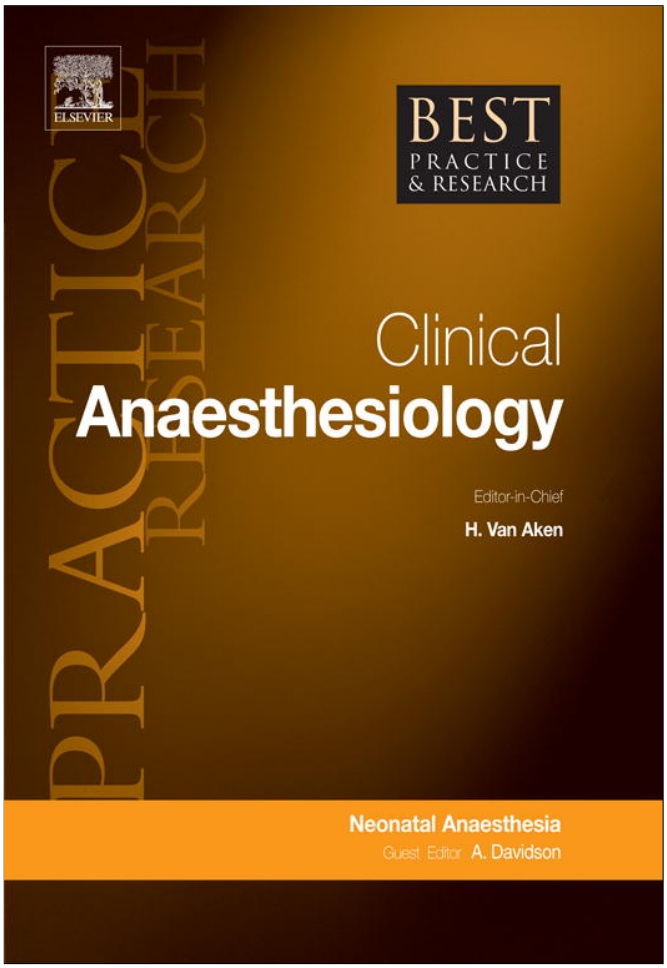

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4

Spinal anaesthesia in the neonate

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Postoperative apnoea in ex-premature infants is inversely proportional to gestational age at birth and postmenstrual age (PMA). Spinal anaesthesia is an important technique in ex-premature infants as it reduces the risk of postoperative apnoea, provided intra-operative sedation is avoided. Recent studies have provided more data on recommended doses of local anaesthetics for infant spinal anaesthesia as well as adjuvants used to prolong the duration of surgical anaesthesia. Spinal anaesthesia is also used for surgical procedures other than inguinal hernia repair. There are a variety of reasons why awake regional is not the preferred technique for ex-premature infants undergoing lower abdominal surgery in many centres, and there is also controversy over the appropriate anaesthetic technique for outpatient surgery in infants <60 weeks PMA. A pragmatic decision analysis on the selection of anaesthetic techniques for inguinal hernia repair in infants is presented.

History

Spinal anaesthesia was described originally by Bier in 1895.[1] In 1901, Bainbridge[2] described 12 spinal anaesthetics in children aged 4 months to 6 years using 1–2% cocaine with a dose of 1–2 mg kg^{-1}.

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Subsequently, Tyrell Grey[3,4] reported the experience of 300 stovaine spinal anaesthetics in infants at the Great Ormond Street Hospital. Spinal anaesthesia was described as a safe technique even in gravely ill infants and children. For that era, the overall mortality rate (1.5%), even in the presence of sepsis, peritonitis and impending septic shock, was impressively low. The postoperative morbidity (largely vomiting) was 25% despite infants being fed milk during surgery and older children being given cake.

The ex-premie

The renaissance of spinal anaesthesia was triggered by a marked increase in the survival rate of extremely pre-term infants (63% since the early 1980s). In Australia, 1.3% of all live births are born at <31 weeks gestational age (GA). This equates to 3450 premature births per year. The 50% survival threshold of live-born infants is achieved between 23 and 24 weeks. The neonatal mortality rates then fall exponentially with survival rates of 89% at 27 weeks gestation and 99% at 31 weeks. Of the survivors, nearly half will suffer moderate to severe disabilities including deafness, blindness, cerebral palsy, behavioural dysfunction and poor school performance. Data from the Australian and New Zealand neonatal network (ANZNN) suggest that of 1112 infants born at <28 weeks GA, 53% are oxygen dependent at 36 weeks and 20% require home oxygen for discharge.[5] A significant number of ex-premature infants require surgery. In particular, inguinal hernias develop in 13% of infants born at <32 weeks gestation and in 30% of those born with a birth weight <1000 g.[6]

A number of authors have identified ex-premature infants as a group at risk of postoperative apnoea and desaturation (Table 1).[7–9] Cote[10] combined data from eight prospective studies (255 patients) to identify risk factors for postoperative apnoea.[11,12] Cote's review found that GA at birth and postconceptual age (PCA) were independent risk factors. (Note: The terms postmenstrual age and postconceptual age are often used interchangeably and indeed mean the same; both ages are measured or calculated from the last menstrual period. If the pregnancy was conceived *in vitro*, then the PCA is still calculated by adding a couple of weeks to the actual date of conception. To avoid confusion, the American Academy of Pediatrics suggests only PMA is used.) There was no relationship between the incidence of apnoea and necrotising enterocolitis (NEC), neonatal apnoea, respiratory distress syndrome (RDS), bronchopulmonary dysplasia Broncho Pulmonary Dysplasia (BPD) or the intra-operative use of opioids or muscle relaxants. Anaemia, however, was an independent risk factor, particularly for patients <43 weeks post conception. The conclusions drawn in this article were that the incidence in an infant born at 35 weeks is not <5% until a PCA of 48 weeks and not <1% until a PCA of 54 weeks (with 95% statistical confidence), and that the risk of apnoea an infant born at 32 weeks does not decrease to <5% until 50 weeks and not <1% until a PCA of 56 weeks.

To reduce the risk of postoperative respiratory compromise, in 1984, Abajian advocated awake spinal anaesthesia for ex-premies.[13] Numerous uncontrolled reports[14–19] followed suggesting a reduced risk for postoperative apnoea with spinal anaesthesia compared to general anaesthesia. Since 1990, five randomised controlled studies comparing spinal with general anaesthesia have been reported.[9,20–23] Welborn[20] demonstrated no apnoeas after awake spinal anaesthesia but intramuscular ketamine prior to spinal anaesthesia produced apnoea in 90% of patients. A Cochrane meta-analysis of 108 infants from four prospective trials comparing GA with spinal anaesthesia[9,20–22,24] suggested overall "there was no convincing evidence to support the use of spinal anaesthesia as standard practice in inguinal

Table 1
Infants in whom spinal anaesthesia offers significant advantages.

Ex-premature infants born at less than 35 weeks gestational age
All Infants with a Post conceptual age less than 45 weeks
Past or current Apnoea of prematurity requiring Caffeine or Methylxanthines
Chronic lung disease requiring home oxygen
Significant neonatal history including IVH, NEC, Retinopathy of prematurity
High-risk infants with congenital heart disease & airway anomalies
Any infant without absolute contraindications.
Infants booked as day-case surgery

herniorrhaphy in ex-premature infants."[25] However, if infants having preoperative ketamine or sedatives were excluded then there was a reduction in postoperative apnoea in the SA group and a reduction of borderline significance in the use of postoperative assisted ventilation in the spinal anaesthesia group. Avoiding supplemental sedation appears to be key in maximising the apnoea-reducing benefit of spinal anaesthesia.

Techniques

Anatomy

The spinal cord ends between L2 and L3 vertebrae in 90% of premature infants and between L1 and L2 vertebrae in 92% of term infants.[26] The dural sac is at the S4 level at birth and reaches the S2 level by the end of the first year (Fig. 1). The line joining the two superior iliac crests (inter-cristal line) crosses at the L5–S1 interspace at birth, L5 vertebra in young children and L3–L4 interspace in adults. As a result, lumbar puncture at the inter-cristal line will always be below the spinal cord.

