1. **Intraneural injection**

While needle-to-nerve proximity correlates with onset of action of a nerve block, injection of local anesthetic within which of the following layers has been implicated in persistent post-operative neurologic symptoms?

A. Circumneural sheath  
B. Epineurium  
C. Perineurium  
D. Epymesium

Correct answer: C

**Explanation:**
Axons are surrounded by connective tissue called the endoneurium. The interstitial fluid inside the endoneurium of the brachial plexus roots consists of cerebral spinal fluid. These roots are surrounded by a dural sleeve, which connects to the dura mater, and fascicles within the nerve roots are extensions of the spinal nerve. Groups of axons together form a fascicle, which is surrounded by a membrane called the perineurium. This perineurium forms a physical and chemical barrier. Currently, it is believed that advancing a needle within the perineurium and injecting local anesthetic results in neurologic injury and should be avoided. This has been referred to as an ‘intraneural intrafascicular’ injection. Unfortunately, current popular ultrasound technology does not have the resolution to discern the perineural layer accurately. Fascicles join to form bundles, which are surrounded by a fibroadipose tissue called the epineurium. The epineurium consists of 2 parts, an interfascicular and an outer epineurium. Injection within the epineurium is also considered an ‘intraneural injection’. Current popular ultrasound technology does not have the resolution to discern the epineurium, and an injection within the epineurium but outside the perineurium can only be noted once the proceduralist injects the solution (increase in cross-sectional diameter of the nerve by more than 15%, separation of the fascicles or fascicular bundles, diffusion of the local anesthetic in a proximal and distal location). There also appears to a paraneural (also been referred to as circumneural sheath) that surrounds the epineurium. This sheath has also been referred to as a gliding apparatus. An injection between the paraneural (circumneural) sheath and the epineurium has been considered the safest location for local anesthetic deposition in order to not damage the nerve integrity while offering a more rapid and effective nerve block. Epymesium is that fascial layer that surrounds the neighboring muscle and is external to the epineurium.
References:


Reina MA, Sala-Blanch X, Monzo E, Nin OC, Bigeleisen PE, Boezaart AP. “Extrafascicular and intraperineural, but no endoneural, spread after deliberate intraneural injections in a cadaveric study.” Anesthesiology 2019;130:1007-16

2. Local anesthetic: mechanism of action

Which voltage-gated channel is the primary receptor target by which local anesthetics exert their effects?

A. Calcium channels
B. Potassium channels
C. Sodium channels  
D. Proton channels

Correct answer C

Explanation:
Voltage-gated sodium channels are protein-based structures within the axon cell membrane. Local anesthetics exert their effects by attaching to the alpha-subunit of the channel on the inner surface cell membrane. Most local anesthetics in clinical use reach this site by traversing the cell membrane as uncharged molecules, and then conjugating with hydrogen ions to attach to the binding site of the channel from the cytoplasm. Local anesthetics bind more readily during depolarization when sodium channels are in an open or inactivated state. This binding results in a reversible and concentration-dependent reduction in the sodium passage into the cell.

Local anesthetic efficacy may be decreased when administered in the region of inflamed tissue. An increase in tissue acidity can change the balance between ionized and unionized forms of administered local anesthetic, lowering the amount of available free base. This decreases the amount of uncharged local anesthetic available to traverse the cell membrane to bind the inner surface of the sodium channel.

References:


3. Local anesthetic: biotransformation and excretion

How are local anesthetics in the amino-amide class metabolized?

A. Hofmann elimination  
B. Cytochrome p450 enzymes of the liver  
C. Plasma cholinesterases  
D. Tissues esterases

Correct answer B

Explanation:
Local anesthetics consist of three components: a hydrophobic aromatic ring, an amide group, and an intermediary ester or amide chain. They are categorized as either ester-linked or amide-linked according to the type of the intermediary chain in its structure.

Amide local anesthetics undergo biotransformation primarily in the liver through the cytochrome P450 enzymatic system, while ester-linked local anesthetics are hydrolyzed by plasma cholinesterases and tissue esterases. The kidneys are the primary excretory organ for local anesthetics and their metabolites.
An alteration in local anesthetic metabolism can potentially increase systemic concentrations and toxicity. Examples include impaired liver function and hepatic perfusion for amide local anesthetics, and plasma cholinesterase deficiency for ester local anesthetics. Significant reductions in renal function can also impair local anesthetic elimination.

References:

4. Liposomal formulations of local anesthetic: mechanism, efficacy, duration

Which of the following statements is TRUE regarding liposomal bupivacaine?

