, Ontario Canada, M4P 3A1, tel 416-480-0602, fax 416-480-0320, email **meetings@cas.ca**.

June 26-29, 2001: *2nd World Congress of the World Institute of Pain: Pain Management in the 21st Century, Istanbul Convention and Exhibition Centre, Istanbul, Turkey.* For further information contact Cengiz Topel Mah, Dilan Tur Congress International, Dereyolu Sok. Umut - 2 Apt., 80630 Etiler, Istanbul, Turkey, tel +90-212 257-86-67 (PBX), fax +90-212-265-54-74, email **info@dilan.com.tr**, web-site **www.dilan.com.tr/wip2001**.

June 15-19, 2003: *International Symposium on Paediatric Pain, Sydney, Australia*. The theme will be "The Big Questions in Paediatric Pain". What are the questions and issues that concern you and the community caring for children in pain? The Scientific Program Committee for the Sydney 2003 meeting would appreciate your participation in an open forum to discuss themes that are important from the perspective of pain researchers, health professionals, parents and children. Ideas can be directed to David Champion **dchampion@prvnw1.stvincents.com.au** and/or Belinda Goodenough **b.goodenough@unsw.edu.au**.

Positions

The Pediatric Chronic Pain Management Program, Department of Anesthesia at the Hospital for Sick Children, Toronto is advertising for a **Fellowship** commencing July 2001. Applications are invited from Board eligible (CA-3 completed or fellowship qualification outside of North America) candidates. It would be expected that applicants would have some prior experience of management of pain in children. Individuals trained in anesthesia or other pain allied specialties will be considered. For further information, please contact Stephen Brown MD FRCPC, email **stephen.brown@sickkids.on.ca** or Hana Zita, email **hana.zita@sickkids.on.ca**, tel 416-813-7240, fax 416-813-7543.

Short announcements on pediatric pain events will be published free of charge.

We need your help

Your participation in abstracting and writing commentaries for the *Pediatric Pain Letter* is welcomed. Please send submissions according to the specifications outlined in our Author's Kit which can be obtained from Jill Hatchette, Managing Editor, *Pediatric Pain Letter*, Psychology Department, Dalhousie University, Halifax, Nova Scotia, B3H 4J1, email **jhatchet@is.dal.ca** (requests can be made in writing or by email). Abstracts and commentaries on any aspect of pain in infants, children and/or adolescents are appropriate. We will attempt to use abstracts and commentaries but the editors reserve the right to edit or reject contributions.

Assistants for this issue: Deanna Braaksma, Frank Elgar, Jill Maclaren, Michael Houlihan, Isabel Redondo and Trudi Walsh.

Editorial Board

Managing Editor: Jill Hatchette, jhatchet@is.dal.ca
Copy Editor: Allan Hennigar, ahennig@is.dal.ca
Psychology Department, Dalhousie University, Halifax, NS, B3H 4J1, Canada, tel 902-494-1938, fax 902-494-6585, web-site **www.dal.ca/~pedpain/pplet/**

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Note: Over the next few issues we will be modifying the format in an effort to improve the usefulness of the *Pediatric Pain Letter*. Your comments are appreciated.