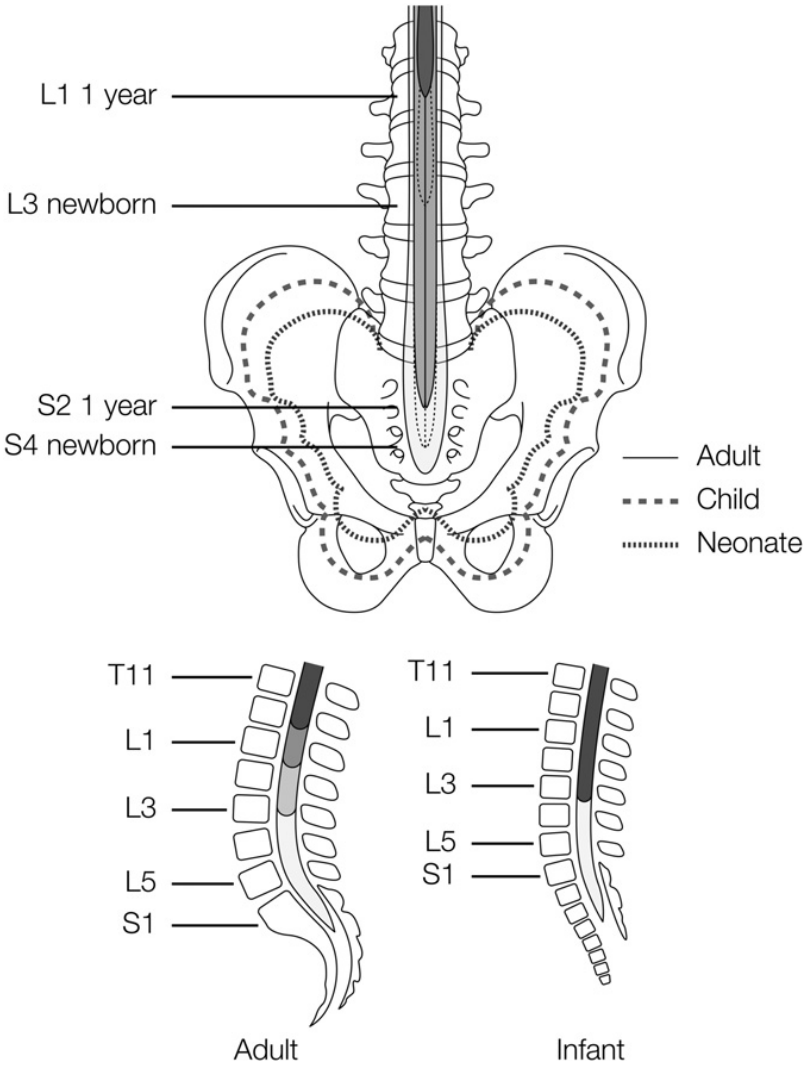

Fig. 1. The spinal cord (dark grey) terminates at a more caudad level in neonates and in infants compared to adults. The conus medullaris ends at approximately L1 in adults and at the L2 level in neonates and infants. In infants the line across the top of both iliac crests (the intercristal line) crosses the vertebral column at the L4–5 or L5–S1 interspace, well below the termination of the spinal cord. The dural sac (light grey) in neonates and infants also terminates in a more caudad location compared to adults, usually at about the level of S3 compared to the adult level of S1. The lack of a lumbar lordosis in infants compared to older children predisposes the infant to high spinal blockade with changes in positioning.

Positioning

Correct positioning and firm holding of the child are crucial to success of the technique. Lumbar puncture can be performed with the infant in either the sitting or lateral decubitus position. The neck should be in extension for lateral positioning as cervical flexion may obstruct the airway during the procedure.[27] The lateral decubitus position is easier to maintain by an assistant. In the sitting position, the patient is less mobile, bony landmarks are more prominent and the cerebrospinal fluid (CSF) hydrostatic pressure is higher but maintaining head support and spine flexion is more difficult. In a study on 30 pre-term infants for inguinal herniotomy, Vila[28] found spinal anaesthesia to be equally effective in both lateral and sitting positions. Apiliogullari[29] recommended 45° head up-tilt in the lateral decubitus position to increase lumbar puncture success and reduce bloody-tap rates.

The distance from the skin to epidural space is age dependent, being 6 mm at birth and increasing to 10–12 mm at 1-year of age.[30] Bosenberg[31] estimated that the distance from skin to epidural space is 1 mm kg^{-1}, whereas Ecoffey[32] reported that the skin to epidural distance ranges from 10–18 mm at the lumbar region to 7–14 mm at the thoracic region in infants <3 years of age. A 25 G quincke spinal needle is 50-mm long and a 25 G hypodermic needle is 16-mm long.

The needles available for paediatric use range from 24 to 29 G, either short-bevelled Quincke or Sprotte and Whitacre with or without introducer with a length shorter than that in adults. Styletted cutting-point Quincke needles, 22 or 25 G with a length of 25 mm are most frequently used. Use of non-styletted needles should be avoided because these can introduce epidermal tissue into the spinal canal resulting in epidermoid tumours.[33] The extent of the sensory block can be assessed with a peripheral nerve stimulator set at tetanus or by a pinch. A L1-level blockade of motor function can be shown by loss of hip flexion.

Drugs and doses

On a per-kilogram basis, infants require doses which are three to five times that of adult doses but with duration that is a quarter of the time of adult spinal anaesthesia.[34] Adult spinal anaesthesia usually requires 12–14 mg of bupivacaine (0.17–0.2 mg kg^{-1} in a 70-kg adult). An infant dose for inguinal hernia repair is 0.8–1 mg kg^{-1} because of a larger volume of distribution (CSF volume of 4 ml kg^{-1} is twice that of adult values) and greater clearance. Infants have a lower pulsatility of CSF but a higher heart rate generates a greater total flow and turnover than adults.

Tetracaine, mepivacaine, lidocaine, racemic bupivacaine and, more recently, levobupivacaine and ropivacaine have all been employed for paediatric spinal anaesthesia (Table 2).[35–37] In the United States, the vast majority of infant spinals have been with hyperbaric tetracaine or hyperbaric bupivacaine with

Table 2
Reported doses of isobaric and hyperbaric local anaesthetics for infant spinal anaesthesia for inguinal hernia repair.

	Agent	Weight	Mean dose	Duration	Author
Hyperbaric	1% tetracaine	<2 kg	0.91 mg/kg	105 min	Williams[53]
		2–3 kg	0.62		Abajian[13]
		3–4 kg	0.54		
		4–6 kg	0.45		
		>6 kg	0.37		
	0.5% tetracaine		0.4 mg/kg	86 min	Rice[54]
	0.5% tetracaine with adrenaline		0.4 mg/kg	128 min	Rice[54]
	0.75% bupivacaine in 8.25% dextrose		0.6–1 mg/kg	84 min	Parkinson[39]
	0.5% bupivacaine		0.3 mg/kg	75 min	Gallagher[16]
Isobaric	0.5% bupivacaine	<2 kg	0.6 ml		Murat[55]
		2–3 kg	0.8 ml		
		>5 kg	1 ml		
			1 mg/kg	82	Frawley[40]
			0.8 mg/kg	70	Mahe[38]
			0.6–0.8 mg/kg	46	Somri[21]
	0.5% bupivacaine with adrenaline		0.86 mg/kg	81	Mahe[38]
	Levobupivacaine		1 mg/kg	87.5	Frawley[36]
	Ropivacaine		1 mg/kg	85	Frawley[35]

or without adrenaline. A common mix consists of an equal volume of 1% tetracaine and 10% dextrose, combined with 0.02 ml of 1:1000 adrenaline (an 'epi wash') with an average dose of 0.5 mg kg^{-1}. Bupivacaine has been used as isobaric (mean dose: 0.8 mg kg^{-1}) [38]or hyperbaric solutions (bupivacaine 0.75% in 8.25% dextrose at 0.6–1 mg kg^{-1}).[39] In our institution, 1 mg kg^{-1} of isobaric 0.5% bupivacaine has recently been replaced by ropivacaine and levobupivacaine. Levobupivacaine, ropivacaine and bupivacaine have different potencies because of differences in formulation, lipid solubility and intrinsic vasoconstrictor activity. In a recent infant spinal potency study[40], ropivacaine and levobupivacaine were 39–45% less potent than bupivacaine at ED50 values but 19–21% less potent at ED95 values.