A. It is produced by the loading of bupivacaine particles into liposomal spheres surrounded by a lipid bilayer
B. It is a selective sodium channel blocker that is naturally produced by animals
C. It is a selective alpha-2 adrenergic agonist in a lipid sphere
D. The lipids in liposomal bupivacaine counteract local anesthetic inhibition of myocardial fatty acid oxidation

Correct Answer: A

Explanation:
Liposomal bupivacaine works by loading local anesthetics into biomaterial-based carriers such as liposome microparticles. The duration is purportedly prolonged by the slow release of local anesthetic. Lower opioid use and lower pain scores compared with plain bupivacaine have been cited as the major benefits to using liposomal bupivacaine, though high quality randomized controlled trials demonstrate only superior analgesia when liposomal bupivacaine is compared to placebo, and not when liposomal bupivacaine is compared against non-liposomal bupivacaine. Current comparative studies of liposomal bupivacaine to bupivacaine is difficult to interpret due to differences in regional anesthetic technique between the liposomal bupivacaine group and the bupivacaine group. The majority of the studies that favorably assess liposomal bupivacaine to non-liposomal bupivacaine compare two different infiltration techniques in addition to the local anesthetic used (liposomal bupivacaine vs bupivacaine). Tetrodotoxin (TTX) and neosaxitoxin (NeoSTX) are referred to in option B; these are selective sodium channel blockers that are naturally produced by animals such as pufferfish and shellfish. These have minimal to no cardiotoxicity and have synergistic effects with conventional local anesthetics. Option C refers to the mechanism of action of dexmedetomidine, which can extend the duration of analgesia when combined with local anesthetics such as lidocaine and bupivacaine. Option D is a proposed mechanism of lipid emulsion therapy in the treatment of local anesthetic systemic toxicity.

References:

5. Local anesthetic dosing for continuous infusion

Which of the following statements is TRUE with regards to continuous infusion of local anesthetic?

A. Less than 1 of 5 cases of local anesthetic systemic toxicity is the result of continuous infusions of local anesthetic.
B. The majority of LAST associated with continuous infusions of local anesthetic is due to undetected placements of intravascular catheters.
C. Patients with renal failure are at high risk for LAST and should not be offered regional anesthetic continuous infusions.
D. In the majority of studies measuring total and free local anesthetic with continuous regional anesthetic infusions, both values are found to increase with increased duration of infusion.

Correct answer: A

Explanation:
The majority of LAST occurs with rapid injection of a high total dose of local anesthetic. In the literature, it appears that LAST is less likely associated with continuous infusions. The majority of LAST cases associated with continuous infusions include systemic reabsorption of local anesthetics in the blood stream. The contribution of renal failure to LAST is less likely than heart failure and liver failure. Amide local anesthetics are metabolized by the liver to mostly inactive metabolites and a very small percentage of the parent local anesthetic compound is excreted unchanged by the kidneys. While a small percentage of local anesthetics are excreted unchanged in the kidneys and reduced dosing and increased vigilance for LAST needs to be exercised in these patients, continuous regional anesthetics can still be offered in these patients. In studies examining plasma concentrations of total and free local anesthetic, authors have found that while plasma concentrations of total local anesthetic (free and bound) increase with increasing duration of the infusion, the plasma concentration of the unbound (free) form has been found to remain unchanged. This is speculated to be due to the fact that trauma and surgery increases the concentration of alpha-1 glycoprotein, which binds the local anesthetic.

References:


6. Local anesthetic systemic toxicity: s/sx, neurotoxicity vs cardiac toxicity

Which of the following clinical scenarios classically typifies the clinical presentation of local anesthetic systemic toxicity?

A. 23-year-old man with OSA has an interscalene block performed with 20 mL of 0.5% bupivacaine with 5 mcg/mL epinephrine. 20 minutes after the block is performed he feels short of breath. He requires oxygen support 2L/min via nasal cannula for hours after the surgery is performed.

B. 82-year-old man with CKD III and cirrhosis has an interscalene block performed for total shoulder arthroplasty. Within minutes of the block, he notes tinnitus, becomes restless, and then has a seizure. Cardiac collapse ensues after.

C. 53-year-old woman has a spinal anesthetic for total knee replacement. 3 mL 0.5% bupivacaine are used. After the uneventful spinal is completed, she complains of nausea and subsequently becomes bradycardic and hypotensive.

D. 18-year-old man has a supraclavicular block for a lesion to be removed from the 5th digit. Under sedation in the operating room, he becomes restless when incision is made. Blood pressure and heart rate elevations are noted concurrently.