Additives and adjuncts

Adrenaline was probably first used by Braun in 1903, and by Tyrell Gray in 1909, to prolong the action of cocaine. Fosel[41] demonstrated that adding 1:200 000 adrenaline to 0.6 ml of isobaric 0.5% bupivacaine increased the duration of spinal anaesthesia from 50 to 95 min. In contrast, Mahe[38] noted that the addition of adrenaline to 0.8 mg kg of isobaric 0.5% bupivacaine increased the duration from 70 to 81 min.[38,42]

Dextrose (in a concentration ranging from 3% to 5%) is frequently added to subarachnoid local anaesthetic solutions to alter the distribution of the local anaesthetic, and hence success and spread of the blockade in children. In 100 children, in the age range of 2–115 months for paediatric day-case surgery under spinal anaesthesia, Kokki[37] compared bupivacaine 5 mg ml^{-1} in saline 0.9%(isobaric) with bupivacaine 5 mg ml^{-1} in 8% glucose (hyperbaric). The success rate of the block was greater with hyperbaric bupivacaine (96%) compared with isobaric bupivacaine (82%). Onset was delayed marginally in the hyperbaric group. Spread and duration of sensory block showed a similar wide scatter in both groups.

Intra-spinal α2-adrenergic agonists (e.g., clonidine and dexmedetomidine) induce analgesia by a pathway involving nitric oxide and acetylcholine release and are potentiated by intra-thecal neostigmine. Rochette added 1 μg kg^{-1} clonidine to spinal isobaric bupivacaine in newborns and doubled the duration of the block without cardiovascular or respiratory side effects.[43] In a subsequent trial of clonidine 1 μg kg^{-1} added to bupivacaine 1 mg kg^{-1} comparing pre-term to term infants, Rochette[44] demonstrated a 22% incidence of postoperative apnoeas in the premature group and a 19% incidence in the term group without sustained bradycardias or significant desaturations. Rakesh reported cephalad migration of intra-thecal clonidine (1 μg kg^{-1} with hyperbaric bupivacaine) with prolonged sedation and respiratory depression in an infant undergoing herniorrhaphy. These authors have advocated caution in the use of intra-thecal Clonidine in ex-premature infants.[45]

Batra[46] reported the use of intra-thecal neostigmine in 75 infants having lower abdominal and urogenital procedures. The infants received 0.5 mg kg^{-1} of hyperbaric bupivacaine with 0.25, 0.5, 0.75 and 1 μg kg^{-1} of neostigmine. They demonstrated there was a linear increase in duration of block from 52 to 92 min with increasing dose of neostigmine. In addition, with doses of neostigmine >0.75 μg kg^{-1}, there was a significant increase in the pain-free interval. The authors further claim that neostigmine does not cause any decrease in spinal cord blood flow or cause any direct spinal cord toxicity in animal or human studies.

Intra-thecal opioids have been reported to reduce the endocrine stress response during infant cardiac surgery.[47–49] Batra[47] reported a dose–response study with four doses of intra-thecal fentanyl (0, 0.25, 0.5 and 1 μg ml^{-1}) added to 0.4–0.5 mg kg^{-1} bupivacaine for lower abdominal surgery in infants. There was a dose-dependent increase in duration of block but four infants developed apnoea requiring bag-and-mask ventilation.

Methylxanthines

The use of methylxanthines is varied. It is not clear whether caffeine needs to be given prophylactically to reduce the rate of postoperative apnoea in ex-premature infants receiving the newer faster insoluble general anaesthetics such as sevoflurane or desflurane. Welborn[50] stated that a single dose of intravenous caffeine (10 mg kg^{-1}) suppresses postoperative apnoea in pre-term infants. In a Cochrane Review, Steer and Henderson-Smart[51], stated that caffeine can be used for this indication, but with a caveat on the small number of patients studied. In general, for any case of irregular breathing after

general anaesthesia, caffeine or aminophylline should be given without delay. Of the methylxanthines, theophylline is the most extensively used but caffeine is at least as effective as theophylline, has a longer half-life, is associated with fewer adverse events and, in addition, has a greater ease of administration.[52]

Why are not spinals the 'Gold standard' of neonatal anaesthesia?

A 1-year study of 24 409 regional blocks in children by the French-Language Society of Pediatric Anaesthesiologists (ADARPEF) suggested spinal anaesthesia represents 18% of all regional blocks in premature infants and 5% of blocks in term infants currently <30 days of age. Rochette[53] reported 10 929 paediatric regional anaesthetic blocks of which 1042 were neonatal spinal anaesthetics. Neonatal spinals represent 30% of all infant neuraxial blocks. Lacroix[54] reported significant decreases in use of caudal anaesthesia from 1994 to 2006, but spinal anaesthesia use increased from 2.1% to 3.2% of all regional procedures. In spite of such widespread use, awake regional techniques are unjustifiably labelled as having an excessive failure rate, inadequate duration of anaesthesia and an unacceptably high rate of unsettled infants requiring intra-operative sedation. Emerging data in animal models have demonstrated accelerated neuronal apoptosis and long-term behavioural changes in rodents exposed in the neonatal period to anaesthetic agents that act on *N*-methyl D-aspartic acid (NMDA) and gamma aminobutyric acid (GABA) receptors.[55] These findings may increase the use of regional anaesthesia in ex-premature infants.

Quality of anaesthesia/success rates

There is a steep learning curve for awake-infant regional anaesthesia. The Vermont registry of spinal anaesthesia in neonates and infants recorded their first infant spinal in 1977[13] and, to date, they have performed >1600 infant spinals (across a 30-year period, this equates to one a week). This database has generated three large series.[13,14,18] In Abajian's first series, the success rate was 100% in high-risk infants but only 76% in larger, term infants. Frumiento[14] reviewed 269 cases of inguinal hernia repair in which successful spinal anaesthesia was achieved in 262 (95% on the first attempt). The success rate in the Vermont Infant Spinal registry's 1554 infants was 97.4%.[56] In contrast, smaller series have reported a significantly higher incidence of failed spinals, bloody taps and blocks requiring supplementation. Williams reported traumatic taps in 20% and failure in four of 17 spinals in ex-premature infants.[22] Shenkman[19] reported a failure rate of 11% and spinal fluid could not be obtained in six of 55 ex-premature infants.

Duration of action

The Holy Grail of Spinal anaesthesia is to have motor block which outlasts even the slowest surgeon. Abajian[13] employed tetracaine at 0.22–0.32 mg kg^{-1} and found that the duration of anaesthesia was 83 min in term infants, 100 min in pre-term infants and 125 min in infants with congenital anomalies. The duration of analgesia increased 29% with 0.01 mg adrenaline (109 vs. 84 min). Harnik[17] used hyperbaric tetracaine doses of 0.24–0.65 mg kg^{-1} in her series of 21 high-risk infants. The duration of block was 71 min and the duration of anaesthesia increased with dose. Rice[57] reported durations of 86 min with 0.4 mg kg^{-1} hyperbaric 0.5% tetracaine, and 128 min in the group receiving 0.4 mg kg^{-1} hyperbaric 0.5% tetracaine with adrenaline. Webster[58] reported a duration of anaesthesia of 70–210 min in 39 high-risk infants receiving 0.5–0.9 mg kg^{-1} hyperbaric tetracaine with adrenaline; however, 12 of these required general anaesthesia and only 59% were unsupplemented.

In neonates, the duration of spinal anaesthesia is less with bupivacaine than with tetracaine. In a recent series[40], duration of motor block at concentrations greater than the ED95 was 81.9 min for bupivacaine, 87.5 for levobupivacaine and 85.2 for ropivacaine. Ramamoorthy reported a series of 60 newborns from 41 to 59 weeks PCA comparing hyperbaric bupivacaine and hyperbaric tetracaine in doses of either 1 or 1.2 mg kg^{-1} with adrenaline. The method of assessment was not mentioned but the duration of spinal anaesthesia was 177 min in the 1 mg kg^{-1} tetracaine group, and 201 min in the 1.2-mg kg^{-1} group. By comparison, the duration of spinal anaesthesia was 147 min in the 1.2 mg kg^{-1} bupivacaine group, and 121 min in the 1-mg kg^{-1} group. Gallagher [16] used 0.06 ml kg^{-1} plus 0.1 ml (mean dose: 0.3 mg kg^{-1}) of hyperbaric 0.5% bupivacaine and reported duration of motor block of 75 min. By contrast,

Somri[21] used 0.6–0.8 mg kg^{-1} isobaric 0.5% bupivacaine and reported durations of 45.9 min. Blaise[59], using 0.6-mg kg^{-1} hyperbaric 0.75% bupivacaine in older children, reported a duration of 70 min. Parkinson[39], using 0.75% bupivacaine in 8.25% glucose with epinephrine, reported a duration of 84 min.