Correct Answer: B

Explanation:
Local anesthetic systemic toxicity (LAST) is more likely to occur in patients at the extremes of age and who have underlying cardiac, neurologic, pulmonary, renal, hepatic, or metabolic disease. While LAST can occur in any patient, case reports to date associate the condition with these physiologic states, as well as a trend toward delayed presentation. Epidemiological data now suggests a lower frequency of LAST as reported by single institutions and some registries. There has also been an increase in the number of reported events outside of the traditional hospital setting by non-anesthesiologists. Of the listed options, option B is the most prototypical of LAST. The initial presenting symptoms of LAST include neurologic excitement such as agitation, metallic taste, auditory symptoms, and seizures. This is typically followed by CNS depression with drowsiness, coma, or respiratory arrest. Cardiac excitement such as tachycardia and arrhythmias and ultimately collapse (hypotension, bradycardia) ensue after neurologic symptoms. Variations may occur in how LAST manifests, such as cardiac symptoms without prodromal neurologic symptoms. The lack of neurotoxicity symptoms prior to cardiac symptoms usually manifest during procedures where there is rapid injection of greater doses of local anesthetic (such as with single injection nerve block).

Option A is most likely hypoxia secondary to hypoventilation due to phrenic nerve paralysis with an interscalene block in a patient with obstructive sleep apnea. Option C is most suggestive of a Bezold-Jarish reflex resulting in reflex bradycardia from preload reduction. The nausea is likely due to a low cardiac output state. Option D suggests an inadequate block with ulnar nerve sparing requiring greater analgesia.

References:
7. LAST Treatment

A 79-year-old man with a history of CAD and liver disease is having a supraclavicular block performed for a ganglion cyst removal. Immediately after the block, he complains of perioral numbness and becomes agitated with hypertension and ventricular tachycardia. Within a minute he has a tonic clonic seizure. Which of the following medications is NOT recommended in the treatment of this condition?

A. Calcium channel blocker
B. Epinephrine
C. 20% lipid emulsion
D. Benzodiazepine

Correct Answer: A

Explanation:
This 79-year-old patient presents with local anesthetic systemic toxicity (LAST). The initial presenting symptoms of LAST include neurologic excitement such as agitation, metallic taste, auditory symptoms, and seizures. This is typically followed by CNS depression with drowsiness, coma, or respiratory arrest. Cardiac excitement (tachycardia, arrhythmias) and then ultimately collapse (hypotension, bradycardia) ensue after neurologic symptoms. Variations, such as cardiac symptoms without prodromal neurologic symptoms, also exist and should be considered if clinical suspicion arises. Of note, calcium channel blockers are contraindicated due to the additive myocardial depressant effect when used in combination with bupivacaine. Vasopressin also is associated with poor outcomes and pulmonary hemorrhage and should not be used. Low dose-epinephrine, 20% lipid emulsion, and benzodiazepine medications are all recommended on the ASRA checklist for LAST treatment.

References:


8. Transient Neurologic Symptoms
Which of the following is a known risk factor for transient neurologic symptoms after a spinal anesthetic?

A. Lithotomy position
B. Dose of local anesthetic
C. Paresthesia during placement
D. Hypotension

Correct answer: A

Explanation: Transient neurologic symptoms (TNS), also known as transient radicular irritation, can occur following a spinal anesthetic. It presents as pain and/or dysesthesia in the buttocks and legs after spinal anesthesia. Known risk factors including spinal lidocaine (though less frequent, tetracaine or bupivacaine can also cause TNS as well), lithotomy position, and outpatient status. Variables not shown to increase the risk of TNS include the following: dose of local anesthetic, addition of epinephrine to local anesthetic, presence of dextrose, paresthesia, hypotension, and presence of blood-tinged cerebrospinal fluid.

References:

9. Local anesthetic: transient neurologic syndrome

A 54-year-old woman presents on POD 1 after a lidocaine spinal anesthetic for right side meniscectomy. She complains of 6/10 “shooting pain” radiating down from her buttocks to her lower leg, and denies loss of bowel or bladder incontinence. Which is the following is the MOST likely cause of her symptoms?

A. Cauda equina syndrome
B. Transient neurologic symptoms
C. Epidural hematoma
D. Epidural abscess

Correct answer: B

Explanation: This patient most likely presents with transient neurologic symptoms (TNS). This is supported by the presentation of pain in her leg and buttocks, the use of lidocaine spinal anesthetic, and positioning with flexed knee (meniscectomy). Other known risk factors for TNS include positioning in the lithotomy position and outpatient surgery. The pain usually resolves in 72 hours and is treated with NSAIDs, though some cases have lasted much longer. While also
possible, a less likely scenario is cauda equina syndrome. Symptoms of cauda equina syndrome would include severe back pain, bowel or bladder incontinence and dysfunction, and anesthesia or paresthesia of the perineum, external genitalia, and anus (“saddle anesthesia”). Epidural hematoma is unlikely without a history of traumatic tap or anticoagulation medications and would likely present sooner. The absence of fever and POD 1 make the diagnosis of epidural abscess extremely unlikely.

References:


10. Preservatives

A 56-year-old man with a history of non-invasive bladder cancer is scheduled for a cystoscopy and laser ablation. A spinal anesthetic is performed using 60 mg preservative-free 2-chloroprocaine. The addition of 200 mcg epinephrine to the chloroprocaine spinal solution would INCREASE the risk of which of the following?

A. Epidural hematoma
B. Spinal cord ischemia
C. Fever, malaise, and myalgias
D. High spinal

Correct answer: C

Explanation:
In a study evaluating the spinal dosing using 2-chloroprocaine and epinephrine, investigators found a 100% incidence of flu-like symptoms, malaise and myalgias in patients who received the epinephrine additive. Symptoms resolved in 6 to 48 hours. Some patients also reported non-radiating back stiffness, backache, and lower extremity pain. Spinal dosing of lidocaine is not as commonly used due to transient neurologic symptoms while bupivacaine spinals last too long for ambulatory procedures. The etiology of the association of epinephrine and chloroprocaine is unclear as epinephrine is commonly used in bupivacaine spinals with no such symptoms. Possible explanations include a small amount of bisulfate preservative in the epinephrine.

References:

11. Methemoglobinemia

A 54-year-old man has a peripheral nerve block prior to hand surgery. The pulse oximetry reading changes from 98% on 2L/min oxygen via nasal cannula to 85%. Blood is aspirated from an arterial line in place and is noted to be chocolate colored. An ABG is checked and while the
SaO\textsubscript{2} is less than 90\%, the PaO\textsubscript{2} is measured to be greater than 70 mmHg. Which of the following local anesthetics is most likely implicated in this clinical scenario?

A. Bupivacaine  
B. Ropivacaine  
C. Prilocaine  
D. Mepivacaine

Correct Answer: C

Explanation:
This scenario is suggestive of methemoglobinemia. The following four anesthetics have been reported as possibly causing methemoglobinemia: prilocaine (ortho-toluidine is responsible for hemoglobin oxidation), benzocaine, lidocaine, and tetracaine. Local anesthetic-related methemoglobinemia is a clinically important problem. It is diagnosed with an elevated direct co-oximeter measurement of methemoglobin (>1 – 2\%), but it can also present as a drop in the oxygen saturation (though the pulse oximeter typically grossly underestimates the degree of hypoxia), chocolate-colored blood, and a discrepancy between SaO\textsubscript{2} and PaO\textsubscript{2}. The treatment for methemoglobinemia is IV methylene blue.

Of note, prilocaine should not be used in infants less than 6 months (unless for transcutaneous anesthesia), pregnant patients, and patients with glucose-6-phosphate dehydrogenase deficiency.

References:

12. Neuraxial opioids: mechanism of action

The use of neuraxial opioids in combination with local anesthetics has proven to be beneficial in providing equal or superior pain relief and less sedation as compared to parenteral opioid dosing. What is the mechanism of action of epidural opioids?

A. Inhibit descending transmission of nociceptive information  
B. Inhibition of the release of substance P in the substantia gelatinosa.  
C. Systemic absorption through dura mater and uptake into posterior spinal arteries.  
D. Mu receptor agonism in the spinothalamic tract.

Correct answer: B

Explanation:
The combined use of opioids with local anesthetic in the epidural space allows for dose reductions in each class in order to provide analgesia. Neuraxial opioids do not result in motor blockade. Epidural opioids can be used alone when there are concerns regarding hemodynamic instability. The mechanism of action is in the substantia gelatinosa in the spinal cord dorsal horn. Opioids act at synapses either presynaptically or postsynaptically. Opioid receptors are
abundantly expressed in the substantia gelatinosa. Neuraxial opioid use inhibits substance P release from the primary sensory.

References:
Miller’s Anesthesia, Eighth Edition, 2015 by Saunders Miller, Pages 870 and 1705

13. Neuraxial opioids

Which of the following side effects is LEAST likely a direct consequence of the use of neuraxial opioids?

A. Pruritus  
B. Hypotension  
C. Nausea/vomiting  
D. Urinary retention

Correct answer: B

Explanation:
Hypotension is usually a result of a sympathectomy that is associated with local anesthetics. Neuraxial opioids can result in reduced blood pressure if analgesia allows for less of a sympathetic discharge due to poorly controlled pain. Pruritus, nausea and vomiting, and respiratory depression occur with the use of neuraxial opioids.

References:

14. Neuraxial opioids: Monitoring

Which of the following statements is TRUE regarding the use of neuraxial opioids for postoperative analgesia?

A. There is no increased risk of respiratory depression in patients with OSA  
B. Neuraxial opioid can be used safely in combination with other sedatives, such as benzodiazepines or systemic opioids  
C. The use of a bolus of extended release neuraxial morphine does not require any further monitoring beyond the first 24 hours  
D. The use of lipophilic agents (fentanyl, sufentanil) would result in greater systemic absorption compared to hydrophilic opioids (morphine, hydromorphone).