Supplementation and sedation

Supplementation is required for infants with an inadequate spinal block, for unsettled babies and for procedures where the surgical duration exceeds block duration. In the Vermont Infant registry study[56], >75% of infants required only comforting with stroking and a pacifier, 2.7% required local anaesthetic and 1.2% required general anaesthesia for inadequate duration. Other studies recommend small doses of midazolam (20–50 μg kg^{-1}) or propofol (0.25–0.5 mg kg^{-1}) to calm unsettled babies intra-operatively.[37,56] Cassady[60] suggested an alternative for avoidance of general anaesthesia for infants when bilateral inguinal herniorrhaphy outlasts subarachnoid block. They recommend the use of single-shot caudal anaesthesia at the completion of the first inguinal hernia repair if it is likely surgery will proceed past 60 min.

Welborn[20] initially used intramuscular ketamine prior to the lumbar puncture but ceased this practice when excessive apnoea rates were recorded. For unsupplemented spinal anaesthetics, infants were, instead, comforted by a pacifier dipped in either a sugar solution or peach schnapps as needed. A systematic review of studies using sucrose analgesia in newborns has demonstrated the clinical efficacy of doses of 0.05–2 ml of 12–50% sucrose solutions in alleviating procedural pain.[61] These studies demonstrate the superiority of either glucose or sucrose over breast milk. Potential mechanisms include a direct activation of opioid receptors by the sugar, an enhancement of the effects of endogenous opioids on their receptor systems or an indirect effect promoting the release of endogenous opioids in the central nervous system (CNS).[62]

Infants undergoing procedures with spinal anaesthesia commonly fall asleep. Sedation was evaluated by Hermanns[63] using the bispectral index (BIS) score and the 95% spectral edge frequency (SEF95). BIS values began to decrease significantly 15 min after spinal anaesthesia and fell <70 after 25 min. Disma[64], using cerebral state index monitoring, also noted burst suppression. The presumed mechanism for sedation after spinal anaesthesia is a diminished afferent conduction to reticulo–thalamo–cortical projection pathways, reducing their excitability and hence decreasing the arousal level of the brain.

New volatile agents

The uses of new insoluble agents, such as sevoflurane and desflurane, have been associated with fewer adverse respiratory events in the recovery period but are not completely protective for postoperative apnoea. O'Brien[65] compared halothane, desflurane and sevoflurane for the incidence of postoperative apnoea in a study of pre-term infants. No major apnoeic events occurred in any of the 40 infants <60 weeks PCA, although there was at least one episode of breath-holding or self-limiting apnoea in each group. Sale[66] monitored ex-prems for apnoeas and bradycardias using nasal thermistry and impedance for 12 h pre and post operation. The incidence of preoperative apnoeas was 27% in the sevoflurane group and 40% in the desflurane group, with the incidence increasing postoperatively to 33% and 60%, respectively. Two infants in the sevoflurane group and four in the desflurane group recorded new apnoea postoperatively. There is only one published study comparing awake spinal anaesthesia with sevoflurane.[22] In this study, an excess of postoperative cardiorespiratory complications was defined as a threefold increase in the incidence of postoperative apnoeas and bradycardias relative to preoperative values. The sevoflurane group demonstrated excess events in patients with pre-existing apnoeas and also those without respiratory disease. Three patients with oxygen-dependent chronic lung disease accounted for 26 of the 39 episodes of apnoea and bradycardia.

Changing surgical management of hernias and hydrocoeles

In a survey of members of the surgical section of the American Academy of Pediatrics, laparoscopic evaluation for contralateral inguinal hernia was reported by 37% compared to only 6% in the 1993

survey.[67] Compared with a prior survey, more surgeons now prefer an earlier repair of the contralateral side to reduce the risk of incarceration.[68] Despite concerns that laparoscopic evaluation of the contralateral groin prior to hernia repair would increase the failure rate of spinal anaesthesia, the use of spinal anaesthesia has remained constant at 15%.

Day-case surgery?

Current evidence does not define a 'safe' PMA for outpatient surgery in former premature infants. Cote[10] and others[12,69] suggest the risk of apnoeas was nearly absent by 44–46 postconceptual weeks but may persists until 60 weeks PCA. They recommended that any infant who has a history of apnoea or is anaemic should not undergo outpatient surgery. Cote's study, however, was underpowered to predict apnoea risk in infants >45 weeks PCA as only 68 of their 255 patients were 46–50 weeks PCA and only 41 exceeded 50 weeks. In addition, volatile anaesthetic agents currently in use have a markedly different postoperative complication profile to those used (i.e., halothane and enflurane) in the Cote study (collected from 1988–93).

A survey of surgical management of inguinal hernias in infants by the American Society of Pediatric Surgeons in 1996[70] reports that, for an infant who has presented with an inguinal hernia after discharge from neonatal intensive care, 65% will operate when convenient and 35% will operate at 40–60 weeks PCA (mean 53 weeks). For an inpatient born at <29 weeks and weighing <1000 g, 71% would operate just before neonatal intensive care unit (NICU) discharge and 20% would operate at 49 weeks PCA and a weight >3.5 kg. A follow-up survey in 2005[67] suggested no change in this practice.

A number of authors have strongly advocated day-case surgery for ex-premature infants.[14,71–73] Melone[73] reported on 1294 outpatient inguinal herniorrhaphies performed between 1985 and 1990, but only 124 patients (9.6%) were identified as being premature (≤36 weeks GA) and the average PCA was 45.3 weeks. They recommended that "Outpatient inguinal herniorrhaphy can be performed in this patient group with minimal morbidity and no mortality." Veverka et al. [72] observed no apnoea after spinal anaesthesia in 62 ex-premies who were discharged home after an average observation period of 5.6 h for those with a history of apnoea and 3.5 h for those without history. Frumiento[14] even argued against routine overnight apnoea monitoring of outpatients.

Murphy suggested the frequency of apnoea after inguinal hernia repair with new anaesthetic agents was much less (4.7%) than reported by Cote.[71] Sevoflurane was the only anaesthetic factor which predisposed to postoperative apnoeas. The risk of postoperative apnoeas was increased in babies with a past history of apnoeas, those born at a GA of <30 weeks, small for GA, mechanical ventilation after birth and history of patent ductus arteriosus (PDA), Intra Ventricular Haemorrhage (IVH) or BPD.

Abajian and Williams[56] recommend day-case surgery and early discharge for uncomplicated cases in infants who receive unsupplemented spinal anaesthesia and who demonstrate no apnoea, bradycardia or desaturations during the surgery and for 8 h postoperatively (Fig. 2). Infants on apnoea monitors or methylxanthine drugs and those who have received any form of perioperative CNS-depressing medication should be admitted overnight. Postoperative apnoea has been reported after spinal anaesthesia[19,58,74,75], especially in infants with pre-existing apnoea and those who were sedated during the procedure (midazolam, ketamine, etc.) or received morphine or codeine[74] in the perioperative period. In some reports of apnoea, it is likely that a high spinal block contributed to the apnoea.[76] Kim[77] and Davidson[75] have both identified failed spinal anaesthetics requiring ketamine or general anaesthesia as a risk factor for postoperative apnoea. In Kim's series, 44% of infants with inadequate spinal anaesthesia developed postoperative apnoea. They suggest that the sedative effect of neuraxial blockade acts synergistically with supplemental pharmacological sedation to increase risk. Davidson[75] found that, in children where spinal anaesthesia was unsuccessful, early apnoea was particularly common.