Correct answer: D

Explanation:
The ASA and ASRA has updated practice guidelines for the prevention, detection and management of respiratory depression associated with neuraxial opioid administration since death and persistent vegetative states have occurred as a result of respiratory depression due to
opioid use. Specifically, a history of sleep apnea and concurrent use of systemic opioids or other sedatives/hypnotics can place patients at risk for respiratory depression and requires increased monitoring. For single bolus neuraxial lipophilic agents (fentanyl, sufentanil), monitoring for adequate oxygenation, ventilation and level of consciousness should be continual for the first 20 minutes followed by once hourly monitoring for 2 hours. For a single bolus of neuraxial morphine, monitoring should be a minimum of 24 hours after administration (hourly for first 12 hours and every 2 hours for second 12 hours). For extended release neuraxial morphine, monitoring should be a minimum of 48 hours (once hourly first 12 hours, every 2 hours from 12h-24h, and every 4 hours from 24h-48h). The use of lipophilic agents (fentanyl, sufentanil) results in greater systemic absorption of the opioids as compared to hydrophilic agents (morphine, hydromorphone).

References:

15. Opioid-induced Hyperalgesia, Opioid tolerance

A patient who chronically takes oral morphine in a dose in excess of 100 mg per day for many years is admitted after lumbar spine decompressive surgery and finds that with escalating doses of hydromorphone (greater than 50mg intravenous hydromorphone in a 5-hour window), he is becoming increasingly more uncomfortable. Which of the following therapeutic measures would MOST LIKELY improve this patient’s pain?

A. The patient is experiencing opioid withdrawal due to inadequate doses of hydromorphone. Therefore, hydromorphone dose needs to be increased.
B. This patient is experiencing opioid-induced hyperalgesia. The hydromorphone should be switched to morphine, and nonopioid multimodal analgesia (NSAIDs, gabapentinoids, ketamine, regional anesthesia) should be used to control his pain.
C. This patient is experiencing tolerance to opioids and a higher dose of hydromorphone is required for improved efficacy.
D. This patient is experiencing opioid-induced allodynia, and a low dose naloxone infusion should be initiated to counteract this mu receptor mediated effect.

Correct answer: B

Explanation:
This patient is experiencing opioid-induced hyperalgesia. Opioid-induced hyperalgesia is an increased sensitivity to pain stimulus with increasing opioid doses. Opioid rotation especially to an opioid with a longer half-life, eventual and gradual opioid reduction, and use of non-opioid multimodal analgesics results in improved pain management. Opioid tolerance is the requirement of higher doses of opioids to achieve an equivalent analgesic effect, and escalating doses of opioids should improve analgesia. Opioid withdrawal is a set of symptoms (nausea, diarrhea, piloerection, rhinorrhea, sweating, pupil dilation, anxiety, restlessness, tachycardia, increased pain, fevers/chills, flu-like symptoms) that occur due to underdosing or withdrawal of
opioids and requires re-initiation of the patient’s home opioid regimen (or equivalent) in order to ablate these effects. Allodynia occurs when a usually non-painful stimulus (e.g. light touch) results in pain, and is a product of central sensitization, but is not typically an opioid-induced problem. It may respond to neuropathic medications or sympathetic blockade.

References:


16. Management of Acute on Chronic Pain

A patient who has been on maintenance oral methadone 80mg once a day for a history of opioid abuse is now scheduled for an open colectomy in one week. Which of the following analgesic management options is LEAST recommended?

A. Continue methadone therapy, converting methadone to IV with a 2:1 or 3:1 PO:IV ratio once a day while patient is unable to tolerate PO.
B. Offer regional anesthetic technique such as thoracic epidural for postoperative pain management with local anesthetic and hydrophilic opioid.
C. Add acetaminophen, nonsteroidal anti-inflammatory agent, and dexamethasone as multimodal analgesics.
D. Use higher doses of opioids to counteract opioid tolerance

Correct answer: D

Explanation:
While patients on opioids can become tolerant within 2-3 weeks of potent opioid consumption and will require higher doses of opioids to achieve an analgesic effect, patients who undergo a bowel surgery would benefit from minimizing any further escalations of their opioids. Tolerance to the side effects of opioids (respiratory depression, bowel dysmotility) occurs much slower than tolerance to opioid’s analgesic effects. Therefore, use of higher than baseline dose of opioids will not be favorable for enhanced recovery after bowel surgery. The use of non-opioid analgesic adjuncts (acetaminophen, NSAIDs, gabapentinoids) can be considered, but good regional analgesia, whether it be in the form of a thoracic epidural, bilateral thoracic paravertebral catheters or bilateral TAP (transversus abdominis plane) catheters can be considered to reduce the need for opioid consumption. In patients who have been on high dose of opioids for
maintenance therapy (such as methadone), the medication should be continued to avoid withdrawal in these patients. In a patient who is NPO, methadone can be converted to IV in order to be delivered. IV methadone has a very quick onset, and depending on the dose, a very prolonged analgesic effect. As the doses of PO methadone increase, the conversion ratio from PO:IV also escalates. Therefore, at lower doses, a 1:1 or 2:1 ratio can be used. However, with high methadone doses (>100mg/day), consider dosing ratios of 4-10:1. The literature on methadone conversion is sparse.

References:


17. Opioid Epidemic

Which of the following statements concerning the opioid crisis is FALSE?

A. Since 2013, opioid abuse has surpassed motor vehicle accidents as the leading cause of preventable deaths in the United States.
B. In 2012, enough opioids were prescribed that every adult American would have around the clock pills for 3-4 weeks.
C. Opioid withdrawal results in significant mortality
D. Due to the rise of deaths from prescription opioids, the CDC recommended more restrictive use of opioid prescriptions for non-cancer pain.

Correct answer: C

Explanation:
Since pain was designated as a fifth vital sign and opioid prescription increased, so did prescription opioid-related deaths. Since 2013, opioid has surpassed motor vehicle accidents as the leading cause of preventable deaths in the United States. The number of opioid prescriptions surged to the point that the number of opioids prescribed was enough to provide for each individual in the United States to have 5mg of oxycodone around the clock for 30 days. Due to this opioid epidemic, the CDC published guidelines recommending more conscientious prescription of opioids in non-cancer pain conditions in 2016. Mortality is mostly due to opioid abuse, not opioid withdrawal. In adults, opioid withdrawal is unpleasant, but rarely results in mortality. Though early literature suggests that opioid withdrawal in parturients can result in neonatal abstinence syndrome with resultant fetal/neonatal demise, this link has not been confirmed. Opioid withdrawal symptoms include insomnia, tachycardia, fevers/chills, nausea,
diarrhea, dilated pupils, restlessness, anxiety and other flu-like symptoms. Withdrawal can be managed most effectively with buprenorphine, but methadone may also be used.

References:


Committee on Obstetric Practice and American Society of Addiction Medicine. “Opioid Use and Opioid Use Disorder in Pregnancy.” Aug 2017; ACOG Committee Opinion # 711


18. Opioid-induced respiratory depression

Which of the following contributes LEAST to opioid-induced respiratory depression?

A. Use of opioids with active metabolites in patients with significant renal dysfunction
B. Multiple concurrent routes of opioid administration (e.g. systemic + neuraxial) or concurrent use of non-opioid sedatives
C. Obstructive Sleep Apnea
D. Chronic use of a stable dose of opioids

Correct answer: D

Explanation:
Opioid-induced hypventilatory effects can result in life threatening morbidity, though the incidence is low. A closed-claims analysis noted 92 claims that were judged as possible, probable or definite amongst 9799 claims from 1990 to 2009. Post-operative use of naloxone (after transfer out of post anesthesia recovery unit) as an indicator of incidence of postoperative respiratory depression after general anesthesia for surgery was calculated to be 1.6 per 1000 anesthetics (Weingarten et al). Physiologic effects of opioids include a decreased respiratory drive, decreased level of consciousness, and upper airway obstruction. The use of opioids with active metabolites that are renally excreted (morphine, tramadol, codeine) in patients with significant renal dysfunction can result in significant opioid-induced respiratory depression.
Obstructive sleep apnea has been associated with the risk of significant respiratory depression as is the concurrent use of multiple routes of opioids and/or the combined use of opioids with other non-opioid sedatives. Chronic use of opioids can result in a higher resting PaCO2 (tolerance to opioid-induced respiratory depression occurs less frequently than expected) though the risk of opioid-induced respiratory depression in this patient population is not excessively increased beyond that of opioid-naïve patients.

References:

19. Multimodal analgesia: tramadol

Which of the following is TRUE of tramadol?

A. In order to achieve analgesic effects, it must be metabolized to its active form, O-desmethotramadol (ODT).
B. Its active metabolite is excreted by the kidneys and, therefore, increased vigilance for opioid-induced respiratory depression should occur in patients with severe renal dysfunction.
C. Use of naloxone is unlikely to improve respiratory depression from tramadol since its mechanism of action is serotonin and norepinephrine reuptake inhibition.
D. The incidence of tramadol abuse is no different than that of stronger opioids such as morphine and hydrocodone.

Correct answer: B

Explanation:
The parent drug, tramadol, actually has analgesic effects mediated by monoaminergic action. Tramadol is metabolized to ODT (O-desmethyl-tramadol), which demonstrates an affinity for mu-opioid receptors greater than the parent compound. Both tramadol and its active metabolite are excreted by the kidneys, and therefore significant renal dysfunction may result in accumulation and increased respiratory depressant effects. Increased vigilance should be exercised in these patients. Use of naloxone has resulted in partial reversal of tramadol's respiratory depressant effects. The incidence of tramadol abuse (estimated to be less than one in 100,000 patients), due to its lower mu-opioid effect, has been much less significant than for other opioids. Tramadol's analgesic potency is approximately 1/6th to 1/10th that of morphine.
References:

20. Acetaminophen Efficacy and Side Effects

Which of the following is TRUE regarding the administration of acetaminophen?