Spinal anaesthesia for procedures other than herniorrhaphy

Spinal anaesthesia has been used for a variety of procedures other than inguinal hernia repair (Table 3). The Vermont infant spinal registry[56] has collected data since 1978 on infants or neonates considered to be at risk of postoperative apnoea or respiratory impairment. Inguinal herniorrhaphies

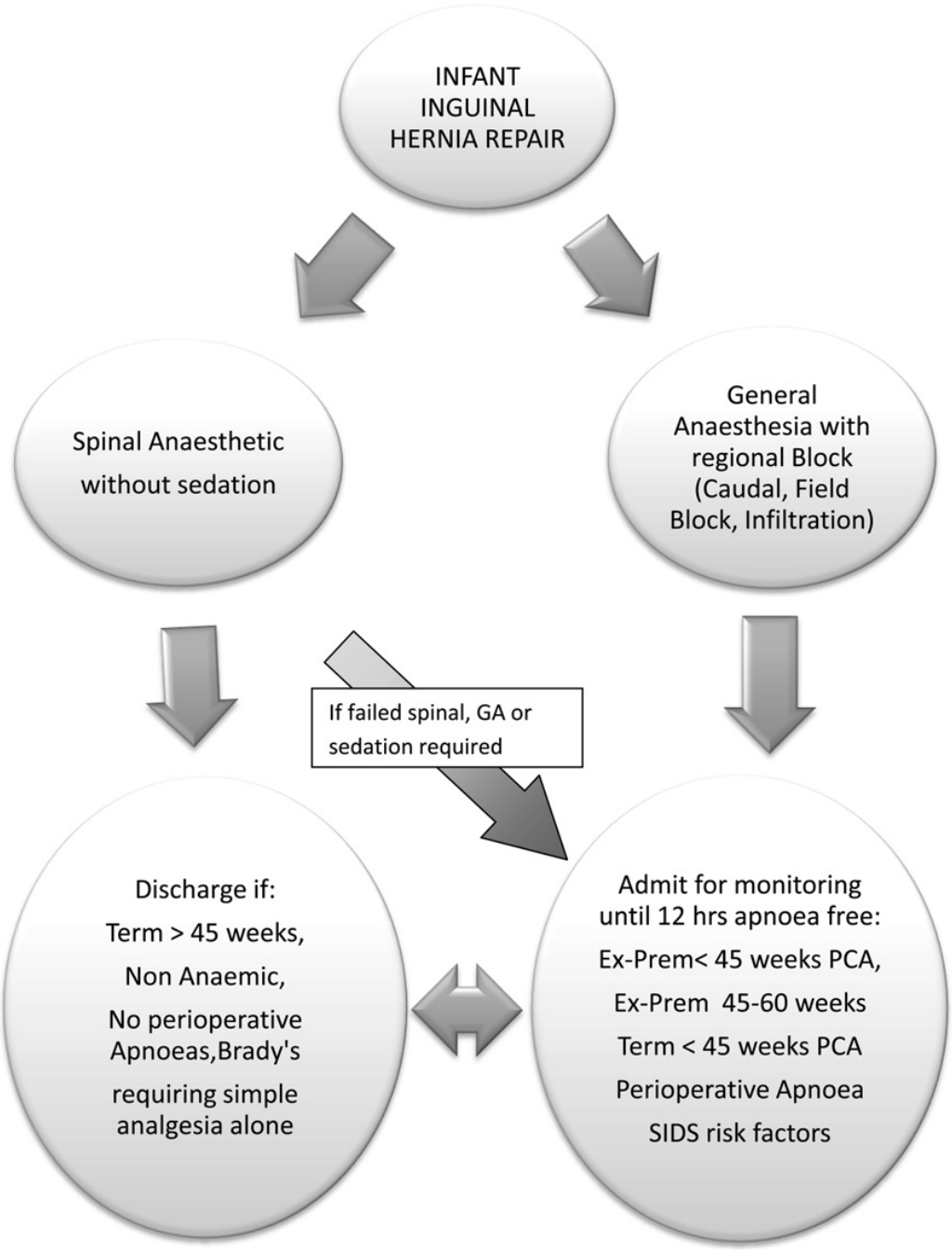

Fig. 2. Decision tree algorithm for management of infants presenting for inguinal hernia repair. Infants at risk of postoperative apnoeas include all those with pre-existing apnoeas, all infants less than 45 weeks post conceptional age (PCA), all on methyl-xanthines, all ex-premature infants with neurological injury and with. Sudden Infant Death Syndrome (SIDS) risk factors include smoking parents, low socioeconomic status and single parents. Analgesics other than paracetamol are associated with postoperative apnoea.

represent 55% of all procedures, but various intra-abdominal procedures were also performed. Williams and Abajian[78] described subarachnoid tetracaine with steep Trendelenburg position for PDA-closure in 14 pre-term and neonates, Hammer[49] used spinal tetracaine (0.5–2 mg kg^{-1}) and morphine (7 μg kg^{-1}) in cardiac surgery with a remifentanil-based anaesthetic technique, and Suominen[79] used 20 μg kg^{-1} intra-thecal morphine to reduce postoperative analgesic requirements after cardiac surgery. The relatively stable cardiovascular properties of spinal anaesthesia have also been used for non-cardiac surgery in infants with complex cardiac lesions.[80]

Table 3
Reported doses for infant spinal anaesthesia for surgery other than inguinal hernia repair.

Procedure		Mean dose (mg kg^{-1})	Agent	Author
Upper abdominal	Gastroschisis	0.5–0.6	0.5% hyperbaric tetracaine	Vane[80]
	Gastrostomy	1	0.5% hyperbaric bupivacaine	Shenkman[81]
	Pyloromyotomy	0.75–1.0	0.5% hyperbaric tetracaine	Williams[53]
		0.8	0.5% isobaric bupivacaine	Somri[82]
Lower Abdominal	Colostomy	0.56	0.5% hyperbaric tetracaine	Williams[53]
	Inguinal hernia	0.50	1% hyperbaric tetracaine	Abajian[13]
	Anorectoplasty	1	0.5% hyperbaric tetracaine with 15 mcg morphine	Tobias[83]
	Peritoneal dialysis catheter	0.95	0.5% isobaric bupivacaine	McCormick[84]
Neurosurgical	Meningo-myelocoele repair	0.56 (1st dose) 0.44 (2nd dose) 0.51 (3rd dose)	0.5% hyperbaric tetracaine with adrenaline	Viscomi[85]
Cardiac	PDA ligation	2.42	0.5% hyperbaric tetracaine	Williams[78]
	Cardiac catheter	1	0.5% hyperbaric bupivacaine	Katznelson[86]
Orthopaedic		0.5	0.5% hyperbaric tetracaine	Aronnson[87]

Continuous spinal anaesthesia and CSEA

In two ex-premature infants with chronic lung disease, Tobias[81] reported the use of continuous spinal anaesthesia with bupivacaine in procedures lasting 2–2.5 h. Payne and Moore[82] described continuous spinal anaesthesia with general anaesthesia for major abdominal surgery in 10 patients in the age range of 2–59 months. In these cases, spinal anaesthesia was provided by intermittent doses of 0.5% bupivacaine (0.2 ml kg^{-1} to a maximum of 1 ml). Infants <1-year of age required repeat boluses at 45–60-min intervals, whereas older infants required re-dosing at 0–80-min intervals.

Bouchet evaluated the tolerance and the efficiency of awake caudal anaesthesia performed in 25 consecutive conscious ex-premature infants for inguinal herniotomies. Two infants with a prior history of apnoea or bronchopulmonary dysplasia had apnoea during and after surgery. Total spinal anaesthesia was the major complication in one infant and prolonged surgery requiring general anaesthesia was the main limitation of this technique in another child.

Somri reported the use of combined spinal–epidural anaesthesia in major abdominal surgery in 28 high-risk neonates and infants.[83] Spinal anaesthesia with isobaric bupivacaine 0.5%, 1 mg kg^{-1} was followed by placement of a caudal epidural catheter to thoracic spinal segments. Satisfactory surgical anaesthesia was achieved in 24 neonates and infants, four patients were converted to general anaesthesia and 20 infants required intravenous midazolam. The issue of epidural volume extension of spinal block was not discussed.

Contraindications

Apart from limitations inherent in duration or site of surgery, there are no clear contraindications to spinal anaesthesia. Contraindications in the adult, such as coagulopathy, are tempered by the fact that coagulation studies[84] are often prolonged in this age group. Spinal anaesthesia has been described even in the presence of a ventriculo-peritoneal shunts devices.[85]

Complications

Complications during infant spinal anaesthesia are rare. A 1-year study of 24 409 regional blocks in children by the French-Language Society of Pediatric Anesthesiologists, reported a complication rate of 1.5 per 1000 in the 60% of children receiving central neuraxial blocks.[86] Intravascular injection was the only reported complication in the 506 spinal anaesthetics.[86]

Systemic absorption of local anaesthetic

Beauvoir[42] measured total and free bupivacaine after spinal anaesthesia in 22 newborns and evaluated a possible influence of adrenaline on bupivacaine absorption. Ten minutes after spinal injection total bupivacaine concentration was 0.31 pg ml^{-1} (87% bound) in the plain group and 0.25 pg ml^{-1} (88% bound) in the adrenaline group. Tetracaine undergoes rapid hydrolysis by plasma esterases including plasma cholinesterase; therefore, in theory, toxicity is less likely. However, there are no reports of total or free plasma tetracaine levels after infant spinal anaesthesia.

High blocks

A unique feature in infants is that there is only one anterior concave curvature of the vertebral column at birth (Fig. 1). The cervical lordosis begins in the first 3 months of life with the child's ability to hold their head upright. The lumbar lordosis starts as the child begins to walk at the age of 6–9 months. Therefore, the spread of hyperbaric local anaesthetics is position dependent in infants and inadvertent high blocks have been reported. Tetracaine has been associated with high spinal blockade with doses as low as 0.5 mg kg^{-1}.[87] Williams[56] used 0.54 mg kg^{-1} hyperbaric tetracaine but reported a 3.8% incidence of high blocks with 0.57 mg kg^{-1} and five infants who required intubation received 0.7 mg kg^{-1}. Jetzek-Zader[88] reported a high spinal in an ex-premature infant undergoing pyloromyotomy but used 1.3 mg kg^{-1} of hyperbaric 0.5% bupivacaine.

Postdural puncture headache

Postdural puncture headache (PDPH) is rare in infants. Kokki[89] found 5% PDPH rate despite 25 G and 29 G Quinke spinal needles, whereas Puncuh[90] reported a 0.5% incidence.

Neuraxial haematoma

Epidural hematoma formation after Sub Arachnoid Blockade (SAB) has not been reported in neonates after neuraxial blockade even following cardiac surgery and patients receiving anticoagulant therapy. It is relevant to note that it is difficult to interpret coagulation studies in infants. De Saint Blanquat[84] performed coagulation studies in 141 ex-premature infants undergoing hernia repair and found prolonged activated partial thromboplastin time (aPTT) values in 60%.

Aseptic meningitis

Aseptic and septic meningitis are rare complications of spinal anaesthesia. Easley and Tobias[91] reported the first documented occurrence of aseptic meningitis in an infant after spinal anaesthesia. Because of the infant's underlying status and recent life-threatening illness, it was not possible to definitely prove a causal relationship between the aseptic meningitis and the spinal anaesthetic.

Conclusion

Infant spinal anaesthesia offers significant benefits to ex-premature infants who are at risk of postoperative apnoea. Infants most likely to benefit include term infants currently <45 weeks PMA and ex-premature infants between 45 and 60 weeks PMA. Recent studies have demonstrated a 98% success rate in performance of the block, but this success rate cannot be expected to be replicated in units where awake regional techniques are uncommonly performed. Even in centres with long-standing experience in spinal anaesthesia, there is a significant incidence of infants requiring intra-operative sedation or supplementation of the block when surgical duration exceeds 75 min. All currently available local anaesthetic agents have now been described for infant spinal anaesthesia with the choice of agent determined by institutional preference. Attempts to increase the duration of motor block by addition of $\alpha 2$ agonists, such as clonidine, have been hampered by a significant incidence of postoperative sedation and apnoeas. Despite strong opinions for and against awake regional

techniques, there are limited studies comparing spinal anaesthesia to general anaesthesia with modern agents such as desflurane or sevoflurane and no studies comparing awake caudal anaesthesia to awake spinal anaesthesia. On current evidence, there is no anaesthetic technique which reliably reduces the apnoeic risk in ex-premature infants to a level which would allow lower abdominal surgery day-case surgery in ex-premature infants.

Research agenda

A large controlled prospective study comparing differences in peri- and postoperative complications between regional anaesthesia and general anaesthesia with modern volatile agents in ex-premature infants is required.
A randomised controlled trial comparing apnoea outcome between awake caudal anaesthesia and awake spinal anaesthesia is required.
A suitable adjuvant to prolong the duration of intra-spinal local anaesthetics without inducing apnoea is required.

Practice points

Awake spinal anaesthesia without intravenous sedation produces the lowest incidence of postoperative apnoeas and bradycardias.
Spinal anaesthesia is most appropriate for neonatal inguinal hernia repair but many other surgical procedures have been described.
Bupivacaine, tetracaine, levobupivacaine and ropivacaine have all been described for neonatal spinal anaesthesia
Duration of spinal anaesthesia varies from 80 to 120 min depending on the agent and dose.
Postoperative monitoring is recommended for all infants currently <45 weeks PMA and ex-premature infants with ongoing apnoeas and complex medical histories.
There is no consensus on appropriate postconceptual age for day-case lower abdominal surgery in infants.

Conflict of interest statement

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References

1. Bier A. Verusche uber cocainisuring des ruckenmarkes. *Deutsche Zeitschrift Für Chirurgie* 1899; **51:** 361–369.
2. Bainbridge WS. A report of twelve operations on infants and young children during spinal analgesia. *Archives de Pédiatrie* 1901; **18:** 510–520.
3. Gray HT. A study of spinal anaesthesia in children and infants. *Lancet* 1909**:** 913–917 (Sept 25).
4. Gray HT. A further study of spinal anaesthesia in children and infants. *Lancet* 1910; **1**(June 11)**:** 1611–1616.
5. Askie LM, Henderson-Smart DJ & Jones RA. Management of infants with chronic lung disease of prematurity in Australasia. *Early Human Development* 2005; **81**(2)**:** 135–142.
6. Brandt ML. Pediatric hernias. *The Surgical Clinics of North America* 2008; **88**(1)**:** 27–43. pp. vii–viii.
7. Steward DJ. Preterm infants are more prone to complications following minor surgery than are term infants. *Anesthesiology* 1982; **56**(4)**:** 304–306.
8. Kurth CD, Spitzer AR, Broennle AM & Downes JJ. Postoperative apnea in preterm infants. *Anesthesiology* 1987; **66**(4)**:** 483–488.