A. The most common adverse effects include nausea, vomiting, and insomnia.
B. The half-life of a therapeutic dose is 12 hours.
C. Acetaminophen can affect platelet function and should be used with care in bleeding patients.
D. Most of the absorption of an oral dose occurs in the stomach.

Correct answer: A

Explanation:
The most common adverse effects of acetaminophen include nausea, vomiting, and insomnia. Serious side effects can occur by exceeding the maximum recommended dose; these effects include acute liver failure and even death. Dosing should be reduced in patients with liver disease, renal impairment, chronic alcohol abuse, and hypovolemia. The half-life of a therapeutic dose of acetaminophen is 1-3 hours, and its duration of action is 4-6 hours, which explains why acetaminophen is usually redosed within 4-6 hours. Acetaminophen, unlike NSAIDs, does not affect platelet function. Most of the absorption of acetaminophen occurs in the small intestine.

Reference:

21. Acetaminophen Efficacy and Side Effects

Which of the following statements regarding the use of acetaminophen is FALSE?

A. Acetaminophen has a relatively safe side effect profile when taken at the recommended doses.
B. The use of acetaminophen as part of a multimodal analgesic regimen has reduced the incidence of opioid-related adverse events.
C. Acetaminophen overdose is the leading cause for acute hepatic failure in the United States.
D. N-acetylcysteine, an antidote for acetaminophen-induced hepatotoxicity, is effective when given within 8 to 10 hours of acetaminophen ingestion.

Correct answer: B

Explanation:
The use of acetaminophen has been linked to at best modest reductions in opioids, but that has not resulted in reductions in opioid-related side effects. Acetaminophen is administered at doses of up to 4 grams per day (up to 15mg/kg/dose every 6 hours in patients less than 50kg) in patients without significant renal/hepatic insufficiency. Acetaminophen overdose is the leading cause for acute hepatic failure in the United States. Unintentional overdose occurs due to the multiple different combination drugs that include acetaminophen such as with hydrocodone (Lortab, Vicodin, Norco), oxycodone (Percocet, Roxicet), butalbital/caffeine (Fioricet), and tramadol (Ultracet). The antidote for acetaminophen overdose is N-acetylcysteine and it is most effective when given within 8 to 10 hours of ingestion.

References:

22. NSAIDS: nonselective vs selective COX-2 inhibitors, indications and side effects

Which of the following statements is NOT true of the use of nonsteroidal anti-inflammatory agents as analgesics?

A. The use of H2 blockers in concert with non-selective COX inhibitors is as effective as the use of COX-2 inhibitors in reducing rates of upper G1 bleed.
B. NSAIDs have been implicated in increased rates of cardiovascular events with selective COX-2 inhibitors resulting in greater risks than nonselective COX inhibitors of myocardial and cerebral thrombotic events.
C. All NSAIDs, regardless of COX selectivity, negatively impact renal function through afferent arteriolar constriction, glomerular filtration rate (GFR) reduction and inhibition of the kidneys’ ability to excrete salt and water.
D. NSAIDs are generally regarded unfavorably in parturients during all three trimesters, though the third trimester is the period that can result in potentially greater harm to the fetus due to risks of fetal renal injury, oligohydramnios, ductus arteriosus constriction and intracranial hemorrhage.

Correct answer: A

Explanation:
Selective COX-2 inhibitors are more effective than the combination of nonselective COX inhibitors and H2 blockers in preventing upper GI bleed. COX-2 inhibitors have been associated with increased risks of myocardial infarctions and thrombotic strokes, resulting in the withdrawal of rofecoxib (Vioxx) from the market. Non-selective COX inhibitors also increase risk of cardiovascular morbidity. COX inhibitors have also been associated with increased risks of heart failure in patients. All NSAIDs negatively impact renal function. Use of NSAIDs in the third trimester should only be reserved for tocolysis with indomethacin and low-dose aspirin as an anti-coagulant due to risks of fetal renal injury, oligohydramnios, ductus arteriosus constriction, and intracranial hemorrhage.

References:


23. g-aminobutyric acid-pentanoid agents: efficacy, indications, contraindications

Which of the following statements regarding the use of gabapentin as an analgesic is FALSE?

A. Side effects of gabapentin include dizziness, sedation, gait disturbance, headache, difficulty with concentration, peripheral edema, and visual disturbances when used for longer periods of time.

B. Meta-analyses of perioperative gabapentin use noted no increased risk of sedation and dizziness with short duration prescription of gabapentinoids though this result may be confounded by the use of sedation and general anesthesia in this patient population.