9. Krane EJ, Haberkern CM & Jacobson LE. Postoperative apnea, bradycardia, and oxygen desaturation in formerly premature infants: prospective comparison of spinal and general anesthesia. *Anesthesia and Analgesia* 1995; **80**(1)**:** 7–13.
*10. Cote CJ, Zaslavsky A, Downes JJ et al. Postoperative apnea in former preterm infants after inguinal herniorrhaphy. A combined analysis. *Anesthesiology* 1995; **82**(4)**:** 809–822.
11. Welborn LG, Hannallah RS, Higgins T et al. Postoperative apnoea in former preterm infants: does anaemia increase the risk? *Canadian Journal of Anaesthesia* 1990; **37**(4 Pt 2)**:** S92.
12. Malviya S, Swartz J & Lerman J. Are all preterm infants younger than 60 weeks postconceptual age at risk for post-anesthetic apnea? *Anesthesiology* 1993; **78**(6)**:** 1076–1081.
*13. Abajian JC, Mellish RW, Browne AF et al. Spinal anesthesia for surgery in the high-risk infant. *Anesthesia and Analgesia* 1984; **63**(3)**:** 359–362.
14. Frumiento C, Abajian JC & Vane DW. Spinal anesthesia for preterm infants undergoing inguinal hernia repair. *Archives of Surgery* 2000; **135**(4)**:** 445–451.
15. Gerber A, Baitella L & Dangel P. Spinal anaestehsia in former preterm infants. *Paediatric Anaesthesia* 1993; **3:** 153–156.
16. Gallagher TM & Crean PM. Spinal anaesthesia in infants born prematurely. *Anaesthesia* 1989; **44**(5)**:** 434–436.
17. Harnik EV, Hoy GR, Potolicchio S et al. Spinal anesthesia in premature infants recovering from respiratory distress syndrome. *Anesthesiology* 1986; **64**(1)**:** 95–99.
18. Sartorelli KH, Abajian JC, Kreutz JM & Vane DW. Improved outcome utilizing spinal anesthesia in high-risk infants. *Journal of Pediatric Surgery* 1992; **27**(8)**:** 1022–1025.
19. Shenkman Z, Hoppenstein D, Litmanowitz I et al. Spinal anesthesia in 62 premature, former-premature or young infants–technical aspects and pitfalls. *Canadian Journal of Anaesthesia* 2002; **49**(3)**:** 262–269.
*20. Welborn LG, Rice LJ, Hannallah RS et al. Postoperative apnea in former preterm infants: prospective comparison of spinal and general anesthesia. *Anesthesiology* 1990; **72**(5)**:** 838–842.
21. Somri M, Gaitini L, Vaida S et al. Postoperative outcome in high-risk infants undergoing herniorrhaphy: comparison between spinal and general anaesthesia. *Anaesthesia* 1998; **53**(8)**:** 762–766.
22. William JM, Stoddart PA, Williams SA & Wolf AR. Postoperative recovery after inguinal herniotomy in ex-premature infants: comparison between sevoflurane and spinal anaesthesia. *British Journal of Anaesthesia* 2001; **86**(3)**:** 366–371.
23. Broadman LM. Use of spinal or continuous caudal anesthesia for inguinal hernia repair in premature infants: are there advantages? *Regional Anesthesia* 1996; **21**(6 Suppl.)**:** 108–113.
24. Kunst G, Linderkamp O, Holle R et al. The proportion of high risk preterm infants with postoperative apnea and bradycardia is the same after general and spinal anesthesia. *Canadian Journal of Anaesthesia* 1999; **46**(1)**:** 94–95.
25. Craven PD, Badawi N, Henderson-Smart DJ & O'Brien M. Regional (spinal, epidural, caudal) versus general anaesthesia in preterm infants undergoing inguinal herniorrhaphy in early infancy. *Cochrane Database of Systematic Reviews* 2003 (3): CD003669.
26. Sahin F, Selcuki M, Ecin N et al. Level of conus medullaris in term and preterm neonate s. *Archives of Disease in Childhood. Fetal and Neonatal Edition* 1997; **77**(1)**:** F67–69.
27. Weisman LE, Merenstein GB & Steenbarger JR. The effect of lumbar puncture position in sick neonates. *American Journal of Diseases of Children* 1983; **137**(11)**:** 1077–1079.
28. Vila R, Lloret J, Munar F & Vinzo J. Spinal anaesthesia for inguinal herniotomy in preterm infants sedated with nitrous oxide: a comparison of lumbar puncture in the lateral or sitting position. *Anaesthesia* 2002; **57**(12)**:** 1164–1167.
29. Apiliogullari S, Duman A, Gok F et al. The effects of 45 degree head up tilt on the lumbar puncture success rate in children undergoing spinal anesthesia. *Paediatric Anaesthesia* 2008; **18**(12)**:** 1178–1182.
30. Shenkman Z, Rathaus V, Jedeikin R et al. The distance from the skin to the subarachnoid space can be predicted in premature and former-premature infants. *Canadian Journal of Anaesthesia* 2004; **51**(2)**:** 160–162.
31. Bosenberg AT & Gouws E. Skin-epidural distance in children. *Anaesthesia* 1995; **50**(10)**:** 895–897.
32. Ecoffey C, Dubousset AM & Samii K. Lumbar and thoracic epidural anesthesia for urologic and upper abdominal surgery in infants and children. *Anesthesiology* 1986; **65**(1)**:** 87–90.
33. Krane EJ. Spinal epidermoid tumors: will a forgotten complication rise again? *Regional Anesthesia and Pain Medicine* 1999; **24**(6)**:** 494–496.
34. Sukhani R, Wahood A & Black PR. Calculating local anesthetic dose for infant spinal: body weight versus spinal length. *Anesthesia and Analgesia* 1993; **76**(4)**:** 917–918.
35. Frawley G, Skinner A, Thomas J & Smith S. Ropivacaine spinal anesthesia in neonates: a dose range finding study. *Paediatric Anaesthesia* 2007; **17**(2)**:** 126–132.
36. Frawley GP, Farrell T & Smith S. Levobupivacaine spinal anesthesia in neonates: a dose range finding study. *Paediatric Anaesthesia* 2004; **14**(10)**:** 838–844.
37. Kokki H, Tuovinen K & Hendolin H. Spinal anaesthesia for paediatric day-case surgery: a double-blind, randomized, parallel group, prospective comparison of isobaric and hyperbaric bupivacaine. *British Journal of Anaesthesia* 1998; **81**(4)**:** 502–506.
38. Mahe V & Ecoffey C. Spinal anesthesia with isobaric bupivacaine in infants. *Anesthesiology* 1988; **68**(4)**:** 601–603.
39. Parkinson SK, Little WL, Malley RA et al. Use of hyperbaric bupivacaine with epinephrine for spinal anesthesia in infants. *Regional Anesthesia* 1990; **15**(2)**:** 86–88.
*40. Frawley G, Ingelmo P & Smith K. Relative potencies of bupivacaine, levobupivacaine and ropivacaine for neonatal spinal anaesthesia. *British Journal of Anaesthesia* 2009; doi:10.1093/bja/aep259.
41. Fosel T, Wilhelm W, Gruness V & Molter G. Spinal anesthesia in infancy using bupivacaine 0.5%. The effect of an adrenaline addition on duration and hemodynamics. *Anaesthesist* 1994; **43**(1)**:** 26–29.
42. Beauvoir C, Rochette A, Desch G & D'Athis F. Spinal anaesthesia in newborns: total and free bupivacaine plasma concentration. *Paediatric Anaesthesia* 1996; **6**(3)**:** 195–199.
43. Rochette A, Raux O, Troncin R et al. Clonidine prolongs spinal anesthesia in newborns: a prospective dose-ranging study. *Anesthesia and Analgesia* 2004; **98**(1)**:** 56–59. table of contents.
*44. Rochette A, Troncin R, Raux O et al. Clonidine added to bupivacaine in neonatal spinal anesthesia: a prospective comparison in 124 preterm and term infants. *Paediatric Anaesthesia* 2005; **15**(12)**:** 1072–1077.

45. Aouad MT, Moukaddem FH, Akel SR & Kanazi GE. Respiratory failure in a former preterm infant following high spinal anesthesia with bupivacaine and clonidine. *Paediatric Anaesthesia* 2008; **18**(10)**:** 1000–1001.
46. Batra YK, Rajeev S, Panda NB et al. Intrathecal neostigmine with bupivacaine for infants undergoing lower abdominal and urogenital procedures: dose response. *Acta Anaesthesiologica Scandinavica* 2009; **53**(4)**:** 470–475.
47. Batra YK, Lokesh VC, Panda NB et al. Dose-response study of intrathecal fentanyl added to bupivacaine in infants undergoing lower abdominal and urologic surgery. *Paediatric Anaesthesia* 2008; **18**(7)**:** 613–619.
48. Humphreys N, Bays SM, Parry AJ et al. Spinal anesthesia with an indwelling catheter reduces the stress response in pediatric open heart surgery. *Anesthesiology* 2005; **103**(6)**:** 1113–1120.
49. Hammer GB, Ramamoorthy C, Cao H et al. Postoperative analgesia after spinal blockade in infants and children undergoing cardiac surgery. *Anesthesia and Analgesia* 2005; **100**(5)**:** 1283–1288. table of contents.
50. Welborn LG, Hannallah RS, Fink R et al. High-dose caffeine suppresses postoperative apnea in former preterm infants. *Anesthesiology* 1989; **71**(3)**:** 347–349.
51. Henderson-Smart DJ & Steer P. Prophylactic caffeine to prevent postoperative apnea following general anesthesia in preterm infants. *Cochrane Database of Systematic Reviews* 2001 (4):CD000048.
52. Steer PA & Henderson-Smart DJ. Caffeine versus theophylline for apnea in preterm infants. *Cochrane Database of Systematic Reviews* 2000 (2):CD000273.
53. Rochette A, Dadure C, Raux O et al. A review of pediatric regional anesthesia practice during a 17-year period in a single institution. *Paediatric Anaesthesia* 2007; **17**(9)**:** 874–880.
54. Lacroix F. Epidemiology and morbidity of regional anaesthesia in children. *Current Opinion in Anaesthesiology* 2008; **21**(3)**:** 345–349.
*55. Jevtovic-Todorovic V, Hartman RE, Izumi Y et al. Early exposure to common anesthetic agents causes widespread neurodegeneration in the developing rat brain and persistent learning deficits. *The Journal of Neuroscience* 2003; **23**(3)**:** 876–882.
*56. Williams RK, Adams DC, Aladjem EV et al. The safety and efficacy of spinal anesthesia for surgery in infants: the Vermont Infant Spinal Registry. *Anesthesia and Analgesia* 2006; **102**(1)**:** 67–71.
57. Rice LJ, DeMars PD, Whalen TV et al. Duration of spinal anesthesia in infants less than one year of age. Comparison of three hyperbaric techniques. *Regional Anesthesia* 1994; **19**(5)**:** 325–329.
58. Webster AC, McKishnie JD, Kenyon CF & Marshall DG. Spinal anaesthesia for inguinal hernia repair in high-risk neonates. *Canadian Journal of Anaesthesia* 1991; **38**(3)**:** 281–286.
59. Blaise GA & Roy WL. Spinal anaesthesia for minor paediatric surgery. *Canadian Anaesthetists' Society Journal* 1986; **33**(2)**:** 227–230.
60. Cassady Jr. JF & Lederhaas G. An alternative for avoidance of general anaesthesia for infants when bilateral inguinal herniorrhaphy outlasts subarachnoid blockade. *Paediatric Anaesthesia* 2000; **10**(6)**:** 674–677.
*61. Blass EM & Watt LB. Suckling- and sucrose-induced analgesia in human newborns. *Pain* 1999; **83**(3)**:** 611–623.
62. Blass EM & Hoffmeyer LB. Sucrose as an analgesic for newborn infants. *Pediatrics* 1991; **87**(2)**:** 215–218.
63. Hermanns H, Stevens MF, Werdehausen R et al. Sedation during spinal anaesthesia in infants. *British Journal of Anaesthesia* 2006; **97**(3)**:** 380–384.
64. Disma N, Tuo P, Astuto M & Davidson AJ. Depth of sedation using Cerebral State Index in infants undergoing spinal anesthesia. *Paediatric Anaesthesia* 2009; **19**(2)**:** 133–137.
65. O'Brien K, Robinson DN & Morton NS. Induction and emergence in infants less than 60 weeks postconceptual age: comparison of thiopental, halothane, sevoflurane and desflurane. *British Journal of Anaesthesia* 1998; **80**(4)**:** 456–459.
*66. Sale SM, Read JA, Stoddart PA & Wolf AR. Prospective comparison of sevoflurane and desflurane in formerly premature infants undergoing inguinal herniotomy. *British Journal of Anaesthesia* 2006; **96**(6)**:** 774–778.
67. Antonoff MB, Kreykes NS, Saltzman DA & Acton RD. American Academy of Pediatrics Section on Surgery hernia survey revisited. *Journal of Pediatric Surgery* 2005; **40**(6)**:** 1009–1014.
68. Lau ST, Lee YH & Caty MG. Current management of hernias and hydroceles. *Seminars in Pediatric Surgery* 2007; **16**(1)**:** 50–57.
69. Liu LM, Cote CJ, Goudsouzian NG et al. Life-threatening apnea in infants recovering from anesthesia. *Anesthesiology* 1983; **59**(6)**:** 506–510.
70. Wiener ES, Touloukian RJ, Rodgers BM et al. Hernia survey of the Section on Surgery of the American Academy of Pediatrics. *Journal of Pediatric Surgery* 1996; **31**(8)**:** 1166–1169.
71. Murphy JJ, Swanson T, Ansermino M & Milner R. The frequency of apneas in premature infants after inguinal hernia repair: do they need overnight monitoring in the intensive care unit? *Journal of Pediatric Surgery* 2008; **43**(5)**:** 865–868.
72. Veverka TJ, Henry DN, Milroy MJ et al. Spinal anesthesia reduces the hazard of apnea in high-risk infants. *The American Surgeon* 1991; **57**(8)**:** 531–534. discussion 534–535.
73. Melone JH, Schwartz MZ, Tyson KR et al. Outpatient inguinal herniorrhaphy in premature infants: is it safe? *Journal of Pediatric Surgery* 1992; **27**(2)**:** 203–207. discussion 207–208.
74. Cox RG & Goresky GV. Life-threatening apnea following spinal anesthesia in former premature infants. *Anesthesiology* 1990; **73**(2)**:** 345–347.
75. Davidson A, Frawley GP, Sheppard S et al. Risk factors for apnea after infant inguinal hernia repair. *Paediatric Anaesthesia* 2009; **19**(4)**:** 402–403.
76. Tobias JD, Burd RS & Helikson MA. Apnea following spinal anaesthesia in two former pre-term infants. *Canadian Journal of Anaesthesia* 1998; **45**(10)**:** 985–989.
77. Kim GS, Song JG, Gwak MS & Yang M. Postoperative outcome in formerly premature infants undergoing herniorrhaphy: comparison of spinal and general anesthesia. *Journal of Korean Medical Science* 2003; **18**(5)**:** 691–695.
78. Williams RK & Abajian JC. High spinal anaesthesia for repair of patent ductus arteriosus in neonates. *Paediatric Anaesthesia* 1997; **7**(3)**:** 205–209.
79. Suominen PK, Ragg PG, McKinley DF et al. Intrathecal morphine provides effective and safe analgesia in children after cardiac surgery. *Acta Anaesthesiologica Scandinavica* 2004; **48**(7)**:** 875–882.
80. Sacrista S, Kern D, Fourcade O et al. Spinal anaesthesia in a child with hypoplastic left heart syndrome. *Paediatric Anaesthesia* 2003; **13**(3)**:** 253–256.

81. Tobias JD, Lowe S, O'Dell N et al. Continuous regional anaesthesia in infants. *Canadian Journal of Anaesthesia* 1993; **40**(11)**:** 1065–1068.
82. Payne KA & Moore SW. Subarachnoid microcatheter anesthesia in small children. *Regional Anesthesia* 1994; **19**(4)**:** 237–242.
*83. Somri M, Tome R, Yanovski B et al. Combined spinal-epidural anesthesia in major abdominal surgery in high-risk neonates and infants. *Paediatric Anaesthesia* 2007; **17**(11)**:** 1059–1065.
84. De Saint Blanquat L, Simon L, Laplace C et al. Preoperative coagulation tests in former preterm infants undergoing spinal anaesthesia. *Paediatric Anaesthesia* 2002; **12**(4)**:** 304–307.
85. Kachko L, Platis CM, Livni G et al. Spinal anesthesia in infants with ventriculoperitoneal shunt: report of five cases and review of literature. *Paediatric Anaesthesia* 2006; **16**(5)**:** 578–583.
86. Giaufre E, Dalens B & Gombert A. Epidemiology and morbidity of regional anesthesia in children: a one-year prospective survey of the French-Language Society of Pediatric Anesthesiologists. *Anesthesia and Analgesia* 1996; **83**(5)**:** 904–912.
87. Wright TE, Orr RJ, Haberkern CM & Walbergh EJ. Complications during spinal anesthesia in infants: high spinal blockade. *Anesthesiology* 1990; **73**(6)**:** 1290–1292.
88. Jetzek-Zader M. High spinal anaesthesia in a formerly preterm infant undergoing pyloromyotomy. *Paediatric Anaesthesia* 2001; **11**(4)**:** 507.
89. Kokki H, Heikkinen M, Turunen M et al. Needle design does not affect the success rate of spinal anaesthesia or the incidence of postpuncture complications in children. *Acta Anaesthesiologica Scandinavica* 2000; **44**(2)**:** 210–213.
90. Puncuh F, Lampugnani E & Kokki H. Use of spinal anaesthesia in paediatric patients: a single centre experience with 1132 cases. *Paediatric Anaesthesia* 2004; **14**(7)**:** 564–567.
91. Easley RB, George R, Connors D & Tobias JD. Aseptic meningitis after spinal anesthesia in an infant. *Anesthesiology* 1999; **91**(1)**:** 305–307.