C. The data is inadequate to recommend the optimal dose and duration of gabapentinoid use for acute postoperative pain control.

D. Gabapentin’s effect as a multimodal analgesic agent has been shown to be very strong, resulting in reducing opioid consumption by greater than a morphine equivalent of 10mg in the first 24 hours after surgery, based on randomized controlled trials with good scientific validity.

Correct answer: D

Explanation:
In the most extensive meta-analysis to date of randomized controlled trials using gabapentin, Fabritius demonstrated that the effects of gabapentin on postoperative analgesia, when examining only trials with low risk of bias, has been minimal to modest, and less than a 5mg of morphine reduction in the first 24 hours after surgery. There are many randomized controlled trials looking at gabapentin’s efficacy in the perioperative period, but these studies are limited by low sample size and heterogeneous doses of gabapentin. In light of gabapentin’s minimal to modest effects and its known side effects when used chronically (dizziness and sedation most reported side effect), it would be difficult to make recommendations about optimal dosing of gabapentin in the perioperative setting and caution should be exercised when considering this drug in patients with cognitive impairment and patients at risk for falls. This systematic review by Fabritius also noted no difference in risks of dizziness and sedation in patients receiving gabapentin perioperatively, although use of general or neuraxial anesthesia would confound data collected on sedation and dizziness in the first 24 hours after surgery.

References:


24. Steroids: systemic vs perineural use

Which of the following concerning the use of intravenous compared to perineural dexamethasone is TRUE?

A. There is no evidence of neurotoxicity in animal studies.
B. Higher doses of perineural dexamethasone such as 8-10 mg are more effective in prolonging analgesic duration compared to lower doses.
C. Intravenous dexamethasone in doses of 0.1 mg/kg or more have shown to have analgesic benefits.
D. Efficacy of perineural dexamethasone is highly dependent on the type of peripheral nerve blockade and the type of local anesthetic used.

Correct answer: C

Explanation:
Perioperative steroid use, both systemic and perineural, have been associated with improved postoperative analgesia and decreased narcotic consumption. Dexamethasone represents the steroid that is most widely studied in the perioperative setting. In a 2011 meta-analysis, single dose intravenous dexamethasone administration of 0.1mg/kg or more have been shown to be effective in reducing postoperative pain and opioid consumption. This is in addition to the known antiemetic benefits of dexamethasone that occurs with lower doses. In the same systematic review, higher doses of systemic dexamethasone did not demonstrate any additional analgesic benefit. Similarly, use of perineural dexamethasone is associated with prolonged...
sensory and motor blocks that confers analgesic advantages. This prolongation in blocks with dexamethasone does not appear to be dose dependent and is independent of the type of block or the local anesthetic that it is mixed with. Small amount of dexamethasone (2-4mg) has been added with different long acting local anesthetics (bupivacaine and ropivacaine) in various upper and lower extremity nerve blocks to achieve similar block prolongation and analgesic effects. While both routes of administration indicate some efficacy, there is still controversy in the literature about which route is more superior. Due to some concerns about neurotoxicity related to perineural use of dexamethasone in rats, perineural administration of steroids remains an off-label use.

References:


25. Nerve stimulation: principles & operation

Which of the following statements about the use of nerve stimulation for regional anesthesia is FALSE?

A. A positive Raj test is due to the fact that local anesthetic spread results in decreased current density surrounding the needle tip.
B. A lower frequency of current pulses allows the physician to advance the needle more quickly.
C. The inability to solicit a motor response despite high stimulating currents does not demonstrate a lack of intraneural needle placement.
D. Motor fibers are more easily activated using shorter pulse duration as compared to sensory fibers, which require longer pulse durations to activate.

Correct answer: B

Explanation:
The Raj test is the loss of a motor response upon injection of a local anesthetic solution; it is due to the fact that local anesthetic solutions usually contain sodium chloride, which conducts electricity, and its presence next to the needle tip results in a distribution of the current and reduction in current density at the needle tip. The Raj test was more important in the era before insulated needles were introduced, where both the tip and the shaft of the needle could elicit a motor stimulation and the use of the Raj test could differentiate between whether it was the needle tip or shaft that elicited the motor stimulation.

Current dispersion is for this reason that with traumatic needle passes, blood can redistribute the current, resulting in a greater stimulation threshold to elicit motor response. The frequency is a rate-limiting factor of needle advancement. It correlates with speed of motor feedback. A
faster, not slower frequency, allows the physician to advance the needle faster with less of a chance to miss eliciting a motor response when the needle is in close proximity to the nerve. The absence of a motor response with higher stimulating currents does not preclude intraneural needle placement. Motor nerve fibers are larger and can be activated with a shorter pulse duration (< 0.1 millisecond) compared with smaller A-delta and C sensory fibers, which are more readily activated with longer pulse durations (>0.3 millisecond).

References: